Department of Investigational Cancer Therapeutics

Phase I Clinical Trials

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THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Making Cancer History®

FROM THE CHAIR

Funda Meric-Bernstam, MD, Chair, Department of Investigational Cancer Therapeutics

This has been an outstanding year for the Department of Investigational Cancer Therapeutics (ICT)!

In fiscal year 2015, we saw 1,731 new patients and consults. During this time, we put more patients on clinical trials than any other department at The University of Texas MD Anderson Cancer Center. We are increasingly sought out as a clinical trials unit for first-in-human trials and trials with novel combination therapies. We have more trial options with a variety of novel therapeutic approaches for our patients, allowing us to offer personalized, state-of-the-art research-driven patient care.

This year, precision medicine has remained at the forefront. MD Anderson's genomic testing platforms have expanded, and coupled with that we not only attracted dozens of industry-sponsored genotype-selected trials, but we also designed several interesting investigator-initiated trials. Now we have more than 40 genotype-selected trials and at least one trial available for the majority of known actionable genomic alterations. Several targets (such as BRAF, HER2, and NTRK) are emerging as compelling targets across several different tumor types. Our efforts in building an extensive research portfolio in genomic medicine is coupled with a major emphasis in decision support. With the backing of a recent grant from the Cancer Prevention and Research Institute of Texas (CPRIT), we created a Precision Oncology Decision Support team, an amazing group of scientists who help us provide thoughtful interpretation of genomic alterations and their therapeutic implications at the point of care. Further, we are expanding our precision oncology efforts beyond genomics to optimize selection of investigational agents—including antibody-drug conjugates and immunotherapy—as well as approved therapies.

We are fortunate that the NCI awarded us both a UM1 grant and a UM1 Phase II supplement to work closely with Dr. James Yao, chair of MD Anderson's Department of Gastrointestinal Medical Oncology, and Drs. Gail Eckhardt and Thomas Flaig from the University of Colorado to form the Southwest Early Clinical Trials Consortium. This allows us to participate in the NCI Experimental Therapeutics Clinical Trials Network and access the Cancer Therapy Evaluation Program (CTEP) portfolio to design investigator-initiated, hypothesis-driven, biomarker-intensive trials with plans for seamless transition into Phase II trials.

It has been striking to see how many new therapeutic opportunities are entering trials in immuno-oncology. This year we are participating in a variety of novel single-agent trials as well as novel-novel combinations, including combinations with other immunotherapies, targeted therapies, chemotherapy, and radiation therapy. Immuno-oncology is a very exciting field with many opportunities for patient impact and discovery of novel combinations, predictors of sensitivity, and resistance.

Our goal is truly to be able to go from bench to bedside and back. Over the past year, we gained significant momentum in the ICT laboratory. We established basic molecular oncology techniques as well as high-throughput approaches for combination therapy screening, and we are working closely with the Institute of Applied Cancer Sciences to establish a pipeline for synthetic lethality studies *in vitro* and *in vivo*. We developed a patient-derived xenograft biobank for *in vivo* modeling, and by working closely with the Institute for Personalized Cancer Therapy we have access to a variety of molecular testing platforms including exome sequencing, RNAseq, and reverse-phase proteomic arrays. We recruited Dr. Coya Tapia, a talented pathologist who has a joint appointment in the departments of Translational Molecular Pathology and ICT, to co-lead our biomarker efforts. Thus, we are increasingly poised to initiate preclinical studies with novel compounds, and to assess target inhibition and adaptive response. We are embarking on studies with novel combinations to help design the next generation of trials and co-clinical trials. We expect that our capabilities in this arena will grow over the next year, allowing us to develop larger collaborations that will facilitate preclinical to clinical transition of new molecular entities as well as provide biomarker decision support for ongoing trials.

