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Henry Ford Health Publication List – August 2024

This bibliography aims to recognize the scholarly activity and provide ease of access to journal articles, meeting abstracts, book chapters, books and other works published by Henry Ford Health personnel. Searches were conducted in PubMed, Embase, Web of Science, and CINAHL during the month, and then imported into EndNote for formatting. There are 214 unique citations listed this month, including 124 articles and 90 conference abstracts.

Articles are listed first, followed by conference abstracts. Because of various limitations, this does not represent an exhaustive list of all published works by Henry Ford Health authors.

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Articles

Conference Abstracts

Articles

Allergy and Immunology
Anderson WC, 3rd, **Baptist AP**, Eakin MN, Federman A, and Murphy VE. Adherence challenges and strategies in specific groups with asthma: adolescents, pregnancy, older adults. *J Allergy Clin Immunol Pract* 2024; Epub ahead of print. PMID: 39122111. Full Text

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Poor adherence to controller therapies is a universal challenge to asthma control. Several high-risk groups, including adolescents, pregnant women, and older adults, have their own unique challenges to adherence. The rates of asthma controller therapy use are low in each of these populations, but secondary to different causes. Adolescents have increased independence and a transition to new self-management responsibilities; pregnant women may be concerned about adverse effects of medications to the fetus; and older adults may have age-related physical and cognitive challenges to effectively taking medication. Only by understanding the nuances of care in these populations can healthcare professionals develop strategies to address barriers to adherence. Tailored education focused on empowering patients and dispelling misconceptions can serve as tools to improve adherence and ultimately asthma control.

Allergy and Immunology
Fulkerson PC, Lussier SJ, Bendixsen CG, Castina SM, Gebretsadik T, Marlin JS, Russell PB, Seibold MA, Everman JL, Moore CM, Snyder BM, Thompson K, Tregoning GS, Wellford S, Arbes SJ, Bacharier LB, Calatroni A, Camargo CA, Jr., Dupont WD, Furuta GT, Gruchalla RS, Gupta RS, Hershey GK, Jackson DJ, **Johnson CC**, Kattan M, Liu AH, Murrison L, O'Connor GT, Phipatanakul W, Rivera-Spoljaric K, Rothenberg ME, Seroogy CM, Teach SJ, **Zoratti EM**, Togias A, Hartert TV, and Heros Study Team O. Human Epidemiology and RespOnse to SARS-CoV-2 (HEROS): Objectives, Design and Enrollment Results of a 12-City Remote Observational Surveillance Study of Households with Children using Direct-to-Participant Methods. *Am J Epidemiol* 2024; Epub ahead of print. PMID: 38775275. Full Text

The Human Epidemiology and Response to SARS-CoV-2 (HEROS) is a prospective multi-city 6-month incidence study which was conducted from May 2020-February 2021. The objectives were to identify risk factors for SARS-CoV-2 infection and household transmission among children and people with asthma and allergic diseases, and to use the host nasal transcriptome sampled longitudinally to understand infection risk and sequelae at the molecular level. To overcome challenges of clinical study implementation due to the coronavirus pandemic, this surveillance study used direct-to-participant methods to remotely enroll and prospectively follow eligible children who are participants in other NIH-funded pediatric research studies and their household members. Households participated in weekly surveys and biweekly nasal sampling regardless of symptoms. The aim of this report is to widely share the methods and study instruments and to describe the rationale, design, execution, logistics and characteristics of a large, observational, household-based, remote cohort study of SARS-CoV-2 infection and transmission in households with children. The study enrolled a total of 5,598 individuals, including 1,913 principal participants (children), 1,913 primary caregivers, 729 secondary caregivers and 1,043 other household children. This study was successfully implemented without necessitating any in-person research visits and provides an approach for rapid execution of clinical research.

Allergy and Immunology
Kakumanu S, Szefler S, Pappalardo AA, Sales AE, **Baptist AP**, Stern J, and Nyenhuis SM. Applying the dissemination and implementation sciences to allergy and immunology: A Work Group Report from the

AAAAI Quality, Adherence, and Outcomes Committee. *J Allergy Clin Immunol* 2024; Epub ahead of print. PMID: 39162669. Full Text

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Translating evidence-based practice (EBP) into real-world clinical settings often takes a considerable amount of time and resources. In allergy and immunology, the dissemination and implementation (D&I) sciences facilitate the study of how variations in knowledge, resources, patient populations, and staffing models lead to differences in the clinical care of asthma, allergic disease, and primary immunodeficiency. Despite the need for validated approaches to study how to best apply EBP in the real world, the D&I sciences are underutilized. To address this gap, an American Academy of Allergy, Asthma & Immunology (AAAAI) work group was convened to provide an overview for the role of the D&I sciences in clinical care and future research within the field. For the D&I sciences to be leveraged effectively, teams should be multidisciplinary and inclusive of community and clinical partners, and multimethods approaches to data collection and analyses should be used. Used appropriately, the D&I sciences provide important tools to promote EBP and health equity as well as optimization of clinical practice in allergy and immunology.

Allergy and Immunology

Larson PS, Steiner AL, Bennion E, **Baptist AP**, O'Neill MS, and Gronlund CJ. Pollen effects in a changing climate: Ragweed pollen exposure and sleepiness in immunotherapy patients of a Southeastern Michigan allergy clinic. *Int J Biometeorol* 2024; Epub ahead of print. PMID: 39141134. Full Text

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Allergic rhino-conjunctivitis (AR) is a globally relevant health disorder characterized by sneezing, rhinorrhea and sleep disturbance. Ragweed (Ambrosia artemisiifolia) is a plant common to North America and an important allergen. Coarse methods of measuring airborne pollen counts are used to predict seasonal allergy symptoms. This research used a longitudinal study design with a novel, model-based raster of predicted pollen counts to test associations with self-reported symptoms of AR collected from patients receiving immunotherapy for pollen allergies at an allergy clinic. Researchers visited a clinic six

times over three weeks. Immunotherapy patients were asked to fill out a brief intake survey on allergic and symptomatic profiles, daytime sleepiness, housing quality, and demographics. Participants responded to a daily, emailed survey on sleepiness and asthma symptoms for 21 days. Using the date and location of responses, ragweed pollen counts were extracted from a prognostic, model based raster (25km pixels). Lag associations of pollen counts with sleepiness were tested using a logistic regression model , adjusted for housing and demographic characteristics, in a distributed lag non-linear model (DLNM) framework. 49 people participated in the study. 26 (52%) were female. The mean age was 37.9 years. Asthma/allergy symptoms were not associated with ragweed pollen but sleepiness was highest two days after exposure (Estimate: 0.33 [0.04,0.62]). Subjects traveled widely during the study period. Intense exposures to ragweed pollen may be associated with daytime sleepiness within small exposure windows. Model-based predicted pollen counts could be used to study health impacts of pollen in people with disease severe enough to receive immunotherapy. Daytime sleepiness can affect productivity and injury risk, and pollen season length and allergenicity may be increasing with climate change. Thus our results may have important implications for population health.

Anesthesiology

Karamchandani K, Nasa P, **Jarzebowski M**, Brewster DJ, De Jong A, Bauer PR, Berkow L, Brown CA, 3rd, Cabrini L, Casey J, Cook T, Divatia JV, Duggan LV, Ellard L, Ergan B, Jonsson Fagerlund M, Gatward J, Greif R, Higgs A, Jaber S, Janz D, Joffe AM, Jung B, Kovacs G, Kwizera A, Laffey JG, Lascarrou JB, Law JA, Marshall S, McGrath BA, Mosier JM, Perin D, Roca O, Rollé A, Russotto V, Sakles JC, Shrestha GS, Smischney NJ, Sorbello M, Tung A, Jabaley CS, and Myatra SN. Tracheal intubation in critically ill adults with a physiologically difficult airway. An international Delphi study. *Intensive Care Med* 2024; Epub ahead of print. PMID: 39162823. Full Text

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PURPOSE: Our study aimed to provide consensus and expert clinical practice statements related to airway management in critically ill adults with a physiologically difficult airway (PDA). METHODS: An international Steering Committee involving seven intensivists and one Delphi methodology expert was convened by the Society of Critical Care Anaesthesiologists (SOCCA) Physiologically Difficult Airway Task Force. The committee selected an international panel of 35 expert clinician-researchers with expertise in airway management in critically ill adults. A Delphi process based on an iterative approach was used to obtain the final consensus statements. RESULTS: The Delphi process included seven survey rounds. A stable consensus was achieved for 53 (87%) out of 61 statements. The experts agreed that in addition to pathophysiological conditions, physiological alterations associated with pregnancy and obesity also constitute a physiologically difficult airway. They suggested having an intubation team consisting of at least three healthcare providers including two airway operators, implementing an appropriately designed checklist, and optimizing hemodynamics prior to tracheal intubation. Similarly, the

experts agreed on the head elevated laryngoscopic position, routine use of videolaryngoscopy during the first attempt, preoxygenation with non-invasive ventilation, careful mask ventilation during the apneic phase, and attention to cardiorespiratory status for post-intubation care. CONCLUSION: Using a Delphi method, agreement among a panel of international experts was reached for 53 statements providing guidance to clinicians worldwide on safe tracheal intubation practices in patients with a physiologically difficult airway to help improve patient outcomes. Well-designed studies are needed to assess the effects of these practice statements and address the remaining uncertainties.

Behavioral Health Services/Psychiatry/Neuropsychology
Fedson S, **Bryce K**, Courtwright A, Dark J, Egan T, Holm AM, Kates O, Lavee J, and Olland A. The Relevance of the Ethics Statement of the ISHLT. *J Heart Lung Transplant* 2024; Epub ahead of print. PMID: 39181521. Full Text

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Behavioral Health Services/Psychiatry/Neuropsychology
Rossom R, Knowlton G, **Yeh HH**, Penfold R, Owen-Smith A, Hooker S, Simon G, **Miller-Matero L**, **Akinyemi E**, and **Ahmedani B**. Psychotherapy Engagement Before and After a Rapid Transition to Telehealth During COVID-19 for Older Adults With Dementia. *J Appl Gerontol* 2024; Epub ahead of print. PMID: 39102577. Full Text

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Objective: To understand the impact of the transition to telehealth during COVID-19 on psychotherapy visits for patients with dementia. Method: Retrospective study of older adults with dementia who had at least one psychotherapy visit in the 9 months before and after the onset of COVID-19 at 3 U.S. health systems. Care disruptions were gaps of 45+ days. Descriptive statistics and logistic mixed-effects models examined factors associated with care disruption. Results: 4953 patients with dementia made 19,902 psychotherapy visits. Gaps in psychotherapy were less frequent during COVID-19 (29.4%) than before (48.9%), with the odds of a patient experiencing a care disruption during COVID-19 0.54 times the odds prior to COVID-19 (95% CI: 0.50-0.59). Almost all patient subgroups had lower adjusted odds of care disruption during COVID-19. Discussion: There were fewer disruptions in psychotherapy care following the rapid shift to virtual care. Telehealth may be a viable option for patients with dementia.

Cardiology/Cardiovascular Research

Al-Abdouh A, Samadi D, Sukhon F, Mhanna M, **Jabri A**, Alhuneafat L, Alabduh T, Bizanti A, Madanat L, Alqarqaz M, Paul TK, and Kundu A. Paclitaxel-Coated Balloon Versus Uncoated Balloon Angioplasty For Coronary In-Stent Restenosis: A Systematic Review And Meta-Analysis Of Randomized Controlled Trials. *Am J Cardiol* 2024; Epub ahead of print. PMID: 39222739. Full Text

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In-stent restenosis (ISR) accounts for 10% of percutaneous coronary intervention (PCI) in the Unites States. Paclitaxel coated balloons (PCBs) have been evaluated as a therapy for coronary ISR in multiple randomized controlled trials (RCTs). We searched PubMed/MEDLINE, Cochrane library, and ClinicalTrials.gov (from inception to April 1, 2024) for RCTs evaluating PCBs versus uncoated balloon angioplasty (BA) in patients with coronary ISR. The outcomes of interest were target lesion revascularization (TLR), major adverse cardiovascular events (MACE), all-cause mortality, cardiovascular mortality, myocardial infarction (MI), and stent thrombosis. We pooled the estimates using inverse variance random-effects model. The effect sizes were reported as risk ratio (RR) with 95% confidence interval (CI). A total of 6 RCTs with 1,343 patients were included. At a follow-up ranging from 6-12 months from randomization, use of PCBs was associated with a statistically significant decrease in TLR (RR 0.28; 95% CI 0.11 to 0.68), and MACE (RR 0.35; 95% CI 0.20 to 0.64) when compared with BA for coronary ISR. However, there was no significant difference in risk between PCBs and BA in terms of all-cause mortality (RR 0.56; 95% CI 0.14 to 2.31), cardiovascular mortality (RR 0.61; 95% CI 0.02 to 16.85), MI (RR 0.60; 95% CI 0.27 to 1.31), and stent thrombosis (RR 0.13; 95% CI 0.00 to 5.06). In conclusion, this meta-analysis suggests that PCBs compared with uncoated BA for treatment of coronary ISR at intermediate term follow-up of one-year was associated with significant decrease in TLR, and MACE without any difference in mortality, MI, or stent thrombosis.

Cardiology/Cardiovascular Research

Alexandrou M, Rempakos A, Mutlu D, Al Ogaili A, Carvalho PEP, Strepkos D, Choi JW, Poommipanit P, **Alaswad K**, **Basir MB**, Davies R, Jaffer FA, Dattilo P, Doing AH, Azzalini L, Aygul N, Chandwaney RH, Jefferson BK, Gorgulu S, Khatri JJ, Young LD, Krestyaninov O, Khelimskii D, Frizzell J, Goktekin O, Flaherty JD, Schimmel DR, Benzuly KH, Uluganyan M, Ozdemir R, Ahmad Y, Rangan BV, Mastrodemos OC, Burke MN, Voudris K, Sandoval Y, and Brilakis ES. Peripheral artery disease in chronic total occlusion percutaneous coronary intervention. *J Invasive Cardiol* 2024; Epub ahead of print. PMID: 39121079. Request Article

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Cardiology/Cardiovascular Research
Blumer V, Kanwar MK, Barnett CF, **Cowger JA**, Damluji AA, Farr M, Goodlin SJ, Katz JN, McIlvennan CK, Sinha SS, and Wang TY. Cardiogenic Shock in Older Adults: A Focus on Age-Associated Risks and Approach to Management: A Scientific Statement From the American Heart Association. *Circulation* 2024; 149(14):e1051-e1065. PMID: 38406869. Full Text

Cardiogenic shock continues to portend poor outcomes, conferring short-term mortality rates of 30% to 50% despite recent scientific advances. Age is a nonmodifiable risk factor for mortality in patients with cardiogenic shock and is often considered in the decision-making process for eligibility for various therapies. Older adults have been largely excluded from analyses of therapeutic options in patients with cardiogenic shock. As a result, despite the association of advanced age with worse outcomes, focused strategies in the assessment and management of cardiogenic shock in this high-risk and growing population are lacking. Individual programs oftentimes develop upper age limits for various interventional strategies for their patients, including heart transplantation and durable left ventricular assist devices. However, age as a lone parameter should not be used to guide individual patient management decisions in cardiogenic shock. In the assessment of risk in older adults with cardiogenic shock, a comprehensive, interdisciplinary approach is central to developing best practices. In this American Heart Association scientific statement, we aim to summarize our contemporary understanding of the epidemiology, risk assessment, and in-hospital approach to management of cardiogenic shock, with a unique focus on older adults.

Cardiology/Cardiovascular Research
Carnicelli AP, Diepen SV, Gage A, Bernhardt AM, **Cowger J**, Houston BA, Siuba MT, Kataria R, Beavers CJ, John KJ, Meyns B, Kapur NK, Tedford RJ, and Kanwar M. Pragmatic approach to temporary mechanical circulatory support in acute right ventricular failure. *J Heart Lung Transplant* 2024; Epub ahead of print. PMID: 39059594. Full Text

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Acute right ventricular failure (RVF) is prevalent in multiple disease states and is associated with poor clinical outcomes. Right-sided temporary mechanical circulatory support (tMCS) devices are used to unload RV congestion and increase cardiac output in cardiogenic shock (CS) with hemodynamically significant RVF. Several RV-tMCS device platforms are available; however consensus is lacking on patient selection, timing of escalation to RV-tMCS, device management, and device weaning. The purposes of this review are to 1) describe the current state of tMCS device therapies for acute RVF with CS, 2) discuss principles of escalation to RV-tMCS device therapy, 3) examine important aspects of clinical management for patients supported by RV-tMCS devices including volume management, anticoagulation, and positive pressure ventilation, and 4) provide a framework for RV-tMCS weaning.

Cardiology/Cardiovascular Research

Cowger JA, Molina E, Deng L, Kanwar M, Shah P, Cogswell R, Gosev I, Cantor RS, Dardas TF, Kirklin JK, Rogers JG, Cleveland JC, Sandau KE, McIlvennan CK, Kaczorowski D, Estep JD, and Pagani FD. Defining optimal left ventricular assist device short-term outcomes may provide insight into programmatic quality assessment. *J Heart Lung Transplant* 2024; Epub ahead of print. PMID: 39142525. Full Text

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BACKGROUND: Patients have substantial variability in perioperative outcomes after left ventricular assist device (LVAD) implant. A perioperative multidimensional tool integrating mortality, adverse events (AEs), and patient-reported outcomes to assist in quality improvement initiatives is needed. METHODS: Patients undergoing HeartMate 3 LVAD implant (January 1, 2017 to January 31, 2024) in the Society of Thoracic Surgeons' Intermacs registry were studied. Cox proportional hazard multivariable analyses incorporating AEs as time-varying covariates for mortality out to 180 days was used to generate the INtermacs Short term composITE quality score (INSITE score derivation), reflecting the adjusted hazard ratio (HR) for mortality contributed by each AE, applying the global ranking methodology. In those alive and on support at 6 months, multivariable logistic regression (odds ratio) was used to examine the impact of AEs on health-related quality of life (QOL) at 180 days, captured through the INSITE-QOL score. Failure to achieve ≥1 point increase in visual analog scale from baseline was the event. RESULTS: Of 13,148 patients, 4,389 (33.4%) suffered at least 1 AE or death through 180 days. Stroke (survival: HR 13.1; QOL: HR 1.7), dialysis (survival: HR 31.4; QOL: HR 4.2), prolonged respiratory failure (survival: HR 5.7; QOL: HR 2.3), reoperation (survival: HR 3.4; QOL: HR 1.6), and right heart failure (survival: 5.0; QOL: HR 1.4), contributed to both mortality and failure to improve QOL at 180 days (all $p < 0.05$). The median INSITE

and INSITE-QOL scores were 0.0 [0.0, 1.6] and 0.0 [0.0, 0.0], respectively. At 9.4% (n = 17) of centers, a high INSITE score (≥13) was present in 15% of patients, while the top 25% of centers had perfect INSITE-QOL scores in at least 75% of patients. CONCLUSIONS: AEs after LVAD confer differential impact on mortality and QOL, enabling the development of global rank outcome scores. Given the high mortality hazard conferred by 180-day AEs, center-specific quality interventions aimed at reducing early complications provide the greatest opportunity to improve long-term survival and QOL.

Cardiology/Cardiovascular Research

Eng MH, Khalili H, Vavalle J, Al-Azizi KM, Waggoner T, Southard JA, Fang K, Hahn RT, **Lee J**, Wang DD, Eleid MF, **O'Neill WW**, and Abbas AE. 3-Year Outcomes of Balloon-Expandable Valves: 20-mm vs Larger Valves (≥23 mm). *JACC Cardiovasc Interv* 2024; Epub ahead of print. PMID: 39177555. Full Text

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BACKGROUND: A prior Society of Thoracic Surgeons/American College of Cardiology TVT (Transcatheter Valve Therapy) Registry-based analysis reported similar 1-year clinical outcomes with small (20-mm) vs large (≥23-mm) balloon-expandable valves (BEV). OBJECTIVES: The aim of this study was to describe mid-term 3-year clinical outcomes for small vs large BEV and the relationship between discharge echocardiographic mean gradient (MG) and different definitions of prothesis-patient mismatch (PPM) with clinical outcomes. METHODS: Using the TVT Registry with Centers for Medicare and Medicaid Services linkage, a propensity-matched analysis of patients receiving 20- vs ≥23-mm BEVs was performed. Spline curves and Kaplan-Meier plots with adjusted HRs determined the relationship between MG and 3-year mortality. RESULTS: In total, 316,091 patients were analyzed; after propensity matching, 8,100 pairs of each group were compared. The 20-mm BEV was associated with higher MGs compared with ≥23-mm BEVs (16.2 ± 7.2 mm Hg vs 11.8 ± 5.7 mm Hg; P < 0.0001). At 3 years, there was no difference in mortality between 20- and ≥23-mm BEVs (31.5% vs 32.5%, respectively; HR: 0.97; 95% CI: 0.90-1.05). Compared with an MG of 10 to 30 mm Hg, an MG <10 mm Hg (HR: 1.25; 95% CI:1.22-1.27) was associated with increased 3-year mortality. Measured severe PPM and predicted no PPM were associated with increased 3-year mortality (33.5% vs 32.9% vs 32.1%; P < 0.0001) and (33.5% vs 31.1% vs 30%; P < 0.0001), respectively. Low MG and severe measured PPM were associated with lower left ventricular ejection fraction (LVEF). CONCLUSIONS: Patients with small-prosthesis BEVs (20 mm) had identical 3-year survival as those with larger (≥23-mm) BEV valves. Severe measured PPM and low MG (<10 mm Hg), but not predicted severe PPM, were associated with lower LVEF and increased mortality, suggesting that LVEF is the culprit for worse outcomes.

Cardiology/Cardiovascular Research

Fadel RA, **Almajed MR**, **Parsons A**, **Kalsi J**, **Shadid M**, **Maki M**, **Alqarqaz M**, **Aronow H**, **Cowger J**, **Fuller B**, **Frisoli T**, **Grafton G**, **Kim H**, **Jones C**, **Koenig G**, Khandelwal A, **Nemeh H**, **O'Neill B**, **Tanaka D**, **Williams C**, **Villablanca P**, **O'Neill W**, **Alaswad K**, and **Basir MB**. Feasibility and Outcomes of a Cardiovascular Medicine Inclusive Extracorporeal Membrane Oxygenation (ECMO) Service. *J Soc Cardiovasc Angiogr Interv* 2024; 3(6):101359. PMID: 39132589. Full Text

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BACKGROUND: There has been a significant increase in the utilization of venoarterial extracorporeal membrane oxygenation (VA-ECMO) in recent years. Cardiothoracic surgery teams have historically led VA-ECMO care teams, with little data available on alternative care models. METHODS: We performed a retrospective review of a cardiovascular medicine inclusive VA-ECMO service, analyzing patients treated with peripheral VA-ECMO at a large quaternary care center from 2018 to 2022. The primary outcome was death while on VA-ECMO or within 24 hours of decannulation. Univariate and multivariate analyses were used to identify predictors of the primary outcome. RESULTS: Two hundred forty-four patients were included in the analysis (median age 61 years; 28.7% female), of whom 91.8% were cannulated by interventional cardiologists, and 84.4% were managed by a cardiology service comprised of interventional cardiologists, cardiac intensivists or advanced heart failure cardiologists. Indications for VA-ECMO included acute myocardial infarction (34.8%), decompensated heart failure (30.3%), and refractory cardiac arrest (10.2%). VA-ECMO was utilized during cardiopulmonary resuscitation in 26.6% of cases, 48% of which were peri-procedural arrest. Of the patients, 46% survived to decannulation, the majority of whom were decannulated percutaneously in the cardiac catheterization laboratory. There was no difference in survival following cannulation by a cardiac surgeon vs interventional cardiologist (50% vs 45%; P = .90). Complications included arterial injury (3.7%), compartment syndrome (4.1%), cannulation site infection (1.2%), stroke (14.8%), acute kidney injury (52.5%), access site bleeding (16%) and need for blood transfusion (83.2%). Elevated baseline lactate (odds ratio [OR], 1.13 per unit increase) and sequential organ failure assessment score (OR, 1.27 per unit increase) were independently associated with the primary outcome. Conversely, an elevated baseline survival after VA ECMO score (OR, 0.92 per unit increase) and 8-hour serum lactate clearance (OR, 0.98 per % increase) were independently associated with survival. CONCLUSIONS: The use of a cardiovascular medicine inclusive ECMO service is feasible and may be practical in select centers as indications for VA-ECMO expand.

Cardiology/Cardiovascular Research
Fang JX, **Frisoli TM**, **Giustino G**, **Villablanca PA**, **Engel Gonzalez P**, **O'Neill BP**, **Wang DD**, **O'Neill WW**, and **Lee JC**. ECG-gated CT improves diagnosis in prosthetic valve degeneration. *Eur Heart J Imaging Methods Pract* 2024; 2(1):qyae049. PMID: 39224105. Full Text

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Cardiology/Cardiovascular Research
Fang JX, **Villablanca PA**, **O'Neill BP**, **Wang DD**, **Engel Gonzalez P**, **Dali S**, **Giustino G**, **Lee JC**, **O'Neill WW**, and **Frisoli TM**. Mechanical Circulatory Support-Assisted Percutaneous Rescue of Ventricularly Embolized Transcatheter Heart Valve. *JACC Cardiovasc Interv* 2024; Epub ahead of print. PMID: 39177559. Full Text

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Cardiology/Cardiovascular Research
Godinez B, Weinberg A, Azmat R, **Balic N**, Parker A, Kaur R, Lerret N, and Collins JA. Comparison of microbial growth on primed extracorporeal membrane oxygenation circuits in varying environments using different priming solutions. *Perfusion* 2024; Epub ahead of print. PMID: 39196790. Full Text

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BACKGROUND: Extracorporeal Membrane Oxygenation (ECMO) is a life support device for patients with severe heart and/or lung failure. Emergency situations require immediate ECMO response. Primed circuits have become a routine practice, as it may take 30-60 min to assemble and prime. There remains a lack of data to support the sterility of primed and stored ECMO circuits. This bench study assessed the impact of storage environment and priming solution on specific microbial growth of primed ECMO circuits. METHODS: Twelve adult ECMO circuits were tested for sterility for 56 days between September-December 2020. Circuits were assembled and primed in a perfusion lab in Chicago, IL. Six were stored in a sterile environment and six in a non-sterile environment, with three circuits primed using normal saline (NaCl) and three with Plasmalyte-A for each environment. Samples were collected on days 0, 3, 7, 14, 28, 42, and 56 in anaerobic bottle cultures testing for potential pathogen growth, such as Staphylococcus aureus, Pseudomonas aeruginosa, and Escherichia coli. RESULTS: Samples obtained from the 12 primed ECMO circuits demonstrated no microbial growth of S. aureus, P. aeruginosa, and E. coli in the bottle cultures. Similarly, there was no difference in the circuit sterility based on the storage environment (sterile vs nonsterile) or priming solution (NaCl vs Plasmalyte-A). CONCLUSION: Our findings showed that ECMO circuits can be primed for 56 days without evidence of the specified bacterial growth. Furthermore, the storage conditions and the prime utilized did not affect the sterility of the primed ECMO circuits.

Cardiology/Cardiovascular Research

Guichard JL, Bonno EL, Nassif ME, Khumri TM, Miranda D, Jonsson O, Shah H, Alexy T, Macaluso GP, Sur J, Hickey G, McCann P, **Cowger JA**, Badiye A, Old WD, Raza Y, Masha L, Kunavarapu CR, Bennett M, Sharif F, Kiernan M, Mullens W, Chaparro SV, Mahr C, Amin RR, Stevenson LW, Hiivala NJ, Owens MM, Sauerland A, Forouzan O, and Klein L. Seated Pulmonary Artery Pressure Monitoring in Patients With Heart Failure: Results of the PROACTIVE-HF Trial. *JACC Heart Fail* 2024; Epub ahead of print. PMID: 39152983. Full Text

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BACKGROUND: Monitoring supine pulmonary artery pressures to guide heart failure (HF) management has reduced HF hospitalizations in select patients. OBJECTIVES: The purpose of this study was to evaluate the effect of managing seated mean pulmonary artery pressure (mPAP) with the Cordella Pulmonary Artery sensor on outcomes in patients with HF. METHODS: Following GUIDE-HF (Hemodynamic-GUIDEd Management of Heart Failure Trial), with U.S. Food and Drug Administration input, PROACTIVE-HF (A Prospective, Multi-Center, Open Label, Single Arm Clinical Trial Evaluating the Safety and Efficacy of the Cordella Pulmonary Artery Sensor System in NYHA Class III Heart Failure Patients trial) was changed from a randomized to a single-arm, open label trial, conducted at 75 centers in the USA and Europe. Eligible patients had chronic HF with NYHA functional class III symptoms, irrespective of the ejection fraction, and recent HF hospitalization and/or elevated natriuretic peptides. The primary effectiveness endpoint at 6 months required the HF hospitalization or all-cause mortality rate to be lower than a performance goal of 0.43 events/patient, established from previous hemodynamic monitoring trials. Primary safety endpoints at 6 months were freedom from device- or system-related complications or pressure sensor failure. RESULTS: Between February 7, 2020, and March 31, 2023, 456 patients were successfully implanted in modified intent-to-treat cohort. The 6-month event rate was 0.15 (95% CI: 0.12-0.20) which was significantly lower than performance goal (0.15 vs 0.43; $P < 0.0001$). Freedom from device- or system-related complications was 99.2% and freedom from sensor failure was 99.8% through 6 months. CONCLUSIONS: Remote management of seated mPAP is safe and results in a low rate of HF hospitalizations and mortality. These results support the use of seated mPAP monitoring and extend the growing body of evidence that pulmonary artery pressure-guided management improves outcomes in heart failure. (Multi-Center, Open Label, Single Arm Clinical Trial Evaluating the Safety and Efficacy of the Cordella Pulmonary Artery Sensor System in NYHA Class III Heart Failure Patients trial [PROACTIVE-HF]; NCT04089059).

Cardiology/Cardiovascular Research

Gupta K, **Villablanca P**, **Gonzalez PE**, **O'Neill B**, **O'Neill WW**, **Wang DD**, **Fang JX**, **Giustino G**, **Frisoli T**, and **Lee JC**. Association of Relative Left Ventricular Outflow Tract Area and Transcatheter Aortic Valve Replacement Related Paravalvular Leak. *J Soc Cardiovasc Angiogr Interv* 2024; 3(3Part B):101294. PMID: 39131220. Full Text

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BACKGROUND: Post-transcatheter aortic valve replacement (TAVR), paravalvular leak (PVL) is a quality metric associated with worse clinical outcomes. Transcatheter heart valve (THV) sizing is based primarily on the systolic annular size without regard to the left ventricular outflow tract (LVOT), which also lies within the THV landing zone. We hypothesized that LVOT size relative to the annulus is associated with post-TAVR PVL. METHODS: Data from consecutive patients undergoing TAVR in a single high-volume center from January 2018 to March 2019 were used. Pre-TAVR data from multidetector computed tomography (MDCT) were collected. Relative LVOT area was defined as LVOT area/annular area during systole. Logistic regression analysis was used to evaluate association with post-TAVR mild or greater PVL by transthoracic echocardiography before discharge. RESULTS: Among 293 patients (median age, 81.1 years; female, 49.5%; White, 88.0%), 81.6% received SAPIEN 3 and 18.4% received CoreValve THV models. Aortic valve morphology was bicuspid in 10.9% of patients. Prevalence of mild or greater

PVL was 23.5% (mild in 20.1%). Relative LVOT area had a significant inverse association such that the odds of mild or greater PVL decreased significantly with every 1% increase in relative LVOT area (adjusted odds ratio, 0.96; 95% CI, 0.93-0.98; P = .002). There was no interaction between the type of implanted valve and the relative LVOT area. Patients in the highest relative LVOT tertile had significantly lower odds of mild or greater PVL (adjusted odds ratio, 0.42; 95% CI, 0.21-0.87; P = .018 vs first tertile). CONCLUSIONS: In patients undergoing TAVR with the newer generation of THV (SAPIEN 3 and CoreValve models), a relatively narrower LVOT area vs annular area was independently associated with increased odds of mild or greater PVL before discharge.

Cardiology/Cardiovascular Research
Jabri A, and **Aronow HD**. Navigating Our Way Through Peripheral Vascular Intervention: Blind or Bolstered? *Am J Cardiol* 2024; Epub ahead of print. PMID: 39097152. Full Text

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Cardiology/Cardiovascular Research
Jabri A, Ayyad M, Albandak M, Al-Abdouh A, Madanat L, Khalefa BB, Alhuneafat L, **Ayyad A**, Lemor A, Mhanna M, **Al Jebaje Z**, **Fadel R**, **Gonzalez PE**, **O'Neill B**, Bagur R, Hanson ID, Abbas AE, **Frisoli T**, **Lee J**, **Wang DD**, **Aggarwal V**, **Alaswad K**, **O'Neill WW**, **Aronow HD**, **AlQarqaz M**, and **Villablanca P**. Outcomes following TAVR in patients with cardiogenic shock: A systematic review and meta-analysis. *Cardiovasc Revasc Med* 2024; Epub ahead of print. PMID: 39209579. Full Text

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BACKGROUND: While transcatheter aortic valve replacement (TAVR) has broadened treatment options for critically ill patients, outcomes among those with concomitant cardiogenic shock (CS) are not well-explored. METHODS: We conducted a comprehensive search of major databases for studies comparing outcomes following TAVR in patients with and without CS since inception up to October 31, 2023. Our meta-analysis included five non-randomized observational. Dichotomous outcomes were assessed using the Mantel-Haenszel method (risk ratio, 95 % CI), and continuous outcomes were evaluated using mean difference and 95 % CI with the inverse variance method. Statistical heterogeneity was determined using the inconsistency test (I(2)). RESULTS: Among 26,283 patients across five studies, 30-day mortality was higher in the CS group (7267 patients; 27.6 %) compared to those without CS (OR 3.41, 95 % CI [2.01, 5.76], p < 0.01), as well as 30-day major vascular complications (OR 1.72, 95 % CI [1.54, 1.92], p < 0.01). At 1-year follow-up, there was no statistically significant difference in mortality rates between the compared groups (OR 2.68, 95 % CI [0.53, 13.46], p = 0.12). No significant between-group differences were observed in the likelihood of 30-day aortic valve reintervention (OR 3.20, 95 % CI [0.63, 16.22], p = 0.09) or post-TAVR aortic insufficiency (OR 0.91, 95 % CI [0.33, 2.51], p = 0.73). Furthermore, 30-day stroke, pacemaker implantation, and in-hospital major bleeding were comparable between both cohorts. CONCLUSION: Among patients undergoing TAVR, short-term mortality is higher but one-year outcomes are similar when comparing those with, to those without, CS. Future studies should examine whether

TAVR outcomes are improved when the procedure is delayed to optimize CS and when delay is not possible, whether particular management strategies lead to more favorable periprocedural outcomes.

Cardiology/Cardiovascular Research
Khalil C, Lazar S, **Megaly M**, Mekritthikrai R, Vipparthy SC, Doukky R, Mortada ME, Huang HD, and Sharma PS. Trends and outcomes of inpatient cardiac implantable electronic device transvenous lead extractions: a nationwide analysis. *J Interv Card Electrophysiol* 2024; Epub ahead of print. PMID: 39105957. Full Text

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BACKGROUND: Higher rates of CIED implantations have been associated with an increased rate of lead failures and complications resulting in higher rates of transvenous lead extractions (TLE). OBJECTIVE: To assess the trends TLE admissions and evaluate the patient related predictors of safety outcomes. METHODS: National Readmission Database was queried to identify patients who underwent TLE from January 2016 to December 2019. We conducted a multivariate regression analysis to identify variables associated with in-hospital mortality in patients undergoing TLE. Additionally, we compared trends and outcomes of TLE among patients with prior sternotomy versus those without prior sternotomy and analyzed sex-based differences among patients undergoing TLE. RESULTS: We identified 30,128 hospitalizations for TLE. The index admission in-hospital mortality rate was 3.21% with cardiac tamponade happening in 1.46% of the admissions. Age, infective endocarditis, CKD, congestive heart failure and anemia were associated with higher in-hospital mortality rates. There was a lower rate of in-hospital mortality in patients with history of prior sternotomy versus patients without (OR 0.72, CI: 0.59-0.87, p-value < 0.001). There was no difference in in-hospital mortality rate between males and females. Females had a shorter length and a higher cost of stay when compared to male gender. CONCLUSION: TLE admissions continue to increase. Overall rates of mortality and complications are relatively low. Patients with prior sternotomy had better outcomes and less complications when compared to those without prior sternotomy. Female gender is associated with higher rates of cardiac tamponade, yet shorter length of stay with lower cost.

Cardiology/Cardiovascular Research
Korsholm K, Iriart X, Saw J, **Wang DD**, Berti S, Galea R, Freixa X, Arzamendi D, De Backer O, Kramer A, Cademartiri F, Cochet H, Odenstedt J, Aminian A, Räber L, Cruz-Gonzalez I, Garot P, Jensen JM, Alkhouli M, and Nielsen-Kudsk JE. Position Statement on Cardiac Computed Tomography Following Left Atrial Appendage Occlusion. *JACC Cardiovasc Interv* 2024; 17(15):1747-1764. PMID: 39142755. Full Text

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Left atrial appendage occlusion (LAAO) is rapidly growing as valid stroke prevention therapy in atrial fibrillation. Cardiac imaging plays an instrumental role in preprocedural planning, procedural execution, and postprocedural follow-up. Recently, cardiac computed tomography (CCT) has made significant advancements, resulting in increasing use both preprocedurally and in outpatient follow-up. It provides a noninvasive, high-resolution alternative to the current standard, transesophageal echocardiography, and may display advantages in both the detection and characterization of device-specific complications, such as peridevice leak and device-related thrombosis. The implementation of CCT in the follow-up after LAAO has identified new findings such as hypoattenuated thickening on the atrial device surface and left atrial appendage contrast patency, which are not readily assessable on transesophageal echocardiography. Currently, there is a lack of standardization for acquisition and interpretation of images and consensus on definitions of essential findings on CCT in the postprocedural phase. This paper intends to provide a practical and standardized approach to both acquisition and interpretation of CCT after LAAO based on a comprehensive review of the literature and expert consensus among European and North American interventional and imaging specialists.

Cardiology/Cardiovascular Research

Krittanawong C, Ahuja T, Wang Z, **Qadeer YK**, Moras E, Virk HUH, Alam M, Jneid H, and Sharma S. Bivalirudin versus heparin in patients undergoing percutaneous coronary intervention in acute coronary syndromes. *Crit Pathw Cardiol* 2024; Epub ahead of print. PMID: 39133562. Full Text

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INTRODUCTION: Data on outcomes between unfractionated heparin and bivalirudin anticoagulation during percutaneous coronary intervention (PCI) in acute coronary syndromes (ACS) remains inconclusive. We aimed to systematically analyze PCI outcomes comparing unfractionated heparin and bivalirudin. METHODS: We systematically searched Ovid MEDLINE, Ovid Embase, Ovid Cochrane Database of Systematic Reviews, Scopus, and Web of Science from database inception in 1966 through January 2024 for studies evaluating PCI outcomes comparing unfractionated heparin and bivalirudin. Two investigators independently reviewed data. Conflicts were resolved through consensus. Random-effects meta-analyses were used. RESULTS: Ten prospective trials were identified that enrolled 42,253 individuals who presented with an acute coronary syndrome. Our analysis found that heparin when compared to bivalirudin was associated with an increased risk of trial-based definition of major bleeding (RR 1.68, 95% CI 1.29-2.20), non-access site complications (RR 4.6, 95% CI 1.75-12.09), TIMI major

bleeding (RR 1.70, 95% CI 1.20-2.41), major bleeding risks (RR 1.87, 95% CI 1.49-2.36), cardiovascular disease death (RR 1.26, 95% CI 1.02-1.57), and thrombocytopenia (RR 1.67, 95% CI 1.07-2.62). There were no statistically significant differences between heparin and bivalirudin for all-cause mortality, MACE, stroke, reinfarction, target vessel revascularization, acute or stent thrombosis. CONCLUSIONS: The present meta-analysis demonstrates bivalirudin reduces major bleeding when used for anticoagulation during PCI in patients with acute coronary syndromes and is not associated with an increased risk of stent thrombosis or MACE.

Cardiology/Cardiovascular Research

Lamas GA, Anstrom KJ, Navas-Acien A, Boineau R, Nemeth H, Huang Z, Wen J, Rosenberg Y, Stylianou M, Jones TLZ, Joubert BR, Yu Q, Santella RM, Mon AC, Ujueta F, Escolar E, Nathan DM, Fonseca VA, Aude YW, **Ehrman JK**, Elliott T, Prashad R, Lewis EF, Lopes RD, Farkouh ME, Elliott AM, Newman JD, and Mark DB. Edetate Disodium-Based Chelation for Patients With a Previous Myocardial Infarction and Diabetes: TACT2 Randomized Clinical Trial. *JAMA* 2024; Epub ahead of print. PMID: 39141382. Full Text

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IMPORTANCE: In 2013, the Trial to Assess Chelation Therapy (TACT) reported that edetate disodium (EDTA)-based chelation significantly reduced cardiovascular disease (CVD) events by 18% in 1708 patients with a prior myocardial infarction (MI). OBJECTIVE: To replicate the finding of TACT in individuals with diabetes and previous MI. DESIGN, SETTING, AND PARTICIPANTS: A 2 × 2 factorial, double-masked, placebo-controlled, multicenter trial at 88 sites in the US and Canada, involving participants who were 50 years or older, had diabetes, and had experienced an MI at least 6 weeks before recruitment compared the effect of EDTA-based chelation vs placebo infusions on CVD events and compared the effect of high doses of oral multivitamins and minerals with oral placebo. This article reports on the chelation vs placebo infusion comparisons. INTERVENTIONS: Eligible participants were randomly assigned to 40 weekly infusions of an EDTA-based chelation solution or matching placebo and to twice daily oral, high-dose multivitamin and mineral supplements or matching placebo for 60 months. This article addresses the chelation study. MAIN OUTCOMES AND MEASURES: The primary end point was the composite of all-cause mortality, MI, stroke, coronary revascularization, or hospitalization for unstable angina. Median follow-up was 48 months. Primary comparisons were made from patients who received at least 1 assigned infusion. RESULTS: Of the 959 participants (median age, 67 years [IQR, 60-72 years]; 27% females; 78% White, 10% Black, and 20% Hispanic), 483 received at least 1 chelation infusion and 476 at least 1 placebo infusion. A primary end point event occurred in 172 participants (35.6%) in the chelation group and in 170 (35.7%) in the placebo group (adjusted hazard ratio [HR], 0.93; 95% CI, 0.76-1.16; P = .53). The 5-year primary event cumulative incidence rates were 45.8% for the

chelation group and 46.5% for the placebo group. CV death, MI, or stroke events occurred in 89 participants (18.4%) in the chelation group and in 94 (19.7%) in the placebo group (adjusted HR, 0.89; 95% CI, 0.66-1.19). Death from any cause occurred in 84 participants (17.4%) in the chelation group and in 84 (17.6%) in the placebo group (adjusted HR, 0.96; 95% CI, 0.71-1.30). Chelation reduced median blood lead levels from 9.03 µg/L at baseline to 3.46 µg/L at infusion 40 (P < .001). Corresponding levels in the placebo group were 9.3 µg/L and 8.7 µg/L, respectively. CONCLUSIONS AND RELEVANCE: Despite effectively reducing blood lead levels, EDTA chelation was not effective in reducing cardiovascular events in stable patients with coronary artery disease who have diabetes and a history of MI. TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT02733185.

Cardiology/Cardiovascular Research
Lee Adawi Awdish R, **Grafton G**, and Berry LL. Never-Words: What Not to Say to Patients With Serious Illness. *Mayo Clin Proc* 2024; Epub ahead of print. PMID: 39177542. Full Text

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Cardiology/Cardiovascular Research
Machanahalli Balakrishna A, Alla VM, **Aronow HD**, Secemsky E, Altin SE, Jayasuriya S, and Goldsweig AM. Endovascular versus surgical revascularization for patients with chronic limb-threatening ischemia: A systematic review and meta-analysis of randomized controlled trials. *Catheter Cardiovasc Interv* 2024; Epub ahead of print. PMID: 39162243. Full Text

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Cardiology/Cardiovascular Research
Medranda GA, Faraz HA, Thompson JB, Zhang Y, Bharadwaj AS, Osborn EA, Abu-Much A, Lansky AJ, **Basir MB**, Moses JW, **O'Neill WW**, Grines CL, and Baron SJ. Association of Preprocedural SYNTAX Score With Outcomes in Impella-Assisted High-Risk Percutaneous Coronary Intervention. *J Soc Cardiovasc Angiogr Interv* 2024; 3(8):101981. PMID: 39166169. Full Text

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BACKGROUND: Patients with complex coronary artery disease, as defined by high SYNTAX scores, undergoing percutaneous coronary intervention (PCI) have poorer outcomes when compared with patients with lower SYNTAX I scores. This study aimed to assess if mechanical circulatory support using Impella mitigates the effect of the SYNTAX I score on outcomes after high-risk percutaneous coronary intervention (HRPCI). METHODS: Using data from the PROTECT III study, patients undergoing Impella-assisted HRPCI between March 2017 and March 2020 were divided into 3 cohorts based on SYNTAX I score-low (≤22), intermediate (23-32), and high (≥33). Procedural and clinical outcomes out to 90 days were compared between groups. Multivariable regression analysis was used to assess the impact of SYNTAX I score on major adverse cardiovascular and cerebrovascular events (MACCE) at 90 days. RESULTS: A total of 850 subjects with core laboratory-adjudicated SYNTAX I scores were identified (low: n = 310; intermediate: n = 256; high: n = 284). Patients with high SYNTAX I scores were older than those with low or intermediate SYNTAX I scores (72.7 vs 69.7 vs 70.1 years, respectively; P < .01). After adjustment for covariates, high SYNTAX I score remained a significant predictor of 90-day MACCE (hazard ratio [HR], 2.14; 95% CI, 1.42-3.69; P < .01 vs low), whereas intermediate SYNTAX I score was not (HR, 0.92; 95% CI, 0.47-1.77; P = .80 vs low). These findings persisted after adjustment for post-PCI SYNTAX I score. CONCLUSIONS: A high SYNTAX I score was associated with higher rates of 90-day MACCE in patients who underwent Impella-assisted HRPCI. Further research is needed to understand the patient and procedural factors driving this finding.

Cardiology/Cardiovascular Research

Mena-Hurtado C, **Aronow HD**, Beckman J, Bikdeli B, Bronas U, Castro-Dominguez Y, Chatterjee S, Elgendy IY, Kadian-Dodov D, Hogan S, Sethi S, Mohamad Yusoff F, and Mukherjee D. Executive Summary of Standard Operating Procedures for Society for Vascular Medicine (SVM) publications. *Vasc Med* 2024; Epub ahead of print. PMID: 39177502. Full Text

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Cardiology/Cardiovascular Research
Mufarrih SH, Qureshi NQ, Khan MS, Kazimuddin M, Secemsky E, Bloch MJ, Giri J, Cohen D, Swaminathan RV, Feldman DN, **Alaswad K**, Kirtane A, Kandzari D, and Aronow HD. Randomized Trials of Renal Denervation for Uncontrolled Hypertension: An Updated Meta-Analysis. *J Am Heart Assoc* 2024; 13(16):e034910. PMID: 39140334. Full Text

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BACKGROUND: Despite optimal medical therapy, a significant proportion of patients' blood pressure remains uncontrolled. Catheter-based renal denervation (RDN) has been proposed as a potential intervention for uncontrolled hypertension. We conducted an updated meta-analysis to assess the efficacy and safety of RDN in patients with uncontrolled hypertension, with emphasis on the differential effect of RDN in patients on and off antihypertensive medications. METHODS AND RESULTS: Online databases were searched to identify randomized clinical trials comparing efficacy and safety of RDN versus control in patients with uncontrolled hypertension. Subgroup analyses were conducted for sham-controlled trials and studies that used RDN devices that have gained or are currently seeking US Food and Drug Administration approval. Fifteen trials with 2581 patients (RDN, 1723; sham, 858) were included. In patients off antihypertensive medications undergoing RDN, a significant reduction in 24-hour ambulatory (-3.70 [95% CI, -5.41 to -2.00] mm Hg), office (-4.76 [95% CI, -7.57 to -1.94] mm Hg), and home (-3.28 [95% CI, -5.96 to -0.61] mm Hg) systolic blood pressures was noted. In patients on antihypertensive medications, a significant reduction was observed in 24-hour ambulatory (-2.23 [95% CI, -3.56 to -0.90] mm Hg), office (-6.39 [95% CI, -11.49 to -1.30]), home (-6.08 [95% CI, -11.54 to -0.61] mm Hg), daytime (-2.62 [95% CI, -4.14 to -1.11]), and nighttime (-2.70 [95% CI, -5.13 to -0.27]) systolic blood pressures, as well as 24-hour ambulatory (-1.16 [95% CI, -1.96 to -0.35]), office (-3.17 [95% CI, -5.54 to -0.80]), and daytime (-1.47 [95% CI, -2.50 to -0.27]) diastolic blood pressures. CONCLUSIONS: RDN significantly lowers blood pressure in patients with uncontrolled hypertension, in patients off and on antihypertensive medications, with a favorable safety profile. The efficacy of RDN was consistent in sham-controlled trials and contemporary trials using US Food and Drug Administration-approved devices.

Cardiology/Cardiovascular Research
Nathan AS, Reddy KP, Eberly LA, Fanaroff A, Julien HM, Fiorilli P, Wald J, Mutaawe S, Cevasco M, Bermudez C, Kapur NK, **Basir MB**, Roswell R, Groeneveld PW, and Giri J. Racial, Ethnic, Socioeconomic, and Geographic Inequities in Access to Mechanical Circulatory Support. *J Soc Cardiovasc Angiogr Interv* 2024; 3(1):101193. PMID: 39131979. Full Text

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BACKGROUND: Hospital admissions for cardiogenic shock have increased in the United States. Temporary mechanical circulatory support (tMCS) can be used to acutely stabilize patients. We sought to evaluate the presence of racial, ethnic, and socioeconomic inequities in access to MCS in the United States among patients with cardiogenic shock. METHODS: Medicare data were used to identify patients with cardiogenic shock admitted to hospitals with advanced tMCS (microaxial left ventricular assist device [mLVAD] or extracorporeal membranous oxygenation [ECMO]) capabilities within the 25 largest core-based statistical areas, all major metropolitan areas. We modeled the association between patient race, ethnicity, and socioeconomic status and use of mLVAD or ECMO. RESULTS: After adjusting for age and clinical comorbidities, dual eligibility for Medicaid was associated with a 19.9% (95% CI, 11.5%-27.4%) decrease in odds of receiving mLVAD in a patient with cardiogenic shock ($P < .001$). After adjusting for age, clinical comorbidities, and dual eligibility for Medicaid, Black race was associated with 36.7% (95% CI, 28.4%-44.2%) lower odds of receiving mLVAD in a patient with cardiogenic shock. Dual eligibility for Medicaid was associated with a 62.0% (95% CI, 60.8%-63.1%) decrease in odds of receiving ECMO in a patient with cardiogenic shock ($P < .001$). Black race was associated with 36.0% (95% CI, 16.6%-50.9%) lower odds of receiving ECMO in a patient with cardiogenic shock, after adjusting for Medicaid eligibility. CONCLUSIONS: We identified large and significant racial, ethnic, and socioeconomic inequities in access to mLVAD and ECMO among patients presenting with cardiogenic shock to metropolitan hospitals with active advanced tMCS programs. These findings highlight systematic inequities in access to potentially lifesaving therapies.

Cardiology/Cardiovascular Research

Perkins SJ, Funes M, Cheah D, Argenti C, Vinales J, Gordon D, Haft JW, Williams DM, McLaughlin VV, Agarwal PP, Moles VM, Cascino T, Obi A, Pandey A, Shih A, and **Aggarwal V**. Safety Window for Effective Lesion Crossing in Patients With Chronic Thromboembolic Pulmonary Hypertension. *J Soc Cardiovasc Angiogr Interv* 2024; 3(8):102142. PMID: 39166161. Full Text

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BACKGROUND: Balloon pulmonary angioplasty for chronic thromboembolic pulmonary hypertension (CTEPH) is limited by a lack of safe and effective tools for crossing these lesions. We aim to identify a

safety window for an intraluminal crossing device in this vascular bed by studying the piercing properties of pulmonary arterial vessel walls and intraluminal CTEPH lesion specimens. As a secondary objective, we also describe the histopathologic features of CTEPH lesions. METHODS: Specimens were procured from 9 patients undergoing pulmonary endarterectomy. The specimens were subsampled and identified grossly as arterial wall or intraluminal CTEPH lesions. The force needed for tissue penetration was measured using a 0.38-mm (0.015-in) diameter probe in an ex vivo experimental model developed in our lab. Concurrent histology was also performed. RESULTS: The mean force needed to penetrate the arterial wall and intraluminal CTEPH lesions was 1.75 ± 0.10 N (n = 121) and 0.30 ± 0.04 N (n = 56), respectively (P < .001). Histology confirmed the presence of intimal hyperplasia with calcium and hemosiderin deposition in the arterial wall as well as an old, organized thrombus in the lumen. CONCLUSIONS: The pulmonary arterial wall is friable and prone to perforation during instrumentation with workhorse coronary guide wires. However, the results of this study demonstrate that a much lower force is needed for the 0.38-mm (0.015-in) probe to penetrate an intraluminal CTEPH lesion compared to pulmonary arterial intima. This finding suggests the existence of a safety window for lesion-crossing devices, enabling effective balloon pulmonary angioplasty.

Cardiology/Cardiovascular Research

Perpetua EM, Palmer R, Le VT, Al-Khatib SM, Beavers CJ, Beckman JA, Bozkurt B, Coylewright M, Lloyd Doherty C, Guibone KA, Hawkey M, Keegan PA, Kirkpatrick JN, Laperle J, Lauck SB, Levine G, Lindman BR, Mack MJ, Price AL, Strong S, **Wyman JF**, Youmans QR, and Gulati M. JACC: Advances Expert Panel Perspective: Shared Decision-Making in Multidisciplinary Team-Based Cardiovascular Care. *JACC Adv* 2024; 3(7):100981. PMID: 39130036. Full Text

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Shared decision-making (SDM) and multidisciplinary team-based care delivery are recommended across several cardiology clinical practice guidelines. However, evidence for benefit and guidance on implementation are limited. Informed consent, the use of patient decision aids, or the documentation of these elements for governmental or societal agencies may be conflated as SDM. SDM is a bidirectional

exchange between experts: patients are the experts on their goals, values, and preferences, and clinicians provide their expertise on clinical factors. In this Expert Panel perspective, we review the current state of SDM in team-based cardiovascular care and propose best practice recommendations for multidisciplinary team implementation of SDM.

Cardiology/Cardiovascular Research
Riley RF, Miller LE, Davies R, **Alaswad K**, **Al-Jebaje Z**, Doshi D, Jaffer FA, Adusumalli S, Frizzell JD, Kumar K, Patel MP, Dakroub A, and Ali ZA. Retrospective Multicenter Analysis of Intravascular Lithotripsy Use During Calcified Left Main Coronary Artery Percutaneous Coronary Interventions. *J Soc Cardiovasc Angiogr Interv* 2024; 3(2):101213. PMID: 39132218. Full Text

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BACKGROUND: Intravascular lithotripsy (IVL) safely and effectively modifies calcified coronary lesions during percutaneous coronary interventions (PCI). Data regarding its utility in modifying calcified left main coronary artery (LMCA) disease are limited. This study aimed to evaluate short-term outcomes of IVL-assisted LMCA PCI. METHODS: This retrospective multicenter all-comers study analyzed patients who underwent intravascular imaging-guided, IVL-assisted PCI for calcified LMCA disease. Clinical and procedural characteristics were obtained, including intravascular imaging measurements. Technical success was defined as successful stent deployment with <30% residual diameter stenosis. Major adverse cardiac events (MACE) was a composite of all-cause death, myocardial infarction, and target vessel revascularization evaluated immediately postprocedure and at 30-day follow-up. RESULTS: Among 184 patients treated at 7 centers from 2019-2023, IVL-assisted LMCA PCI achieved 99.4% technical success. Calcium fracture was identified in 136/165 cases (82.4%) on post-IVL imaging. Pretreatment minimal luminal area increased significantly compared to post-PCI minimal stent area (MSA) (4.1 ± 1.3 to 9.3 ± 2.5 mm(2), respectively; P < .001). There was a direct correlation between IVL balloon size and the final MSA (P = .002). In-hospital MACE was 4.4% and 30-day MACE was 8.8%. In multivariate logistic regression, presentation with troponin-positive myocardial infarction was the sole predictor of 30-day MACE. CONCLUSIONS: IVL-assisted PCI for calcified LMCA lesions was safe and resulted in high technical success rates, confirming its utility as an effective treatment in this challenging lesion subset.

Cardiology/Cardiovascular Research
Rymer J, Alhanti B, Kemp S, Bhatt DL, Kochar A, Angiolillo DJ, Diaz M, Garratt KN, Wimmer NJ, Waksman R, Kirtane AJ, Ang L, Bach R, Barker C, Jenkins R, **Basir MB**, Sullivan A, El-Sabae H, Brothers L, Ohman EM, Jones WS, Washam JB, and Wang TY. Risk of Bleeding Among Cangrelor-Treated Patients Administered Upstream P2Y(12) Inhibitor Therapy: The CAMEO Registry. *J Soc Cardiovasc Angiogr Interv* 2024; 3(2):101202. PMID: 39132213. Full Text

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BACKGROUND: Little is known about the bleeding risk associated with cangrelor use in patients with myocardial infarction (MI) who are exposed to an oral P2Y(12) inhibitor before coronary angiography. METHODS: Cangrelor in Acute MI: Effectiveness and Outcomes (CAMEO) is an observational registry studying platelet inhibition for patients with MI. Upstream oral P2Y(12) inhibition was defined as receipt of an oral P2Y(12) inhibitor within 24 hours before hospitalization or in-hospital before angiography. Among cangrelor-treated patients, we compared bleeding after cangrelor use through 7 days postdischarge between patients with and without upstream oral P2Y(12) inhibitor exposure. RESULTS: Among 1802 cangrelor-treated patients with MI, 385 (21.4%) received upstream oral P2Y(12) inhibitor treatment. Of these, 101 patients (33.8%) started cangrelor within 1 hour, 103 (34.4%) between 1 and 3 hours, and 95 (31.8%), >3 hours after in-hospital oral P2Y(12) inhibitor administration; the remaining received an oral P2Y(12) inhibitor before hospitalization. There was no statistically significant difference in rates of bleeding among cangrelor-treated patients with and without upstream oral P2Y(12) inhibitor exposure (6.5% vs 8.8%; adjusted odds ratio [OR], 0.62; 95% CI, 0.38-1.01). Bleeding was observed in 5.0%, 10.7%, and 3.2% of patients treated with cangrelor <1, 1 to 3, and >3 hours after the last oral PY(12) inhibitor dose, respectively; bleeding rates were not statistically different between groups (1-3 hours vs <1 hour: adjusted OR, 2.70; 95% CI, 0.87-8.32; >3 hours vs <1 hour: adjusted OR, 0.65; 95% CI, 0.15-2.85). CONCLUSIONS: Bleeding risk was not observed to be significantly higher after cangrelor treatment in patients with and without upstream oral P2Y12 inhibitor exposure.

Cardiology/Cardiovascular Research
Sabra M, Kabani S, and **Maskoun W**. Role of cardiac event monitor in the detection of delayed high-grade atrioventricular block after negative electrophysiological study in patients with post–transcatheter aortic valve replacement. *Heart Rhythm O2* 2024; 5(8):587-591. PMID: Not assigned. Full Text

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Cardiology/Cardiovascular Research
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BACKGROUND: Data on procedural and early outcomes after transjugular transcatheter tricuspid valve replacement (TTVR) are limited. OBJECTIVES: This study sought to evaluate first-in-man procedural and clinical outcomes after transjugular TTVR with a special focus on patients who received large device sizes in whom TTVR outcomes have been questioned. METHODS: The retrospective registry included patients who underwent TTVR using the LuX-Valve Plus system (Jenscare Biotechnology Co Ltd) for symptomatic tricuspid regurgitation (TR) from January 2022 until February 2024 at 15 international centers in a compassionate use setting. The endpoints were procedural TR reduction, in-hospital death, adverse events, and 1-month survival. We further stratified results according to the size of the implanted device (<55 vs ≥55 mm). RESULTS: The registry included a total of 76 patients at a median age of 78 years (Q1-Q3: 72-83 years, 47.4% women). TR was reduced to ≤2+ and ≤1+ in 94.7% and 90.8% of patients (75.0% of patients received TTVR devices ≥55 mm) with well-sustained results at 1-month follow-up (TR ≤2+ in 95.0% and ≤1+ 86.8%). Residual TR was paravalvular in all cases. In-hospital death occurred in 4 patients (5.3%). Four patients (5.3%) underwent cardiac surgery during index hospitalization. Major in-hospital bleeding events occurred in 5 patients (6.6%). New in-hospital pacemaker implantation was required in 3.9% of patients in the overall cohort (5.7% in "pacemaker-naive" individuals). No cases of valve thrombosis, stroke, myocardial infarction, or pulmonary embolism were observed. At 1-month follow-up, survival was 94.4%, and NYHA functional class significantly improved. One further patient received a pacemaker, 1 further bleeding event occurred, and 2 patients underwent reintervention or surgery within the first 30 days after TTVR. No differences in procedural outcomes or adverse events were observed after stratification for valve size. CONCLUSIONS: Transjugular TTVR appears to be a safe and effective treatment option for patients with severe TR with comparable outcomes in very large tricuspid anatomies.

Cardiology/Cardiovascular Research

Zahr F, Elmariah S, Vemulapalli S, Kodali SK, Hahn RT, Anderson AS, Eleid MF, Davidson CJ, Sharma RP, **O'Neill WW**, Bethea B, Thourani VH, Chakravarty T, Gupta A, and Makkar RR. Impact of Tricuspid Regurgitation on Outcomes of Transcatheter Aortic Valve Replacement With Balloon-Expandable Valves. *JACC Cardiovasc Interv* 2024; 17(16):1916-1931. PMID: 39197990. Full Text

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BACKGROUND: Tricuspid regurgitation (TR) is highly prevalent in the transcatheter aortic valve replacement (TAVR) population, but clear management guidelines are lacking. OBJECTIVES: The aims of this study were to elucidate the prevalence and consequences of severe TR in patients with aortic stenosis undergoing TAVR and to examine the change in TR post-TAVR, including predictors of improvement and its impact on longer term mortality. METHODS: Using Centers for Medicare and Medicaid Services-linked TVT (Transcatheter Valve Therapy) Registry data, a propensity-matched analysis was performed among patients undergoing TAVR with baseline mild, moderate, or severe TR. Kaplan-Meier estimates were used to assess the impact of TR on 3-year mortality. Multivariable analysis identified predictors of 30-day TR improvement. RESULTS: Of the 312,320 included patients, 84% had mild, 13% moderate, and 3% severe TR. In a propensity-matched cohort, severe baseline TR was associated with higher in-hospital mortality (2.5% vs 2.1% for moderate TR and 1.8% for mild TR; $P = 0.009$), higher 1-year mortality (24% vs 19.6% for moderate TR and 16.6% for mild TR; $P < 0.0001$), and 3-year mortality (54.2% vs 48.5% for moderate TR and 43.3% for mild TR; $P < 0.0001$). Among the patients with severe TR at baseline, 76.4% improved to moderate or less TR 30 days after TAVR. Baseline mitral regurgitation moderate or greater, preserved ejection fraction, higher aortic valve gradient, and better kidney function predicted TR improvement after TAVR. However, severe 30-day residual TR was associated with higher 1-year mortality (27.4% vs 18.7% for moderate TR and 16.8% for mild TR; $P < 0.0001$). CONCLUSIONS: Severe baseline and 30-day residual TR after TAVR are associated with increased mortality up to 3 years. This analysis identifies a higher risk group that could be evaluated for the recently approved tricuspid interventions.

Center for Health Policy and Health Services Research

McGlothen-Bell K, Cartagena D, Malin KJ, Vittner D, McGrath JM, Koerner RL, **Vance AJ**, and Crawford AD. Reimagining Supportive Approaches at the Intersection of Mandatory Reporting Policies for the Mother-Infant Dyad Affected by Substance Use. *Adv Neonatal Care* 2024; 24(5):424-434. PMID: 39133542. Full Text

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BACKGROUND: As rates of substance use during pregnancy persist, the health and optimal development of infants with prenatal substance exposure remain a key priority. Nurses are tasked with identifying and reporting suspected cases of child maltreatment, including abuse and neglect, which is often assumed to be synonymous with substance use during pregnancy. While policies aimed at protecting infants from child abuse and neglect are well intentioned, literature regarding the short- and long-term social and legal implications of mandatory reporting policies is emerging. PURPOSE: In this article, we explore the intersections between the condition of substance use in pregnancy and policies

related to mandatory reporting. METHODS: We provide an overview of historical and current trends in mandatory reporting policies for nurses related to substance use in pregnancy and related ethical and social implications for mother-infant dyads. RESULTS: Nurses often function at the intersection of healthcare and social services, underscoring the important role they play in advocating for ethical and equitable care for both members of the mother-infant dyad affected by substance use. IMPLICATIONS FOR PRACTICE AND RESEARCH: We offer recommendations for practice including the integration of respectful care and family-centered support for the mother-infant dyad affected by substance use. Cross-sectoral collaborations, inclusive of the family, are important to the advancement of evidence-based and equity-focused research, advocacy, and policy initiatives to support familial preservation and reduce mother-infant separation.

Center for Health Policy and Health Services Research

Moe AM, **Llamocca E**, Wastler HM, Steelesmith DL, Brock G, Oluwoye O, and Fontanella CA. Racial and Ethnic Disparities in the Diagnosis and Early Treatment of First-Episode Psychosis. *Schizophr Bull Open* 2024; 5(1):sgae019. PMID: 39206276. Full Text

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BACKGROUND: Despite recognition that early intervention for first-episode psychosis (FEP) improves outcomes, Black youth with FEP continue to experience critical disparities in care. A historical lack of scientific focus on racial and ethnic factors in the study of psychosis and scant investigations among publicly insured (ie, Medicaid-enrolled) youth hinder our ability to understand and address factors that contribute to disparities in early FEP care. Strategies for improving FEP services for Black youth are reliant on more precise identification of who faces disparities and when during the early course of illness disparities are experienced. STUDY DESIGN: A retrospective longitudinal analysis of Ohio Medicaid claims data was performed for 987 982 youth aged 15-24 years between 2010 and 2020 to examine: (1) the likelihood of FEP diagnosis, (2) the type of psychotic disorder diagnosis received, and (3) receipt of treatment following psychosis onset. STUDY RESULTS: Non-Hispanic Black (NHB) youth, relative to non-Hispanic White (NHW) peers, were more likely to be diagnosed with a psychotic disorder and were further more likely to receive a diagnosis of schizophrenia relative to an affective psychotic disorder. In the first year following FEP diagnosis, NHB youth were also less likely to receive psychotherapy than NHW youth; this disparity was no longer present when examined at 2 years following FEP. CONCLUSIONS: In this study, Black youth experienced disparities in both the diagnosis and early treatment of FEP. Additional efforts are needed to understand and address these observed disparities and to promote equitable access to FEP care during the critical early illness phases.

