THE TRIAL BLAZER

UPMC HILLMAN CANCER CENTER

A QUARTERLY NEWSLETTER FROM
CLINICAL RESEARCH SERVICES

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INTRODUCTION

We have been very busy in CRS. As discussed in previous newsletters, the implementation of the regulatory software (eReg), Clinical Trial Management System (OnCore), and data entry for IITs (REDCap) is moving ahead as planned. A small group of super-users is being trained on the eReg platform. Over the next few months, four disease centers will begin full use of the system: first for new studies and then it will be open to currently accruing trials, prioritized by monitoring activity. We hope to roll out physician and staff training in phases over the next few months, in preparation for the department-wide rollout. All physician-investigators should anticipate training and the complete transition to eSignatures by early Fall.

Data mapping and script writing for data migration is underway to transition from CTMA to OnCore. We plan to start training sessions in February 2022 with an anticipated go-live date in May 2022. By then, we hope to integrate various institutional IT systems with OnCore to improve efficiency and accuracy of clinical trial tracking. We have completed a pilot project to create an IIT study in REDCap and migrate existing data from CTMA's case report forms (CRFs) to the REDCap environment. The CRS team has created several CRFs in REDCap to serve as templates for all UPMC Hillman IITs. In the next phase, we are preparing for data entry into REDCap by our collaborators across the nation, eliminating the need for CRS to enter data for other participating sites. We hope to transition around 80 IITs from CTMA to REDCap in the next year.

In very important developments, it is our pleasure to introduce the latest addition to our senior leadership team, a highly accomplished physician scientist, Taofeek Owonikoko, MD, PhD, as the new chief of the Division of Hematology/Oncology at UPMC Hillman and in the Department of Medicine. Dr. Owonikoko, whose appointment commenced July 1, 2021, will also act as the associate director for translational research and co-leader of the Cancer Therapeutics Program, while holding the Stanley M. Marks – OHA Endowed Chair in Hematology/Oncology Leadership. He also serves as a co-chair of the Clinical Research Oversight Committee (CROC) along with Dr. Wozniak. Dr. Owonikoko's clinical focus is on thoracic malignancies and his research interests are in preclinical biomarker discovery in lung cancer and other solid tumor types, and translation of promising laboratory findings into clinical trials in collaboration with academic and industry partners. Please join us in extending Dr. Owonikoko a warm welcome as we look forward to what we believe will be a rewarding tenure.

We are pleased to announce the appointment of Jan Drappatz, MD, as the new chair of Hillman Data and Safety Monitoring Committee (DMSC). We sincerely thank Nathan Bahary, MD, PhD, for serving as the chair for many years. We are excited to introduce Yana Najjar, MD, as the new director of the Clinical and Translational Research Center (CTRC) and sincerely thank the outgoing director Michael Boyiadzis, MD, who has done an outstanding job.

Continued

Points of Interest

Spotlight Trials

- GBM AGILE - The Clinical Trial of the Future
- PSMA Theranostics in Prostate Cancer

CRS Spotlight Team

- Brain Malignancies Research Team

Priority Trials

- Genitourinary and Prostate Cancers
- Breast Cancers
- Gynecologic Cancers
- Biobehavioral Trials
- Cancer Immunotherapy Center
- Lung Cancers
- Head and Neck Cancers

Current Accrual Statistics for Second Quarter 2021

- Open Studies and Accruals Jan–Jun 2021

ACHIEVEMENTS AND ACCOLADES

- **Dr. Ashok Muthukrishnan invited to write commentary in the Targeted Oncology journal.**
- **Brenda Lee Steele, senior clinical research manager, retires.**

The "Spotlight Trials" of interest in this edition are by Dr. Drappatz, entitled **HCC 19-048: GBM AGILE Global Adaptive Trial Master Protocol: An International, Seamless Phase II/III Response Adaptive Randomization Platform Trial Designed To Evaluate Multiple Regimens In Newly Diagnosed and Recurrent Glioblastoma (GBM)** and by Ashok Muthukrishnan, MD, MS, entitled **Phase II Study of 18F-DCFPyL Positron Emission Tomography (PET) in Men with Intermediate or High Risk Biochemically Recurrent Prostate Cancer**. The Brain Malignancies CRS Team takes center stage as the Spotlight Team.

