# THE **TRIAL** BLAZER

UPMC HILLMAN CANCER CENTER

A quarterly newsletter from CLINICAL RESEARCH SERVICES

## INTRODUCTION

In view of the ongoing federal mandate and decisions made in the interest of patient safety at UPMC Hillman Cancer Center as a result of COVID-19, we are continuing the suspension of in-person monitoring visits. While most treatment trials are open and accruing patients, CRS staff are currently supporting all research activities using a dynamic staffing model to maintain social distancing and reduce exposure. We have instituted a new process for granting remote-EMR access to continue study monitoring and source data verification. CRS management is taking all the necessary steps to minimize the impact of restrictions placed on research due to COVID-19, keep the investigators and physicians abreast of latest developments with timely communication, and make clinical trials available for our patients. Despite all the difficulties that this pandemic presents to our clinical research efforts, patient accruals have continued at a steady pace. This is a credit to all the members of the Clinical Research Service, patients, and physicians.

In other "trial business," we do have an encouraging update on the HCC 19-135 "randomized non-inferiority trial evaluating the length of treatment with PD-1/PD-L1 inhibitors in patients with advanced solid tumors." The details are in the "Spotlight Trials" section. This quarter, the CRS Team Spotlight is focused on the CIC Disease center team under the joint leadership of Drs. Jason Luke and Leisha Emens, and supervision of Krystle Eaton. Please check out the center team members and their profile pictures in this edition to recognize and get to know them a little better. As always, our progress would not be attainable without the efforts of the entire staff and we continue to deeply appreciate all of you for going the extra mile, from those working tirelessly from home to those coming in when necessary. Finally, we are in this together, and we are here to support you in any way we can, so please feel free to reach out if you need to.

**Antoinette (Toni) Wozniak, MD, FACP, FASCO**
Associate Director of Clinical Research

**Bhanu P. Pappu, PhD, MHA**
Vice President of Clinical Research Operations and Strategy

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## SPOTLIGHT TRIAL

### ADaptiVe Biomarker Trial that InformS Evolution of Therapy (ADVISE)

**HCC 19-078: ADaptiVe Biomarker Trial that InformS Evolution of Therapy (ADVISE)**

***Principal Investigator: Dr. Jason Luke, lukejj@upmc.edu***

Biomarker analyses to guide molecularly targeted therapies has been described as feasible through studies such as the lung cancer BATTLE trial and ongoing efforts are attempting to extend this approach independent of tumor type (NCI MATCH, ASCO TAPUR etc.). In immuno-oncology (IO), such an approach has not yet been described and may require a more complex biomarker analysis in selecting therapies. To provide an initial path toward identifying rational IO combination selection, the ADaptiVe Biomarker Trial that InformS Evolution of Therapy (ADVISE) multicenter, pilot, open-label study has the primary goal of understanding the feasibility and early efficacy of pretreatment tumor biopsies obtainment and feasibility in selecting treatment of PD1-based combination. Tumor biopsies are taken and analyzed for immune markers including lymphocyte activation gene 3 (LAG-3), colony-stimulating factor 1 receptor (CSF1R), forkhead box P3 (FoxP3), indoleamine 2,3-dioxygenase (IDO), cluster of differentiation 8 (CD8), and programmed death ligand 1 (PD-L1). If identified, patients are assigned to a corresponding combination of nivolumab + relatlimab (LAG3), cabiralizumab (CSF1R), ipilimumab (FOXP3), or linrodostat (IDO). Should none be identified, the analysis suggests a non-T cell-inflamed tumor and the subject is assigned to nivolumab + multisite stereotactic body radiation therapy (SBRT).

*Continued on next page >*

## POINTS OF INTEREST

## SPOTLIGHT TRIAL *Continued*

The study is recruiting up to 50 participants with six tumor histologies: melanoma (A), non-small cell lung cancer (B), renal cell carcinoma (C), urothelial bladder cancer (D), squamous cell cancer of the head and neck (E), and gastric or gastroesophageal junction cancer (F). Patients can be PD1/L1 treatment naïve or experience though the later are the direct population of highest interest in the study.