The ICT department remains on an upward trajectory. We are working hard and innovating to deserve our reputation as one of the top research centers in the world. We appreciate the productive relationships we have built with our industry partners and many academic collaborators to allow us access to new treatment options for our patients. We are grateful for the support of our colleagues across MD Anderson and referring oncologists across the world. And as always, and most importantly, we are grateful for the honor and privilege to be there for our patients. • • •

MD Anderson wins $6 million CPRIT grant for genomic knowledge base

Funda Meric-Bernstam, MD, chair of the Department of Investigational Cancer Therapeutics (ICT), was awarded the largest of six Core Facility Support Awards announced in May 2015 by the Cancer Prevention Research Institute of Texas (CPRIT). Meric-Bernstam is the Medical Director of the Sheikh Khalifa Bin Zayed Al Nahyan Institute of Personalized Cancer Therapy (IPCT), working closely with the institute's Directors Gordon Mills, MD, PhD, John Mendelsohn, MD, and Executive Director Kenna Shaw, PhD. The grant will support development of the Precision Oncology Decision Support Core, a vast knowledge base of annotated genes and genotype-relevant trials to guide clinicians in choosing appropriate targeted therapeutic trials for their individual patients. The core will integrate tumor-specific data to generate personalized annotation reports. Investigators will also add variants of unknown significance (VUSs) to their functional genomics analysis at a rate of up to 30 per month over the five-year life of the project. That's 1,800 VUSs! "We're very ambitious in general," Meric- Bernstam said.

A portion of the knowledge base is available through the website www.personalizedcancertherapy.org, which went live in April 2014. It currently contains 26 annotated genes and has clocked almost 100,000 page views. The framework for the project was published in the April 2015 edition of the Journal of the National Cancer Institute.

Meric-Bernstam is the principal investigator of the team, which includes scientists with the Khalifa Institute for Personalized Cancer Therapy; faculty from Systems Biology, Pathology, and Hematopathology; and several division faculty: Scott Kopetz, MD, PhD, Gastrointestinal Medical Oncology; Michael Davies, MD, PhD, Melanoma Medical Oncology; Sarina Piha-Paul, MD, David Hong, MD, and Apostolia Tsimberidou, MD, PhD, all from ICT; John Mendelsohn, MD, Genomic Medicine; as well as Elmer Bernstam, MD, and Amy Franklin, PhD, from The University of Texas School of Biomedical Informatics.

"A treating oncologist has limited time to extrapolate the therapeutic implications of the alteration and what is known in the literature and ongoing clinical trials," Meric-Bernstam said. That is where the decision support team and knowledge base comes in. "If there's no clinical data publicly available, the team can interact with physicians and exchange data on whether these mutations are activating. So that will be unique."

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The team has granularly annotated MD Anderson trials that seek specific genomic alterations, and other studies that may be a good match. "That's something we will continue to build on with this grant," she said. The knowledge base also contains public information from www.clinicaltrials.gov.

"Our goal is to start with MD Anderson and expand throughout Texas for greater impact," Meric-Bernstam said. That has already begun with the Clearinghouse Protocol, which has enrolled about 6,000 patients to date. In that trial, treating physicians receive email alerts containing information about clinical trials that are relevant to their patients' genomic alterations. The physicians can then access the decision support tool to learn more about how to interpret and use the test results.

"We're working to make the clinical trial database more useful for people who are looking, and eventually that will be external facing," she said. "To date we've received 1,800 requests for genomic annotations. This grant will really help us enhance the knowledge base and clinical trial efforts and get to a more systematic way of putting reports together, ultimately adding tumor-specific information as an extra layer," Meric-Bernstam said. • • •

– by Claire Blondeau

David Hong, MD

Joint research retreat provides symposium to spark alliances

The joint Experimental Therapeutics (ET), Investigational Cancer Therapeutics (ICT), Institute for Applied Cancer Science (IACS), and Oncology Research for Biologics and Immunotherapy Translation (ORBIT) research retreat took place Aug. 8, 2015, in the South Campus Research Building 4 conference room. In all, 44 participants attended the meeting. Hosted by David Hong, MD, *(left)* associate professor of ICT, Varsha Gandhi, PhD, chair *ad interim* of ET, Funda Meric-Bernstam, MD, chair of ICT, and William Plunkett, PhD, professor of ET, the central goal for the symposium was to allow a medium for faculty to share their research in hopes of fostering productive collaborations among departments.