Finally, on a bittersweet note, we are saying goodbye to Brenda Lee Steele, one of our long serving Senior Clinical Managers. Brenda retired effective July 2, 2021, and as she sets off to chart a new trajectory in life, we will miss her and wish her nothing but the best in her future endeavors. Please take the time to read her farewell tribute by Deidre Cleary, senior director, Clinical Research Services in the **Accomplishments and Accolades** section.

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

Bhanu P. Pappu, PhD, MHA
Vice President for Clinical Operations and Strategy

CRS TEAM SPOTLIGHT: Brain Malignancies Center

Physicians and CRS Members

Dr. Frank Lieberman

Dr. Frank Lieberman is the director of the adult neuro-oncology program at UPMC Hillman Cancer Center. His brain tumor translational investigations focus on the application of molecular genetic techniques and functional imaging techniques to develop strategies for individually optimized molecularly targeted treatment of patients with malignant gliomas. In addition, Dr. Lieberman has many extracurricular life passions, and he is deeply involved in Torah learning, which is a source of purpose, resilience, and joy. He also could not live without classical music and one of his proudest accomplishments is his role in the creation of the Clarion Quartet, which comprised members of the Pittsburgh Symphony. He is blessed to be the husband of Beverly for 44 years; the father of Moti, Ranit, and Eli Lieberman; and has a daughter-in-law, Marissa Lieberman. As of 20 months ago, the new joy in his life is their grandson, Nathan Joshua.

Dr. Robert Friedlander

Dr. Robert Friedlander is chairman of the Department of Neurological Surgery and UPMC distinguished professor of neurological surgery and neurobiology at the University of Pittsburgh School of Medicine. Clinically, he focuses on the operative management of complex cerebrovascular disorders and brain tumors, while his specialized research interests include aneurysms, vascular malformations, brain tumors, carotid disease, cerebrovascular disease, Chiari malformation, spinal cord tumors. Dr. Friedlander has published extensively in several high-impact journals such as Proceedings of the *National Academy of Sciences of the United States of America*, *National Neuroscience*, and *New England Journal of Medicine*.

Dr. Jan Drappatz

Dr. Jan Drappatz is an associate professor at the University of Pittsburgh School of Medicine, and the associate director of the Adult Neuro-oncology program at UPMC. Dr. Drappatz's primary areas of research involve the development of novel agents for the treatment of glioblastoma, CNS lymphoma, and other primary and metastatic brain tumors. He has served as the principal investigator of numerous clinical trials to identify effective therapies for patients with brain tumors and other neurological ailments associated with cancer. Dr. Drappatz has published over 200 peer-reviewed manuscripts, book chapters, and abstracts.

Dr. John Flickinger

Dr. John Flickinger is a professor of radiation oncology and neurological surgery at the University of Pittsburgh School of Medicine. Dr. Flickinger holds an interest in spine tumors, brain tumors, metastatic diseases, effects of radiation on normal tissue, and the mathematical modeling of radiation response. He helped establish the first Gamma Knife radiosurgery center in the United States at UPMC Presbyterian in 1987 and has continued to direct the radiation oncology component of the Gamma Knife center there.

Dr. Zaid Siddiqui

Dr. Zaid Siddiqui is a radiation oncologist specializing in the treatment of CNS tumors, such as brain metastases, gliomas, and meningiomas, with external beam radiotherapy and Gamma Knife® radiosurgery. His research focuses on the use of computational and machine learning methods for optimizing treatment planning efficiency, performing oncology outcomes analysis, and discovering new biology in preclinical models. Dr. Siddiqui has numerous publications in prestigious journals such as *JAMA Oncology*, *Medical Physics*, and *Neuro-Oncology Practice*.

Dr. Ajay Niranjan

Dr. Ajay Niranjan is an associate professor of neurological surgery at the University of Pittsburgh School of Medicine. As a leading expert on stereotactic radiosurgery, Dr. Niranjan has helped develop guidelines for stereotactic radiosurgery for trigeminal neuralgia, pituitary adenomas, arteriovenous malformations, acoustic neuromas, and brain metastases. He also has co-authored more than 120 articles in journals such as *Neurosurgery*, *Journal of Neurosurgery*, and *Journal of Neuro-oncology*; contributed more than 55 book chapters; and edited two books on stereotactic radiosurgery.