Center for Health Policy and Health Services Research

Rossom R, Knowlton G, **Yeh HH**, Penfold R, Owen-Smith A, Hooker S, Simon G, **Miller-Matero L**, **Akinyemi E**, and **Ahmedani B**. Psychotherapy Engagement Before and After a Rapid Transition to Telehealth During COVID-19 for Older Adults With Dementia. *J Appl Gerontol* 2024; Epub ahead of print. PMID: 39102577. Full Text

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Objective: To understand the impact of the transition to telehealth during COVID-19 on psychotherapy visits for patients with dementia. Method: Retrospective study of older adults with dementia who had at least one psychotherapy visit in the 9 months before and after the onset of COVID-19 at 3 U.S. health systems. Care disruptions were gaps of 45+ days. Descriptive statistics and logistic mixed-effects models examined factors associated with care disruption. Results: 4953 patients with dementia made 19,902 psychotherapy visits. Gaps in psychotherapy were less frequent during COVID-19 (29.4%) than before (48.9%), with the odds of a patient experiencing a care disruption during COVID-19 0.54 times the odds prior to COVID-19 (95% CI: 0.50-0.59). Almost all patient subgroups had lower adjusted odds of care disruption during COVID-19. Discussion: There were fewer disruptions in psychotherapy care following the rapid shift to virtual care. Telehealth may be a viable option for patients with dementia.

Center for Health Policy and Health Services Research
Shamaa O, Ahmed A, **Rupp L**, **Trudeau S**, and **Gordon SC**. Beyond the Surface: Unveiling Hidden Hurdles to Primary Biliary Cholangitis Care. *Cureus* 2024; 16(7):e64753. PMID: 39156427. Full Text

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INTRODUCTION: Ursodeoxycholic acid (UDCA) slows disease progression among patients with primary biliary cholangitis (PBC), yet not all patients receive this standard-of-care medication. Our study aims to identify reasons why PBC patients did not receive the recommended UDCA treatment. METHODS: Using medical record data collected by the Fibrotic Liver Disease (FOLD) Consortium for 2006-2016, we identified PBC patients from a single site with no UDCA therapy record. Two independent reviewers used a structured data collection instrument to systematically confirm and record the reasons for the lack of treatment. RESULTS: Among 494 PBC patients (11% men and 13.2% Black patients) with a median follow-up of 5.2 years, 35 (7%) had never received UDCA (16% men and 24% Black patients). Of these, 18 (51%) had laboratory indications of PBC but were not formally diagnosed. Among the remaining 17 patients with recognized PBC, six were never offered UDCA, seven declined treatment, and four remained untreated despite being offered treatment. We did not find a statistically significant association between the lack of PBC diagnosis and treatment and patients' age ($p = 0.139$), gender ($p = 0.222$), race ($p = 0.081$), or insurance coverage ($p = 0.456$), perhaps due to our small sample size. CONCLUSIONS: Multiple factors influencing the lack of evaluation and treatment in PBC patients were identified at the provider and patient levels. The most common reasons included financial barriers, loss to follow-up, severe decompensated disease at diagnosis, and lack of referral to specialists for further evaluation. Future interventions targeting modifiable provider and patient barriers may improve rates and timeliness of PBC diagnosis and treatment.

Center for Health Policy and Health Services Research
Stewart CC, Simon G, **Ahmedani BK**, Beck A, Daida YG, Lynch FL, Owen-Smith AA, Negriff SL, Rossom R, Sterling SA, Lu CY, and Schoenbaum M. Variation in completeness of coding external cause of injuries under ICD-10-CM. *Inj Prev* 2024; Epub ahead of print. PMID: 38906684. Full Text

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INTRODUCTION: Information about causes of injury is key for injury prevention efforts. Historically, cause-of-injury coding in clinical practice has been incomplete due to the need for extra diagnosis codes in the International Classification of Diseases-Ninth Revision-Clinical Modification (ICD-9-CM) coding. The transition to ICD-10-CM and increased use of clinical support software for diagnosis coding is expected to improve completeness of cause-of-injury coding. This paper assesses the recording of external cause-of-injury codes specifically for those diagnoses where an additional code is still required. METHODS: We used electronic health record and claims data from 10 health systems from October 2015 to December 2021 to identify all inpatient and emergency encounters with a primary diagnosis of injury. The proportion of encounters that also included a valid external cause-of-injury code is presented. RESULTS: Most health systems had high rates of cause-of-injury coding: over 85% in emergency departments and over 75% in inpatient encounters with primary injury diagnoses. However, several sites had lower rates in both settings. State mandates were associated with consistently high external cause recording. CONCLUSIONS: Completeness of cause-of-injury coding improved since the adoption of ICD-10-CM coding and increased slightly over the study period at most sites. However, significant variation remained, and completeness of cause-of-injury coding in any diagnosis data used for injury prevention planning should be empirically determined.

Center for Health Policy and Health Services Research
Zivin K, Zhang X, Tilea A, Hall SV, Admon LK, **Vance AJ**, and Dalton VK. Perinatal Psychotherapy Use and Costs Before and After Federally Mandated Health Insurance Coverage. *JAMA Netw Open* 2024; 7(8):e2426802. PMID: 39120900. Full Text

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IMPORTANCE: Insurance coverage affects health care access for many delivering women diagnosed with perinatal mood and anxiety disorders (PMADs). The Mental Health Parity and Addiction Equity Act (MHPAEA; passed in 2008) and the Patient Protection and Affordable Care Act (ACA; passed in 2010) aimed to improve health care access. OBJECTIVE: To assess associations between MHPAEA and ACA implementation and psychotherapy use and costs among delivering women overall and with PMADs. DESIGN, SETTING, AND PARTICIPANTS: This cross-sectional study conducted interrupted time series analyses of private insurance data from January 1, 2007, to December 31, 2019, for delivering women aged 15 to 44 years, including those with PMADs, to assess changes in psychotherapy visits in the year before and the year after delivery. It estimated changes in any psychotherapy use and per-visit out-of-pocket costs (OOPCs) for psychotherapy associated with MHPAEA (January 2010) and ACA (January 2014) implementation. Data analyses were performed from August 2022 to May 2023. EXPOSURES: Implementation of the MHPAEA and ACA. MAIN OUTCOMES AND MEASURES: Any psychotherapy use and per-visit OOPCs for psychotherapy standardized to 2019 dollars. RESULTS: The study included 837 316 overall deliveries among 716 052 women (mean [SD] age, 31.2 [5.4] years; 7.6% Asian, 8.8% Black, 12.8% Hispanic, 64.1% White, and 6.7% unknown race and ethnicity). In the overall cohort, a nonsignificant step change was found in the delivering women who received psychotherapy after MHPAEA implementation of 0.09% (95% CI, -0.04% to 0.21%; P = .16) and a nonsignificant slope change of delivering women who received psychotherapy of 0.00% per month (95% CI, -0.02% to 0.01%; P = .69). A nonsignificant step change was found in delivering individuals who received psychotherapy after ACA implementation of 0.11% (95% CI, -0.01% to 0.22%; P = .07) and a significantly increased slope change of delivering individuals who received psychotherapy of 0.03% per month (95% CI, 0.00% to 0.05%; P = .02). Among those with PMADs, the MHPAEA was associated with an immediate increase (0.72%; 95% CI, 0.26% to 1.18%; P = .002) then sustained decrease (-0.05%; -0.09% to -0.02%; P = .001) in psychotherapy receipt; the ACA was associated with immediate (0.77%; 95% CI, 0.26% to

1.27%; P = .003) and sustained (0.07%; 95% CI, 0.02% to 0.12%; P = .005) monthly increases. In both populations, per-visit monthly psychotherapy OOPCs decreased (-$0.15; 95% CI, -$0.24 to -$0.07; P < .001 for overall and -$0.22; -$0.32 to -$0.12; P < .001 for the PMAD population) after MHPAEA passage with an immediate increase ($3.14 [95% CI, $1.56-$4.73]; P < .001 and $2.54 [95% CI, $0.54-$4.54]; P = .01) and steady monthly increase ($0.07 [95% CI, $0.02-$0.12]; P = .006 and $0.10 [95% CI, $0.03-$0.17]; P = .004) after ACA passage. CONCLUSIONS AND RELEVANCE: This study found complementary and complex associations between passage of the MHPAEA and ACA and access to psychotherapy among delivering individuals. These findings indicate the value of continuing efforts to improve access to mental health treatment for this population.

Dermatology

Grant GJ, **Robinson CG**, **Rambhatla PV**, and **Mohammad TF**. A comparison of tinted sunscreen availability in urban versus suburban settings in the Detroit area. *Arch Dermatol Res* 2024; 316(8):570. PMID: 39180553. Full Text

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Dermatology

Hamzavi IH, Ganesan AK, Mahmoud BH, Weiss E, Ahmed AM, Robinson D, Goldman MP, Munavalli G, Kahn SA, Huang V, Waibel J, Desai A, Elbuluk N, Desai S, and Pandya AG. Effective and durable repigmentation for stable vitiligo: a randomized within-subject controlled trial assessing treatment with autologous skin cell suspension transplantation. *J Am Acad Dermatol* 2024; Epub ahead of print. PMID: 39182674. Full Text

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BACKGROUND: Vitiligo lesions are often challenging to repigment with conventional medical therapies. Surgical autologous melanocyte transfer methods can be utilized for stable vitiligo but demand specialized skills and equipment. A point-of-care autologous cell harvesting device was designed

enabling simple preparation of autologous skin cell suspension (ASCS) containing melanocytes, keratinocytes, and fibroblasts providing a straightforward approach for cellular transplantation. OBJECTIVE: To evaluate the safety and effectiveness of ASCS for repigmentation of stable vitiligo lesions among adults. METHODS: A US multicenter, randomized, within-subject controlled trial compared ASCS to NB-UVB only (Control) in similar vitiligo lesions. ASCS was applied after laser skin resurfacing and followed by NB-UVB treatment. The primary effectiveness endpoint was the proportion of lesions achieving ≥80% repigmentation at week-24. Repigmentation durability was assessed at week-52. RESULTS: Among 25 subjects, 36% of ASCS-treated lesions achieved ≥80% repigmentation at week-24 compared to 0% for Control ($p<0.025$), with durability through week-52. The safety profile of ASCS was acceptable, with favorable patient- and investigator-reported outcomes. LIMITATIONS: Study sample size limited robust subgroup analyses. CONCLUSION: Application of ASCS is a safe and effective treatment for repigmentation of stable vitiligo lesions with the potential to improve health-related quality of life and reduce burden of disease.

Dermatology
Karns JP, **Nguyen A**, **Wong N**, **True-Malhotra A**, **Smythe D**, and **Vemulapalli R**. A 27-Year-Old Female With JAK2 Mutation: A Case of Budd-Chiari Syndrome Secondary to Prolonged Oral Contraceptive Pill Use. *Cureus* 2024; 16(7):e64858. PMID: 39156349. Full Text

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Individuals with Philadelphia chromosome-negative myeloproliferative neoplasms (MPNs) such as polycythemia vera and essential thrombocythemia (ET) demonstrate an increased thrombotic risk associated with JAK2 mutations. Physicians must take heed when treating these patients, to mitigate this pro-thrombotic state as much as possible. Failure to do so, or exacerbating the state, can lead to dire consequences. We present the case of a 27-year-old female with a history of ulcerative colitis (UC) and ET, currently taking estrogen-containing oral contraceptive pills (OCPs). She presented to the emergency department with rapid weight gain, jaundice, nausea, and diarrhea and was found to have obstructive jaundice and thrombotic burden that extended into the portal, mesenteric, splenic, and hepatic veins. On the second attempt, a successful transjugular intrahepatic portosystemic shunt procedure was performed, resulting in improved venous flow. This case underscores the importance of cautious medication use, especially OCPs, in patients with hypercoagulable states due to JAK2 mutations, for example, the V617F mutation in JAK2. It emphasizes the need for vigilant monitoring, individualized management, and a multidisciplinary approach to mitigate thrombotic complications. Increased awareness and continued research are crucial for optimizing treatment strategies for patients with MPNs and associated genetic mutations.

Dermatology
Lebwohl M, Bukhalo M, **Stein Gold L**, Glick B, Llamas-Velasco M, Sanchez-Rivera S, Pan A, Zhan T, Drogaris L, Douglas K, St John G, Espaillat R, and Bissonnette R. A randomized phase 3b study evaluating the safety and efficacy of risankizumab in adult patients with moderate-to-severe plaque psoriasis with non-pustular palmoplantar involvement. *J Am Acad Dermatol* 2024; Epub ahead of print. PMID: 39208985. Full Text

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BACKGROUND: In plaque psoriasis, palmoplantar areas are more difficult to treat. OBJECTIVE: Evaluate the safety and efficacy of risankizumab (RZB) versus placebo (PBO) for the treatment of palmoplantar psoriasis (PPPsO). METHODS: Patients were randomized to RZB or PBO for 16 weeks followed by RZB through week 52. The primary and secondary endpoints were achievement of palmoplantar Investigator's Global Assessment of "clear" or "almost clear" with ≥2-point reduction from baseline (ppIGA 0/1), achievement of ≥75%, ≥90% and 100% improvement in Palmoplantar Psoriasis Area and Severity Index (PPASI 75, PPASI 90, PPASI 100) and achievement of static Physician Global Assessment of "clear" or "almost clear" with ≥2-point reduction from baseline (sPGA 0/1) at week 16. Safety was based on treatment-emergent adverse events (TEAEs). RESULTS: RZB demonstrated significant efficacy compared to PBO at week 16 in the patients achieving ppIGA 0/1 (33.3% vs 16.1% [P = .006]), PPASI 75 (42.5% vs 14.9% [P < .001]), PPASI 90 (27.6% vs 5.7% [P < 0.001]), sPGA 0/1 (32.2% vs 11.5% [P < .001]) and PPASI 100 (17.2% vs 1.1% [P < .001]). Results improved through week 52 with no new safety signals. LIMITATION: No biologic comparator CONCLUSIONS: RZB demonstrated safety and efficacy in PPPsO.

Dermatology

Lim HW, Passeron T, Goh CL, Kang HY, Ly F, Morita A, Ocampo-Candiani J, Puig S, Schalka S, Wei L, Demessant AL, Le Floc'h C, Kerob D, Dreno B, and Krutmann J. Evaluating the Frequency of Mole Checks by a Dermatologist and Correlated Variables in a Global Survey across 17 Countries: HELIOS Project. *Acta Derm Venereol* 2024; 104:adv40929. PMID: 39177162. Full Text

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Secondary prevention of skin cancer consists in early detection of malignant lesions through patients' mole self-examination and medical examination. The objective of this study was to assess the self-reported frequency of mole examination in a large, representative sample of the adult general population of 17 countries from all continents. Of a total of 17,001 participants, 4.8% had their moles checked by a dermatologist more than once a year, 11.3% once a year, 8.4% every 2-3 years, 12.4% once in a while, 10.3% once in lifetime, and 52.6% of participants had never performed a mole examination. Egypt was the country with the highest prevalence of people who performed a moles check more than once a year (15.9%), followed by Brazil and the USA. A higher frequency of mole checks was associated with sex (man vs woman), higher education, higher income, fair phototype, history of skin cancer, medical insurance, and sun-protective behaviours. Despite recommendations by health providers, it appears that the frequency of mole checks in the general population is still low. It is necessary for dermatologists to keep informing at-risk populations about the importance of moles check, with particular care regarding categories that less frequently adhere to secondary prevention measures.

Dermatology
Maghfour J, Genelin X, Olson J, **Wang A**, **Schultz L**, and Blalock TW. The epidemiology of dermatofibrosarcoma protuberans incidence, metastasis, and death among various population groups: A Surveillance, Epidemiology, and End Results database analysis. *J Am Acad Dermatol* 2024; Epub ahead of print. PMID: 38908718. Full Text

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BACKGROUND: Limited information exists regarding the epidemiology, metastasis, and survival of dermatofibrosarcoma protuberans (DFSP). OBJECTIVE: To measure DFSP incidence and assess metastasis and survival outcomes. METHODS: Incidence rate, overall and DFSP-specific survival outcomes for primary DFSP tumors contained in the Surveillance, Epidemiology, and End Results (SEER) registry were analyzed via quasi-Poisson regression, Cox, and competing risk analyses. RESULTS: DFSP incidence rate was 6.25 (95% CI, 5.93-6.57) cases per million person-years with significantly higher incidence observed among Black individuals than White individuals (8.74 vs 4.53). DFSP with larger tumor size (≥3 cm, odds ratio [OR]: 2.24; 95% CI, 1.62-3.12; P < .001) and tumors located on the head and neck (OR: 4.88; 95% CI, 3.31-7.18; P < .001), and genitalia (OR: 3.16; 95% CI, 1.17-8.52; P = .023) were associated with significantly increased risk of metastasis whereas higher socioeconomic status was associated with significantly decreased risk of metastasis. Larger tumor size (≥3 cm), regardless of location, and age (≥60 years) were associated with significantly worse overall and cancer-specific survival. LIMITATIONS: Retrospective design of SEER. CONCLUSION: DFSP incidence is 2-fold higher among Black than White individuals. The risk of DFSP metastasis is significantly increased with tumor size ≥3 cm and tumors located on head and neck, and genitalia. Larger tumor size (≥ 3 cm), regardless of location, and age (≥60 years) are the most important prognostic indicators of survival.

Dermatology
Rosales Santillan M, **Ozog D**, and Wu W. Using Neuromodulators to Improve Scar Formation, Keloids, Rosacea, and Antiaging. *Dermatol Surg* 2024; 50(9s):S91-s96. PMID: 39196841. Full Text

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BACKGROUND: Botulinum toxin A (BoNT-A) treatment has many uses in dermatology. Its mechanism of action and long-term effects for scar formation, rosacea, and antiaging are still being investigated. OBJECTIVE: To conduct a literature review on BoNT-A to further investigate its use in scar formation, rosacea, and antiaging. METHODS: A literature review was conducted using PubMed on botulinum toxin treatment for scar formation, rosacea, and antiaging. Studies discussing the toxin mechanism of action and treatment algorithm were included. The authors also provided their personal experience in BoNT-A use for these 3 conditions. RESULTS: The mechanism of action of Botulinum toxin A in improving scar formation, rosacea, and antiaging is now better understood. While it is effective in the short term, little is still known about how frequently treatment needs to be repeated and if there are any long-term effects. CONCLUSION: While in vitro studies have supporting evidence on the mechanism of action of BoNT-A on scar formation, rosacea, and antiaging, further studies are needed to identify long-term treatment effects.

Dermatology
Silverberg JI, Wollenberg A, **Stein Gold L**, Del Rosso J, Yosipovitch G, Lio P, Carrascosa JM, Gallo G, Ding Y, Xu Z, Casillas M, Pierce E, Agell H, and Ständer S. Patients with Moderate-to-Severe Atopic

Dermatitis Maintain Stable Response with No or Minimal Fluctuations with 1 Year of Lebrikizumab Treatment. *Dermatol Ther (Heidelb)* 2024; 14(8):2249-2260. PMID: 39123054. Full Text

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INTRODUCTION: Lebrikizumab is a novel monoclonal antibody with established efficacy in patients with moderate-to-severe atopic dermatitis (AD) in multiple Phase 3 trials. One of the ultimate treatment goals for patients with moderate-to-severe AD is to achieve stable disease control without concern for planning future life events. METHODS: In ADvocate1 and ADvocate2, lebrikizumab-treated patients meeting the protocol-defined response criteria at Week 16 were re-randomized 2:2:1 to receive lebrikizumab every 2 weeks (Q2W), lebrikizumab every 4 weeks (Q4W), or placebo Q2W (lebrikizumab withdrawal) for 36 additional weeks. In this post hoc analysis, we evaluated the proportions of patients with no or minimal fluctuations of efficacy during the 36-week maintenance period and plotted individual patient trajectories. We defined no or minimal fluctuations as achieving and maintaining the defined endpoint (≥ 75% improvement in the Eczema Area and Severity Index [EASI 75], ≥ 90% improvement in EASI, Pruritus Numeric Rating Scale [NRS] ≥ 4-point improvement, or Pruritus NRS ≥ 3-point improvement) for ≥ 80% of the study visits. If patients used rescue medication, discontinued treatment, or transferred to the escape arm, data collected at or after the event were imputed as non-response. RESULTS: The proportions of lebrikizumab responders who maintained EASI 75 with no or minimal fluctuations were 70.8% (lebrikizumab Q2W), 71.2% (lebrikizumab Q4W), and 60.0% (lebrikizumab withdrawal). Of the patients with baseline Pruritus NRS ≥ 4 and who achieved ≥ 4-point improvement at Week 16, 66.1% (lebrikizumab Q2W), 62.7% (lebrikizumab Q4W), and 55.2% (lebrikizumab withdrawal) maintained ≥ 4-point Pruritus NRS improvement with no or minimal fluctuations. CONCLUSIONS: Patients who met the response criteria at Week 16 and continued treatment with lebrikizumab Q2W or Q4W demonstrated a stable response with no or minimal fluctuations of efficacy in measures of skin and itch up to Week 52. CLINICAL TRIAL REGISTRATION: NCT04146363 (ADvocate1) and NCT04178967 (ADvocate2). Atopic dermatitis, also known as atopic eczema (or just eczema), is a common skin disease that causes itchy, dry skin. Patients with eczema are often unsure of when disease flares will happen, even while receiving treatment. In two global studies, ADvocate1 and ADvocate2, lebrikizumab improved the signs and symptoms of moderate-to-severe eczema after 16 weeks of treatment. Most of these patients also saw improvement up to 52 weeks. We wanted to know if patients continued to feel better between Week 16 and Week 52. Patients who responded to lebrikizumab after 16 weeks were given lebrikizumab every 2 weeks, lebrikizumab every 4 weeks, or placebo every 2 weeks. We tested how many patients experienced stable response to therapy, which we said was maintaining the same level of improvement on skin signs and itch symptoms for at least 80% of study visits from Week 16 to Week 52. In patients treated with lebrikizumab every 2 weeks or every 4 weeks, we saw that about seven of every ten patients maintained a stable response in skin improvement and about six of every ten patients maintained stable response in itch symptoms. In patients who stopped lebrikizumab therapy, six out of every ten patients maintained a stable skin improvement and more than five of every ten patients maintained a stable improvement in itch symptoms. In ADvocate1 and ADvocate2, most lebrikizumab-treated patients showed a stable response over time on skin and itch with dosing every 2 weeks or every 4 weeks.

Dermatology
Tisack A, and **Mohammad TF**. Drug-Induced Pigmentation: A Review. *Drugs* 2024; Epub ahead of print. PMID: 39085684. Full Text

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Drug-induced pigmentation (DIP) is estimated to account for 20% of all cases of acquired hyperpigmentation. Over 50 agents have been implicated, including antibiotics, antimalarials, antiretrovirals, antipsychotics, prostaglandin analogs, heavy metals, and chemotherapeutic agents. The skin, mucosal surfaces, nails, and hair can all be affected, with the color, distribution, onset, and duration of pigmentation varying between offending agents. Both a thorough physical examination and medication history are necessary to determine the offending agent. In terms of mechanism, DIP occurs most frequently through the accumulation of melanin within the dermis but also by drug accumulation, pigment synthesis, and iron deposition. Photoprotection, including applying a broad-spectrum sunscreen, wearing photoprotective clothing, and seeking shade, plays an important role in the prevention of exacerbation of DIP. Multiple lasers, including the picosecond alexandrite, Q-switched Nd:YAG, Q-switched alexandrite, and Q-switched ruby lasers, have been successful in obtaining clearance of DIP. In this review, we examine the unique characteristics of each of the inciting agents in terms of incidence, clinical presentation, time to onset and resolution, and pathogenesis.

Diagnostic Radiology
Hembroff G, **Klochko C**, **Craig J**, Changarnkothapeecherikkal H, and **Loi RQ**. Improved Automated Quality Control of Skeletal Wrist Radiographs Using Deep Multitask Learning. *J Imaging Inform Med* 2024; Epub ahead of print. PMID: 39187704. Full Text

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Radiographic quality control is an integral component of the radiology workflow. In this study, we developed a convolutional neural network model tailored for automated quality control, specifically designed to detect and classify key attributes of wrist radiographs including projection, laterality (based on the right/left marker), and the presence of hardware and/or casts. The model's primary objective was to ensure the congruence of results with image requisition metadata to pass the quality assessment. Using a dataset of 6283 wrist radiographs from 2591 patients, our multitask-capable deep learning model based on DenseNet 121 architecture achieved high accuracy in classifying projections (F1 Score of 97.23%), detecting casts (F1 Score of 97.70%), and identifying surgical hardware (F1 Score of 92.27%). The model's performance in laterality marker detection was lower (F1 Score of 82.52%), particularly for partially visible or cut-off markers. This paper presents a comprehensive evaluation of our model's performance, highlighting its strengths, limitations, and the challenges encountered during its development and implementation. Furthermore, we outline planned future research directions aimed at refining and expanding the model's capabilities for improved clinical utility and patient care in radiographic quality control.

Diagnostic Radiology
Karns JP, **Nguyen A**, **Wong N**, **True-Malhotra A**, **Smythe D**, and **Vemulapalli R**. A 27-Year-Old Female With JAK2 Mutation: A Case of Budd-Chiari Syndrome Secondary to Prolonged Oral Contraceptive Pill Use. *Cureus* 2024; 16(7):e64858. PMID: 39156349. Full Text

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Individuals with Philadelphia chromosome-negative myeloproliferative neoplasms (MPNs) such as polycythemia vera and essential thrombocythemia (ET) demonstrate an increased thrombotic risk associated with JAK2 mutations. Physicians must take heed when treating these patients, to mitigate this pro-thrombotic state as much as possible. Failure to do so, or exacerbating the state, can lead to dire consequences. We present the case of a 27-year-old female with a history of ulcerative colitis (UC) and ET, currently taking estrogen-containing oral contraceptive pills (OCPs). She presented to the emergency department with rapid weight gain, jaundice, nausea, and diarrhea and was found to have obstructive jaundice and thrombotic burden that extended into the portal, mesenteric, splenic, and hepatic veins. On the second attempt, a successful transjugular intrahepatic portosystemic shunt procedure was performed, resulting in improved venous flow. This case underscores the importance of cautious medication use, especially OCPs, in patients with hypercoagulable states due to JAK2 mutations, for example, the V617F mutation in JAK2. It emphasizes the need for vigilant monitoring, individualized management, and a multidisciplinary approach to mitigate thrombotic complications. Increased awareness and continued research are crucial for optimizing treatment strategies for patients with MPNs and associated genetic mutations.

Emergency Medicine
Gunaga S, **Smythe D**, **Shearer N**, **Hashem M**, and **Al-Hage A**. Man with convulsive syncope. *J Am Coll Emerg Physicians Open* 2024; 5(4):e13249. PMID: 39104917. Full Text

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Department of Emergency Medicine Envision Healthcare Ann Arbor Michigan USA.
Department of Osteopathic Medical Specialties Michigan State University College of Osteopathic Medicine East Lansing Michigan USA.
Department of Internal Medicine Division of Cardiology Henry Ford Wyandotte Hospital Wyandotte Michigan USA.

Emergency Medicine
Jayaprakash N, Sarani N, Nguyen HB, and Cannon C. State of the art of sepsis care for the emergency medicine clinician. *J Am Coll Emerg Physicians Open* 2024; 5(4):e13264. PMID: 39139749. Full Text

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Sepsis impacts 1.7 million Americans annually. It is a life-threatening disruption of organ function because of the body's host response to infection. Sepsis remains a condition frequently encountered in emergency departments (ED) with an estimated 850,000 annual visits affected by sepsis each year in the United States. The pillars of managing sepsis remain timely identification, initiation of antimicrobials while aiming for source control and resuscitation with a goal of restoring tissue perfusion. The focus herein is current evidence and best practice recommendations for state-of-the-art sepsis care that begins in the ED.

Endocrinology and Metabolism
Hood K, Bergenstal RM, **Cushman T**, Gal RL, Raghinaru D, **Kruger D**, Johnson ML, McArthur T, Bradshaw A, Olson BA, Oser SM, Oser TK, Kollman C, Weinstock RS, Beck RW, and Aleppo G. Patient-Reported Outcomes Improve with a Virtual Diabetes Care Model that Includes Continuous Glucose Monitoring. *Telemed J E Health* 2024; Epub ahead of print. PMID: 39166322. Full Text

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Henry Ford Health System, Detroit, Michigan, USA.
JAEB Center for Health Research, Tampa, Florida, USA.
Cecelia Health, New York City, New York, USA.
Lagoon Health, Minneapolis, Minnesota, USA.
University of Colorado School of Medicine, Aurora, Colorado, USA.
SUNY Upstate Medical University, Syracuse, New York, USA.
Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA.

Background: The objective was to examine patient-reported outcomes (PROs) associated with access to a virtual clinic model for diabetes care. Methods: Adults with diabetes (N = 234) received virtual care, including support for continuous glucose monitoring (CGM) over a 6-month study period. Care was led by a Certified Diabetes Care and Education Specialist and focused on optimizing self-management skills and response to glucose values observed on CGM. After 6 months of CGM use and access to diabetes education, participants could opt in to another 6 months of follow-up with access to the virtual care team. Participants completed PRO surveys and had health and glycemic measures collected at baseline, 3, 6, and 12 months. Results: Participants with type 1 diabetes (N = 160) were 44 ± 14 years and had mean baseline HbA1c of 61 mmol/mol (7.7%). Participants with type 2 diabetes (N = 74) were 52 ± 12 years and had mean baseline HbA1c of 66 mmol/mol (8.2%). Compared with baseline levels, at 6 months participants experienced less depression, diabetes distress, and hypoglycemic fears while also experiencing greater satisfaction with glucose monitoring, diabetes technology and specifically with CGM, and confidence for managing hypoglycemic ($p < 0.05$). For participants with type 1 diabetes, more time in the target range for glucose levels (70-180 mg/dL) was associated with less depression, diabetes distress, and hypoglycemic fears. Conclusions: PROs improved for adults with diabetes utilizing virtual diabetes care, including support for CGM use. Paired with the glycemic improvements observed in this virtual clinic study, there were robust benefits on the quality of life of adults with diabetes. ClinicalTrials.gov Identifier: NCT04765358.

Endocrinology and Metabolism

Johnson G, Griffin LV, **Qiu S**, and **Rao SD**. Differences in tissue-level properties as assessed by nano-scratching in patients with and without atypical femur fractures on long-term bisphosphonate therapy: a proof-of-concept pilot study. *JBMR Plus* 2024; 8(9):ziae097. PMID: 39135632. Full Text

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Atypical femur fractures (AFFs) are a well-established complication of long-term bisphosphonate (BP) therapy, but their pathogenesis is not fully understood. Although many patients on long-term BP therapy have severe suppression of bone turnover (SSBT), not all such patients experience AFF, even though SSBT is a major contributor to AFF. Accordingly, we evaluated tissue level properties using nano-scratch testing of trans-iliac bone biopsy specimens in 12 women (6 with and 6 without AFF matched for age and race). Nano-scratch data were analyzed using a mixed-model ANOVA with volume-normalized scratch energy as a function of AFF (Yes or No), region (periosteal or endosteal), and a first-order interaction between region and AFF. Tukey post hoc analyses of the differences of least squared means of scratch energy were performed and reported as significant if $p<.05$. The volume-normalized scratch energy was 10.6% higher in AFF than in non-AFF patients ($p=.003$) and 17.9 % higher in the periosteal than in the endosteal region ($p=.004$). The differences in normalized scratch energy are suggestive of a higher hardness of the bone tissue after long-term BP therapy. The results of this study are consistent with other studies in the literature and demonstrate the efficacy of using Nano-Scratch technique to evaluate bone tissue that exhibits SSBT and AFF. Further studies using nano-scratch may help quantify and elucidate underlying mechanisms for the pathogenesis of AFF.

Endocrinology and Metabolism

Sweeney AT, Hamidi O, Dogra P, **Athimulam S**, Correa R, Blake MA, McKenzie T, Vaidya A, Pacak K, Hamrahian AH, and Bancos I. Clinical Review: The Approach to the Evaluation and Management of Bilateral Adrenal Masses. *Endocr Pract* 2024; Epub ahead of print. PMID: 39103149. Full Text

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Division of Endocrinology, Cleveland Clinic, Cleveland, Ohio.
Division of Abdominal Imaging, Department of Radiology, Massachusetts General Hospital, Boston, Massachusetts.
Division of Endocrine Surgery, Department of Surgery, Mayo Clinic, Rochester, Minnesota.
Center for Adrenal Disorders, Division of Endocrinology, Diabetes, Hypertension, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts.
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Division of Endocrinology, Joint appointment Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, Minnesota.

OBJECTIVE: This white paper provides practical guidance for clinicians encountering bilateral adrenal masses. METHODS: A case-based approach to the evaluation and management of bilateral adrenal masses. Specific clinical scenarios presented here include cases of bilateral adrenal adenomas, hemorrhage, pheochromocytomas, metastatic disease, myelolipomas, as well as primary bilateral macronodular adrenal hyperplasia. RESULTS: Bilateral adrenal masses represent approximately 10% to 20% of incidentally discovered adrenal masses. The general approach to the evaluation and management of bilateral adrenal masses follows the same protocol as the evaluation of unilateral adrenal masses, determined based on the patient's clinical history and examination as well as the imaging characteristics of each lesion, whether the lesions could represent a malignancy, demonstrate hormone excess, or possibly represent a familial syndrome. Furthermore, there are features unique to bilateral adrenal masses that must be considered, including the differential diagnosis, the evaluation, and the management depending on the etiology. Therefore, considerations for the optimal imaging modality, treatment (medical vs surgical therapy), and surveillance are included. These recommendations were developed through careful examination of existing published studies as well as expert clinical opinion consensus. CONCLUSION: The evaluation and management of bilateral adrenal masses require a comprehensive systematic approach which includes the assessment and interpretation of the patient's clinical history, physical examination, dynamic hormone evaluation, and imaging modalities to determine the key radiographic features of each adrenal nodule. In addition, familial syndromes should be considered. Any final treatment options and approaches should always be considered individually.

Family Medicine

Karns JP, **Nguyen A**, **Wong N**, **True-Malhotra A**, **Smythe D**, and **Vemulapalli R**. A 27-Year-Old Female With JAK2 Mutation: A Case of Budd-Chiari Syndrome Secondary to Prolonged Oral Contraceptive Pill Use. *Cureus* 2024; 16(7):e64858. PMID: 39156349. Full Text

Medical School, College of Osteopathic Medicine, Michigan State University, Detroit, USA.
Family Medicine, Henry Ford Health System, Detroit, USA.
Dermatology, Henry Ford Health System, Detroit, USA.
Interventional Radiology, Henry Ford Health System, Detroit, USA.

Individuals with Philadelphia chromosome-negative myeloproliferative neoplasms (MPNs) such as polycythemia vera and essential thrombocythemia (ET) demonstrate an increased thrombotic risk

associated with JAK2 mutations. Physicians must take heed when treating these patients, to mitigate this pro-thrombotic state as much as possible. Failure to do so, or exacerbating the state, can lead to dire consequences. We present the case of a 27-year-old female with a history of ulcerative colitis (UC) and ET, currently taking estrogen-containing oral contraceptive pills (OCPs). She presented to the emergency department with rapid weight gain, jaundice, nausea, and diarrhea and was found to have obstructive jaundice and thrombotic burden that extended into the portal, mesenteric, splenic, and hepatic veins. On the second attempt, a successful transjugular intrahepatic portosystemic shunt procedure was performed, resulting in improved venous flow. This case underscores the importance of cautious medication use, especially OCPs, in patients with hypercoagulable states due to JAK2 mutations, for example, the V617F mutation in JAK2. It emphasizes the need for vigilant monitoring, individualized management, and a multidisciplinary approach to mitigate thrombotic complications. Increased awareness and continued research are crucial for optimizing treatment strategies for patients with MPNs and associated genetic mutations.

Family Medicine

Okon-Umoren A, **Yaphe S**, **Smith A**, **Passalacqua KD**, and **Budzynska K**. Transient Hyperglycemia in a Patient With Type 2 Diabetes After COVID-19 Messenger RNA Vaccination: A Case Report. *Cureus* 2024; 16(7):e63983. PMID: 39105031. Full Text

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The development of new vaccines against the SARS-CoV-2 virus in response to the COVID-19 pandemic represents a milestone in the history of public health. However, due to the rapid development and short duration of these new vaccines, the full spectrum of side effects is not yet known. A 76-year-old man presented to the clinic for follow-up after being discharged from the emergency department for hyperglycemia. His medical history included well-controlled type 2 diabetes for two years, hypertension, and hyperlipidemia. He had recently noticed high home blood glucose readings over 400 mg/dL, and his hemoglobin A1c (mean 90-day glucose level) had increased from 6.5% to 12.6%. Notably, the patient reported having excellent health behaviors, including daily exercise, a closely monitored healthy diet, and regular blood glucose testing. After extensive endocrinology workup, the rapid change in blood glucose was thought to be due to his having recently received the COVID-19 messenger RNA (mRNA) vaccine. He was started on long- and short-acting insulin and a glucagon-like peptide-1 agonist (novel injectable type 2 diabetes medication), with improvement in blood glucose. He was tapered off all medications and remains on metformin 1,000 mg twice daily after one year.Whether the new COVID-19 mRNA vaccines directly incur hyperglycemia within certain groups of patients with diabetes is not known; thus, studies exploring the relationship between vaccine antigen binding and pancreatic function are needed.

Gastroenterology

Buti M, Heo J, Tanaka Y, Andreone P, Atsukawa M, Cabezas J, Chak E, Coffin CS, Fujiwara K, Gankina N, **Gordon SC**, Janczewska E, Komori A, Lampertico P, McPherson S, Morozov V, Plesniak R, Poulin S, Ryan P, Sagalova O, Sheng G, Voloshina N, Xie Q, Yim HJ, Dixon S, Paff M, Felton L, Lee M, Greene T, Lim J, Lakshminarayanan D, McGonagle G, Plein H, Youssef A, Elston R, Kendrick S, and Theodore D. Sequential Peg-IFN after bepirovirsen may reduce post-treatment relapse in chronic hepatitis B. *J Hepatol* 2024; Epub ahead of print. PMID: 39214467. Full Text

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BACKGROUND & AIMS: Bepirovirsen, an antisense oligonucleotide, induces sustained hepatitis B surface antigen (HBsAg) and hepatitis B virus (HBV) DNA below lower limit of quantification (<LLOQ) in a subset of patients. The B-Together study investigated if sequential bepirovirsen and pegylated interferon-α-2a (Peg-IFN) therapy can reduce relapse and improve response rates. METHODS: Phase 2b, multicentre, randomised, open-label trial. Participants on stable nucleos(t)ide analog (NA) therapy were randomised 1:1 to bepirovirsen 300 mg once weekly (plus loading dose on Days 4 and 11) for 24 (Arm 1) or 12 (Arm 2) weeks followed by Peg-IFN 180 mcg once weekly for up to 24 weeks, with up to 36 weeks follow-up. Participants continued NA therapy throughout. PRIMARY OUTCOME: proportion of participants with HBsAg <0.05 IU/mL and HBV DNA <LLOQ for 24 weeks after planned end of Peg-IFN treatment, in the absence of newly initiated antiviral therapy. RESULTS: The intent-to-treat population included 108 participants (Arm 1=55; Arm 2=53). The primary outcome was achieved by 5 (9%) participants in Arm 1 and 8 (15%) in Arm 2. All responders had baseline HBsAg ≤3000 IU/mL. Indirect comparison with the Phase 2b study B-Clear indicates that sequential addition of Peg-IFN may reduce the relapse rates previously observed with bepirovirsen alone. The proportions of participants with adverse events (AEs) and treatment-related AEs in both treatment windows were similar between treatment arms. CONCLUSIONS: Sequential therapy with bepirovirsen followed by Peg-IFN is tolerable and effective in participants with chronic HBV infection on stable NA. This proof-of-concept trial demonstrates a potential strategy to extend responses to bepirovirsen by reducing relapse. FUNDING: GSK (study 209348/NCT04676724). CLINICAL TRIAL NUMBER: NCT04676724.

Gastroenterology

Caines A, **Trudeau S**, and **Gordon SC**. Evaluating the safety and efficacy of seladelpar for adults with primary biliary cholangitis. *Expert Opin Pharmacother* 2024; 25(11):1517-1523. PMID: 39107982.
Request Article

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INTRODUCTION: Seladelpar (MBX-8025) is a once-daily administered highly specific PPAR-δ agonist in Phase 3 and extension trials for use in patients with primary biliary cholangitis (PBC). AREAS COVERED: This review provides background on current treatment options for PBC, and summarizes clinical trial data regarding the safety and effectiveness of seladelpar within the context of these treatments. EXPERT OPINION: Clinical trials results demonstrate the safety and tolerability of seladelpar use for PBC, including in patients with cirrhosis. The primary composite endpoint (ALP <1.67 times ULN, decrease ≥ 15% from baseline, and TB ≤ULN) was met in 61.7% of the patients treated with seladelpar and in 20% receiving placebo ($p < 0.001$). Moreover, pruritus - a cardinal and often intractable symptom of PBC - was improved with seladelpar treatment, as were overall quality of life measurements. Improvements in markers of inflammation were likewise observed. These biochemical and clinical findings therefore represent landmark developments in PBC treatment and offer a therapeutic option for PBC.

Gastroenterology
Chaudhary AJ, **Jamali T**, **Dababneh Y**, **Saleem A**, and **Salgia R**. Late Presentation of Recurrent Solid Pseudopapillary Pancreatic Neoplasm With Liver Metastases During Pregnancy. *ACG Case Rep J* 2024; 11(8):e01418. PMID: 39108614. Full Text

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Our case highlights a rare instance of recurrent metastatic solid pseudopapillary epithelial neoplasms of the pancreas, emerging 8 years after radical pancreatic resection-an extended interval surpassing the reported average. Managing solid pseudopapillary epithelial neoplasm during pregnancy is uniquely challenging, given the increase in the expression of progesterone receptors during the intrapartum period, leading to tumor growth. Although surgical resection remains the primary approach, systemic chemotherapy, radiation therapy, and liver transplant are other considerations. The absence of consensus guidelines for recurrence monitoring emphasizes the need for vigilant, long-term surveillance extending beyond the conventional 5-year mark.

Gastroenterology
Shamaa O, Ahmed A, **Rupp L**, **Trudeau S**, and **Gordon SC**. Beyond the Surface: Unveiling Hidden Hurdles to Primary Biliary Cholangitis Care. *Cureus* 2024; 16(7):e64753. PMID: 39156427. Full Text

Gastroenterology and Hepatology, Henry Ford Health System, Detroit, USA.
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INTRODUCTION: Ursodeoxycholic acid (UDCA) slows disease progression among patients with primary biliary cholangitis (PBC), yet not all patients receive this standard-of-care medication. Our study aims to identify reasons why PBC patients did not receive the recommended UDCA treatment. METHODS: Using medical record data collected by the Fibrotic Liver Disease (FOLD) Consortium for 2006-2016, we identified PBC patients from a single site with no UDCA therapy record. Two independent reviewers used a structured data collection instrument to systematically confirm and record the reasons for the lack of treatment. RESULTS: Among 494 PBC patients (11% men and 13.2% Black patients) with a median follow-up of 5.2 years, 35 (7%) had never received UDCA (16% men and 24% Black patients). Of these, 18 (51%) had laboratory indications of PBC but were not formally diagnosed. Among the remaining 17 patients with recognized PBC, six were never offered UDCA, seven declined treatment, and four remained untreated despite being offered treatment. We did not find a statistically significant association between the lack of PBC diagnosis and treatment and patients' age ($p = 0.139$), gender ($p = 0.222$), race ($p = 0.081$), or insurance coverage ($p = 0.456$), perhaps due to our small sample size. CONCLUSIONS: Multiple factors influencing the lack of evaluation and treatment in PBC patients were identified at the

provider and patient levels. The most common reasons included financial barriers, loss to follow-up, severe decompensated disease at diagnosis, and lack of referral to specialists for further evaluation. Future interventions targeting modifiable provider and patient barriers may improve rates and timeliness of PBC diagnosis and treatment.

Gastroenterology
Toiv A, **Saleh Z**, **Ishak A**, **Alsheik E**, **Venkat D**, Nandi N, and **Zuchelli TE**. Digesting Digital Health: A Study of Appropriateness and Readability of ChatGPT-Generated Gastroenterological Information. *Clin Transl Gastroenterol* 2024; Epub ahead of print. PMID: 39212302. Full Text

Department of Internal Medicine, Henry Ford Hospital, Detroit, MI, USA.
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BACKGROUND AND AIMS: The advent of artificial intelligence-powered large language models capable of generating interactive responses to intricate queries marks a groundbreaking development in how patients access medical information. Our aim was to evaluate the appropriateness and readability of gastroenterological information generated by ChatGPT. METHODS: We analyzed responses generated by ChatGPT to 16 dialogue-based queries assessing symptoms and treatments for gastrointestinal conditions and 13 definition-based queries on prevalent topics in gastroenterology. Three board-certified gastroenterologists evaluated output appropriateness with a 5-point Likert-scale proxy measurement of currency, relevance, accuracy, comprehensiveness, clarity, and urgency/next steps. Outputs with a score of 4 or 5 in all 6 categories were designated as "appropriate." Output readability was assessed with Flesch Reading Ease score, Flesch-Kinkaid Reading Level, and Simple Measure of Gobbledygook scores. RESULTS: ChatGTP responses to 44% of the 16 dialogue-based and 69% of the 13 definition-based questions were deemed appropriate, and the proportion of appropriate responses within the 2 groups of questions was not significantly different (P = .17). Notably, none of ChatGTP's responses to questions related to gastrointestinal emergencies were designated appropriate. The mean readability scores showed that outputs were written at a college-level reading proficiency. CONCLUSION: ChatGPT can produce generally fitting responses to gastroenterological medical queries, but responses were constrained in appropriateness and readability, which limits the current utility of this large language model. Substantial development is essential before these models can be unequivocally endorsed as reliable sources of medical information.

Gastroenterology
Yang D, Mohammed A, Yadlapati R, Wang AY, Jeyalingam T, Draganov PV, Robalino Gonzaga E, Hasan MK, Schlachterman A, Xu MM, Saeed A, Aadam A, Sharaiha RZ, Law R, Wong Kee Song LM, Saumoy M, Pandolfino JE, Nishimura M, Kahaleh M, Hwang JH, Bechara R, Konda VJ, DeWitt JM, Kedia P, Kumta NA, Inayat I, Stavropoulos SN, Kumbhari V, Siddiqui UD, Jawaid S, Andrawes S, Khashab M, Triggs JR, Sharma N, Othman M, Sethi A, Baumann AJ, **Priraka C**, Dunst CM, Wagh MS, Al-Haddad M, Gayawali CP, Kantsevoy S, and Elmunzer BJ. NORTH AMERICAN EXPERT CONSENSUS ON THE POST-PROCEDURAL CARE OF PATIENTS AFTER PER-ORAL ENDOSCOPIC MYOTOMY USING A DELPHI PROCESS. *Clin Gastroenterol Hepatol* 2024; Epub ahead of print. PMID: 39214390. Full Text

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BACKGROUND AND AIMS: There is significant variability in the immediate post-operative and long-term management of patients undergoing per-oral endoscopic myotomy (POEM), largely stemming from the lack of high-quality evidence. We aimed to establish a consensus on several important questions on the after care of post-POEM patients through a modified Delphi process. METHODS: A steering committee developed an initial questionnaire consisting of 5 domains (33 statements): post-POEM admission/discharge, indication for immediate post-POEM esophagram, peri-procedural medications and diet resumption, clinic follow-up recommendations, and post-POEM reflux surveillance and management. A total of 34 experts participated in the 2 rounds of the Delphi process, with quantitative and qualitative data analyzed for each round to achieve consensus. RESULTS: A total of 23 statements achieved high degree of consensus. Overall, the expert panel agreed on the following: (1) same-day discharge after POEM can be considered in select patients, (2) a single dose of prophylactic antibiotics may be as effective as a short course, (3) a modified diet can be advanced as tolerated, (4) all patients should be followed in clinic and undergo objective testing for surveillance and management of reflux. Consensus could not be achieved on the indication of post-POEM esophagram to evaluate for leak. CONCLUSIONS: The results of this Delphi process established expert agreement on several important issues and provides a practical guidance on key aspects in the care of patients following POEM.

Gastroenterology
Zhang B, Magnaye KM, Stryker E, Moltzau-Anderson J, Porsche CE, Hertz S, McCauley KE, Smith BJ, Zydek M, Pollard KS, Ma A, **El-Nachef N**, and Lynch SV. Sustained mucosal colonization and fecal metabolic dysfunction by Bacteroides associates with fecal microbial transplant failure in ulcerative colitis patients. *Sci Rep* 2024; 14(1):18558. PMID: 39122767. Full Text

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Fecal microbial transplantation (FMT) offers promise for treating ulcerative colitis (UC), though the mechanisms underlying treatment failure are unknown. This study harnessed longitudinally collected colonic biopsies (n = 38) and fecal samples (n = 179) from 19 adults with mild-to-moderate UC undergoing serial FMT in which antimicrobial pre-treatment and delivery mode (capsules versus enema) were assessed for clinical response (≥ 3 points decrease from the pre-treatment Mayo score). Colonic biopsies underwent dual RNA-Seq; fecal samples underwent parallel 16S rRNA and shotgun metagenomic sequencing as well as untargeted metabolomic analyses. Pre-FMT, the colonic mucosa of non-responsive (NR) patients harbored an increased burden of bacteria, including Bacteroides, that expressed more antimicrobial resistance genes compared to responsive (R) patients. NR patients also exhibited muted mucosal expression of innate immune antimicrobial response genes. Post-FMT, NR and R fecal microbiomes and metabolomes exhibited significant divergence. NR metabolomes had elevated concentrations of immunostimulatory compounds including sphingomyelins, lysophospholipids and taurine. NR fecal microbiomes were enriched for Bacteroides fragilis and Bacteroides salyersiae strains that encoded genes capable of taurine production. These findings suggest that both effective mucosal microbial clearance and reintroduction of bacteria that reshape luminal metabolism associate with FMT success and that persistent mucosal and fecal colonization by antimicrobial-resistant Bacteroides species may contribute to FMT failure.

Global Health Initiative

Lakew M, Tadesse B, **Srinivasan S**, Aschalew M, Andarge B, Kebede D, Etifu A, Alemu T, Yalew B, Benti T, Olani A, Abera S, Bedada W, Fromsa A, Mekonnen GA, Almaw G, Ameni G, Ashenafi H, Gumi B, Bakker D, and Kapur V. Assessing the feasibility of test-and-cull and test-and-segregation approaches for the control of high-prevalence bovine tuberculosis in Ethiopian intensive dairy farms. *Sci Rep* 2024; 14(1):14298. PMID: 38906922. Full Text

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Bovine tuberculosis (bTB) is endemic and has a substantial impact on the livestock sector in Ethiopia and other low and middle-income countries (LMICs). With a national emphasis on dairy farm intensification to boost milk production and spur economic growth, the incidence of bTB is anticipated to rise. However, Ethiopia, like other LMICs, lacks a comprehensive national bTB control strategy due to the economic and social infeasibility of traditional test-and-cull (TC) approaches. To inform the development of such a strategy, we evaluated the effectiveness and feasibility of TC and test-and-segregation (TSg) strategies for bTB control on Ethiopian dairy farms. A TC approach was used at Farm A [N = 62; comparative cervical test (CCT) > 4 mm, starting prevalence 11.3%] while TSg was implemented at Farm B (N = 45; CCT > 4 mm, prevalence 22.2%), with testing intervals of 2-4 months. Both strategies achieved a reduction in bTB prevalence to 0%, requiring seven rounds of TC over 18 months at Farm A, and five rounds of TSg over 12 months at Farm B's negative herd. The results show that adopting more sensitive thresholds [CCT > 0 mm or single cervical test (SCT) > 2 mm] during later rounds was pivotal in identifying and managing previously undetected infections, emphasizing the critical need for optimized diagnostic thresholds. Cost analysis revealed that TC was approximately twice as expensive as TSg, primarily due to testing, labor, and cow losses in TC, versus construction of new facilities and additional labor for TSg. This underscores the economic and logistical challenges of bTB management in resource-limited settings. Taken together, our study highlights an urgent need for the exploration of alternative approaches including TSg and or vaccination to mitigate within herd transmission and enable implementation of bTB control in regions where TC is not feasible.

Graduate Medical Education

Gunaga S, **Smythe D**, **Shearer N**, **Hashem M**, and **Al-Hage A**. Man with convulsive syncope. *J Am Coll Emerg Physicians Open* 2024; 5(4):e13249. PMID: 39104917. Full Text

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Graduate Medical Education

Okon-Umoren A, **Yaphe S**, **Smith A**, **Passalacqua KD**, and **Budzynska K**. Transient Hyperglycemia in a Patient With Type 2 Diabetes After COVID-19 Messenger RNA Vaccination: A Case Report. *Cureus* 2024; 16(7):e63983. PMID: 39105031. Full Text

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The development of new vaccines against the SARS-CoV-2 virus in response to the COVID-19 pandemic represents a milestone in the history of public health. However, due to the rapid development and short duration of these new vaccines, the full spectrum of side effects is not yet known. A 76-year-old man presented to the clinic for follow-up after being discharged from the emergency department for hyperglycemia. His medical history included well-controlled type 2 diabetes for two years, hypertension, and hyperlipidemia. He had recently noticed high home blood glucose readings over 400 mg/dL, and his hemoglobin A1c (mean 90-day glucose level) had increased from 6.5% to 12.6%. Notably, the patient reported having excellent health behaviors, including daily exercise, a closely monitored healthy diet, and regular blood glucose testing. After extensive endocrinology workup, the rapid change in blood glucose was thought to be due to his having recently received the COVID-19 messenger RNA (mRNA) vaccine. He was started on long- and short-acting insulin and a glucagon-like peptide-1 agonist (novel injectable type 2 diabetes medication), with improvement in blood glucose. He was tapered off all medications and remains on metformin 1,000 mg twice daily after one year.Whether the new COVID-19 mRNA vaccines

directly incur hyperglycemia within certain groups of patients with diabetes is not known; thus, studies exploring the relationship between vaccine antigen binding and pancreatic function are needed.

Hematology-Oncology

Dowlati A, Hummel HD, Champiat S, Olmedo ME, Boyer M, He K, Steeghs N, Izumi H, Johnson ML, Yoshida T, Bouchaab H, Borghaei H, Felip E, Jost PJ, **Gadgeel S**, Chen X, Yu Y, Martinez P, Parkes A, and Paz-Ares L. Sustained Clinical Benefit and Intracranial Activity of Tarlatamab in Previously Treated Small Cell Lung Cancer: DeLLphi-300 Trial Update. *J Clin Oncol* 2024; Epub ahead of print. PMID: 39208379. Full Text

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Clinical trials frequently include multiple end points that mature at different times. The initial report, typically based on the primary end point, may be published when key planned co-primary or secondary analyses are not yet available. Clinical Trial Updates provide an opportunity to disseminate additional results from studies, published in JCO or elsewhere, for which the primary end point has already been reported.Tarlatamab, a bispecific T-cell engager immunotherapy targeting delta-like ligand 3, has shown durable anticancer activity and manageable safety in previously treated small cell lung cancer (SCLC) in DeLLphi-300 phase I and DeLLphi-301 phase II trials. Here, we report extended follow-up of DeLLphi-300 (median follow-up, 12.1 months [range, 0.2-34.3]) in fully enrolled cohorts treated with tarlatamab ≥10 mg dose administered once every two weeks, once every three weeks, or once on day 1 and once on day 8 of a 21-day cycle (N = 152). Overall, the objective response rate (ORR) was 25.0%; the median duration of response (mDOR) was 11.2 months (95% CI, 6.6 to 22.3), and the median overall survival (mOS) was 17.5 months (95% CI, 11.4 to not estimable [NE]). Among 17 patients receiving 10 mg tarlatamab once every two weeks, the ORR was 35.3%, the mDOR was 14.9 months (95% CI, 3.0 to NE), the mOS was 20.3 months (95% CI, 5.1 to NE), and 29.4% had sustained disease control with time on treatment ≥52 weeks. No new safety signals were identified. In modified Response Assessment in Neuro-Oncology Brain Metastases analyses, CNS tumor shrinkage of ≥30% was observed in 62.5% of patients (10 of 16) who had a baseline CNS lesion of ≥10 mm, including in a subset of patients with tumor shrinkage long after previous brain radiotherapy. In DeLLphi-300 extended follow-up, tarlatamab demonstrated unprecedented survival and potential findings of intracranial activity in previously treated SCLC.

Hematology-Oncology

Graff JN, Hoimes CJ, Gerritsen WR, Vaishampayan UN, Elliott T, **Hwang C**, Ten Tije AJ, Omlin A, McDermott RS, Fradet Y, Tagawa ST, Kilari D, Ferrario C, Uemura H, Jones RJ, Fukasawa S, Peer A, Niu C, Poehlein CH, Qiu P, Suttner L, de Wit R, Schloss C, de Bono JS, and Antonarakis ES. Pembrolizumab plus enzalutamide for metastatic castration-resistant prostate cancer progressing on enzalutamide: cohorts 4 and 5 of the phase 2 KEYNOTE-199 study. *Prostate Cancer Prostatic Dis* 2024; Epub ahead of print. PMID: 39134652. Request Article

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BACKGROUND: KEYNOTE-199 (NCT02787005) is a multicohort phase 2 study evaluating pembrolizumab in patients with metastatic castration-resistant prostate cancer (mCRPC). Results from cohorts 4 (C4) and 5 (C5) are presented. METHODS: Eligible patients had not received chemotherapy for mCRPC and had responded to enzalutamide prior to developing resistance as defined by Prostate Cancer Clinical Trials Working Group 3 guidelines. Patients with RECIST-measurable disease were enrolled in C4, and patients with bone-only or bone-predominant disease were enrolled in C5. All patients received pembrolizumab 200 mg every 3 weeks for ≤35 cycles with ongoing enzalutamide until progression, unacceptable toxicity, or withdrawal. The primary end point was objective response rate (ORR) per RECIST v1.1 by blinded independent central review in C4. Secondary end points included disease control rate (DCR), overall survival, and safety in each cohort and both cohorts combined. RESULTS: A total of 126 patients were treated (C4, n = 81; C5, n = 45). Median age was 72 years (range 43-92), and 87.3% had received ≥6 months of enzalutamide prior to study entry. Confirmed ORR was 12.3% (95% CI 6.1-21.5%) for C4. Median duration of response in C4 was 8.1 months (range, 2.5+ to 15.2), and 5 of these patients experienced an objective response lasting ≥6 months. DCR was 53.1% (95% CI 41.7-64.3%) in C4 and 51.1% (95% CI 35.8-66.3%) in C5. Median overall survival was 17.6 months (95% CI 14.0-22.6) in C4 and 20.8 months (95% CI 14.1-28.9) in C5. Grade ≥3 treatment-related adverse events occurred in 35 patients (27.8%); 2 patients in C4 died from immune-related adverse events (myasthenic syndrome and Guillain-Barré syndrome). CONCLUSIONS: The addition of pembrolizumab to ongoing enzalutamide treatment in patients with mCRPC that progressed on enzalutamide after initial response demonstrated modest antitumor activity with a manageable safety profile. CLINICAL TRIAL REGISTRY AND ID: ClinicalTrials.gov, NCT02787005.

Hematology-Oncology

Graham LS, Henderson NC, Kellezi O, **Hwang C**, Barata PC, Bilen MA, Kilari D, Pierro M, Thapa B, Tripathi A, Mo G, Labriola M, Park JJ, Rothstein S, Garje R, Koshkin VS, Patel VG, Dorff T, Armstrong AJ, McKay RR, Alva A, and Schweizer MT. DNA-Damaging Therapies in Patients With Prostate Cancer and Pathogenic Alterations in Homologous Recombination Repair Genes. *JCO Precis Oncol* 2024; 8:e2400014. PMID: 39178368. Request Article

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PURPOSE: Outcomes data for DNA-damaging therapeutics for men with prostate cancer (PC) and non-BRCA1/2 homologous recombination repair (HRR) mutations are limited. We evaluated outcomes by HRR alteration in men with PC treated with poly(ADP-ribose)polymerase inhibitors (PARPi) and/or platinum chemotherapy. METHODS: Retrospective data from the PROMISE consortium were used. Clinical outcomes differences were assessed between patients with BRCA1/2 mutations (cohort A) and those with HRR mutations without direct BRCA complex interaction (cohort B: ATM, CDK12, CHEK1, CHEK2, and FANCL). Outcomes in patients with HRR mutations with direct BRCA complex interaction were also explored (cohort C: RAD51B/C/D, RAD54L2, BARD1, GEN1, PALB2, FANCA, and BRIP1). RESULTS: One hundred and forty-six patients received PARPi (cohort A: 94, cohort B: 45, cohort C: 7) and 104 received platinum chemotherapy (cohort A: 48, cohort B: 44, cohort C: 10). PSA50 response rate to PARPi was higher in cohort A (61%) than cohort B (5%), P < .001. Median clinical/radiographic progression-free survival (crPFS) with PARPi in cohort A was significantly longer than in cohort B: 15.9 versus 8.7 months, P = .005. PSA50 response rate to platinum therapy was higher in cohort A (62%) than in cohort B (32%), P = .024, although crPFS was not significantly different. PSA50 response rate to PARPi and platinum was 40% and 32%, respectively, in cohort C. In multivariable analysis, cohort A had significantly improved overall survival and crPFS compared with cohort B with PARPi but not platinum chemotherapy. CONCLUSION: Patients with BRCA1/2-mutated PC had significantly improved outcomes to PARPi but not platinum chemotherapy compared with those with HRR mutations without direct BRCA complex interaction.

Hematology-Oncology

Philip PA, Sahai V, Bahary N, Mahipal A, Kasi A, Rocha Lima CMS, Alistar AT, Oberstein PE, Golan T, Metges JP, Lacy J, Fountzilas C, Lopez CD, Ducreux M, Hammel P, Salem M, Bajor D, Benson AB, Luther S, Pardee T, and Van Cutsem E. Devimistat (CPI-613) With Modified Fluorouarcil, Oxaliplatin, Irinotecan, and Leucovorin (FFX) Versus FFX for Patients With Metastatic Adenocarcinoma of the Pancreas: The Phase III AVENGER 500 Study. *J Clin Oncol* 2024; Epub ahead of print. PMID: 39088774. Full Text

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PURPOSE: Metastatic pancreatic adenocarcinoma (mPC) remains a difficult-to-treat disease. Fluorouarcil, oxaliplatin, irinotecan, and leucovorin (FFX) is a standard first-line therapy for mPC for patients with a favorable performance status and good organ function. In a phase I study, devimistat (CPI-613) in combination with modified FFX (mFFX) was deemed safe and exhibited promising efficacy in mPC. METHODS: The AVENGER 500 trial (ClinicalTrials.gov identifier: NCT03504423) is a global, randomized phase III trial conducted at 74 sites across six countries to investigate the efficacy and safety of devimistat in combination with mFFX (experimental arm) compared with standard-dose FFX (control arm) in treatment-naïve patients with mPC. Treatment, administered in once-every-2-weeks cycles until disease progression or intolerable toxicity, included intravenous devimistat at 500 mg/m(2) total per day on days 1 and 3 in the experimental arm. The primary end point of the study was overall survival (OS). RESULTS: Five hundred and twenty-eight patients were randomly assigned (266 in the experimental arm and 262 in the control arm). The median OS was 11.10 months for devimistat plus mFFX versus 11.73 months for FFX (hazard ratio [HR], 0.95 [95% CI, 0.77 to 1.18]; P = .655) and median progression-free survival was 7.8 months versus 8.0 months, respectively (HR, 0.99 [95% CI, 0.76 to 1.29]; P = .94). Grade ≥3 treatment-emergent adverse events with >10% frequency in the devimistat plus mFFX arm versus the FFX arm were neutropenia (29.0% v 34.5%), diarrhea (11.2% v 19.6%), hypokalemia (13.1% v 14.9%), anemia (13.9% v 13.6%), thrombocytopenia (11.6% v 13.6%), and fatigue (10.8% v 11.5%), respectively. CONCLUSION: Devimistat in combination with mFFX did not improve long- and short-term mPC patient outcomes compared with standard FFX. There were no new toxicity signals with the addition of devimistat.

Hospital Medicine

Ardeshna N, Feldeisen T, Kong X, Haymart B, **Kaatz S**, Ali M, Barnes GD, and Froehlich JB. Comparing DOAC and warfarin outcomes in an obese population using the 'real-world' Michigan Anticoagulation Quality Improvement Initiative (MAQI(2)) registry. *Vasc Med* 2024; Epub ahead of print. PMID: 39177515.
Full Text

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INTRODUCTION: Direct oral anticoagulants (DOACs) have overtaken warfarin in the treatment of nonvalvular atrial fibrillation (AF) and venous thromboembolism (VTE). Limited data explore the safety of DOACs in obesity. METHODS: This multicenter retrospective study between June 2015 and September 2019 uses the Michigan Anticoagulation Quality Improvement Initiative (MAQI(2)) registry to compare DOACs and warfarin across weight classes (not obese: body mass index (BMI) $\geqslant$ 18.5 and < 30; obese: BMI $\geqslant$ 30 and < 40; severely obese: BMI $\geqslant$ 40). Primary outcomes include major, clinically relevant nonmajor (CRNM), and minor bleeding events per 100 patient-years. Secondary outcomes include stroke, recurrent VTE, and all-cause mortality. RESULTS: DOACs were prescribed to 49% of the 4089 patients with AF and 46% of the 3162 patients with VTE. Compared to patients treated with warfarin, those treated with DOACs had a higher estimated glomerular filtration rate across BMI categories regardless of indication. In the AF population, severely obese patients treated with DOACs had more major (3.4 vs 1.8, p = 0.004), CRNM (8.6 vs 5.9, p = 0.019), and minor bleeding (11.4 vs 9.9, p = 0.001). There was no difference in stroke or all-cause mortality. In the VTE population, both CRNM (7.5 vs 6.7, p = 0.042) and minor bleeding (19.3 vs 10.5, p < 0.001) events occurred at higher rates in patients treated with DOACs. There was no difference in recurrent pulmonary embolism, stroke, or all-cause mortality. CONCLUSION: There is a higher rate of bleeding in severely obese patients with VTE and AF treated with DOACs compared to warfarin, without a difference in secondary outcomes. Further studies to compare the anticoagulant classes and understand bleeding drivers in this population are needed.

Hypertension and Vascular Research
Zahoor I, **Pan G**, **Cerghet M**, Elbayoumi T, Mao-Draayer Y, **Giri S**, and **Palaniyandi SS**. Current understanding of cardiovascular autonomic dysfunction in multiple sclerosis. *Heliyon* 2024; 10(15):e35753. PMID: 39170118. Full Text

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Autoimmune diseases, including multiple sclerosis (MS), are proven to increase the likelihood of developing cardiovascular disease (CVD) due to a robust systemic immune response and inflammation. MS can lead to cardiovascular abnormalities that are related to autonomic nervous system dysfunction by causing inflammatory lesions surrounding tracts of the autonomic nervous system in the brain and spinal cord. CVD in MS patients can affect an already damaged brain, thus worsening the disease course by causing brain atrophy and white matter disease. Currently, the true prevalence of cardiovascular dysfunction and associated death rates in patients with MS are mostly unknown and inconsistent. Treating vascular risk factors is recommended to improve the management of this disease. This review provides an updated summary of CVD prevalence in patients with MS, emphasizing the need for more preclinical studies using animal models to understand the pathogenesis of MS better. However, no distinct studies exist that explore the temporal effects and etiopathogenesis of immune/inflammatory cells on cardiac damage and dysfunction associated with MS, particularly in the cardiac myocardium. To this end, a thorough investigation into the clinical presentation and underlying mechanisms of CVD must be conducted in patients with MS and preclinical animal models. Additionally, clinicians should monitor for cardiovascular complications while prescribing medications to MS patients, as some MS drugs cause severe CVD.