The study population of men and women will be expected to be at least 18 years old and meet the following, among other, main eligibility criteria:

- Diagnosed with selected solid tumors
- Eastern Cooperative Oncology Group (ECOG) performance status ≤ 1
- At least two lesions with measurable disease, defined by Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1
- One lesion must be easily biopsied with intent to obtain five core biopsy specimens for analysis
- Received prior therapy, which may include prior IO therapy; however, at least 10 participants must be IO-naïve
- Consent to tumor tissue requirements of the study
- Adequate organ function, as defined by prespecified examinations

Interested physicians can contact Dr. Luke, Krystle Easton, program supervisor (mientkiewiczk@upmc.edu), or Samantha Devine (perkinssj@upmc.edu) for additional eligibility criteria and with other inquiries.

## ☆ CRS TEAM SPOTLIGHT: CANCER IMMUNOTHERAPEUTICS CENTER

***Dr. Jason Luke***

He's the black sheep in his family as the only one who isn't a professional musician. But he was a music major first semester in college and is the trumpet player in the SITC CheckPoints Band.

***Dr. Leisha Emens***

She enjoys hiking and has climbed some big mountains: to the top of Mt. Cotopaxi in Ecuador and Mt. Kilimanjaro in Tanzania.

***Dr. Diwakar Davar***

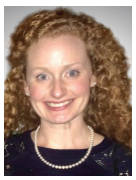
He's interested in long distance cycling.

***Dr. Yana Najjar***

She's a great cook and has been invited to guest chef at different restaurants. She loves to travel, has done so globally, and her favorite trip was to the Galapagos Islands.

***Dr. Dan Zandberg***

He's an amateur drummer who would love to form a band.



***Grace Davis***

She likes triathlons and participates in at least two each year.

***Jode Craig***

He likes history, reads when he can, and enjoys movies and DIY home improvement.

***Krystle Eaton***

She enjoys spending time with her family, loves playing soccer, and wishes she had more time to crochet.

***Sarah Brodeur***

She likes to cook and worked as a cook/baker briefly after college.

***Thomas Last***

His favorite hobby is traveling, and he has family all over the country he enjoys visiting.

## HIGH PRIORITY TRIALS IN THE COMMUNITY

### Update On Optimal Duration Of Immunotherapy For Solid Tumors Trial

**HCC 19-135: A randomized non-inferiority trial evaluating the length of treatment with PD-1/PD-L1 inhibitors in patients with advanced solid tumors**

***Principal Investigator: Dr. Antoinette Wozniak, wozniakaj@upmc.edu***

The study is now open at all community sites, including UPMC Pinnacle and UPMC Mercy. Work is currently underway to roll out the prescreening tool for all sites, so stay tuned for more information as developments unfold. Specific malignancies currently included are NSCLC, bladder, HNSCC, renal, melanoma, MMR/MSI [colon, rectal, cholangio, esophageal, ovarian, uterine], anal, gastric and GE junction, hepatocellular, and triple negative breast cancers. Study PIs are working with the biostatistician to incorporate other disease types. If any disease of interest is not on the list please, let us know and it can be discussed. Physicians and CRCs can self-identify patients in addition to receiving notification from the study team. Finally, the 19-135 RA has been hired and is currently in training. More information to come.

*Any additional questions regarding eligibility should be directed to Dr. Antoinette Wozniak, Dr. Vincent Reyes (reyesv@upmc.edu), or Dan Goldstein (goldsteindj@upmc.edu.)*

## PRIORITY TRIALS IN THE COMMUNITY

### Gastrointestinal Cancers

*Interested physicians can contact the principal investigators or Daniel Goldstein (goldsteindj@upmc.edu) with inquiries.*

**HCC 19-149: A Phase 1 Study to Evaluate the Safety and Tolerability of AB680 Combination Therapy in Participants with Gastrointestinal Malignancies**

***Principal Investigator: Dr. Nathan Bahary, baharyn@upmc.edu***

The CD73-adenosine axis has emerged as one of the most promising pathways in immuno-oncology. This phase 1, open-label, dose-escalation, and dose-expansion study is primarily aimed at evaluating the safety, tolerability, pharmacokinetics, pharmacodynamics, and clinical activity of the CD73 inhibitor AB680 in combination with the programmed cell death-1 inhibitor AB122 and standard chemotherapy (nab-paclitaxel [NP] and gemcitabine [Gem]) in participants with advanced pancreatic cancer.