Dr. Pascal Zinn

Dr. Pascal Zinn is an assistant professor of neurological surgery at the University of Pittsburgh School of Medicine and associate director of the Adult Neurosurgical Oncology Program at UPMC Hillman Cancer Center. Dr. Zinn is the principal investigator of a molecular biology laboratory studying approaches in hyper-personalized tumor treatments and patient care where he uses humanoid brain organoid cancer models to simulate tumor conditions of patients in the laboratory and studies the origins of tumor formation and strategies for treatment using tumor genetics precision approaches. Dr. Zinn has several publications in notable journals such as *Nature Communication, Molecular Cancer Research, and Neurosurgery*.

Dr. Georgio Zenonos

Dr. Georgio Zenonos is an assistant professor and the associate director of the UPMC Center for Cranial Base Surgery. His research interests include genetics of skull base tumors, surgical anatomy (refinement of skull base approaches, and surgical technique), skull base outcomes research, and high-definition fiber tactography. Dr. Zenonos has published extensively and given numerous presentations nationally and internationally. He has been frequently invited as a scientific reviewer by prominent neurosurgical journals.

Dr. Ray Sekula

Dr. Ray Sekula is professor of neurosurgery at the University of Pittsburgh School of Medicine and director of the Cranial Nerve Disorders Program at UPMC. He specializes in minimally invasive neurosurgery, with particular interest in trigeminal neuralgia, hemifacial spasm, acoustic neuroma, Chiari malformation, tumors of the brainstem and skull base, and degenerative and traumatic spinal disorders. Dr. Sekula has several publications in widely circulated journals such as *Brain, Genomic Medicine,* and *Neurosurgery*.

Dr. Megan Mantica

Dr. Megan Mantica is an assistant professor of neurology and medicine at the University of Pittsburgh School of Medicine in the division of hematology/oncology. She specializes in the treatment of adult high-grade gliomas, central nervous system lymphoma, and neurological complications of cancer treatment. Her translational research interests include women's neuro-oncology, reproductive neuro-oncology and metastatic brain disease, and high-grade gliomas. Dr. Mantica enjoys deep sea fishing in her "spare" time.

Clare Grzejka

Clare Grzejka is a senior clinical research manager who has had an illustrious almost 17-year and counting career with CRS. When she's not at work, Clare enjoys weekend happy hours with her family, feeding the birds and squirrels, organizing closets and cupboards, and working in the yard.

Melinda Vargas-Jaffe

Melinda Vargas-Jaffe is a clinical research supervisor, and she has been with the CRS Brain Center for over nine years. She enjoys travelling and trying new restaurants. She plans to do pet therapy with her Aussie shepherd, Joe, when she retires.

Jackie Hahn-Efrati

Jackie Hahn-Efrati is a senior regulatory specialist who has been with CRS for 13 years. Her biggest passions, outside of work, are all aspects of animal rescue and welfare which she has been involved in for more than 30 years both in Pittsburgh and in Jerusalem. Jackie is pictured here at a recent fundraiser with her current foster dog, Nefertiti.

Allison Hoffman

Allison Hoffman is a clinical research associate and has been with the brain team for about two years. She loves to travel, hike, and attempt recipes from The Great British Bake Off.

Logan Baylor

Logan Baylor has been a float research associate with the Brain Center for about seven months. When she is not in the office, you might find her in the kitchen experimenting with a new dish or baking up some treats to share. In her free time, she also enjoys hiking and going on little adventures with her dog and her fiancé, Shawn.

Samantha Schaeffer

Samantha Schaeffer is a clinical research coordinator and has been with CRS for about five months. She enjoys reading, caring for her houseplant collection, and snuggling with her dog, Kiwi.

SPOTLIGHT TRIALS

GBM AGILE - The Clinical Trial of the Future

HCC 19-048: GBM AGILE: Global Adaptive Trial Master Protocol: An International, Seamless Phase II/III Response Adaptive Randomization Platform Trial Designed to Evaluate Multiple Regimens in Newly Diagnosed and Recurrent Glioblastoma (GBM)

Principal Investigator: Dr. Jan Drappatz, drappatzj@upmc.edu

Glioblastoma (GBM) adaptive, global, innovative learning environment (AGILE) is a biomarker-based, multi-arm, two-stage trial designed to evaluate multiple therapies in newly diagnosed and recurrent GBM. The goals of the trial are to identify effective therapies for GBM and match them with patient subtypes. In the initial screening stage, Bayesian response adaptive randomization is used within subtypes of the disease to assign patients to experimental arms, or a control based on their performance. Those with evidence of efficacy in at least one of several "biomarker signatures" will continue therapies in GBM AGILE uninterrupted. Furthermore, they will transition to a confirmatory stage with fixed randomization in an expansion cohort to control type I error, intended to support marketing approval. GBM AGILE provides an efficient mechanism to screen and develop robust information regarding the efficacy of proposed novel therapeutics and associated biomarkers for GBM and to quickly move therapies and biomarkers into the clinic.