Infectious Diseases

Ma KC, Surie D, Lauring AS, Martin ET, Leis AM, Papalambros L, Gaglani M, Columbus C, Gottlieb RL, Ghamande S, Peltan ID, Brown SM, Ginde AA, Mohr NM, Gibbs KW, Hager DN, Saeed S, Prekker ME, Gong MN, Mohamed A, Johnson NJ, Srinivasan V, Steingrub JS, Khan A, Hough CL, Duggal A, Wilson JG, Qadir N, Chang SY, Mallow C, Kwon JH, Parikh B, Exline MC, **Vaughn IA**, **Ramesh M**, Safdar B, Mosier J, Harris ES, Shapiro NI, Felzer J, Zhu Y, Grijalva CG, Halasa N, Chappell JD, Womack KN, Rhoads JP, Baughman A, Swan SA, Johnson CA, Rice TW, Casey JD, Blair PW, Han JH, Ellington S, Lewis NM, Thornburg N, Paden CR, Atherton LJ, Self WH, Dawood FS, and DeCuir J. Effectiveness of Updated 2023-2024 (Monovalent XBB.1.5) COVID-19 Vaccination Against SARS-CoV-2 Omicron XBB and BA.2.86/JN.1 Lineage Hospitalization and a Comparison of Clinical Severity-IVY Network, 26 Hospitals, October 18, 2023-March 9, 2024. *Clin Infect Dis* 2024; Epub ahead of print. PMID: 39107255.
Full Text

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Baylor Scott & White, Temple, Texas, USA.
Intermountain Medical Center, Murray, Utah, USA.
University of Colorado, Aurora, Colorado, USA.
University of Iowa, Iowa City, Iowa, USA.
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Johns Hopkins University, Baltimore, Maryland, USA.
Hennepin County Medical Center, Minneapolis, Minnesota, USA.
Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York, USA.
University of Washington, Seattle, Washington.
Baystate Medical Center, Springfield, Massachusetts.
Oregon Health & Science University, Portland, Oregon, USA.
Cleveland Clinic, Cleveland, Ohio, USA.
Stanford University, Stanford, California, USA.
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University of Miami, Miami, Florida, USA.
Washington University, St. Louis, Missouri, USA.
The Ohio State Medical Center, Columbus, Ohio, USA.
Henry Ford Health, Detroit, Michigan, USA.
Yale University, New Haven, Connecticut, USA.
University of Arizona, Tuscon, Arizona, USA.
University of Utah, Salt Lake City, Utah, USA.
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BACKGROUND: Assessing variant-specific COVID-19 vaccine effectiveness (VE) and severity can inform public health risk assessments and decisions about vaccine composition. BA.2.86 and its descendants, including JN.1 (referred to collectively as "JN lineages"), emerged in late 2023 and exhibited substantial divergence from co-circulating XBB lineages. METHODS: We analyzed patients hospitalized with COVID-19-like illness at 26 hospitals in 20 U.S. states admitted October 18, 2023-March 9, 2024. Using a test-negative, case-control design, we estimated effectiveness of an updated 2023-2024 (Monovalent XBB.1.5) COVID-19 vaccine dose against sequence-confirmed XBB and JN lineage hospitalization using logistic regression. Odds of severe outcomes, including intensive care unit (ICU) admission and invasive mechanical ventilation (IMV) or death, were compared for JN versus XBB lineage hospitalizations using logistic regression. RESULTS: 585 case-patients with XBB lineages, 397 case-patients with JN lineages, and 4,580 control-patients were included. VE in the first 7-89 days after receipt of an updated dose was 54.2% (95% CI = 36.1%-67.1%) against XBB lineage hospitalization and 32.7% (95% CI = 1.9%-53.8%) against JN lineage hospitalization. Odds of ICU admission (adjusted odds ratio [aOR] 0.80; 95% CI = 0.46-1.38) and IMV or death (aOR 0.69; 95% CI = 0.34-1.40) were not significantly different among JN compared to XBB lineage hospitalizations. CONCLUSIONS: Updated 2023-2024 COVID-19 vaccination

provided protection against both XBB and JN lineage hospitalization, but protection against the latter may be attenuated by immune escape. Clinical severity of JN lineage hospitalizations was not higher relative to XBB.

Internal Medicine
Ali S, Ali MJ, **Chaudhary AJ**, Rehman SU, and Maqsood MA. The Broad Spectrum of Gallbladder Paraneoplastic Syndromes. *Gastro Hep Adv* 2024; 3(5):565-572. PMID: 39165415. Full Text

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Gallbladder carcinoma (GBC) is a rare gastrointestinal tumor with a reported incidence of 1 in 100,000 in the United States. GBC may present with subtle signs and symptoms that can be missed on routine examination and/or confused with other conditions. Unfortunately, its subtle presentation frequently leads to late diagnosis and, thus, a poor prognosis. Several paraneoplastic syndromes have been associated with GBC. Despite their strong associations with neoplastic disease, the precise pathophysiologic mechanisms underlying the development of these syndromes remain poorly understood. Given the vague nature of their initial signs and symptoms, these syndromes are frequently diagnosed as independent entities and only later associated with occult malignancies that may have already metastasized to other organs. Physicians need to be aware of the signs and symptoms of these paraneoplastic syndromes and include an underlying malignancy as part of the differential diagnosis. This review provides a detailed discussion of the paraneoplastic syndromes associated with GBC.

Internal Medicine
Chaudhary AJ, **Jamali T**, **Dababneh Y**, **Saleem A**, and **Salgia R**. Late Presentation of Recurrent Solid Pseudopapillary Pancreatic Neoplasm With Liver Metastases During Pregnancy. *ACG Case Rep J* 2024; 11(8):e01418. PMID: 39108614. Full Text

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Our case highlights a rare instance of recurrent metastatic solid pseudopapillary epithelial neoplasms of the pancreas, emerging 8 years after radical pancreatic resection-an extended interval surpassing the reported average. Managing solid pseudopapillary epithelial neoplasm during pregnancy is uniquely challenging, given the increase in the expression of progesterone receptors during the intrapartum period, leading to tumor growth. Although surgical resection remains the primary approach, systemic chemotherapy, radiation therapy, and liver transplant are other considerations. The absence of consensus guidelines for recurrence monitoring emphasizes the need for vigilant, long-term surveillance extending beyond the conventional 5-year mark.

Internal Medicine
Fadel RA, **Almajed MR**, **Parsons A**, **Kalsi J**, **Shadid M**, **Maki M**, **Alqarqaz M**, **Aronow H**, **Cowger J**, **Fuller B**, **Frisoli T**, **Grafton G**, **Kim H**, **Jones C**, **Koenig G**, Khandelwal A, **Nemeh H**, **O'Neill B**, **Tanaka D**, **Williams C**, **Villablanca P**, **O'Neill W**, **Alaswad K**, and **Basir MB**. Feasibility and Outcomes of a Cardiovascular Medicine Inclusive Extracorporeal Membrane Oxygenation (ECMO) Service. *J Soc Cardiovasc Angiogr Interv* 2024; 3(6):101359. PMID: 39132589. Full Text

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BACKGROUND: There has been a significant increase in the utilization of venoarterial extracorporeal membrane oxygenation (VA-ECMO) in recent years. Cardiothoracic surgery teams have historically led VA-ECMO care teams, with little data available on alternative care models. METHODS: We performed a retrospective review of a cardiovascular medicine inclusive VA-ECMO service, analyzing patients treated with peripheral VA-ECMO at a large quaternary care center from 2018 to 2022. The primary outcome was death while on VA-ECMO or within 24 hours of decannulation. Univariate and multivariate analyses were used to identify predictors of the primary outcome. RESULTS: Two hundred forty-four patients were included in the analysis (median age 61 years; 28.7% female), of whom 91.8% were cannulated by interventional cardiologists, and 84.4% were managed by a cardiology service comprised of interventional cardiologists, cardiac intensivists or advanced heart failure cardiologists. Indications for VA-ECMO included acute myocardial infarction (34.8%), decompensated heart failure (30.3%), and refractory cardiac arrest (10.2%). VA-ECMO was utilized during cardiopulmonary resuscitation in 26.6% of cases, 48% of which were peri-procedural arrest. Of the patients, 46% survived to decannulation, the majority of whom were decannulated percutaneously in the cardiac catheterization laboratory. There was no difference in survival following cannulation by a cardiac surgeon vs interventional cardiologist (50% vs 45%; P = .90). Complications included arterial injury (3.7%), compartment syndrome (4.1%), cannulation site infection (1.2%), stroke (14.8%), acute kidney injury (52.5%), access site bleeding (16%) and need for blood transfusion (83.2%). Elevated baseline lactate (odds ratio [OR], 1.13 per unit increase) and sequential organ failure assessment score (OR, 1.27 per unit increase) were independently associated with the primary outcome. Conversely, an elevated baseline survival after VA ECMO score (OR, 0.92 per unit increase) and 8-hour serum lactate clearance (OR, 0.98 per % increase) were independently associated with survival. CONCLUSIONS: The use of a cardiovascular medicine inclusive ECMO service is feasible and may be practical in select centers as indications for VA-ECMO expand.

Internal Medicine
Farooq U, Tarar ZI, **Chaudhary AJ**, Alayli AE, Kamal F, Niu C, and Qureshi K. Infection-Related Readmissions Are Rising among Patients with Hepatorenal Syndrome: A Nationwide Analysis. *Livers* 2024; 4(2):268-274. PMID: Not assigned. Full Text

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Internal Medicine
Toiv A, **Saleh Z**, **Ishak A**, **Alsheik E**, **Venkat D**, Nandi N, and **Zuchelli TE**. Digesting Digital Health: A Study of Appropriateness and Readability of ChatGPT-Generated Gastroenterological Information. *Clin Transl Gastroenterol* 2024; Epub ahead of print. PMID: 39212302. Full Text

Department of Internal Medicine, Henry Ford Hospital, Detroit, MI, USA.
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BACKGROUND AND AIMS: The advent of artificial intelligence-powered large language models capable of generating interactive responses to intricate queries marks a groundbreaking development in how patients access medical information. Our aim was to evaluate the appropriateness and readability of gastroenterological information generated by ChatGPT. METHODS: We analyzed responses generated by ChatGPT to 16 dialogue-based queries assessing symptoms and treatments for gastrointestinal conditions and 13 definition-based queries on prevalent topics in gastroenterology. Three board-certified gastroenterologists evaluated output appropriateness with a 5-point Likert-scale proxy measurement of currency, relevance, accuracy, comprehensiveness, clarity, and urgency/next steps. Outputs with a score of 4 or 5 in all 6 categories were designated as "appropriate." Output readability was assessed with Flesch Reading Ease score, Flesch-Kinkaid Reading Level, and Simple Measure of Gobbledygook

scores. RESULTS: ChatGTP responses to 44% of the 16 dialogue-based and 69% of the 13 definition-based questions were deemed appropriate, and the proportion of appropriate responses within the 2 groups of questions was not significantly different (P = .17). Notably, none of ChatGTP's responses to questions related to gastrointestinal emergencies were designated appropriate. The mean readability scores showed that outputs were written at a college-level reading proficiency. CONCLUSION: ChatGPT can produce generally fitting responses to gastroenterological medical queries, but responses were constrained in appropriateness and readability, which limits the current utility of this large language model. Substantial development is essential before these models can be unequivocally endorsed as reliable sources of medical information.

Nephrology

Besarab A, **Frinak S**, Margassery S, and Wish JB. Hemodialysis Vascular Access: A Historical Perspective on Access Promotion, Barriers, and Lessons for the Future. *Kidney Med* 2024; 6(9):100871. PMID: 39220002. Full Text

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This review describes the history of vascular access for hemodialysis (HD) over the past 8 decades. Reliable, repeatable vascular access for outpatient HD began in the 1960s with the Quinton-Scribner shunt. This was followed by the autologous Brecia-Cimino radial-cephalic arteriovenous fistula (AVF), which dominated HD vascular access for the next 20 years. Delayed referral and the requirement of 1.5-3 months for AVF maturation led to the development of and increasing dependence on synthetic arteriovenous grafts (AVGs) and tunneled central venous catheters, both of which have higher thrombosis and infection risks than AVFs. The use of AVGs and tunneled central venous catheters increased progressively to the point that, in 1997, the first evidence-based clinical practice guidelines for HD vascular access recommended that they only be used if a functioning AVF could not be established. Efforts to promote AVF use in the United States during the past 2 decades doubled their prevalence; however, recent practice guidelines acknowledge that not all patients receiving HD are ideally suited for an AVF. Nonetheless, improved referral for AVF placement before dialysis initiation and improved conversion of failing AVGs to AVFs may increase AVF use among patients in whom they are appropriate.

Nephrology

Halloran PF, Madill-Thomsen KS, Böhmig G, Bromberg J, Budde K, Barner M, Mackova M, Chang J, Einecke G, Eskandary F, Gupta G, Myślak M, Viklicky O, Akalin E, Alhamad T, Anand S, Arnol M, Baliga R, Banasik M, Bingaman A, Blosser C, Brennan D, Chamienia A, Chow K, Ciszek M, de Freitas D, Dęborska-Materkowska D, Debska-Ślizień A, Djamali A, Domański L, Durlik M, Fatica R, **Francis I**, Fryc J, Gill J, Gill J, Glyda M, Gourishankar S, Grenda R, Gryczman M, Hruba P, Hughes P, Jittirat A, Jurekovic Z, Kamal L, Kamel M, Kant S, Kasiske B, Kojc N, Konopa J, Lan J, Mannon R, Matas A, Mazurkiewicz J, Miglinas M, Mueller T, Narins S, Naumnik B, **Patel A**, Perkowska-Ptasińska A, Picton M, Piecha G, Poggio E, Bloudíčkova SR, Samaniego-Picota M, Schachtner T, Shin S, Shojai S, Sikosana M, Slatinská J, Smykal-Jankowiak K, Solanki A, Haler Ž V, Vucur K, Weir MR, Wiecek A, Włodarczyk Z, Yang H, and Zaky Z. Subthreshold rejection activity in many kidney transplants currently classified as having no rejection. *Am J Transplant* 2024; Epub ahead of print. PMID: 39117038. Full Text

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Methodist Transplant and Specialty Hospital, San Antonio, TX, USA.
University of Washington, Seattle, WA, USA.
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Medical University of Gdańsk, Gdańsk. Poland.
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Most kidney transplant patients who undergo biopsies are classified as having no rejection based on consensus thresholds. However, we hypothesized that because these patients have normal adaptive immune systems, T cell-mediated rejection (TCMR) and antibody-mediated rejection (ABMR) may exist as subthreshold activity in some transplants currently classified as no rejection. To examine this question, we studied genome-wide microarray results from 5086 kidney transplant biopsies (4170 patients). An updated archetypal analysis designated 56% of biopsies as no rejection. Subthreshold molecular TCMR and/or ABMR activity molecular activity was detectable as elevated classifier scores in many biopsies classified as no rejection, with ABMR activity in many TCMR biopsies and TCMR activity in many ABMR biopsies. In biopsies classified as no rejection histologically and molecularly, molecular TCMR classifier scores correlated with increases in histologic TCMR features and molecular injury, lower eGFR, and higher risk of graft loss, and molecular ABMR activity correlated with increased glomerulitis and donor-specific antibody. No rejection biopsies with high subthreshold TCMR or ABMR activity had a higher probability of having TCMR or ABMR respectively diagnosed in a future biopsy. We conclude that many kidney transplant recipients have unrecognized subthreshold TCMR or ABMR activity, with significant implications for future problems.

Neurology
Bossie E, and **Zeidman LA**. Adolf Heidenhain (1893-1937). *J Neurol* 2024; Epub ahead of print. PMID: 39172279. Full Text

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Neurology
Ding G, **Li L**, **Chopp M**, **Zhang L**, **Li Q**, **Luo H**, **Wei M**, **Zhang J**, **Boyd E**, **Zhang Z**, and **Jiang Q**. Velocity of cerebrospinal fluid in the aqueduct measured by phase-contrast MRI in rat. *NMR Biomed* 2024; Epub ahead of print. PMID: 39104053. Full Text

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Cerebrospinal fluid (CSF) circulation plays a key role in cerebral waste clearance via the glymphatic system. Although CSF flow velocity is an essential component of CSF dynamics, it has not been sufficiently characterized, and particularly, in studies of the glymphatic system in rat. To investigate the relationship between the flow velocity of CSF in the brain aqueduct and the glymphatic waste clearance rate, using phase-contrast MRI we performed the first measurements of CSF velocity in rats. Phase-contrast MRI was performed using a 7 T system to map mean velocity of CSF flow in the aqueduct in rat brain. The effects of age (3 months old versus 18 months old), gender, strain (Wistar, RNU, Dark Agouti), anesthetic agents (isoflurane versus dexmedetomidine), and neurodegenerative disorder (Alzheimer' disease in Fischer TgF344-AD rats, males and females) on CSF velocity were investigated in eight independent groups of rats (12 rats per group). Our results demonstrated that quantitative velocities of CSF flow in the aqueduct averaged 5.16 ± 0.86 mm/s in healthy young adult male Wistar rats. CSF flow velocity in the aqueduct was not altered by rat gender, strain, and the employed anesthetic agents in all rats, also age in the female rats. However, aged (18 months) Wistar male rats exhibited significantly reduced the CSF flow velocity in the aqueduct (4.31 ± 1.08 mm/s). In addition, Alzheimer's disease further reduced the CSF flow velocity in the aqueduct of male and female rats.

Neurology **Ewing JR**. Editorial for "Assessment of Tumor Cell Invasion and Radiotherapy Response in Experimental Glioma by Magnetic Resonance Elastography". *J Magn Reson Imaging* 2024; Epub ahead of print. PMID: 39212105. Full Text

Department of Neurology, Henry Ford Hospital, Detroit, Michigan, USA.
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Neurology
Karthik G, Cao CZ, Demidenko MI, Jahn A, Stacey WC, **Wasade VS**, and Brang D. Auditory cortex encodes lipreading information through spatially distributed activity. *Curr Biol* 2024; Epub ahead of print. PMID: 39153482. Full Text

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Watching a speaker's face improves speech perception accuracy. This benefit is enabled, in part, by implicit lipreading abilities present in the general population. While it is established that lipreading can alter the perception of a heard word, it is unknown how these visual signals are represented in the auditory system or how they interact with auditory speech representations. One influential, but untested,

hypothesis is that visual speech modulates the population-coded representations of phonetic and phonemic features in the auditory system. This model is largely supported by data showing that silent lipreading evokes activity in the auditory cortex, but these activations could alternatively reflect general effects of arousal or attention or the encoding of non-linguistic features such as visual timing information. This gap limits our understanding of how vision supports speech perception. To test the hypothesis that the auditory system encodes visual speech information, we acquired functional magnetic resonance imaging (fMRI) data from healthy adults and intracranial recordings from electrodes implanted in patients with epilepsy during auditory and visual speech perception tasks. Across both datasets, linear classifiers successfully decoded the identity of silently lipread words using the spatial pattern of auditory cortex responses. Examining the time course of classification using intracranial recordings, lipread words were classified at earlier time points relative to heard words, suggesting a predictive mechanism for facilitating speech. These results support a model in which the auditory system combines the joint neural distributions evoked by heard and lipread words to generate a more precise estimate of what was said.

Neurology

Osuala KO, Chalasani A, Aggarwal N, **Ji K**, and Moin K. Paracrine Activation of STAT3 Drives GM-CSF Expression in Breast Carcinoma Cells, Generating a Symbiotic Signaling Network with Breast Carcinoma-Associated Fibroblasts. *Cancers (Basel)* 2024; 16(16). PMID: 39199680. Full Text

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This study evaluated the paracrine signaling between breast carcinoma-associated fibroblasts (CAFs) and breast cancer (BCa) cells. Resolving cell-cell communication in the BCa tumor microenvironment (TME) will aid the development of new therapeutics. Here, we utilized our patented TAME (tissue architecture and microenvironment engineering) 3D culture microphysiological system, which is a suitable pathomimetic avatar for the study of the BCa TME. We cultured in 3D BCa cells and CAFs either alone or together in cocultures and found that when cocultured, CAFs enhanced the invasive characteristics of tumor cells, as shown by increased proliferation and spread of tumor cells into the surrounding matrix. Secretome analysis from 3D cultures revealed a relatively high secretion of IL-6 by CAFs. A marked increase in the secretion of granulocyte macrophage-colony stimulating factor (GM-CSF) when carcinoma cells and CAFs were in coculture was also observed. We theorized that the CAF-secreted IL-6 functions in a paracrine manner to induce GM-CSF expression and secretion from carcinoma cells. This was confirmed by evaluating the activation of STAT3 and gene expression of GM-CSF in carcinoma cells exposed to CAF-conditioned media (CAF-CM). In addition, the treatment of CAFs with BCa cell-CM yielded a brief upregulation of GM-CSF followed by a marked decrease, indicating a tightly regulated control of GM-CSF in CAFs. Secretion of IL-6 from CAFs drives the activation of STAT3 in BCa cells, which in turn drives the expression and secretion of GM-CSF. As a result, CAFs exposed to BCa cell-secreted GM-CSF upregulate inflammation-associated genes such as IL-6, IL-6R and IL-8, thereby forming a positive feedback loop. We propose that the tight regulation of GM-CSF in CAFs may be a novel regulatory pathway to target for disrupting the CAF:BCa cell symbiotic relationship. These data provide yet another piece of the cell-cell communication network governing the BCa TME.

Neurology

Zahoor I, **Pan G**, **Cerghet M**, Elbayoumi T, Mao-Draayer Y, **Giri S**, and **Palaniyandi SS**. Current understanding of cardiovascular autonomic dysfunction in multiple sclerosis. *Heliyon* 2024; 10(15):e35753. PMID: 39170118. Full Text

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Autoimmune diseases, including multiple sclerosis (MS), are proven to increase the likelihood of developing cardiovascular disease (CVD) due to a robust systemic immune response and inflammation. MS can lead to cardiovascular abnormalities that are related to autonomic nervous system dysfunction by causing inflammatory lesions surrounding tracts of the autonomic nervous system in the brain and spinal cord. CVD in MS patients can affect an already damaged brain, thus worsening the disease course by causing brain atrophy and white matter disease. Currently, the true prevalence of cardiovascular dysfunction and associated death rates in patients with MS are mostly unknown and inconsistent. Treating vascular risk factors is recommended to improve the management of this disease. This review provides an updated summary of CVD prevalence in patients with MS, emphasizing the need for more preclinical studies using animal models to understand the pathogenesis of MS better. However, no distinct studies exist that explore the temporal effects and etiopathogenesis of immune/inflammatory cells on cardiac damage and dysfunction associated with MS, particularly in the cardiac myocardium. To this end, a thorough investigation into the clinical presentation and underlying mechanisms of CVD must be conducted in patients with MS and preclinical animal models. Additionally, clinicians should monitor for cardiovascular complications while prescribing medications to MS patients, as some MS drugs cause severe CVD.

Neurosurgery
Jimenez MJD, **Kantak P**, and Raskin J. Why Pimping Works: The Neurophysiology of Emotional Memories. *Cureus* 2024; 16(7):e64237. PMID: 39130900. Full Text

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A time-honored medical ritual that combines emotion and cognition into a seamless consolidation of lucid memories is a feared teaching method in medical education. The resulting neurophysiology is explained from a neurosurgeon's perspective - equal parts guilt and dread as a prescription for an improved and sustained trainee fund of knowledge. Much of the available literature published with regard to pimping explores its pedagogy and use in medical practice. This review aims to explore the neurobehavioral and biological aspects of pimping in why it remains a popular teaching model. We describe the neuromodulatory process of integrating emotions and memory as observed during pimping. Additionally, we explore the neuronal pathways and circuits involved in memory encoding, consolidation, and retrieval. Finally, we explored the effects of this methodology as it is currently used in the United States medical education system.

Neurosurgery
van den Bent MJ, French PJ, Brat D, Tonn JC, Touat M, Ellingson BM, Young RJ, Pallud J, von Deimling A, Sahm F, Figarella Branger D, Huang RY, Weller M, Mellinghoff IK, Cloughsey TF, Huse JT, Aldape K, Reifenberger G, Youssef G, Karschnia P, **Noushmehr H**, Peters KB, Ducray F, Preusser M, and Wen PY. The biological significance of tumor grade, age, enhancement and extent of resection in IDH mutant gliomas: how should they inform treatment decision in the era of IDH inhibitors? Invited review. *Neuro Oncol* 2024; Epub ahead of print. PMID: 38912846. Full Text

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The 2016 and 2021 World Health Organization (WHO) 2021 Classification of Central Nervous System (CNS) tumors have resulted in a major improvement of the classification of IDH-mutant gliomas. With more effective treatments many patients experience prolonged survival . However, treatment guidelines are often still based on information from historical series comprising both patients with IDHwt and IDH mutant tumors. They provide recommendations for radiotherapy and chemotherapy for so-called high-risk patients, usually based on residual tumor after surgery and age over 40. More up-to-date studies give a better insight into clinical, radiological and molecular factors associated with outcome of patients with IDH-mutant glioma. These insights should be used today for risk stratification and for treatment decisions. In many patients with an IDH-mutant grade 2 and grade 3 glioma, if carefully monitored postponing radiotherapy and chemotherapy is safe, and will not jeopardize overall outcome of patients. With the INDIGO trial showing patient benefit from the IDH inhibitor vorasidenib, there is a sizable population in which it seems reasonable to try this class of agents before recommending radio-chemotherapy with its delayed adverse event profile affecting quality of survival. Ongoing trials should help to further identify the patients that are benefiting from this treatment.

Nursing

Hallman MJ, Hauff NJ, Mooney M, and Brandt DJ. Evaluation of a weight-based enteral feeding program for the very low birth weight infant in the neonatal intensive care unit. *J Neonatal Nurs* 2024; 30(4):353-359. PMID: Not assigned. Full Text

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This project was a program evaluation of the first year of implementation of weight-based fast advancement enteral feeding programs for very low birthweight preterm infants, related to adherence to the guidelines, length of indwelling central line days, and infection and growth rates. The sample consists of infants born at less than 33 weeks and less than 1500 g, n = 221; defined as pre-(n = 107) and post-program (n = 114) implementation groups further stratified into adherent (n = 53) and non-adherent (n = 58) cohorts. In the post-program adherent cohort, central line days were decreased from 17 to 10 days ($p < 0.001$) with no documented infection events in the first 14 days of life ($p < 0.001$) compared to the post-program non-adherent cohort. This feeding program is an evidence-based conservative approach to fast advancement. There is evidence to support more aggressive feeding advancement in all weight categories that could further decrease both indwelling central line days and infection events.

Obstetrics, Gynecology and Women's Health Services

Smith N, **Kwon Kim S**, **Goyert G**, **Lin CH**, **Rose C**, and **Pitts DS**. Nifedipine outperforms labetalol: A comparative analysis of hypertension management in black pregnancies. *Pregnancy Hypertens* 2024; 37:101147. PMID: 39153458. Full Text

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BACKGROUND: Nifedipine has previously exhibited superior efficacy to labetalol in managing hypertension in the non-pregnant Black population, establishing itself as a first-line treatment option. However, the unique challenges of hypertension during pregnancy, especially prevalent in Black individuals, remain underexplored in terms of effective medication choices. This gap highlights the need for targeted research on antihypertensive efficacy specifically within this population. OBJECTIVE: This study aims to evaluate the effectiveness of nifedipine versus labetalol in managing blood pressure in Black pregnancies. The primary measure is the mean systolic and diastolic blood pressure trajectories throughout pregnancy, determining the superiority of nifedipine in this context. STUDY DESIGN: A retrospective cohort study was conducted at a multi-center institution in the metropolitan Detroit area, encompassing data from 1,235 Black pregnancies affected by chronic hypertension between 2015 and 2022. Mean blood pressure trajectories during pregnancy were fit by linear mixed effects model with a random intercept and time effect. RESULTS: Patients on nifedipine had an estimated 2.08 mmHg lower mean systolic and 1.60 mmHg lower mean diastolic blood pressure compared to those on labetalol, with significant p-values of 0.040 and 0.028. Additionally, nifedipine users were less likely to need increased doses, with an odds ratio of 0.28 (95 % CI: 0.19-0.40, $p < 0.001$) compared to labetalol users. CONCLUSION: This study provides compelling evidence that nifedipine outperforms labetalol in managing blood pressure during Black pregnancies. These findings suggest that the initiation of nifedipine should be considered in the management of chronic hypertension among Black pregnant individuals, offering a potentially more effective treatment option.

Orthopedics/Bone and Joint Center

Abbas MJ, Markel DC, Hallstrom BR, Zheng H, and **Charters MA**. The Impact of Surgeon Volume on Unicompartmental Knee Arthroplasty Survivorship: A Michigan Arthroplasty Registry Collaborative Quality Initiative (MARCQI) Database Analysis. *J Arthroplasty* 2024; Epub ahead of print. PMID: 39147075. Full Text

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BACKGROUND: The utilization of unicompartmental knee arthroplasty (UKA) has remained low when compared to total knee arthroplasty (TKA), possibly due to higher rates of revision and reoperation. This study aimed to quantify surgeon UKA case-volumes and measure the effect of surgeon volume on early revision. We hypothesized that surgeons who have high case volumes would have lower revision rates compared to medium- and low-volume surgeons. METHODS: Primary UKAs were performed between February 2012 and November 2021, and associated revisions were identified utilizing the Michigan Arthroplasty Registry Collaborative Quality Initiative (MARCQI). Surgeon information, including total cases and annual UKA volume, was collected. Case volume per year was stratified as High (≥ 35 cases per year), Medium (15 to 34 cases per year), and low (< 15 cases per year). RESULTS: There were a total of 15,542 UKAs performed. Of these, 701 (4.5%) were revised, and 412 (58.8%) revisions occurred within 2 years. Of the 287 surgeons who performed an UKA in the registry, 237 (82.6%) were low-volume surgeons, 36 (12.5%) were medium-volume, and 14 (4.9%) were high-volume. High-volume surgeons were more likely to operate on older patients ($P < 0.01$), Medicare patients ($P < 0.01$), and patients who had ASA (American Society of Anesthesiologists) scores of III and IV ($P < 0.01$). High-volume surgeons had significantly lower 5-year revision rates compared to medium and low-volume surgeons (high: 4.3% (95% CI [confidence interval]: 3.70 to 4.90), medium: 5.2% (4.44 to 6.12), low: 7.2% (6.37 to 8.02); $P < 0.001$). In comparison, the 5-year revision rate for TKA in Michigan was 3.0% (95% CI: 2.90 to 3.08). CONCLUSION: When UKAs were performed by high-volume surgeons in the state of Michigan, there was better survivorship when compared to low-volume and medium-volume surgeons. High-volume surgeons were more likely to perform UKA on older patients, Medicare patients, and patients who had ASA scores of III and IV. The revision rate for the high-volume surgeons still exceeded the 5-year revision rate for total knee arthroplasty in Michigan.

Orthopedics/Bone and Joint Center

Chougule A, **Zhang C**, **Vinokurov N**, **Mendez D**, **Vojtisek E**, Shi C, Zhang J, and **Gardinier J**. Purinergic signaling through the P2Y2 receptor regulates osteocytes' mechanosensitivity. *J Cell Biol* 2024; 223(11). PMID: 39212624. Full Text

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Osteocytes' response to dynamic loading plays a crucial role in regulating the bone mass but quickly becomes saturated such that downstream induction of bone formation plateaus. The underlying mechanisms that downregulate osteocytes' sensitivity and overall response to loading remain unknown. In other cell types, purinergic signaling through the P2Y2 receptor has the potential to downregulate the sensitivity to loading by modifying cell stiffness through actin polymerization and cytoskeleton organization. Herein, we examined the role of P2Y2 activation in regulating osteocytes' mechanotransduction using a P2Y2 knockout cell line alongside conditional knockout mice. Our findings demonstrate that the absence of P2Y2 expression in MLO-Y4 cells prevents actin polymerization while increasing the sensitivity to fluid flow-induced shear stress. Deleting osteocytes' P2Y2 expression in conditional-knockout mice enabled bone formation to increase when increasing the duration of exercise.

Overall, P2Y2 activation under loading produces a negative feedback loop, limiting osteocytes' response to continuous loading by shifting the sensitivity to mechanical strain through actin stress fiber formation.

Orthopedics/Bone and Joint Center

Harrison AK, **Braman JP**, and Cagle PJ. What's New in Shoulder and Elbow Surgery. *J Bone Joint Surg Am* 2024; Epub ahead of print. PMID: 39172885. Full Text

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Otolaryngology – Head and Neck Surgery

Abiri A, Hong EM, Dilley KK, Nguyen TV, Salmon MK, Grose EM, Tripathi SH, Venkatesh S, Kim Y, Lee DJ, Douglas JE, **Eide JG**, Kshirsagar RS, Phillips KM, Sedaghat AR, Lee JM, Tong CCL, Adappa ND, Palmer JN, and Kuan EC. Quality-of-Life Outcomes Following Endoscopic Resection of Sinonasal Inverted Papilloma. *Laryngoscope* 2024; Epub ahead of print. PMID: 39180440. Full Text

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OBJECTIVES: There is growing interest in assessing patient quality of life (QOL) following treatment of sinonasal tumors, including inverted papilloma (IP). We aimed to elucidate the natural history of postoperative QOL outcomes in IP patients treated with surgery. METHODS: Cases of sinonasal IP treated surgically at 4 tertiary academic rhinology centers were retrospectively reviewed. SNOT-22 scores were used to evaluate QOL preoperatively and postoperatively (1, 3, 6, 12 months). Repeated-measures ANOVA assessed for differences in mean scores over time. Linear regression identified factors associated with QOL longitudinally. RESULTS: 373 patients were analyzed. Mean preoperative SNOT-22 score was 20.6 ± 20.4, which decreased to 16.3 ± 18.8 ($p = 0.041$) and 11.8 ± 15.0 ($p < 0.001$) at 1 and 3 months postoperatively, respectively. No further changes in SNOT-22 scores occurred beyond 3 months postoperatively ($p > 0.05$). When analyzed by SNOT-22 subdomains, nasal, sleep, and otologic/facial subdomain scores (all $p < 0.05$) demonstrated improvement at 12-month follow-up compared with preoperative scores; this was not observed for the emotional subdomain score ($p = 0.800$). Recurrent cases were associated with higher long-term SNOT-22 scores ($\beta = 7.08$; $p = 0.017$). Age, sex, degree of dysplasia, prior surgery, primary site, and smoking history did not correlate with symptoms (all $p > 0.05$). CONCLUSIONS: QOL outcomes related to IP resection are largely driven by nasal, sleep, and otologic/facial subdomains, though patients appear to experience enduring improvement as early as 3 months postoperatively. Recurrent disease is a major driver of negative QOL. LEVEL OF EVIDENCE: 4 Laryngoscope, 2024.

Otolaryngology – Head and Neck Surgery

Al-Saghir T, **Hall J**, **Diffley M**, **Tang A**, Teitelbaum A, **Tepper DG**, **Darian V**, **Evangelista M**, and **Atisha D**. Marijuana's Impact On Implant-based Breast Reconstruction: A Retrospective Cohort Study. *Plast Reconstr Surg Glob Open* 2024; 12(8):e6082. PMID: 39171243. Full Text

From the Division of Otolaryngology, Henry Ford Health System, Detroit, Mich.
Division of Plastic Surgery, Henry Ford Health System, Detroit, Mich.
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Division of General Surgery, Corewell Health, Royal Oak, Mich.

BACKGROUND: Studies have shown that chronic marijuana use is associated with increased vascular inflammation, endothelial damage, myocardial infarctions, strokes, arteritis, and cardiomyopathies; however, cannabis's effect on wound healing in immediate direct-to-implant (DTI) breast reconstruction is unknown. With the increasing prevalence of marijuana use, it is imperative to understand its effects on surgical outcomes. METHODS: We performed a retrospective cohort study of consecutive patients in a quaternary-care breast cancer center undergoing immediate DTI reconstruction. Patient demographics, operative details, and surgical complications were extracted through chart review. Active cannabis use was defined as use within 12 weeks of operation. Univariate and multivariable analyses were performed. RESULTS: In total, 243 consecutive patients underwent immediate DTI reconstruction, and 12 reported active cannabis use. There were no significant differences in patient demographics, cancer treatment, or operative details. Active marijuana users demonstrated higher rates of cellulitis treated with IV antibiotics ($P = 0.004$), explantation for infection ($P = 0.004$), emergency department visits ($P = 0.028$), readmission ($P = 0.037$), takeback to the operating room in 90 days ($P < 0.001$), and overall major complications ($P < 0.001$). Multivariable analysis demonstrated that active marijuana users were more likely to experience cellulitis treated with IV antibiotics [odds ratio (OR) = 3.55, $P = 0.024$], takeback to the OR within 90 days of operation (OR = 4.75, $P = 0.001$), and major complications (OR = 2.26, $P = 0.048$). CONCLUSIONS: The consumption of cannabis in the perioperative setting is associated with increased rates of complications in patients undergoing immediate DTI reconstruction; however, an analysis with a larger patient population is needed to conclude that abstinence from its use should be highly encouraged.

Otolaryngology – Head and Neck Surgery
Craig JR, and Saibene AM. Odontogenic Sinusitis: The Next Step. *Otolaryngol Clin North Am* 2024; Epub ahead of print. PMID: 39138074. Full Text

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Otolaryngology – Head and Neck Surgery
Craig JR, Saibene AM, Adappa ND, Douglas JE, **Eide JG**, Felisati G, Kohanski MA, Kshirsagar RS, Kwiecien C, Lee D, Makary CA, Palmer JN, **Ray A**, **Wilson C**, and Kuan EC. Maxillary Antrostomy Versus Complete Sinus Surgery for Odontogenic Sinusitis With Frontal Sinus Extension. *Laryngoscope* 2024; Epub ahead of print. PMID: 39189339. Full Text

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OBJECTIVES: Endoscopic sinus surgery (ESS) is often necessary when managing odontogenic sinusitis (ODS), but ESS extent for ODS with extramaxillary sinus involvement has been incompletely studied. This study compared outcomes after wide maxillary antrostomy (MA) alone versus complete ESS for ODS with frontal sinus involvement. METHODS: A multicenter prospective cohort study was conducted on patients with uncomplicated ODS (no extrasinus spread) who underwent ESS when computed

tomography demonstrated maxillary, anterior ethmoid (AE), and frontal sinus opacification. Multiple preoperative and postoperative variables were recorded, including 22-item sinonasal outcome tests (SNOT-22) and endoscopic findings. Ultimate SNOT-22 and endoscopic resolution, and time to SNOT-22 and endoscopic resolution were compared between patients who underwent MA alone versus "complete" ESS (maxillary, ethmoid, frontal; not sphenoid). RESULTS: Of 70 patients, mean age was 59.2 years, and 55.7% were male. Thirty-five underwent MA alone, and 35 had complete ESS. At first postoperative visits (mean 9.3 days), AE sinus purulence was more likely resolved after complete ESS compared with MA (97.1% vs. 71.4%, p = 0.006). However, time to resolution of AE purulence was comparable by 6 weeks postoperatively (p = 0.158). There were no significant differences in times to foul smell resolution and achieving ≥9 point SNOT-22 reduction (p > 0.05). CONCLUSIONS: For ODS with frontal sinus involvement, MA alone and complete ESS both resulted in rapid and long-term symptomatic resolution. While ultimate resolution of sinus purulence was equivalent between surgery groups, complete ESS did lead to faster resolution of frontoethmoidal purulence in a significant number of cases. LEVEL OF EVIDENCE: 2 Laryngoscope, 2024.

Otolaryngology – Head and Neck Surgery

Craig JR, Saibene AM, Felisati EG, and Felisati G. Collaboration between otolaryngologists and oral surgeons in maxillary sinus elevation planning. *Clin Implant Dent Relat Res* 2024; Epub ahead of print. PMID: 39187918. Full Text

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BACKGROUND: The collaboration between otolaryngologists and dental providers is crucial for the planning and execution of maxillary sinus elevation (MSE) procedures, which are integral to successful dental implant placements. PURPOSE: This article examines the essential role of otolaryngological assessments in identifying potential sinonasal risks that could impact the outcomes of MSE. MATERIALS AND METHODS: A comprehensive narrative review of existing literature was conducted. DISCUSSION: The review underscores the importance of thorough preoperative evaluations, including patient history, computed tomography (CT) or cone-beam CT (CBCT) scans, and nasal endoscopy, to mitigate sinonasal health risks. It details various clinical scenarios and patient assessments, emphasizing a systematic approach to diagnosing and managing sinonasal conditions proactively. The discussion reveals that while some sinus conditions may not significantly affect MSE success, conditions impacting mucociliary clearance and sinus drainage are critical risk factors requiring otolaryngological intervention. Additionally, the article introduces a grading system to assist clinicians in identifying patients who would benefit from otolaryngological evaluations prior to MSE. CONCLUSION: This review highlights the value of interdisciplinary collaboration and standardized protocols in enhancing the predictability and safety of MSE procedures, ultimately improving patient outcomes.

Otolaryngology – Head and Neck Surgery

Eide JG, Kuan EC, Adappa ND, Chang J, Cho DY, Garg R, Govindaraj S, Grayson J, **Im E**, Keschner D, Kohanski M, Locke T, Palmer JN, Welch KC, Woodworth BA, Yoo F, and **Craig JR**. Subtotal Middle Turbinate Resection in Patients with Chronic Rhinosinusitis with Nasal Polyps is Unlikely to Cause Empty Nose Syndrome: A Multi-Institutional Prospective Study. *Laryngoscope* 2024; Epub ahead of print. PMID: 39136246. Full Text

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BACKGROUND: Empty nose syndrome (ENS) is a poorly understood, debilitating condition affecting a minority of patients who underwent nasal airway surgery, most commonly following inferior turbinate surgery. Few publications have demonstrated middle turbinate resection (MTR) causing ENS, but MTR is still considered a potential cause of ENS. The Empty Nose Syndrome 6-item Questionnaire (ENS6Q) is validated for ENS diagnosis, with ENS6Q ≥ 11 considered highly suggestive of ENS. The purpose of this multicenter study was to determine the incidence of patients with ENS6Q ≥ 11 following subtotal MTR during endoscopic sinus surgery (ESS) for chronic rhinosinusitis with nasal polyps (CRSwNP) by comparing preoperative and postoperative ENS6Q scores. METHODS: A multi-institutional prospective cohort study (8 US institutions) was conducted on patients who underwent bilateral subtotal MTR during ESS for CRSwNP. Preoperative and postoperative ENS6Q scores were compared after at least 12 months of postoperative follow-up. RESULTS: Of 110 patients, mean age was 51.6 years and 59.1% were male. Mean follow-up was 14.5 ± 2.5 months (range 12.1-22.3 months). Mean preoperative and postoperative ENS6Q were 7.7 and 2.2, respectively, demonstrating a mean 5.5 point decrease postoperatively ($p < 0.0001$). At final follow-up, no patient had an ENS6Q ≥ 11. Of note, 20% of patients had preoperative ENS6Q scores ≥11, but all decreased to <11 postoperatively. CONCLUSIONS: Based on prospective multicenter data over 1-2 years postoperatively, subtotal MTR for CRSwNP never led to ENS6Q scores ≥11, and patients experienced significant decreases in ENS6Q postoperatively. Subtotal MTR during ESS for CRSwNP was, therefore, unlikely to cause ENS even with long-term follow-up. LEVEL OF EVIDENCE: 4 Laryngoscope, 2024.

Otolaryngology – Head and Neck Surgery
Kwiatkowska MA, and **Craig JR**. Unilateral Sinus Disease: What Is, and Is Not Odontogenic Sinusitis? *Otolaryngol Clin North Am* 2024; Epub ahead of print. PMID: 39147657. Full Text

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The differential diagnosis of unilateral sinus disease (USD) is broad, and while concerning etiologies like sinonasal neoplasia, invasive fungal sinusitis, and cerebrospinal fluid rhinorrhea should always be considered, most cases are due to noninvasive inflammatory or infectious conditions. To diagnose USD appropriately, clinicians must integrate the clinical history and examination, nasal endoscopy, computed tomography (CT), and possibly MRI. Odontogenic sinusitis (ODS) is the most common cause of unilateral maxillary sinus opacification on CT, with 45% to 75% of such cases being odontogenic in nature. This study provides USD diagnostic considerations and reinforces the diagnostic approach to ODS.

Otolaryngology – Head and Neck Surgery
Pannkuk TF, **Craig JR**, Tušas P, and Simuntis R. Management of Endodontic Disease for Odontogenic Sinusitis. *Otolaryngol Clin North Am* 2024; Epub ahead of print. PMID: 39214736. Full Text

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Primary dental treatments for odontogenic sinusitis (ODS) due to endodontic infections (pulpal necrosis and apical periodontitis ± periapical abscess) include extraction and root canal treatment (RCT).

Published evidence is lacking on the success of primary endodontic treatment for purulent ODS, with the majority of RCT-related series reporting on its success at resolving reactive maxillary sinus mucositis. Dental extraction is the most definitive treatment of endodontic disease causing ODS, but compromises the functional dentition and still often fails to resolve the purulent sinusitis. This article highlights key concepts of RCT and dental extraction techniques, as well as their published success at resolving ODS.

Otolaryngology – Head and Neck Surgery
Pollick SA, **Mansour Y**, and Pesch MH. Newborn congenital cytomegalovirus screening and hearing outcomes: a systematic review of current literature. *Curr Opin Otolaryngol Head Neck Surg* 2024; Epub ahead of print. PMID: 39146216. Full Text

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PURPOSE OF REVIEW: The purpose of this review is to summarize the very recent literature surrounding hearing outcomes of children with congenital cytomegalovirus (cCMV) detected through systematic screening programs. RECENT FINDINGS: There are several different approaches to cCMV screening including forms of targeted vs. universal screening of newborns as well as maternally-derived prenatal testing. However, many studies fail to document hearing-related outcomes both in the newborn period and further into childhood when late-onset sensorineural hearing loss (SNHL) can occur. This systematic review included studies of neonates screened for cCMV reporting hearing outcomes for at least one point in time. Hearing targeted screening appeared the most widely reported for detection of unilateral and bilateral SNHL in those with cCMV. A few studies examined these clinical findings in relation to antiviral treatment. SUMMARY: Congenital CMV is an important and common cause of childhood hearing loss. Newborn screening programs may expand opportunities for early diagnosis and treatment of the infection and its sequelae.

Otolaryngology – Head and Neck Surgery
Testori T, Scaini R, Friedland B, Saibene AM, Felisati G, **Craig JR**, Deflorian M, Zuffetti F, Del Fabbro M, and Wang HL. Maxillary sinus opacification after surgery in asymptomatic patients: Transient swelling of the sinus mucosa or graft dispersion into the maxillary sinus. A radiographic report of three cases after a follow-up period of at least 5 years. *Int J Oral Implantol (Berl)* 2024; 17(2):189-198. PMID: 38801332. Request Article

Maxillary sinus grafting is a predictable regenerative technique to facilitate maxillary posterior implant placement when there is insufficient vertical bone height inferior to the maxillary sinuses to allow placement of implants of adequate dimensions. It enables an increase in vertical bone height, which makes implant placement easier. Maxillary sinus mucosal membrane perforation is one of the most common intraoperative complications during maxillary sinus grafting and may result in extrusion of graft material into the sinus. When this occurs, the mucociliary function of the maxillary sinus may expel the extruded graft material through its natural ostium, though graft particles may remain in the sinus or possibly occlude the natural ostium. After grafting, transient maxillary sinus mucosal oedema may occur. A postoperative CBCT scan may reveal varying degrees of sinus opacification, namely partial, subtotal or total. Although it is always possible to identify graft material, which may enter the sinus as a result of membrane perforation that might not even be visible to the implantologist during the surgical procedure, it is challenging to assess whether sinus opacification is due to mucosal thickening or mucus accumulation. The aim of the present case series was to offer a pragmatic approach to managing asymptomatic patients whose CBCT scans demonstrated partial, subtotal or total maxillary sinus opacification with bone graft particles that seemed to have been extruded into the sinus.

Pathology and Laboratory Medicine
Al-Obaidy KI, and Cheng L. Advancing the molecular understanding of renal tumorigenesis: Acquired cystic disease-associated renal cell carcinoma (ACD-RCC) as a model system. *Ann Diagn Pathol* 2024; 73:152366. PMID: 39121515. Full Text

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In summary, the study's investigation of KMT2C and TSC2 variants in ACD-RCC marks a significant advancement in comprehending this distinct kidney tumor. By illuminating the molecular landscape of ACD-RCC, the research sets the stage for future studies aimed at revealing the complex mechanisms driving tumor development and progression. This understanding could eventually lead to more effective management and treatment strategies for renal cancer patients.

Pathology and Laboratory Medicine

Deignan JL, Aggarwal V, Bale AE, Bellissimo DB, Booker JK, Cao Y, Crooks KR, Deak KL, Del Gaudio D, Funke B, Hoppman NL, Horner V, Hufnagel RB, Jackson-Cook C, Koduru P, Leung ML, Li S, Liu P, Luo M, Mao R, Mason-Suares H, Mikhail FM, Moore SR, Naeem RC, Pollard LM, Repnikova EA, Shao L, **Shaw BM**, Shetty S, Smolarek TA, Spiteri E, Van Ziffle J, Vance GH, Vnencak-Jones CL, and Williams ES. The challenges and opportunities of offering and integrating training in clinical molecular genetics and clinical cytogenetics: A survey of LGG Fellowship Program Directors. *Genet Med Open* 2024; 2. PMID: 39175871. Full Text

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PURPOSE: The specialty of Laboratory Genetics and Genomics (LGG) was created in 2017 in an effort to reflect the increasing convergence in technologies and approaches between clinical molecular genetics and clinical cytogenetics. However, there has not yet been any formal evaluation of the merging of these disciplines and the challenges faced by Program Directors (PDs) tasked with ensuring the successful training of laboratory geneticists under the new model. METHODS: An electronic multi-question Qualtrics survey was created and was sent to the PD for each of the Accreditation Council for Graduate Medical Education-accredited LGG fellowship programs at the time. The data were collected, and the responses were aggregated for each question. RESULTS: All of the responding PDs had started training at least 1 LGG fellow. PDs noted challenges with funding, staff shortages, molecular/cytogenetics content integration, limited total training time, increased remote work, increased sendout testing, and a lack of prior cytogenetics knowledge among incoming fellows. CONCLUSION: This survey attempted to assess the challenges that LGG PDs have been facing in offering and integrating clinical molecular genetics and clinical cytogenetics fellowship training. Common challenges between programs were noted, and a set of 6 concluding comments are provided to facilitate future discussion.

Pathology and Laboratory Medicine

Otrock ZK, and Eby CS. Zoonotic Bacterial Infections Triggering Cytokine Storm Syndrome. *Adv Exp Med Biol* 2024; 1448:285-291. PMID: 39117822. Request Article

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Zoonotic infections can result in life-threatening complications that can manifest with hemophagocytic lymphohistiocytosis (HLH)/cytokine storm syndrome (CSS). Bacteria constitute the largest group of zoonotic infection-related HLH cases. The growing list of zoonotic bacterial infections associated with HLH/CSS include Brucella spp., Rickettsia spp., Ehrlichia, Coxiella burnetii, Mycobacterium spp., and Bartonella spp. Patients most commonly present with fever, cytopenias, hepatosplenomegaly, myalgias, and less frequently with rash, jaundice, and lymphadenopathy.

Pathology and Laboratory Medicine
Sangoi AR, **Al-Obaidy KI**, Akgul M, Mehra R, Chan E, and Williamson SR. Cowper Glands Identified in Prostate and Urethral Specimens: A Comprehensive Immunohistochemical Characterization and Potential Diagnostic Pitfall. *Int J Surg Pathol* 2024; Epub ahead of print. PMID: 39165181. Full Text

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Cowper glands recognition remains one of the key histoanatomic benign mimics of prostatic adenocarcinoma. In most instances, these can be identified based on the dimorphic population of lobulated acini and duct(s). However, in the prostate biopsy setting with incomplete/distorted cores, this may not be immediately apparent and may warrant use of immunohistochemistry to argue against prostatic adenocarcinoma. Although immunohistochemical pitfalls in Cowper glands have been described, to our knowledge a comprehensive evaluation of both traditional and purportedly prostate-specific novel markers in Cowper glands has not been previously performed. Herein, we studied the clinicopathological and immunohistochemical features of 21 male patients (age range 39-81 years; mean = 63 years), including 15 prostate biopsies (7 of which also had prostate cancer in the same specimen set and 2 of which had both prostate cancer and Cowper glands in the same biopsy core). Immunohistochemistry showed the following results in Cowper glands: 100% positive for NKX3.1, 100% positive (basal cells) for both high molecular weight keratin and p63, 57% positive for PSAP, 25% positive for PSMA, 5% positive for AMACR, and 0% positive for PSA. In conclusion, for specimens lacking appreciable dimorphic morphology, caution should be rendered when using prostate-specific markers (PSA, PSAP, PSMA, and NKX3.1) as these can show considerable staining in Cowper glands and be a pitfall. Instead, findings from this cohort indicate relying on basal markers (high molecular weight keratin/p63; either individually or in a "cocktail" approach) and PSA are most useful in distinguishing Cowper glands (retained basal cell markers staining) from prostatic adenocarcinoma.

Pathology and Laboratory Medicine
Xu JM, Cao MG, Gao QC, Lu YX, and **Stark AT**. Nurses' Workplace Social Capital and Sustainable Development: An Integrative Review of Empirical Studies. *J Nurs Manag* 2024; 2024:14. PMID: Not assigned. Full Text

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Aim. The purpose of our review was to assess the role of nurses' workplace social capital in meeting the Sustainable Development Goals (SDGs) of the United Nations (UN). Background. In 2015, the 2030 Agenda for Sustainable Development with 17 universal goals was adopted by members of the UN. Although nurses have been acknowledged as important contributors to sustainable development, they still have difficulties in connecting their work to the SDGs. Nurses' workplace social capital is an important concept in nursing management due to its constructive consequences. However, the potential association between nurses' workplace social capital and the SDGs has not been evaluated. Evaluation. We conducted an integrative review, following the methodology of Whittemore and Knafl. Seven databases, Medline, CINAHL, Web of Science, Cochrane Library, Embase, PsycINFO, and Scopus with no restriction on publication year, were searched in May 2023 to identify statistically significant empirical evidence. Only peer-reviewed research papers published in English language journals were considered. We applied the Mixed Methods Appraisal Tool to evaluate the quality of the selected articles. We categorized outcomes of nurses' workplace social capital into themes and connected them to the SDGs through

repeated comparisons and discussions. Key Issues. Twenty-nine of 2,188 retrieved articles were included in the final data analysis. Twenty-three outcomes of nurses' workplace social capital were identified, and three themes were abstracted. Nurses' workplace social capital is positively associated with SDG 3 (good health and well-being), SDG 8 (decent work and economic growth), and SDG 17 (partnerships for the goals). Conclusion. Findings of our integrative review shed light on the importance of nurses' workplace social capital and the role of nurses in achieving the global movement for sustainable development. Implication for Nursing Management. Investment in nursing workforce and nurses' workplace social capital can further strengthen the position of nurses to support and deliver the SDGs.

Pharmacy

Liske J, **Patel N**, **Makowski C**, **Awdish R**, and **Smith ZR**. Risk evaluation and mitigation strategy compliance for pulmonary hypertension medications after policy implementation with computerized provider order entry support. *Am J Health Syst Pharm* 2024; Epub ahead of print. PMID: 39096261. Full Text

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DISCLAIMER: In an effort to expedite the publication of articles, AJHP is posting manuscripts online as soon as possible after acceptance. Accepted manuscripts have been peer-reviewed and copyedited, but are posted online before technical formatting and author proofing. These manuscripts are not the final version of record and will be replaced with the final article (formatted per AJHP style and proofed by the authors) at a later time. PURPOSE: Treatment for pulmonary hypertension includes medications with risk evaluation and mitigation strategy (REMS) programs. Health-system inpatient pharmacies dispensing these agents must comply with inpatient REMS dispensing criteria. Implementing a health-system policy with computerized provider order entry (CPOE) decision support may improve REMS compliance. METHODS: This was a retrospective, quasi-experimental study comparing REMS compliance before and after development of a policy with CPOE decision support that was implemented in August 2019. Patients 18 years of age or older with a diagnosis of pulmonary hypertension were included if they received at least one dose of an endothelin receptor antagonist or riociguat while hospitalized. Patients were included in the preintervention group if they were hospitalized between August 1, 2017, and August 31, 2019, and in the postintervention group if they were hospitalized between September 1, 2019, and August 31, 2021. The primary outcome was the REMS compliance rate. Secondary endpoints included the time to REMS compliance and independent factors associated with failed or delayed REMS compliance. RESULTS: A total of 150 patients were included, with 75 patients in both the pre- and postintervention groups. Compliance increased significantly from the preintervention (50%) to postintervention (92%) group ($P < 0.001$). Time to compliance was also significantly reduced from 770 minutes in the preintervention group to 140 minutes in the postintervention group ($P = 0.031$). Factors independently associated with REMS compliance were being in the postintervention group (odds ratio, 16.9; 95% confidence interval, 5.8-49.2) and being admitted to a pulmonary hypertension center for comprehensive care. (odds ratio, 7.8; 95% confidence interval, 2.9-21.2). CONCLUSION: A health-system policy with CPOE decision support improved both the rate of and time to compliance with inpatient REMS dispensing procedures.

Plastic Surgery

Al-Saghir T, **Hall J**, **Diffley M**, **Tang A**, Teitelbaum A, **Tepper DG**, **Darian V**, **Evangelista M**, and **Atisha D**. Marijuana's Impact On Implant-based Breast Reconstruction: A Retrospective Cohort Study. *Plast Reconstr Surg Glob Open* 2024; 12(8):e6082. PMID: 39171243. Full Text

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BACKGROUND: Studies have shown that chronic marijuana use is associated with increased vascular inflammation, endothelial damage, myocardial infarctions, strokes, arteritis, and cardiomyopathies;

however, cannabis's effect on wound healing in immediate direct-to-implant (DTI) breast reconstruction is unknown. With the increasing prevalence of marijuana use, it is imperative to understand its effects on surgical outcomes. METHODS: We performed a retrospective cohort study of consecutive patients in a quaternary-care breast cancer center undergoing immediate DTI reconstruction. Patient demographics, operative details, and surgical complications were extracted through chart review. Active cannabis use was defined as use within 12 weeks of operation. Univariate and multivariable analyses were performed. RESULTS: In total, 243 consecutive patients underwent immediate DTI reconstruction, and 12 reported active cannabis use. There were no significant differences in patient demographics, cancer treatment, or operative details. Active marijuana users demonstrated higher rates of cellulitis treated with IV antibiotics ($P = 0.004$), explantation for infection ($P = 0.004$), emergency department visits ($P = 0.028$), readmission ($P = 0.037$), takeback to the operating room in 90 days ($P < 0.001$), and overall major complications ($P < 0.001$). Multivariable analysis demonstrated that active marijuana users were more likely to experience cellulitis treated with IV antibiotics [odds ratio (OR) = 3.55, $P = 0.024$], takeback to the OR within 90 days of operation (OR = 4.75, $P = 0.001$), and major complications (OR = 2.26, $P = 0.048$). CONCLUSIONS: The consumption of cannabis in the perioperative setting is associated with increased rates of complications in patients undergoing immediate DTI reconstruction; however, an analysis with a larger patient population is needed to conclude that abstinence from its use should be highly encouraged.

Public Health Sciences

Al-Saghir T, **Hall J**, **Diffley M**, **Tang A**, Teitelbaum A, **Tepper DG**, **Darian V**, **Evangelista M**, and **Atisha D**. Marijuana's Impact On Implant-based Breast Reconstruction: A Retrospective Cohort Study. *Plast Reconstr Surg Glob Open* 2024; 12(8):e6082. PMID: 39171243. Full Text

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BACKGROUND: Studies have shown that chronic marijuana use is associated with increased vascular inflammation, endothelial damage, myocardial infarctions, strokes, arteritis, and cardiomyopathies; however, cannabis's effect on wound healing in immediate direct-to-implant (DTI) breast reconstruction is unknown. With the increasing prevalence of marijuana use, it is imperative to understand its effects on surgical outcomes. METHODS: We performed a retrospective cohort study of consecutive patients in a quaternary-care breast cancer center undergoing immediate DTI reconstruction. Patient demographics, operative details, and surgical complications were extracted through chart review. Active cannabis use was defined as use within 12 weeks of operation. Univariate and multivariable analyses were performed. RESULTS: In total, 243 consecutive patients underwent immediate DTI reconstruction, and 12 reported active cannabis use. There were no significant differences in patient demographics, cancer treatment, or operative details. Active marijuana users demonstrated higher rates of cellulitis treated with IV antibiotics ($P = 0.004$), explantation for infection ($P = 0.004$), emergency department visits ($P = 0.028$), readmission ($P = 0.037$), takeback to the operating room in 90 days ($P < 0.001$), and overall major complications ($P < 0.001$). Multivariable analysis demonstrated that active marijuana users were more likely to experience cellulitis treated with IV antibiotics [odds ratio (OR) = 3.55, $P = 0.024$], takeback to the OR within 90 days of operation (OR = 4.75, $P = 0.001$), and major complications (OR = 2.26, $P = 0.048$). CONCLUSIONS: The consumption of cannabis in the perioperative setting is associated with increased rates of complications in patients undergoing immediate DTI reconstruction; however, an analysis with a larger patient population is needed to conclude that abstinence from its use should be highly encouraged.

Public Health Sciences

Bolderston A, McCuaig C, **Ghosh S**, McEntee MF, and Kiely E. Mind the gap: Gender disparities in authorship in the Journal of Medical Imaging and Radiation Sciences. *J Med Imaging Radiat Sci* 2024; 55(4):101726. PMID: 39106559. Full Text

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INTRODUCTION: Research studies tracking gender and academic publication productivity in healthcare find gender disparities in research activity, publication, and authorship. Article authorship is one of the important metrics to track when seeking to understand gender inequality in academic career advancement. Research on gender disparities in publication productivity in the field of Medical Radiation Science (MRS) is very limited thus this study analyses and explains potential gender differences in article authorship and acceptance for publication in the Journal of Medical Imaging and Radiation Sciences (JMIRS) for a 5-year period (2017-2021). METHODS: Gender was inferred based on the author's first name or title (e.g., Mr, Mrs or Ms). For those who left the title blank or reported as 'Dr' or 'Prof,' a series of steps were taken to identify their gender. Where gender was impossible to ascribe, these authors were excluded. Descriptive and inferential statistics are reported for the study population. Descriptive and inferential statistics are used. Percentages of females are reported, and males constitute the other portion. Chi-square, slope analysis and z-tests were used to test hypotheses. RESULTS: Results show that female authorship overall and in all categories of authorship placement (i.e., first, last and corresponding) increased over the timeframe reviewed. The percentage gain in the increase was higher than that for male authorship. However, male authorship started from a higher baseline in 2017 and has also increased year on year and overall, as well as in each placement category examined. More female authors were in the MRS sub-specialism Radiation Therapy (RT) than in the other MRS sub-specialisms. Analysis of the acceptance rate of articles with female authors shows a weak downward trend, and this may be related to higher submission and acceptance rates of articles by male authors during the same period. CONCLUSION: Male authors are overrepresented in all categories, which raises questions about the persistence of gender disparities in JMIRS authorship and article acceptance. Positive trends in female authorship indicate progress, yet there is the persistence of the significant under-representation of women in the Medical Radiation Sciences workforce in academic publishing. Recruiting more males to address the gender imbalance in the profession should not be at the expense of females' career progression.

Public Health Sciences

Caines A, **Trudeau S**, and **Gordon SC**. Evaluating the safety and efficacy of seladelpar for adults with primary biliary cholangitis. *Expert Opin Pharmacother* 2024; 25(11):1517-1523. PMID: 39107982.
Request Article

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INTRODUCTION: Seladelpar (MBX-8025) is a once-daily administered highly specific PPAR-δ agonist in Phase 3 and extension trials for use in patients with primary biliary cholangitis (PBC). AREAS COVERED: This review provides background on current treatment options for PBC, and summarizes clinical trial data regarding the safety and effectiveness of seladelpar within the context of these treatments. EXPERT OPINION: Clinical trials results demonstrate the safety and tolerability of seladelpar use for PBC, including in patients with cirrhosis. The primary composite endpoint (ALP <1.67 times ULN, decrease ≥ 15% from baseline, and TB ≤ULN) was met in 61.7% of the patients treated with seladelpar and in 20% receiving placebo ($p < 0.001$). Moreover, pruritus - a cardinal and often intractable symptom of PBC - was improved with seladelpar treatment, as were overall quality of life measurements.

Improvements in markers of inflammation were likewise observed. These biochemical and clinical findings therefore represent landmark developments in PBC treatment and offer a therapeutic option for PBC.

Public Health Sciences
Fulkerson PC, Lussier SJ, Bendixsen CG, Castina SM, Gebretsadik T, Marlin JS, Russell PB, Seibold MA, Everman JL, Moore CM, Snyder BM, Thompson K, Tregoning GS, Wellford S, Arbes SJ, Bacharier LB, Calatroni A, Camargo CA, Jr., Dupont WD, Furuta GT, Gruchalla RS, Gupta RS, Hershey GK, Jackson DJ, **Johnson CC**, Kattan M, Liu AH, Murrison L, O'Connor GT, Phipatanakul W, Rivera-Spoljaric K, Rothenberg ME, Seroogy CM, Teach SJ, **Zoratti EM**, Togias A, Hartert TV, and Heros Study Team O. Human Epidemiology and RespOnse to SARS-CoV-2 (HEROS): Objectives, Design and Enrollment Results of a 12-City Remote Observational Surveillance Study of Households with Children using Direct-to-Participant Methods. *Am J Epidemiol* 2024; Epub ahead of print. PMID: 38775275. Full Text

The Human Epidemiology and Response to SARS-CoV-2 (HEROS) is a prospective multi-city 6-month incidence study which was conducted from May 2020-February 2021. The objectives were to identify risk factors for SARS-CoV-2 infection and household transmission among children and people with asthma and allergic diseases, and to use the host nasal transcriptome sampled longitudinally to understand infection risk and sequelae at the molecular level. To overcome challenges of clinical study implementation due to the coronavirus pandemic, this surveillance study used direct-to-participant methods to remotely enroll and prospectively follow eligible children who are participants in other NIH-funded pediatric research studies and their household members. Households participated in weekly surveys and biweekly nasal sampling regardless of symptoms. The aim of this report is to widely share the methods and study instruments and to describe the rationale, design, execution, logistics and characteristics of a large, observational, household-based, remote cohort study of SARS-CoV-2 infection and transmission in households with children. The study enrolled a total of 5,598 individuals, including 1,913 principal participants (children), 1,913 primary caregivers, 729 secondary caregivers and 1,043 other household children. This study was successfully implemented without necessitating any in-person research visits and provides an approach for rapid execution of clinical research.