The morning began with a brief introduction from Gandhi. The first session focused on novel molecular targets, with a talk on nanocarriers from Gabriel Lopez, MD, professor of ET, and on the ORBIT pipeline and partnerships from Michael Curran, PhD, assistant professor of Immunology. Following was a session on strategies to enhance therapeutic activity or overcome resistance mechanisms, which included a clinical trials overview from Meric-Bernstam; details of a Phase I/II study of AZD1775 and vorinostat in patients with head and neck cancer from Siqing Fu, MD, PhD, associate professor of ICT; a discussion on PI3K inhibition, resistance, and combination therapies from Gandhi; and reversal of resistance in cancers marked by wild-type p53 by Zahid Siddik, PhD, professor of ET. The third session shifted to establishing biomarkers for patient selection and resistance. During this late morning block, Filip Janku, MD, PhD, assistant professor of ICT, spoke about liquid biopsies; Chang-Gong Liu, PhD, professor of ET, gave a brief talk about the sequencing and non-coding RNA program; and Geoffrey Bartholomeusz, PhD, associate professor of ET, focused on target identification and validation care. The final module of the day was centered around translational study-associated proof-of-principle trials, and was kicked off by Vivek Subbiah, MD, assistant professor of ICT, with a discussion about the search for the science behind exceptional responders. Within this session was a working lunch during which Shuxing Zhang, PharmD, PhD, associate professor of ET, delivered a talk on targeting ubiquitination for cancer therapy. The afternoon ended with two open discussions, the first led by Hong on molecules targeting cancer pathophysiology, and the second led by Plunkett on translation of mechanism-based therapy combinations. • • •

– by Erica Di Pierro

Pioneering liquid biopsy: Janku taps into the bloodstream to see tumor dynamics

As medicine evolves, techniques to diagnosis, treat, and track disease are becoming less invasive and more targeted to minimize unnecessary pain and unintended side effects. Through efforts in the clinic and the laboratory, Filip Janku, MD, PhD, assistant professor of Investigational Cancer Therapeutics (ICT), hopes to improve cancer patient outcomes by refining how we obtain information about tumors over the course of disease. After completing medical and research education in his native Czech Republic, Janku transferred to Bon Secours Hospital in Ireland where he practiced oncology and put together a clinical trial unit. This experience affirmed his passion for organizing and conducting trials, which he pursued further during a clinical research fellowship here at MD Anderson. Originally intending to return to Ireland after this training, Janku found himself at home in this institution's diverse, ambitious environment, and earned an assistant professorship in 2011.

Janku's Phase I trial portfolio includes therapies targeting the PI3K pathway and IDH1/IDH2, genes commonly mutated in brain tumors, cholangiocarcinomas, and some sarcomas. In the laboratory, he focuses on the non-invasive liquid biopsy method, which operates on the principle that cells, both malignant and normal, shed short fragments of DNA into the bloodstream that can be recovered from the serum fraction of whole blood. Known as cell-free DNA (cfDNA), these circulating fragments allow for convenient and minimally invasive retrieval of tumor DNA that can be sequenced to determine mutation profiles and real-time genetic changes that may correlate with various disease events including progression and therapy response. This concept is particularly useful in the Phase I clinical trial setting where there is a need for serial biopsy to track treatment responses and emergence of resistance. Indeed, clinical research is frequently limited by availability of high quality tissue specimens, the collection of which is also often associated with uncomfortable or even harmful complications for the patient.

Several major principles drive Janku's exploration into potential applications of this technique. First, to support wider use of liquid biopsy, a significant amount of work has shown strong concordance between liquid and tissue biopsy in mutation status for several commonly mutated genes including BRAF, KRAS, and PIK3CA in advanced cancers. Such results suggest that this method could be used in lieu of tissue, although Janku believes the new technology will instead add a new, more convenient dimension to monitoring cancer status. Additionally, mounting evidence shows that changes in cfDNA may correlate with response and resistance to therapy. For example, quantitative levels of circulating tumor DNA in the plasma have been shown to change after administration of therapy, indicating that this metric could be used as a biomarker for therapy response. Further, liquid biopsy may be able to identify mutations in cfDNA that drive therapy resistance, possibly allowing for pre-emptive intervention through treatment modification. "The only way for us to try to understand the mechanism causing therapy resistance in an individual patient is to do serial biopsy," Janku noted, a process made much easier by liquid biopsy. Levels of cfDNA may also predict prognosis in some cases; surprising recent findings from Janku's group have shown that patients with higher fractions of BRAF-, KRAS-, and EGFR-mutant DNA fare worse than patients with less, despite the fact that all three of these mutations have corresponding targeted therapies. In addition to blood, Janku has found that both urine and cerebral spinal fluid contain detectable amounts of cfDNA; he is also investigating the utility of genetic material-containing exosomes shed from tumor cells into plasma and other biological fluids.