Prospective male and female participants must be ≥ 18 years and meet the following main, among other, inclusion criteria to be eligible to enroll in this study:

Newly Diagnosed GBM Criteria:

- Histologically confirmed Grade IV GBM, inclusive of gliosarcoma (WHO criteria; IDH wild-type by immunohistochemistry or sequencing for IDH) established by surgical resection or biopsy
- MRI scan with required imaging sequences performed within 21 days prior to randomization
- Post-operative MRI within 96 hours of surgery
- Use of dexamethasone ≤ 4 mg/per day within five days prior to randomization
- Karnofsky performance status ≥ 60% performed within a 14-day window prior to randomization
- Availability of GBM tumor tissue

Recurrent GBM Criteria

- Histologically confirmed Grade IV GBM inclusive of gliosarcoma (WHO criteria, IDH wild-type) at first or second recurrence after initial standard, control, or experimental therapy that includes radiotherapy, at a minimum
- Evidence of recurrent disease demonstrated by disease progression using slightly modified RANO criteria with post-chemoradiation time point as baseline
- Two scans to confirm progression
- Baseline MRI performed within 14 days prior to randomization
- Use of dexamethasone ≤ 4 mg/day within five days prior to randomization
- Karnofsky performance status ≥ 70% performed within a 14-day window prior to randomization
- Availability of GBM tumor tissue from initial definitive or recurrent surgery, if performed

PSMA Theranostics in Prostate Cancer

HCC 20-009: Phase II Study of 18F-DCFPyL Positron Emission Tomography (PET) in Men with Intermediate or High Risk Biochemically Recurrent Prostate Cancer

Principal Investigator: Dr. Ashok Muthukrishnan, muthukrishnana@upmc.edu

Prostate-specific membrane antigen (PSMA) is a transmembrane glycoprotein expressed by virtually all prostate cancers, and its expression is further increased in metastatic and hormone-refractory prostate carcinomas, making it a useful target for developing agents for the diagnosis and staging of prostate cancer. 18F-DCFPyL injection is a radiolabeled small molecule that binds to the extracellular domain of PSMA with high affinity. This study is an interventional, single-group assignment, prospective non-randomized, open label Phase II trial designed to evaluate the positive predictive value of 18F-DCFPyL PET imaging in men diagnosed with prostate cancer with increasing PSA levels. Approximately 300 participants are planned for enrollment, and they will receive a single dose of 18F-DCFPyL PET and undergo a PET imaging study. The PET imaging maybe repeated at a later date if the biopsy of the lesion is negative and if the lesion is present on follow-up imaging.

Potential male participants ≥ 18 years of age are expected to meet the following main, among other, eligibility criteria:

- Histologically confirmed diagnosis of prostate cancer
- Biochemical recurrence defined as a PSA ≥ 0.2 ng/mL measured more than 6 weeks after prostatectomy or a PSA increase ≥ 2 ng/mL above nadir following radiation therapy (ASTRO Phoenix consensus definition)
- Age ≥ 18 years of age
- ECOG performance status ≤ 2 (Karnofsky ≥ 60%)

PRIORITY TRIALS

Genitourinary/Prostate Cancers

HCC 20-241: A Phase III, Randomized, Placebo-controlled, Double-blind Study of Niraparib in Combination with Abiraterone Acetate and Prednisone Versus Abiraterone Acetate and Prednisone for the Treatment of Participants with Deleterious Germline or Somatic Homologous Recombination Repair (HRR) Gene-Mutated Metastatic Castration-Sensitive Prostate Cancer (mCSPC) (AMPLITUDE)

