Findings: The findings fell into four categories: (1) impressions of participants toward their providers, (2) reflections on the clinical trial recruitment experience, (3) communication relationships with medical and research providers, (4) and cultural aspects of patient-provider communication. One major finding was that an important way women learn about clinical trials is through conversations with their oncologists. However, only 29% of Black women interviewed were informed of their clinical trial by a healthcare provider, suggesting that Black women may not be receiving the information they need to participate in clinical trials.

Conclusion: By understanding existing patient-provider communication typologies, we can improve these methods of communication to increase the interest and participation of Black women in breast cancer clinical trials.

Implications: Clinical trials provide data to healthcare providers about treatment options for breast cancer. If minoritized populations are continually underrepresented in clinical trials, these treatments might not prove to be efficacious in Black women. Researchers must make the necessary investment of resources and effort to better understand the needs of Black women in clinical trial recruitment.

Complications in Burn Patients Following Fluid Over-Resuscitation

Peipert LJ, Kraatz J

Background/Objective: Over-resuscitation of burn patients leads to dangerous edema-related sequelae. The Parkland formula is commonly used to predict fluid requirements in the 24 hours following burn injury, yet studies report widely varying resuscitation rates. This study aims to assess fluid resuscitation practices at Lutheran Hospital and evaluate correlations between resuscitation rates and fluid-overload complications.

Methods: A retrospective chart review assessed fluid resuscitation of 36 adult patients with burns affecting at least 15% total surface body area (TBSA) between May 2020-May 2022 at Lutheran Hospital. Intravenous fluid rates and urine output (UO) were recorded for the first 24 hours of each patient's hospital stay. Complications and mortality were recorded for the entirety of a patient's hospital stay. Patients who received volumes exceeding those recommended by the Parkland formula were placed in the high-volume group whereas patients who received a lesser volume were placed in the low-volume group. Statistical analyses were performed using Microsoft Excel ($p = 0.05$).

Results: The study included 36 patients with an average fluid resuscitation of 4.13 ±2.14 mL/kg/%TBSA in the first 24 hours following hospital admission. Average UO in the high-volume group ($n=14$) was 1.33 ±0.76 mL/kg/hr compared to 0.75 ±0.47 mL/kg/hr in the low-volume group ($n=22$). Fluid complications were more common in the high-volume group (41.7%) compared to the low-volume group (19.0%), but this difference was not statistically significant ($p=0.230$). No difference in mortality was observed ($p=1.000$).

Conclusion: The high-volume group had an average UO exceeding the recommended range (0.5-1.0 mL/kg/hr) and experienced greater rates of fluid-overload complications (pulmonary edema, compartment syndromes, etc.). Due to the small sample size and limited power of this study, the difference in fluid-related complications was not statistically significant.

Clinical Impact and Implications: Physicians should limit fluid volumes exceeding the Parkland formula when resuscitating burn patients to avoid fluid overload sequelae.

Development of PET Tracers of Glutamine Metabolism

Rehman I, Arkin Cs, Knapek E, Snyder S, Schulte M

The labeling of amino acids with positron-emitting radionuclides (such as fluorine-18) has been a widely used approach for the imaging of tumors as it often provides higher diagnostic accuracy than what is observed with [18F]FDG. In particular, PET tracers of glutamine metabolism have garnered significant attention in recent years. O-(2-[18F]fluoroethyl-L-tyrosine (18F-FET) is a promising PET tracer in this regard and is currently under investigation at Indiana University (IU) through an expanded access IND for patients with brain malignancies. Clinical production of 18F-FET at IU previously required the use of HPLC for purification, following the reaction of fluorine-18 with the precursor molecule for FET. While this method has been successful in removing undesirable impurities and byproducts, HPLC significantly increases synthesis time and is a common failure point in the synthesis of FET on our current radiochemistry module. To address this issue, we aimed to deploy a solid-phase-extraction (SPE) method for the purification of FET, thereby eliminating the need for HPLC purification. Several methods for the SPE purification of FET have been previously reported; however, none of these strategies afforded pure [18F]FET on our synthesis module, thus development of new methods was required.

While several tracers capable of measuring different aspects of glutamine metabolism have been evaluated in both preclinical and clinical studies, there are metabolic liabilities that limit their utility and complicate data analysis. [18F]-4F-glutamine is one such tracer that has shown promise but has limitations due to undesirable metabolism in vivo. Herein we report our progress towards an improved synthesis of [18F]FET for ongoing clinical studies as well as our progress towards the development of a novel tracer that would

address metabolic liabilities associated with currently available PET tracers of glutamine metabolism.