Public Health Sciences
Grady SC, Pavan A, **Qiong Z**, Rachael P, and Ligmann-Zielinska A. COVID-19 in nursing homes: Geographic diffusion and regional risk factors from January 1 to July 26, 2020 of the pandemic. *PLoS One* 2024; 19(8):e0308339. PMID: 39146332. Full Text

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BACKGROUND: COVID-19 deaths in nursing homes accounted for 30.2% of all COVID-19 deaths in the United States during the early weeks (1-January to 26-July, 2020) of the pandemic. This study presents the geographic diffusion of COVID-19 cases and deaths in nursing homes during this time period, while also providing explanation of regional risk factors. METHODS AND FINDINGS: Nursing home COVID-19 data on confirmed cases (n = 173,452) and deaths (n = 46,173) were obtained from the Centers for Medicare and Medicaid Services. Weekly COVID-19 case counts were spatially smoothed to identify nursing homes in areas of high COVID-19 infection. Bivariate spatial autocorrelation was used to visualize High vs. Low-case counts and related deaths. Zero-inflated negative binomial models were estimated within Health and Human Service (HHS) Regions at three-week intervals to evaluate facility and area-level risk factors. The first reported nursing home resident to die of COVID-19 was in the state of Washington on 28-February, 2020. By 24-May, 2020 there were simultaneous epicenters in the Northeast (HHS Regions 1 and 2) and Midwest (HHS Region 5) with diffusion into the South (HHS Regions 4 and 6) from 15-June to 5-July, 2020. The case-fatality rate was highest from 25-May to 14-June, 2020 (30.9 deaths per 1000 residents); thereafter declining to 24.1 (15-June to 5-July, 2020) and

19.4 (6-July to 26-July, 2020) (overall case-fatality rate 1-January to 26-July = 26.6). Statistically significant risk factors for COVID-19 deaths were admission of patients with COVID-19 into nursing homes, staff confirmed infections and nursing shortages. COVID-19 deaths were likely to occur in nursing homes in high minority and non-English speaking neighborhoods and neighborhoods with a high proportion of households with disabilities. CONCLUSIONS: Enhanced communication between HHS regional administrators about "lessons learned" could provide receiving state health departments with timely information to inform clinical practice to prevent premature death in nursing homes in future pandemics.

Public Health Sciences

Issaka RB, Ibekwe LN, Todd KW, Burnett-Hartman AN, Clark CR, Del Vecchio NJ, Kamineni A, **Neslund-Dudas C**, Chubak J, Corley DA, Haas JS, Honda SA, Li CI, Winer RL, and Pruitt SL. Association between racial residential segregation and screening uptake for colorectal and cervical cancer among Black and White patients in five US health care systems. *Cancer* 2024; Epub ahead of print. PMID: 39119731. Full Text

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BACKGROUND: Despite increased recognition that structural racism contributes to poorer health outcomes for racial and ethnic minorities, there are knowledge gaps about how current patterns of racial residential segregation are associated with cancer screening uptake. The authors examined associations between Black residential segregation and screening for colorectal cancer (CRC) and cervical cancer among non-Hispanic Black and non-Hispanic White adults. METHODS: This was a retrospective study of CRC and cervical cancer screening-eligible adults from five health care systems within the Population-Based Research to Optimize the Screening Process (PROSPR II) Consortium (cohort entry, 2010-2012). Residential segregation was measured using site-specific quartiles of the Black local isolation score (LIS). The outcome was receipt of CRC or cervical cancer screening within 3 years of cohort entry (2010-2015). Logistic regression was used to calculate associations between the LIS and screening completion, adjusting for patient-level covariates. RESULTS: Among CRC (n = 642,661) and cervical cancer (n = 163,340) screening-eligible patients, 456,526 (71.0%) and 106,124 (65.0%), respectively, received screening. Across PROSPR sites, living in neighborhoods with higher LIS tended to be associated with lower odds of CRC screening (Kaiser Permanente Northern California: adjusted odds ratio [aOR] LIS trend in Black patients, 0.95 [p < .001]; aOR LIS trend in White patients, 0.98 [p < .001]; Kaiser Permanente Southern California: aOR LIS trend in Black patients, 0.98 [p = .026]; aOR LIS trend in White patients, 1.01 [p = .023]; Kaiser Permanente Washington: aOR LIS trend in White patients, 0.97 [p = .002]. However, for cervical cancer screening, associations with the LIS varied by site and race

(Kaiser Permanente Washington: aOR LIS trend in White patients, 0.95 [p < .001]; Mass General Brigham: aOR LIS trend in Black patients, 1.12 [p < .001]; aOR LIS trend in White patients, 1.03 [p < .001]). CONCLUSIONS: Across five diverse health care systems, the direction of the association between Black residential segregation and screening varied by PROSPR site, race, and screening type. Additional research, including studies that examine multiple dimensions of segregation and structural racism using intersectional approaches, are needed to further disentangle these relationships.

Public Health Sciences

Ma KC, Surie D, Lauring AS, Martin ET, Leis AM, Papalambros L, Gaglani M, Columbus C, Gottlieb RL, Ghamande S, Peltan ID, Brown SM, Ginde AA, Mohr NM, Gibbs KW, Hager DN, Saeed S, Prekker ME, Gong MN, Mohamed A, Johnson NJ, Srinivasan V, Steingrub JS, Khan A, Hough CL, Duggal A, Wilson JG, Qadir N, Chang SY, Mallow C, Kwon JH, Parikh B, Exline MC, **Vaughn IA**, **Ramesh M**, Safdar B, Mosier J, Harris ES, Shapiro NI, Felzer J, Zhu Y, Grijalva CG, Halasa N, Chappell JD, Womack KN, Rhoads JP, Baughman A, Swan SA, Johnson CA, Rice TW, Casey JD, Blair PW, Han JH, Ellington S, Lewis NM, Thornburg N, Paden CR, Atherton LJ, Self WH, Dawood FS, and DeCuir J. Effectiveness of Updated 2023-2024 (Monovalent XBB.1.5) COVID-19 Vaccination Against SARS-CoV-2 Omicron XBB and BA.2.86/JN.1 Lineage Hospitalization and a Comparison of Clinical Severity-IVY Network, 26 Hospitals, October 18, 2023-March 9, 2024. *Clin Infect Dis* 2024; Epub ahead of print. PMID: 39107255.
Full Text

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Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York, USA.
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Cleveland Clinic, Cleveland, Ohio, USA.
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BACKGROUND: Assessing variant-specific COVID-19 vaccine effectiveness (VE) and severity can inform public health risk assessments and decisions about vaccine composition. BA.2.86 and its descendants, including JN.1 (referred to collectively as "JN lineages"), emerged in late 2023 and exhibited substantial divergence from co-circulating XBB lineages. METHODS: We analyzed patients hospitalized with COVID-19-like illness at 26 hospitals in 20 U.S. states admitted October 18, 2023-March 9, 2024. Using a test-negative, case-control design, we estimated effectiveness of an updated 2023-2024 (Monovalent XBB.1.5) COVID-19 vaccine dose against sequence-confirmed XBB and JN lineage hospitalization using logistic regression. Odds of severe outcomes, including intensive care unit (ICU) admission and invasive

mechanical ventilation (IMV) or death, were compared for JN versus XBB lineage hospitalizations using logistic regression. RESULTS: 585 case-patients with XBB lineages, 397 case-patients with JN lineages, and 4,580 control-patients were included. VE in the first 7-89 days after receipt of an updated dose was 54.2% (95% CI = 36.1%-67.1%) against XBB lineage hospitalization and 32.7% (95% CI = 1.9%-53.8%) against JN lineage hospitalization. Odds of ICU admission (adjusted odds ratio [aOR] 0.80; 95% CI = 0.46-1.38) and IMV or death (aOR 0.69; 95% CI = 0.34-1.40) were not significantly different among JN compared to XBB lineage hospitalizations. CONCLUSIONS: Updated 2023-2024 COVID-19 vaccination provided protection against both XBB and JN lineage hospitalization, but protection against the latter may be attenuated by immune escape. Clinical severity of JN lineage hospitalizations was not higher relative to XBB.

Public Health Sciences

Maghfour J, Genelin X, Olson J, **Wang A**, **Schultz L**, and Blalock TW. The epidemiology of dermatofibrosarcoma protuberans incidence, metastasis, and death among various population groups: A Surveillance, Epidemiology, and End Results database analysis. *J Am Acad Dermatol* 2024; Epub ahead of print. PMID: 38908718. Full Text

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BACKGROUND: Limited information exists regarding the epidemiology, metastasis, and survival of dermatofibrosarcoma protuberans (DFSP). OBJECTIVE: To measure DFSP incidence and assess metastasis and survival outcomes. METHODS: Incidence rate, overall and DFSP-specific survival outcomes for primary DFSP tumors contained in the Surveillance, Epidemiology, and End Results (SEER) registry were analyzed via quasi-Poisson regression, Cox, and competing risk analyses. RESULTS: DFSP incidence rate was 6.25 (95% CI, 5.93-6.57) cases per million person-years with significantly higher incidence observed among Black individuals than White individuals (8.74 vs 4.53). DFSP with larger tumor size (≥3 cm, odds ratio [OR]: 2.24; 95% CI, 1.62-3.12; P < .001) and tumors located on the head and neck (OR: 4.88; 95% CI, 3.31-7.18; P < .001), and genitalia (OR: 3.16; 95% CI, 1.17-8.52; P = .023) were associated with significantly increased risk of metastasis whereas higher socioeconomic status was associated with significantly decreased risk of metastasis. Larger tumor size (≥3 cm), regardless of location, and age (≥60 years) were associated with significantly worse overall and cancer-specific survival. LIMITATIONS: Retrospective design of SEER. CONCLUSION: DFSP incidence is 2-fold higher among Black than White individuals. The risk of DFSP metastasis is significantly increased with tumor size ≥3 cm and tumors located on head and neck, and genitalia. Larger tumor size (≥ 3 cm), regardless of location, and age (≥60 years) are the most important prognostic indicators of survival.

Public Health Sciences

Platt A, Truong T, Boulos M, Carlson NE, Desai M, Elam MM, Slade E, Hanlon AL, Hurst JH, Olsen MK, **Poisson LM**, Rende L, and Pomann GM. A guide to successful management of collaborative partnerships in quantitative research: An illustration of the science of team science. *Stat (Int Stat Inst)* 2024; 13(2). PMID: 39176388. Full Text

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Data-intensive research continues to expand with the goal of improving healthcare delivery, clinical decision-making, and patient outcomes. Quantitative scientists, such as biostatisticians, epidemiologists, and informaticists, are tasked with turning data into health knowledge. In academic health centres, quantitative scientists are critical to the missions of biomedical discovery and improvement of health. Many academic health centres have developed centralized Quantitative Science Units which foster dual goals of professional development of quantitative scientists and producing high quality, reproducible domain research. Such units then develop teams of quantitative scientists who can collaborate with researchers. However, existing literature does not provide guidance on how such teams are formed or how to manage and sustain them. Leaders of Quantitative Science Units across six institutions formed a working group to examine common practices and tools that can serve as best practices for Quantitative Science Units that wish to achieve these dual goals through building long-term partnerships with researchers. The results of this working group are presented to provide tools and guidance for Quantitative Science Units challenged with developing, managing, and evaluating Quantitative Science Teams. This guidance aims to help Quantitative Science Units effectively participate in and enhance the research that is conducted throughout the academic health centre-shaping their resources to fit evolving research needs.

Public Health Sciences

Shamaa O, Ahmed A, **Rupp L**, **Trudeau S**, and **Gordon SC**. Beyond the Surface: Unveiling Hidden Hurdles to Primary Biliary Cholangitis Care. *Cureus* 2024; 16(7):e64753. PMID: 39156427. Full Text

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INTRODUCTION: Ursodeoxycholic acid (UDCA) slows disease progression among patients with primary biliary cholangitis (PBC), yet not all patients receive this standard-of-care medication. Our study aims to identify reasons why PBC patients did not receive the recommended UDCA treatment. METHODS: Using medical record data collected by the Fibrotic Liver Disease (FOLD) Consortium for 2006-2016, we identified PBC patients from a single site with no UDCA therapy record. Two independent reviewers used a structured data collection instrument to systematically confirm and record the reasons for the lack of treatment. RESULTS: Among 494 PBC patients (11% men and 13.2% Black patients) with a median follow-up of 5.2 years, 35 (7%) had never received UDCA (16% men and 24% Black patients). Of these, 18 (51%) had laboratory indications of PBC but were not formally diagnosed. Among the remaining 17 patients with recognized PBC, six were never offered UDCA, seven declined treatment, and four remained untreated despite being offered treatment. We did not find a statistically significant association between the lack of PBC diagnosis and treatment and patients' age ($p = 0.139$), gender ($p = 0.222$), race ($p = 0.081$), or insurance coverage ($p = 0.456$), perhaps due to our small sample size. CONCLUSIONS: Multiple factors influencing the lack of evaluation and treatment in PBC patients were identified at the provider and patient levels. The most common reasons included financial barriers, loss to follow-up, severe decompensated disease at diagnosis, and lack of referral to specialists for further evaluation. Future interventions targeting modifiable provider and patient barriers may improve rates and timeliness of PBC diagnosis and treatment.

Public Health Sciences

Smith N, **Kwon Kim S**, **Goyert G**, **Lin CH**, **Rose C**, and **Pitts DS**. Nifedipine outperforms labetalol: A comparative analysis of hypertension management in black pregnancies. *Pregnancy Hypertens* 2024; 37:101147. PMID: 39153458. Full Text

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BACKGROUND: Nifedipine has previously exhibited superior efficacy to labetalol in managing hypertension in the non-pregnant Black population, establishing itself as a first-line treatment option. However, the unique challenges of hypertension during pregnancy, especially prevalent in Black individuals, remain underexplored in terms of effective medication choices. This gap highlights the need for targeted research on antihypertensive efficacy specifically within this population. OBJECTIVE: This study aims to evaluate the effectiveness of nifedipine versus labetalol in managing blood pressure in Black pregnancies. The primary measure is the mean systolic and diastolic blood pressure trajectories throughout pregnancy, determining the superiority of nifedipine in this context. STUDY DESIGN: A retrospective cohort study was conducted at a multi-center institution in the metropolitan Detroit area, encompassing data from 1,235 Black pregnancies affected by chronic hypertension between 2015 and 2022. Mean blood pressure trajectories during pregnancy were fit by linear mixed effects model with a random intercept and time effect. RESULTS: Patients on nifedipine had an estimated 2.08 mmHg lower mean systolic and 1.60 mmHg lower mean diastolic blood pressure compared to those on labetalol, with significant p-values of 0.040 and 0.028. Additionally, nifedipine users were less likely to need increased doses, with an odds ratio of 0.28 (95 % CI: 0.19-0.40, $p < 0.001$) compared to labetalol users. CONCLUSION: This study provides compelling evidence that nifedipine outperforms labetalol in managing blood pressure during Black pregnancies. These findings suggest that the initiation of nifedipine should be considered in the management of chronic hypertension among Black pregnant individuals, offering a potentially more effective treatment option.

Public Health Sciences

Tinsley SA, **Arora S**, **Stephens A**, **Finati M**, **Chiarelli G**, **Cirulli GO**, **Morrison C**, **Richard C**, **Hares K**, **Rogers CG**, and **Abdollah F**. The impact of cannabis use disorder on urologic oncologic surgery morbidity, length of stay, and inpatient cost: analysis of the National Inpatient Sample from 2003 to 2014. *World J Urol* 2024; 42(1):465. PMID: 39090376. Full Text

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PURPOSE: This study examined the impact of cannabis use disorder (CUD) on inpatient morbidity, length of stay (LOS), and inpatient cost (IC) of patients undergoing urologic oncologic surgery. METHODS: The National Inpatient Sample (NIS) from 2003 to 2014 was analyzed for patients undergoing prostatectomy, nephrectomy, or cystectomy ($n = 1,612,743$). CUD was identified using ICD-9 codes. Complex-survey procedures were used to compare patients with and without CUD. Inpatient major complications, high LOS (4th quartile), and high IC (4th quartile) were examined as endpoints. Univariable and multivariable analysis (MVA) were performed to compare groups. RESULTS: The incidence of CUD increased from 51 per 100,000 admissions in 2003 to 383 per 100,000 in 2014 ($p < 0.001$). Overall, 3,503 admissions had CUD. Patients with CUD were more frequently younger (50 vs. 61), male (86% vs. 78.4%), Black (21.7% vs. 9.2%), and had 1st quartile income (36.1% vs. 20.6%); all $p < 0.001$. CUD had no impact on any complication rates (all $p > 0.05$). However, CUD patients had higher LOS (3 vs. 2 days; $p < 0.001$) and IC ($15,609 vs. $12,415; $p < 0.001$). On MVA, CUD was not an independent predictor of major complications ($p = 0.6$). Conversely, CUD was associated with high LOS (odds ratio (OR) 1.31; 95% CI 1.08-1.59) and high IC (OR 1.33; 95% CI 1.12-1.59), both $p < 0.01$. CONCLUSION: The incidence of CUD at the time of urologic oncologic surgery is increasing. Future

research should look into the cause of our observed phenomena and how to decrease LOS and IC in CUD patients.

Public Health Sciences

Wesselink AK, Claus Henn B, Fruh V, Geller RJ, Coleman CM, Schildroth S, Sjodin A, Bethea TN, Noel NL, Baird DD, **Wegienka G**, and Wise LA. Persistent endocrine-disrupting chemicals and incident uterine leiomyomata: A mixtures analysis. *Sci Total Environ* 2024; 951:175871. PMID: 39216750. Request Article

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BACKGROUND: Uterine leiomyomata (UL; fibroids) are hormone-dependent neoplasms that can cause significant gynecologic morbidity. Studies have documented associations between concentrations of persistent endocrine-disrupting chemicals (EDCs) and UL incidence; however, few have assessed the effects of EDC mixtures on UL. METHODS: In the Study of Environment, Lifestyle, and Fibroids, a prospective cohort study, participants attended study visits at baseline and approximately every 20 months for up to 10 years; at each visit, they completed questionnaires, provided blood samples, and underwent standardized ultrasound examinations. In baseline plasma samples (n = 1155), we quantified concentrations of polychlorinated biphenyls (PCBs), polybrominated diphenyl ethers (PBDEs), and organochlorine pesticides using high-resolution mass spectrometry. We selected nine EDCs detected in >60 % of samples (4 PCBs, 4 PBDEs, and 2,2-bis(4-chlorophenyl)-1,1-dichloroethene (p,p'-DDE)) and conducted probit Bayesian kernel machine regression with hierarchical variable selection to estimate effects of the EDC mixture and individual EDCs on UL incidence, adjusting for potential confounders. RESULTS: During 10 years of follow-up, 32 % of participants developed ultrasound-detected UL. The EDC mixture was not appreciably associated with the probit of UL (β comparing all EDCs at their 75th vs. 50th percentile:= - 0.01, 95 % credible interval [CrI]: -0.11, 0.10). However, individual EDC concentrations were associated with UL in opposing directions: PCB138/158 was positively associated with UL (β for 25th-to-75th-percentile increase when all other chemicals were set to their 50th percentile = 0.18, 95 % CrI: -0.09, 0.44), whereas PBDE99 and p,p'-DDE were inversely associated with UL (β = -0.06, 95 % CrI: -0.21, 0.10 and β = -0.12, 95 % CrI: -0.34, 0.10, respectively). There was little evidence of interaction between EDCs. CONCLUSION: In this prospective ultrasound study, a mixture of persistent EDCs was not appreciably associated with incident UL during 10 years of follow-up, but individual EDCs were associated with UL in opposite directions.

Public Health Sciences

White MC, Osazuwa-Peters OL, Abouelella DK, Barnes JM, Cannon TY, Watts TL, **Adjei Boakye E**, and Osazuwa-Peters N. Trends and factors associated with receipt of human papillomavirus (HPV) vaccine in private, public, and alternative settings in the United States. *Vaccine* 2024; 42(22):126036. PMID: 38876838. Full Text

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BACKGROUND: One of the goals of the President's Cancer Panel was to maximize access to human papillomavirus (HPV) vaccination through expansion of alternative settings for receiving the vaccine, such as in public health settings, schools, and pharmacies. METHODS: In a cross-sectional analysis, we utilized the National Immunization Survey-Teen data from 2014 to 2020 (n = 74,645) to describe trends and factors associated with HPV vaccine uptake in private, public, and alternative settings. We calculated annual percent change (APC) between 2014 and 2020, estimating rate of HPV vaccine uptake across settings. Using multinomial logistic regression, we estimated the odds of receipt of HPV vaccine in public health settings and other alternative settings compared to private healthcare settings, adjusting for sociodemographic covariates. RESULTS: We found a 5 % annual increase in the use of private facilities between 2014-2018 (APC = 5.3; 95 % CI 3.4, 7.1), and almost 7 % between 2018-2020 (APC = 6.7; 95 % CI 1.4, 12.3). Adjusted multinomial logistic regression analyses found that odds of receiving vaccinations at a public facility vs. a private facility increased almost two times for adolescents living below poverty (aOR = 1.82, 95 % CI: 1.60, 2.08) compared to above poverty. Additionally, adolescents without physician recommendations had lower odds of receiving vaccines at public versus private facilities (aOR = 1.75, 95 % CI: 1.44, 2.12). Finally, odds of receiving HPV vaccines at public facilities vs. private facilities decreased by 33 % for White adolescents (aOR = 0.67, 95 % CI: 0.57, 0.78) versus Black adolescents. CONCLUSIONS: Sociodemographic factors such as race, and socioeconomic factors such as poverty level, and receipt of physician HPV recommendations are associated with receiving the vaccine at private settings vs. public health facilities and alternative settings. This information is important in strengthening alternative settings for HPV vaccine uptake to increase access to the vaccine among disadvantaged individuals.

Pulmonary and Critical Care Medicine

Lee Adawi Awdish R, **Grafton G**, and Berry LL. Never-Words: What Not to Say to Patients With Serious Illness. *Mayo Clin Proc* 2024; Epub ahead of print. PMID: 39177542. Full Text

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Pulmonary and Critical Care Medicine

Liske J, **Patel N**, **Makowski C**, **Awdish R**, and **Smith ZR**. Risk evaluation and mitigation strategy compliance for pulmonary hypertension medications after policy implementation with computerized provider order entry support. *Am J Health Syst Pharm* 2024; Epub ahead of print. PMID: 39096261. Full Text

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are posted online before technical formatting and author proofing. These manuscripts are not the final version of record and will be replaced with the final article (formatted per AJHP style and proofed by the authors) at a later time. PURPOSE: Treatment for pulmonary hypertension includes medications with risk evaluation and mitigation strategy (REMS) programs. Health-system inpatient pharmacies dispensing these agents must comply with inpatient REMS dispensing criteria. Implementing a health-system policy with computerized provider order entry (CPOE) decision support may improve REMS compliance. METHODS: This was a retrospective, quasi-experimental study comparing REMS compliance before and after development of a policy with CPOE decision support that was implemented in August 2019. Patients 18 years of age or older with a diagnosis of pulmonary hypertension were included if they received at least one dose of an endothelin receptor antagonist or riociguat while hospitalized. Patients were included in the preintervention group if they were hospitalized between August 1, 2017, and August 31, 2019, and in the postintervention group if they were hospitalized between September 1, 2019, and August 31, 2021. The primary outcome was the REMS compliance rate. Secondary endpoints included the time to REMS compliance and independent factors associated with failed or delayed REMS compliance. RESULTS: A total of 150 patients were included, with 75 patients in both the pre- and postintervention groups. Compliance increased significantly from the preintervention (50%) to postintervention (92%) group ($P < 0.001$). Time to compliance was also significantly reduced from 770 minutes in the preintervention group to 140 minutes in the postintervention group ($P = 0.031$). Factors independently associated with REMS compliance were being in the postintervention group (odds ratio, 16.9; 95% confidence interval, 5.8-49.2) and being admitted to a pulmonary hypertension center for comprehensive care. (odds ratio, 7.8; 95% confidence interval, 2.9-21.2). CONCLUSION: A health-system policy with CPOE decision support improved both the rate of and time to compliance with inpatient REMS dispensing procedures.

Pulmonary and Critical Care Medicine

Lisznyai E, **Hutchings H**, **Debiane L**, and **Okereke I**. Central airway carcinoid tumor mimicking chronic asthma and necessitating pneumonectomy: A case report. *Int J Surg Case Rep* 2024; 122:110167. PMID: 39137644. Full Text

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INTRODUCTION: Central airway tumors can occasionally be misdiagnosed as a chronic disease. We present a case of a central airway carcinoid tumor that was mistaken as chronic asthma for many years. PRESENTATION OF CASE: A 29-year-old male bodybuilder presented to our emergency department with shortness of breath and hemoptysis. He was an avid bodybuilder who participated in competitions. He had been diagnosed with asthma for years and used an albuterol inhaler chronically. Computed tomography of the chest showed diffuse opacification of the left hemithorax, multiple air-fluid levels and a 4-cm mass of the proximal left mainstem bronchus with intraluminal calcifications. Bronchoscopy demonstrated a large endobronchial mass, and biopsy was positive for typical carcinoid tumor. Stabilization was achieved with rigid bronchoscopy and partial endobronchial debridement of the tumor to allow some patency to the left lung. After stabilization, he subsequently underwent left pneumonectomy. He recovered well and was discharged home on postoperative day 2. On surveillance 2.5 years after pneumonectomy, he has resumed bodybuilding and has no evidence of recurrent disease. DISCUSSION: Proximal airway tumors can mimic asthma. Careful management can achieve successful results even in very complex cases. There should be an increased level of suspicion for other diagnoses, especially in young and healthy individuals with asthma that is refractory to medical treatment. CONCLUSION: Proximal airway tumors can mimic chronic diseases such as asthma. Other diagnoses should be considered, especially in young and health individuals with asthma symptoms that do not respond to conventional therapies.

Pulmonary and Critical Care Medicine

Xie F, Zhang Q, Mu C, Zhang Q, Yang H, Mao J, **Simoff MJ**, Huang J, Zhang X, and Sun J. Shape-sensing Robotic-assisted Bronchoscopy (SS-RAB) in Sampling Peripheral Pulmonary Nodules: A Prospective, Multicenter Clinical Feasibility Study in China. *J Bronchology Interv Pulmonol* 2024; 31(4). PMID: 39115240. Full Text

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BACKGROUND: The ION system is a shape-sensing robotic-assisted bronchoscopy (SS-RAB) platform developed to biopsy peripheral pulmonary nodules (PPNs). There is a lack of data describing the use of this system in the Chinese population. The study aimed to assess the feasibility and safety of using SS-RAB to diagnose PPNs across multiple centers within China. METHODS: This prospective, multicenter study used SS-RAB in consecutive patients with solid or sub-solid PPNs 8 to 30 mm in largest diameter. Primary endpoints were diagnostic yield and the rates of procedure- or device-related complications. Radial endobronchial ultrasound (rEBUS) was to confirm lesion localization, followed by sampling, using the Flexision biopsy needle, biopsy forceps, and cytology brush. Subjects with nonmalignant index biopsy results were followed up to 6 months. RESULTS: A total of 90 PPNs were biopsied from 90 subjects across 3 centers using SS-RAB. The median nodule size was 19.4 mm (IQR: 19.3, 24.6) in the largest dimension. In all (100%) cases, the catheter successfully reached the target nodule with tissue samples obtained. The diagnostic yield was 87.8% with a sensitivity for malignancy of 87.7% (71/81). In a univariate analysis, nodule lobar location, presence of bronchus sign, and rEBUS view were associated with a diagnostic sample, but only rEBUS view showed an association in a multivariate analysis. The overall pneumothorax rate was 1.1% without pneumothorax requiring intervention, and there was no periprocedural bleeding. CONCLUSION: As an emerging technology in the Chinese population, SS-RAB can safely biopsy PPNs with strong diagnostic performance.

Rehabilitation Services/Physical Therapy/Occupational Health

Daniels CJ, Cupler ZA, Napuli JG, Walsh RW, Ziegler AL, Meyer KW, Knieper MJ, Walters SA, Salsbury SA, Trager RJ, Gliedt JA, Young MD, Anderson KR, Kirk EJ, Mooring SA, Battaglia PJ, Paris DJ, **Brown AG**, Goehl JM, and Hawk C. Development of Preliminary Integrated Health Care Clinical Competencies for United States Doctor of Chiropractic Programs: A Modified Delphi Consensus Process. *Glob Adv Integr Med Health* 2024; 13:27536130241275944. PMID: 39157778. Full Text

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BACKGROUND: There has been rapid growth of chiropractors pursuing career opportunities in both public and private hospitals and other integrated care settings. Chiropractors that prosper in integrated care settings deliver patient-centered care, focus on the institutional mission, understand and adhere to organizational rules, and are proficient in navigating complex systems. The Council on Chiropractic Education Accreditation Standards do not outline specific meta-competencies for integrated care clinical training. OBJECTIVE: The purpose of this study was to develop preliminary integrated health care competencies for DC programs to guide the advancement of clinical chiropractic education. METHODS: A systematic literature search was performed. Articles were screened for eligibility and extracted in duplicate. Domains and seed statements were generated from this literature, piloted at a conference workshop, and evaluated via a modified Delphi consensus process. Of 42 invited, 36 chiropractors participated as panelists. Public comment period yielded 20 comments, none resulting in substantive changes to the competencies. RESULTS: Of 1718 citations, 23 articles met eligibility criteria. After 2 modified Delphi rounds, consensus was reached on all competency statements. A total of 78 competency statements were agreed upon, which encompassed 4 domains and 11 subdomains. The 4 domains were: 1) Collaboration, (2) Clinical Excellence, (3) Communication, and (4) Systems Administration. CONCLUSION: We identified 78 preliminary competencies appropriate for preparing DC students and early career chiropractors for clinical practice in integrated healthcare settings. Educational programs may consider these competencies for curricular design and reform to strengthen DC program graduates for integrated practice, advanced training, and employment.

Research Administration

Duarte JD, Thomas CD, Lee CR, Huddart R, Agundez JAG, Baye JF, Gaedigk A, Klein TE, **Lanfear DE**, Monte AA, Nagy M, Schwab M, Stein CM, Uppugunduri CRS, van Schaik RHN, Donnelly RS, Caudle KE, and Luzum JA. Clinical Pharmacogenetics Implementation Consortium Guideline (CPIC) for CYP2D6, ADRB1, ADRB2, ADRA2C, GRK4, and GRK5 Genotypes and Beta-Blocker Therapy. *Clin Pharmacol Ther* 2024; Epub ahead of print. PMID: 38951961. Full Text

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Beta-blockers are widely used medications for a variety of indications, including heart failure, myocardial infarction, cardiac arrhythmias, and hypertension. Genetic variability in pharmacokinetic (e.g., CYP2D6) and pharmacodynamic (e.g., ADRB1, ADRB2, ADRA2C, GRK4, GRK5) genes have been studied in relation to beta-blocker exposure and response. We searched and summarized the strength of the evidence linking beta-blocker exposure and response with the six genes listed above. The level of evidence was high for associations between CYP2D6 genetic variation and both metoprolol exposure and heart rate response. Evidence indicates that CYP2D6 poor metabolizers experience clinically significant greater exposure and lower heart rate in response to metoprolol compared with those who are not poor metabolizers. Therefore, we provide therapeutic recommendations regarding genetically predicted CYP2D6 metabolizer status and metoprolol therapy. However, there was insufficient evidence to make therapeutic recommendations for CYP2D6 and other beta-blockers or for any beta-blocker and the other five genes evaluated (updates at www.cpicpgx.org).

Sleep Medicine

Dauvilliers Y, **Roth T**, Bogan R, Thorpy MJ, Morse AM, Ascencion F, and Gudeman J. Improvements in daytime sleepiness and disrupted nighttime sleep with once-nightly sodium oxybate in people with narcolepsy type 1 and type 2: a plain language summary. *J Comp Eff Res* 2024; 13(9):e240031. PMID: 39088033. Full Text

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WHAT IS THIS SUMMARY ABOUT? This is a plain language summary of a published article in the journal Sleep. Narcolepsy is a sleep condition that has 2 different subtypes: narcolepsy type 1 and narcolepsy type 2. These are called NT1 and NT2 for short. Sodium oxybate (SXB) is approved to treat excessive daytime sleepiness (EDS) and cataplexy. People with NT1 and NT2 both have EDS, but cataplexy is only present in people with NT1. Limited information is available about how SXB works in people with NT2. This is because previous trials have included only people with NT1 or people with unspecified narcolepsy. For more than 20 years, the only available formulation of this medicine had to be given twice during the night. Many people with narcolepsy find that chronically waking up in the middle of the night for a second dose of SXB is disruptive to themselves or others in their household. People have also reported sleeping through alarm clocks, missing their second dose, and feeling worse the next day. Some people have accidentally taken the second dose too early, putting them at risk for serious adverse effects. These adverse effects may include slow breathing, low blood pressure, or sedation. The US Food and Drug Administration (FDA) approved a medicine called LUMRYZ(™) (sodium oxybate) for extended-release oral suspension in May 2023. LUMRYZ is a once-nightly formulation of SXB (ON-SXB for short) and is taken as a single dose before bedtime. This medicine treats EDS and muscle weakness (also known as cataplexy) in people with narcolepsy. A clinical trial called REST-ON studied ON-SXB to find out if it was better at treating narcolepsy symptoms than a medicine with no active ingredients (placebo). This summary describes a study that tested whether ON-SXB was better than placebo at treating narcolepsy symptoms in people with NT1 or NT2. WHAT WERE THE RESULTS? This study showed that compared to people who took placebo, people who took ON-SXB were able to stay awake longer during the day, felt less sleepy during the daytime, had less cataplexy, and had more improvements in their symptoms overall than people who took placebo. WHAT DO THE RESULTS MEAN? ON-SXB has been proven effective for people with NT1 or NT2. Unlike prior formulations of SXB, ON-SXB is taken once at bedtime, without requiring waking up in the middle of the night for a second dose.

Sleep Medicine
Garcia-Borreguero D, Black J, Earley CJ, Fulda S, Högl B, Manconi M, Ondo W, **Roth T**, Trenkwalder C, and Winkelman JW. Rethinking clinical trials in restless legs syndrome: A roadmap. *Sleep Med Rev* 2024; 77:101978. PMID: 39102777. Full Text

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The number of large clinical trials of restless legs syndrome (RLS) have decreased in recent years, this coincides with reduced interest in developing and testing novel pharmaceuticals. Therefore, the International Restless Legs Syndrome Study Group (IRLSSG) formed a task force of global experts to

examine the causes of these trends and make recommendations to facilitate new clinical trials. In our article, we delve into potential complications linked to the diagnostic definition of RLS, identify subpopulations necessitating more attention, and highlight issues pertaining to endpoints and study frameworks. In particular, we recommend developing alternative scoring methods for more accurate RLS diagnosis, thereby improving clinical trial specificity. Furthermore, enhancing the precision of endpoints will increase study effect sizes and mitigate study costs. Suggestions to achieve this include developing online, real-time sleep diaries with high-frequency sampling of nightly sleep latency and the use of PLMs as surrogate markers. Furthermore, to reduce the placebo response, strategies should be adopted that include placebo run-in periods. As RLS is frequently a chronic condition, priority should be given to long-term studies, using a randomized, placebo-controlled, withdrawal design. Lastly, new populations should be investigated to develop targeted treatments such as mild RLS, pregnancy, hemodialysis, or iron-deficient anemia.

Sleep Medicine

Roth T, Morse AM, Bogan R, Roy A, Gudeman J, and Dauvilliers Y. Weight Loss With Once-nightly Sodium Oxybate for the Treatment of Narcolepsy: Analysis From the Phase III Randomized study Evaluating the efficacy and SafeTy of a ONce nightly formulation of sodium oxybate (REST-ON) Trial. *Clin Ther* 2024; Epub ahead of print. PMID: 39153911. Full Text

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PURPOSE: Individuals with narcolepsy are more likely to be obese than the general population. Changes in weight-related measures with extended-release, once-nightly sodium oxybate (ON-SXB) and characteristics of participants with ≥5% weight loss were assessed in a Randomized study Evaluating the efficacy and SafeTy of a ONce nightly formulation of sodium oxybate (REST-ON) trial post hoc analysis. METHODS: REST-ON (NCT02720744) was a Phase III, double-blind, placebo-controlled, multicenter, randomized clinical trial. Participants aged ≥16 years with narcolepsy type 1 (NT1) or NT2 received ON-SXB or placebo for 13 weeks (week 1, 4.5 g; weeks 2-3, 6 g; weeks 4-8, 7.5 g; and weeks 9-13, 9 g). Weight and body mass index were measured at baseline and study end. FINDINGS: Weights were similar between groups at baseline (mean [SD]; ON-SXB, 81.2 [20.8] kg; N = 107 [NT1, n = 80; NT2, n = 27]; placebo, 82.1 [22.5] kg; N = 105 [NT1, n = 82; NT2, n = 23]). At week 13 (9 g), mean (SD) weight decreased 1.3 (3.6) kg with ON-SXB and increased 0.2 (2.6) kg with placebo; 17.8% (19/107; NT1, n = 14; NT2, n = 5) of participants receiving ON-SXB had ≥5% weight loss versus 3.8% receiving placebo (4/105; NT1, n = 3; NT2, n = 1; P = 0.001). At week 13, least squares mean (SE) body mass index change from baseline was –0.51 (0.13) kg/m(2) with ON-SXB and 0.08 (0.13) kg/m(2) with placebo (least squares mean difference [95% CI], -0.59 [-0.95 to -0.23] kg/m(2); P = 0.001). Excessive daytime sleepiness improved for both groups with ON-SXB, the ≥5% weight-loss subgroup exhibited larger improvement in the Maintenance of Wakefulness Test and Epworth Sleepiness Scale versus the other subgroup (weight loss <5%, no change, or weight gain) (Maintenance of Wakefulness Test, P = 0.019; Epworth Sleepiness Scale score, P < 0.001). IMPLICATIONS: Narcolepsy is often associated with obesity, which may increase cardiometabolic risks. ON-SXB, an effective treatment for excessive daytime sleepiness and cataplexy, may be preferred in overweight or obese individuals to provide a more tailored treatment approach. GOV IDENTIFIER: NCT02720744.

Surgery

Al-Saghir T, **Hall J**, **Diffley M**, **Tang A**, Teitelbaum A, **Tepper DG**, **Darian V**, **Evangelista M**, and **Atisha D**. Marijuana's Impact On Implant-based Breast Reconstruction: A Retrospective Cohort Study. *Plast Reconstr Surg Glob Open* 2024; 12(8):e6082. PMID: 39171243. Full Text

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BACKGROUND: Studies have shown that chronic marijuana use is associated with increased vascular inflammation, endothelial damage, myocardial infarctions, strokes, arteritis, and cardiomyopathies; however, cannabis's effect on wound healing in immediate direct-to-implant (DTI) breast reconstruction is unknown. With the increasing prevalence of marijuana use, it is imperative to understand its effects on surgical outcomes. METHODS: We performed a retrospective cohort study of consecutive patients in a quaternary-care breast cancer center undergoing immediate DTI reconstruction. Patient demographics, operative details, and surgical complications were extracted through chart review. Active cannabis use was defined as use within 12 weeks of operation. Univariate and multivariable analyses were performed. RESULTS: In total, 243 consecutive patients underwent immediate DTI reconstruction, and 12 reported active cannabis use. There were no significant differences in patient demographics, cancer treatment, or operative details. Active marijuana users demonstrated higher rates of cellulitis treated with IV antibiotics ($P = 0.004$), explantation for infection ($P = 0.004$), emergency department visits ($P = 0.028$), readmission ($P = 0.037$), takeback to the operating room in 90 days ($P < 0.001$), and overall major complications ($P < 0.001$). Multivariable analysis demonstrated that active marijuana users were more likely to experience cellulitis treated with IV antibiotics [odds ratio (OR) = 3.55, $P = 0.024$], takeback to the OR within 90 days of operation (OR = 4.75, $P = 0.001$), and major complications (OR = 2.26, $P = 0.048$). CONCLUSIONS: The consumption of cannabis in the perioperative setting is associated with increased rates of complications in patients undergoing immediate DTI reconstruction; however, an analysis with a larger patient population is needed to conclude that abstinence from its use should be highly encouraged.

Surgery
Halloran PF, Madill-Thomsen KS, Böhmig G, Bromberg J, Budde K, Barner M, Mackova M, Chang J, Einecke G, Eskandary F, Gupta G, Myślak M, Viklicky O, Akalin E, Alhamad T, Anand S, Arnol M, Baliga R, Banasik M, Bingaman A, Blosser C, Brennan D, Chamienia A, Chow K, Ciszek M, de Freitas D, Dęborska-Materkowska D, Debska-Ślizień A, Djamali A, Domański L, Durlik M, Fatica R, **Francis I**, Fryc J, Gill J, Gill J, Glyda M, Gourishankar S, Grenda R, Gryczman M, Hruba P, Hughes P, Jittirat A, Jurekovic Z, Kamal L, Kamel M, Kant S, Kasiske B, Kojc N, Konopa J, Lan J, Mannon R, Matas A, Mazurkiewicz J, Miglinas M, Mueller T, Narins S, Naumnik B, **Patel A**, Perkowska-Ptasińska A, Picton M, Piecha G, Poggio E, Bloudíčkova SR, Samaniego-Picota M, Schachtner T, Shin S, Shojai S, Sikosana M, Slatinská J, Smykal-Jankowiak K, Solanki A, Haler Ž V, Vucur K, Weir MR, Wiecek A, Włodarczyk Z, Yang H, and Zaky Z. Subthreshold rejection activity in many kidney transplants currently classified as having no rejection. *Am J Transplant* 2024; Epub ahead of print. PMID: 39117038. Full Text

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Most kidney transplant patients who undergo biopsies are classified as having no rejection based on consensus thresholds. However, we hypothesized that because these patients have normal adaptive immune systems, T cell-mediated rejection (TCMR) and antibody-mediated rejection (ABMR) may exist as subthreshold activity in some transplants currently classified as no rejection. To examine this question, we studied genome-wide microarray results from 5086 kidney transplant biopsies (4170 patients). An updated archetypal analysis designated 56% of biopsies as no rejection. Subthreshold molecular TCMR and/or ABMR activity molecular activity was detectable as elevated classifier scores in many biopsies classified as no rejection, with ABMR activity in many TCMR biopsies and TCMR activity in many ABMR biopsies. In biopsies classified as no rejection histologically and molecularly, molecular TCMR classifier scores correlated with increases in histologic TCMR features and molecular injury, lower eGFR, and higher risk of graft loss, and molecular ABMR activity correlated with increased glomerulitis and donor-specific antibody. No rejection biopsies with high subthreshold TCMR or ABMR activity had a higher probability of having TCMR or ABMR respectively diagnosed in a future biopsy. We conclude that many kidney transplant recipients have unrecognized subthreshold TCMR or ABMR activity, with significant implications for future problems.

Surgery

Lin H, Baker JW, Meister K, Lak KL, Martin Del Campo SE, Smith A, Needleman B, Nadzam G, Ying LD, **Varban O**, Reyes AM, Breckenbridge J, Tabone L, Gentles C, Echeverri C, Jones SB, Gould J, Vosburg W, Jones DB, Edwards M, Nimeri A, Kindel T, and Petrick A. American society for metabolic and bariatric surgery: intra-operative care pathway for minimally invasive Roux-en-Y gastric bypass. *Surg Obes Relat Dis* 2024; Epub ahead of print. PMID: 39097472. Full Text

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BACKGROUND: Clinical care pathways help guide and provide structure to clinicians and providers to improve healthcare delivery and quality. The Quality Improvement and Patient Safety Committee (QIPS) of the American Society for Metabolic and Bariatric Surgery (ASMBS) has previously published care pathways for the performance of laparoscopic sleeve gastrectomy (LSG) and pre-operative care of patients undergoing Roux-en-Y gastric bypass (RYGB). OBJECTIVE: This current RYGB care pathway was created to address intraoperative care, defined as care occurring on the day of surgery from the preoperative holding area, through the operating room, and into the postanesthesia care unit (PACU). METHODS: PubMed queries were performed from January 2001 to December 2019 and reviewed according to Level of Evidence regarding specific key questions developed by the committee. RESULTS: Evidence-based recommendations are made for care of patients undergoing RYGB including the pre-operative holding area, intra-operative management and performance of RYGB, and concurrent procedures. CONCLUSIONS: This document may provide guidance based on recent evidence to bariatric surgeons and providers for the intra-operative care for minimally invasive RYGB.

Surgery
Lisznyai E, **Hutchings H**, **Debiane L**, and **Okereke I**. Central airway carcinoid tumor mimicking chronic asthma and necessitating pneumonectomy: A case report. *Int J Surg Case Rep* 2024; 122:110167. PMID: 39137644. Full Text

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INTRODUCTION: Central airway tumors can occasionally be misdiagnosed as a chronic disease. We present a case of a central airway carcinoid tumor that was mistaken as chronic asthma for many years. PRESENTATION OF CASE: A 29-year-old male bodybuilder presented to our emergency department with shortness of breath and hemoptysis. He was an avid bodybuilder who participated in competitions. He had been diagnosed with asthma for years and used an albuterol inhaler chronically. Computed tomography of the chest showed diffuse opacification of the left hemithorax, multiple air-fluid levels and a 4-cm mass of the proximal left mainstem bronchus with intraluminal calcifications. Bronchoscopy demonstrated a large endobronchial mass, and biopsy was positive for typical carcinoid tumor. Stabilization was achieved with rigid bronchoscopy and partial endobronchial debridement of the tumor to allow some patency to the left lung. After stabilization, he subsequently underwent left pneumonectomy.

He recovered well and was discharged home on postoperative day 2. On surveillance 2.5 years after pneumonectomy, he has resumed bodybuilding and has no evidence of recurrent disease. DISCUSSION: Proximal airway tumors can mimic asthma. Careful management can achieve successful results even in very complex cases. There should be an increased level of suspicion for other diagnoses, especially in young and healthy individuals with asthma that is refractory to medical treatment. CONCLUSION: Proximal airway tumors can mimic chronic diseases such as asthma. Other diagnoses should be considered, especially in young and health individuals with asthma symptoms that do not respond to conventional therapies.

Surgery

Magyar CTJ, Li Z, Aceituno L, Claasen M, **Ivanics T**, Choi WJ, Rajendran L, Sayed BA, Bucur R, Rukavina N, Selzner N, Ghanekar A, Cattral M, and Sapisochin G. Temporal evolution of living donor liver transplantation survival - A UNOS registry study. *Am J Transplant* 2024; Epub ahead of print. PMID: 39163907. Full Text

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Living donor liver transplantation (LDLT) is a curative treatment for various liver diseases, reducing waitlist times and associated mortality. We aimed to assess the overall survival (OS), identify predictors for mortality, and analyze differences in risk factors over time. Adult patients undergoing LDLT were selected from the United Network for Organ Sharing database from inception (1987) to 2023. The Kaplan-Meier method was used for analysis, and multivariable Cox proportional hazard models were conducted. 7,257 LDLT recipients with a median age of 54years (IQR:45,61), 54% male, 80% non-Hispanic White, BMI 26.3kg/m(2) (IQR:23.2,30.0), and MELD 15 (IQR:11,19) were included. The median cold ischemic time was 1.6hours (IQR:1.0,2.3) with 88% right-lobe-grafts. The follow-up was 4.0years (IQR:1.0,9.2).

The contemporary reached median overall survival was 17.0years (95%CI:16.1,18.1) with OS estimates: 1-year 95%, 3-years 89%, 5-years OS 84%, 10-years 72%, 15-years 56% and 20-years 43%. Nine independent factors associated with mortality were identified, with an independent improved OS in the recent time era (aHR 0.53; 95%CI:0.39,0.71). The median center-caseload per year was 5 (IQR:2,10) with observed center-specific improvement of OS. LDLT is a safe procedure with excellent OS. Its efficacy has improved despite an increase of risk parameters, suggesting its limits are yet to be met.

Urology

Corey Z, Lehman E, Lemack GE, Clifton MM, Klausner AP, Mehta A, **Atiemo H**, Lee R, Sorensen M, Smith R, Buckley J, Thompson RH, Breyer BN, Badalato GM, Wallen EM, Cain M, Wolf JS, Jr., and Raman JD. Practice Readiness? Trends in Chief Resident Case Logs vs Subsequent Case Log Data in Clinical Practice. *Urol Pract* 2024; Epub ahead of print. PMID: 39196730. Full Text

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INTRODUCTION: Limited information exists regarding the association between resident surgical case experience and subsequent case mix in practice. We compare the case log distribution residents completed during their chief year to those completed by these graduates in their first 2 years in independent practice. METHODS: Resident chief year case logs from 10 institutions were analyzed across 4 categories of index procedures: (1) general urology, (2) endourology, (3) reconstructive urology, and (4) urologic oncology. Current Procedural Terminology codes for associated index procedures were used to query case log data during their first 2 years in practice collected by the American Board of Urology. Interactions were tested between the trends of chief year case logs relative to trends in practice case logs. RESULTS: Amongst 292 residents, a total of 104,827 cases were logged during chief year and 77,976 cases in the first 2 years as an attending. Most cases completed during chief year were in oncology followed by general urology, endourology, and reconstructive urology. As attendings, most cases completed were in general urology, followed by endourology, reconstructive urology, and oncology. Chief year case logs showed decreasing trends in the median number of case logs in reconstructive urology, endourology, and general urology, while case logs in independent practice noted increasing trends in all index procedure categories over time. CONCLUSIONS: Urology residents perform more cases during their chief year compared to their first 2 years of independent practice. Case types completed as chief residents vs subsequent clinical practice also differ significantly. These observations may have implications for residency training, particularly regarding curriculum design.

Urology

Goradia R, **Abdollah F**, and Sood A. Re: Integrative Multi-Region Molecular Profiling of Primary Prostate Cancer in Men with Synchronous Lymph Node Metastasis. *Eur Urol* 2024; Epub ahead of print. PMID: 39112304. Full Text

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Urology

Tinsley SA, **Arora S**, **Stephens A**, **Finati M**, **Chiarelli G**, **Cirulli GO**, **Morrison C**, **Richard C**, **Hares K**, **Rogers CG**, and **Abdollah F**. The impact of cannabis use disorder on urologic oncologic surgery morbidity, length of stay, and inpatient cost: analysis of the National Inpatient Sample from 2003 to 2014. *World J Urol* 2024; 42(1):465. PMID: 39090376. Full Text

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PURPOSE: This study examined the impact of cannabis use disorder (CUD) on inpatient morbidity, length of stay (LOS), and inpatient cost (IC) of patients undergoing urologic oncologic surgery. METHODS: The National Inpatient Sample (NIS) from 2003 to 2014 was analyzed for patients undergoing prostatectomy, nephrectomy, or cystectomy (n = 1,612,743). CUD was identified using ICD-9 codes. Complex-survey procedures were used to compare patients with and without CUD. Inpatient major complications, high LOS (4th quartile), and high IC (4th quartile) were examined as endpoints. Univariable and multivariable analysis (MVA) were performed to compare groups. RESULTS: The incidence of CUD increased from 51 per 100,000 admissions in 2003 to 383 per 100,000 in 2014 ($p < 0.001$). Overall, 3,503 admissions had CUD. Patients with CUD were more frequently younger (50 vs. 61), male (86% vs. 78.4%), Black (21.7% vs. 9.2%), and had 1st quartile income (36.1% vs. 20.6%); all $p < 0.001$. CUD had no impact on any complication rates (all $p > 0.05$). However, CUD patients had higher LOS (3 vs. 2 days; $p < 0.001$) and IC ($15,609 vs. $12,415; $p < 0.001$). On MVA, CUD was not an independent predictor of major complications ($p = 0.6$). Conversely, CUD was associated with high LOS (odds ratio (OR) 1.31; 95% CI 1.08-1.59) and high IC (OR 1.33; 95% CI 1.12-1.59), both $p < 0.01$. CONCLUSION: The incidence of CUD at the time of urologic oncologic surgery is increasing. Future research should look into the cause of our observed phenomena and how to decrease LOS and IC in CUD patients.

Urology

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OBJECTIVES: We sought to determine whether bladder cuff excision and its technique influence outcomes after radical nephroureterectomy (RNU) for upper tract urothelial carcinoma (UTUC). METHODS AND MATERIALS: A multicenter, international, retrospective analysis using the ROBotic surgery for Upper tract Urothelial cancer Study (ROBUUST) 2.0 registry identified 1,718 patients undergoing RNU for UTUC between 2015 and 2023 at 17 centers across the United States, Europe, and Asia. Data was gathered on (1) whether bladder cuff excision was performed and (2) what technique was used, including formal excision or other techniques (pluck technique, stripping/intussusception technique) and outcomes. Multivariate and survival analyses were performed to compare the groups. RESULTS: Most patients (90%, 1,540/1,718) underwent formal bladder cuff excision in accordance with EAU and AUA guidelines. Only 4% (68/1,718) underwent resection using other techniques, and 6% (110/1,718) did not have a bladder cuff excised. Median follow up for the cohort was 24 months (IQR 9-44). When comparing formal bladder cuff excision to other excision techniques, there were no differences in oncologic or survival outcomes including bladder recurrence-free survival (BRFS), recurrence-free survival (RFS), metastasis-free survival (MFS), overall survival (OS), or cancer-specific survival (CSS). However, excision of any kind conferred a decreased risk of bladder-specific recurrence compared to no excision. There was no difference in RFS, MFS, OS, or CSS when comparing bladder cuff excision, other techniques, and no excision. CONCLUSIONS: Bladder cuff excision improves recurrence-free survival, particularly when considering bladder recurrence. This benefit is conferred regardless of technique, as long as the intramural ureter and ureteral orifice are excised. However, the benefit of bladder cuff excision on metastasis-free, overall, and cancer-specific survival is unclear.

Cardiology/Cardiovascular Research
Buda KG, Hryniewicz K, Eckman PM, **Basir MB**, **Cowger JA**, **Alaswad K**, Mukundan S, Sandoval Y, Elliott A, Brilakis ES, and Megaly MS. National Trends and Outcomes of Early versus Delayed Mechanical Circulatory Support in Patients with Acute Myocardial Infarction Complicated by Cardiogenic Shock. *US Cardiology Review* 2024; 18:3. Full Text

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Background: Despite increased temporary mechanical circulatory support (tMCS) utilization for acute MI complicated by cardiogenic shock (AMI-CS), observational and randomized data regarding tMCS efficacy are conflicting. Objectives: The aim of the study was to describe outcomes based on tMCS timing in AMI-CS and to identify predictors of in-hospital and 30-day mortality and readmission. Methods: Patients with AMI-CS identified in the National Readmissions Database (NRD) were grouped according to the use of tMCS and early (<24 hours) versus delayed tMCS (≥24 hours) utilization. The correlation between the timing of tMCS support and inpatient outcomes was evaluated using linear regression. Multivariate logistic regression (OR [95% CI]) using backward stepwise elimination was used to identify variables associated with 30-day mortality and readmission. Results: Patients who underwent tMCS (n=109,148) for AMI-CS had lower in-hospital mortality (33.9% versus 36.4%, p<0.001), longer lengths of stay (median [IQR]) (9 [4-17] days versus 7 [3-14] days, p<0.001), and twice the hospital cost (US$64,069 [$39,455-$105,441] versus US$31,832 [$17,595- $57,742] p<0.001) compared to those who did not have tMCS (n=185,691) in the unadjusted analysis. Patients who received tMCS within 24 hours of admission (n=79,906) had shorter length of stay (7 days versus 15 days, p<0.001), lower hospital cost (US$55,644 versus US$88,644, p<0.001), and lower rates of ischemic and bleeding complications than those with tMCS placed ≥24 hours after admission (n=32,241). After adjustment, early tMCS was associated with lower mortality (OR 0.92 [CI 0.88-0.96]) and readmission (OR 0.91 [CI 0.85-0.97]). Conclusion: Among patients receiving tMCS for AMI-CS, early tMCS was associated with shorter lengths of stay, lower hospital costs, and fewer deaths and readmissions at 30 days. In AMI-CS, early tMCS may be preferable to delayed tMCS.

Cardiology/Cardiovascular Research
Cherabuddi MR, **Goodman BD**, **Ayyad A**, **Almajali DA**, **Nadeem O**, **Bradley P**, **Russell C**, and **Ouellette DR**. Exploring Disparate Access to Care in Sarcoidosis Patients in Detroit, Michigan. *Am J Respir Crit Care Med* 2024; 209. Full Text

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Rationale Sarcoidosis is a multisystem granulomatous inflammatory disease with immense ongoing research. Previous studies assessed the role of social predictors on severity at presentation and found Black, older individuals, with lower income, without insurance to have more severe disease. The city of Detroit, Michigan is at greater risk of disparities with 5 times greater Black population and almost thrice in poverty compared to the nation. We aimed to explore these potential disparities to incorporate our findings into future practice at provider, patient and healthcare system level. Methods This is a retrospective chart review study of all patients seen in pulmonary clinics at Henry Ford Health between January 1st, 2020, and December 31st, 2022, with sarcoidosis patients identified as those with ICD diagnosis code D86. Data collected included date of office visit(s), age, race (Black, White, Other), sex, area deprivation index (ADI), insurance type (Medicare, Medicaid, Commercial), MyChart status, chest x-rays, pulmonary function tests (PFTs), missed clinic visits, number of hospitalizations, mortality, positive biopsy on file, communication of results after bronchoscopy and visits around the time of bronchoscopy. Categorical variables were described using frequency. Numerical variables were described using median, mean and standard deviation. Statistical analysis included Chi-square test, Two-sample T-test and Wilcoxon Rank Sum test and a p-value of <0.05 was considered statistically significant. Results Sarcoidosis patients (N=788), when compared to those seen for other pulmonary problems (N=13,036) were typically slightly younger, Black, female, belonging to higher ADI (greater socioeconomic disadvantage) based on national and state ranks, more likely to use commercial insurance and Medicaid

compared to Medicare, have active MyChart access, more noshows, more PFTs on file. Among sarcoidosis patients, significant findings included presence of active MyChart among younger patients, lower ADI and with commercial insurance; more X-rays and PFTs were done in Medicare patients; no-show rate was higher in higher ADI; hospitalizations were higher in those with government insurance. Sarcoidosis patients with positive biopsies on file from 2013-2023 were more likely to be male, White or other races, younger and belonged to lower national ADI ranks. Conclusions This study identified an intricate pattern of demographic and socioeconomic variables affecting access to care in sarcoidosis patients, raising concerns for healthcare barriers especially based on race and ADI, and higher bronchoscopies in those demographic groups thought less likely to have sarcoidosis. Understanding these is vital for equitable high-quality care, assisting in timely and efficient management of the patient's disease. (Figure Presented).

Center for Health Policy and Health Services Research

Tam S, **Boakye EA**, **Springer K**, **Poisson L**, **Al-Antary N**, **Elsiss F**, **Nair M**, **Zatirka T**, **Ryan M**, **Chang SS**, and **Movsas B**. Age-normed patient-reported outcome measures among cancer survivors. *J Clin Oncol* 2024; 42(16). Full Text

S. Tam

Background: Patient-reported outcome measures (PROMs) are instruments used to collect health-related outcomes that are derived completely from the patient without interpretation from healthcare providers. Monitoring and subsequent intervention based on PROMs collection has demonstrated efficacy in clinical trial settings. This has resulted in implementation of PROMs in routine clinical cancer practices throughout the nation. PROMs have been normed to the general population, but establishing the norms among cancer patients is essential to understanding how PROMs can be evaluated on an individual basis in routine clinical cancer care. This study aims to characterize age-normed PROMs scores among survivors of cancer using the National Institute of Health's Patient-Reported Outcome Measures Information System (PROMIS) depression, fatigue, pain interference, and physical function domains. Methods: Routine collection of PROMs using 4 domains (depression, fatigue, pain interference, and physical function) of PROMIS were offered to all patients with a diagnosis of cancer of any disease site at visits with an oncologic provider using computer adaptive testing. All patients ≥18 years old with a completed PROM at least 2 years since their diagnosis of cancer were eligible for inclusion in the analysis. Only completed PROMs were included in the final analysis. Generalized estimating equation models were used to assess the relationship between age and the estimated mean T-score for each PROMs domain, considering repeat measures within a single patient. Results: A total of 3,636 patients were included in this retrospective cohort study with a total of 26,173 completed PROMs among all 4 domains. Mean age at diagnosis was 61.2 years (SD=12.44), 64% (n=2324) were female, 68% (n=2,461) identified as White, and 25% (n=893) identified as Black. For fatigue, mean T-score ranged from 48.4 points (SD=9.6) among 18-29 years olds to 56.5 points (SD=10.1) among 90-99 years olds, with no significant change with age (p=0.27). For depression, mean T-score ranged from 48.9 points (SD=9.0) among 60-69 year olds to 51.1 points (SD=8.8) among 80-89 year olds with a 0.3 point/decade decrease in T-score (p=0.01). Pain interference T-scores ranged from 48.6 points (SD=10.5) among 18-29 year olds to 55.0 points (SD=9.4) among 80-89 year olds with a 0.4 point/decade average increase (p,0.001). The largest differences were observed in physical function, where scores ranged from 53.5 points (SD=11.0) among 18-29 year olds to 34.3 points (SD=9.2) among 90-99 year olds. There was a 2.1 point/decade decrease in T-score (p,0.001). Conclusions: Among survivors of cancer, mean PROMIS scores differed by age in the depression, pain interference, and physical function domains but not fatigue. These age-normed PROMIS T-scores, which are required to understand individualized assessments of PROMs, are essential as PROMs are integrated into routine cancer care.

Dermatology

Bissonnette R, Lee MS, Forman SB, **Gold LS**, Kallender H, Angel B, Kuo Y, and Paller AS. Ruxolitinib cream 1.5% twice daily for the treatment of extensive atopic dermatitis in children aged 2-11 years: 52 week results from a maximum-use trial. *Br J Dermatol* 2024; 191:ii3. Full Text

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Background Eight-week safety and tolerability, efficacy, and limited systemic absorption of ruxolitinib cream 1.5% in an open-label, single-arm, maximum-use trial (MUsT) of children with moderate to severe atopic dermatitis (AD; NCT05034822) were previously described. This is the first report of longer-term data from the same study. Objectives Data on tolerability, safety, systemic exposure, and clinical and patient-reported outcomes are presented from the entire 52-week treatment period to assess whether clinical benefits and tolerability observed through Week 8 are sustained during the as-needed treatment long-term safety period through Week 52. Methods In this open-label, single-arm MUsT, patients 2-11 years old with AD ≥3 months, ≥35% affected body surface area (BSA), and Investigator's Global Assessment (IGA) ≥3 applied twice-daily ruxolitinib cream 1.5% for 4 weeks to baseline lesions, then as-needed to active lesions for 4 weeks; patients could continue into the as-needed 44-week long-term safety period. Results This MUsT included 29 patients with moderate to severe AD. Treatment-emergent adverse events through Week 52 occurred in 31.0% of patients. One patient (3.4%) had 2 treatment-related application site reactions (paresthesia and folliculitis); no adverse events resulted in treatment interruption/discontinuation; none were serious or suggested systemic Janus kinase (JAK) inhibition. Through the 4-week continuous-use twice-daily treatment period, the mean (SD) application quantity was 8.5 (6.29) g/day, which was associated with a mean steady-state ruxolitinib plasma concentration of 98.2 nM, well below half-maximal concentration of JAK-mediated myelosuppression in adults (281 nM). From Week 8 to Week 52 (as-needed use), mean (SD) application quantity was 3.2 (2.79) g/day, consistent with lower, as-needed use in this long-term safety period. At Weeks 4 and 52 (assessed in n=26 and n=13 patients, respectively), 53.8%/53.8% achieved IGA-Treatment Success (IGA 0/1 with ≥2-grade improvement from baseline). Mean BSA decreased from 58.0% (range, 35.0%-92.0%) at baseline (n=29) to 11.4% at Week 4 and continued to decrease to 2.2% through Week 52 (n=26 and n=14, respectively). Patient-reported outcomes, such as the Patient-Oriented Eczema Measure, Children's Dermatology Life Quality Index, and Infants' Dermatitis Quality of Life Index, were collected through Week 52. Conclusions Ruxolitinib cream 1.5% demonstrated consistently good tolerability and safety over 52 weeks in children aged 2 to 11 years with extensive moderate to severe AD. Rapid lesion clearance over 4 weeks with twice-daily therapy, which was sustained with longer-term as-needed use associated with low quantities of ruxolitinib cream being applied, may address application burden concerns.

Dermatology

Eichenfield LF, Armstrong AW, **Stein Gold LF**, Zaenglein AL, Lee LW, Brar KK, Joyce JC, Holland KE, Angel B, Sturm D, Li Q, and Simpson EL. Efficacy and safety of ruxolitinib cream in children aged 2 to 11 years with moderate and/or more extensive atopic dermatitis: subgroup analysis from the TRuE-AD3 study. *Br J Dermatol* 2024; 191:ii80-ii81. Full Text

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Introduction/Background Atopic dermatitis (AD) is a chronic, inflammatory skin disease with onset usually occurring in childhood. Topical therapy is the mainstay of AD treatment and is typically used prior to systemic therapy in patients with moderate disease. Ruxolitinib (Janus kinase [JAK] 1/JAK2 inhibitor) cream is approved by the US Food and Drug Administration for patients aged ≥12 years with mild to moderate AD, and has demonstrated efficacy and was well tolerated in children (aged 2-11 y) with AD in TRuE-AD3 (NCT04921969), a phase 3, double-blind, randomized, vehicle-controlled study. Objectives Here we investigated the effects of ruxolitinib cream in a subset of patients from TRuE-AD3 with moderate and/or more extensive disease at baseline. Methods TRuE-AD3 included children aged 2-11 years with AD for ≥3 months, an Investigator's Global Assessment (IGA) score of 2 or 3, and an affected body surface area (BSA) of 3%-20%. Patients were randomized 2:2:1 to apply 1.5% ruxolitinib cream, 0.75% ruxolitinib cream, or vehicle cream twice daily for 8 weeks. Rescue treatment was not permitted. Patients from TRuE-AD3 with moderate and/or more extensive disease at baseline (defined as an IGA score of 3, ≥10% affected BSA, or a combined IGA score of 3 and ≥10% BSA) were included in this analysis. Efficacy was assessed as the proportion of patients in each treatment group who achieved IGA treatment success (IGA-TS; a score of 0 or 1 with a ≥2-grade improvement from baseline), ≥75% improvement from baseline in the Eczema Area and Severity Index (EASI75), and ≥90% improvement from baseline in the Eczema Area and Severity Index (EASI-90) at Weeks 2, 4, and 8. Statistical significance was assessed at Week 8 using exact logistic regression. Patients with missing post-baseline

data were imputed as nonresponders. Results Patients in TRuE-AD3 (N=330) had a median (range) age of 6 (2-11) years, 54.2% were girls, and 54.5% were White. The mean (SD) BSA was 10.5% (5.4%), the mean (SD) EASI was 8.6 (5.4), and 252 patients (76.4%) had a baseline IGA of 3. Among patients with an IGA of 3 at baseline, more patients who applied 1.5% ruxolitinib cream or 0.75% ruxolitinib cream versus vehicle achieved IGA-TS (40.0% and 29.1%, respectively, vs 6.1%), EASI-75 (43.0% and 38.8% vs 8.2%), and EASI-90 (17.0% and 21.4% vs 0%) at Week 2. Improvements were also observed at Week 8 (IGA-TS, 59.0% [P<0.0001] and 37.9% [P=0.004] vs 14.3%; EASI-75, 64.0% [P<0.0001] and 48.5% [P<0.0001] vs 14.3%; EASI90, 40.0% [P<0.0001] and 33.0% [P=0.001] vs 8.2%), with 1.5% ruxolitinib cream consistently resulting in numerically better improvements than 0.75% ruxolitinib cream. Similar improvements were observed with ruxolitinib cream versus vehicle among patients with ≥10% affected BSA at baseline and a combined baseline IGA of 3 and ≥10% BSA. Both strengths of ruxolitinib cream were well tolerated among patients with an IGA of 3 at baseline; no serious treatment-emergent adverse events (TEAEs) were reported. Conclusions Children with moderate and/or more extensive AD in this study had substantially higher rates of clinical responses with ruxolitinib cream monotherapy versus vehicle as early as Week 2 (first assessment), with further improvement throughout the 8-week treatment period. Ruxolitinib cream was well tolerated with no serious TEAEs.