Abiraterone acetate (AA) plus prednisone (AAP) is an established standard of care for the treatment of patients with metastatic castration-sensitive prostate cancer (mCSPC). Niraparib is an oral, highly selective PARP inhibitor with potent activity against PARP-1 and PARP-2 DNA-repair polymerases that is currently approved for epithelial ovarian, fallopian tube, or primary peritoneal cancer in multiple lines of therapy, and is under investigation for use in prostate cancer. We hypothesize that adding niraparib to the AAP backbone regimen may improve initial disease control and long-term outcomes compared with AAP alone in a biomarker selected population. In this study to prove this hypothesis, approximately 788 participants receiving background androgen deprivation therapy (ADT; i.e., gonadotropin-releasing hormone analog or surgical castration) will be randomized in a 1:1 ratio to receive either niraparib 200 mg and AA 1000 mg, plus prednisone 5 mg daily (experimental group) or AA 1000 mg plus prednisone 5 mg daily (control group).

Potential male participants ≥ 18 years of age are expected to meet the following main, among other, eligibility criteria:

- Diagnosis of prostate adenocarcinoma
- Metastatic disease documented by ≥1 bone lesion(s) on 99mTc bone scan
- At least one of the specified deleterious germline or somatic HRR gene alterations
- ECOG PS Grade < 2
- Started ADT (either medical or surgical castration) >14 days prior to randomization and willing to continue through the treatment phase
- Docetaxel-treated patients must meet additional requirements
- Demonstrate adequate pre-defined clinical laboratory values at screening
- Willing to providing a DNA sample

For more information, please contact Dr. Leonard Appleman, principal investigator, at applemanlj@upmc.edu, or Clare Grzejka, senior clinical research manager, at grzejkac@upmc.edu.

Breast Cancers

HCC 21-007: CompassHER2 Residual Disease (RD), a Double-blinded, Phase III Randomized Trial of T-DM1 and Placebo Compared with T-DM1 and Tucatinib

Ado trastuzumab emtansine (T-DM1) is an antibody-drug conjugate of the monoclonal antibody trastuzumab, which is a targeted antitumor therapy and the cytotoxic compound, emtansine (DM1), a microtubule inhibitor and maytansine derivative. T-DM1 has FDA approval for use in patients with HER2-positive metastatic breast cancer (MBC). Tucatinib is a potent oral HER2-specific TKI that is currently in clinical development for HER2-positive MBC. In this study, we hypothesize that T-DM1 and tucatinib may be superior in preventing breast cancer from relapsing in patients with HER2 positive breast cancer compared to T-DM1 alone. Eligible patients will be randomized to receive T-DM1 with or without tucatinib for up to 14 cycles in the absence of disease progression or unacceptable toxicity.

This study, which is open at all UPMC Hillman Cancer Center sites has the following, among other, main eligibility criteria that prospective participants are expected to meet:

- HER2-positive status will be based on pretreatment biopsy material and defined as an immunohistochemistry (IHC) score of 3+ and/or positive by in situ hybridization (ISH)
- Patients with clinical stage T1-4, N0-3 disease at presentation and residual invasive disease
- Patients with residual HR-negative, HER2+ disease in the breast and/or lymph nodes per the surgical pathology report are eligible; however, patients with HR+ HER2+ cancers must have node-positive residual disease per the surgical pathology report in order to qualify for the study.

For more information, please contact Dr. Sarah Taylor, principal investigator, at taylorse2@upmc.edu or Josh Plassmeyer, manager, Breast/Gynecological Cancer Center, at plassmeyerjm@upmc.edu.

Biobehavioral Trials

HCC 20-282: Writing Interventions for Aromatase Inhibitor Medication Adherence

We are conducting a self-affirmation intervention with breast cancer patients prescribed aromatase inhibitors to examine whether this intervention (compared to a control intervention) leads to less stress, fewer physical symptoms, and improved medication adherence. Participants will be randomly assigned to either the self-affirmation or control condition, in which they will complete a monthly writing task online. Each month we will assess symptoms of stress, side effects, and other physical and mental symptoms, as well as medication adherence. The intervention will last for six months, but we will continue to assess medication adherence using a Smart Pill Bottle that tracks when participants open it to take their daily pill for one year. Half of the sample in each condition will complete their third intervention activity on CMU's campus in the fMRI scanner so that we can assess neural mechanisms for the outcomes of interest.