Once a major rate-limiting step in the process, sequencing technologies have matured to a point where they are now central to the success of liquid biopsy. Janku employs multiple methods including droplet digital polymerase chain reaction (PCR), which partitions thousands of individual PCR reactions into water-oil emulsion droplets for high-throughput amplification within one tube. He also uses BEAMing (beads, emulsion, amplification, and magnetics), an exquisitely sensitive process that separates low levels of mutated DNA from abundant normal DNA using magnetic beads, then amplifies the mutant fraction. Janku and his collaborators also investigate next-generation sequencing platforms. Among Janku's lab instrument arsenal is a fully automated, real-time PCR-based system that rapidly processes input DNA, spitting out a mutation profile panel in under an hour. In Janku's experience, mutation profiles from plasma DNA processed by a fully automated, real-time quantitative PCR demonstrate high concordance with profiles from biopsied tissue samples.

Research scientist Helen Huang, MD, assists Janku in the lab to isolate cfDNA, circulating fragments that can be sequenced to determine mutation profiles.

Key to establishing liquid biopsy as a go-to tool is to prove that information obtained from the procedure can improve patient outcomes. "We need to design clinical trials that will utilize the results of serial profiling of liquid biopsies. This way, we can test the question of if we act on what we see in these profiles, does it make a difference to the patient," Janku said. This will be the next major goal for the field. • • •

– by Erica Di Pierro

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Phase I program welcomes newest faculty member


Shubham Pant, MD

Shubham Pant, MD, joined MD Anderson in March 2016 as an associate professor in the Department of Investigational Cancer Therapeutics and as the associate medical director of the Clinical and Translational Research Center (CTRC), our patient care center for those on Phase I clinical trials. Pant was an associate professor of medicine and the director of clinical trials in the Section of Hematology-Oncology at the University of Oklahoma Health Sciences Center, the Mai Eager Anderson Chair in Cancer Clinical Trials, and associate director of the Tobacco Settlement Endowment Trust (TSET) Phase I program for the Stephenson Cancer Center in Oklahoma City. Pant previously served as an elected member at large and site principal investigator (PI) to the Board of Directors of the Cancer and Leukemia Group B (CALGB) of the National Cancer Institute (NCI) National Clinical Trials Network, and was a member of the Board of Trustees for the NCI's Alliance in Clinical Trials In Oncology (ACTION). He is currently on the board of the Oklahoma Society of Clinical Oncology and serves as their ASCO/State Affiliate Council Representative.

Pant tells us in his own words what he strives to achieve at MD Anderson.

- **Collaboration:** I plan to partner with basic science colleagues at MD Anderson to develop compounds from the bench to the bedside, and design and lead investigator-initiated studies.
- **Clinical trials portfolio:** At the University of Oklahoma, I was a PI or co-PI on approximately 80 Phase I trials, including several first-in-human trials. I intend to continue developing early phase clinical trials, assisting with the design, and directing research as a PI.
- **Patient care:** MD Anderson is world renowned for excellence in patient care. As in Oklahoma, I will provide empathetic and exemplary care to my patients.
- **Process improvement:** I firmly believe in the quote "Learn as if you were to live forever" (M.K. Gandhi). In that vein, I achieved a Green Belt certification from the University of Oklahoma College of Engineering in Lean Six Sigma. I will collaborate with my colleagues and staff at MD Anderson to develop more efficient systems, looking for areas to improve in the clinic as well as the clinical trials process, and then design solutions that address workflow and the quality of care for patients with cancer.
- **Education:** I enjoy working and collaborating with fellows. I hope to mentor fellows and educate them on the nuances of early phase drug development and clinical trial methodology.