Dermatology

Gold LS, Weidinger S, Staumont-Salle D, Nakajima S, Simpson EL, De Bruin Weller M, Davey S, Rahawi K, and Bernigaud C. Amlitelimab (an anti-OX40 ligand antibody) vs placebo in patients with moderate-to-severe atopic dermatitis: study design of phase 3 OCEANA clinical trials COAST 1/2, SHORE, AQUA, and ESTUARY. *Br J Dermatol* 2024; 191:ii59-ii60. Full Text

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Introduction/Background Amlitelimab is a fully human, nondepleting anti-OX40 Ligand (OX40L) monoclonal antibody that blocks OX40L-OX40 interactions. In addition to an acceptable safety profile, phase 2a and 2b trials showed the clinical efficacy of amlitelimab in achieving lesional and symptomatic (pruritus) endpoints and demonstrating a continued durable response when patients with moderate-to-severe atopic dermatitis (AD) were withdrawn from amlitelimab during a 28-week period, suggesting the viability of extended interval dosing (every 12 weeks [Q12W]). Objectives Phase 3 clinical trials will determine the efficacy and safety of amlitelimab every four weeks (Q4W) and Q12W dosing in patients with moderate-to-severe AD with various treatment histories. Methods OCEANA phase 3 clinical trials (COAST 1, COAST 2, SHORE, AQUA, and ESTUARY) are multinational, multicenter, randomized, double-blind, parallel group, placebo-controlled trials evaluating efficacy and safety of subcutaneous amlitelimab with two different dosing regimens. Key inclusion criteria for COAST 1/2, SHORE, and AQUA include: adults and adolescents (≥12 years old) having AD ≥1 year with inadequate response to topical treatments (within 6 months before screening) and/or systemic treatment (within 12 months before screening), validated Investigator Global Assessment scale for Atopic Dermatitis (vIGA-AD) baseline score of 3 or 4, Eczema Area and Severity Index (EASI) baseline score of ≥16, AD involvement of ≥10% of body surface area at baseline, and weekly average Peak Pruritus Numerical Rating Scale score of ≥4. COAST 1/2 are 24-week monotherapy studies, while SHORE is a 24-week study with background topical corticosteroids (TCSs) and topical calcineurin inhibitors (TCIs). AQUA is a 36-week study with background TCSs and TCIs that exclusively includes participants with an inadequate response to prior treatment with AD biologics or oral Janus kinase inhibitors. Primary endpoints for COAST 1/2, SHORE, and AQUA include vIGA-AD 0/1 and a reduction from baseline of ≥2 points (for US and US reference countries) and vIGA-AD 0/1 and EASI-75 (for Japan, EU, and EU reference countries). Adult patients ≥40 kg will be randomized to amlitelimab 250 mg Q4W + 500 mg loading dose (LD), amlitelimab 250 mg Q12W + 500 mg LD, or placebo; dose will be adjusted for patients <40 kg. Trials have a 2- to 4-week screening period. Primary endpoints will be evaluated at Week 24 for COAST 1/2 and SHORE and at Week 36 for AQUA, with expected enrollment of 420, 420, 496, and 249 patients in each study, respectively. Patients who have completed COAST 1/2 or SHORE can elect to enter the ESTUARY blinded extension study; patients completing AQUA can enter RIVER-AD, an open-label long-term study. Upon entering ESTUARY, clinical responders previously on 250 mg Q4W +LD will be randomized to 250 mg Q4W, 250 mg Q12W, or treatment withdrawal (placebo), while nonresponders will continue on 250 mg Q4W. Clinical responders previously on 250 mg Q12W +LD will be randomized to 250 mg Q12W or

treatment withdrawal (placebo), while nonresponders will be randomized to 250 mg Q12W or 250 mg Q4W. Clinical responders previously on placebo will continue placebo, while nonresponders on placebo will receive amlitelimab 250 mg Q4W +LD. Participants not entering the ESTUARY or RIVER-AD trials will be included in a 16-week safety follow-up. ESTUARY and RIVER-AD will evaluate long-term safety and efficacy. Biopsies and blood samples will be collected at various timepoints in the OCEANA phase 3 trials. Results Enrollment for the OCEANA phase 3 trials began Q4 2023. COAST 1/2, SHORE, and AQUA trials are expected to be completed in 2026. Conclusions Results of the clinical trials should provide further evidence demonstrating the efficacy and safety of amlitelimab in treating moderate-to-severe AD using two different dosing regimens, including an extended dosing regimen, in patients with various treatment histories.

Dermatology

Prajapati VH, Bunick CG, Eyerich K, **Gold LS**, Galimberti F, Calimlim B, Teixeira H, Hu X, Yang Y, Sancho C, Grada A, and Irvine AD. Sustained improvements over 140 weeks in signs, symptoms, and quality of life with upadacitinib in adolescents and adults with moderate-to-severe atopic dermatitis: integrated results from the phase 3 Measure Up 1 and Measure Up 2 studies. *Br J Dermatol* 2024; 191:ii72-ii73. Full Text

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Introduction/Background Atopic dermatitis (AD) is a chronic, recurrent, immune-mediated inflammatory disease associated with burdensome symptoms including itch, skin pain, sleep disruption, as well as reduced quality of life (QoL).1 It is therefore important to consider signs, symptoms, and QoL impairments when evaluating long-term benefits of AD treatments. Upadacitinib is an oral selective Janus kinase inhibitor approved to treat moderate-to-severe AD.2 Objective To evaluate the effects of upadacitinib monotherapy on skin and patient-reported outcomes (PROs) in patients with moderate-to-severe AD over 140 weeks. Methods Measure Up 1 (NCT03569293) and Measure Up 2 (NCT03607422) were replicate, multicenter, phase 3 studies evaluating once-daily oral upadacitinib monotherapy for adolescents (aged 12-17 years) and adults (aged ≥ 18 years) with moderate-to-severe AD.3,4 At baseline, patients were randomized 1:1:1 to upadacitinib 15 mg, upadacitinib 30 mg, or placebo. In this analysis, data for patients who were randomized to upadacitinib 15 mg or upadacitinib 30 mg at baseline in Measure Up 1 and Measure Up 2 were integrated and reported based on observed cases from week 16 (the end of the double-blind period) through week 140 of the blinded extension period; week 16 data for patients randomized to placebo were also reported. Assessments included itch (Worst Pruritus Numerical Rating Scale [WP-NRS]); Eczema Area and Severity Index (EASI); skin pain (AD Symptom Scale [ADerm-SS] Skin Pain); skin symptoms (ADerm-SS 7-item Total Symptom Score [TSS-7]); skin symptom severity (Patient-Oriented Eczema Measure [POEM]); QoL (Dermatology Life Quality Index [DLQI; patients aged ≥ 16 years], and Children's DLQI [CDLQI; patients aged < 16 years]); and sleep, daily activities, and emotional state (AD Impact Scale [ADerm-IS]). Assessed outcomes included achievement of (1) minimal clinically important differences vs baseline (WP-NRS, ADerm-SS Skin Pain, and POEM improvement ≥ 4; ADerm-SS TSS-7 improvement ≥ 28; ADerm-IS Sleep, Daily Activities, and Emotional State improvements ≥ 12, ≥ 14, and ≥ 11, respectively), (2) no/minimal disease burden or impact (WP-NRS 0/1, ≥ 90% improvement from baseline in EASI [EASI 90], DLQI 0/1,and CDLQI 0/1), and (3) simultaneous achievement of EASI 90 and WP-NRS 0/1, an endpoint that aligns with the recently proposed minimal disease activity concept.5 Results Data for 1213 patients (upadacitinib 15 mg, n = 603; upadacitinib 30 mg, n = 610), including 241 adolescents (19.9%) and 972 adults (80.1%), from Measure Up 1 and Measure Up 2 were analyzed. At week 16, over 50% of patients receiving either dose of upadacitinib reported clinically meaningful improvements in PROs; among patients receiving upadacitinib 15 mg and upadacitinib 30 mg, 36.7% and 53.1% achieved WP-NRS 0/1, while 29.0% and 44.1% achieved DLQI 0/1, and 23.5% and 50.0% achieved CDLQI 0/1, respectively. Response rates at week 16 were sustained or improved further through week 140. At week 140, the proportion of patients treated with upadacitinib 15 mg and upadacitinib 30 mg from baseline who achieved clinically meaningful improvements were 64.8% and 70.9% for itch, 74.6% and 81.5% for skin pain, 67.6% and 75.4% for skin symptoms, 89.0% and 94.2% for skin symptom severity, 76.5% and 84.0% for sleep, 79.2% and 84.0% for daily activities, and 78.6% and 82.7% for emotional state, respectively. At week 140, achievement rates with upadacitinib

15 mg and upadacitinib 30 mg were 45.1% and 51.4% for WP-NRS 0/1, 67.3% and 75.6% for EASI 90, 40.5% and 47.1% for simultaneous EASI 90 and WP-NRS 0/1 achievement, 40.2% and 48.5% for DLQI 0/1, and 35.7% and 65.0% for CDLQI 0/1, respectively. Conclusions Patients with moderate-to-severe AD experienced sustained improvements in skin signs/symptoms through 140 weeks while receiving upadacitinib. Rates of long-term PRO improvements were numerically higher with upadacitinib 30 mg compared with upadacitinib 15 mg.

Dermatology

Silverberg JI, Bunick C, Hong HCH, Mendes-Bastos P, **Gold LS**, Costanzo A, Ibrahim N, Sancho C, Wu X, Han Y, Levy G, Altman K, and Eyerich K. Efficacy and safety of upadacitinib vs dupliumab in adults and adolescents with moderate-to-severe atopic dermatitis: results of an open-label, efficacy assessor-blinded head-to-head phase 3b/4 study (Level Up). *Br J Dermatol* 2024; 191:ii112-ii113. Full Text

J.I. Silverberg, Department of Dermatology, George Washington University, School of Medicine and Health Sciences, Washington, DC, United States

Introduction/Background Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by intense itch and eczematous skin lesions. Some patients with AD continue to experience flares and substantial clinical burden despite the use of systemic therapy. Upadacitinib is a selective oral Janus kinase (JAK) inhibitor with greater inhibitory potency for JAK1 versus JAK2, JAK3, and tyrosine kinase 2. Dupilumab is a monoclonal antibody inhibiting interleukin-4 and interleukin-13 signaling. Both upadacitinib and dupilumab are approved in multiple countries for the treatment of moderate-to-severe AD in adolescents and adults. Objectives This monotherapy study assessed the efficacy and safety of upadacitinib, initiated at 15 mg once daily (QD) and dose-escalated to 30 mg QD based on clinical response, compared with dupilumab per its label. Results presented here are based on the Week 16 primary analysis. Methods Level Up is a phase 3b/4 global, randomized, open-label, efficacy assessor blinded, head-to-head, multi-center study evaluating upadacitinib vs dupilumab in adolescents and adults with moderate-to-severe AD who had inadequate response to systemic therapy or when use of those therapies was inadvisable. Patients were randomized to upadacitinib 15 mg or dupilumab per its label for 16 weeks of treatment (Period 1), with an extension period to 32 weeks (Period 2) for patients not achieving at least 75% reduction in Eczema Area and Severity Index from baseline (EASI 75) at Week 16. Patients on upadacitinib 15 mg were dose-escalated to 30 mg starting from Week 4 if they had a <EASI 50 response, or a <4-point improvement from baseline for their weekly rolling average of Worst Pruritus Numerical Rating Scale (WP-NRS) score. Patients taking upadacitinib 15 mg who did not achieve EASI 75 starting at Week 8 also had their dose increased to 30 mg. Starting at Week 4, rescue with topical therapy was optional and per investigator's discretion if protocol criteria were met. The primary endpoint of the study was the simultaneous achievement of 90% or greater reduction in EASI from baseline (EASI 90) and a WP-NRS of 0 or 1 (WP-NRS 0/1) at Week 16. Results A total of 920 patients (803 adults, 117 adolescents) were randomized to upadacitinib (458) or dupilumab (462). At Week 16, upadacitinib showed superior efficacy versus dupilumab in the primary endpoint, where a significantly higher proportion of patients simultaneously achieved EASI 90 and WP-NRS 0/1 at Week 16 (19.9% vs 8.9% for upadacitinib and dupilumab respectively, $p<0.0001$). Upadacitinib also showed superiority versus dupilumab for all ranked secondary endpoints including skin and itch response endpoints at varying response levels and timepoints. No new safety signals were identified during Period 1. Proportions of patients with any treatment-emergent adverse event were higher for upadacitinib (65.3%) than dupilumab (52.7%). Severe adverse events (AEs) and AEs leading to discontinuation of study treatment were similar between upadacitinib and dupilumab, with no difference in the proportion of serious AEs (0.9%). The most common AE reported was nasopharyngitis for both upadacitinib and dupilumab. One serious infection (0.2%) was reported for dupilumab, and none for upadac - itinib. Five opportunistic infections (excluding tuberculosis and herpes zoster) occurred for upadacitinib (all eczema her - peticum) with none for dupilumab. No malignancies, adju - dicated major adverse cardiac events, adjudicated venous thromboembolic events (VTEs) or deaths were reported in either treatment group. Conclusions Treatment of moderate-to-severe AD with upadacitinib demonstrated superiority versus dupilumab for the primary endpoint of simultaneous achievement of near complete skin clearance (EASI 90) and no to little itch (WP-NRS 0/1) at Week 16 and for all ranked secondary endpoints. There were no new safety risks compared to the known safety profile of upadacitinib.

Dermatology

Silverberg JI, Irvine A, Foley P, Del Rosso J, Schacht A, Dossenbach M, Casillas M, Johansson E, Gallo G, and **Gold LS**. A novel efficacy index for long-term therapy outcomes expressed by maintenance of EASI 75 and IGA 0,1 response in atopic dermatitis. *Br J Dermatol* 2024; 191:ii14-ii15. Full Text

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Introduction Atopic dermatitis (AD) is a common, chronic inflammatory disease requiring long-term, continuous therapy, yet in real life, patients may need to temporarily interrupt therapy. Objectives To indirectly compare long-term outcomes with lebrikizumab, tralokinumab, and dupilumab, we present an exploratory efficacy index, which accounts for on-drug and off-drug combined outcomes at Week 52. Methods The data set consisted of patients who, after 16 weeks, responded to treatment, defined as achieving either an IGA 0,1 or EASI 75 score, and who were randomized to receive maintenance dosages of lebrikizumab 250 mg Q4W (ADvocate1; ADvocate2), tralokinumab 300 mg Q2W (ECZTRA1; ECZTRA 2), and dupilumab 300 mg QW, Q2W (SOLO-CONTINUE) or were randomized to withdraw these treatments up to Week 52. The efficacy index is based on a weighted combination of response rates at Week 52, using non-responder imputation results, for IGA 0,1 or EASI 75, for patients who were either in the treatment continuation or the withdrawal arm. Here, we report the efficacy index, in which the weight places equal emphasis on continuing or stopping treatment, and we compare the efficacy index of tralokinumab and dupilumab with lebrikizumab. Results The efficacy index (95% CI) for lebrikizumab, tralokinumab, and dupilumab, respectively, was 53% (45%-61%), 45% (37%-53%), and 34% (28%-40%) with IGA 0,1; 63% (55%-71%), 42% (35%-49%), and 51% (45%-57%) with EASI 75. With IGA 0,1, lebrikizumab was statistically different from dupilumab; with EASI 75, lebrikizumab was statistically different from dupilumab and tralokinumab. Conclusions This novel efficacy index, which accounts for the importance of continuing or stopping therapy after Week 16, may be a useful tool to indirectly compare long-term treatment outcomes. Lebrikizumab's higher efficacy index may translate to improved long-term management of AD.

Dermatology

Silverberg JI, **Stein-Gold L**, Thaçi D, Pink AE, Papp KA, Legat FJ, Laquer VT, Cheong SY, Ulianov L, Ryzhkova A, and Piketty C. Nemolizumab elicits fast itch response in atopic dermatitis within 2 days: a post hoc analysis of ARCADIA 1 and 2 data. *Br J Dermatol* 2024; 191:ii111-ii112. Full Text

J.I. Silverberg, George Washington University, School of Medicine and Health Sciences, Washington, DC, United States

Background Itch is the most burdensome symptom of atopic dermatitis (AD) that severely affects sleep and overall and quality of life.1,2 Rapid control of itch could be instrumental in minimizing disease symptoms and the associated burden for patients.3,4 Nemolizumab, an interleukin-31 (IL-31) alpha antagonist, inhibits the IL-31 pathway of itch and inflammation in AD.5 Objectives To evaluate speed of onset of itch relief and sleep improvements with nemolizumab in moderate-to-severe AD. Methods ARCADIA-1 and ARCADIA-2 were two identical, randomized, double-blinded, placebo-controlled studies. Patients (≥12 years) with moderate-to-severe AD and inadequate response to topical corticosteroids (TCS) were randomized (2:1) to receive nemolizumab 30mg every 4 weeks (60mg baseline loading dose) or matching placebo, both with background TCS of low/medium potency with/without topical calcineurin inhibitors (TCI). Results Significant improvements in itch (least squares [LS] mean±- standard error [SE] change from baseline [CFB] in Peak Pruritus Numeric Rating Scale [PP-NRS]) were noted in nemolizumab-treated vs placebo-treated patients by Day 1 in ARCADIA-1 (-0.9±0.08 vs -0.4±0.10) and ARCADIA-2 (-1.1±0.09 vs -0.4±0.12), reaching -2.4±0.08 vs -1.2±0.11 and -2.3 ±0.09 vs -0.9±0.12 respectively at Day 14 ($p<0.001$ for all). Significantly greater proportions of nemolizumab-treated vs placebo-treated patients achieved ≥4-point improvement in PP-NRS by Day 2 in ARCADIA-1 (9.4% vs 3.4%, $p<0.01$) and Day 1 in ARCADIA-2 (8.2% vs 1.9%, $p<0.001$) and through Day 14 (ARCADIA-1: 22.7% vs 10.6%, $p<0.0001$; ARCADIA-2: 23.4% vs 6.8%, $p<0.0001$). Conclusions Treatment with

nemolizumab plus TCS/TCI resulted in rapid, statistically and clinically significant improvements in itch in moderate-to-severe AD.

Dermatology
Simpson E, Fenske C, Li A, Dawson Z, Maldonado YM, Ho K, Callahan K, **Gold LS**, Desai S, Golant A, Di Ruggiero D, and Silverberg JI. Characteristics of adult patients with atopic dermatitis initiating biologics and JAK inhibitors in the CorEvitas AD Registry. *Br J Dermatol* 2024; 191:ii43-ii45. Full Text

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Introduction/Background Biologics and Janus kinase inhibitors (JAKi) are promising treatment options for patients with atopic dermatitis (AD)1; however, no studies, to our knowledge, have evaluated differences in characteristics of patients on these medications in a real-world setting. Objective This study sought to describe the demographics, clinical characteristics, treatment patterns, and disease severity and patient-reported outcome measures of adult patients with AD initiating either a biologic or JAKi in the prospective, non-interventional CorEvitas AD Registry. Methods This cross-sectional study included patients initiating either a biologic (dupilumab or tralokinumab) or JAKi (abrocitinib or upadacitinib) in the CorEvitas AD Registry between 7/21/2020 and 7/31/2023. Patient characteristics were summarized at initiation of therapy using descriptive statistics, overall and by prior experience with biologic/JAKi therapy and systemic therapy (any registry-eligible systemic medication). Additionally, exploratory multivariable modified-Poisson regression was used to identify factors associated with biologic vs. JAKi initiation. Variables were selected by first using bivariate regression, and covariates with p-values ≤0.15 were submitted to a backward selection process. Age, sex, and race were included in the final model for representation purposes. Results The study reported 1,958 initiations, with 1,604 biologic initiations and 354 JAKi initiations. The initiated medication was the first-line systemic among 86.4% of the biologic initiators and 40.7% of the JAKi initiators. Biologic initiators were slightly older than JAKi initiators (mean age 50.7 years, SD 18.5 vs. mean 47.9, SD 17.0 years), with no major differences in sex, race/ethnicity, education, or work status. Differences were seen in history of infections (32.7% in biologic initiators vs. 44.9% in JAKi initiators) and rosacea (12.1% biologics vs. 5.9% JAKi). Furthermore, biologic initiators had greater disease severity than JAKi initiators as measured by body surface area % involvement (mean 26.0, SD 20.2 vs. mean 18.3, SD 19.4), validated Investigator Global Assessment for AD (severe vIGA-AD™, 34.4% vs. 24.6%), Eczema Area and Severity Index (EASI, mean 14.5, SD 12.0 vs. mean 10.7, SD 11.1) and SCoring AD (SCORAD, mean 48.2, SD 19.8 vs. mean 42.2, SD 20.1). Patient-reported outcomes were similar between groups. In adjusted analyses, factors positively associated with JAKi initiation compared to biologics included living in the Midwest US (vs. Northeast US, RR: 1.50, 95% CI: 1.14, 1.97), worst skin pain in 24 hours (RR: 1.05, 95% CI: 1.02, 1.09), and prior use of 1 or 2+ systemic therapies (vs. none, RR: 4.30, 95% CI: 2.29, 8.07 and RR: 5.49, 95% CI: 3.06, 9.84, respectively). Factors positively associated with biologic initiation included having a history of cancer (RR: 0.33, 95% CI: 0.22, 0.49), moderate vIGA-AD™ (vs. clear, RR: 0.74, 95% CI: 0.56, 0.98), hand involvement (RR: 0.73, 95% CI: 0.62, 0.86), and worst itch in 24 hours (RR: 0.97, 95% CI: 0.94, 0.99). Conclusions In this real-world assessment, certain characteristics differed between adult patients with AD initiating either biologics which were most commonly first-line agents or JAKi (more likely used after other systemic agents), although some effect sizes were small and may not be clinically meaningful. Study limitations to consider include that characteristics associated with biologic or JAKi initiation may be influenced by timing of medication approval and availability. These foundational results highlight the importance of individualized patient assessment when deciding among different therapeutic approaches.

Dermatology
Strober B, **Gold LS**, Gisondi P, Orroth K, Cordey M, Kent ST, Deignan C, Jardon S, Hernandez RK, Brookhart MA, and Armstrong A. REAL WORLD EFFECTIVENESS OF INITIATING TOPICAL THERAPY COMPARED WITH INITIATING APREMILAST EARLY OR LATE. *Acta Derm Venereol* 2024; 104:102. Full Text

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Shauna; Hernandez, Rohini K.] Amgen Inc, Thousand Oaks, CA USA. [Brookhart, M. Alan] Duke Univ, Durham, NC USA. [Armstrong, April] Univ Calif Los Angeles, Los Angeles, CA USA. University of California System; University of California Los Angeles

Dermatology
Strober B, Sofen H, Imafuku S, Paul C, Gooderham M, Spelman L, Seo SJ, Passeron T, Kisa RM, Berger V, Vritzali E, Hoyt K, Colombo MJ, Banerjee S, Augustin M, **Stein Gold L**, Alexis A, Thaçi D, Blauvelt A, and Lebwohl M. DEUCRAVACITINIB IN PLAQUE PSORIASIS: MAINTENANCE OF RESPONSE OVER 3 YEARS. *Ann Rheum Dis* 2024; 83:2039-2040. Full Text

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Background: Deucravacitinib, a first-in-class, oral, selective, allosteric tyrosine kinase 2 inhibitor, is approved in multiple countries for the treatment of adults with plaque psoriasis. Deucravacitinib was superior to placebo and apremilast in the global, 52-week, phase 3 POETYK PSO-1 (NCT03624127) and PSO-2 (NCT03611751) trials in psoriasis. [1] Deucravacitinib is being investigated in several immune-mediated diseases and has shown efficacy vs placebo in phase 2 trials in systemic lupus erythematosus (SLE) (NCT03252587) and psoriatic arthritis (PsA) (NCT03881059). The POETYK long-term extension (LTE) trial (NCT04036435) showed that deucravacitinib maintained long-term efficacy through 2 years, with no new safety signals. [2] Objectives: We report clinical efficacy up to 3 years (148 weeks) in the POETYK LTE trial in a subset of patients with plaque psoriasis who received continuous deucravacitinib from day 1 in the parent trials. Methods: In POETYK PSO-1 and PSO-2, patients were randomized 1:2:1 to placebo, deucravacitinib 6 mg once daily (QD), or apremilast 30 mg twice daily. At week 52, patients could enter the POETYK LTE trial and receive open-label deucravacitinib 6 mg QD. Deucravacitinib efficacy through week 148 was evaluated in patients from pooled POETYK PSO-1 and PSO-2 populations; these patients received continuous deucravacitinib from day 1, achieved ≥ 75% reduction from baseline in Psoriasis Area and Severity Index score (PASI 75) at week 16 (primary endpoint) or week 24 (peak response), and were enrolled in the POETYK LTE trial. Maintenance of response was assessed through the data cutoff (June 15, 2022); responses assessed included PASI 75 and ≥ 90% reduction from baseline in PASI (PASI 90). A static Physician's Global Assessment (sPGA) score of 0 (clear) or 1 (almost clear) with a ≥ 2-point improvement from baseline was assessed. Results: A total of 513 patients completed 52 weeks in the parent trials and received continuous deucravacitinib from day 1, including 313 patients (61.4%; 95% CI, 57.0-65.6) who achieved PASI 75 at week 16 and 336 patients (66.5%; 95% CI, 62.2-70.6) who achieved PASI 75 at week 24. Among these patients, PASI 75 response rates were maintained from weeks 52 to 148 (Table 1). PASI 90 response rates were maintained in > 50% of patients from the start of the POETYK LTE trial (Table 1). Response rates for sPGA score of 0/1 were maintained from weeks 52 to 148 (Table 1). Conclusion: Clinical efficacy was maintained for up to 148 weeks with continuous deucravacitinib in most patients who were week 16 and week 24 PASI 75 responders in the parent trials and enrolled in the POETYK LTE trial. These findings further support the long-term use of once-daily oral deucravacitinib as an effective treatment for patients with psoriasis.

Dermatology
Yamaguchi Y, Peeva E, Adiri R, Ghosh P, Napatalung L, **Hamzavi I**, Pandya AG, Shore RN, Ezzedine K, and Guttman-Yassky E. Response to ritlecitinib with or without narrow band ultraviolet B (nbUVB) add-on therapy in patients with active non-segmental vitiligo (NSV). *Br J Dermatol* 2024; 191:ii27-ii28. Full Text

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Introduction/Background Ritlecitinib, a JAK3/TEC family kinase inhibitor, demonstrated efficacy in a Phase 2b trial of patients with NSV. Objectives To evaluate the efficacy and tolerability of ritlecitinib with or without nbUVB add-on therapy in patients with NSV. Methods In a Phase 2b trial, following a 24-week placebo-controlled dose-ranging period, patients with NSV received ritlecitinib 200 mg for 4 weeks then 50 mg for 20 weeks, with or without nbUVB phototherapy 2x/week. Missing data were handled using observed case (OC) and last observation carried forward (LOCF). Results 43 and 187 patients received ritlecitinib+nbUVB and ritlecitinib-monotherapy, respectively. Nine patients receiving ritlecitinib+nbUVB

discontinued due to nbUVB group-specific efficacy criteria requiring >10% improvement in %change from baseline (CFB) in Total-Vitiligo Area Scoring Index (T-VASI) at Week 12. At Week 24, mean (90% CI) %CFB in Facial-VASI (F-VASI) was -69.6 (-79.1, -60.1) vs -55.1 (-59.4, -50.7) (OC; P=0.009) and -57.0 (-65.3, -48.7) vs -51.5 (-55.9, -47.1) (LOCF; P=0.158), for ritlecitinib+nbUVB vs ritlecitinib-monotherapy, respectively. 60.9% (43.1%, 77.2%) vs 29.2% (22.8%, 35.9%) (OC; P=0.007) and 44.4% (30.2%, 59.1%) vs 27.4% (21.7%, 33.4%) (LOCF; P=0.081) of patients, respectively, achieved ≥75% improvement in F-VASI. Mean (90% CI) %CFB in T-VASI at Week 24 was -46.8 (-54.5, -39.2) vs -24.5 (-28.1, -21.0) (OC; P<0.001) and -29.4 (-36.5, -22.2) vs -21.2 (-25.0, -17.4) (LOCF; P=0.043) for ritlecitinib+nbUVB vs ritlecitinib-monotherapy, respectively. 50.0% (33.3%, 66.7%) vs 15.2% (11.1%, 20.3%) (OC; P<0.001) and 32.6% (22.1%, 44.7%) vs 14.4% (10.6%, 19.0%) (LOCF, P=0.014) of patients, respectively, achieved ≥50% improvement in T-VASI. nbUVB addition to ritlecitinib was well-tolerated with no new safety signals. Conclusions Ritlecitinib alone and with nbUVB therapy improved facial and total body repigmentation and was well-tolerated. nbUVB may improve ritlecitinib efficacy.

Diagnostic Radiology

George M, **Clark J**, **Hartway K**, **Zwernik S**, **Gartrelle K**, **Salas-Escabillas D**, **Long D**, **Nassif G**, **Pichardo T**, **Wombwell A**, **Wen HJ**, **Benitz S**, **Philip PA**, **Khan G**, **Shah RA**, **Park H**, **Crawford H**, **Kwon DS**, **Theisen B**, and **Steele N**. Longitudinal tissue-based evaluation of TIGIT expression in patients with pancreatic cancer: Effect of expression with advancing clinical stages and across racial groups. *J Clin Oncol* 2024; 42(16). Full Text

M. George

Background: While ground has been gained, pancreatic ductal adenocarcinoma (PDAC) continues to have a low 5-year survival of 13%. This is owed partially to a lack of early detection biomarkers and resistance to standard therapeutic options. TIGIT, an immune checkpoint receptor, is a marker of T-cell exhaustion and plays a key role in the inhibition of anti-tumor immune responses. TIGIT inhibitors are being explored in clinical trials in PDAC. Here we evaluate TIGIT expression in a cohort of PDAC patients and correlate level and intensity of expression with clinical parameters. We also examine changes in expression as the disease progresses from primary to metastatic disease. Methods: We performed RNAscope in situ hybridization (ISH) with a probe specific for human TIGIT mRNA on 82 formalin-fixed paraffin-embedded (FFPE) tissue samples. The cohort of tissue samples included 9 biopsies, 67 primary resections and 6 metastatic lesions. We evaluated the total TIGIT expression (%) as well as the intensity of TIGIT expression (% of cells with 3+ punctae, signifying putative immune cells), and compared these values between samples. Utilizing linear regression for continuous outcomes and logistic regression for binary outcomes, we tested for associations between TIGIT expression and clinical covariates. Results: Staining analysis showed that TIGIT expression did not differ significantly between racial groups. The mean percentage of TIGIT positive cells was 64.0%. High expression of TIGIT was associated with more advanced clinical stage ($p < 0.05$). Evaluation of three longitudinal samples from the same patient revealed decreased TIGIT expression from the initial biopsy (41.6%) to resection (33.4%) and metastasis (2.8%). In these specimens, 3+ TIGIT expression also declined (2.1%, 1.2% and 0.02%, respectively). Conclusions: Anti-TIGIT therapy has potential to reverse immune suppression and, with other therapeutic modalities, may provide survival benefit. Here we demonstrate that increased TIGIT expression correlates with more advanced stage at diagnosis and also present data demonstrating that overall TIGIT expression, as detected by RNAscope ISH, may decrease as PDAC progresses to metastasis. As such, anti-TIGIT therapy may have important implications for evading an important mechanism of cancer progression.

Emergency Medicine

Jaehne A, Naiman M, **Cook B**, **Wilson I**, **Veryser D**, **Kelly W**, **Ghosh S**, and **Rivers EP**. Value of Monocyte Distribution Width in Bacteremia Assessment in Emergency Department Patients. *Am J Respir Crit Care Med* 2024; 209. Full Text

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Rationale Monocyte distribution width (MDW) is a pathogen-agnostic marker of immune response and dysregulation reported as part of a Complete Blood Count (CBC) with differential. MDW is derived from the distribution of peripheral blood monocyte volumes and aids in the identification of severe infections and sepsis in adult Emergency Department (ED) patients. Several prospective clinical trials have demonstrated that elevated MDW values are associated with severe infection in the general adult ED population. Additional real-world examination can help refine interpretation in early clinical scenarios. MDW could play a useful role in assessing bacteremia and septicemia risk. Bacteremia, defined as the presence of viable bacteria in the bloodstream, is present in up to 20% of sepsis patients. Blood culture establishes pathogen presence and identity but requires time. This may limit a more aggressive treatment strategy. The purpose of this study was to characterize MDW clinical behavior in the context of bacteremia upon hospital presentation. Methods This was a prospective, observational cohort study. All patients who presented to the ED, were over 18 years of age, and had a blood culture order along with a CBC with differential were enrolled into the study. MDW values were blinded to those involved in direct patient care. An MDW value ≥20 is the published cut-off for increased severe infection risk. We calculated the diagnostic accuracy of MDW values ≥20 for positive blood cultures using SPSS Version 25. Results From July 2021 to September 2023 a total of 185,405 ED visits were registered. During this time 9,400 ED blood cultures were ordered. A total of 5,316 ED blood culture results were matched with MDW results. The overall blood culture positivity rate was 14.5%. MDW sensitivity and specificity for positive blood culture were 83.9% and 36.2%, respectively. Positive and negative predictive values were 18.2% and 93.0%, respectively. Conclusion This interim analysis suggests that MDW may be a useful adjunct for early detection of bacteremia in ED patients. The observed sensitivity is consistent with the known relationship between positive blood culture and sepsis. Since MDW results can be available well before blood culture results, this biomarker could help early risk stratification among suspected infection patients. MDW values below 20 have a high predicative value for negative blood cultures. Further analysis incorporating additional clinical information will provide guidance for interpreting MDW values in combination blood culture results.

Gastroenterology
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Chaudhary A, Harris K, **Faisal MS**, **Toiv A**, Shahzil M, **Samad M**, **Youssef R**, Farooq U, Tarar Z, and **Suresh S**. USE OF AN ENDOCUFF COLONOSCOPE ATTACHMENT INCREASES SESSILE SERRATED POLYP DETECTION. *Gastrointest Endosc* 2024; 99(6):AB518-AB519. Full Text

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Gastroenterology
Chaudhary A, Harris K, **Toiv A**, Shahzil M, **Faisal MS**, **Ichkhanian Y**, **Dababneh Y**, **Patel-Rodrigues P**, **Salgia R**, and **Watson A**. INCREASED RECEIPT OF CURATIVE INTENT THERAPY FOR LIVER CANCER AFTER EUS-GUIDED ASSESSMENT OF PORTAL HYPERTENSION. *Gastrointest Endosc* 2024; 99(6):AB807-AB808. Full Text

Henry Ford Hlth Syst, Detroit, MI USA. Resilience Healthcare Weiss Mem Hosp LLC, Chicago, IL USA. Indiana Univ Sch Med, Indianapolis, IN 46202 USA. System; Indiana University Bloomington

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Chavan AK, **Adil S**, Chaudhari R, Satyavada S, Jha P, Vachhani R, and Wong R. ENDOSCOPIC CYANOACRYLATE INJECTION 2.0: DOPPLER ENDOSCOPIC PROBE GUIDED TECHNIQUE FOR THE TREATMENT OF GASTRIC VARICES. *Gastrointest Endosc* 2024; 99(6):AB752-AB753. Full Text

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Gastroenterology
Faisal MS, **Ashraf T**, **Faisal MS**, **Harris K**, **Khan MZ**, **Chaudhary A**, **Watson A**, **Dang DY**, **Pompa R**, **Elatrache M**, **Piraka C**, **Singla S**, and **Zuchelli T**. CYSTIC DUCT STENTING VERSUS OTHER TREATMENT MODALITIES FOR MANAGEMENT OF ACUTE CHOLECYSTITIS IN PATIENTS WITH DECOMPENSATED CIRRHOSIS. *Gastrointest Endosc* 2024; 99(6):AB651-AB652. Full Text

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Faisal MS, **Faisal MS**, **Chaudhary A**, **Shamaa O**, **Alomari A**, **Dang DY**, **Watson A**, **Elatrache M**, **Pompa R**, **Piraka C**, **Singla S**, and **Zuchelli T**. AMPULLARY ADENOMAS GREATER THAN 20 MM IN SIZE HAVE HIGHER RISK OF RECURRENCE COMPARED TO SMALLER LESIONS. *Gastrointest Endosc* 2024; 99(6):AB628-AB628. Full Text

[Faisal, Muhammad Salman; Faisal, Muhammad Saad; Chaudhary, Ammad; Shamaa, Omar; Alomari, Ahmad; Dang, Duyen; Watson, Andrew; Elatrache, Mazen; Pompa, Robert; Piraka, Cyrus; Singla, Sumit; Zuchelli, Tobias] Henry Ford Hlth Syst, Detroit, MI USA.

Gastroenterology
Faisal MS, **Shamaa O**, **Faisal MS**, **Dang D**, **Watson A**, **Elatrache M**, **Pompa R**, **Piraka C**, **Zuchelli T**, and **Singla S**. SAFETY AND EFFICACY OF BILIARY RADIOFREQUENCY ABLATION IN MANAGEMENT OF AMPULLARY LESIONS. *Gastrointest Endosc* 2024; 99(6):AB630-AB631. Full Text

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Gastroenterology
Jamali T, **Faisal MS**, **Chaudhary A**, **Faisal MS**, **Nimri F**, **Khan MZ**, **Alomari A**, **Saleem A**, **Kostecki P**, **Youssef R**, **Vemulapalli K**, **Ali SA**, **Patel-Rodrigues P**, **Watson A**, **Dang D**, **Elatrache M**, **Piraka C**, **Singla S**, **Pompa R**, and **Zuchelli T**. RISK OF CHOLECYSTITIS WITH PLACEMENT OF FULLY COVERED METAL BILIARY STENT: REAL WORLD EXPERIENCE FROM A TERTIARY CARE REFERRAL CENTER. *Gastrointest Endosc* 2024; 99(6):AB696-AB697. Full Text

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Gastroenterology
Jamali T, **Nimri F**, **Chaudhary A**, **Saleem A**, **Faisal MS**, **Alomari A**, **Abusuliman M**, **Faisal MS**, **Watson A**, **Pompa R**, **Elatrache M**, **Dang D**, **Piraka C**, **Singla S**, and **Zuchelli T**. ADVERSE EVENTS RELATED TO DILATION OF LUMEN APPOSING METAL STENTS DURING ENDOSCOPIC ULTRASOUND GUIDED INTERVENTIONS. *Gastrointest Endosc* 2024; 99(6):AB915-AB916. Full Text

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Jamali T, **Nimri F**, **Chaudhary A**, **Saleem A**, **Faisal MS**, **Samad M**, **Faisal MS**, **Dang D**, **Zuchelli T**, and **Singla S**. ADVERSE EVENTS RELATED TO ERCP WITH CHOLANGIOSCOPY IN LIVER TRANSPLANT RECIPIENTS. *Gastrointest Endosc* 2024; 99(6):AB636-AB637. Full Text

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Gastroenterology
Jamali T, **Nimri F**, and **Elatrache M**. A FISHY CASE: ECTOPIC PANCREATIC TISSUE CONTAINING A MUCINOUS CYSTIC NEOPLASM WITHIN THE DUODENUM IDENTIFIED BY "FISH-MOUTH" APPEARANCE ON ENDOSCOPY. *Gastrointest Endosc* 2024; 99(6):AB103-AB103. Full Text

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Nimri F, **Jamali T**, **Ali SA**, **Dawod S**, **Alluri S**, **Youssef R**, **Faisal MS**, **Omeish H**, **Abusuliman M**, **Saleem A**, **Alomari A**, **Faisal MS**, **Singla S**, and **Zuchelli T**. THE SAFETY OF SPHINCTEROTOMY IN ERCP AMONG PATIENTS WITH CIRRHOSIS: INSIGHTS FROM A QUATERNARY CARE TRANSPLANT CENTER. *Gastrointest Endosc* 2024; 99(6):AB683-AB684. Full Text

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Gastroenterology
Patel-Rodrigues P, **Jamali T**, **Shamaa O**, **Nimri F**, **Piraka C**, and **Elatrache M**. NAVIGATING HEPATOLITHIASIS: A CASE REPORT OF ENDOSCOPIC MANAGEMENT OF HEPATOLITHIASIS IN A TERTIARY CARE SETTING. *Gastrointest Endosc* 2024; 99(6):AB117-AB118. Full Text

[Patel-Rodrigues, Palak; Jamali, Taher; Shamaa, Omar; Nimri, Faisal; Piraka, Cyrus; Elatrache, Mazen] Henry Ford Hosp, Detroit, MI USA.

Gastroenterology
Pohl H, Rex D, Barber J, Moyer M, Elmunzer B, Rastogi A, **Gordon S**, Zolotarevsky E, Levenick J, Aslanian H, **Elatrache M**, Von Renteln D, Brahmbhatt B, Keswani R, Kumta N, Pleskow D, Smith Z, Abu Ghanimeh M, Sanaei O, Jensen L, Mackenzie T, and **Piraka C**. COLD SNARE ENDOSCOPIC RESECTION FOR LARGE COLON POLYPS - A RANDOMIZED TRIAL. *Gastrointest Endosc* 2024; 99(6):AB442-AB442. Full Text

Dartmouth Hitchcock Med Ctr, Lebanon, NH USA. Indiana Univ Sch Med, Indianapolis, IN USA. Corewell Hlth Butterworth Hosp, Grand Rapids, MI USA. Penn State Hlth Milton S Hershey Med Ctr, Hershey, PA USA. Med Univ South Carolina, Columbia, SC USA. Univ Kansas, Med Ctr, Lawrence, KS USA. Yale New Haven Hosp, New Haven, CT USA. Henry Ford Hosp, Detroit, MI USA. Ctr Hosp Univ Montreal, Montreal, PQ, Canada. Mayo Clin, Jacksonville, FL USA. Northwestern Univ, Feinberg Sch Med, Evanston, IL USA. Icahn Sch Med Mt Sinai, New York, NY USA. Beth Israel Deaconess Med Ctr, Boston, MA USA. Med Coll Wisconsin, Milwaukee, WI USA. Univ Nebraska Med Ctr, Lincoln, NE USA. Dartmouth Inst Hlth Policy & Clin Practice, Lebanon, NH USA. White River Junct VA Med Ctr, Hartford, CT USA. Bloomington; Pennsylvania Commonwealth System of Higher Education (PCSHE); Pennsylvania State University; Penn State Health; Medical University of South Carolina; University of Kansas; University of Kansas Medical Center; Yale University; Henry Ford Health System; Henry Ford Hospital; Universite de Montreal; Mayo Clinic; Northwestern University; Feinberg School of Medicine; Icahn School of Medicine at Mount Sinai; Harvard University; Beth Israel Deaconess Medical Center; Medical College of Wisconsin; University of Nebraska System; University of Nebraska Medical Center; University of Nebraska Lincoln; Dartmouth College

Gastroenterology
Samad M, **Kostecki P**, **Nabaty R**, **Faisal MS**, **Jamali T**, **Chaudhary A**, **Youssef R**, **Zuchelli T**, **Singla S**, and **Piraka C**. ROLE OF ENDOSCOPIC ULTRASOUND AND PROGRESSION OF PANCREATIC CYSTS IN SOLID ORGAN TRANSPLANT PATIENTS. *Gastrointest Endosc* 2024; 99(6):AB933-AB933. Full Text

[Samad, Momin; Kostecki, Polo; Nabaty, Renieh; Faisal, Muhammad Salman; Jamali, Taher; Chaudhary, Ammad; Youssef, Rami; Zuchelli, Tobias; Singla, Sumit; Piraka, Cyrus] Henry Ford Hosp, Detroit, MI USA.

Gastroenterology
Shahzil M, **Chaudhary A**, Qureshi AA, Hasan F, **Jamali T**, Khan MZ, **Faisal MS**, Khaqan MA, **Alsheik E**, and **Zuchelli T**. "ENDOSCOPIC FULL-THICKNESS PLICATION FOR THE TREATMENT OF GASTROESOPHAGEAL REFLUX DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED, SHAM-CONTROLLED TRIALS". *Gastrointest Endosc* 2024; 99(6):AB154-AB155. Full Text

Henry Ford Hlth Syst, Detroit, MI USA. Weiss Mem Hosp LLC, Resilience Healthcare, Chicago, IL USA. King Edward Med Univ, Lahore, Pakistan. Cooper Univ Hlth Care, Camden, NJ USA. John H Stroger Jr Hosp Cook Cty, Chicago, IL USA. Hospital Cook County; University of Illinois System; University of Illinois Chicago; University of Illinois Chicago Hospital

Gastroenterology
Shamaa O, **Ali SA**, **Omeish H**, **Alomari A**, **Dababneh Y**, **Piraka C**, and **Zuchelli T**. ASSESSING PROCEDURE OUTCOMES FOLLOWING PIECEMEAL COLD SNARE ENDOSCOPIC MUCOSAL RESECTION OF LARGE NON-PEDUNCULATED COLORECTAL POLYPS. *Gastrointest Endosc* 2024; 99(6):AB520-AB521. Full Text

[Shamaa, Omar; Ali, Suhib Alhaj; Omeish, Haya; Alomari, Ahmad; Dababneh, Yara; Piraka, Cyrus; Zuchelli, Tobias] Henry Ford Hosp, Detroit, MI USA.

Global Health Initiative
Antwi S, **Kaljee L**, **Dankerlui D**, **Walker EM**, **Larrious-Lartey H**, Brush B, Israel B, Harris D, Chue S, Cawthome N, Mills C, **Aboah VO**, Daniels G, Aduse-Poku L, Coombe CM, Rowe Z, Patman L, Ramocan W, **Perkins DW**, and **Jiagge EM**. Black/African American participation in cancer clinical trials: A qualitative study of community members, patients with cancer, and survivors (Detroit, MI) using CBPR. *J Clin Oncol* 2024; 42(16). Full Text

S. Antwi

Background: Black/African Americans (B/AA) have a disproportionate cancer burden and the highest mortality rates of any racial/ethnic group for most cancers. Racial/ethnic variation in cancer burden reflects health inequities, differences in risk factors, heredity and genomic diversity, and lack of access to and participation in cancer prevention, screening, treatment, and clinical trials. Twelve percent of the United States population are B/AA; however, only about 5% B/AA participate in clinical trials. As a result, data regarding tumors from B/AA are not equally represented in new drug discovery efforts. Methods: Participatory Action for Access to Clinical Trials (PAACT) used a Community Based Participatory Research (CBPR) approach to support a partnership between Henry Ford Health (HFH) and eight African American, Caribbean, and continental African community-based organizations (CBOs). Focus group data were collected in-person and virtually with representatives from the CBOs and HFH cancer survivors. CBOs participated in Steering Committee meetings throughout the project and two community forums to obtain feedback on recommendations identified through the qualitative data. Results: Factors contributing to participation in cancer clinical trials included systemic issues related to racism, health disparities and trust in government, health systems, and clinical research. Other factors included personal experiences with healthcare systems, healthcare provider-patient communication, socio-economic barriers (e.g., time away from work, family), and perceptions of future benefits from trials for B/AA communities. Recommendations included: 1) on-going health system outreach to B/AA communities regarding cancer prevention and treatment, as well as clinical trials. 2) B/AA community liaisons and cancer survivors as providers of information related to clinical trials; 3) two-way provider-patient communication to address questions and concerns about treatment options and trial information; 4) monetary compensation for indirect trial costs; 5) information on the importance of diversity within trials; and 6) ensuring information is provided to patients' support networks. Conclusions: CBPR is effective in the identification of factors that influence participation in clinical trials. Building trust between patients and the healthcare system begins before patients walk into a clinic and every interaction contributes to institutional worthiness of community and patient trust. It is possible and imperative for health systems to work with B/AA communities and jointly identify and implement recommendations to ensure informed decision-making regarding trial

participation. We are currently designing intervention strategies based on the recommendations for implementation at HFH.

Hematology-Oncology
Abu Rous F, Sussell J, Kochounian CN, Zhang Q, Majda T, Sheinson D, Ogale S, Bara I, and **Gadgeel S**. Patient Characteristics and Treatment Patterns in Biomarker Selected Early Non-Small Cell Lung Cancer. *J Thorac Oncol* 2024; 19(7):E47-E47. Full Text

[Abu Rous, Fawzi; Gadgeel, Shirish] Henry Ford Hlth, Detroit, MI USA. [Sussell, Jesse; Kochounian, Celina Ngiam; Zhang, Qing; Majda, Thomas; Sheinson, Danny; Ogale, Sarika; Bara, Ilze] Genentech Inc, San Francisco, CA USA.

Hematology-Oncology
Aerts J, Paz-Ares LG, Helissey C, Cappuzzo F, Quere G, Kowalski D, Benitez JC, Guisier F, Besse B, **Gadgeel SM**, Wehler T, Gil-Bazo I, Chisamore MJ, Gorgun C, Celik I, Mørch MH, Castro PG, Ong TJ, and Felip E. Acasunlimab (DuoBody-PD-L1x4-1BB) alone or in combination with pembrolizumab (pembro) in patients (pts) with previously treated metastatic non-small cell lung cancer (mNSCLC): Initial results of a randomized, open-label, phase 2 trial. *J Clin Oncol* 2024; 42(16). Full Text

J. Aerts

Background: Most pts with mNSCLC without actionable gene alterations have limited options after progression on first-line checkpoint inhibitor (CPI)-containing treatment (tx). Given failures of recent trials in this setting, single-agent chemotherapy remains the main tx option despite limited effectiveness (eg, docetaxel ORR 10-14%) and considerable toxicity. Acasunlimab is a bispecific antibody designed to elicit antitumor immune response via conditional 4- 1BB activation strictly dependent on simultaneous PD-L1 binding. Preclinical and PK/PD findings support combining acasunlimab with additional PD-1 blockade to further potentiate anti-tumor activity and potentially extend durability. Initial results from the ongoing randomized, phase 2 trial (NCT05117242) evaluating acasunlimab as monotherapy (mono) and in combination with pembro (combo) in pts with mNSCLC are reported. Methods: Eligible pts had PD-L1+ mNSCLC, with progression after ≥1 prior anti-PD-(L)1 tx. Tumor PD-L1 status was assessed by central testing (TPS≥1%, PD-L1 IHC 22C3 PharmDx); this subset is presented in the efficacy analyses. Following safety run-in, pts were randomized to acasunlimab mono (arm A, 100 mgQ3W x 2 cycles then 500mg Q6W) or combo (arm B, 100mg + pembro 200mg Q3W; arm C, 100 mg + pembro 400 mg Q6W). Primary efficacy endpoint was ORR per RECIST v1.1. Stratification factors were PD-L1 expression and histology. Results: As of Jan 9, 2024, 98 pts (63 with central PD-L1+ status) were enrolled: 23 (16) pts arm A; 39 (22) pts arm B; 36 (25) pts arm C. Among evaluable PD-L1+ pts, 86% received prior pembro tx; 64% had prior concurrent CPI + chemotherapy. Unconfirmed ORR and DCR were 31% and 50% for arm A, 25%and65%for arm B, and30%and75%for arm C, respectively. Confirmed ORRs (and mDoR) were 13% (2 mo), 21% (6 mo), and 22% (NR), with 6-mo PFS rates of 0%, 18%, and 33% for arms A, B, and C, respectively. No responses were observed among centrally confirmed PD-L1- negative pts. The most common TRAEs (all grades; grade ≥3) were asthenia (17.4%; 8.7%), diarrhea (17.4%; 0%), nausea (17.4%, 0%), anemia (13%; 4.3%) and liver-related events (13%; 8.7%) for mono, and liver-related events (18.7%; 13.3%), fatigue (14.7%; 0%), asthenia (13.3%; 0%), and diarrhea (12%; 0%) for combo. Transaminase elevations were generally asymptomatic and manageable with steroids and/or tx delay. Early peripheral pharmacodynamics were consistent with acasunlimab-mediated immune activation in all arms, with a more pronounced increase in CD8 T-cell proliferation with combo. Conclusions: In PD-L1+ pts with mNSCLC following progression on prior CPI tx, acasunlimab + pembro combo showed a manageable safety profile and promising efficacy, with deeper responses and durable disease control in pts treated Q6W. Enrollment is ongoing.

Hematology-Oncology
Antwi S, **Kaljee L**, **Dankerlui D**, **Walker EM**, **Larrious-Lartey H**, Brush B, Israel B, Harris D, Chue S, Cawthome N, Mills C, **Aboah VO**, Daniels G, Aduse-Poku L, Coombe CM, Rowe Z, Patman L, Ramocan W, **Perkins DW**, and **Jiagge EM**. Black/African American participation in cancer clinical trials: A

qualitative study of community members, patients with cancer, and survivors (Detroit, MI) using CBPR. *J Clin Oncol* 2024; 42(16). Full Text

S. Antwi

Background: Black/African Americans (B/AA) have a disproportionate cancer burden and the highest mortality rates of any racial/ethnic group for most cancers. Racial/ethnic variation in cancer burden reflects health inequities, differences in risk factors, heredity and genomic diversity, and lack of access to and participation in cancer prevention, screening, treatment, and clinical trials. Twelve percent of the United States population are B/AA; however, only about 5% B/AA participate in clinical trials. As a result, data regarding tumors from B/AA are not equally represented in new drug discovery efforts. Methods: Participatory Action for Access to Clinical Trials (PAACT) used a Community Based Participatory Research (CBPR) approach to support a partnership between Henry Ford Health (HFH) and eight African American, Caribbean, and continental African community-based organizations (CBOs). Focus group data were collected in-person and virtually with representatives from the CBOs and HFH cancer survivors. CBOs participated in Steering Committee meetings throughout the project and two community forums to obtain feedback on recommendations identified through the qualitative data. Results: Factors contributing to participation in cancer clinical trials included systemic issues related to racism, health disparities and trust in government, health systems, and clinical research. Other factors included personal experiences with healthcare systems, healthcare provider-patient communication, socio-economic barriers (e.g., time away from work, family), and perceptions of future benefits from trials for B/AA communities. Recommendations included: 1) on-going health system outreach to B/AA communities regarding cancer prevention and treatment, as well as clinical trials. 2) B/AA community liaisons and cancer survivors as providers of information related to clinical trials; 3) two-way provider-patient communication to address questions and concerns about treatment options and trial information; 4) monetary compensation for indirect trial costs; 5) information on the importance of diversity within trials; and 6) ensuring information is provided to patients' support networks. Conclusions: CBPR is effective in the identification of factors that influence participation in clinical trials. Building trust between patients and the healthcare system begins before patients walk into a clinic and every interaction contributes to institutional worthiness of community and patient trust. It is possible and imperative for health systems to work with B/AA communities and jointly identify and implement recommendations to ensure informed decision-making regarding trial participation. We are currently designing intervention strategies based on the recommendations for implementation at HFH.

Hematology-Oncology

Cho BC, Hamid O, Zhu X, Keam B, Kaczmar JM, Williamson SK, Birnbaum AE, Dowlati A, Dy GK, Hager SJ, Lynce F, McDermott RS, Sarker D, **Weise AM**, Yap TA, Yilmaz E, Fang F, Mani J, Kroog GS, and Papadopoulos KP. A phase 1 study of fianlimab (anti-LAG-3) in combination with cemiplimab (anti-PD-1) in patients with advanced HNSCC. *J Clin Oncol* 2024; 42(16). Full Text

B.C. Cho

Background: Concurrent blockade of LAG-3 may enhance efficacy of anti-PD-1 therapies. We present safety and clinical activity data from a Phase 1 study in patients (pts) with head and neck squamous cell carcinomas (HNSCC) treated with anti-LAG-3 (fianlimab) + anti-PD-1 (cemiplimab). Methods: Two expansion cohorts of adult pts with recurrent and/or metastatic HNSCC with no curative options who were anti-PD-1/PD-L1-naïve (cohort 11) or anti-PD-1/L1- experienced with most recent dose within 3 months (mos) prior to screening (cohort 12) were enrolled. All pts received fianlimab 1600 mg + cemiplimab 350 mg intravenously every 3 weeks (wks) for up to 24 mos. Tumor measurements were performed every 6 wks for 24 wks, then every 9 wks. Results: 15 pts each in cohort 11 and 12 (total N=30; median age: 69 years) were enrolled and treated with fianlimab + cemiplimab as of 04 Oct 2023 data cutoff.For cohorts 11 and 12 respectively, 80% and 87% of pts were male, and 53% and 80% were White. All pts had prior cancer-related systemic therapy. 33% (5/15) and 87% (13/15) of pts in cohorts 11 and 12 had ≥2 lines of prior therapies, respectively. For cohorts 11 and 12, median treatment duration was 12 wks (mean: 41 wks) and 13 wks (mean: 24 wks), and median follow-up was 12 mos and 10 mos, respectively. Grade ≥3 treatment-emergent adverse events (TEAEs) occurred in 47% of pts each in cohorts 11 and 12. Serious

TEAEs occurred in 13% and 20% of pts in cohorts 11 and 12, respectively. Treatment-related TEAEs (TRAEs) were reported in 67% of pts in cohorts 11 and 53% of pts in cohort 12. The most common TRAEs (any grade) were hypothyroidism (33%) in cohort 11; and fatigue (20%) and pneumonitis (20%) in cohort 12. Grade ≥3 TRAEs occurred in 7% of pts in cohorts 11 and 13% of pts in cohorts 12. Treatment-related immune-related AEs were reported in 47% and 40% of pts in cohorts 11 and 12, respectively. Treatment was discontinued due to any TEAE in 2 pts in cohort 12. In cohort 12, there was one death due to grade 5 respiratory failure attributable to aspiration pneumonia. RECIST 1.1-based investigator-assessed objective response rate (ORR) was 33% (5 partial responses [PRs]) in cohort 11 and7%(1 PR) in cohort 12. The disease control rate (DCR) was47%and67%in cohorts 11 and 12, respectively. Kaplan-Meier estimation of median progression-free survival was 2 mos (95% CI, 1-14) in cohort 11 and 4 mos (95% CI, 1-7) in cohort 12 pts. Duration of responses were 17, 10, 20, 22, and 20 mos in 5 responders in cohort 11; and 32 mos in 1 responder in cohort 12. Estimated event-free probability at 12 month was 33% (95% CI, 12-56) in cohort 11 and 16% (95% CI, 3-40) in cohort 12 pts. Conclusions: Fianlimab + cemiplimab in pts with HNSCC showed signs of clinical activity with durable responses among pts with anti-PD-1/PD-L1- naïve (cohort 11) and anti-PD-1/L1-experienced (cohort 12), with an acceptable safety profile which warrants further investigation.

Hematology-Oncology
Connell B, **Hwang C**, Folefac E, Lawlor C, Koethe B, and Mathew P. Fractionated docetaxel (D) and radium 223 (Ra223) in metastatic castrationresistant prostate cancer (CRPC): A modular phase I trial. *J Clin Oncol* 2024; 42(16). Full Text

B. Connell

Background: Disease progression following novel hormonal therapy in CRPC remains bonedominant and D-responsive. D+ Ra223 would be a logical combination but myelosuppression is dose-limiting. Prior combinations have required a reduction in dose intensity (DI) in both agents. Fractionated schedules of D Q2weekly (DQ2) have comparable activity to D 75mg/m2 Q3weekly with mitigated myelosuppression. We hypothesized that a fractionated schedule of DQ2 with standard Ra223 dosing would be feasible while preserving DI. Methods: Subjects had progressive bone-metastatic CRPC, ECOG PS 0-2, and no bulky visceral disease. Design was phase I, 6+6, dose escalation plus expansion with 28-day cycles. DQ2 was given in a 4-week lead-in, then with Ra223 every 4 weeks. Dose-level (DL) 1: D 40mg/m2; if neutropenia, then 1a: D 40mg/m2 with G-CSF on Day 16, 2a: D 50mg/m2 with G-CSF on Day 16. Up to 6 cycles of the combination were given. Primary objective was the feasibility and maximum tolerated DL explored (MTD). Secondary objectives included PSA response, ORR, PFS, OS, and quality of life. Results: 43 patients (pts) enrolled including 34.9% non-white pts and 76.7% with ≥ 4 bony mets. 8 dropped out during the D lead in (1 each neutropenia, stroke, failure to thrive, anorexia/ fatigue, thrombocytopenia, infusion reaction and 2 hospitalized for other reasons). At DL1, 2 of 3 had DLT (both neutropenia). No DLT occurred at DL1a (n=5) or DL2a (n=5). MTD was DL2a. 22 subjects enrolled to expansion cohort at DL2a. Of the 35 pts treated with D + Ra223, adverse events of interest listed in the table. No febrile neutropenia, fractures, or G5 toxicity were seen. 19/35 completed all 6 cycles of combination therapy. PSA50 response was seen in 18 (51.4%) and PSA90 in 9 (25.7%) pts. Of 31 pts with evaluable data, best response (RECIST 1.1) was 1 CR, 5 PR, 23 SD, 2 PD. Median PFS was 50.0 weeks (95% CI: 37.3-86.1) and OS was 86.1 weeks (95% CI: 60.0-130.9). 10 pts progressed exclusively in nodal/visceral metastases compared to 6 in bone only. Quality of life measures remained stable on study. Conclusions: Utilizing a D lead-in strategy, combination DQ2 and Ra223 was feasible and well tolerated, with a favorable PFS and evidence of preferential control of osseous metastases. Dose-intensity for both docetaxel and Ra223 was preserved and comparable to the FDA-approved dose-schedules for each of the single agents. The lead-in design and use of G-CSF contributes significantly to the feasibility.

Hematology-Oncology
Felip E, Cho BC, Gutiérrez V, Alip A, Besse B, Lu S, Spira AI, Girard N, Califano R, **Gadgeel SM**, Yang JCH, Nogami N, Azuma K, Curtin JC, Zhang J, Panchal A, Ennis M, Sethi SN, Bauml JM, and Lee SH. Amivantamab plus lazertinib vs osimertinib in first-line EGFR-mutant advanced non-small cell lung cancer (NSCLC) with biomarkers of high-risk disease: A secondary analysis from the phase 3 MARIPOSA study. *J Clin Oncol* 2024; 42(16). Full Text

E. Felip

Background: Amivantamab (ami) is an EGFR-MET bispecific antibody with immune celldirecting activity. Lazertinib (laz) is a CNS-penetrant, 3rd-generation EGFR TKI. In MARIPOSA (NCT04487080), first-line ami+laz provided a statistically significant improvement in progression-free survival (PFS) vs osimertinib (osi) in patients (pts) with EGFR-mutant advanced NSCLC (HR, 0.70; P< 0.001), including in pts with a history of brain metastases (HR, 0.69; Cho Ann Oncol 2023;34:S1306, LBA14). Pts with TP53co-mutations, detectable circulating tumor DNA (ctDNA), and baseline brain or liver metastases have poor prognoses. We evaluated outcomes for pts in these high-risk subgroups from MARIPOSA. Methods: MARIPOSA enrolled pts with treatment-naïve, EGFR-mutant (Ex19del or L858R) advanced NSCLC. This analysis included pts randomized to ami+laz (n = 429) or osi (n = 429). Pathogenic alterations were analyzed by next-generation sequencing (NGS) of baseline blood ctDNA with Guardant360 CDx. Ex19del and L858R ctDNA in blood was analyzed at baseline and Cycle (C) 3 Day (D) 1 with Biodesix droplet digital PCR (ddPCR). Results: Baseline ctDNA for NGS analysis of pathogenic alterations was available for 636 pts (ami+laz, n = 320; osi, n = 316). Among pts with TP53 co-mutation, mPFS was 18.2 months (mo) for ami+laz vs 12.9 mo for osi (HR, 0.65; P= 0.003). Pts with TP53 wild-type had a trend favoring ami+laz for mPFS (HR, 0.75; P =0.11). In pts with ddPCR-detectable ctDNA at baseline, ami+laz significantly prolonged mPFS vs osi (20.3 vs 14.8 mo; HR, 0.68; P= 0.002). Further, ami+laz significantly improved mPFS vs osi in pts with ctDNA clearance at C3D1 (24.0 vs 16.5 mo; HR, 0.64; P= 0.004) and in pts who did not clear ctDNA (16.5 vs 9.1 mo; HR, 0.48; P= 0.014). For pts with liver metastases at baseline, ami+laz significantly prolonged mPFS vs osi (18.2 vs 11.0 mo; HR, 0.58; P= 0.017), which is consistent with the improved PFS for ami+laz vs osi in pts with a history of brain metastases. Conclusions: Ami+laz demonstrated significantly improved mPFS vs osi in pts with biomarkers of high-risk disease. Given these features can occur in up to 85% of pts, ami+laz represents an important new standard of care for treatment-naïve EGFR-mutant advanced NSCLC.

Hematology-Oncology

George M, **Clark J**, **Hartway K**, **Zwernik S**, **Gartrelle K**, **Salas-Escabillas D**, **Long D**, **Nassif G**, **Pichardo T**, **Wombwell A**, **Wen HJ**, **Benitz S**, **Philip PA**, **Khan G**, **Shah RA**, **Park H**, **Crawford H**, **Kwon DS**, **Theisen B**, and **Steele N**. Longitudinal tissue-based evaluation of TIGIT expression in patients with pancreatic cancer: Effect of expression with advancing clinical stages and across racial groups. *J Clin Oncol* 2024; 42(16). Full Text

M. George

Background: While ground has been gained, pancreatic ductal adenocarcinoma (PDAC) continues to have a low 5-year survival of 13%. This is owed partially to a lack of early detection biomarkers and resistance to standard therapeutic options. TIGIT, an immune checkpoint receptor, is a marker of T-cell exhaustion and plays a key role in the inhibition of anti-tumor immune responses. TIGIT inhibitors are being explored in clinical trials in PDAC. Here we evaluate TIGIT expression in a cohort of PDAC patients and correlate level and intensity of expression with clinical parameters. We also examine changes in expression as the disease progresses from primary to metastatic disease. Methods: We performed RNAscope in situ hybridization (ISH) with a probe specific for human TIGIT mRNA on 82 formalin-fixed paraffin-embedded (FFPE) tissue samples. The cohort of tissue samples included 9 biopsies, 67 primary resections and 6 metastatic lesions. We evaluated the total TIGIT expression (%) as well as the intensity of TIGIT expression (% of cells with 3+ punctae, signifying putative immune cells), and compared these values between samples. Utilizing linear regression for continuous outcomes and logistic regression for binary outcomes, we tested for associations between TIGIT expression and clinical covariates. Results: Staining analysis showed that TIGIT expression did not differ significantly between racial groups. The mean percentage of TIGIT positive cells was 64.0%. High expression of TIGIT was associated with more advanced clinical stage ($p < 0.05$). Evaluation of three longitudinal samples from the same patient revealed decreased TIGIT expression from the initial biopsy (41.6%) to resection (33.4%) and metastasis (2.8%). In these specimens, 3+ TIGIT expression also declined (2.1%, 1.2% and 0.02%, respectively). Conclusions: Anti-TIGIT therapy has potential to reverse immune suppression and, with other therapeutic modalities, may provide survival benefit. Here we demonstrate that increased TIGIT expression correlates

with more advanced stage at diagnosis and also present data demonstrating that overall TIGIT expression, as detected by RNAscope ISH, may decrease as PDAC progresses to metastasis. As such, anti-TIGIT therapy may have important implications for evading an important mechanism of cancer progression.