Eligible participants will be breast cancer patients who:

- Have been prescribed aromatase inhibitors within the last week or
- Will be prescribed aromatase inhibitors as part of their treatment plan
- Willing to use a special pill bottle during the duration of the study

For more information, please contact Dr. Carissa Low, principal investigator, at lowca@upmc.edu or 412-623-5973, Janine Dutcher at jdutcher@andrew.cmu.edu or cmubreastcancerstudy@gmail.com, or Ella Chobin at chobanem@upmc.edu.

Cancer Immunotherapies

HCC 19-096: Phase II Study of IDH1 Inhibitor Ivosidenib and Nivolumab in IDH1 Mutant Gliomas and Advanced Solid Tumors

Current data suggest that aberrant isocitrate dehydrogenase 1 (IDH) activity may play a role in limiting the efficacy of immunotherapy. This study is aimed at describing the safety, response rate, progression-free and overall survival, and summarizing safety events of ivosidenib, a novel, first-in-class compound targeted selectively at inhibiting the mutated IDH1 enzyme in combination with the immunotherapeutic, nivolumab, in participants with advanced solid tumors (nonresectable or metastatic) or enhancing gliomas. Participants with a histologically consistent diagnosis of an IDH1 gene-mutated tumor that is not eligible for curative therapy will be enrolled to receive orally administered ivosidenib dosed daily on 28-day cycles and nivolumab infused every 28 days. Participants will be assessed at every visit for adverse events starting from the first dose of study treatment. Disease response will be assessed using CT or MRI every eight weeks (±7 days) from the first day of treatment cycle 1 and/or at any time disease progression is suspected. A post-treatment follow-op Visit for safety will occur 28 (±5) days after the last dose of the study drug.

Prospective participants > 18 years of age are expected to meet the following main, among other, eligibility criteria:

- Histopathological diagnosis of an advanced solid tumor with no available curative treatment and previous appropriate standard of care treatment options in the opinion of the treating investigator
- For glioma, must have both contrast-enhancing disease and WHO 2016 grade ≥ 2
- ECOG PS score of 0 or 1
- At least one evaluable and measurable lesion as defined by RECIST v1.1 (solid tumors) or RANO criteria (glioma)
- Recovered from toxicities associated with prior anticancer therapy to baseline or ≤ grade 1 unless stabilized under medical management per investigator
- Adequate bone marrow, hepatic, and renal function as evidenced by specified laboratory analyses

For more information, please contact Dr. Jason Luke, principal investigator, at lukejj@upmc.edu, or Amy Rose, clinical research manager, at kennaj@upmc.edu.

HCC 20-047: CART-TnMUC1-01: A Phase I Open-Label, Multi-Center First in Human Study of TnMUC1-Targeted Genetically Modified Chimeric Antigen Receptor T Cells in Patients with Advanced TnMUC1-Positive Solid Tumors and Multiple Myeloma

Current data suggest that aberrant isocitrate dehydrogenase 1 (IDH) activity may play a role in limiting the efficacy of immunotherapy. This study aims to evaluate the safety, tolerability, feasibility, and preliminary efficacy of administering genetically modified autologous T cells engineered to express a chimeric antigen receptor (CAR) that recognizes the tumor antigen, TnMUC1, and activates T cells. The dose escalation phase of the study is designed to identify the dose and regimen of CART-TnMUC1 cells that can be safely administered intravenously following the lymphodepletion regimen to patients with (1) advanced TnMUC1+ solid tumors (triple negative breast cancer [TNBC]), epithelial ovarian cancer, pancreatic cancer, and non-small cell lung cancer [NSCLC]) and (2) advanced TnMUC1+ multiple myeloma in a parallel two-arm dose escalation study. The Dose Escalation phase will enroll approximately 40 patients. The Expansion phase of the study, designed to assess the preliminary efficacy of CART-TnMUC1 cells administered intravenously to patients with TnMUC1+ refractory solid tumors, will enroll approximately 72 patients (18/tumor indication).

Prospective participants > 18 years of age are expected to meet the following main, among other, eligibility criteria:

- Confirmed diagnosis of metastatic treatment-resistant epithelial ovarian cancer (including cancers of the fallopian tube), pancreatic adenocarcinoma, TNBC or NSCLC, or relapsed/refractory multiple myeloma
- ECOG score of 0 or 1
- Received or be intolerant to prespecified therapies for the included cancer types
- Evaluable disease qualified based on the pre-established criteria for the cancer types
- Have TnMUC1+ disease, determined by centrally tested TnMUC1 expression in a tumor biopsy
- Toxicities from any previous therapy must have recovered to grade 1 or baseline
- Adequate vital organ function as defined by established standard criteria

For more information, please contact Dr. Jason Luke, principal investigator, at lukejj@upmc.edu, or Amy Rose, clinical research manager, at kennaj@upmc.edu.