Outcomes of Arterial and Caval Resection During Post-Chemotherapy Retroperitoneal Lymph Node Dissection in Metastatic Testicular Cancer

Smith R, Cary C

Background/Objective: In the United States, testicular cancer is the most common solid tumor in men aged 15 to 34. Fortunately, testicular cancer has a cure rate greater than 90% and a 97% five-year survival rate. For the men not cured, a relapse to the retroperitoneum (RP) is most common. Of the patients with RP metastases, a minimal number may require post-chemotherapy retroperitoneal lymph node dissection (PC-RPLND) with resection of the aorta, external iliac, or inferior vena cava (IVC). We hypothesized this procedure would yield reasonable cure rates with acceptable levels of postoperative complications to warrant the indication for surgery.

Methods: Between 2000 and 2020, 2,054 patients with metastatic testicular cancer underwent a PC-RPLND; of those men, 39 also underwent an aortic, external iliac, and/or IVC resection. For the men with a PC-RPLND and vascular resection, demographic, clinical, pathologic, and operative information were reviewed. Next, a Kaplan-Meier curve was created to determine overall survival.

Results: In this retrospective cohort study of 39 patients, PC-RPLND and vascular resection occurred at a median age of 40. The median follow-up of the cohort was 9 months. The median pre-operative mass size was 9 cm and 19 cm in the RP and pelvis, respectively. At PC-RPLND, 54%, 13%, 18%, and 15% of patients demonstrated cancer, teratoma, teratoma and cancer, and necrosis, respectively. Following PC-RPLND and vascular resection, 22 (56%) patients recurred. The median (IQR) time to relapse was 4.2 (2.5 – 8.2) months. Recurrence to the lung was most common, followed by the RP and liver. In total, 17 (44%) patients died of disease with a median overall survival of 14.8 months.

Conclusion: With an overall survival rate of 45% at two years in this heavily pretreated patient population, PC-RPLND with resection of the aorta, external iliac, and/or IVC is reasonable in very select cases.

Targeting Arg-1 and PD-L1 in M2-Tumor Associated Macrophages Impairs Juvenile Myelomonocytic Leukemia (JMML) Cell Proliferation and Migration

Young K, Pasupuleti SK, Stieglitz E, Kapur R

Background and Hypothesis: Tumor-associated macrophages (TAMs) are a key component of tumor-infiltrating immune cells. They are largely characterized into M1 or M2 types. TAMs express an anti-inflammatory M2-like phenotype, promote tumor progression. However, the role of M2-TAMs in driving disease pathogenesis in patients with Juvenile myelomonocytic leukemia (JMML), a rare form of pediatric leukemia driven to a large extent by mutations in the PTPN11 gene, which encodes the phosphatase SHP2 is unclear. We hypothesized that in JMML, inflammatory myeloid cells including neutrophils and M2-TAMs express higher levels of arginase-1 (Arg-1) and PD-L1, which may contribute to the local suppression of immune responses and support the development of JMML.

Methods: To study how alterations in M1/M2 macrophages contribute to JMML development, we utilized a mouse model bearing Shp2E76K mutation (Ptpn11E76K/+) which manifests the cardinal features of human JMML. We hypothesized that Shp2E76K/+ mutations enhance the function of bone marrow derived macrophages (BMDMs), including M2-TAMs and contribute to T-cell suppression.

Results: Our analysis of the bulk RNA-sequence data from 90 JMML patients showed an increase in the expression of Arg-1 and PD-1. Furthermore, single cell RNA-seq analysis of macrophages from 4 JMML patients revealed higher expression of M2-macrophage markers/genes. Our results show that in M2-TAMs, Arg-1 and PD-L1 levels are elevated in BM and spleens of Shp2E76K/+ mice compared to WT. Moreover, M2-TAMs, Arg-1 and PD-L1 levels were also higher in BMDMs derived from Shp2E76K/+ mice compared to WT. The BMDMs from Shp2E76K/+ mice have greater proliferation and migration potential compared to WT BMDMs, which was significantly reduced by inhibiting the function of Arg-1 and PD-L1.

Conclusion: Our results show that M2-TAMs, arginase-1, and PD-L1 create a pro-tumor microenvironment, which likely contributes to the growth of JMML cells. Inhibition of Arg-1 and PD-L1 is a novel therapeutic approach to treat patients with JMML.