Hematology-Oncology
Gor R, Gwalani P, **Gor D**, Shah A, Thakur RK, and Gartrell BA. The silent burden: A SEER-based analysis of potential years of life lost due to genitourinary cancers in the United States (1975-2017). *J Clin Oncol* 2024; 42(16). Full Text

R. Gor

Background: Genitourinary (GU) cancers significantly impact United States (US) public health, not just in mortality but also in premature deaths. We evaluated the potential years of life lost (PYLL) due to these cancers (prostate, kidney, bladder, testicular, penile, and others) from 1975 to 2017 using the SEER database and stratified it across racial groups. Methods: From 1975 to 2017, GU cancers were identified using SEER∗Stat 8.4.2 using ICD-10 CM codes. We analyzed premature deaths and calculated PYLL as [Life expectancy minus (age at diagnosis + survival time)]. Due to non-homogeneity, the Kruskal-Wallis test (a = 5%) was employed for subgroup PYLL analysis. Spearman correlation coefficient (r) assessed the relationship between the year of diagnosis and PYLL. Analyses were conducted using SAS OnDemand. Results: Of the 1,715,763 GU cancer cases (1975-2017), 235,279 had premature deaths, totaling 2,406,551.20 PYLL. Testicular cancer showed the highest median PYLL (33.3 years) compared to other sites, followed by penile cancer with a median PYLL of 12.2 years. Non-Hispanic (NH) Blacks had higher PYLL for prostate, kidney, ureteral, and bladder cancers ($p<0.05$), while Hispanics had higher PYLL for penile and testicular cancers ($p<0.0001$). r value for PYLL and year of diagnosis was 0.23. Conclusions: Our study reveals a substantial impact of GU cancers on premature mortality and PYLL in the US. Despite the lower prevalence, testicular and penile cancers contribute significantly to PYLL, likely related to younger age at diagnosis. Racial disparities were evident, with NH-Blacks and Hispanics experiencing higher PYLL for specific GU cancers compared to other racial groups. These findings underscore the pressing need for targeted interventions to address disparities and enhance GU cancer management and prevention outcomes. (Table Presented).

Hematology-Oncology
Gor R, Gwalani P, **Gor D**, Shah A, Thakur RK, and Kumar A. Pain, palliation, and opioid use patterns: A nationwide analysis of neoplasm-related pain admissions and trends (2016-2020). *J Clin Oncol* 2024; 42(16). Full Text

R. Gor

Background: Neoplasm-related pain (NRP) remains a significant contributor to the diminished quality of life in cancer patients. We aimed to study the epidemiological characteristics and trends among patients hospitalized for NRP from 2016 to 2020. Methods: A retrospective study of patients hospitalized for primary or secondary diagnosis of NRP from 2016-2020 was conducted using the National Inpatient Sample (NIS) database. Temporal trends in the prevalence, mortality rate (MR), length of stay (LOS), hospitalization cost, palliative care consults, and opioid use/dependence/abuse (OUD) were assessed using linear regression or the Cochran- Armitage test. Further, the NIS database was searched to identify all patients admitted with a diagnosis of OUD. Amongst them, the proportion of patients with a coexisting diagnosis of NRP was calculated. Analysis was done using R 4.3.2 and SAS 9.4. Results: 174,530 cases with NRP were identified from 2016-2020, with a median age at hospitalization of 61(IQR: 52,70). The number of hospitalizations increased from 28,036 in 2016 to 41,013 in 2019 and then dropped to 38,040 in 2020 ($p < 0.001$). The total inpatient MR was 7.8%, decreasing from 8.5%in 2017 to 7.0% in 2020 ($p < 0.0001$). The mean cost of hospitalization increased significantly from $64,162.5 in 2016 to $82,943.8 in 2020 ($p<0.001$). There was no significant change in the mean LOS. The number of palliative care consults increased from 29.8% in 2016 to 31.5% in 2019 and then dropped to 31.3% in 2020 ($p < 0.001$). Among 174,530 NRP patients, 5,844 (3.4%) had a coexisting diagnosis of OUD, which increased from 832 (3.0%) in 2016 to 1419 (3.7%) in 2020 ($p < 0.001$). A total of 737,971 patients with a diagnosis of

OUD were admitted from 2016-2020, of which 5844 (0.79%) had a coexisting diagnosis of NRP. Conclusions: We observed increased hospitalizations for NRP and related palliative care consults from 2016 to 2019, with a subsequent decline in 2020. This drop could be related to the impact of the COVID-19 pandemic. Despite the rise in the cost of hospitalizations, there has been a declining trend in MR, potentially due to improved quality of care. The gradual rise in the coexistence of OUD among NRP patients is notable. Yet, NRP patients remain a minority within the broader context of OUD-related admissions, underscoring the need for nuanced, patient-centered approaches in NRP management. (Table Presented).

Hematology-Oncology

Gupta A, Singh A, Tarimci B, Sindhu AK, Bathvar P, Bedi S, Theik NWY, Shah V, Malhotra S, Khealani M, Obulareddy SUJ, **Kukreja G**, and Kanitkar A. PM2.5 and risk of lung cancer and associated mortality: An umbrella meta-analysis. *J Clin Oncol* 2024; 42(16). Full Text

A. Gupta

Background: PM 2.5, particulate matter with a diameter of 2.5 micrometers or less, is a major contributor to lung cancer and associated mortality. Epidemiological studies reveal a concerning trend, with each 10 micrograms per cubic meter increase in PM 2.5 associated with a 15% higher risk of lung cancer and a 13% increase in mortality rates, underscoring the significant burden it imposes on public health systems globally. We aimed to evaluate the odds of association between environmental exposure to PM 2.5 and the risk of lung cancer and associated mortality. Methods: We performed a systematic review and umbrella meta-analysis using studies containing quantitative data onPM2.5 and lung cancer.Weused PRISMA guidelines and the MOOSE protocol using PubMed and MeSH terms like PM 2.5, non-small cell cancer, lung cancer, pollutants, particulate matter 2.5, and environmental factors. We had excluded nonfull- length articles, non-meta-analysis studies, and non-human studies. RavMan 5.4 was used, and generic inverse variance methods with mixed effect models were applied to identify a pooled risk ratio with a 95% confidence interval. Forest plots were obtained, and sensitivity analysis was performed based on funnel plots and I2 (heterogeneity) values. Results: Of the 245,529 articles evaluated for the quality of the data, 99 met the inclusion and exclusion criteria. Out of 99, we used six articles to derive the quantitative data. In umbrella metaanalysis, PM 2.5 exposure was associated with a 1.16 times higher risk (95%CI: 1.1-1.22, p<0.00001, I2=0%) of lung cancer and a 1.22 times higher risk of non-lung cancers (95%CI: 1.15-1.30, p<0.00001, I2=0%). PM 2.5 was associated with non-significant higher mortality (RR: 1.06, 95%CI: 0.99-1.13, p=0.09, I2=97%) with leave-on-out analysis (excluding Chen et al.) significant association between mortality and PM 2.5 (RR: 1.08, 95%CI: 1.06-1.10, p<0.00001, I2=0%). Conclusions: Our umbrella meta-analysis shows a significant risk of lung cancer and mortality from PM 2.5 exposure. Further investigation and increased consciousness are necessary to mitigate the risk of lung cancer associated with this pollutant.

Hematology-Oncology

Hussein MA, **Khan G**, Chandana SR, Cid RAP, Kiss I, Gallego J, Macarulla T, De la Fouchardiere C, Goetze T, Dean AP, O'Reilly EM, Wainberg ZA, Lee WJ, Van Cutsem E, Hubner R, Paulson AS, Bekaii-Saab TS, Pant S, Maxwell F, and Melisi D. NALIRIFOX versus nab-paclitaxel and gemcitabine in treatment-naive patients with metastatic pancreatic ductal adenocarcinoma (mPDAC): Updated overall survival analysis with 29-month follow-up of NAPOLI 3. *J Clin Oncol* 2024; 42(16):1. Full Text

Florida Canc Specialists North Div, St Petersburg, FL USA. Henry Ford Hlth Syst, Detroit, MI USA. Canc & Hematol Ctr, Grand Rapids, MI USA. Hosp Univ Miguel Servet, Zaragoza, Spain. Masaryk Mem Canc Inst, Brno, Czech Republic. Gen Univ Elche Hosp, Dept Med Oncol, Alicante, Spain. Vall dHebron Univ Hosp, Gastrointestinal & Endocrine Tumor Unit, Barcelona, Spain. Vall dHebron Inst Oncol VHIO, Barcelona, Spain. Ctr Leon B prime erard, Lyon, France. Univ Canc Ctr Frankfurt, Krankenhaus Nordwest, Frankfurt, Germany. Frankfurter Inst Klin Krebsforschung IKF GmbH Kra, Frankfurt, Germany. St John God Hosp, Subiaco, WA, Australia. Mem Sloan Kettering Canc Ctr, Dept Med, New York, NY USA. Univ Calif Los Angeles, David Geffen Sch Med, Los Angeles, CA USA. Natl Canc Ctr, Res Inst & Hosp, Goyang, South Korea. Univ Hosp Gasthuisberg, Leuven, Belgium. Univ Leuven, KU Leuven, Leuven, Belgium. Christie NHS Fdn Trust, Dept Med Oncol, Manchester, England. Baylor Charles

Sammons Canc Ctr, Texas Oncol, Dallas, TX USA. Mayo Clin, Comprehens Canc Ctr, Phoenix, AZ USA. Univ Texas MD Anderson Canc Ctr, Dept Invest Canc Therapeut, Houston, TX USA. IPSEN Bioinnovat Ltd, Abingdon, England. Univ Verona, Verona, Italy. Azienda Osped Univ Integrata, Verona, Italy. Hospital; Masaryk Memorial Cancer Institute; Hospital Universitari Vall d'Hebron; Vall d'Hebron Institut d'Oncologia (VHIO); Krankenhaus Nordwest; St John of God Subiaco Hospital; St John of God Health Care; Memorial Sloan Kettering Cancer Center; University of California System; University of California Los Angeles; University of California Los Angeles Medical Center; David Geffen School of Medicine at UCLA; National Cancer Center - Korea (NCC); KU Leuven; University Hospital Leuven; KU Leuven; Christie NHS Foundation Trust; Baylor University Medical Center; Texas Oncology; Mayo Clinic; Mayo Clinic Phoenix; University of Texas System; UTMD Anderson Cancer Center; University of Verona; University of Verona; Azienda Ospedaliera Universitaria Integrata Verona

Hematology-Oncology

Johnson ML, Arriola E, Kato T, Girard N, **Gadgeel SM**, Wang J, Li X, Lowery C, Krug LM, and Ahn MJ. eVOLVE-Lung02: A phase 3 study of first-line (1L) volrustomig plus chemotherapy (CT) versus pembrolizumab plus CT in metastatic non-small-cell lung cancer (mNSCLC) with PD-L1 tumor cell (TC) expression <50%. *J Clin Oncol* 2024; 42(16). Full Text

M.L. Johnson

Background: Immunotherapies targetingprogrammed cell death-1 (PD-1) and its ligand PD-L1 have transformed 1L mNSCLC. However, in a subset of patients (pts) with PD-L1-low or PD-L1- negative disease (i.e. PD-L1 TC expression ,50% or ,1%, respectively), anti-PD-(L)1 therapies, with or without CT, are associated with shorter overall survival (OS) than in pts with PDL1- high disease. Dual inhibition of PD-1 and CTLA-4 is often undertaken in PD-L1-low, and especially PD-L1-negative, mNSCLC to address the poorer prognosis in these pts. Although combination therapy using lower doses of CTLA-4 inhibitors has shown benefit in this setting, toxicity at higher doses has limited the clinical utility of this approach. Volrustomig (MEDI5752) is a monovalent, PD-1/CTLA-4 bispecific, humanized IgG1 monoclonal antibody engineered to specifically inhibit PD-1, with increased CTLA-4 blockade on PD-1+ activated T cells compared to PD-1- resting peripheral T cells. This mode of action may facilitate enhanced CTLA-4 inhibition at tolerable doses beyond those achievable with current PD-1/ CTLA-4 combinations. Data from the first-in-human phase 1/2 study (NCT03530397) showed encouraging antitumor activity and acceptable tolerability with 1L volrustomig plus carboplatin/pemetrexed (CP) in NSCLC, particularly in pts with PD-L1 TC ,1%. The phase 3, two-arm, parallel-group, randomized, multicenter, open-label eVOLVE-Lung02 study (NCT05984277) is designed to evaluate the efficacy of 1L volrustomig plus CT versus pembrolizumab plus CT in mNSCLC pts with PD-L1 TC ,50%. Methods: Eligibility criteria include age ≥18 years; ECOG performance status 0 or 1; histologically or cytologically documented squamous (sq) or non-squamous (non-sq) stage IV NSCLC with PD-L1 TC expression ,50%; wild-type EGFR, ALK, or ROS1; and no prior systemic therapy for mNSCLC. Approximately 900 pts will be randomized 1:1 to receive histology-specific CT (sq, paclitaxel plus carboplatin; nonsq, CP with pemetrexed maintenance at investigator discretion) in combination with either volrustomig or pembrolizumab (200 mg) every 3 weeks (Q3W) for 4 cycles; after this volrustomig or pembrolizumab will be administered Q3W until completion of 24 months of treatment or disease progression, or other discontinuation criteria are met. Randomization will be stratified according to histology (sq vs non-sq), PD-L1 (,1% vs 1-49%), smoking (never vs former/current), and region (Asia vs rest of world). Primary endpoints are progression-free survival (PFS) per RECIST v1.1 and OS in the PD-L1 TC ,1% population. Secondary endpoints include PFS and OS in all randomized pts (PD-L1 TC ,50%), overall response rate, duration of response, PFS2, safety and tolerability, patient-reported outcomes, pharmacokinetics, and immunogenicity. Enrollment is ongoing.

Hematology-Oncology

Khawaja MRRUH, Naqash AR, Schneider R, Shastri A, Stahl M, Moser JC, Karim NFA, Madanat Y, Jonas BA, Stein E, **Gadgeel SM**, McCloskey JK, Gollerkeri A, Perea R, Chutake Y, Agarwal S, Henrick P, Shi K, and Daver NG. Safety, pharmacokinetics (PK), pharmacodynamics (PD) and efficacy of KT-253, a targeted protein degrader of MDM2, in patients with relapsed/refractory (R/R) solid tumors, lymphoma, high grade myeloid malignancies and acute lymphoblastic leukemia (ALL). *J Clin Oncol* 2024; 42(16). Full Text

M.R.R.-U.-H. Khawaja

Background: The tumor suppressor p53 is mutated in approximately 50% of cancers. In those cancers with wild-type p53, its activity is controlled by mouse double minute 2 (MDM2), an E3 ligase that tags p53 for degradation. KT-253 is a novel, highly potent heterobifunctional MDM2 degrader that upregulates p53 activity and overcomes the p53-MDM2 feedback loop, resulting in .200-fold higher potency compared to MDM2 inhibitors. In preclinical PDX models of sensitive p53WT solid tumors, AML and ALL, KT-253 robustly activates p53, induces apoptosis, and results in tumor regressions with every 3-week dosing. The ability to rapidly induce an acute apoptotic response and dose intermittently may result in a therapeutic index that has eluded previous MDM2 targeting agents. Methods: The ongoing open-label Phase 1 study evaluates safety, PK, PD and preliminary efficacy of IV KT-253 administered on Day 1 of 21-day cycles. Patients (pts) with advanced (≥2 prior therapies) solid tumors (ST)/lymphomas (Arm A) and relapsed/refractory (R/R) high grade myeloid malignancies (AML, high/very-high risk myelodysplastic syndrome (MDS), MDS/myeloproliferative neoplasms) and ALL (Arm B) are eligible. Blood samples are collected for KT-253 PK/PD analyses. Results: As of 26 January 2024, 18 pts have been treated, 13 in Arm A dose levels (A: DL) 1-4 and 5 in Arm B dose levels (B: DL) 1- 2, with mean number of 3 and 2 doses, respectively. The most common solid tumor types were Merkel cell carcinoma ((MCC) n=3), adenoid cystic carcinoma ((ACC) n=2) and uveal melanoma (n=2). Arm B included 5 pts with R/R AML. The median age was 61 years (yrs) (range 42, 81) in Arm A and 66 yrs (range 57, 70) in Arm B. The most common adverse events (AEs) in > 20% of pts included nausea, fatigue, headache, and vomiting. There was 1 DLT of AEs leading to discontinuation that included Grade (G) 2 nausea and fatigue in A: DL4. There were no neutropenia or thrombocytopenia AEs in either arm. KT-253 related SAEs included G3 hypotension in a pt with decreased oral intake (A: DL1). Overall best response: 1 CR (B: DL2, AML); 2 PRs (A: DL1, MCC; B: DL1, AML); 3 SD (A: DL1, fibromyxoid sarcoma; DL2, ACC; DL3, renal cell cancer). PD data from A: DL1-4 and B: DL1-2 demonstrated rapid upregulation of plasma GDF- 15 protein and upregulation of CDKN1A and PHLDA3 mRNA levels in blood. KT-253 demonstrated dose-dependent increase in plasma exposure with levels approximating efficacious doses. Conclusions: KT-253 results in potent upregulation of p53-dependent biomarkers and has demonstrated early signs of anti-tumor activity including objective responses in MCC and AML at doses that are well tolerated. Dose escalation is ongoing at DL4 in Arm A and at DL2 in Arm B and analyses from additional pts will be presented at the meeting.

Hematology-Oncology

Lara PN, Kroll S, Chatzkel JA, Teoh DGK, Ma VT, Kilari D, **Hwang C**, Sweis RF, Yalamanchili K, Peguero JA, Li T, and Parikh M. Leukocyte immunoglobulin-like receptor (LILRB2)-targeted JTX-8064 plus the anti- PD1 inhibitor JTX-4014 (pimivalimab) in immune-checkpoint inhibitor (ICI) pretreated patients (pts) with advanced or metastatic renal cell cancer (mRCC): Results from the multi-stage phase 1-2 INNATE trial. *J Clin Oncol* 2024; 42(16). Full Text

P.N. Lara

Background: Disease progression following treatment of mRCC pts with ICI-based therapy (tx) is nearly universal, warranting evaluation of novel immunotherapeutic approaches. LILRB2 is an immune checkpoint molecule expressed primarily in cells of myeloid origin (e.g., monocytes/macrophages). Inhibition of LILRB2 reprograms macrophages from an immunosuppressive (M2) to an immunostimulatory (M1) phenotype. JTX-8064 is a humanized monoclonal antibody that binds to LILRB2, blocking its interaction with MHC1 molecules. Preclinical studies suggest that JTX-8064 can overcome anti-PD(L)1 resistance mechanisms. Here we report the results of an expansion cohort of previously-treated mRCC pts in INNATE, a multistage phase 1-2 trial of JTX-8064 in combination with anti-PD1 agents in solid tumors. Methods: Pts with pathologically-confirmed clear cell mRCC progressing on or after anti- PD(L)1 tx in the most recent prior line, acceptable end-organ function, and ECOG PS 0-1 were treated with JTX-8064 700mgand JTX-4014 500mgIV q3 weeks. Primary endpoint was overall response rate (ORR); secondary endpoints were safety, disease control rate (DCR), progressionfree survival (PFS), & overall survival (OS). A Simon 2-stage design (n=10+19) was employed where ORR .= 20% was deemed to be of further interest versus null hypothesis of ORR ,= 5%, with alpha=0.05. Results: 31 pts were enrolled,

with median age of 64 years (range 38-85); 84% males; 16% Hispanic; 93% White; 45% PS=0; 71% one prior tx line. Of 28 pts evaluable for response, 1 CR, 1 PR, 14 SD (± SD.= 6 months), and 11 PD were seen for an ORR of 7% & DCR of 54%.Median PFS was 4 months (95%CI: 2, 6.8); 12-month OS was 75% (95%CI: 55,88). Txrelated adverse events (AE) of all grades were reported in 11 pts (45%), most commonly fatigue (16%) & diarrhea (10%). Only 4 protocol-related G3-4 AEs were reported: thrombocytopenia (G4); diplopia, diarrhea, & bradycardia (all G3). Three on-study deaths (hypotension; cardiorespiratory arrest; & unknown) were deemed unrelated to protocol tx. Conclusions: While ORR did not meet the protocol-defined efficacy target, evidence of anti tumor activity was seen in ICI pre-treated mRCC pts with combination JTC-8064 + JTX-4014. Treatment was reasonably well-tolerated. Identification & evaluation of clinical and molecular phenotypes most likely to benefit from LILRB2-targeted therapies are warranted.

Hematology-Oncology
Le X, Spira AI, **Gadgeel SM**, Riess JW, Yu Y, Zhao Y, Cheng Y, Juan-Vidal O, Gao B, Yoh K, Forster M, Kitazono S, Hayashi H, Planchard D, Jiang Y, Baio N, Kowanetz M, Leung W, Hsu JY, and Wang J. FURTHER: A global study to evaluate furmonertinib in patients with EGFR mutant NSCLC including uncommon EGFR mutations (FURMO-002). *J Clin Oncol* 2024; 42(16). Full Text

X. Le

Background: Furmonertinib (AST2818) is an oral, highly brain-penetrant, and broadly active mutation-selective epidermal growth factor receptor (EGFR) inhibitor engineered for broad activity and selectivity across EGFRmutations (mts) (1). Furmonertinib is approved in China for first-line advanced NSCLC with EGFR Ex19del or L858R mts based on the progression-free survival benefit observed in the Phase 3 study versus gefitinib (FURLONG). Furmonertinib has also demonstrated promising interim efficacy and safety in patients (pts) with NSCLC harboring EGFR exon 20 insertion (ex20ins) mts with a confirmed overall response rate (ORR) of 78.6% (n=28) by blinded independent central review (BICR) and a preliminary median duration of response (DoR) of 15.2 months in the front-line setting (FAVOUR study; see Han et al., WCLC 2023). Furmonertinib recently obtained FDA Breakthrough Therapy Designation for the treatment of pts with advanced NSCLC with EGFR ex20ins mts. P-loop and aC-helix Compressing (PACC) mts represent another subset of uncommon EGFR mts (2) that are similar to ex20ins mts in narrowing the drug-binding pocket; including G719X, S768I, E709X, L747X, V774M. Preclinical data indicating that furmonertinib is potent in models harboring EGFR PACC mts Developing efficacious, well-tolerated, and CNS-penetrant medicines for NSCLC pts with EGFR ex20ins mts and PACC mts remains an unmet need. Methods: FURTHER (FURMO-002) is the first global trial evaluating furmonertinib in NSCLC pts with EGFR and HER2 mts in North America, Europe, and the Asia-Pacific. FURTHER is a phase 1b, open-label, multicenter study in which pts will be treated orally with furmonertinib daily. For Stage 1 dose-escalation, the primary endpoint is incidence and severity of adverse events, including dose limiting toxicities and has been completed. For Stage 2 dose expansion, approximately 120 pts will be enrolled across 4 expansion cohorts. Stage 2 Cohorts 1-3 dose expansion cohorts will enroll pts with previously treated, locally advanced or metastatic NSCLC pts with either EGFR ex20ins mts, HER2 ex20ins mts, or EGFR activating mts, respectively. Cohorts 1-3 allow enrollment of pts with prior EGFR or HER2-directed therapy. Stage 2 Cohort 4 will enroll EGFR TKI-naïve NSCLC pts with EGFR PACC mts. Key inclusion criteria include documented EGFR or HER2 mts by local testing and measurable disease per RECIST v1.1. Stage 2 primary endpoint is ORR using RECIST v1.1. Key secondary endpoints include progression-free survival and overall survival. Stage 2 enrollment is ongoing. 1. Musib et al., NACLC 2022. 2. Robichaux et al., 2021. Clinical trial information: NCT05364073.

Hematology-Oncology
Meranda M, **Sheqwara J**, **Shallal A**, **Alangaden G**, **Dillon W**, **Veve M**, **Mann Y**, **Tamr A**, and **Raslan S**. Patterns of vancomycin use in high-risk febrile neutropenia. *J Clin Oncol* 2024; 42(16). Full Text

M. Meranda

Background: Febrile neutropenia (FN) is a common complication in patients with hematologic malignancy. ASCO guidelines on the management of FN endorse empiric anti-Pseudomonas coverage while

reserving the use of agents targeting gram-positive organisms and methicillinresistant Staphylococcus aureus (MRSA) for select criteria-defined patients such as those with severe mucositis, hemodynamic instability, radiographic pneumonia, or history of MRSA colonization among others. We sought to examine our institutional management of FN, hypothesizing that local use of empiric vancomycin for high-risk FN will deviate from ASCO guidelines reflected in institutional policy. Methods: Case data from 1/1/2016 - 6/1/2023 was collected retrospectively, comprising patients admitted to the general medical floor with known leukemia, lymphoma, or multiple myeloma meeting ASCO criteria for FN. Patients admitted to intensive care at time of FN or for less than 48-hours were excluded. For each patient, use of vancomycin at time of FN diagnosis (t0) and 48-hours later (t48) was evaluated for congruence with society guidelines. Results: 91 patients were reviewed with amedian age of 68 years old (IQR 59-74, 15). Median length of stay (LOS) was 20 days (IQR 7-29, 22) with FN occurring on day seven of hospitalization on average. Most patients receiving vancomycin were admitted to the hematology specialty unit at time of diagnosis (63%). Acute leukemia was the most common malignancy represented (62.8%), while high grade lymphoma comprised 23.1%. 98.9% of patients were on active chemotherapy at time of FN. 81 patients (89%) received vancomycin as empiric treatment for FN with 76 (93.8%) receiving vancomycin at t0. Of this latter cohort, 29.7% of patients received vancomycin at t0 without indication. At t48, vancomycin was discontinued in 28.4% of patients, 44.4% received vancomycin with true indication, and 27.2% were continued on vancomycin without indication. The median duration of therapy for patients receiving vancomycin incongruently at t48 was 4 days. Of those meeting criteria for vancomycin use at t48, severe mucositis and soft tissue infection were each cited in 22.2% of cases, followed by pneumonia, persistent fever, and hemodynamic instability. Notably, the presence of any grade mucositis was significantly associated with the continued use of empiric vancomycin at t48 ($p = .025$). Admission to hematology specialty unit did not significantly affect adherence to FN management guidelines. Conclusions: These data suggest that the use of vancomycin for FN at our institution deviates from society guidelines including on specialized hematology wards. This study was underpowered to assess adverse outcomes seen with vancomycin use such as renal injury, prolonged LOS and greater cost of care. Given the high complexity of this patient population, detailed provider education is indicated to promote safe, evidence-based care and broader antimicrobial stewardship.

Hematology-Oncology
Mosquera LG, Balanchivadze N, Ali F, **Meranda M**, **Castro OH**, and **Kuriakose P**. Factors influencing career choices and post-fellowship perspectives in adult hematology/oncology fellows: A nationwide cross-sectional study. *J Clin Oncol* 2024; 42(16):1. Full Text

Henry Ford Hosp, Detroit, MI USA. Virginia Oncol Associates, Norfolk, VA USA. Coastal Canc Ctr, Myrtle Beach, SC USA.

Hematology-Oncology
Panian J, Henderson N, Barata PC, Bilen MA, Graham L, Heath EI, Herchenhorn D, **Hwang C**, Kilari D, Koshkin VS, Nauseef JT, Sokolova A, Zakharia Y, Schweizer MT, Dorff TB, Armstrong AJ, Alva AS, and McKay RR. Association of tumor genetics with outcomes in patients (pts) with PSMA-positive metastatic castration-resistant prostate cancer (mCRPC) treated with 177Lu-PSMA- 617. *J Clin Oncol* 2024; 42(16). Full Text

J. Panian

Background: 177Lu-PSMA-617 is approved for the treatment (tx) of mCRPC. Though tx is associated with improved survival, not all pts experience a benefit. Acquired resistance is common and some pts have intrinsic resistance. There is a lack of data on genomic markers that could aid in selecting pts for tx. In this study, we aim to characterize molecular predictors of benefit to 177Lu-PSMA-617. Methods: We used the retrospective Prostate Cancer Precision Medicine Multi-Institutional Collaborative Effort (PROMISE) clinical-genomic database (n=2100). The primary endpoint was to investigate the association of genomic alterations with a ≥50% PSA decline (PSA50) from baseline following 177Lu-PSMA-617. Associations were assessed using Wald-chi square test and Cox regression in multivariable analysis. Secondary endpoints included clinical progression-free survival (PFS) and overall survival (OS). Results: We identified 115 pts with PSMA PET+ mCRPC treated with 177Lu-PSMA-617 who had commercial genetic

sequencing prior to tx (median age 72 yrs, 25% non-white). Median number of prior lines for mCRPC was 3 with 71 pts (62%) receiving .1 androgen receptor signaling inhibitor (ARSI) and 55 pts (48%) receiving .1 taxane; 11 pts (9%) received ARSI with 177Lu-PSMA-617. Overall, the PSA50 was 49% with median OS and PFS of 14.0 and 7.6 months (mos), respectively. In pts with a PSA50, median OS and PFS were 22.6 and 11.6 mos, respectively, vs 11.2 and 5.6 mos for those without a PSA50. Genetic alterations associated with PSA50 are in the table. PSA50 was48%in pts with (n=32) vs49%in pts without DDR alterations (n=83). PSA50 was 44% in pts with tumor suppressor gene alterations (TSGa) (PTEN, p53, RB1) (n=68) vs 56% in pts without (n=47). Median PFS was 7.6 vs 7.3 mos for pts with and without any TSGa (p=0.90), and median OS was 12.2 mos vs 22.6 mos for pts with and without TSGa (p=0.004). Of the 43 pts with AR alterations, 8/15 (53%) with LBD mutations, 10/27 (37%) with AR amplification, and 0/1 with AR-V7 had a PSA50. FGFR, CDK12 and MYC alterations were enriched in individuals without a PSA50 (75-83%). Conclusions: We demonstrate that CDK12, MYC and FGFR alterations were associated with a lower PSA50 with 177Lu-PSMA-617. Larger cohorts should be investigated for confirmation, as biomarkers to inform relative benefit of tx could be useful in prioritizing options for mCRPC.

Hematology-Oncology
Pichardo R, **Jacob B**, **Jamil M**, **Jamil D**, **Raslan S**, **Rose CM**, **Boakye EA**, **Poisson L**, **Tam S**, and **Philip PA**. Patient-reported and clinical outcomes among patients with pancreatic cancer. *J Clin Oncol* 2024; 42(16). Full Text

R. Pichardo

Background: Pancreatic cancer is associated with poor survival, high symptom burden, and psychological distress. Conventional assessments such as performance status (PS) have relied on provider-generated data to evaluate the selection of treatment and prognosis. Patientreported outcome measures (PROMs) represent a patient-centric representation of the patient experience and are increasingly applied as tools to help improve outcomes and quality of life. However, little is known about the correlation of PROMs with ECOG PS and clinical outcomes in pancreatic cancer. Methods: We performed a retrospective analysis of patients with pancreatic cancer seen at the Henry Ford Health System between 09/2020 and7/2023, using ICD codes. The NIH's validated and standardized Patient-Reported Outcomes Measurement Information System was used to capture 4 core domains: fatigue, pain interference, physical function, and depression. Patient-level variables and disease-specific variables were obtained by chart review from EHR. Kruskal-Wallis tests for continuous variables and or Fisher's exact tests for categorial variables were used to compare the different ECOG scores and PROM scores and patient-level and disease-specific variables. Results: 176 patients were analyzed, with a median age of 65, 58% were male. Most patients had Stage 1 32.9% followed by Stage 4 25.9%, stage 3 22.9%, 1 32.9%. The majority had an ECOG score of 1, followed by, 0, 2, and only 10 had an ECOG PS of 3. There was no statistically significant difference in PS scores according to smoking status, race, or AJCC Stage but differed by age (P = 0.0007). PS score was not significantly associated with PROMscores on depression, fatigue, or pain interference. However, increasing PS scores were associated with a significant increase in low physical function PROM scores (P , 0.0001). Conclusions: Clinician-assessed PS is a single assessment of the patient's tolerance to therapies subject to physician bias; our study provides encouraging data on the association between PS and patients' reported physical function. The other PROM domains did not provide additional meaningful information on the patient's function although are part of clinical decision-making.

Hematology-Oncology
Piha-Paul SA, De La Fuente MI, Iwamoto F, Nagpal S, **Weise AM**, Zhu JJ, Chandra S, Chen C, Fu Y, Yang Z, and Tsai KK. Interim analysis of ABM-1310, a blood-brain barrier-penetrant BRAF inhibitor, in patients with BRAF V600-mutated solid tumors. *J Clin Oncol* 2024; 42(16). Full Text

S.A. Piha-Paul

Background: ABM-1310 is a novel, small-molecule BRAF inhibitor with preclinical evidence of high blood-brain barrier penetration. Here we report interim results from a Phase 1 study of ABM-1310 in patients

(pts) with BRAF V600 mutations (NCT04190628). Methods: This multicenter, open-label, two-part study enrolled adult pts with advanced BRAF V600-mutated solid tumors, including those with recurrent or metastatic solid tumors or primary CNS tumors. Pts who failed previous BRAF±MEK inhibitor treatment were eligible. In the dose-escalation (Part 1), pts received either ABM-1310 monotherapy (25-250 mg bid) continuously or ABM-1310 (100-200mgbid) + cobimetinib (60mgQD on d1-21) q28d. Escalation followed a 3+3 design with dose-limiting toxicities assessed during Cycle 1. Part 2 was cohort expansion (ABM-1310 150-200 mg bid). Primary objectives were maximum tolerated dose (MTD) of ABM-1310 6 cobimetinib. Secondary objectives included safety, tolerability, pharmacokinetics, and anticancer activity. Results: As of 28 Nov 2023, 51 pts (36 male; median age 56 years; 38 pts refractory to BRAF ±hibitors) were enrolled. Of these, 74.5% (38/51) experienced treatment-related adverse events (TRAEs). The most frequent (≥10%) TRAEs were skin rash (n=15) and asymptomatic electrocardiogram QT prolongation (AQTP, n=18), most (97.4%) of which were grade (G) 1-2. Nine pts (17.6%) had G3 TRAEs including AQTP, rash, neutropenia, nausea, vomiting, lipase increased and myalgia. There were no treatment-related early discontinuations, G4 AEs, or treatment-related deaths. Among 28 efficacy-evaluable pts who received any dose of ABM-1310 monotherapy, the ORR was 21.4% and disease control rate (DCR) was 60.7%, including 6 partial responses (PR) (glioblastoma multiforme n=2, pleomorphic xanthoastrocytoma n=2, papillary thyroid carcinoma [PTC] n=1, and pancreatic cancer [PC] n=1). Eleven pts had stable disease (SD). Among 16 efficacy-evaluable pts treated with ABM- 1310 + cobimetinib, the ORR was 12.5% and DCR was 68.8% including 2 PR (1 each with melanoma and PTC) and 9 SD. Among 10 pts with primary CNS tumors treated with ABM- 1310 monotherapy, the ORR was 40% (4 PR, 4 SD), and the median PFS was 4.6 months. In 6 pts with PTC, the ORR was 33.3% (2 PR, 4 SD), and the median PFS was 6.0 months. In 4 pts with PC treated with ABM-1310 monotherapy, the ORR was 25% (1 PR for >6 months; pt remains on study treatment). The MTD for ABM-1310 either as monotherapy or in combination with cobimetinib was 200 mg bid. Preliminary assessment of ABM-1310 drug exposure vs. dose showed a linear dose-proportional relationship. Conclusions: ABM-1310, either alone or in combination with cobimetinib, was well tolerated without new or unexpected side effects or safety issues. Preliminary efficacy of ABM-1310 was seen in pts with BRAF V600-mutated solid tumors, including those who were refractory to prior BRAF 6 MEK inhibitors.

Hematology-Oncology

Purtell JPP, **Ralston A**, **Rose CM**, **McElyea K**, **Ibrahim F**, **Thompson A**, **Ghosh S**, and **Hwang C**. Race and decisional conflict about genetic testing in patients with advanced prostate cancer. *J Clin Oncol* 2024; 42(16). Full Text

J.P.P. Purtell

Background: Guideline recommended genetic testing in advanced prostate cancer (PC) is underutilized and not always accepted by patients (pts). We assessed attitudes and decisional conflict (DC) surrounding genetic testing associated with subsequent test completion, and differences between white and nonwhite pts. Methods: Eligibility for this prospective single institution study included pts with N1 or M1 PC who had not yet completed genetic testing. Upon informed consent, pts were given a 24-question survey using a Likert scale of 0 (strongly agree) to 4 (strongly disagree) to assess attitudes toward genetic testing including a validated assessment of DC. DC and DC subscores (range 0-100, with 100 being highest DC) were calculated from subsets of survey responses. Self-identified race was obtained from the EMR. Two-group comparisons between white and nonwhite pts, and between those who completed genetic testing and who did not, were conducted with SAS v9.4 software using Fisher's exact test for categorical variables and Wilcoxon rank sum test for Likert scale survey questions and DC score variables. Results: Of 42 enrolled pts (21 white, 17 black, 1 Asian, 3 declined), 22 (52.4%) completed genetic testing. Compared to white pts, nonwhite pts expressed more concern about test result privacy (mean = 1.72 v 2.95, p = 0.002), test results being used for non-healthcare purposes (1.78 v 3.00, p = 0.003), and trying unproven treatments (1.72 v 2.67, p = 0.01). Nonwhite pts felt more external pressure in decision-making compared to white pts (0.67 v 0.29, p = 0.04). No significant differences were appreciated in completion of testing, DC, or any subscore between racial groups. Compared to pts who did not complete testing, those who completed testing were more likely to report they knew which options were available (0.73. v 1.25, p = 0.05), knew the benefits of each option (0.77 v 1.30, p = 0.04), knew the risk and side effects of each option (0.95 v 1.50, p = 0.05), were clear about which benefits matter most to

themselves (0.73 v 1.37, p = 0.02), and were clear about the best choice for themselves (0.73 v 1.35, p = 0.02). DC (28.59 v 18.11, p = 0.03) was higher in pts who did not complete testing, along with uncertainty (31.25 v 19.32, p = 0.02) and informed (31.25 v 20.45, p = 0.03) subscores. No differences were seen in values clarity, support, or effective decision subscores. Conclusions: In our study, nonwhite pts expressed greater concern about privacy, data misuse, and trying unproven treatments. Those who did not complete testing had more DC with greater uncertainty about knowledge and decision making. These findings will help direct targeted interventions to increase knowledge, trust, and decisional certainty about genetic testing in pts with advanced PC. Ongoing studies will assess the impact of these interventions on rates of testing completion at our institution.

Hematology-Oncology
Rous FA, Sussell J, Ngiam C, Zhang Q, Majda T, Sheinson D, Ogale S, Bara I, Schulze K, and **Gadgeel SM**. Real-world outcomes in patients with biomarker-selected early-stage non-small cell lung cancer. *J Clin Oncol* 2024; 42(16). Full Text

F.A. Rous

Background: Extensive literature has assessed the prognostic value of Lung driver mutations (LDMs) in advanced non-small cell lung cancer (aNSCLC). However, their role in predicting outcomes in early-stage cases (eNSCLC) is less defined due to limited data on biomarkerselected eNSCLC. Study variations have led to diverse findings on the prognostic value of individual LDMs in eNSCLC. Methods: We retrospectively analyzed patients with resected stage I-IIIa NSCLC diagnosed between 2011-2023 using the nationwide (US-based) de-identified Flatiron Health-Foundation Medicine lung clinico-genomic database, which consolidates data from approximately 280 US cancer clinics (~800 sites of care). We allocated patients to five cohorts classified by early-stageLDMstatus: ALK+, EGFR+, KRAS G12C+, KRAS non-G12C+ and wild-type (WT - negative for the listed biomarkers). The clinical attributes and treatment patterns for this cohort were described by our group in a previous abstract; here we analyze recurrence-free and overall survival (RFS and OS) by cohort, using the Kaplan-Meier method. We used Cox regression for multivariate analysis, controlling for demographic and clinical characteristics including age, race, insurance status, stage, histology, and smoking status. Results: The sample contained 1,595 stage I-IIIa patients with known LDM status. Of these, 2.8%, 20.4%, 10.7%, 19.3%, and 46.8% were ALK+, EGFR+, KRAS G12C+, KRAS non-G12C+, and WT. Median OS and RFS were shorter in the WT group compared to any LDM group; results can be found in the table. These differences in OS and RFS persisted in multivariate analysis; hazard ratios (HR) were all statistically significant (p,0.05) and can be found in the table below. Conclusions: In this real-world analysis, patients with eNSCLC LDM-positive tumors had improved OS and RFS relative toWTpatients. Differences in OS betweenWTand LDM+ patients are likely due to frequent receipt of targeted therapy (TT) following progression to advanced disease. However, the small fraction of patients that received adjuvant TT within 6 months of surgery (described in our previous abstract) is not likely to explain observed differences in RFS; thus the differences may be due to innate characteristics of these LDMs.

Hematology-Oncology
Sborov DW, Pawlyn C, Ishida T, Huang JSY, Benjamin R, Iida S, Popat R, Kuroda J, Pianko MJ, Ramakrishnan A, Schuster SR, **Dabak VS**, Lesokhin AM, Conte U, Soltantabar P, Hong F, Vandendries E, and Fonseca R. Evaluation of cytokine release syndrome (CRS) in patients with relapsed or refractory multiple myeloma (RRMM) receiving step-up priming doses and longer dosing intervals of elranatamab: MagnetisMM-9. *J Clin Oncol* 2024; 42(16). Full Text

D.W. Sborov

Background: Elranatamab (ELRA) is a humanized BCMA-CD3 bispecific antibody. In the phase 2 registrational MagnetisMM-3 (MM-3) trial, SC ELRA was given as 2 step-up priming doses (12mgon C1D1 and 32 mgon C1D4) followed by 76mgQWin patients (pts) with RRMM. Overall, 56.3% of pts had CRS (grade 2, 14.3%; no grade≥3). Most events occurred after doses 1 (44.5%), 2 (20.2%), and 3 (5.9%); 0.8% (1 pt) had CRS with doses 4+. Recurrent CRS (>1 event) occurred in 15.1% of pts (Lesokhin Nat Med 2023). Methods: MagnetisMM-9 (MM-9; NCT05014412) is a phase 1/2, open-label,

nonrandomized study of ELRA examining an alternative 2-dose step-up priming regimen (4 and 20mgon C1D1 and C1D4, respectively). Eligible pts had RRMM and were refractory to ≥1 IMiD, ≥1 PI, and ≥1 anti-CD38 antibody. After the priming doses, ELRA 76 mg was given QW for 6 cycles (Part 1) or for 1 cycle followed by 116 or 152 mg Q2W for 5 cycles (Part 2A). The RP2D from Part 2A (152 mg) was evaluated in Part 2B (dose expansion). The rate of grade ≥2 CRS per ASTCT criteria during C1 is the primary endpoint for both parts. Secondary endpoints include evaluation of AEs and PK. Here, we report the overall safety and CRS profile associated with the 4/20 mg priming regimen. Results: For 85 treated pts, median age was 64.0 y; 49.4% were male; 23.5% had EMD; 31.8% had high-risk cytogenetics. Pts had a median of 5.0 (range, 1-12) prior LOTs; 85.9% had triple-class refractory disease. After amedian follow-up of 7.4 mo, the most common (>50%) AEs were CRS (63.5%; grade ≥2, 15.3%) and neutropenia (54.1%; all grade ≥2). ICANS occurred in 4.7% of pts (all grade ≤2). The grade ≥2 CRS rate in C1 was 14.1% (90% CI, 8.4-21.9). CRS rates after the first 3 doses are in the the table. For doses 4+, any grade (grade ≥2) CRS was observed in 10.6% (3.5%) of pts overall, 12.1% (3.0%) of pts continuing to receive 76 mg (n=33), 25.0% (0%) of pts receiving 116 mg (n=12), and 5.0% (5.0%) of pts receiving 152 mg (RP2D; n=40). Overall, recurrent CRS was observed in 20.0% of pts. The geometric means (CV%) of free ELRA concentrations 24 h (Cmax-24h) after step-up doses 1 and 2 were 85.64 (48%) and 242.8 (55%). Conclusions: The 4/20 mg step-up priming regimen and alternative dosing schedules resulted in similar safety and incidence of overall and grade ≥2 CRS events vs the regimen used in MM-3 (12/32 mg), with no new safety signals identified. However, the CRS profile in this study differed, with more CRS after doses 2, 3, and 4+ and a higher prevalence of recurrent CRS. The Cmax-24h of free ELRA (CV%) after the priming doses were lower than those in MM-3 (107.4 [47%] and 405.1 [72%], respectively). Thus, the priming regimen used in MM-3 remains the optimal regimen for mitigating CRS. Future analyses of ongoing studies will be used to confirm these results. (Table Presented).

Hematology-Oncology

Shah A, Gwalani P, Gor R, **Gor D**, Sivanandam A, and Nehra AH. Beyond the initial diagnosis: Epidemiological factors associated with second primary cancers among patients with head and neck squamous cell carcinoma (a SEER-based study). *J Clin Oncol* 2024; 42(16). Full Text

A. Shah

Background: Patients with Head and Neck cancer squamous cell carcinoma (HNSSC) have an increased risk of developing a Second Primary Cancer (SPC). We evaluated the epidemiological factors associated with SPC among patients with Stage 1-4 HNSCC using the SEER database from 2004-2020. Methods: Stage 1-4 HNSSC cases from 2004-2020, with a minimum of six months of follow-up, were identified using SEER.Stat 8.4.2 using ICD-10 CM codes. Adjusted odd's ratios (aOR) for developing SPC (dependent variable) and the independent variables (sex, age, race and ethnicity, site of primary cancer, and marital status) were generated using multivariate logistic regression. All the analyses were performed on SAS OnDemand. Results: 127,919 cases of HNSCC were identified from 2004-2020. Oral cavity cancer accounted for 41.2% of the cases. 18,192 (14.2%) patients developed SPC. Patients with primary hypopharynx, laryngeal, and oral cavity cancer had the highest odds of developing SPC (p, 0.0001). The most prevalent sites for developing SPC were the lung (25.0%), head and neck (24.1%), and prostate (10.6 %). Males had significantly higher odds of developing SPC than females (aOR - 1.11 (1.07, 1.5)). When compared to the NH-white population, Hispanics and NH-Asian had significantly lower odds of developing SPC (aOR - 0.72 (0.68, 0.77) and 0.72 (0.68, 0.78) respectively), while NH-Blacks had higher odds of developing SPC (aOR - 1.1(1.01,1.23)). Conclusions: Our study emphasizes the substantial risk of SPC in HNSCC patients, with oral cavity cancer as the predominant primary cancer subtype. Specific HNSCC sites show elevated SPC odds, mainly primary hypopharyngeal cancer, emphasizing the need for targeted surveillance. Demographic variations reveal gender and racial disparities in SPC susceptibility, advocating for tailored monitoring and preventive strategies in high-risk subpopulations to enhance overall cancer care and survivorship.

Hematology-Oncology

Shahid MA, **Kulkarni RB**, **Albusoul L**, **Jacob B**, **Rose CM**, **Springer K**, and **Dabak VS**. Evaluation and treatment response in patients with hormone receptor-positive, HER2 low metastatic breast cancer: A single center retrospective analysis. *J Clin Oncol* 2024; 42(16). Full Text

M.A. Shahid, Henry Ford Hospital, Detroit, MI, United States

Background: Patients with Hormone Receptor (HR)+ metastatic breast cancer have seen several new options that improve overall survival. Recently, there are new treatment options for patients with HER2 low expression (defined as HER2 1+ on IHC or 2+ on IHC with a negative FISH). Currently, patients who have HR+ metastatic breast cancer are treated with a combination of an aromatase inhibitor and a Cyclin Dependent Kinase (CDK) 4/6 Inhibitor as first line. Information regarding response to therapy in this group and a correlation with HER2 expression is limited. Methods: This is a retrospective study that aimed to evaluate patients with metastatic, HR+, HER2 low or HER2 negative breast cancer between January 1, 2015 and December 31, 2022. Patients were stratified based on their HER2 status, race, presence of de-novo metastatic disease versus progression, treatment with a CDK 4/6 Inhibitor, and time to progression (defined as the date of biopsy-proved diagnosis to the date of radiographic progression). Comparative data analyses were performed using Fisher Exact and Kruskal-Wallis testing. Kaplan Meier estimates with a log rank p-value were used for survival curves, and a Pvalue of < 0.05 was considered statistically significant. Results: 143 patients were included in our study. Patients were divided based on their HER2 status; 33.5% had HER2 2+ disease, 55.9% had HER2 1+, and 8.4% had HER2 0. Of the patients evaluated, 66% (94/143) were Caucasian, 25% (36/143) were African American (AA), and 9% (13/143) were of other race. There was a significant difference amongst patients treated with CDK 4/6 inhibitors when stratified by race; AA patients had a higher proportion of not using a CDK4 inhibitor (43.3% vs 20.3%; p-value 0.0109). There was a significant difference between the survival curves of HER2 0, 1+, and 2+ (log rank p-value = 0.043). HER2 0 patients progressed quicker than HER2 1+ and 2+ patients. When comparing HER2 negative and low disease, a significant difference was found between the survival curves (log rank p-value = 0.0190). In patients with HER2 low (1+ and 2+ with negative FISH) and HER2 negative disease, there was no difference noted among patients who had de-novo or progression to metastatic disease, high MiB1 status (defined as >20%), whether treatment with CDK 4/6 inhibitor was used, and tumor histology. Conclusions: In our study, patients who had any HER2 expression had a longer time to progression compared to patients with no expression. Patients who had a higher expression (2+ vs 1+) displayed a longer time to progression. This may suggest that as the HER2 expression increases, they may derive a longer benefit with first line therapy. Interestingly, African American patients had a higher proportion of not using a CDK4/6 inhibitor. Larger studies are needed to evaluate these differences and determine whether any expression can be used as a prognostic marker.

Hematology-Oncology

Tam S, **Boakye EA**, **Springer K**, **Poisson L**, **Al-Antary N**, **Elsiss F**, **Nair M**, **Zatirka T**, **Ryan M**, **Chang SS**, and **Movsas B**. Age-normed patient-reported outcome measures among cancer survivors. *J Clin Oncol* 2024; 42(16). Full Text

S. Tam

Background: Patient-reported outcome measures (PROMs) are instruments used to collect health-related outcomes that are derived completely from the patient without interpretation from healthcare providers. Monitoring and subsequent intervention based on PROMs collection has demonstrated efficacy in clinical trial settings. This has resulted in implementation of PROMs in routine clinical cancer practices throughout the nation. PROMs have been normed to the general population, but establishing the norms among cancer patients is essential to understanding how PROMs can be evaluated on an individual basis in routine clinical cancer care. This study aims to characterize age-normed PROMs scores among survivors of cancer using the National Institute of Health's Patient-Reported Outcome Measures Information System (PROMIS) depression, fatigue, pain interference, and physical function domains. Methods: Routine collection of PROMs using 4 domains (depression, fatigue, pain interference, and physical function) of PROMIS were offered to all patients with a diagnosis of cancer of any disease site at visits with an oncologic provider using computer adaptive testing. All patients ≥18 years old with a completed PROM at least 2 years since their diagnosis of cancer were eligible for inclusion in the analysis. Only completed PROMs were included in the final analysis. Generalized estimating equation models were used to assess the relationship between age and the estimated mean T-score for each PROMs domain, considering repeat measures within a single patient. Results: A total of 3,636 patients were included in

this retrospective cohort study with a total of 26,173 completed PROMs among all 4 domains. Mean age at diagnosis was 61.2 years (SD=12.44), 64% (n=2324) were female, 68% (n=2,461) identified as White, and 25% (n=893) identified as Black. For fatigue, mean T-score ranged from 48.4 points (SD=9.6) among 18-29 years olds to 56.5 points (SD=10.1) among 90-99 years olds, with no significant change with age (p=0.27). For depression, mean T-score ranged from 48.9 points (SD=9.0) among 60-69 year olds to 51.1 points (SD=8.8) among 80-89 year olds with a 0.3 point/decade decrease in T-score (p=0.01). Pain interference T-scores ranged from 48.6 points (SD=10.5) among 18-29 year olds to 55.0 points (SD=9.4) among 80-89 year olds with a 0.4 point/decade average increase (p,0.001). The largest differences were observed in physical function, where scores ranged from 53.5 points (SD=11.0) among 18-29 year olds to 34.3 points (SD=9.2) among 90-99 year olds. There was a 2.1 point/decade decrease in T-score (p,0.001). Conclusions: Among survivors of cancer, mean PROMIS scores differed by age in the depression, pain interference, and physical function domains but not fatigue. These age-normed PROMIS T-scores, which are required to understand individualized assessments of PROMs, are essential as PROMs are integrated into routine cancer care.

Hematology-Oncology
Thomas DM, Daniele G, Kim JE, **Gadgeel SM**, Ahn ER, Paz-Ares LG, Prenen H, Chen D, Fang J, Wilson TR, Simmons BP, and Barlesi F. Ipatasertib in patients with AKT1/2/3 mutation-positive (AKTmut) tumors: TAPISTRY study. *J Clin Oncol* 2024; 42(16). Full Text

D.M. Thomas

Background: AKT1/2/3 point mutations are found in ~1% of all solid tumors, with varying prevalence across different tumor types. Ipatasertib is an inhibitor of the AKT kinase, but its antitumor activity as monotherapy in patients with AKTmut tumors is unknown. We present efficacy and safety data of ipatasertib in patients with advanced/metastatic AKTmut solid tumors from Cohort E of the TAPISTRY trial (NCT04589845). Methods: TAPISTRY is a phase II, global, open-label, multi-cohort trial evaluating the efficacy and safety of different therapies in patients with advanced/metastatic solid tumors. Patients in Cohort E were aged ≥12 years and had solid tumors harboring an AKT1/2/3mutation identified by next-generation sequencing and measurable disease by RECIST v1.1. Oral ipatasertib 400 mg was administered once daily. Tumor assessments were performed at screening, every eight weeks from Day 1/ Cycle 1 for one year, and every 12 weeks after that. The primary endpoint was objective response rate (ORR) by independent review committee (IRC). Key secondary endpoints included ORR by investigator, duration of response, progression-free survival, overall survival and safety. Results: At data cut-off (16 Jul 2023), 50 patients were safety evaluable and 48 were efficacy evaluable. In the safety-evaluable population, median age was 59 years (range, 30-79); 98% of patients (n/N = 49/50) had an AKT1 mutation (AKT1 E17K, n=47) and 2% (n/N = 1/50) had an AKT2 E17K mutation; 41/50 patients (82%) had received ≥2 prior lines of treatment. Efficacyevaluable patients had 10 different tumor types, the most common being breast cancer (n/N = 21/48; 44%). Key outcomes are summarized in the Table. After a median follow-up of 11.3 months, ORR by IRC in efficacy-evaluable patients was 31.3% (n/N = 15/48; 95% CI 18.7-46.3), driven by responses in three tumor types: breast (n/N = 7/21; 33%), endometrial (n/N = 7/7; 100%), and head and neck (n/N = 1/2; 50%). The most frequent adverse event was diarrhea (n/N = 39/50; 78%). Safety was consistent with the known profile of ipatasertib; no new safety signals were identified. Conclusions: Treatment with ipatasertib led to a marked and durable antitumor activity in some tumor types such as endometrial cancer, but not in the overall tumor-agnostic cohort. Further studies are needed to understand the relevance of AKT inhibition in these tumor types.

Hematology-Oncology
Tsai FYC, Birrer MJ, Brown JR, Chandrasekaran S, Chung V, Frank RC, Garmey EG, **Gadgeel SM**, George TJ, Jalal SI, Poklepovic AS, Segar JM, Spira AI, Zhang JJ, and Kasi A. A phase 2 clinical trial of first-in-class fascin inhibitor NP-G2-044 as monotherapy and in combination therapy with anti-PD-1 immunotherapy in patients with advanced solid tumor malignancies. *J Clin Oncol* 2024; 42(16). Full Text.

F.Y.-C. Tsai

Background: Fascin is the main actin cross-linker in filopodia and its elevated levels are correlated with increased risk of cancer metastasis, disease progression and mortality. Preclinical evidence shows that deletion of the fascin gene (FSCN1) delays tumor development, slows tumor growth, reduces metastatic colonization and increases overall survival. NP-G2- 044 is a novel, small molecule antagonist of fascin that blocks tumor metastasis, inhibits cancer growth and increases antigen uptake by intra-tumoral dendritic cells. In a previously presented phase 1 clinical trial, the drug was well tolerated and demonstrated signals of anti-tumor and anti-metastatic activity. Methods: This open-label study was designed to establish the recommended phase 2 dose (RP2D) of orally administered NP-G2-044 administered as both monotherapy (MT) and in combination (CT) with anti-PD-1 immunotherapy (IO). Efficacy was assessed by RECIST 1.1 and iRECIST [CT patients (pts.) only]. Following MT-RP2D identification, additional treatment-refractory pts. with advanced/metastatic gynecologic (GYN) malignancies were evaluated at the MT-RP2D. The CT-RP2D was established by a 3+3 design followed by an expansion cohort in pts. experiencing stable disease (SD) or progressive disease (PD) on prior anti-PD(L)-1 therapy. Results: MT-RP2D of 2100mg QD was selected based on a 16-pt. comparative review of PK, safety, and efficacy between two highest doses previously identified in phase 1. No DLTs or drug-related SAEs were observed among MT-RP2D pts. Median PFS for 12 GYN pts. receiving the MT-RP2D was 20 weeks and greater than 70% of these pts did not develop new metastases while on study. One pt. (treatment-refractory ovarian cancer) continues on study with SD exceeding 24 months. A CT-RP2D of 1600 mg. QD was selected and enrollment is ongoing. Among 29 enrolled CT pts. evaluated to-date, no DLTs were observed. Multiple tumor bulk reductions were observed among CT pts. incl one confirmed RECIST PR (53% reduction in tumor bulk) for a pt. with cutaneous squamous cell cancer who progressed on prior anti-PD(L)-1 therapy. Most common TEAEs observed for CT were diarrhea, fatigue and nausea with the safety monitoring is ongoing. Conclusions: The first-in-class fascin inhibitor, NP-G2-044, appears safe and well tolerated administered both as MT and in CT with IO. Signals of anti-cancer and anti-metastatic activity were observed with both mono and combination therapy. A phase 3 randomized clinical trial evaluating NP-G2-044 in combination with chemo in pts. with platinum-resistant ovarian cancer is in development with enrollment anticipated to start later this year. Additionally, a phase 2 study to further evaluate NP-G2-044 in combination with anti-PD-1 therapy in IO-naïve pts is planned.

Hematology-Oncology

Waliany S, Hung YP, **Abu Rous F**, Do A, Peterson J, **Meservey C**, Digumarthy SR, **Gadgeel SM**, Lin JJ, and Meadori CB. Atypical Lung Carcinoids with EML4-ALK Fusion and Responses to ALK Inhibitors. *J Thorac Oncol* 2024; 19(7):E32-E33. Full Text.

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Infectious Diseases

Meranda M, **Sheqwara J**, **Shallal A**, **Alangaden G**, **Dillon W**, **Veve M**, **Mann Y**, **Tamr A**, and **Raslan S**. Patterns of vancomycin use in high-risk febrile neutropenia. *J Clin Oncol* 2024; 42(16). Full Text

M. Meranda

Background: Febrile neutropenia (FN) is a common complication in patients with hematologic malignancy. ASCO guidelines on the management of FN endorse empiric anti-Pseudomonas coverage while reserving the use of agents targeting gram-positive organisms and methicillinresistant Staphylococcus aureus (MRSA) for select criteria-defined patients such as those with severe mucositis, hemodynamic instability, radiographic pneumonia, or history of MRSA colonization among others. We sought to examine our institutional management of FN, hypothesizing that local use of empiric vancomycin for high-risk FN will deviate from ASCO guidelines reflected in institutional policy. Methods: Case data from

1/1/2016 - 6/1/2023 was collected retrospectively, comprising patients admitted to the general medical floor with known leukemia, lymphoma, or multiple myeloma meeting ASCO criteria for FN. Patients admitted to intensive care at time of FN or for less than 48-hours were excluded. For each patient, use of vancomycin at time of FN diagnosis (t0) and 48-hours later (t48) was evaluated for congruence with society guidelines. Results: 91 patients were reviewed with amedian age of 68 years old (IQR 59-74, 15). Median length of stay (LOS) was 20 days (IQR 7-29, 22) with FN occurring on day seven of hospitalization on average. Most patients receiving vancomycin were admitted to the hematology specialty unit at time of diagnosis (63%). Acute leukemia was the most common malignancy represented (62.8%), while high grade lymphoma comprised 23.1%. 98.9% of patients were on active chemotherapy at time of FN. 81 patients (89%) received vancomycin as empiric treatment for FN with 76 (93.8%) receiving vancomycin at t0. Of this latter cohort, 29.7% of patients received vancomycin at t0 without indication. At t48, vancomycin was discontinued in 28.4% of patients, 44.4% received vancomycin with true indication, and 27.2% were continued on vancomycin without indication. The median duration of therapy for patients receiving vancomycin incongruently at t48 was 4 days. Of those meeting criteria for vancomycin use at t48, severe mucositis and soft tissue infection were each cited in 22.2% of cases, followed by pneumonia, persistent fever, and hemodynamic instability. Notably, the presence of any grade mucositis was significantly associated with the continued use of empiric vancomycin at t48 ($p = .025$). Admission to hematology specialty unit did not significantly affect adherence to FN management guidelines. Conclusions: These data suggest that the use of vancomycin for FN at our institution deviates from society guidelines including on specialized hematology wards. This study was underpowered to assess adverse outcomes seen with vancomycin use such as renal injury, prolonged LOS and greater cost of care. Given the high complexity of this patient population, detailed provider education is indicated to promote safe, evidence-based care and broader antimicrobial stewardship.

Internal Medicine

Abosheaishaa H, Nassar M, Abdelhalim O, Ali A, Mohamed I, Haseeb-ul-Rasool M, **Abusuliman M**, Morsi S, Abbas S, Amin T, Bahbah A, Salem A, Karna R, and Bilal M. PREVALENCE OF LESIONS PREDISPOSING TO ANEMIA IN THE UPPER GASTROINTESTINAL TRACT IN END-STAGE RENAL DISEASE PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS. *Gastrointest Endosc* 2024; 99(6):AB1149-AB1150. Full Text

Icahn Sch Med Mt Sinai, New York, NY USA. Univ Buffalo, Buffalo, NY USA. Donald & Barbara Zucker Sch Med Hofstra Northwell, Hempstead, NY USA. Univ Missouri Kansas City, Kansas City, KS USA. Henry Ford Hosp, Detroit, MI USA. Johns Hopkins Univ, Baltimore, MD USA. Koc Univ, Istanbul, Turkiye. Menoufia Univ, Shibin Al Kawm, Egypt. Maimonides Hosp, Brooklyn, NY USA. Allegheny Hlth Network, Pittsburgh, PA USA. Minneapolis VA Med Ctr, Minneapolis, MN USA. (SUNY) System; State University of New York (SUNY) Buffalo; Northwell Health; University of Missouri System; University of Missouri Kansas City; Henry Ford Health System; Henry Ford Hospital; Johns Hopkins University; Koc University; Egyptian Knowledge Bank (EKB); Menofia University; Maimonides Medical Center; US Department of Veterans Affairs; Veterans Health Administration (VHA); Minneapolis VA Health Care System

Internal Medicine

Aljbour Almajali D, **Ayyad A**, **Alhaj ali S**, and **Godfrey AM**. A Case of Idiopathic Pneumonia Syndrome in a Patient With Recent Stem Cell Transplant. *Am J Respir Crit Care Med* 2024; 209. Full Text

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Introduction:Idiopathic pneumonia syndrome (IPS) represents a rare but severe complication observed in up to 10% of patients undergoing allogeneic stem cell transplantation (SCT), that carries a high mortality rate. IPS usually manifests within four months post-SCT, making it crucial to promptly identify and manage. Case Presentation:A 68 year-old male with a medical history of acute myeloid leukemia on chemotherapy who received allogenic SCT 26 days prior to admission presented to the emergency department with fever and dyspnea. Upon arrival, the patient exhibited hypoxia and increased work of breathing necessitating BiPAP support and subsequent intubation. CT of the chest showed diffuse bilateral consolidative and ground-glass opacities. Broad-spectrum antibiotics were initiated while awaiting results of additional workup. Bronchoscopy and bronchoalevoar lavage (BAL) did not reveal an

infectious etiology. Transbronchial biopsies not completed given thrombocytopenia. Respiratory culture, fungal culture, and AFB smear and culture were unrevealing. Respiratory viral PCR, PJP PCR, fungitell, and aspergillus galactomannan were negative. No eosinophils were seen on BAL given the recent Daptomycin thus excluding acute eosinophilic pneumonia. CMV DNA quant was elevated at 1002 so the patient was transitioned to Ganciclovir and given Cytogam. Levels were 123 a week later but felt presentation was less consistent with CMV pneumonitis. Given lack of improvement within 72 hours of presentation and that infectious etiology seemed less likely, the patient was started on methylprednisolone 2 mg/kg divided twice daily for treatment of suspected IPS. Additionally, Etanercept was started twice weekly. After ten days of mechanical ventilation, the patient was extubated to heated high flow nasal cannula. Discussion:The exact etiology of IPS remains elusive, thought to be a complex interplay of factors, including lung lining damage from conditioning regimens and graftversus- host disease. IPS diagnosis is based on the exclusion of infectious and cardiac etiologies in the presence of clinical and radiographic findings suggestive of pneumonia, typically confirmed through lung biopsy. However, obtaining a lung biopsy may not always be feasible, as in the presented case, due to patient-specific factors. Treatment for IPS involves a combination of approaches, including oxygen therapy, ventilatory support if needed, systemic corticosteroids, and immunosuppressive medications such as Etanercept which block tumor necrosis factor. Early recognition and intervention are crucial for achieving favorable outcomes in these challenging cases. This also highlights the importance of treating possible infectious etiologies while awaiting workup and when unable to rule out certain infections.

Internal Medicine

Aljbour Almajali D, **Cherabuddi MR**, **Ayyad A**, **Fram F**, and **Abu Sayf A**. Brivaracetam-Related Neurological Decline in a Patient With Complex Medical History. *Am J Respir Crit Care Med* 2024; 209. Full Text

D. Aljbour Almajali, Internal Medicine, Henry Ford Hospital, Detroit, MI, United States

Introduction: Brivaracetam is a newer anticonvulsant that is a propyl analogue of levetiracetam. The medication was initially approved in 2016 as an add-on treatment and was later approved in 2018 as monotherapy for treatment of partial-onset seizures. A review article published in January 2023 concluded that Brivaracetam had a limited impact on cognition and behavior. This case report explores the potential role of Brivaracetam in the patient's deteriorating neurological status. Case Description: A 68-year-old female with past medical history of chronic kidney disease, hypertension and foot osteomyelitis presented with generalized weakness. Of note, during a recent hospitalization, the patient was started on Cefepime for treatment of UTI and developed seizures afterwards, she was later discharged on Brivaracetam. Generalized weakness was thought to be related to Malnutrition. Subsequently, the patient underwent placement of gastrostomy tube and was started on tube feeds. Her hospital course was complicated by gradually worsening mental status and later an episode of somnolence. The patient had stable vital signs at that time. Workup revealed ammonia level of 258, ALP 363, ALT 60, AST 187 and lactate of 2.7. Imaging, including a CT head and abdomen, ruled out acute intracranial or intra-abdominal processes. Further investigations, including infectious workup and EEG did not reveal a possible etiology. Ammonia levels improved with holding tube feeds and treatment with lactulose and Rifaximin; however, there was no improvement in mental status. The patient was transferred to the ICU for airway monitoring in the setting of AMS. A multidisciplinary approach suggested a possible role of Brivaracetam. After holding Brivaracetam, the patient had significant improvement in cognition within 48 hours, further supporting the possibility of Brivaracetam-induced cognitive decline. Case Discussion: Previous studies have generally failed to establish a link between Brivaracetam use and serious neurological side effects. One case report was published in 2022 describing Brivaracetam-induced hyperammonemia and encephalopathy. In our case ammonia levels were elevated as well suggesting a possible association. Further research is needed to better understand the relationship between Brivaracetam and neurological decline in patients with complex medical backgrounds, shedding light on the importance of careful medication reconciliation and close monitoring in such cases.