Lung Cancers

HCC 21-034: Phase II Randomized Study of Maintenance Atezolizumab Versus Atezolizumab in Combination with Talazoparib in Patients with SLFN11 Positive Extensive Stage Small Cell Lung Cancer (ES-SCLC)

Immunotherapy with monoclonal antibodies such as atezolizumab may help the immune system attack cancer cells, interfering with tumor cell grow and metastasis. Poly ADP ribose polymerases (PARPs) are DNA-repair polymerases and mutations in DNA cause tumor cells to grow rapidly and uncontrollably. PARP inhibitors such as talazoparib may interfere in the functions of PARP, and thereby prevent tumor cells from self-repair and inhibit their growth. Administering atezolizumab in combination with talazoparib may contribute to reducing the growth and metastasis of extensive-stage small cell lung cancer (ES-SCLC) compared to atezolizumab alone. In this study, participants with Schlafen family member 11 (SLFN11)-positive ES-SCLC will be randomized to receive atezolizumab alone or plus talazoparib as maintenance therapy, using a dynamic balancing algorithm. Randomization will be stratified on Zubrod performance status (0–1 versus 2) and whether patients received radiation therapy.

Prospective participants must be ≥ 18 years and meet the following main, among other, inclusion criteria to be eligible to enroll in this study:

- Histologically or pathologically confirmed diagnosis of ES-SCLC
- Completed at least one cycle of frontline induction treatment with platinum plus etoposide plus atezolizumab prior to Screening Registration
- Have adequate tumor tissue available from a core biopsy
- Have adequate cardiac function and normal organ and marrow function
- Have Zubrod performance status 0–2

For more information, please contact Dr. Antoinette Wozniak, principal investigator, at wozniakaj@upmc.edu, or Jen Ruth, clinical research manager, at ruthj2@upmc.edu.

Head and Neck Cancers

HCC-19-082: Phase II Study Evaluating HPV-16 Vaccination (ISA101b) and Pembrolizumab plus Cisplatin Chemoradiotherapy for "Intermediate Risk" HPV-16 Associated Head and Neck Squamous Cell Carcinoma

Novel therapeutic approaches are needed to improve disease control in head and neck squamous cell carcinoma (HNSCC) and immunotherapy has been proven promising and clinically effective. Data also support HPV-specific vaccination with anti-PD-1 immunotherapy with pembrolizumab to enhance the efficacy of primed and expanded HPV-16 E6/E7-specific cellular immunity against intermediate risk HPV+ HNSCC. Furthermore, data also support a hypothesis that checkpoint inhibitors administered prior to or concomitant with radiotherapy can induce clinically significant antitumor immune responses induced by "vaccination" to tumor-specific antigens exposed during radiation-induced cell death, which may be particularly relevant to viral-induced tumors such as HPV-positive HNSCC. This present study primarily aims to evaluate treatment intensification using fixed-dose pembrolizumab (concurrent) plus the HPV-specific vaccine ISA101b added to standard, concurrent cisplatin- intensity modulated radiotherapy (IMRT) in patients with previously untreated locally advanced HPV-16+, "intermediate risk" HNSCC. The goal here is to recommend survival estimates in a subsequent definitive randomized trial as determined by the endpoint of two-year progression-free survival (PFS) rate.

This trial is open at UPMC Hillman Cancer Center in Shadyside and the main, among other, eligibility criteria for prospective participants ≥ 18 years old are as follows:

- Histologically confirmed HNSCC with no evidence of distant metastasis and oropharynx primary site with intermediate risk disease as predefined
- No prior systemic (chemotherapy or biologic/molecular targeted therapy) or radiation treatment for head and neck cancer
- Patients with a history of curatively treated non-HNSCC malignancy must be disease-free for at least 2 years
- Consent to research biopsy at baseline and during week 2 of pembrolizumab/ISA101b vaccination, prior to start of cisplatin-IMRT, and another optional biopsy at week 2 after start of IMRT
- ECOG PS 0–1

For more information, please contact Dr. Robert Ferris, principal investigator, at ferrrl@upmc.edu, or Jen Ruth, clinical research manager, at ruthj2@upmc.edu.