In the dose-escalation phase, approximately 30 participants will receive increasing AB680 doses of 25, 50, 75, 100, and 125 mg (Cohorts 1-5, respectively) every two weeks in combination with AB122 and NP/Gem with assessments based on a 3+3 design, including a 28-day dose-limiting (DLT) evaluation period. The subsequent dose-expansion phase will evaluate the recommended phase II dose of AB680 identified during dose escalation in combination with AB122 and NP/Gem in 15 to 40 participants with advanced pancreatic cancer.

Potential eligible male and female participants ≥ 18 years of age, are expected to meet the following major, among other, inclusion criteria:

- ≥ One measurable lesion according to RECIST 1.1
- ECOG performance status score of 0 or 1
- Histologically or cytologically confirmed metastatic pancreatic adenocarcinoma
- No prior treatment including chemotherapy, biological therapy, or targeted therapy for metastatic disease
- Prior adjuvant therapy (including chemotherapy and/or radiotherapy) for pancreatic adenocarcinoma is permitted if neoadjuvant or adjuvant therapy was completed at least six months prior to study enrollment; prior adjuvant therapy may include NP and/or Gem
- Patients with initial diagnosis of locally advanced pancreatic cancer with chemotherapy and resection and no evidence of disease are eligible if metastatic disease has relapsed and last chemotherapy dose was received more than six months before study entry.

**HCC 19-163: Randomized Double-Blind Phase III Trial of Vitamin D3 Supplementation in Patients with Previously Untreated Metastatic Colorectal Cancer (Solaris)**

***Principal Investigator: Dr. Anuradha Krishnamurthy, krishnamurthya2@upmc.edu***

The hypothesis that vitamin D status is related to colorectal cancer (CRC) has been supported for decades by preclinical and epidemiologic data as well as observational studies. Based on the positive findings of the SUNSHINE multicenter, randomized, double-blind phase II trial addressing causality in the relationship between vitamin D and CRC, this present larger, confirmatory phase III trial with more robust power, has the primary objective of comparing the progression-free survival (PFS) of patients administered high-dose vitamin D3 in combination with standard chemotherapy. To this end, patients will be randomized to either experimental arm 1, which will receive chemotherapy + bevacizumab + high-dose vitamin D3 or control arm 2, which will be treated with chemotherapy + bevacizumab + standard-dose vitamin D3. Chemotherapy will consist of mFOLFOX6 or FOLFIRI at the treating physician's discretion.

The prospective eligible patient population will be expected to meet the following main, among other, inclusion criteria:

- Histologically confirmed locally advanced/metastatic colorectal
- Adenocarcinoma with no planned metastasectomy
- No deficient mismatch repair (dMMR) or microsatellite instability-high (MSI-H) disease
- Measurable disease per RECIST v1.1
- No prior systemic treatment for metastatic disease

## Melanoma and Cutaneous Tumors

*Interested physicians can contact the respective principal investigators or Amy Rose (kennaj@UPMC.edu) with inquiries.*

**HCC 18-071: A Phase II Study of Anti-PD1 Monoclonal Antibody (Nivolumab, BMS-936558) Administered in Combination with Anti-LAG3 Monoclonal Antibody (Relatlimab, BMS-986016) in Patients with Metastatic Melanoma Naïve to Prior Immunotherapy in the Metastatic Setting**

***Principal Investigator: Dr. John Kirkwood, kirkwoodjm@upmc.edu***

This study has the primary objective of assessing change in immune biomarkers by analyzing serial peripheral blood and tumor biopsy samples from patients administered relatlimab and nivolumab, alone or in combination and estimating the association between changes in immune biomarkers and tumors.