Collaboration is key to successful immunotherapy clinical trials


Aung Naing, MD

One of the objectives of Investigational Cancer Therapeutics (ICT) is to facilitate collaboration that will help move promising agents as swiftly as possible through the clinical trials pipeline from pre-clinical studies to the Phase I setting, and then to Phase II and III trials. Aung Naing, MD, associate professor of ICT, emphasized that this cooperative spirit is particularly important to the department as new immunotherapeutic agents make their way through the Phase I clinics. Collaboration among experts across disease-specific departments is invaluable in expediting the movement of novel, complex therapies from Phase I through later stage trials so they can reach patients. As with any new treatment, some immunotherapeutic agents come with challenging side effects that must be understood to be properly managed. Naing and others in ICT frequently collaborate with faculty in Internal Medicine, including professor Maria Suarez-Almazor, MD, PhD, to co-manage such reactions and recognize the mechanisms behind them. Further, investigators in Diagnostic Radiology use innovative imaging techniques to determine which patients may be more susceptible to side effects. ICT also interfaces heavily with the Immunotherapy Moon Shot Platform, which provides analyses that clarify Phase I trial results. In all, the success and momentum of these game-changing agents through the clinical trials pipeline relies on sharing of data and ideas.

Active Phase I Program Protocols

April 2016

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ADVANCED CANCER

Protocol #	Title	Mechanism of Action	Principal Investigator	Age Requirement	Stable CNS Metastases Allowed?
ECOGEAY131	NCI-MATCH	Multiple	Funda Meric-Bernstam	≥18	Yes
NCI9591	A Phase I Trial of Single Agent Trametinib (GSK1120212) in Advanced Cancer Patients with Hepatic Dysfunction	MEK inhibitor	Vivek Subbiah, MD	≥18	Yes, if treated and asymptomatic.
2015-0480	A Phase I Open-label, Multicenter, Dose-escalation Study of PRN1371, a FGFR1-4 Kinase Inhibitor, in Adult Patients with Advanced Solid Tumors, followed by an Expansion Cohort in Patients with FGFR1, 2, 3, or 4 Genetic Alterations	FGFR1-4 kinase inhibitor	Sarina Piha-Paul, MD	≥18	Yes
2015-0465	A Phase I Open-label Study to Determine the Safety and Tolerability of ALRN-6924 in Patients with Advanced Solid Tumors or Lymphomas Expressing Wild-type p53 Protein	MDM2/MDMX inhibitor	Funda Meric-Bernstam, MD	≥18	Yes, it treated and stable at least 30 days prior to study enrollment.
2015-0263	A Phase I/II, Open-label, Multicenter Study of the Safety and Efficacy of LAG525 Single Agent and in Combination with PDR001 Administered to Patients with Advanced Malignancies	Anti-LAG-3 IgG4 antibody + anti-PD1 IgG4 antibody (LAG = lymphocyte activation gene)	David Hong, MD	≥18	Yes, if asymptomatic and don't require radiotherapy or surgery, and no increasing doses of corticosteroids within 2 weeks prior to dosing.
2015-0220	A Phase I Dose-escalation Study of Radio-labeled Immunotherapeutic, FF-21101(90Y), for the Treatment of Advanced Cancer	DOTA-conjugated chimeric human/ mouse monoclonal antibody	Vivek Subbiah, MD	≥18	Yes, if treated and stable.
2015-0158	A Phase I/IIa Study to Assess the Safety, Pharmacokinetics, and Pharmacodynamics of PLX8394 in Patients with Advanced, Unresectable Solid Tumors	BRAF inhibitor	Filip Janku, MD, PhD	≥18	Yes, if clinically stable and off corticosteroids.
2015-0054	A Phase I, Open-label, Dose-escalation, Safety and Tolerability Study of INCB054329 in Subjects with Advanced Malignancies	BET inhibitor	Sarina Piha-Paul, MD	≥18	Yes, if clinically stable and off corticosteroids for ≥4 weeks from start of study.