Internal Medicine
Chaudhary A, Harris K, **Faisal MS**, **Toiv A**, Shahzil M, **Samad M**, **Youssef R**, Farooq U, Tarar Z, and **Suresh S**. USE OF AN ENDOCUFF COLONOSCOPE ATTACHMENT INCREASES SESSILE SERRATED POLYP DETECTION. *Gastrointest Endosc* 2024; 99(6):AB518-AB519. Full Text

Henry Ford Hlth Syst, Franklin, MI USA. Weiss Mem Hosp LLC, Resilience Healthcare, Chicago, IL USA. St Louis Univ, St Louis, MO USA. Univ Missouri Kansas City, Kansas City, MO USA. System; University of Missouri Kansas City

Internal Medicine
Chaudhary A, Harris K, **Toiv A**, Shahzil M, **Faisal MS**, **Ichkhanian Y**, **Dababneh Y**, **Patel-Rodrigues P**, **Salgia R**, and **Watson A**. INCREASED RECEIPT OF CURATIVE INTENT THERAPY FOR LIVER CANCER AFTER EUS-GUIDED ASSESSMENT OF PORTAL HYPERTENSION. *Gastrointest Endosc* 2024; 99(6):AB807-AB808. Full Text

Henry Ford Hlth Syst, Detroit, MI USA. Resilience Healthcare Weiss Mem Hosp LLC, Chicago, IL USA. Indiana Univ Sch Med, Indianapolis, IN 46202 USA. System; Indiana University Bloomington

Internal Medicine
Cherabuddi MR, **Goodman BD**, **Ayyad A**, **Almajali DA**, **Nadeem O**, **Bradley P**, **Russell C**, and **Ouellette DR**. Exploring Disparate Access to Care in Sarcoidosis Patients in Detroit, Michigan. *Am J Respir Crit Care Med* 2024; 209. Full Text

M.R. Cherabuddi, Internal Medicine, Henry Ford Hospital, Detroit, MI, United States

Rationale Sarcoidosis is a multisystem granulomatous inflammatory disease with immense ongoing research. Previous studies assessed the role of social predictors on severity at presentation and found Black, older individuals, with lower income, without insurance to have more severe disease. The city of Detroit, Michigan is at greater risk of disparities with 5 times greater Black population and almost thrice in poverty compared to the nation. We aimed to explore these potential disparities to incorporate our findings into future practice at provider, patient and healthcare system level. Methods This is a retrospective chart review study of all patients seen in pulmonary clinics at Henry Ford Health between January 1st, 2020, and December 31st, 2022, with sarcoidosis patients identified as those with ICD diagnosis code D86. Data collected included date of office visit(s), age, race (Black, White, Other), sex, area deprivation index (ADI), insurance type (Medicare, Medicaid, Commercial), MyChart status, chest x-rays, pulmonary function tests (PFTs), missed clinic visits, number of hospitalizations, mortality, positive biopsy on file, communication of results after bronchoscopy and visits around the time of bronchoscopy. Categorical variables were described using frequency. Numerical variables were described using median, mean and standard deviation. Statistical analysis included Chi-square test, Two-sample T-test and Wilcoxon Rank Sum test and a p-value of <0.05 was considered statistically significant. Results Sarcoidosis patients (N=788), when compared to those seen for other pulmonary problems (N=13,036) were typically slightly younger, Black, female, belonging to higher ADI (greater socioeconomic disadvantage) based on national and state ranks, more likely to use commercial insurance and Medicaid compared to Medicare, have active MyChart access, more noshows, more PFTs on file. Among sarcoidosis patients, significant findings included presence of active MyChart among younger patients, lower ADI and with commercial insurance; more X-rays and PFTs were done in Medicare patients; no-show rate was higher in higher ADI; hospitalizations were higher in those with government insurance. Sarcoidosis patients with positive biopsies on file from 2013-2023 were more likely to be male, White or other races, younger and belonged to lower national ADI ranks. Conclusions This study identified an intricate pattern of demographic and socioeconomic variables affecting access to care in sarcoidosis patients, raising concerns for healthcare barriers especially based on race and ADI, and higher bronchoscopies in those demographic groups thought less likely to have sarcoidosis. Understanding these is vital for equitable high-quality care, assisting in timely and efficient management of the patient's disease. (Figure Presented).

Internal Medicine

Cherabuddi MR, **Schloop M**, **Shakaroun D**, and **Abu Sayf A**. Pulmonary Tumor Thrombotic Microangiopathy Leading to the Discovery of Underlying Gastric Adenocarcinoma. *Am J Respir Crit Care Med* 2024; 209. Full Text

M.R. Cherabuddi, Internal Medicine, Henry Ford Hospital, Detroit, MI, United States

Introduction- Pulmonary tumor thrombotic microangiopathy (PTTM), coined in 1989, is a rare fatal complication of gastric carcinoma involving widespread tumor emboli, thrombi, reactive pulmonary vascular changes, pulmonary hypertension and is almost always diagnosed post-mortem. There is limited literature on pathophysiology and effective management. Description- A 45-year-old man with remote smoking and recent vaping developed progressively worsening shortness of breath over 2 months. Initial imaging was concerning for interstitial lung disease, was started on prednisone taper and developed a new oxygen requirement of 2-4 L. He then developed sudden onset bilateral hip pain with mobility impairment causing him to present to the emergency department. Workup was remarkable for new bicytopenia with hemoglobin 7 g/dL, platelet count 34000/µL, D-dimer >20 ug/mL FEU, LDH 1035 IU/L, CT abdomen and pelvis concerning for primary gastric malignancy, numerous predominantly sclerotic lesions throughout the osseous pelvis, proximal femurs, sacrum and lumbar spine, peritoneal involvement, diffuse pulmonary ground-glass opacities with interlobular septal thickening and fissural nodularity with upper lobe predominance and widespread lymphadenopathy suspicious for lymphangitic metastatic spread. He rapidly decompensated requiring ICU admission for heated high-flow nasal cannula. Echocardiogram could not determine pulmonary artery pressure. He developed diplopia and dizziness, MRI brain showed 10x20 mm left middle cranial fossa enhancing mass with edema, was started on highdose steroid taper. A CT-guided cervical lymph node biopsy revealed gastric adenocarcinoma with signet ring morphology, HER2 IHC 2+, FISH negative, PD-L1 CPS < 1, microsatellite stable. He started dose-reduced FOLFOX chemotherapy while in the ICU, eventually discharged and tolerated chemotherapy and radiation to gastric and brain lesions, with disease stability, and eventual resolution of hypoxia. Discussion- This presentation is likely due to aggressive gastric carcinoma with pulmonary lymphangitic spread, initially mistaken for interstitial lung disease. A clinical picture of right heart failure may have been masked by initiating early diuresis. Case series describe patterns of cough, dyspnea, right heart failure, anemia, thrombocytopenia, elevated LDH and D-dimer, CT with diffuse septal thickening, mediastinal and hilar lymphadenopathy and nodules, elevated pulmonary artery pressures and presence of malignancy and immunohistochemical expression of tissue and vascular endothelial growth factors. PTTM can lead to pulmonary stenosis and manifest as right heart failure leading to the diagnosis of underlying gastric carcinoma. Acute hypoxic respiratory failure in an otherwise healthy male with a cancer diagnosis should raise suspicion for PTTM. Further research is warranted to better understand this lethal condition for earlier diagnosis and timely management.

Internal Medicine

Cherabuddi MR, **Srikanth A**, and **Ouellette DR**. Pan-positive PET-CT - Metastasis or Multisystem Sarcoidosis? *Am J Respir Crit Care Med* 2024; 209. Full Text

M.R. Cherabuddi, Internal Medicine, Henry Ford Hospital, Detroit, MI, United States

Introduction Sarcoidosis is a multisystem granulomatous disorder of unknown etiology commonly affecting lungs, lymph nodes, skin and eyes. Less commonly, involvement of bones and spleen is seen. Description A 36-year-old woman with a history of mild childhood exercise-induced asthma developed an upper respiratory infection after exposure to sick contacts, after which she developed shortness of breath with no improvement with albuterol, budesonide-formoterol and a short steroid course. Her symptoms progressed to dyspnea with normal activity, wheezing and dry cough. Despite an unremarkable chest x-ray, CT and PET scans revealed nodular and ground-glass pulmonary parenchymal lesions, bony lesions, splenic involvement, and diffuse adenopathy in the neck, mediastinum and abdomen. Lesions were PET-avid and thought consistent with metastatic neoplasm. The patient had hypercalcemia. Pulmonary function testing (PFT) revealed airway obstruction with moderate to severe reduction in FEV1 with moderate diffusion impairment. The patient was diagnosed with sarcoidosis after multiple sites were biopsied to include transbronchial lung, cervical lymph node and bone with non-caseating granulomas.

She was prescribed daily prednisone, methotrexate, and mometasone-formoterol, which gradually led to improvement in shortness of breath and resolution of serum hypercalcemia. A CT scan one year later showed improvement in thoracic lymphadenopathy and pulmonary nodules and marked improvement in bony lesions. The patient developed tachycardia but did not have evidence of active cardiac involvement. The patient failed initial sarcoidosis therapy when she developed calcium oxalate kidney stones and hypercalciuria despite having a normal serum calcium level. Infliximab was added to her treatment regimen with resolution of hypercalciuria. The patient subsequently had gradual onset of sarcoid arthropathy, worsened with cold exposure and is being considered for hydroxychloroquine. Discussion Bone involvement is rarely seen in sarcoidosis and is usually asymptomatic and discovered incidentally as in our case. Osseous lesions often mimic metastases, difficult to differentiate on imaging. Splenic involvement is rarely seen in sarcoidosis, is usually nodular rather than diffuse as is in this case, and is a risk factor for chronic sarcoidosis with extrapulmonary involvement. Hypercalciuria without hypercalcemia in sarcoidosis has previously been reported and is an indication for aggressive treatment. Prompt biopsy ruled out malignancy in this patient and revealed sarcoidosis. This patient displayed a constellation of unusual findings due to sarcoidosis, including multiple lesions mimicking metastatic neoplasm, diffuse splenic involvement, and hypercalciuria and nephrolithiasis without hypercalcemia. Biopsy is vital for accurate diagnosis and timely management of sarcoidosis.

Internal Medicine

Elfert K, Beran A, Abosheaishaa H, Salem A, Mohamed M, Elromisy E, **Abusuliman M**, Nassar M, and Elhanafi S. RISK OF PERCUTANEOUS ENDOSCOPIC GASTROSTOMY-RELATED BLEEDING WITH UNINTERRUPTED ANTICOAGULATION: A MULTI-CENTER RETROSPECTIVE COHORT STUDY. *Gastrointest Endosc* 2024; 99(6):AB152-AB152. Full Text

St Barnabas Hosp, Bronx, NY USA. Univ Buffalo, Jacobs Sch Med & Biomed Sci, Buffalo, NY USA. Indiana Univ, Sch Med, Indianapolis, IN USA. Texas Tech Univ Hlth Sci Ctr El Paso, Paul L Foster Sch Med, El Paso, TX USA. Maimonides Hosp, Brooklyn, NY USA. Tanta Univ, Fac Med, Tanta, Egypt. CUNY, City Coll New York, Sch Med, New York, NY USA. Brown Univ, Warren Alpert Med Sch, Providence, RI USA. Henry Ford Hlth Syst, Detroit, MI USA. State University of New York (SUNY) Buffalo; Indiana University System; Indiana University Indianapolis; Maimonides Medical Center; Egyptian Knowledge Bank (EKB); Tanta University; City University of New York (CUNY) System; City College of New York (CUNY); Brown University; Henry Ford Health System; Henry Ford Hospital

Internal Medicine

Faisal MS, **Ashraf T**, **Faisal MS**, **Harris K**, **Khan MZ**, **Chaudhary A**, **Watson A**, **Dang DY**, **Pompa R**, **Elatrache M**, **Piraka C**, **Singla S**, and **Zuchelli T**. CYSTIC DUCT STENTING VERSUS OTHER TREATMENT MODALITIES FOR MANAGEMENT OF ACUTE CHOLECYSTITIS IN PATIENTS WITH DECOMPENSATED CIRRHOSIS. *Gastrointest Endosc* 2024; 99(6):AB651-AB652. Full Text

[Faisal, Muhammad Salman; Ashraf, Taha; Faisal, Muhammad Saad; Harris, Kevin; Khan, Muhammad Zarrar; Chaudhary, Ammad; Watson, Andrew; Dang, Duyen; Pompa, Robert; Elatrache, Mazen; Piraka, Cyrus; Singla, Sumit; Zuchelli, Tobias] Henry Ford Hlth Syst, Detroit, MI USA.

Internal Medicine

Faisal MS, **Faisal MS**, **Chaudhary A**, **Shamaa O**, **Alomari A**, **Dang DY**, **Watson A**, **Elatrache M**, **Pompa R**, **Piraka C**, **Singla S**, and **Zuchelli T**. AMPULLARY ADENOMAS GREATER THAN 20 MM IN SIZE HAVE HIGHER RISK OF RECURRENCE COMPARED TO SMALLER LESIONS. *Gastrointest Endosc* 2024; 99(6):AB628-AB628. Full Text

[Faisal, Muhammad Salman; Faisal, Muhammad Saad; Chaudhary, Ammad; Shamaa, Omar; Alomari, Ahmad; Dang, Duyen; Watson, Andrew; Elatrache, Mazen; Pompa, Robert; Piraka, Cyrus; Singla, Sumit; Zuchelli, Tobias] Henry Ford Hlth Syst, Detroit, MI USA.

Internal Medicine

Faisal MS, **Shamaa O**, **Faisal MS**, **Dang D**, **Watson A**, **Elatrache M**, **Pompa R**, **Piraka C**, **Zuchelli T**, and **Singla S**. SAFETY AND EFFICACY OF BILIARY RADIOFREQUENCY ABLATION IN MANAGEMENT OF AMPULLARY LESIONS. *Gastrointest Endosc* 2024; 99(6):AB630-AB631. Full Text

[Faisal, Muhammad Salman; Shamaa, Omar; Faisal, Muhammad Saad; Dang, Duyen; Watson, Andrew; Elatrache, Mazen; Pompa, Robert; Piraka, Cyrus; Zuchelli, Tobias; Singla, Sumit] Henry Ford Hlth Syst, Detroit, MI USA.

Internal Medicine

Farooq U, Tarar Z, Jaan A, Hayat U, Gondal A, **Chaudhary A**, Schlachterman A, Kumar A, Kowalski T, and Kamal F. ANALYZING TRENDS AND PATTERNS IN ERCP-RELATED ADVERSE EVENTS: WHERE WE NEED TO DO BETTER. *Gastrointest Endosc* 2024; 99(6):AB671-AB671. Full Text

St Louis Univ, St Louis, MO USA. Univ Missouri, Columbia, MO USA. Rochester Gen Hosp, Rochester, NY USA. Thomas Jefferson Univ, Philadelphia, PA USA. Guthrie Healthcare Syst, Sayre, PA USA. Geisinger Wyoming Valley Med Ctr, Wilkes Barre, PA USA. Henry Ford Hlth Syst, Detroit, MI USA. Missouri Columbia; Rochester General Hospital; Jefferson University; Henry Ford Health System; Henry Ford Hospital

Internal Medicine

Gandy R, **Andrews T**, **Graham M**, **Jurayj K**, **Tirgari S**, and **Kelly B**. Use of Multiple Treatment Modalities for Management of High-Risk Pulmonary Embolism Complicated by Clot-In-Transit. *Am J Respir Crit Care Med* 2024; 209. Full Text

R. Gandy, Henry Ford Hospital, Detroit, MI, United States

Introduction: Treatment of high-risk pulmonary Embolism (PE) is a challenging hemodynamic and logistical process. With contraindications to systemic thrombolytics, standard therapy involves choosing another treatment modality, the comparative outcomes of which are either mixed or not well studied. We present a case of a high-risk PE managed with systemic anticoagulation, catheter directed thrombolytics and mechanical embolectomy. Case Description: A 53-year-old female with uncontrolled diabetes, hypertension, peripheral arterial disease, schizoaffective disorder, and recent right leg osteomyelitis was admitted for myonecrosis of the thigh. During her hospitalization she developed tachycardia, hypoxia, and hypotension requiring vasopressors and admission to the intensive care unit (ICU). Point-of-care ultrasound (POCUS) was performed which incidentally showed inferior vena cava (IVC) and severe right ventricular (RV) dilation, and several mobile hyperechoic masses in the right atrium (RA) (Fig. 1a). Unfractionated heparin was initiated, and the Pulmonary Embolism Response Team (PERT) was activated. Computed Tomography (CT) imaging showed filling defects in the RA consistent with clots-in-transit and a large saddle pulmonary embolus (Fig. 1b) with extension to all segments of the pulmonary arteries (PA) (Fig. 1c: example of embolic burden in the right pulmonary vasculature). Systemic thrombolytics were contraindicated due to high risk of bleeding and compartment syndrome of the infected lower extremity. She underwent emergent embolectomy via AlphaVac system of RA/RV thrombus and central pulmonary arteries with an associated decline in systolic PA pressure, from 53 to 43 mmHg. With concern for distal clot, persistent shock, and consideration of bleeding risk, she received six hours of EkoSonic catheter-directed thrombolysis with rapid improvement in oxygen and vasopressor requirements. The patient was eventually discharged on warfarin pending further thrombotic workup. Follow-up echocardiogram and CT imaging showed normal hemodynamics and without any noted residual embolic disease. Discission: This case highlights a positive outcome of a high-risk PE where the rare use of multiple treatment modalities including systemic anticoagulation, catheter-directed thrombolysis, and mechanical embolectomy was required to resolve persistent obstructive shock. While current literature found a 20% mortality at 3-months in patients with PE and thrombi-intransit, use of multiple therapies allowed for complete resolution of right heart strain and pulmonary emboli at just one month after discharge (Ibrahim WH, et al. DOI:10.1177/10760296221140114). This case also demonstrates the diagnostic utility of POCUS in venous thromboembolism. Lastly, this case further

demonstrates the use of a multi-disciplinary PERT program to assist in timely assessment, coordination, and intervention to reduce mortality.

Internal Medicine
Jamali T, **Faisal MS**, **Chaudhary A**, **Faisal MS**, **Nimri F**, **Khan MZ**, **Alomari A**, **Saleem A**, **Kostecki P**, **Youssef R**, **Vemulapalli K**, **Ali SA**, **Patel-Rodrigues P**, **Watson A**, **Dang D**, **Elatrache M**, **Piraka C**, **Singla S**, **Pompa R**, and **Zuchelli T**. RISK OF CHOLECYSTITIS WITH PLACEMENT OF FULLY COVERED METAL BILIARY STENT: REAL WORLD EXPERIENCE FROM A TERTIARY CARE REFERRAL CENTER. *Gastrointest Endosc* 2024; 99(6):AB696-AB697. Full Text

[Jamali, Taher; Faisal, Muhammad Saad; Chaudhary, Ammad; Faisal, Muhammad Salman; Nimri, Faisal; Khan, Muhammad Zarrar; Alomari, Ahmad; Saleem, Abdulmalik; Kostecki, Polo; Youssef, Rami; Vemulapalli, Krishna; Ali, Suhib Alhaj; Patel-Rodrigues, Palak; Watson, Andrew; Dang, Duyen; Elatrache, Mazen; Piraka, Cyrus; Singla, Sumit; Pompa, Robert; Zuchelli, Tobias] Henry Ford Hlth Syst, Detroit, MI USA.

Internal Medicine
Jamali T, **Nimri F**, **Chaudhary A**, **Saleem A**, **Faisal MS**, **Alomari A**, **Abusuliman M**, **Faisal MS**, **Watson A**, **Pompa R**, **Elatrache M**, **Dang D**, **Piraka C**, **Singla S**, and **Zuchelli T**. ADVERSE EVENTS RELATED TO DILATION OF LUMEN APPOSING METAL STENTS DURING ENDOSCOPIC ULTRASOUND GUIDED INTERVENTIONS. *Gastrointest Endosc* 2024; 99(6):AB915-AB916. Full Text

[Jamali, Taher; Nimri, Faisal; Chaudhary, Ammad; Saleem, Abdulmalik; Faisal, Muhammad Saad; Alomari, Ahmad; Abusuliman, Mohammed; Faisal, Muhammad Salman; Watson, Andrew; Pompa, Robert; Elatrache, Mazen; Dang, Duyen; Piraka, Cyrus; Singla, Sumit; Zuchelli, Tobias] Henry Ford Hlth Syst, Detroit, MI USA.

Internal Medicine
Meranda M, **Sheqwara J**, **Shallal A**, **Alangaden G**, **Dillon W**, **Veve M**, **Mann Y**, **Tamr A**, and **Raslan S**. Patterns of vancomycin use in high-risk febrile neutropenia. *J Clin Oncol* 2024; 42(16). Full Text

M. Meranda

Background: Febrile neutropenia (FN) is a common complication in patients with hematologic malignancy. ASCO guidelines on the management of FN endorse empiric anti-Pseudomonas coverage while reserving the use of agents targeting gram-positive organisms and methicillinresistant Staphylococcus aureus (MRSA) for select criteria-defined patients such as those with severe mucositis, hemodynamic instability, radiographic pneumonia, or history of MRSA colonization among others. We sought to examine our institutional management of FN, hypothesizing that local use of empiric vancomycin for high-risk FN will deviate from ASCO guidelines reflected in institutional policy. Methods: Case data from 1/1/2016 - 6/1/2023 was collected retrospectively, comprising patients admitted to the general medical floor with known leukemia, lymphoma, or multiple myeloma meeting ASCO criteria for FN. Patients admitted to intensive care at time of FN or for less than 48-hours were excluded. For each patient, use of vancomycin at time of FN diagnosis (t0) and 48-hours later (t48) was evaluated for congruence with society guidelines. Results: 91 patients were reviewed with amedian age of 68 years old (IQR 59-74, 15). Median length of stay (LOS) was 20 days (IQR 7-29, 22) with FN occurring on day seven of hospitalization on average. Most patients receiving vancomycin were admitted to the hematology specialty unit at time of diagnosis (63%). Acute leukemia was the most common malignancy represented (62.8%), while high grade lymphoma comprised 23.1%. 98.9% of patients were on active chemotherapy at time of FN. 81 patients (89%) received vancomycin as empiric treatment for FN with 76 (93.8%) receiving vancomycin at t0. Of this latter cohort, 29.7% of patients received vancomycin at t0 without indication. At t48, vancomycin was discontinued in 28.4% of patients, 44.4% received vancomycin with true indication, and 27.2% were continued on vancomycin without indication. The median duration of therapy for patients receiving vancomycin incongruently at t48 was 4 days. Of those meeting criteria for vancomycin use at t48, severe mucositis and soft tissue infection were each cited in 22.2% of cases, followed by pneumonia, persistent fever, and hemodynamic instability. Notably, the presence of any

grade mucositis was significantly associated with the continued use of empiric vancomycin at t48 (p = .025). Admission to hematology specialty unit did not significantly affect adherence to FN management guidelines. Conclusions: These data suggest that the use of vancomycin for FN at our institution deviates from society guidelines including on specialized hematology wards. This study was underpowered to assess adverse outcomes seen with vancomycin use such as renal injury, prolonged LOS and greater cost of care. Given the high complexity of this patient population, detailed provider education is indicated to promote safe, evidence-based care and broader antimicrobial stewardship.

Internal Medicine
Mosquera LG, Balanchivadze N, Ali F, **Meranda M**, **Castro OH**, and **Kuriakose P**. Factors influencing career choices and post-fellowship perspectives in adult hematology/oncology fellows: A nationwide cross-sectional study. *J Clin Oncol* 2024; 42(16):1. Full Text

Henry Ford Hosp, Detroit, MI USA. Virginia Oncol Associates, Norfolk, VA USA. Coastal Canc Ctr, Myrtle Beach, SC USA.

Internal Medicine
Nimri F, **Jamali T**, **Ali SA**, **Dawod S**, **Alluri S**, **Youssef R**, **Faisal MS**, **Omeish H**, **Abusuliman M**, **Saleem A**, **Alomari A**, **Faisal MS**, **Singla S**, and **Zuchelli T**. THE SAFETY OF SPHINCTEROTOMY IN ERCP AMONG PATIENTS WITH CIRRHOSIS: INSIGHTS FROM A QUATERNARY CARE TRANSPLANT CENTER. *Gastrointest Endosc* 2024; 99(6):AB683-AB684. Full Text

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Internal Medicine
Nimri F, **Jamali T**, **Dawod S**, **Ali SA**, **Alluri S**, **Youssef R**, **Faisal MS**, **Omeish H**, **Alomari A**, **Abusuliman M**, **Saleem A**, **Faisal MS**, **Singla S**, and **Zuchelli T**. EXPLORING THE SAFETY OF CONDUCTING ERCP IN DECOMPENSATED CIRRHOSIS: INSIGHTS FROM A QUATERNARY CARE TRANSPLANT CENTER. *Gastrointest Endosc* 2024; 99(6):AB656-AB656. Full Text

[Nimri, Faisal; Jamali, Taher; Dawod, Sanad; Ali, Suhib Alhaj; Alluri, Spandana; Youssef, Rami; Faisal, Muhammad Saad; Omeish, Haya; Alomari, Ahmad; Abusuliman, Muhammad; Saleem, Abdulmalik; Faisal, Muhammad Salman; Singla, Sumit; Zuchelli, Tobias] Henry Ford Hosp, Detroit, MI USA.

Internal Medicine
Pichardo R, **Jacob B**, **Jamil M**, **Jamil D**, **Raslan S**, **Rose CM**, **Boakye EA**, **Poisson L**, **Tam S**, and **Philip PA**. Patient-reported and clinical outcomes among patients with pancreatic cancer. *J Clin Oncol* 2024; 42(16). Full Text

R. Pichardo

Background: Pancreatic cancer is associated with poor survival, high symptom burden, and psychological distress. Conventional assessments such as performance status (PS) have relied on provider-generated data to evaluate the selection of treatment and prognosis. Patientreported outcome measures (PROMs) represent a patient-centric representation of the patient experience and are increasingly applied as tools to help improve outcomes and quality of life. However, little is known about the correlation of PROMs with ECOG PS and clinical outcomes in pancreatic cancer. Methods: We performed a retrospective analysis of patients with pancreatic cancer seen at the Henry Ford Health System between 09/2020 and7/2023, using ICD codes. The NIH's validated and standardized Patient-Reported Outcomes Measurement Information System was used to capture 4 core domains: fatigue, pain interference, physical function, and depression. Patient-level variables and disease-specific variables were obtained by chart review from EHR. Kruskal-Wallis tests for continuous variables and or Fisher's exact tests for categorial variables were used to compare the different ECOG scores and PROM scores and patient-level and disease-specific variables. Results: 176 patients were analyzed, with a median age of 65, 58% were male. Most

patients had Stage 1 32.9% followed by Stage 4 25.9%, stage 3 22.9%, 1 32.9%. The majority had an ECOG score of 1, followed by, 0, 2, and only 10 had an ECOG PS of 3. There was no statistically significant difference in PS scores according to smoking status, race, or AJCC Stage but differed by age (P = 0.0007). PS score was not significantly associated with PROMscores on depression, fatigue, or pain interference. However, increasing PS scores were associated with a significant increase in low physical function PROM scores (P , 0.0001). Conclusions: Clinician-assessed PS is a single assessment of the patient's tolerance to therapies subject to physician bias; our study provides encouraging data on the association between PS and patients' reported physical function. The other PROM domains did not provide additional meaningful information on the patient's function although are part of clinical decision-making.

Internal Medicine
Samad M, **Kostecki P**, **Nabaty R**, **Faisal MS**, **Jamali T**, **Chaudhary A**, **Youssef R**, **Zuchelli T**, **Singla S**, and **Piraka C**. ROLE OF ENDOSCOPIC ULTRASOUND AND PROGRESSION OF PANCREATIC CYSTS IN SOLID ORGAN TRANSPLANT PATIENTS. *Gastrointest Endosc* 2024; 99(6):AB933-AB933. Full Text

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Internal Medicine
Shahid MA, **Kulkarni RB**, **Albusoul L**, **Jacob B**, **Rose CM**, **Springer K**, and **Dabak VS**. Evaluation and treatment response in patients with hormone receptor-positive, HER2 low metastatic breast cancer: A single center retrospective analysis. *J Clin Oncol* 2024; 42(16). Full Text

M.A. Shahid, Henry Ford Hospital, Detroit, MI, United States

Background: Patients with Hormone Receptor (HR)+ metastatic breast cancer have seen several new options that improve overall survival. Recently, there are new treatment options for patients with HER2 low expression (defined as HER2 1+ on IHC or 2+ on IHC with a negative FISH). Currently, patients who have HR+ metastatic breast cancer are treated with a combination of an aromatase inhibitor and a Cyclin Dependent Kinase (CDK) 4/6 Inhibitor as first line. Information regarding response to therapy in this group and a correlation with HER2 expression is limited. Methods: This is a retrospective study that aimed to evaluate patients with metastatic, HR+, HER2 low or HER2 negative breast cancer between January 1, 2015 and December 31, 2022. Patients were stratified based on their HER2 status, race, presence of de-novo metastatic disease versus progression, treatment with a CDK 4/6 Inhibitor, and time to progression (defined as the date of biopsy-proved diagnosis to the date of radiographic progression). Comparative data analyses were performed using Fisher Exact and Kruskal-Wallis testing. Kaplan Meier estimates with a log rank p-value were used for survival curves, and a Pvalue of < 0.05 was considered statistically significant. Results: 143 patients were included in our study. Patients were divided based on their HER2 status; 33.5% had HER2 2+ disease, 55.9% had HER2 1+, and 8.4% had HER2 0. Of the patients evaluated, 66% (94/143) were Caucasian, 25% (36/143) were African American (AA), and 9% (13/143) were of other race. There was a significant difference amongst patients treated with CDK 4/6 inhibitors when stratified by race; AA patients had a higher proportion of not using a CDK4 inhibitor (43.3% vs 20.3%; p-value 0.0109). There was a significant difference between the survival curves of HER2 0, 1+, and 2+ (log rank p-value = 0.043). HER2 0 patients progressed quicker than HER2 1+ and 2+ patients. When comparing HER2 negative and low disease, a significant difference was found between the survival curves (log rank p-value = 0.0190). In patients with HER2 low (1+ and 2+ with negative FISH) and HER2 negative disease, there was no difference noted among patients who had de-novo or progression to metastatic disease, high MiB1 status (defined as >20%), whether treatment with CDK 4/6 inhibitor was used, and tumor histology. Conclusions: In our study, patients who had any HER2 expression had a longer time to progression compared to patients with no expression. Patients who had a higher expression (2+ vs 1+) displayed a longer time to progression. This may suggest that as the HER2 expression increases, they may derive a longer benefit with first line therapy. Interestingly, African

American patients had a higher proportion of not using a CDK4/6 inhibitor. Larger studies are needed to evaluate these differences and determine whether any expression can be used as a prognostic marker.

Internal Medicine
Shahzil M, **Chaudhary A**, Qureshi AA, Hasan F, **Jamali T**, Khan MZ, **Faisal MS**, Khaqan MA, **Alsheik E**, and **Zuchelli T**. "ENDOSCOPIC FULL-THICKNESS PLICATION FOR THE TREATMENT OF GASTROESOPHAGEAL REFLUX DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED, SHAM-CONTROLLED TRIALS". *Gastrointest Endosc* 2024; 99(6):AB154-AB155. Full Text

Henry Ford Hlth Syst, Detroit, MI USA. Weiss Mem Hosp LLC, Resilience Healthcare, Chicago, IL USA. King Edward Med Univ, Lahore, Pakistan. Cooper Univ Hlth Care, Camden, NJ USA. John H Stroger Jr Hosp Cook Cty, Chicago, IL USA. Hospital Cook County; University of Illinois System; University of Illinois Chicago; University of Illinois Chicago Hospital

Internal Medicine
Shamaa O, **Ali SA**, **Omeish H**, **Alomari A**, **Dababneh Y**, **Piraka C**, and **Zuchelli T**. ASSESSING PROCEDURE OUTCOMES FOLLOWING PIECEMEAL COLD SNARE ENDOSCOPIC MUCOSAL RESECTION OF LARGE NON-PEDUNCULATED COLORECTAL POLYPS. *Gastrointest Endosc* 2024; 99(6):AB520-AB521. Full Text

[Shamaa, Omar; Ali, Suhib Alhaj; Omeish, Haya; Alomari, Ahmad; Dababneh, Yara; Piraka, Cyrus; Zuchelli, Tobias] Henry Ford Hosp, Detroit, MI USA.

Nephrology
Obeidat A, Mansour N, **Mahfouz R**, and Aldiabat M. Potential impact of malnutrition on patients with hepatocellular carcinoma undergoing liver transplantation: A nationwide analysis. *J Clin Oncol* 2024; 42(16):1. Full Text

Presbyterian Hlth Syst, Albuquerque, NM USA. Wageningen Univ & Res, Wageningen, Netherlands. Henry Ford Hosp, Detroit, MI 48202 USA. Washington Univ, St Louis, MO 63110 USA. Hospital; Washington University (WUSTL)

Neurology
De Groot JF, Cloughesy TF, Berry DA, Buxton MB, Colman H, Ellingson BM, Gordon GB, Lassman AB, Lim M, Mellinghoff IK, Sulman EP, Weller M, Wen PY, Hyddmark EMV, **Mikkelsen T**, Owen SP, Mason WP, Drappatz J, Blondin NA, and Perry JR. Evaluation of VAL-083 in GBM AGILE, a phase 3 registration platform trial for newly diagnosed and recurrent glioblastoma. *J Clin Oncol* 2024; 42(16). Full Text

J.F. De Groot

Background: GBM AGILE (NCT03970447) is a phase 2/3 Bayesian adaptive registration platform trial testing multiple therapies efficiently against a common control (C) with a primary endpoint of overall survival (OS). VAL-083 (VAL) is a DNA targeting agent that, independent of O6-methylguanine DNA methyltransferase promoter methylation status, targets the N7 position of guanine residues and facilitates inter-strand DNA crosslinks, leading to DNA doublestrand breaks and cell death. It entered the trial in January 2021, and it is the 2nd arm (of 6) to complete its evaluation. Methods: Patient subtypes considered in GBM AGILE are newly diagnosed methylated (NDM), ND unmethylated (NDU), & recurrent disease (RD). C is temozolomide (in ND) & lomustine (in RD). Arms open to all 3 subtypes are evaluated in = prospectively defined signatures (sig): NDU, NDM, RD, all ND and All. Randomization to C is 20% in each subtype. Exp arms in GBM AGILE have 1 or 2 stages. Efficacy is based on OS hazard ratio (HR) of arm/C. Efficacy goal is a final Bayesian probability ≥ 98% for HR <1.00 in combined Stages 1 & 2. Arms stop accruing in Stage 1 if they reach max sample size (N) or drop for futility or safety. Exp arms in Stage 1 are adaptively randomized with allocation being proportional to an arm's current probability of having ≥ 30% benefit in OS, P(HR <0.70). In stage 1, exp arms are evaluated monthly, and arms showing Bayesian predictive power (PP) ≥ 0.8, graduate into Stage 2 with fixed randomization in one sig. For all

exp arms, follow up continues for 12 mos after accrual stops (clinical cutoff). Arms are declared futile at any monthly analysis when PP is <0.25 for all sigs. Open to all 3 subtypes, VAL entered as the 1st arm in NDM and was randomized 1:1 to C in this subtype until additional arms entered. The target max N for VAL in its Stages 1 & 2 were 150 and 50, resp. Results: At the interim after VAL reached max sample size in Stage 1, the PP for all signatures was <0.8 and >0.25 for at least one sig. Thus, VAL did not graduate nor drop for futility, but accrual stopped for maximum N in Stage 1 (see table). Final results will be presented at the meeting. Columns 2-5 show results at the interim after which VAL stopped for max N. Columns 6-8 show near final results. Conclusions: GBM AGILE is an efficient & effective model for phase 3 drug development. VAL did not increase OS compared to C in any glioblastoma subtype. GBM AGILE evaluated this agent in less time, at lower cost, & with fewer patients than typical registration trials & is currently evaluating several other arms. (Table Presented).

Obstetrics, Gynecology and Women's Health Services

Salleh M, Alkaram W, Zaiem F, **Kheil M**, Jain D, Wahidi M, Boerner J, Jang H, Kim S, Morris R, Bandyopadhyay S, and Ali-Fehmi R. The role of epithelial-mesenchymal transition markers in invasive breast cancer among patients of Arab descent. *J Clin Oncol* 2024; 42(16). Full Text

M. Salleh

Background: Epithelial-mesenchymal transition (EMT) is the process wherein polarized and cohesive epithelial cells lose their epithelial characteristics and acquire a mesenchymal phenotype and proceed to the invasive form of the tumor. Numerous regulators play a role in the complex signaling pathways that mediate the EMT process. This study aims to investigate the immunohistochemical (IHC) expression of several EMT-related markers and their implications on the diagnosis and prognosis of breast cancer in a cohort of Arab descent women. Methods: Patients of Arab descent treated surgically for invasive and in-situ breast cancer between 2017- 2020 were included in the study. Expressions of Ki-67, Transforming growth factor- β (TGFβ), NF-kappaB (NF-κB), Snail, Vimentin, E-cadherin (E-Cad), and B-catenin (B-Cat) were evaluated by IHC in tissue microarray slides, as per guidelines in the literature. We examined the association between the tumor markers and other clinicopathological variables and prognosis. Fisher's exact tests were utilized to compare categorical variables between groups. Results: One hundred eleven patients were included, 65.8% had invasive ductal carcinoma (IDC); 19.8% had invasive lobular carcinoma (ILC); 13.5% had both ductal and lobular features, and 0.9% had ductal carcinoma in situ. 91 (54.1%) were grade 2 and 303 (41.4%) were grade 3 tumors. Most tumors were ER positive (81.8%), PR positive (75.7%), and HER-2 negative (77.5%). The median age at diagnosis was 52 years. High TGF- β expression was associated with higher frequency of grade 3 tumors (p=0.036), AJCC stage III (p=0.042), and larger tumor size (p=0.036) compared to those with low TGF-B expression. Patients with positive B-Cat expression had a higher risk of death compared to those with negative B-Cat expression (HR, 3.90; 95% CI, 1.19 to 15.93; p=0.024). IDC had a statistically significant increased expression of TGF-B (69.9% vs.45.5%, p=0.045), E-Cad (76.7% vs. 13.6%, p<0.001), and B-Cat (P 39.7% vs. 0%, p<0.001) when compared to ILC. The overall survival at 1 and 5 years were 96.3% (95% CI, 92.7- 99.9) and 81.7% (95% CI, 73.8-90.3), respectively. Conclusions: Tumors with high expression for TGF- β and B-Cat exhibit more aggressive clinical behavior, suggesting the potential prognostic and therapeutic value of these markers. Due to the limited research focused on Arab descent women, findings from this study may provide the foundation for more extensive molecular and clinical studies to assess the validity and clinical utility of these biomarkers in breast cancer patients from diverse ethnic backgrounds.

Otolaryngology – Head and Neck Surgery

Pichardo R, **Jacob B**, **Jamil M**, **Jamil D**, **Raslan S**, **Rose CM**, **Boakye EA**, **Poisson L**, **Tam S**, and **Philip PA**. Patient-reported and clinical outcomes among patients with pancreatic cancer. *J Clin Oncol* 2024; 42(16). Full Text

R. Pichardo

Background: Pancreatic cancer is associated with poor survival, high symptom burden, and psychological distress. Conventional assessments such as performance status (PS) have relied on provider-generated data to evaluate the selection of treatment and prognosis. Patientreported outcome measures (PROMs)

represent a patient-centric representation of the patient experience and are increasingly applied as tools to help improve outcomes and quality of life. However, little is known about the correlation of PROMs with ECOG PS and clinical outcomes in pancreatic cancer. Methods: We performed a retrospective analysis of patients with pancreatic cancer seen at the Henry Ford Health System between 09/2020 and7/2023, using ICD codes. The NIH's validated and standardized Patient-Reported Outcomes Measurement Information System was used to capture 4 core domains: fatigue, pain interference, physical function, and depression. Patient-level variables and disease-specific variables were obtained by chart review from EHR. Kruskal-Wallis tests for continuous variables and or Fisher's exact tests for categorial variables were used to compare the different ECOG scores and PROM scores and patient-level and disease-specific variables. Results: 176 patients were analyzed, with a median age of 65, 58% were male. Most patients had Stage 1 32.9% followed by Stage 4 25.9%, stage 3 22.9%, 1 32.9%. The majority had an ECOG score of 1, followed by, 0, 2, and only 10 had an ECOG PS of 3. There was no statistically significant difference in PS scores according to smoking status, race, or AJCC Stage but differed by age (P = 0.0007). PS score was not significantly associated with PROMscores on depression, fatigue, or pain interference. However, increasing PS scores were associated with a significant increase in low physical function PROM scores (P , 0.0001). Conclusions: Clinician-assessed PS is a single assessment of the patient's tolerance to therapies subject to physician bias; our study provides encouraging data on the association between PS and patients' reported physical function. The other PROM domains did not provide additional meaningful information on the patient's function although are part of clinical decision-making.

Otolaryngology – Head and Neck Surgery

Tam S, **Boakye EA**, **Springer K**, **Poisson L**, **Al-Antary N**, **Elsiss F**, **Nair M**, **Zatirka T**, **Ryan M**, **Chang SS**, and **Movsas B**. Age-normed patient-reported outcome measures among cancer survivors. *J Clin Oncol* 2024; 42(16). Full Text

S. Tam

Background: Patient-reported outcome measures (PROMs) are instruments used to collect health-related outcomes that are derived completely from the patient without interpretation from healthcare providers. Monitoring and subsequent intervention based on PROMs collection has demonstrated efficacy in clinical trial settings. This has resulted in implementation of PROMs in routine clinical cancer practices throughout the nation. PROMs have been normed to the general population, but establishing the norms among cancer patients is essential to understanding how PROMs can be evaluated on an individual basis in routine clinical cancer care. This study aims to characterize age-normed PROMs scores among survivors of cancer using the National Institute of Health's Patient-Reported Outcome Measures Information System (PROMIS) depression, fatigue, pain interference, and physical function domains. Methods: Routine collection of PROMs using 4 domains (depression, fatigue, pain interference, and physical function) of PROMIS were offered to all patients with a diagnosis of cancer of any disease site at visits with an oncologic provider using computer adaptive testing. All patients ≥18 years old with a completed PROM at least 2 years since their diagnosis of cancer were eligible for inclusion in the analysis. Only completed PROMs were included in the final analysis. Generalized estimating equation models were used to assess the relationship between age and the estimated mean T-score for each PROMs domain, considering repeat measures within a single patient. Results: A total of 3,636 patients were included in this retrospective cohort study with a total of 26,173 completed PROMs among all 4 domains. Mean age at diagnosis was 61.2 years (SD=12.44), 64% (n=2324) were female, 68% (n=2,461) identified as White, and 25% (n=893) identified as Black. For fatigue, mean T-score ranged from 48.4 points (SD=9.6) among 18-29 years olds to 56.5 points (SD=10.1) among 90-99 years olds, with no significant change with age (p=0.27). For depression, mean T-score ranged from 48.9 points (SD=9.0) among 60-69 year olds to 51.1 points (SD=8.8) among 80-89 year olds with a 0.3 point/decade decrease in T-score (p=0.01). Pain interference T-scores ranged from 48.6 points (SD=10.5) among 18-29 year olds to 55.0 points (SD=9.4) among 80-89 year olds with a 0.4 point/decade average increase (p,0.001). The largest differences were observed in physical function, where scores ranged from 53.5 points (SD=11.0) among 18-29 year olds to 34.3 points (SD=9.2) among 90-99 year olds. There was a 2.1 point/decade decrease in T-score (p,0.001). Conclusions: Among survivors of cancer, mean PROMIS scores differed by age in the depression, pain interference, and physical function domains but not fatigue. These age-normed PROMIS

T-scores, which are required to understand individualized assessments of PROMs, are essential as PROMs are integrated into routine cancer care.

Pathology and Laboratory Medicine
Abbas O, **Tawil T**, **Inamdar K**, **Liu W**, **Gomez-Gelvez J**, **Shen YL**, **Fang XL**, and **Ghosh SB**. Acute Myeloid Leukemia with Rare T(16;21)(Q24;Q22) and RUNX1::CBFA2T3 Fusion Resembling AML with RUNX1::RUNX1T1: A Case Report and Literature Review. *J Mol Diagn* 2024; 26(6):S28-S29. Full Text.

[Abbas, Omar; Tawil, Tala; Inamdar, Kedar; Liu, Wei; Gomez-Gelvez, Juan; Shen, Yulei; Fang, Xiaolan; Ghosh, Sharmila B.] Henry Ford Hlth, Dept Pathol & Lab Med, Detroit, MI USA. [Inamdar, Kedar; Liu, Wei; Gomez-Gelvez, Juan; Shen, Yulei; Ghosh, Sharmila B.] Henry Ford Hlth, Div Hematopathol, Detroit, MI USA. [Fang, Xiaolan] Henry Ford Hlth, Div Mol Pathol & Genom Med, Detroit, MI USA. System

Pathology and Laboratory Medicine
George M, **Clark J**, **Hartway K**, **Zwernik S**, **Gartrelle K**, **Salas-Escabillas D**, **Long D**, **Nassif G**, **Pichardo T**, **Wombwell A**, **Wen HJ**, **Benitz S**, **Philip PA**, **Khan G**, **Shah RA**, **Park H**, **Crawford H**, **Kwon DS**, **Theisen B**, and **Steele N**. Longitudinal tissue-based evaluation of TIGIT expression in patients with pancreatic cancer: Effect of expression with advancing clinical stages and across racial groups. *J Clin Oncol* 2024; 42(16). Full Text

M. George

Background: While ground has been gained, pancreatic ductal adenocarcinoma (PDAC) continues to have a low 5-year survival of 13%. This is owed partially to a lack of early detection biomarkers and resistance to standard therapeutic options. TIGIT, an immune checkpoint receptor, is a marker of T-cell exhaustion and plays a key role in the inhibition of anti-tumor immune responses. TIGIT inhibitors are being explored in clinical trials in PDAC. Here we evaluate TIGIT expression in a cohort of PDAC patients and correlate level and intensity of expression with clinical parameters. We also examine changes in expression as the disease progresses from primary to metastatic disease. Methods: We performed RNAscope in situ hybridization (ISH) with a probe specific for human TIGIT mRNA on 82 formalin-fixed paraffin-embedded (FFPE) tissue samples. The cohort of tissue samples included 9 biopsies, 67 primary resections and 6 metastatic lesions. We evaluated the total TIGIT expression (%) as well as the intensity of TIGIT expression (% of cells with 3+ punctae, signifying putative immune cells), and compared these values between samples. Utilizing linear regression for continuous outcomes and logistic regression for binary outcomes, we tested for associations between TIGIT expression and clinical covariates. Results: Staining analysis showed that TIGIT expression did not differ significantly between racial groups. The mean percentage of TIGIT positive cells was 64.0%. High expression of TIGIT was associated with more advanced clinical stage ($p < 0.05$). Evaluation of three longitudinal samples from the same patient revealed decreased TIGIT expression from the initial biopsy (41.6%) to resection (33.4%) and metastasis (2.8%). In these specimens, 3+ TIGIT expression also declined (2.1%, 1.2% and 0.02%, respectively). Conclusions: Anti-TIGIT therapy has potential to reverse immune suppression and, with other therapeutic modalities, may provide survival benefit. Here we demonstrate that increased TIGIT expression correlates with more advanced stage at diagnosis and also present data demonstrating that overall TIGIT expression, as detected by RNAscope ISH, may decrease as PDAC progresses to metastasis. As such, anti-TIGIT therapy may have important implications for evading an important mechanism of cancer progression.

Pathology and Laboratory Medicine
Jaehne A, Naiman M, **Cook B**, **Wilson I**, **Veryser D**, **Kelly W**, **Ghosh S**, and **Rivers EP**. Value of Monocyte Distribution Width in Bacteremia Assessment in Emergency Department Patients. *Am J Respir Crit Care Med* 2024; 209. Full Text

A. Jaehne, Emergency Medicine, Henry Ford Hospital, Detroit, MI, United States

Rationale Monocyte distribution width (MDW) is a pathogen-agnostic marker of immune response and dysregulation reported as part of a Complete Blood Count (CBC) with differential. MDW is derived from

the distribution of peripheral blood monocyte volumes and aids in the identification of severe infections and sepsis in adult Emergency Department (ED) patients. Several prospective clinical trials have demonstrated that elevated MDW values are associated with severe infection in the general adult ED population. Additional real-world examination can help refine interpretation in early clinical scenarios. MDW could play a useful role in assessing bacteremia and septicemia risk. Bacteremia, defined as the presence of viable bacteria in the bloodstream, is present in up to 20% of sepsis patients. Blood culture establishes pathogen presence and identity but requires time. This may limit a more aggressive treatment strategy. The purpose of this study was to characterize MDW clinical behavior in the context of bacteremia upon hospital presentation. Methods This was a prospective, observational cohort study. All patients who presented to the ED, were over 18 years of age, and had a blood culture order along with a CBC with differential were enrolled into the study. MDW values were blinded to those involved in direct patient care. An MDW value ≥20 is the published cut-off for increased severe infection risk. We calculated the diagnostic accuracy of MDW values ≥20 for positive blood cultures using SPSS Version 25. Results From July 2021 to September 2023 a total of 185,405 ED visits were registered. During this time 9,400 ED blood cultures were ordered. A total of 5,316 ED blood culture results were matched with MDW results. The overall blood culture positivity rate was 14.5%. MDW sensitivity and specificity for positive blood culture were 83.9% and 36.2%, respectively. Positive and negative predictive values were 18.2% and 93.0%, respectively. Conclusion This interim analysis suggests that MDW may be a useful adjunct for early detection of bacteremia in ED patients. The observed sensitivity is consistent with the known relationship between positive blood culture and sepsis. Since MDW results can be available well before blood culture results, this biomarker could help early risk stratification among suspected infection patients. MDW values below 20 have a high predicative value for negative blood cultures. Further analysis incorporating additional clinical information will provide guidance for interpreting MDW values in combination blood culture results.

Pathology and Laboratory Medicine

Jin M, **Inamdar K**, **Gomez-Gelvez J**, **Liu W**, **Ghosh S**, **Carey J**, and **Shen YL**. A Unique Case of *BCR*::*ABL1*-Positive Chronic Myeloid Leukemia (CML) with Concurrent Chronic Myelomonocytic Leukemia (CMML)-Like Features: A Masked Composite Condition or Disease Progression? *J Mol Diagn* 2024; 26(6):S32-S32. Full Text

[Jin, Michelle; Inamdar, Kedar; Gomez-Gelvez, Juan; Liu, Wei; Ghosh, Sharmila; Carey, John; Shen, Yulei] Henry Ford Hosp, Dept Pathol & Lab Med, Detroit, MI USA.

Pharmacy

Meranda M, **Sheqwara J**, **Shallal A**, **Alangaden G**, **Dillon W**, **Veve M**, **Mann Y**, **Tamr A**, and **Raslan S**. Patterns of vancomycin use in high-risk febrile neutropenia. *J Clin Oncol* 2024; 42(16). Full Text

M. Meranda

Background: Febrile neutropenia (FN) is a common complication in patients with hematologic malignancy. ASCO guidelines on the management of FN endorse empiric anti-Pseudomonas coverage while reserving the use of agents targeting gram-positive organisms and methicillinresistant Staphylococcus aureus (MRSA) for select criteria-defined patients such as those with severe mucositis, hemodynamic instability, radiographic pneumonia, or history of MRSA colonization among others. We sought to examine our institutional management of FN, hypothesizing that local use of empiric vancomycin for high-risk FN will deviate from ASCO guidelines reflected in institutional policy. Methods: Case data from 1/1/2016 - 6/1/2023 was collected retrospectively, comprising patients admitted to the general medical floor with known leukemia, lymphoma, or multiple myeloma meeting ASCO criteria for FN. Patients admitted to intensive care at time of FN or for less than 48-hours were excluded. For each patient, use of vancomycin at time of FN diagnosis (t0) and 48-hours later (t48) was evaluated for congruence with society guidelines. Results: 91 patients were reviewed with amedian age of 68 years old (IQR 59-74, 15). Median length of stay (LOS) was 20 days (IQR 7-29, 22) with FN occurring on day seven of hospitalization on average. Most patients receiving vancomycin were admitted to the hematology specialty unit at time of diagnosis (63%). Acute leukemia was the most common malignancy represented (62.8%), while high grade lymphoma comprised 23.1%. 98.9% of patients were on active chemotherapy

at time of FN. 81 patients (89%) received vancomycin as empiric treatment for FN with 76 (93.8%) receiving vancomycin at t0. Of this latter cohort, 29.7% of patients received vancomycin at t0 without indication. At t48, vancomycin was discontinued in 28.4% of patients, 44.4% received vancomycin with true indication, and 27.2% were continued on vancomycin without indication. The median duration of therapy for patients receiving vancomycin incongruently at t48 was 4 days. Of those meeting criteria for vancomycin use at t48, severe mucositis and soft tissue infection were each cited in 22.2% of cases, followed by pneumonia, persistent fever, and hemodynamic instability. Notably, the presence of any grade mucositis was significantly associated with the continued use of empiric vancomycin at t48 (p = .025). Admission to hematology specialty unit did not significantly affect adherence to FN management guidelines. Conclusions: These data suggest that the use of vancomycin for FN at our institution deviates from society guidelines including on specialized hematology wards. This study was underpowered to assess adverse outcomes seen with vancomycin use such as renal injury, prolonged LOS and greater cost of care. Given the high complexity of this patient population, detailed provider education is indicated to promote safe, evidence-based care and broader antimicrobial stewardship.

Public Health Sciences

Jaehne A, Naiman M, **Cook B**, **Wilson I**, **Veryser D**, **Kelly W**, **Ghosh S**, and **Rivers EP**. Value of Monocyte Distribution Width in Bacteremia Assessment in Emergency Department Patients. *Am J Respir Crit Care Med* 2024; 209. Full Text

A. Jaehne, Emergency Medicine, Henry Ford Hospital, Detroit, MI, United States

Rationale Monocyte distribution width (MDW) is a pathogen-agnostic marker of immune response and dysregulation reported as part of a Complete Blood Count (CBC) with differential. MDW is derived from the distribution of peripheral blood monocyte volumes and aids in the identification of severe infections and sepsis in adult Emergency Department (ED) patients. Several prospective clinical trials have demonstrated that elevated MDW values are associated with severe infection in the general adult ED population. Additional real-world examination can help refine interpretation in early clinical scenarios. MDW could play a useful role in assessing bacteremia and septicemia risk. Bacteremia, defined as the presence of viable bacteria in the bloodstream, is present in up to 20% of sepsis patients. Blood culture establishes pathogen presence and identity but requires time. This may limit a more aggressive treatment strategy. The purpose of this study was to characterize MDW clinical behavior in the context of bacteremia upon hospital presentation. Methods This was a prospective, observational cohort study. All patients who presented to the ED, were over 18 years of age, and had a blood culture order along with a CBC with differential were enrolled into the study. MDW values were blinded to those involved in direct patient care. An MDW value ≥20 is the published cut-off for increased severe infection risk. We calculated the diagnostic accuracy of MDW values ≥20 for positive blood cultures using SPSS Version 25. Results From July 2021 to September 2023 a total of 185,405 ED visits were registered. During this time 9,400 ED blood cultures were ordered. A total of 5,316 ED blood culture results were matched with MDW results. The overall blood culture positivity rate was 14.5%. MDW sensitivity and specificity for positive blood culture were 83.9% and 36.2%, respectively. Positive and negative predictive values were 18.2% and 93.0%, respectively. Conclusion This interim analysis suggests that MDW may be a useful adjunct for early detection of bacteremia in ED patients. The observed sensitivity is consistent with the known relationship between positive blood culture and sepsis. Since MDW results can be available well before blood culture results, this biomarker could help early risk stratification among suspected infection patients. MDW values below 20 have a high predicative value for negative blood cultures. Further analysis incorporating additional clinical information will provide guidance for interpreting MDW values in combination blood culture results.

Public Health Sciences

Pichardo R, **Jacob B**, **Jamil M**, **Jamil D**, **Raslan S**, **Rose CM**, **Boakye EA**, **Poisson L**, **Tam S**, and **Philip PA**. Patient-reported and clinical outcomes among patients with pancreatic cancer. *J Clin Oncol* 2024; 42(16). Full Text

R. Pichardo

Background: Pancreatic cancer is associated with poor survival, high symptom burden, and psychological distress. Conventional assessments such as performance status (PS) have relied on provider-generated data to evaluate the selection of treatment and prognosis. Patientreported outcome measures (PROMs) represent a patient-centric representation of the patient experience and are increasingly applied as tools to help improve outcomes and quality of life. However, little is known about the correlation of PROMs with ECOG PS and clinical outcomes in pancreatic cancer. Methods: We performed a retrospective analysis of patients with pancreatic cancer seen at the Henry Ford Health System between 09/2020 and7/2023, using ICD codes. The NIH's validated and standardized Patient-Reported Outcomes Measurement Information System was used to capture 4 core domains: fatigue, pain interference, physical function, and depression. Patient-level variables and disease-specific variables were obtained by chart review from EHR. Kruskal-Wallis tests for continuous variables and or Fisher's exact tests for categorial variables were used to compare the different ECOG scores and PROM scores and patient-level and disease-specific variables. Results: 176 patients were analyzed, with a median age of 65, 58% were male. Most patients had Stage 1 32.9% followed by Stage 4 25.9%, stage 3 22.9%, 1 32.9%. The majority had an ECOG score of 1, followed by, 0, 2, and only 10 had an ECOG PS of 3. There was no statistically significant difference in PS scores according to smoking status, race, or AJCC Stage but differed by age (P = 0.0007). PS score was not significantly associated with PROMscores on depression, fatigue, or pain interference. However, increasing PS scores were associated with a significant increase in low physical function PROM scores (P , 0.0001). Conclusions: Clinician-assessed PS is a single assessment of the patient's tolerance to therapies subject to physician bias; our study provides encouraging data on the association between PS and patients' reported physical function. The other PROM domains did not provide additional meaningful information on the patient's function although are part of clinical decision-making.

Public Health Sciences

Purtell JPP, **Ralston A**, **Rose CM**, **McElyea K**, **Ibrahim F**, **Thompson A**, **Ghosh S**, and **Hwang C**. Race and decisional conflict about genetic testing in patients with advanced prostate cancer. *J Clin Oncol* 2024; 42(16). Full Text.

J.P.P. Purtell

Background: Guideline recommended genetic testing in advanced prostate cancer (PC) is underutilized and not always accepted by patients (pts). We assessed attitudes and decisional conflict (DC) surrounding genetic testing associated with subsequent test completion, and differences between white and nonwhite pts. Methods: Eligibility for this prospective single institution study included pts with N1 or M1 PC who had not yet completed genetic testing. Upon informed consent, pts were given a 24-question survey using a Likert scale of 0 (strongly agree) to 4 (strongly disagree) to assess attitudes toward genetic testing including a validated assessment of DC. DC and DC subscores (range 0-100, with 100 being highest DC) were calculated from subsets of survey responses. Self-identified race was obtained from the EMR. Two-group comparisons between white and nonwhite pts, and between those who completed genetic testing and who did not, were conducted with SAS v9.4 software using Fisher's exact test for categorical variables and Wilcoxon rank sum test for Likert scale survey questions and DC score variables. Results: Of 42 enrolled pts (21 white, 17 black, 1 Asian, 3 declined), 22 (52.4%) completed genetic testing. Compared to white pts, nonwhite pts expressed more concern about test result privacy (mean = 1.72 v 2.95, p = 0.002), test results being used for non-healthcare purposes (1.78 v 3.00, p = 0.003), and trying unproven treatments (1.72 v 2.67, p = 0.01). Nonwhite pts felt more external pressure in decision-making compared to white pts (0.67 v 0.29, p = 0.04). No significant differences were appreciated in completion of testing, DC, or any subscore between racial groups. Compared to pts who did not complete testing, those who completed testing were more likely to report they knew which options were available (0.73. v 1.25, p = 0.05), knew the benefits of each option (0.77 v 1.30, p = 0.04), knew the risk and side effects of each option (0.95 v 1.50, p = 0.05), were clear about which benefits matter most to themselves (0.73 v 1.37, p = 0.02), and were clear about the best choice for themselves (0.73 v 1.35, p = 0.02). DC (28.59 v 18.11, p = 0.03) was higher in pts who did not complete testing, along with uncertainty (31.25 v 19.32, p = 0.02) and informed (31.25 v 20.45, p = 0.03) subscores. No differences were seen in values clarity, support, or effective decision subscores. Conclusions: In our study, nonwhite pts expressed greater concern about privacy, data misuse, and trying unproven treatments. Those who did not complete

testing had more DC with greater uncertainty about knowledge and decision making. These findings will help direct targeted interventions to increase knowledge, trust, and decisional certainty about genetic testing in pts with advanced PC. Ongoing studies will assess the impact of these interventions on rates of testing completion at our institution.

Public Health Sciences
Semprini J, **Boakye EA**, Barnes JM, Goldston DB, Graboyes EM, and Osazuwa-Peters N. Sociodemographic differences in suicide/intentional self-harm among cancer survivors versus the general United States population. *J Clin Oncol* 2024; 42(16). Full Text

J. Semprini

Background: Suicide is a national public health crisis, and one of the leading causes of death in the United States. Worse yet, the suicide mortality rate is at least double among cancer survivors compared to the general population. Suicide rates vary across the population, but it is unclear how sociodemographic factors explain differences in suicide rates among cancer survivors versus the general United States population. Methods: We analyzed two sets of populationbased data. First, we retrieved suicide/self-harm mortality rates for the general population from the National Vital Statistics System. Next, we accessed cancer case data from the Surveillance, Epidemiology, End Results (SEER) program to estimate number of deaths due to suicide/self-harm among cancer patients, per 100,000 persons, with a 95% confidence interval. All analyses were restricted to contiguous states with full state representation in SEER (CA, CT, GA, ID, IA, KY, LA, NJ,NM, NY, TX, UT).Wethen compared subgroup differences by sex, race/ethnicity, age, and state. Results: In 2020, there were 15,813 deaths in the general population (12.1 suicide/100,000 persons; 95% CI: 11.9, 12.3), and 1,127 among cancer survivors (22.1 suicide/100,000 persons; 95% CI: 22.0, 22.1) due to suicide/intentional self-harm. Among racial/ethnic groups, the largest difference was found in the non-Hispanic White cancer survivors, with 10.4 more suicide/100,000 persons vs. White individuals in the general population. In contrast, two racial minority groups had higher suicide mortality rate in the general population vs. cancer survivors: Non-Hispanic Black individuals (general population = 7.4 suicide/100,000 persons vs cancer survivors = 6.9 suicide/100,000 persons), and Native American Indian (general population = 16.6 suicide/100,000 persons vs. cancer survivors = 11.3 suicide/100,000 persons). Among females, suicide mortality rate was slightly higher by 1.3 suicide/100,000 persons in cancer survivors vs. general population, and much higher among male cancer survivors vs. general population (19.9 suicide/100,000 persons more). For age groups, the lowest difference in suicide mortality between cancer survivors vs. general population was in the 65-84 age group (5.1 more suicide/100,000 persons). Across all other age groups, suicide rates were 11.9 to 14.4 higher in cancer survivors vs. the general population. Across the 12 states in our analysis, the smallest difference was in Iowa (1.9 more suicide/ 100,000 persons), and the largest difference was in Idaho (27.0 more suicide/100,000 persons). Conclusions: In most subgroups, people diagnosed with cancer appear to be at greater risk of death from suicide/intentional self-harm than the general population. As the number of people living with cancer continues to grow, policies increasing the quality of life for cancer patients are warranted.

Public Health Sciences
Shahid MA, **Kulkarni RB**, **Albusoul L**, **Jacob B**, **Rose CM**, **Springer K**, and **Dabak VS**. Evaluation and treatment response in patients with hormone receptor-positive, HER2 low metastatic breast cancer: A single center retrospective analysis. *J Clin Oncol* 2024; 42(16). Full Text

M.A. Shahid, Henry Ford Hospital, Detroit, MI, United States

Background: Patients with Hormone Receptor (HR)+ metastatic breast cancer have seen several new options that improve overall survival. Recently, there are new treatment options for patients with HER2 low expression (defined as HER2 1+ on IHC or 2+ on IHC with a negative FISH). Currently, patients who have HR+ metastatic breast cancer are treated with a combination of an aromatase inhibitor and a Cyclin Dependent Kinase (CDK) 4/6 Inhibitor as first line. Information regarding response to therapy in this group and a correlation with HER2 expression is limited. Methods: This is a retrospective study that aimed to evaluate patients with metastatic, HR+, HER2 low or HER2 negative breast cancer between January 1,

2015 and December 31, 2022. Patients were stratified based on their HER2 status, race, presence of de-novo metastatic disease versus progression, treatment with a CDK 4/6 Inhibitor, and time to progression (defined as the date of biopsy-proved diagnosis to the date of radiographic progression). Comparative data analyses were performed using Fisher Exact and Kruskal-Wallis testing. Kaplan Meier estimates with a log rank p-value were used for survival curves, and a Pvalue of < 0.05 was considered statistically significant. Results: 143 patients were included in our study. Patients were divided based on their HER2 status; 33.5% had HER2 2+ disease, 55.9% had HER2 1+, and 8.4% had HER2 0. Of the patients evaluated, 66% (94/143) were Caucasian, 25% (36/143) were African American (AA), and 9% (13/143) were of other race. There was a significant difference amongst patients treated with CDK 4/6 inhibitors when stratified by race; AA patients had a higher proportion of not using a CDK4 inhibitor (43.3% vs 20.3%; p-value 0.0109). There was a significant difference between the survival curves of HER2 0, 1+, and 2+ (log rank p-value = 0.043). HER2 0 patients progressed quicker than HER2 1+ and 2+ patients. When comparing HER2 negative and low disease, a significant difference was found between the survival curves (log rank p-value = 0.0190). In patients with HER2 low (1+ and 2+ with negative FISH) and HER2 negative disease, there was no difference noted among patients who had de-novo or progression to metastatic disease, high MiB1 status (defined as >20%), whether treatment with CDK 4/6 inhibitor was used, and tumor histology. Conclusions: In our study, patients who had any HER2 expression had a longer time to progression compared to patients with no expression. Patients who had a higher expression (2+ vs 1+) displayed a longer time to progression. This may suggest that as the HER2 expression increases, they may derive a longer benefit with first line therapy. Interestingly, African American patients had a higher proportion of not using a CDK4/6 inhibitor. Larger studies are needed to evaluate these differences and determine whether any expression can be used as a prognostic marker.