The following are the main, among other, inclusion and exclusion criteria prospective, eligible participants will be expected to meet:

- Men and women ≥ 18 years of age
- Meeting AJCC 8th edition criteria for unresectable stage IIIB, stage IIIC, stage IIID, or stage IV melanoma
- Not received treatment with immunotherapy in the metastatic setting

**HCC 19-047: Randomized Phase II Neoadjuvant Study of PD-1 Inhibitor TSR-042 vs. Combination of Tim-3 Inhibitor TSR-042 and PD-1 Inhibitor in Resectable Stage III or Oligometastatic Stage IV Melanoma**

***Principal Investigator: Dr. Diwakar Davar, davard@upmc.edu***

Tim-3 is a co-inhibitory receptor that is expressed on CD8 T cells, FoxP3+ Treg cells, and innate immune cells such as macrophages and dendritic cells. Work from multiple UPMC Hillman Cancer Center Investigators including Dr. Hassane Zarour and Dr. Robert Ferris has demonstrated the role of Tim-3 blockade in multiple cancers including melanoma, NSCLC, and HNSCC. TSR-022 (cobolimab) is a TIM-3 inhibitor that has demonstrated activity in heavily pre-treated melanoma and lung cancer (Dr. Davar, SITC 2018). TSR-042 (dostarlimab) is a PD-1 inhibitor. HCC 19-047 (Neo-Mel-T) is a randomized phase II neoadjuvant study evaluating the role of dual TIM-3/PD-1 blockade vs. PD-1 blockade in high-risk resectable melanoma. This highly innovative study aims to investigate an innovative combination with proven efficacy in advanced cancer in earlier-line disease while obtaining valuable biospecimens to further build upon the scientific advances of HCC investigators.

Prospective study patients aged ≥ 18 years are expected to meet the following main, among other, eligibility criteria:

- Stage III B/C/D and IV-A melanoma
- Melanoma with clinically detected LN, in-transit melanoma, or both

## Genitourinary/Prostate Cancers

*Physicians should contact the study principal investigator or Clare Grzejka (grzejkac@upmc.edu) with inquiries.*

**HCC 18-094: A Single-arm, Open-label, Multicenter Study of Enfortumab Vedotin (ASG-22CE) for Treatment of Patients with Locally Advanced or Metastatic Urothelial Cancer Who Previously Received Immune Checkpoint Inhibitor (CPI) Therapy**

***Principal Investigator: Dr. Leonard Appleman, applemanlj@upmc.edu***

Checkpoint inhibitors (CPIs) are a new treatment strategy for metastatic urothelial cancer, but few patients exhibit tumor response and long-term survival improves by only a few months. Enfortumab vedotin (ASG-22CE) shows promising antitumor activity in metastatic urothelial cancer patients previously treated with CPIs who had either post-baseline imaging or discontinued treatment before imaging. This phase II study primarily aims to determine the antitumor activity of single-agent enfortumab vedotin, measured by confirmed ORR in patients with locally advanced or metastatic urothelial cancer who have previously received systemic therapy with a CPI and either previously received platinum-containing chemotherapy or are platinum-naïve and cisplatin ineligible. In this study, CPIs are defined as programmed cell death protein 1 (PD-1) or PD-1 ligand 1 (PD-L1) inhibitors including, atezolizumab, pembrolizumab, durvalumab, avelumab, and nivolumab.

Prospective patients, both men and women, will be expected to be at least 18 years old and meet the following main, among other, eligibility criteria:

- Histologically documented urothelial carcinoma (i.e., cancer of the bladder, renal pelvis, ureter, or urethra). Patients with squamous differentiation or mixed cell types are eligible.
- Received prior (Cohort 1) or no prior (Cohort 2, platinum-naive) treatment with platinum-containing or other chemotherapy and are ineligible for treatment with cisplatin at enrollment.
- Have locally advanced or metastatic urothelial cancer previously treated with CPI with measurable disease according to RECIST version 1.1
- Received CPI neoadjuvant/adjuvant therapy and had recurrent or progressive disease (PD) during or within 3 months of therapy completion
- Have PD during or following their most recent therapy
- ECOG performance status score of ≤1 for Cohort 1 or ≤2 for Cohort 2
- Anticipated life expectancy ≥3 months as assessed by the investigator
- Adequate baseline hematologic, hepatic, and renal function
- No ongoing sensory or motor neuropathy (Grade 2 or higher), or active central