2015-0028	An Open-label, Dose-escalation/expansion Phase I Study of ASP4132 Given Orally to Subjects with Advanced Refractory Solid Tumors and Lymphomas	Mitochondrial complex I inhibitor	Filip Janku, MD, PhD	≥18	Yes, if asymptomatic and off steroids.
2014-1099	A Phase I, Open-label, Dose-escalation, Safety and Tolerability Study of INCB054828 in Subjects with Advanced Malignancies	FGFR inhibitor	Vivek Subbiah, MD	≥18	Yes, of clinically stable and off all corticosteroid for ≥4 weeks.
2014-1056	Phase Ia/Ib Study of the Oral TRK Inhibitor LOXO-101 in Subjects with Adult Solid Tumors	TRK inhibitor	David Hong, MD	≥18	Yes, if treated and imaging within 28 days prior to enrollment confirms stable disease an sponsor grants approval.
2014-1006	A Phase I Study of IDH305 in Patients with Advanced Malignancies that Harbor IDH1R132 Mutations	IDH1R132 inhibitor	Filip Janku, MD, PhD	≥18	Yes
2014-0959	A Phase I Study Evaluating the Safety and Pharmacokinetics of ABBV-075 in Subjects with Advanced Cancer	BET inhibitor (BRD4, BRD3, BRD2 and BRDT)	Sarina Piha-Paul, MD	≥18	Yes, if stable and off steroids at least 1 week prior to start of study.
2014-0640	A Phase Ib Study to Evaluate the Safety of Selinexor (KPT-330) in Combination with Multiple Standard Chemotherapy Agents in Patients with Advanced Malignancies	Selective inhibitor of nuclear export (SINE)	Aung Naing, MD	≥18	Yes, if clinically stable with no steroids or anticonvulsants and >4 weeks from prior tx.
2014-0512	A Phase I/IIa, Multicenter, Open-label Study of Oral RXDX-101 in Adult Patients with Locally Advanced or Metastatic Cancer Confirmed to be Positive for TRKA, TRKB, TRKC, ROS1, or ALK Molecular Alterations	Multiple tyrosine kinase inhibitor	Shumei Kato, MD	≥18	Yes, if asymptomatic and off anticonvulsants or steroids for at least 2 weeks.
2014-0339	A Phase I Study of Oprozomib to Assess Food Effect, Drug-drug Interactions with Midazolam, and Safety and Tolerability in Patients with Advanced Malignancies	Proteosome inhibitor	Apostolia Tsimberidou, MD	≥18	No
2014-0328	Pharmacokinetics of Oral Alisertib (MLN8237) in Adult Patients with Advanced Solid Tumors or Relapsed/Refractory Lymphomas with Varying Degrees of Hepatic Function	Aurora A kinase inhibitor	Siqing Fu, MD, PhD	≥18	Yes, if clinically stable with no neurologic dysfunction.
2014-0069	A Dose-finding Phase I Study of TAS-120 in Patients with Advanced Solid Tumors with or without Fibroblast Growth Factor/Receptor (FGF/FGFR)-related Abnormalities Followed by a Phase II Study in Patients with Advanced Solid Tumors or Multiple Myeloma with FGF/FGFR-Related Abnormalities	FGFR inhibitor	Funda Meric-Bernstam, MD	≥18	Yes, if clinically stable and off corticosteroids for ≥2 months.
2013-0918	A Phase II, Open-label Study in Subjects with BRAF (V600E) Mutated Rare Cancers with Several Histologies to Investigate the Clinical Efficacy and Safety of the Combination Therapy of Dabrafenib and Trametinib	BRAF inhibitor + MEK inhibitor	Vivek Subbiah, MD	≥18	Yes, if stable.
2013-0833	A Phase I Trial of Regorafenib and Cetuximab in Patients with Advanced Malignancy	Antiangiogenic agent and EGFR inhibitor	Vivek Subbiah, MD	≥18	Yes
2013-0813	A Phase Ib Open-label, Multicenter, Dose-escalation and Expansion Study of Orally Administered MEK162 plus BYL719 in Adult Patients with Selected Advanced Solid Tumors	MEK inhibitor combined with PI3K inhibitor	Filip Janku, MD, PhD	≥18	No brain primaries but allows brain mets if stable.

Continued

TREATMENT PLANNING CONFERENCE

Referring physicians and nurses who want to present patients for possible Phase I clinical trial inclusion are invited to attend the weekly treatment planning conference held every Wednesday from 8 to 8:30 a.m.