ACHIEVEMENTS AND ACCOLADES

Brenda Lee Steele Retires

By Deidre Cleary, RN, BSN, CCRC, Senior Director, Clinical Research Services

Brenda Lee Steele began her career with CRS as a community coordinator at UPMC Hillman Cancer Center, Excela Health's Arnold Palmer Pavilion in Greensburg. She always had a passion for breast cancer and when a vacancy opened in the center, she decided to make the move to the Breast Center at UPMC Magee-Womens Hospital as a clinical research coordinator. Brenda continued to add on responsibilities along with her regular duties and was promoted to supervisor where she helped mentor and train the staff. During her stint as a supervisor, Brenda obtained her Bachelor of Science in nursing and was able to move into the clinical research manager role. Brenda also holds certifications in research, oncology nursing, and breast cancer. During her tenure, she incorporated the Gynecologic Center into CRS and most recently ran the charge to create a CTRC at Magee. We would like to thank Brenda for all her years of service and wish her well in her retirement.

Dr. Ashok Muthukrishnan has been conducting groundbreaking research in the area of theranostics in prostate cancer and was recently invited to present a commentary in the prestigious *Targeted Oncology* journal. We would like to congratulate him on his laudable achievements and below is an excerpt from his article.

PSMA Theranostics Poised to Change Prostate Cancer Landscape

With the recent success of lutetium Lu 177 DOTATATE (Lutathera®) therapy for neuroendocrine tumor, the field of theranostics has come under a vivid spotlight in the last couple of years from oncologists, nuclear radiologists, cancer researchers, and the pharmaceutical industry. Although research focused on prostate-specific membrane antigen (PSMA) has been ongoing for almost two decades, the timing for the emergence of PSMA theranostics could not have been any better. The fact that current conventional imaging is woefully inadequate in detecting low-volume oligometastatic disease burden in prostate cancer makes PSMA targeting valuable from a diagnostic standpoint.

Dr. Muthukrishnan's current research involves examining a PSMA theranostic agent (F-18 PyL) for its diagnostic accuracy in prostate cancer. The study has been enrolling several patients a week due to exceptionally high interest in the medical and radiation oncology community with the UPMC system and elsewhere. The new agent will most likely change the management paradigm in several prostate cancer patients. Future studies will help us understand even more the utility of PSMA imaging and theranostics combined with current standard-of-care drugs such as ZYTIGA® and XTANDI®. The practice of PSMA theranostics is a relatively new concept that, while exciting, portends many organizational and technical challenges for cancer centers across the nation. Despite the challenges, PSMA theranostics will undoubtedly change the prostate cancer landscape in the near future. The preliminary efficacy and safety data on PSMA theranostics hold great promise, and it might be prudent for cancer centers to at least begin discussions on preparing their infrastructure, educating their medical staff, as they get ready to welcome PSMA into their practice.

OPEN STUDIES AND ACCRUALS JAN–JUN 2021

Disease / Modality Center	Open Trials		Accruals	
	Interventional	Therapeutic	Interventional	Therapeutic
Biobehavioral Medicine in Oncology Program	11	0	167	0
Brain Tumor Center	11	11	12	12
Breast Center	27	23	213	36
Early Therapeutics Centers (Phase I and II)	62	62	54	54
GI/Esophageal Cancer Center	17	17	61	61
Gynecological Oncology Center	13	12	9	9
Head and Neck Center	22	19	93	39
Hematological Malignancies Center	35	35	18	18
Immune Therapy Center	52	52	63	63
Lung and Thoracic Malignancies Center	27	25	65	17
Melanoma Center	25	25	67	67
Multi-Disease/Modality Center Trials	2	1	32	32
Pediatric Oncology	55	52	12	12
Prostate and Urologic Cancers	16	15	43	26
Sarcoma Center	11	11	8	8
Supportive Care	1	0	0	0
Radiation Oncology Center	20	19	95	32
Total Accruals	**387**	**360**	**1012**	**486**

**Accruals are calculated from January 1, 2021 through June 30, 2021.

Clinical Research Services (CRS) is made up of over 200 staff members who facilitate development, implementation, coordination, internal data monitoring, and completion of approximately 400 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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