## ☆ IMAGING CORE PROCESS

**It is our great pleasure to announce that the Imaging Core lead by Rivka Colen, MD will be available to staff effective immediately.**

All CRS staff must follow the process below for all tumor assessments:

**Purpose:** This core will serve as a standardized and central imaging service for research faculty and staff. Treatment response assessments including tumor measurements per protocol criteria such as RECIST, irRC, RANO, etc., will be provided for all clinical trial oncology patients.

**Process:** Please follow the indicated link for the process document, which outlines the process. The template below must be used to provide the Imaging Core Team the information necessary to complete the tumor assessments.

| | |
|---|---|
| Patient Name | |
| MRN | |
| DOB | |
| HCC Study | |
| Baseline Scan Date | |
| Current Scan Date | |
| Current Scan Time | |
| Facility Completing Scan | |
| Scan Type (i.e., CT, MRI) | |
| Imaging Criteria | |
| Date Measurements Needed By | |
| Time Measurements Needed By | |
| Date of Physician Appointment | |
| Time of Physician Appointment | |
| Biopsy Lesion | |
| Radiation Lesion | |
| Protocol CRA | |
| Protocol PI | |
| Treating Physician | |
| Were Scans Reviewed by Imaging Core? | |

Any questions with the process should be sent to Josh Plassmeyer at plassmeyerjm@upmc.edu.

The process is saved at the following link: O:\CRSFinalDocuments\Clinical\Guidelines & References

## ☆ ACHIEVEMENTS AND ACCOLADES

For Alliance the UPMC Hillman Cancer Center LAPS was identified as one of the top 50 accruing sites this year. Congratulations to the team!

## 2020 OPEN STUDIES AND ACCRUALS

| Disease / Modality Center | Current Int OTA Trials | Current Rx OTA Trials | Interventional Accruals | Therapeutic Accruals |
|---|---|---|---|---|
| Biobehavioral Medicine in Oncology Program | 8 | 0 | 17 | 0 |
| Brain Tumor Center | 10 | 10 | 11 | 11 |
| Breast Center | 14 | 13 | 13 | 12 |
| Early Therapeutics Centers (Phase I and II) | 42 | 42 | 21 | 21 |
| GI/Esophageal Cancer Center | 18 | 18 | 31 | 31 |
| Gynecological Oncology Center | 5 | 5 | 9 | 9 |
| Head and Neck Center | 23 | 22 | 17 | 17 |
| Hematological Malignancies Center | 32 | 32 | 18 | 17 |
| Immune Therapy Center | 19 | 19 | 19 | 19 |
| Lung and Thoracic Malignancies Center | 32 | 29 | 47 | 24 |
| Melanoma Center | 17 | 17 | 22 | 22 |
| Multi-Disease/Modality Center Trials | 3 | 3 | 343 | 75 |
| Pediatric Oncology | 44 | 43 | 14 | 14 |
| Prostate and Urologic Cancers | 17 | 17 | 22 | 22 |
| Sarcoma Center | 10 | 10 | 3 | 3 |
| Supportive Care | 3 | 0 | 96 | 0 |
| Total | 297 | 280 | 703 | 297 |
| *Radiation Oncology Center | 3 | 3 | 3 | 3 |

* Radiation Oncology accruals are distributed to disease center of care.

All Accruals are calculated through 04/15/2020.

Clinical Research Services (CRS) is made up of over 190 staff members who facilitate development, implementation, coordination, internal data monitoring, and completion of approximately 250 oncology-focused trials at Hillman each year. These trials include institutional (investigator-initiated), multi-center cooperative group/National Clinical Trial Network (NCTN), consortium, and industry-sponsored trials. Using a disease-specific centers model for conducting clinical trials, CRS provides study development and implementation assistance, submissions to the FDA, IRB processing, patient recruitment, study coordination, study-specific training, data collection, and specimen collection and processing.

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