Contact Ly M. Nguyen, senior study coordinator, to add a case to the meeting agenda. (lmnguyen1@mdanderson.org; 713-563-2169)

ADVANCED CANCER

Protocol #	Title	Mechanism of Action	Principal Investigator	Age Requirement	Stable CNS Metastases Allowed?
2013-0684	A Multicenter Phase I Study of MRX34, MicroRNA miR-RX34 Liposomal Injection	Micro ribonucleic acid	David Hong, MD	≥18	Yes
2013-0633	A Phase I/II Open-label, Dose-escalation Study to Investigate the Safety, Pharmacokinetics, Pharmacodynamics, and Clinical Activity of GSK525762 in Subjects with NUT Midline Carcinoma (NMC) and Other Cancers	Bromodomain extra-terminal (BET) inhibitor	Sarina Piha-Paul, MD	Pedi + Part Ia: ≥16; Part Ib: 12 - 15; Part II (expansion): ≥16, then 12 - 15 once Part Ib has been completed.	No brain primaries but allows brain mets.
2013-0616	A Phase I Study of LY3009120 in Patients with Advanced or Metastatic Cancer	Raf/Ras/MEK/ERK inhibitor	David Hong, MD	≥18	No brain primaries but allows brain mets.
2013-0574	A Phase I Dose-escalation, Safety, Pharmacokinetic and Pharmacodynamic Study of BVD-523 in Patients with Advanced Malignances	ERK inhibitor	Filip Janku, MD, PhD	≥18	No brain primaries but allows brain mets.
2013-0525	A Phase I, First-in-human, Dose-escalation Trial of MSC2363318A, a Dual p70S6K/Akt Inhibitor, in Subjects with Advanced Malignancies	p70S6K and AKT inhibitor	Apostolia Tsimberidou, MD	≥18	Yes
2013-0511	A Phase I Study of MLN9708 and Vorinostat to Target Autophagy in Patients with Advanced p53 Mutant Malignancies	Proteasome inhibitor and histone deacetylase inhibitor	Siqing Fu, MD, PhD	≥18	Yes, if controlled.
2013-0466	A Phase I Dose-escalation and Pharmacokinetic Study of NC-4016 in Patients with Advanced Solid Tumors or Lymphomas	Polymeric micellar nanoparticle of oxaliplatin metabolite	Vivek Subbiah, MD	≥18	Yes
2013-0257	A Phase I Multiple Ascending-dose Study of DS-3032b, an Oral MDM2 Inhibitor, in Subjects with Advanced Solid Tumors or Lymphomas	MDM2 inhibitor	David Hong, MD	≥18	Yes, brain mets but not primary.