Public Health Sciences

Tam S, **Boakye EA**, **Springer K**, **Poisson L**, **Al-Antary N**, **Elsiss F**, **Nair M**, **Zatirka T**, **Ryan M**, **Chang SS**, and **Movsas B**. Age-normed patient-reported outcome measures among cancer survivors. *J Clin Oncol* 2024; 42(16). Full Text

S. Tam

Background: Patient-reported outcome measures (PROMs) are instruments used to collect health-related outcomes that are derived completely from the patient without interpretation from healthcare providers. Monitoring and subsequent intervention based on PROMs collection has demonstrated efficacy in clinical trial settings. This has resulted in implementation of PROMs in routine clinical cancer practices throughout the nation. PROMs have been normed to the general population, but establishing the norms among cancer patients is essential to understanding how PROMs can be evaluated on an individual basis in routine clinical cancer care. This study aims to characterize age-normed PROMs scores among survivors of cancer using the National Institute of Health's Patient-Reported Outcome Measures Information System (PROMIS) depression, fatigue, pain interference, and physical function domains. Methods: Routine collection of PROMs using 4 domains (depression, fatigue, pain interference, and physical function) of PROMIS were offered to all patients with a diagnosis of cancer of any disease site at visits with an oncologic provider using computer adaptive testing. All patients ≥18 years old with a completed PROM at least 2 years since their diagnosis of cancer were eligible for inclusion in the analysis. Only completed PROMs were included in the final analysis. Generalized estimating equation models were used to assess the relationship between age and the estimated mean T-score for each PROMs domain, considering repeat measures within a single patient. Results: A total of 3,636 patients were included in this retrospective cohort study with a total of 26,173 completed PROMs among all 4 domains. Mean age at diagnosis was 61.2 years (SD=12.44), 64% (n=2324) were female, 68% (n=2,461) identified as White, and 25% (n=893) identified as Black. For fatigue, mean T-score ranged from 48.4 points (SD=9.6) among 18-29 years olds to 56.5 points (SD=10.1) among 90-99 years olds, with no significant change with age (p=0.27). For depression, mean T-score ranged from 48.9 points (SD=9.0) among 60-69 year olds to 51.1 points (SD=8.8) among 80-89 year olds with a 0.3 point/decade decrease in T-score (p=0.01). Pain interference T-scores ranged from 48.6 points (SD=10.5) among 18-29 year olds to 55.0 points (SD=9.4) among 80-89 year olds with a 0.4 point/decade average increase (p,0.001). The largest differences were observed in physical function, where scores ranged from 53.5 points (SD=11.0) among 18-29 year olds to 34.3 points (SD=9.2) among 90-99 year olds. There was a 2.1 point/decade decrease in T-score

(p,0.001). Conclusions: Among survivors of cancer, mean PROMIS scores differed by age in the depression, pain interference, and physical function domains but not fatigue. These age-normed PROMIS T-scores, which are required to understand individualized assessments of PROMs, are essential as PROMs are integrated into routine cancer care.

Public Health Sciences
Trendowski MR, Watza D, Lusk C, Lonardo F, Ratliff V, Wenzlaff A, Mamdani H, **Neslund-Dudas C**, Boerner J, Schwartz AG, and Gibson HM. Evaluation of the tumor microenvironment in African American and non-Hispanic White patients with non-small cell lung cancer associated with PD-L1 expression or the presence of tertiary lymphoid structures. *J Clin Oncol* 2024; 42(16). Full Text

M.R. Trendowski

Background: African Americans have higher incidence and mortality from lung cancer than non-Hispanic Whites, but investigations into differences in the tumor microenvironment and treatment response have been minimal. Due to the increasing utility of immunotherapy in the treatment of non-small cell lung cancer (NSCLC), we compared the immune cell composition and transcriptomic signature in the tumor microenvironment among African American and non-Hispanic White patients based on PD-L1 or tertiary lymphocyte structure (TLS) status to determine if there were differences of translational relevance. Methods: Using a cohort of 280 NSCLC patients from the INHALE study (non-Hispanic White: n = 155; African American: n = 125) with whole transcriptome microarray data, we determined the PD-L1 tumor proportion score (< 1% vs. ≥ 1%) and TLS status (presence/absence) within tumor tissue sections by immunohistochemistry. TLS were defined as dense aggregates of CD20 stained cells with a minimum diameter of 150 μm. Immune cell distribution within the tumor microenvironment was evaluated relative to differential gene expression. Results: Tumors from African Americans had a higher proportion of plasma cell signatures within the tumor microenvironment than tumors from non-Hispanic Whites. In addition, gene expression patterns in African American PD-L1 positive samples suggest these tumors contained significantly greater numbers of γδ Tcells and resting dendritic cells, along with fewer CD8+ T-cells compared to PD-L1 negative samples after adjusting for stage and histology. We also identified 22 genes that were differentially expressed between PD-L1 positive and negative tumors, along with 37 genes that were differentially expressed between TLS positive and negative tumors. Investigation of differential expression of B-cell/plasma cell related genes between the two patient populations revealed that four immunoglobulin genes in African Americans (IGHA1, IGHD, IGKV2-29, and IGLL5) were associated with decreased mortality risk, while none of these genes were associated with overall survival in the non-Hispanic White population. Conclusions: In the first known race-stratified analysis of tumor microenvironment in lung cancer based on PD-L1 expression or TLS status, differences within the immune cell composition and transcriptomic signature were identified among non-Hispanic White and African American patients that may have therapeutic implications. Future investigation of these unique aspects within the tumor microenvironment will make advances in immunotherapy more equitable, thereby reducing the health disparities African Americans currently experience.

Public Health Sciences
Yao S, Wilbrink R, Czarnota P, Marlin MC, Khatri B, Stolarczyk AM, Pritchett Frazee C, Li C, Wright K, Tessneer KL, James JA, Scofield RH, **Adrianto I**, Rasmussen A, Guthridge JM, Farris AD, and Lessard CJ. SPATIAL TRANSCRIPTOMICS IMPLICATES GLANDULAR CELL INVOLVEMENT IN PATHOPHYSIOLOGY OF SJÖGREN'S DISEASE. *Ann Rheum Dis* 2024; 83:39. Full Text

S. Yao, Oklahoma Medical Research Foundation, Genes and Human Disease Research Program, Oklahoma City, United States

Background: 10X Visium spatial transcriptomics evaluates mRNA-binding tiles (55μm diameter) of a sectioned tissue, yielding heterogeneous cell sampling. The SpatialPCA algorithm was developed to identify like tissue regions and determine the cellular context of spatial coordinates using homogenous tissue types with distinct boundaries [1] However, while proficient in analyzing homogenous tissue types, SpatialPCA is less effective at differentiating like tiles from heterogenous tissue types. Objectives: To develop a novel analysis pipeline, HistoSpatialPCA, that leverages spatially aware dimensional reduction

to model spatially correlated structures across tiles from heterogeneous tissue types such as a target tissue of Sjögren's Disease (SjD), the minor salivary gland (MSG). Then, to apply Histo- SpatialPCA to MSGs biopsied from SjD patients and healthy controls (HC) to identify disease-specific differential gene expression (DE) and pathway dysregulation in the salivary gland. Methods: MSG sections were arranged on 10X Visium capture slide chambers. Nuclei segmentation and classification was performed, followed by images annotation by tissue type (fibrosis, glandular, inflammatory, fat) (HALO Image Analysis Platform). Imaging data were extracted from tiles and integrated with spatial coordinates using HistoPCA. After quality control to filter low-quality and non-tissue tiles, SpatialPCA was performed [1]. Subsequently, data integration (Harmony) and UMAP with KMeans clustering were performed. SjD case-control differential expression (DE) was analyzed using pseudo-bulk gene expression. Finally, DE transcripts were analyzed by Ingenuity Pathway Analysis. Results: HistoSpatialPCA, followed by UMAP with KMeans clustering, detected 34,948 tiles from n=41 subjects, resulting in 8 distinct clusters in the MSG (Figure 1A,B). Comparison of dysregulated genes and pathways revealed cluster-specific differences between Ro+ and Ro- SjD cases verses HCs (Figure 1C). Ro+ SjD cases exhibited dysregulation across all clusters, whereas Ro- cases showed no significant dysregulated pathways in clusters 0, 2, and 7 and fewer altered pathways in clusters 1 and 6. Rank order of the dysregulated pathways also differed between Ro+ and Ro- SjD cases. Interferon gamma was the top pathway in all SjD cases and Ro+ across all clusters, but was only dysregulated in Ro- cluster 5 and modestly in clusters 1 and 3. Cluster 5 was the most similar between Ro+ and Ro- and showed the highest percentage of inflammation (upregulation of many proinflammatory pathways; downregulation of CTLA4, IL-10, and PD-1 signaling). Conclusion: HistoSpatialPCA successfully grouped like tiles from spatial transcriptomic analysis of heterogeneous MSG. Cluster annotation, followed by DE and pathway analyses revealed dysregulation of tiles across all clusters in Ro+ SjD cases, while Ro- cases exhibited the most pronounced dysregulation in cluster 5, 4, and 3. Notably, cluster 5 demonstrated the highest inflammation, sharing many dysregulated pathways between Ro+ and Ro- SjD cases. This spatially aware technology will provide new insights into the role of different cell/tissue types in SjD pathobiology of the salivary gland. (Figure Presented).

Pulmonary and Critical Care Medicine

Aljbour Almajali D, **Ayyad A**, **Alhaj ali S**, and **Godfrey AM**. A Case of Idiopathic Pneumonia Syndrome in a Patient With Recent Stem Cell Transplant. *Am J Respir Crit Care Med* 2024; 209. Full Text

D. Aljbour Almajali, Internal Medicine, Henry Ford Hospital, Detroit, MI, United States

Introduction:Idiopathic pneumonia syndrome (IPS) represents a rare but severe complication observed in up to 10% of patients undergoing allogeneic stem cell transplantation (SCT), that carries a high mortality rate. IPS usually manifests within four months post-SCT, making it crucial to promptly identify and manage. Case Presentation:A 68 year-old male with a medical history of acute myeloid leukemia on chemotherapy who received allogenic SCT 26 days prior to admission presented to the emergency department with fever and dyspnea. Upon arrival, the patient exhibited hypoxia and increased work of breathing necessitating BiPAP support and subsequent intubation. CT of the chest showed diffuse bilateral consolidative and ground-glass opacities. Broad-spectrum antibiotics were initiated while awaiting results of additional workup. Bronchoscopy and bronchoalevoar lavage (BAL) did not reveal an infectious etiology. Transbronchial biopsies not completed given thrombocytopenia. Respiratory culture, fungal culture, and AFB smear and culture were unrevealing. Respiratory viral PCR, PJP PCR, fungitell, and aspergillus galactomannan were negative. No eosinophils were seen on BAL given the recent Daptomycin thus excluding acute eosinophilic pneumonia. CMV DNA quant was elevated at 1002 so the patient was transitioned to Ganciclovir and given Cytogam. Levels were 123 a week later but felt presentation was less consistent with CMV pneumonitis. Given lack of improvement within 72 hours of presentation and that infectious etiology seemed less likely, the patient was started on methylprednisolone 2 mg/kg divided twice daily for treatment of suspected IPS. Additionally, Etanercept was started twice weekly. After ten days of mechanical ventilation, the patient was extubated to heated high flow nasal cannula. Discussion:The exact etiology of IPS remains elusive, thought to be a complex interplay of factors, including lung lining damage from conditioning regimens and graftversus- host disease. IPS diagnosis is based on the exclusion of infectious and cardiac etiologies in the presence of clinical and radiographic findings suggestive of pneumonia, typically confirmed through lung biopsy.

However, obtaining a lung biopsy may not always be feasible, as in the presented case, due to patient-specific factors. Treatment for IPS involves a combination of approaches, including oxygen therapy, ventilatory support if needed, systemic corticosteroids, and immunosuppressive medications such as Etanercept which block tumor necrosis factor. Early recognition and intervention are crucial for achieving favorable outcomes in these challenging cases. This also highlights the importance of treating possible infectious etiologies while awaiting workup and when unable to rule out certain infections.

Pulmonary and Critical Care Medicine

Aljbour Almajali D, **Cherabuddi MR**, **Ayyad A**, **Fram F**, and **Abu Sayf A**. Brivaracetam-Related Neurological Decline in a Patient With Complex Medical History. *Am J Respir Crit Care Med* 2024; 209. Full Text

D. Aljbour Almajali, Internal Medicine, Henry Ford Hospital, Detroit, MI, United States

Introduction: Brivaracetam is a newer anticonvulsant that is a propyl analogue of levetiracetam. The medication was initially approved in 2016 as an add-on treatment and was later approved in 2018 as monotherapy for treatment of partial-onset seizures. A review article published in January 2023 concluded that Brivaracetam had a limited impact on cognition and behavior. This case report explores the potential role of Brivaracetam in the patient's deteriorating neurological status. Case Description: A 68-year-old female with past medical history of chronic kidney disease, hypertension and foot osteomyelitis presented with generalized weakness. Of note, during a recent hospitalization, the patient was started on Cefepime for treatment of UTI and developed seizures afterwards, she was later discharged on Brivaracetam. Generalized weakness was thought to be related to Malnutrition. Subsequently, the patient underwent placement of gastrostomy tube and was started on tube feeds. Her hospital course was complicated by gradually worsening mental status and later an episode of somnolence. The patient had stable vital signs at that time. Workup revealed ammonia level of 258, ALP 363, ALT 60, AST 187 and lactate of 2.7. Imaging, including a CT head and abdomen, ruled out acute intracranial or intra-abdominal processes. Further investigations, including infectious workup and EEG did not reveal a possible etiology. Ammonia levels improved with holding tube feeds and treatment with lactulose and Rifaximin; however, there was no improvement in mental status. The patient was transferred to the ICU for airway monitoring in the setting of AMS. A multidisciplinary approach suggested a possible role of Brivaracetam. After holding Brivaracetam, the patient had significant improvement in cognition within 48 hours, further supporting the possibility of Brivaracetam-induced cognitive decline. Case Discussion: Previous studies have generally failed to establish a link between Brivaracetam use and serious neurological side effects. One case report was published in 2022 describing Brivaracetam-induced hyperammonemia and encephalopathy. In our case ammonia levels were elevated as well suggesting a possible association. Further research is needed to better understand the relationship between Brivaracetam and neurological decline in patients with complex medical backgrounds, shedding light on the importance of careful medication reconciliation and close monitoring in such cases.

Pulmonary and Critical Care Medicine

Bachert HD, **Thavarajah K**, **Abu Sayf A**, **Calo SMS**, and **Abdul Hameed AM**. Interstitial Lung Disease in a Patient With Hydroxyurea-associated Dermatomyositis-like Eruption With Abnormal P53 Expression. *Am J Respir Crit Care Med* 2024; 209. Full Text

H.D. Bachert, Pulmonary and Critical Care Medicine, Henry Ford Hospital, Detroit, MI, United States

Introduction: Although seldom reported, Hydroxyurea has been known to cause pulmonary toxicity and fibrotic Interstitial Lung Disease (ILD). Hydroxyurea is an antineoplastic medication used to treat leukemias, polycythemia vera, psoriasis and sickle cell anemia. It is a cell cycle specific agent that selectively inhibits DNA synthesis. Common side effects include bone marrow suppression and gastrointestinal and cutaneous manifestations. Cutaneous adverse effects of Hydroxyurea include Dermatomyositis-like eruption (DM-LE) and non-melanoma skin cancers (NMSC). We present a case of ILD in a patient with Hydroxyurea-associated DM-LE with abnormal p53 expression. Case Description: A 73-year-old Caucasian male, nonsmoker, with a history of polycythemia vera on hydroxyurea for 22 years, NMSC, and reflux presented for evaluation of dyspnea and cough for 4 months. On physical

examination he had dystrophic nails, Gottron's papules, mechanic's hands, poikiloderma, telangiectasias, hyperkeratotic papules and tenderness in his PIP joints. Autoimmune workup revealed elevated Rheumatoid factor and aldolase levels. Computed tomography chest showed basilar predominant reticulation with traction bronchiectasis in a probable Usual Interstitial Pneumonia pattern. Pulmonary function testing showed a restrictive pattern with diffusion impairment. Skin biopsy showed interface dermatitis with vacuolar alteration and positive p53 staining, consistent with a diagnosis of DM-LE with abnormal p53 expression. Following evaluation in combined Rheumatology-ILD clinic and discussion at ILD multidisciplinary meeting, the differential diagnoses of Idiopathic pulmonary fibrosis (IPF), Hydroxyurea associated ILD, and ILD secondary to amyopathic DM were considered. Hydroxyurea was discontinued and the patient was started on Nintedanib for IPF/Progressive pulmonary fibrosis. He was started on Ruxolitinib, a JAK1 and JAK2 tyrosine kinase inhibitor, for the treatment of polycythemia vera and possible DM and he was referred to oncology for cancer screening for DM. Discussion: In patients on Hydroxyurea, druginduced pulmonary toxicity should be considered in the differential diagnosis of fibrotic ILD. Hydroxyurea can cause DM-LE due to a chronic phototoxic process involving aberrant keratinocyte p53 expression and UV radiation exposure. DM-LE, previously considered a benign entity, may represent a premalignant precursor of NMSC. DM-LE typically resolves after cessation of Hydroxyurea. However, persistence of lesions despite cessation of Hydroxyurea suggests unmasking of true amyopathic DM. JAK/STAT inhibitors such as Ruxolitinib have recently been suggested as a therapeutic option for ILD. This complex case highlights the multidisciplinary approach and diagnostic challenges of ILD with cutaneous manifestations suggestive of DM.

Pulmonary and Critical Care Medicine

Cherabuddi MR, **Goodman BD**, **Ayyad A**, **Almajali DA**, **Nadeem O**, **Bradley P**, **Russell C**, and **Ouellette DR**. Exploring Disparate Access to Care in Sarcoidosis Patients in Detroit, Michigan. *Am J Respir Crit Care Med* 2024; 209. Full Text

M.R. Cherabuddi, Internal Medicine, Henry Ford Hospital, Detroit, MI, United States

Rationale Sarcoidosis is a multisystem granulomatous inflammatory disease with immense ongoing research. Previous studies assessed the role of social predictors on severity at presentation and found Black, older individuals, with lower income, without insurance to have more severe disease. The city of Detroit, Michigan is at greater risk of disparities with 5 times greater Black population and almost thrice in poverty compared to the nation. We aimed to explore these potential disparities to incorporate our findings into future practice at provider, patient and healthcare system level. Methods This is a retrospective chart review study of all patients seen in pulmonary clinics at Henry Ford Health between January 1st, 2020, and December 31st, 2022, with sarcoidosis patients identified as those with ICD diagnosis code D86. Data collected included date of office visit(s), age, race (Black, White, Other), sex, area deprivation index (ADI), insurance type (Medicare, Medicaid, Commercial), MyChart status, chest x-rays, pulmonary function tests (PFTs), missed clinic visits, number of hospitalizations, mortality, positive biopsy on file, communication of results after bronchoscopy and visits around the time of bronchoscopy. Categorical variables were described using frequency. Numerical variables were described using median, mean and standard deviation. Statistical analysis included Chi-square test, Two-sample T-test and Wilcoxon Rank Sum test and a p-value of <0.05 was considered statistically significant. Results Sarcoidosis patients (N=788), when compared to those seen for other pulmonary problems (N=13,036) were typically slightly younger, Black, female, belonging to higher ADI (greater socioeconomic disadvantage) based on national and state ranks, more likely to use commercial insurance and Medicaid compared to Medicare, have active MyChart access, more noshows, more PFTs on file. Among sarcoidosis patients, significant findings included presence of active MyChart among younger patients, lower ADI and with commercial insurance; more X-rays and PFTs were done in Medicare patients; no-show rate was higher in higher ADI; hospitalizations were higher in those with government insurance. Sarcoidosis patients with positive biopsies on file from 2013-2023 were more likely to be male, White or other races, younger and belonged to lower national ADI ranks. Conclusions This study identified an intricate pattern of demographic and socioeconomic variables affecting access to care in sarcoidosis patients, raising concerns for healthcare barriers especially based on race and ADI, and higher bronchoscopies in those demographic groups thought less likely to have sarcoidosis. Understanding

these is vital for equitable high-quality care, assisting in timely and efficient management of the patient's disease. (Figure Presented).

Pulmonary and Critical Care Medicine

Cherabuddi MR, **Schloop M**, **Shakaroun D**, and **Abu Sayf A**. Pulmonary Tumor Thrombotic Microangiopathy Leading to the Discovery of Underlying Gastric Adenocarcinoma. *Am J Respir Crit Care Med* 2024; 209. Full Text

M.R. Cherabuddi, Internal Medicine, Henry Ford Hospital, Detroit, MI, United States

Introduction- Pulmonary tumor thrombotic microangiopathy (PTTM), coined in 1989, is a rare fatal complication of gastric carcinoma involving widespread tumor emboli, thrombi, reactive pulmonary vascular changes, pulmonary hypertension and is almost always diagnosed post-mortem. There is limited literature on pathophysiology and effective management. Description- A 45-year-old man with remote smoking and recent vaping developed progressively worsening shortness of breath over 2 months. Initial imaging was concerning for interstitial lung disease, was started on prednisone taper and developed a new oxygen requirement of 2-4 L. He then developed sudden onset bilateral hip pain with mobility impairment causing him to present to the emergency department. Workup was remarkable for new bicytopenia with hemoglobin 7 g/dL, platelet count 34000/μL, D-dimer >20 ug/mL FEU, LDH 1035 IU/L, CT abdomen and pelvis concerning for primary gastric malignancy, numerous predominantly sclerotic lesions throughout the osseous pelvis, proximal femurs, sacrum and lumbar spine, peritoneal involvement, diffuse pulmonary ground-glass opacities with interlobular septal thickening and fissural nodularity with upper lobe predominance and widespread lymphadenopathy suspicious for lymphangitic metastatic spread. He rapidly decompensated requiring ICU admission for heated high-flow nasal cannula. Echocardiogram could not determine pulmonary artery pressure. He developed diplopia and dizziness, MRI brain showed 10x20 mm left middle cranial fossa enhancing mass with edema, was started on highdose steroid taper. A CT-guided cervical lymph node biopsy revealed gastric adenocarcinoma with signet ring morphology, HER2 IHC 2+, FISH negative, PD-L1 CPS < 1, microsatellite stable. He started dose-reduced FOLFOX chemotherapy while in the ICU, eventually discharged and tolerated chemotherapy and radiation to gastric and brain lesions, with disease stability, and eventual resolution of hypoxia. Discussion- This presentation is likely due to aggressive gastric carcinoma with pulmonary lymphangitic spread, initially mistaken for interstitial lung disease. A clinical picture of right heart failure may have been masked by initiating early diuresis. Case series describe patterns of cough, dyspnea, right heart failure, anemia, thrombocytopenia, elevated LDH and D-dimer, CT with diffuse septal thickening, mediastinal and hilar lymphadenopathy and nodules, elevated pulmonary artery pressures and presence of malignancy and immunohistochemical expression of tissue and vascular endothelial growth factors. PTTM can lead to pulmonary stenosis and manifest as right heart failure leading to the diagnosis of underlying gastric carcinoma. Acute hypoxic respiratory failure in an otherwise healthy male with a cancer diagnosis should raise suspicion for PTTM. Further research is warranted to better understand this lethal condition for earlier diagnosis and timely management.

Pulmonary and Critical Care Medicine

Cherabuddi MR, **Srikanth A**, and **Ouellette DR**. Pan-positive PET-CT - Metastasis or Multisystem Sarcoidosis? *Am J Respir Crit Care Med* 2024; 209. Full Text

M.R. Cherabuddi, Internal Medicine, Henry Ford Hospital, Detroit, MI, United States

Introduction Sarcoidosis is a multisystem granulomatous disorder of unknown etiology commonly affecting lungs, lymph nodes, skin and eyes. Less commonly, involvement of bones and spleen is seen. Description A 36-year-old woman with a history of mild childhood exercise-induced asthma developed an upper respiratory infection after exposure to sick contacts, after which she developed shortness of breath with no improvement with albuterol, budesonide-formoterol and a short steroid course. Her symptoms progressed to dyspnea with normal activity, wheezing and dry cough. Despite an unremarkable chest x-ray, CT and PET scans revealed nodular and ground-glass pulmonary parenchymal lesions, bony lesions, splenic involvement, and diffuse adenopathy in the neck, mediastinum and abdomen. Lesions were PET-avid and thought consistent with metastatic neoplasm. The patient had hypercalcemia.

Pulmonary function testing (PFT) revealed airway obstruction with moderate to severe reduction in FEV1 with moderate diffusion impairment. The patient was diagnosed with sarcoidosis after multiple sites were biopsied to include transbronchial lung, cervical lymph node and bone with non-caseating granulomas. She was prescribed daily prednisone, methotrexate, and mometasone-formoterol, which gradually led to improvement in shortness of breath and resolution of serum hypercalcemia. A CT scan one year later showed improvement in thoracic lymphadenopathy and pulmonary nodules and marked improvement in bony lesions. The patient developed tachycardia but did not have evidence of active cardiac involvement. The patient failed initial sarcoidosis therapy when she developed calcium oxalate kidney stones and hypercalciuria despite having a normal serum calcium level. Infliximab was added to her treatment regimen with resolution of hypercalciuria. The patient subsequently had gradual onset of sarcoid arthropathy, worsened with cold exposure and is being considered for hydroxychloroquine. Discussion Bone involvement is rarely seen in sarcoidosis and is usually asymptomatic and discovered incidentally as in our case. Osseous lesions often mimic metastases, difficult to differentiate on imaging. Splenic involvement is rarely seen in sarcoidosis, is usually nodular rather than diffuse as is in this case, and is a risk factor for chronic sarcoidosis with extrapulmonary involvement. Hypercalciuria without hypercalcemia in sarcoidosis has previously been reported and is an indication for aggressive treatment. Prompt biopsy ruled out malignancy in this patient and revealed sarcoidosis. This patient displayed a constellation of unusual findings due to sarcoidosis, including multiple lesions mimicking metastatic neoplasm, diffuse splenic involvement, and hypercalciuria and nephrolithiasis without hypercalcemia. Biopsy is vital for accurate diagnosis and timely management of sarcoidosis.

Pulmonary and Critical Care Medicine

Gandy R, **Andrews T**, **Graham M**, **Jurayj K**, **Tirgari S**, and **Kelly B**. Use of Multiple Treatment Modalities for Management of High-Risk Pulmonary Embolism Complicated by Clot-In-Transit. *Am J Respir Crit Care Med* 2024; 209. Full Text

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Introduction: Treatment of high-risk pulmonary Embolism (PE) is a challenging hemodynamic and logistical process. With contraindications to systemic thrombolytics, standard therapy involves choosing another treatment modality, the comparative outcomes of which are either mixed or not well studied. We present a case of a high-risk PE managed with systemic anticoagulation, catheter directed thrombolytics and mechanical embolectomy. Case Description: A 53-year-old female with uncontrolled diabetes, hypertension, peripheral arterial disease, schizoaffective disorder, and recent right leg osteomyelitis was admitted for myonecrosis of the thigh. During her hospitalization she developed tachycardia, hypoxia, and hypotension requiring vasopressors and admission to the intensive care unit (ICU). Point-of-care ultrasound (POCUS) was performed which incidentally showed inferior vena cava (IVC) and severe right ventricular (RV) dilation, and several mobile hyperechoic masses in the right atrium (RA) (Fig. 1a). Unfractionated heparin was initiated, and the Pulmonary Embolism Response Team (PERT) was activated. Computed Tomography (CT) imaging showed filling defects in the RA consistent with clots-in-transit and a large saddle pulmonary embolus (Fig. 1b) with extension to all segments of the pulmonary arteries (PA) (Fig. 1c: example of embolic burden in the right pulmonary vasculature). Systemic thrombolytics were contraindicated due to high risk of bleeding and compartment syndrome of the infected lower extremity. She underwent emergent embolectomy via AlphaVac system of RA/RV thrombus and central pulmonary arteries with an associated decline in systolic PA pressure, from 53 to 43 mmHg. With concern for distal clot, persistent shock, and consideration of bleeding risk, she received six hours of EkoSonic catheter-directed thrombolysis with rapid improvement in oxygen and vasopressor requirements. The patient was eventually discharged on warfarin pending further thrombotic workup. Follow-up echocardiogram and CT imaging showed normal hemodynamics and without any noted residual embolic disease. Discission: This case highlights a positive outcome of a high-risk PE where the rare use of multiple treatment modalities including systemic anticoagulation, catheter-directed thrombolysis, and mechanical embolectomy was required to resolve persistent obstructive shock. While current literature found a 20% mortality at 3-months in patients with PE and thrombi-intransit, use of multiple therapies allowed for complete resolution of right heart strain and pulmonary emboli at just one month after discharge (Ibrahim WH, et al. DOI:10.1177/10760296221140114). This case also demonstrates the diagnostic utility of POCUS in venous thromboembolism. Lastly, this case further

demonstrates the use of a multi-disciplinary PERT program to assist in timely assessment, coordination, and intervention to reduce mortality.

Pulmonary and Critical Care Medicine
Khan SL, Danoff SK, Kulkarni T, Reichuber J, Shifren A, Shlobin OA, **Thavarajah K**, Warrior K, and Hajari Case A. Practice Patterns for Screening and Treating Interstitial Lung Disease-related Pulmonary Hypertension at Specialty Care Centers in the United States. *Am J Respir Crit Care Med* 2024; 209. Full Text

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Objectives: Interstitial lung disease (ILD) is frequently complicated by pulmonary hypertension (PH) which confers worse symptoms, functional limitation, increased healthcare utilization, and poorer survival (1). Despite this, there is a dearth of data to guide screening and treatment of ILD-related PH (2). Methods: To better understand current practice patterns for screening and treating PH-ILD, we conducted a survey of ILD specialists at 81 institutions in the Pulmonary Fibrosis Foundation Care Center Network (PFF CCN) and PH specialists at 73 Pulmonary Hypertension Association (PHA) Care Centers. Results: ILD and PH specialists reported similar comfort levels managing PH-ILD and had comparable access to internal referral resources. Both groups reported similar wait times for patients after referral, methods of multidisciplinary case review, limited access to integrated clinics, and availability of clinic providers and staff. ILD specialists varied in their approaches to identifying which patients to screen for PH and the frequency of testing. Transthoracic echocardiography was the most frequently used screening test among both ILD and PH specialists. More PH specialists reported right heart catheterization (RHC) as their preferred method for diagnosing PH. PH specialists were more likely to start medications like diuretics or pulmonary vasodilator therapies. Inhaled prostanoids were the most frequently prescribed medications by both PH and ILD specialists. Finally, ILD and PH specialists were equally likely to refer patients for lung transplantation. More ILD specialists reported referring ILD patients for transplant at the time of PH diagnosis, while more PH specialists reported using functional decline as their threshold for referral. Conclusions: There is variability in the diagnostic and therapeutic approaches to PH-ILD both between and among ILD and PH specialists. RHC is not uniformly used to diagnose PH. The PFF has published a position statement with the PHA statement calling for the standardization of PH-ILD screening and the necessity of hemodynamic testing for a proper diagnosis (3). PH-ILD should be managed in an experienced center and ILD patients should be referred for lung transplantation when diagnosed with concomitant PH. References 1. Nathan SD. Progress in the Treatment of Pulmonary Hypertension Associated with Interstitial Lung Disease. Am J Respir Crit Care Med. 2023 May 9. 2. Nikkho SM, Richter MJ, Shen E, Abman SH, Antoniou K, Chung J, et al. Clinical significance of pulmonary hypertension in interstitial lung disease. Pulm Circ. 2022. 3. Pulmonary Fibrosis Foundation, Pulmonary Hypertension Association. Pulmonary Hypertension related to ILD. PFF Position Statements. 2023.

Pulmonary and Critical Care Medicine
Nader G, Abdelsamia M, **Sharma A**, Wang L, Atti L, and Laird-Fick H. Epidemiologic Study of Overall Survivability of Individuals Diagnosed With Lung and Bronchus Cancer in Michigan Between the Years 1996 to 2017. *Am J Respir Crit Care Med* 2024; 209. Full Text

G. Nader, Michigan State University Sparrow Hospital, Lansing, MI, United States

RATIONALE: Lung and bronchus cancer is a leading cause of death in the United States. Between the years 2013-2019, the national relative survival for lung and bronchus cancer was 25.4%. Compared to the national average, Michigan has an increased mortality rate, and low early screening and treatment rates. Additionally,to date, there is no epidemiologic study investigating survival rates based on race in Michigan. This study aimed to explore the epidemiological trends of patients diagnosed with lung and bronchus cancer in Michigan, compare primary location and stage of diagnosis upon detection and asses overall survival (OS). METHODS: Data was acquired from the Michigan Cancer Surveillance Program (MCSP). Study population consisted of individuals between the ages of 18-90 diagnosed with Lung or Bronchus cancer in Michigan during years 1996 to 2017. Patients with incomplete data for race, gender

and survival time were excluded. Log Rank test was used to test OS among three time periods, Univariant and Multivariate Cox Regression Model was employed to determine factors which significantly affected OS. RESULTS: 153,742 individuals met inclusion criteria; 54.22% male and 45.78% female. Mean age at diagnosis was 69 years (SD=10.86). Majority of individuals were White Non-Hispanic and lived in a Metropolitan community. Median OS was 8 months with an Interquartile range (IQR) of 2-21 months. Majority of lung and bronchus cancers were diagnosed in late stages when distant site/nodes were involved (44.44%) and only 19.0 % of tumors were localized. Univariate analyses identified four individual characteristics associated with reduced OS: age at diagnosis, male sex, American Indian race, and living in rural or urban area. Multivariant analyses identified three races associated with improved OS: Asian race, Black non-Hispanic race, Hispanic non-white non-black race. OS was reduced if the primary tumor site was mainstem bronchus (including the bronchus intermedius), lung base, overlapping lesions of lung lobes or otherwise not specified. SEER stage 7 (presence of distant sites/nodes) was associated with reduced OS HR 1.19 (95% CI 1.17-1.21) p<0.001. Log rank test showed no significant difference in OS among the three time-periods (P =0.99).CONCLUSIONS: In addition to TMN stage, several factors are associated with reduced survivability in Michigan residents with lung and bronchus cancer. Consideration of these factors may be helpful as a community outreach tool to help increase early detection, reduce overall mortality and explain the lack of treatment in Michigan residents when compared to the national average.

Pulmonary and Critical Care Medicine

Nader G, **Sharma A**, Alattal S, Ghnaima H, Joshi A, Choi J, Liu J, and O'Brien CM. A Rare Case of Steroid-dependent Rheumatoid Lung Disease Without Joint Manifestations. *Am J Respir Crit Care Med* 2024; 209. Full Text

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Introduction:Rheumatoid arthritis (RA) is a systemic inflammatory disorder with the most common manifestation extra-articular manifestation being lung involvement. RA can affect any lung compartment with varying presentation. RA-Interstitial lung disease (RA-ILD) is associated with significant morbidity and mortality. Lung involvement in RA typically occurs following articular manifestation, although it may occur prior to joint manifestation. Corticosteroids and Disease modifying anti-rheumatic drugs (DMARDS), have been remarked as mainstay of treatment. Case Presentation:60-year-old Female with significant past medical history of COVID-19 pneumonia 1 year prior, presented to the hospital due to progressively worsening exertional dyspnea of 3 years duration. On presentation, patient was afebrile, hypoxic to 88% requiring 2L nasal cannula, and normotensive. Physical exam was remarkable for female in no acute distress, and inspiratory crackles in bilateral lung fields. On further questioning she reported dry cough but denied fevers, chills, body aches, and chest pain. She denied sick contacts, tobacco, or vaping use. She reported significant social history of working on poultry farm but denied other environmental exposures. CTA chest was ordered in emergency department and showed bilateral ground glass opacities without pulmonary embolism. A high-resolution CT chest was subsequently ordered which showed increased interstitial marking in periphery of both lungs suggestive of chronic interstitial lung disease. Patient was started on high dose corticosteroids and admitted to medicine service with pulmonary consultation. Extensive work-up including infectious, hypersensitivity pneumonitis and auto-immune panel were ordered but resulted as negative with exception of isolated elevation in rheumatoid factor, Anti-CCP antibodies and inflammatory markers. Patient was ultimately diagnosed with Rheumatoid Arthritis associated lung disease (RA-ILD) with plan for bronchoscopy and biopsy outpatient pending clinical improvement. She was discharged on high-dose corticosteroid with taper but had repeated exacerbation of underlying pulmonary symptoms with any attempts to taper corticosteroids precluding bronchoscopy. Follow-up imaging showed continuous progression of diffuse interstitial fibrosis with non-specific interstitial pneumonia (NSIP) pattern. Patient was ultimately started on Mycophenolate in addition to corticosteroids due to disease progression on high dose corticosteroid therapy, with improvement in pulmonary symptoms. Discussion: Treatment strategies in RA-ILD have not been well-studied. Initiation or augmentation of treatment depends on initial disease severity and disease progression. Corticosteroids and other immunosuppressive medications remain the mainstay of treatment, although studies are lacking. This case demonstrates that subset of patients with RA-ILD, particularly without join

manifestations may be poorly responsive to corticosteroids and may benefit from early initiation of concomitant DMARD therapy.

Pulmonary and Critical Care Medicine

Ratwani AP, Grosu H, **Husnain SU**, Sanchez T, Yermakhanova G, Pannu JK, **Debiane L**, Depew ZS, Yarmus LB, Maldonado F, Lentz RJ, Rickman OB, Feller-Kopman DJ, Arai M, New H, Chen H, Chen S, Ost DE, Dana F, Rezai-Ghara L, Parker M, Lee P, Khemasuwan D, Shepherd RW, Rahman N, and Shojaee S. Post-thoracentesis Ultrasound Vs. Chest X-ray for the Evaluation of Effusion Evacuation and Lung Re-expansion: A Multicenter Study. *Am J Respir Crit Care Med* 2024; 209. Full Text

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Rationale: The utility of ultrasound examination as a follow-up imaging modality to thoracentesis, compared to traditional chest radiography (CXR), has not been thoroughly studied. Ultrasound is shown to have comparable sensitivity to CXR for the diagnosis of pneumothorax. However, CXR is still routinely obtained, in part to assess the degree of lung-parietal pleura apposition as an indicator of successful pleural space evacuation and lung re-expansion. Our study explores whether post-thoracentesis ultrasound is comparable to CXR in determining successful evacuation of the pleural space. Methods: Patients with free-flowing pleural effusions with minimal to no septations were recruited from six academic centers. Post-thoracentesis ultrasound was performed immediately following thoracentesis, and CXRs were obtained within 4-hours post-procedure. Our primary outcome was the agreement between US and CXR in their ability to assess complete pleural space evacuation. Complete pleural space evacuation was defined as the absence of pleural fluid on three ultrasound views (anterior, mid-axillary, and posterior) and minimal to no costophrenic angle blunting (CPA) on CXR (portable or PA/lateral technique). Residual postprocedure effusions were categorized as 'small' or 'large' based on pre-specified imaging criteria. Interobserver reliability was assessed through independent image reviews by two pulmonologists and two radiologists blinded to all patient/procedure data, with disagreements resolved by a third reviewer. Concordance of ultrasound-guided vs CXR-guided assessment of lung expandability was the secondary endpoint. In scenarios when most outcomes were categorized as 'present' in an imbalanced contingency table, the Kappa statistic was replaced with Gwet's AC1. Results: From February 2021 to May 2022, 147 patients were recruited for the study. Malignancy was the most frequent effusion etiology (n=49), followed by hepatic hydrothorax (n=22) and heart failure (n=11), and the pleural space was considered non-expandable in 50% of cases. A total of 823 pleural ultrasound images were collected for blind review. The Gwet's AC1 assessing complete pleural evacuation agreement between ultrasound and CXR was 0.93 (95% CI: 0.83-1.00). When assessing US vs. CXR agreement in relation to effusion size, a Cohan's Kappa of 0.64 (95% CI: 0.51-0.77) was observed. Ultrasound vs CXR-guided assessment of expandability showed a Cohan's Kappa of 0.89 (95% CI 0.81 to 0.96). Conclusion: Ultrasound use reduces the risk of radiation exposure and is routinely used before thoracentesis. Our findings show that postthoracentesis ultrasound can be considered an equally effective alternative to CXR when assessing clinically meaningful parameters such as pleural space drainage and lung expansion in noncomplicated pleural effusions.

Pulmonary and Critical Care Medicine

Raymond-Forde S, and **Olexsey K**. A Rare but Potentially Fatal Reaction in Plain Sight: Trimethoprim-Sulfamethoxazole Induced Acute Lung Injury. *Am J Respir Crit Care Med* 2024; 209. Full Text

S. Raymond-Forde, Pulmonary and Critical Care, Henry Ford Hospital, Detroit, MI, United States

Introduction: Trimethoprim/Sulfamethoxazole (TMP/SMX) is a commonly prescribed antibiotic for skin and genito-urinary tract infections. Adverse pulmonary reactions are infrequent, mild, and self-limiting with withdrawal of TMP/SMX1. Recently, however, its use has been associated with severe acute respiratory distress syndrome (ARDS) in adolescents and young adults1. It is associated with a distinct pathology termed diffuse alveolar injury with delayed epithelialization2. Case description: Case #1: A 34-year-old man presented to hospital with cough, shortness of breath, fever, and a rash, three weeks after starting TMP/SMX for prostatitis. He was febrile, tachycardic, and hypoxic, with a diffuse maculo-papular rash and

bilateral wheezing. Laboratory findings included leukopenia, mild thrombocytopenia. Chest imaging revealed peripheral lower lobe opacities with subpleural sparing, which progressed to include pneumothoraces, pneumomediastinum and subcutaneous emphysema (Fig 1). Infectious and autoimmune workup was unrevealing. Despite discontinuation of TMP/SMX, empiric antibiotics and steroids, he progressed to fulminant ARDS requiring mechanical ventilation and extracorporeal membranous oxygenation (ECMO). After a prolonged and complicated course, he expired from refractory respiratory failure and septic shock. Case #2: A 26-year-old woman presented to hospital with fever, rash, shortness of breath, and chest pain, one week after starting TMP/SMX for recurrent vaginal cysts. On presentation, she was febrile, tachycardic, and hypoxic with diffuse wheezing on exam and leukopenia on labs. Chest imaging showed bibasilar ground-glass opacities which progressed to include pneumothoraces, pneumomediastinum, and subcutaneous emphysema. Despite discontinuation of TMP/SMX, empiric antibiotics, and steroids she developed fulminant ARDS requiring mechanical ventilation and subsequently ECMO. Ultimately, she underwent bilateral lung transplantation after nearly 80 days on ECMO. Explanted lung pathology showed severe fibrosing cellular and interstitial pneumonia. Discussion: TMP/SMX-associated ARDS is rare, but lifethreatening. Our cases are consistent with the largest case series published where 74% of patients developed pneumomediastinum and or pneumothorax, 84% required ECMO, 32% required lung transplant, and 37% died1. Conclusions: TMP/SMX-associated ARDS is a rare occurrence in previously healthy young adults with distinct pathology and proposed clinical diagnostic criteria2. Given its high mortality and the common use of TMP/SMX, clinicians should be aware of this entity. Early recognition and transfer to an ECMO and/or transplant center may improve outcomes. (Figure Presented).

Pulmonary and Critical Care Medicine

Raymond-Forde S, **Raymond-Forde S**, **Godfrey AM**, and **Alexander KR**. The Gift of a Heart, With Strings Attached: A Case of Strongyloides Stercoralis Hyperinfection Syndrome With Fulminant Respiratory Failure. *Am J Respir Crit Care Med* 2024; 209. Full Text

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Introduction: Strongyloides stercoralis is an intestinal nematode, endemic to tropical and temperate regions, including the Appalachian region of the southern United States. An estimated 600 million is people infected worldwide1. While most infections are asymptomatic, in immunocompromised patients, particularly from steroid use, it has the potential to cause a highly fulminant and potentially deadly hyper-infection syndrome2. Case Description: A 43-year-old woman with a history of orthotopic heart transplant for nonischemic cardiomyopathy, steroid-induced diabetes, and recent hospital admission for Escherichia Coli bacteriemia of unclear source, was readmitted with persistent fatigue, lethargy, generalized weakness, nausea, non-bloody emesis and shortness of breath. Immunosuppressive regime included prednisone, tacrolimus, and mycophenolate mofetil. She was afebrile, tachycardic and hypotensive, tachypneic and hypoxic, requiring 6L of supplemental oxygen. Laboratory findings included hemoglobin of 6.9g/dL, normal white blood cell count and differential, anion gap metabolic acidosis with hyperglycemia, and elevated amylase at 1081 IU/L. SARS CoV2 was not detected. CT scan of the chest and abdomen revealed acute pancreatitis, extensive ground glass, and consolidative opacities in both lungs. Echocardiography showed hyperdynamic ejection fraction. She was treated for diabetic ketoacidosis secondary to acute pancreatitis and sepsis from pulmonary source. Noninvasive infectious evaluation was negative. Respiratory failure worsened, requiring mechanical ventilation and extracorporeal membranous oxygenation. Repeat chest imaging revealed bilateral dense consolidation with air bronchograms, and smooth septal thickening without pleural effusions. Bronchoscopy confirmed diffuse alveolar hemorrhage, with live Strongyloides organisms on cytology (Figure 1). Notably, transplant coordinators were informed of Strongyloides infection in a kidney recipient from the same donor. She received ivermectin and eventually recovered after a prolonged hospital course. Discussion: Strongyloides hyperinfection occurs from acceleration of the organism's auto-infective life cycle from host T-cell mediated immunosuppression. Increased parasite burden and migration between the gastrointestinal and pulmonary system often occur with enteric gram-negative bacteremia and can lead to alveolar hemorrhage and fulminant pneumonitis3. Conclusions: Strongyloides hyperinfection is potentially fatal and underrecognized. It should be considered in patients who are immunosuppressed, with unexplained enteric gram-negative bacteremia and fulminant respiratory failure. Recipients of organ

transplants and organ donors should be routinely screened for Strongyloides infection. (Figure Presented).

Pulmonary and Critical Care Medicine

Zeid H, **Abu Sayf A**, **Thavarajah K**, **Calo S**, and **Abdul Hameed AM**. From Relief to Risk: Menace of Injecting Crushed Antihistamine Pills: A Case Report. *Am J Respir Crit Care Med* 2024; 209. Full Text

H. Zeid, Pulmonary and Critical Care, Henry Ford Hospital, Detroit, MI, United States

Pulmonary foreign body granulomatosis (PFBG) is a rare disorder characterized by the development of granulomatous inflammation secondary to foreign bodies lodged in the pulmonary capillaries. It can be caused by intravenous injection of grounded oral medications, typically methylphenidate, opiates, antihistamines, and meperidine. We present a case of PFBG induced by injecting crushed antihistamine pills. 31-year-old male, daily marijuana smoker, with a history of a small bowel resection followed by a small bowel transplant complicated by transplant failure, ultimately leading to transplant enterectomy requiring long-term total parenteral nutrition via a peripherally inserted central catheter (PICC) was hospitalized for abdominal pain with staph epidermidis bacteremia. He was asymptomatic from a pulmonary standpoint. Computed tomography (CT) abdomen and pelvis showed new bibasilar diffuse micronodular pulmonary opacities. Confirmatory CT chest showed diffuse bilateral tree-in-bud nodular opacities with centrilobular groundglass opacities. Comprehensive autoimmune review of systems and autoimmune workup was negative and there was no clinical suspicion for chronic aspiration. No other occupational or environmental exposures were identified. Non-invasive work-up for fungal infections and bronchoalveolar lavage cultures ruled out fungal, bacterial, atypical bacterial and mycobacterial infections. Transbronchial biopsy showed perivascular, intra-alveolar and interstitial, irregular, and birefringent (under polarized light) foreign particulates associated with granulomatous inflammation. On H&E stains particulates with coral-like morphology and deep basophilic staining were seen and Elastin van Gieson stain showed fragmentation of elastic laminae of vessels. The histopathological diagnosis was consistent with PFBG. Later, upon questioning, the patient admitted to injecting crushed Benadryl pills into his PICC line. The patient was recommended to discontinue this practice and despite abstinence he had progression of his disease. Unfortunately, our patient died shortly after due a non-pulmonary cause. The clinical manifestations of PFBG range from being asymptomatic to fulminant respiratory failure, pulmonary hypertension and progressive pulmonary fibrosis. Our patient had asymptomatic PFBG with no previous history of substance use making it a challenging diagnosis. Centrilobular micronodules are caused by bronchiolar disorders including endobronchial infections and tumors, hypersensitivity pneumonitis, respiratory bronchiolitis, follicular bronchiolitis, chronic aspiration, and pulmonary vascular disease. Definitive diagnosis requires tissue diagnosis with transbronchial biopsy or open lung biopsy and stopping the use of offending agent is the mainstay of treatment. Periodic reassessment for disease progression is recommended in asymptomatic patients due to the risk of progressive pulmonary fibrosis despite cessation of IV drug use. (Figure Presented).

Radiation Oncology

Antwi S, **Kaljee L**, **Dankerlui D**, **Walker EM**, **Larrious-Lartey H**, Brush B, Israel B, Harris D, Chue S, Cawthome N, Mills C, **Aboah VO**, Daniels G, Aduse-Poku L, Coombe CM, Rowe Z, Patman L, Ramocan W, **Perkins DW**, and **Jiagge EM**. Black/African American participation in cancer clinical trials: A qualitative study of community members, patients with cancer, and survivors (Detroit, MI) using CBPR. *J Clin Oncol* 2024; 42(16). Full Text

S. Antwi

Background: Black/African Americans (B/AA) have a disproportionate cancer burden and the highest mortality rates of any racial/ethnic group for most cancers. Racial/ethnic variation in cancer burden reflects health inequities, differences in risk factors, heredity and genomic diversity, and lack of access to and participation in cancer prevention, screening, treatment, and clinical trials. Twelve percent of the United States population are B/AA; however, only about 5% B/AA participate in clinical trials. As a result, data regarding tumors from B/AA are not equally represented in new drug discovery efforts. Methods: Participatory Action for Access to Clinical Trials (PAACT) used a Community Based Participatory

Research (CBPR) approach to support a partnership between Henry Ford Health (HFH) and eight African American, Caribbean, and continental African community-based organizations (CBOs). Focus group data were collected in-person and virtually with representatives from the CBOs and HFH cancer survivors. CBOs participated in Steering Committee meetings throughout the project and two community forums to obtain feedback on recommendations identified through the qualitative data. Results: Factors contributing to participation in cancer clinical trials included systemic issues related to racism, health disparities and trust in government, health systems, and clinical research. Other factors included personal experiences with healthcare systems, healthcare provider-patient communication, socio-economic barriers (e.g., time away from work, family), and perceptions of future benefits from trials for B/AA communities. Recommendations included: 1) on-going health system outreach to B/AA communities regarding cancer prevention and treatment, as well as clinical trials. 2) B/AA community liaisons and cancer survivors as providers of information related to clinical trials; 3) two-way provider-patient communication to address questions and concerns about treatment options and trial information; 4) monetary compensation for indirect trial costs; 5) information on the importance of diversity within trials; and 6) ensuring information is provided to patients' support networks. Conclusions: CBPR is effective in the identification of factors that influence participation in clinical trials. Building trust between patients and the healthcare system begins before patients walk into a clinic and every interaction contributes to institutional worthiness of community and patient trust. It is possible and imperative for health systems to work with B/AA communities and jointly identify and implement recommendations to ensure informed decision-making regarding trial participation. We are currently designing intervention strategies based on the recommendations for implementation at HFH.

Radiation Oncology

Corn BW, Paulus R, Gondi V, Mehta MP, Fogh SE, Wefel JS, Videtic GMM, Sun A, Yoon H, Heinzerling JH, McGarry RC, Kundapur V, Devisetty K, Wu AJC, Kanner AA, Pugh SL, **Movsas B**, and Kachnic LA. Hope drives quality of life in patients with brain metastases, but the hope center remains elusive: An analysis of NRG-CC003. *J Clin Oncol* 2024; 42(16). Full Text

Background: NRG-CC003, a phase II/III study, randomized 393 patients with small cell lung cancer to prophylactic cranial irradiation (PCI) with or without Hippocampal Avoidance (HA). “Hopefulness” is a cognitive construct based on 3 components: goals; pathways to reach those goals; and agency (i.e., motivation to embark on the pathway). Hope can be measured with validated instruments. Since hope is cognitive in nature, the existence of a “hope center” in the brain - most likely in the hippocampus - has been hypothesized. One exploratory objective of NRG-CC003 posited that if hope levels (measured pre- and post-PCI) were better maintained in patients randomized to PCI+HA (in comparison to patients treated by PCI without hippocampal protection), then the hippocampus would, indeed, be implicated as part of the mechanism of hopefulness. Methods: In both arms, PCI consisted of 10 fractions of 2.5 Gy. The Adult Hope Scale (AHS) was administered at time-zero and at 6-months. With regard to patient reported outcome (PRO) measures, the EORTC QLQ-C30 was administered at baseline and then at 3, 6-, 12-, 18- and 24-month intervals. Comparisons of AHS scores by arm were made using Wilcoxon-Mann-Whitney tests, and correlation of AHS with EORTC QLQ-C30 by Pearson correlation coefficients. Results: Approximately 95% of patients completed the AHS at baseline and 67% filled out the questionnaire at 6-months which paralleled the completion rates of the conventional tools for QOL and neurocognition that were employed in the study. When comparing hope levels (change from baseline to 6 months) there was no significant difference ($p > 0.05$) between the two arms of the trial (PCI vs PCI + HA). There was a significant correlation for the components of hopefulness with QOL; specifically, between change in agency score and QLQ-C30 global health status ($p < 0.0001$) as well as between change in pathways score and QLQ-C30 global health status ($p = 0.022$). Conclusions: It is feasible to study hopefulness in the context of prospective trials conducted within the NCTN. The hippocampus could not be implicated as a critical structure in a central pathway that coordinates hopefulness. Whether these data categorically refute the “hope-hippocampal hypothesis” will be discussed vis-à-vis several caveats (e.g., selection of AHS; presence of sufficient cognitive reserve postirradiation; adequacy of the dose-delta between the 2 arms to cause differential levels of damage to the purported hope center). For the first time, a validated tool prospectively established a relationship between hope and quality of life among patients with cancer. Given previous NRG studies correlating QOL with oncologic endpoints (e.g., local control and survival),

modelling will be carried out to determine if hope mediates, results from, or is associated with these endpoints.

Radiation Oncology

Tam S, **Boakye EA**, **Springer K**, **Poisson L**, **Al-Antary N**, **Elsiss F**, **Nair M**, **Zatirka T**, **Ryan M**, **Chang SS**, and **Movsas B**. Age-normed patient-reported outcome measures among cancer survivors. *J Clin Oncol* 2024; 42(16). Full Text

S. Tam

Background: Patient-reported outcome measures (PROMs) are instruments used to collect health-related outcomes that are derived completely from the patient without interpretation from healthcare providers. Monitoring and subsequent intervention based on PROMs collection has demonstrated efficacy in clinical trial settings. This has resulted in implementation of PROMs in routine clinical cancer practices throughout the nation. PROMs have been normed to the general population, but establishing the norms among cancer patients is essential to understanding how PROMs can be evaluated on an individual basis in routine clinical cancer care. This study aims to characterize age-normed PROMs scores among survivors of cancer using the National Institute of Health's Patient-Reported Outcome Measures Information System (PROMIS) depression, fatigue, pain interference, and physical function domains. Methods: Routine collection of PROMs using 4 domains (depression, fatigue, pain interference, and physical function) of PROMIS were offered to all patients with a diagnosis of cancer of any disease site at visits with an oncologic provider using computer adaptive testing. All patients ≥18 years old with a completed PROM at least 2 years since their diagnosis of cancer were eligible for inclusion in the analysis. Only completed PROMs were included in the final analysis. Generalized estimating equation models were used to assess the relationship between age and the estimated mean T-score for each PROMs domain, considering repeat measures within a single patient. Results: A total of 3,636 patients were included in this retrospective cohort study with a total of 26,173 completed PROMs among all 4 domains. Mean age at diagnosis was 61.2 years (SD=12.44), 64% (n=2324) were female, 68% (n=2,461) identified as White, and 25% (n=893) identified as Black. For fatigue, mean T-score ranged from 48.4 points (SD=9.6) among 18-29 years olds to 56.5 points (SD=10.1) among 90-99 years olds, with no significant change with age (p=0.27). For depression, mean T-score ranged from 48.9 points (SD=9.0) among 60-69 year olds to 51.1 points (SD=8.8) among 80-89 year olds with a 0.3 point/decade decrease in T-score (p=0.01). Pain interference T-scores ranged from 48.6 points (SD=10.5) among 18-29 year olds to 55.0 points (SD=9.4) among 80-89 year olds with a 0.4 point/decade average increase (p,0.001). The largest differences were observed in physical function, where scores ranged from 53.5 points (SD=11.0) among 18-29 year olds to 34.3 points (SD=9.2) among 90-99 year olds. There was a 2.1 point/decade decrease in T-score (p,0.001). Conclusions: Among survivors of cancer, mean PROMIS scores differed by age in the depression, pain interference, and physical function domains but not fatigue. These age-normed PROMIS T-scores, which are required to understand individualized assessments of PROMs, are essential as PROMs are integrated into routine cancer care.

Rheumatology

Alwarawrah Z, El Sharu H, Parekh V, Singh S, Hammami S, and **Bishnoi A**. Rheumatoid Arthritis Associated Asthma Exacerbations: A National Inpatient Sample 2016- 2020. *Am J Respir Crit Care Med* 2024; 209. Full Text

Introduction: Population-based studies have determined a higher likelihood of developing Asthma in patients with Rheumatoid Arthritis (RA). Conversely, there is a higher likelihood of developing RA in patients with Asthma. (1,2,3). We aimed to analyze the prevalence of Asthma Exacerbations (AE) in patients admitted to the hospital with RA compared to asthma patients without RA. Methods: The 2016 - 2020 National Inpatient Sample Database (NIS) was analyzed using the International Classification of Diseases - 10 Clinical Modification codes to identify adult hospitalizations with RA. The study's primary outcome was to assess the prevalence of AE in patients with RA compared to patients without RA. Multivariate logistic regression and linear regression analyses were used to adjust for possible confounders. Results: Out of 782,224 hospitalized with AE, 19,346 (0.012%) had RA. Of these, (91.9%) were females. The mean age of patients with RA hospitalized with AE was 58.6 compared to 32.5 in

patients without RA (p Value <0.001). Moreover, patients with AE and RA had longer lengths of stay and total hospital charges compared to patients without RA, 3.9 days vs. 2.7 days (p-Value <0.001) and 37091$ vs. 27610$ (p-Value <0.001), respectively. Logistic regression analysis showed that patients with RA had a higher risk of hospitalization with an Asthma Exacerbation than the general population (adjusted Odds Ratio [aOR] of 1.09, 95% Confidence Interval [CI] 1.04 - 1.14). Notably, patients with RA and Asthma Exacerbations had a higher risk of Obstructive Sleep Apnea (aOR: 2.38, CI: 2.11 - 2.68), Obesity (aOR: 1.58, CI: 1.43 - 1.75), and Upper Respiratory Tract Infections (aOR: 6.77, CI: 5.68 - 8.06). Patients with RA and Asthma Exacerbations had a lower risk of Heart Failure Exacerbation (aOR: 0.32, CI: 0.23 - 0.43), Tobacco Use Disorder (aOR: 0.28, CI: 0.11 - 0.67), and chronic kidney disease (aOR: 0.45, CI: 0.37 - 0.57). There was no statistically significant difference in ischemic stroke (aOR: 0.14, CI: 0.02 - 1.01) or COPD (aOR: 0.90, CI: 0.60 - 1.35). Conclusion: Patients with RA were more likely to have asthma exacerbations than the general population, but the observed effect is likely not clinically significant. Females with RA were more likely to be hospitalized with asthma exacerbations. Patients with RA and Asthma Exacerbations had a higher risk of Obstructive Sleep Apnea, Obesity, and Upper Respiratory Tract Infections. They had lower odds of Heart Failure Exacerbations, Tobacco Use Disorder, Hemodialysis, and chronic kidney disease.

Rheumatology

Alwarawrah Z, El Sharu H, Singh S, Hammami S, Antia A, and **Bishnoi A**. The Association of Ankylosing Spondylitis and Obstructive Sleep Apnea: A Nationwide Sample 2016-2020. *Am J Respir Crit Care Med* 2024; 209. Full Text

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Introduction: Ankylosing spondylitis (AS) is a chronic seronegative inflammatory axial spondylitis that usually affects young males. Long-standing AS may lead to a restrictive pattern of pulmonary disease, likely due to chest wall and spinal immobility. However, the effect of AS on Obstructive Sleep Apnea (OSA) has been rarely described in the literature. We aimed to assess the association between the two diseases and to describe the morbidity outcomes in hospitalized patients with AS. Methods: Using the National Inpatient Sample (NIS) 2016-2020, we analyzed adult hospitalizations with and without AS using International Classification of Diseases - 10 Clinical Modification (ICD-10-CM) codes. The primary outcome was the association between AS and OSA. Secondary outcomes were inpatient mortality, effect on common comorbidities, mean length of stay (LOS), and mean total hospital charge (THC). Multivariate logistic regression and linear regression analyses were used to adjust for potential confounders. Results: Out of 88034 patients hospitalized with AS, 12.58% had OSA; 72% were males with a mean age of 63. While adjusting for obesity, smoking, acute and chronic respiratory conditions, and patients' characteristics, patients with AS had a 1.53 higher adjusted odds ratio (aOR) of having OSA with a 95% confidence interval (CI) of 1.46-1.62 and a p-value <0.001. Moreover, amongst patients with AS, patients with OSA had a higher risk of cardiac conduction abnormalities (aOR: 1.37, CI 1.11-1.70) and acute heart failure exacerbation (aOR: 1.63, CI: 1.36-1.95). Surprisingly, patients with AS and OSA had a lower chance of mortality (aOR: .59, CI: 0.41-0.84) and a lower chance of having acute coronary syndrome (aOR: 0.61, CI: 0.46-0.81). There was no statistically significant difference in LOS and THC. Figure 1 shows the Forrest plot for multivariate analysis of in-hospital morbidities when adjusted for patient demographics, comorbidities, and hospital characteristics. Conclusion: Patients with AS had higher odds of having OSA. Nevertheless, this has not impacted inpatient mortality and morbidity. This association should highlight the importance of screening for OSA in patients with AS. (Figure Presented).

Surgery

George M, **Clark J**, **Hartway K**, **Zwernik S**, **Gartrelle K**, **Salas-Escabillas D**, **Long D**, **Nassif G**, **Pichardo T**, **Wombwell A**, **Wen HJ**, **Benitz S**, **Philip PA**, **Khan G**, **Shah RA**, **Park H**, **Crawford H**, **Kwon DS**, **Theisen B**, and **Steele N**. Longitudinal tissue-based evaluation of TIGIT expression in patients with pancreatic cancer: Effect of expression with advancing clinical stages and across racial groups. *J Clin Oncol* 2024; 42(16). Full Text

M. George

Background: While ground has been gained, pancreatic ductal adenocarcinoma (PDAC) continues to have a low 5-year survival of 13%. This is owed partially to a lack of early detection biomarkers and resistance to standard therapeutic options. TIGIT, an immune checkpoint receptor, is a marker of T-cell exhaustion and plays a key role in the inhibition of anti-tumor immune responses. TIGIT inhibitors are being explored in clinical trials in PDAC. Here we evaluate TIGIT expression in a cohort of PDAC patients and correlate level and intensity of expression with clinical parameters. We also examine changes in expression as the disease progresses from primary to metastatic disease. Methods: We performed RNAscope in situ hybridization (ISH) with a probe specific for human TIGIT mRNA on 82 formalin-fixed paraffin-embedded (FFPE) tissue samples. The cohort of tissue samples included 9 biopsies, 67 primary resections and 6 metastatic lesions. We evaluated the total TIGIT expression (%) as well as the intensity of TIGIT expression (% of cells with 3+ punctae, signifying putative immune cells), and compared these values between samples. Utilizing linear regression for continuous outcomes and logistic regression for binary outcomes, we tested for associations between TIGIT expression and clinical covariates. Results: Staining analysis showed that TIGIT expression did not differ significantly between racial groups. The mean percentage of TIGIT positive cells was 64.0%. High expression of TIGIT was associated with more advanced clinical stage ($p < 0.05$). Evaluation of three longitudinal samples from the same patient revealed decreased TIGIT expression from the initial biopsy (41.6%) to resection (33.4%) and metastasis (2.8%). In these specimens, 3+ TIGIT expression also declined (2.1%, 1.2% and 0.02%, respectively). Conclusions: Anti-TIGIT therapy has potential to reverse immune suppression and, with other therapeutic modalities, may provide survival benefit. Here we demonstrate that increased TIGIT expression correlates with more advanced stage at diagnosis and also present data demonstrating that overall TIGIT expression, as detected by RNAscope ISH, may decrease as PDAC progresses to metastasis. As such, anti-TIGIT therapy may have important implications for evading an important mechanism of cancer progression.

Urology

Pichardo R, **Jacob B**, **Jamil M**, **Jamil D**, **Raslan S**, **Rose CM**, **Boakye EA**, **Poisson L**, **Tam S**, and **Philip PA**. Patient-reported and clinical outcomes among patients with pancreatic cancer. *J Clin Oncol* 2024; 42(16). Full Text

R. Pichardo

Background: Pancreatic cancer is associated with poor survival, high symptom burden, and psychological distress. Conventional assessments such as performance status (PS) have relied on provider-generated data to evaluate the selection of treatment and prognosis. Patientreported outcome measures (PROMs) represent a patient-centric representation of the patient experience and are increasingly applied as tools to help improve outcomes and quality of life. However, little is known about the correlation of PROMs with ECOG PS and clinical outcomes in pancreatic cancer. Methods: We performed a retrospective analysis of patients with pancreatic cancer seen at the Henry Ford Health System between 09/2020 and7/2023, using ICD codes. The NIH's validated and standardized Patient-Reported Outcomes Measurement Information System was used to capture 4 core domains: fatigue, pain interference, physical function, and depression. Patient-level variables and disease-specific variables were obtained by chart review from EHR. Kruskal-Wallis tests for continuous variables and or Fisher's exact tests for categorial variables were used to compare the different ECOG scores and PROM scores and patient-level and disease-specific variables. Results: 176 patients were analyzed, with a median age of 65, 58% were male. Most patients had Stage 1 32.9% followed by Stage 4 25.9%, stage 3 22.9%, 1 32.9%. The majority had an ECOG score of 1, followed by, 0, 2, and only 10 had an ECOG PS of 3. There was no statistically significant difference in PS scores according to smoking status, race, or AJCC Stage but differed by age ($P = 0.0007$). PS score was not significantly associated with PROMscores on depression, fatigue, or pain interference. However, increasing PS scores were associated with a significant increase in low physical function PROM scores (P , 0.0001). Conclusions: Clinician-assessed PS is a single assessment of the patient's tolerance to therapies subject to physician bias; our study provides encouraging data on the association between PS and patients' reported physical function. The other PROM domains did not provide additional meaningful information on the patient's function although are part of clinical decision-making.