SOLID TUMORS

Protocol #	Title	Mechanism of Action	Principal Investigator	Age Requirement	Stable CNS Metastases Allowed?
2015-0838	Evaluation of an Alternative Schedule for CRLX101 Alone and in Combination with Bevacizumab in Subjects with Advanced Solid Tumor Malignancies	Topoisomerase I and HIF-1α and HIF-2α inhibitor	Sarina Piha-Paul, MD	≥18	No brain primaries. Brain mets allowed if asymptomatic and off steroids at least 2 weeks prior to start of study.
2015-0728	A Phase II Basket Study of the Oral TRK Inhibitor LOXO-101 in Subjects with NTRK Fusion-positive Tumors	TRK inhibitor	David Hong, MD	≥18	Yes, if asymptomatic.
2015-0656	An Open-label, Phase I/Ib, Single-agent Study of RXDX-105 in Patients with Advanced Solid Tumors	RET/BRAF/EGFR inhibitor	Siqing Fu, MD, PhD	≥18	No brain primaries, but brain mets allowed if treated, clinically stable and off steroids ≥3 weeks prior to start of treatment.
2015-0637	A Phase I/Ib/II, Open-label, Multicenter Study of the Safety and Efficacy of MBG453 as Single Agent and in Combination with PDR001 in Adult Patients with Advanced Malignancies	Anti-TIM-3 IgG4 antibody alone or in combination with anti-PD1 IgG4 antibody	Aung Naing, MD	≥18	Yes, if neurologically stable, asymptomatic, and not requiring radiotherapy 4 weeks prior to enrollment and off steroids with 2 weeks prior to first dose.
2015-0627	An Open-label, Non-randomized, Multicenter Phase I Study to Characterize the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Maximum Tolerated Dose of Oral MKNK1 Inhibitor BAY 1143269 Given Alone or in Combination with Intravenous Docetaxel in Subjects with Advanced Solid Tumors	MKNK1 inhibitor +/- chemo	Funda Meric-Bernstam, MD	≥18	Yes, if stable with no evidence of growth of brain or meningeal or spinal metastases on imaging at start of study. No acute steroid therapy.
2015-0468	A Phase Ia/b Study to Evaluate the Safety and Tolerability of ETC-1922159 in Advanced Solid Tumors	Wnt signaling regulator	Vivek Subbiah, MD	≥18	Yes, if treated and stable ≥4 wks prior to dosing.
2015-0411	A Multicenter Phase II Clinical Trial of Lurbinectedin (PM01183) in Selected Advanced Solid Tumors	DNA minor groove binder	Vivek Subbiah, MD	≥18	No known CNS involvement.
2015-0384	An Open-label Multicenter Phase I Study of E7046 in Subjects with Selected Advanced Malignancies	Prostaglandin EP4 receptor inhibitor	David Hong, MD	≥18	Yes, if treated with no evidence of progression for at least 8 weeks and off steroids at least 4 weeks before first dose.
2015-0353	A Phase Ib/II, Open-label, Multicenter Study Assessing the Safety, Tolerability, Pharmacokinetics, and Preliminary Anti-tumour Activity of MEDI4736 in Combination with AZD9150 or AZD5069 in Patients with Advanced Solid Malignancies and Subsequently Comparing AZD9150 and AZD5069 Both as Monotherapy and in Combination with MEDI4736 as Second-line Treatment in Patients with Recurrent and/or Metastatic Squamous Cell Carcinoma of the Head and Neck	PD-L1 inhibitor combined with, STAT3 inhibitor or CRCX2 antagonist	David Hong, MD	≥18	Yes, if previously treated and determined stable for at least 2 months by CT or MRI scan.
2015-0282	A Phase I/II, Multicenter, Open-label, Dose-escalation Study of AG-221 in Subjects with Advanced Solid Tumors, including Glioma, and with Angioimmunoblastic T cell Lymphoma, that Harbor an IDH2 Mutation	IDH2 inhibitor	Filip Janku, MD, PhD	≥18	Yes, if asymptomatic or require therapy to control symptoms (radiation, surgery, etc.) within 2 mos of first dose. Glioma patients with stable mets on steroid-dosing regimen prior to screening MRI may enroll with medical monitor approval.
2015-0261	A First-in-human Study of Repeat Dosing with REGN2810, a Monoclonal, Fully Human Antibody to Programmed Death-1 (PD1), as Single Therapy and in Combination with Other Anti-Cancer Therapies in Patients with Advanced Malignancies	Anti-PD-L1 IgG1 monoclonal antibody alone or combined with radiation therapy and/or chemo	Aung Naing, MD	≥18	Yes, if stable ≥4 weeks prior to treatment, neurologic symptoms have returned to baseline, and there is no evidence of new or enlarging brain mets.
2015-0239	An Open-label, Multicohort, Phase II Study of MPDL3280A in Advanced Solid Tumors	Anti-PD-L1 IgG1 monoclonal antibody	David Hong, MD	≥18	Yes, if treated and asymptomatic, have measureable disease outside the CNS, only supratentorial metastases, no hx of intracranial hemorrhage, no cortico-steroids or anticonvulsants, on stereotactic radiation within 7 days of C1D1. No leptomeningeal disease.

Protocol #	Title	Mechanism of Action	Principal Investigator	Age Requirement	Stable CNS Metastases Allowed?
2015-0093	A Phase I, Multicenter, Open-label, Dose-escalation, Safety, Pharmacokinetics, Pharmacodynamic, and Clinical Activity Study of Orally Administered AG-120 in Subjects with Advanced Solid Tumors, Including Glioma, with an IDH1 Mutation	IDH1 inhibitor	Filip Janku, MD, PhD	≥18	Yes, if asymptomatic and off steroids within 2 months of first dose. Glioma patients on steroid-dosing regimen prior to screening MRI may be permitted to enroll with medical monitor approval.
2015-0076	A Multicenter Study of the Bruton's Tyrosine Kinase (BTK) Inhibitor, Ibrutinib, in Combination with MEDI4736, in Subjects with Relapsed or Refractory Solid Tumors	BTK inhibitor combined with anti-PD-L1 antibody	David Hong, MD	≥18	No
2015-0075	An Open-label Multicenter Phase I/II Study of the Safety and Efficacy of PDR001 Administered to Patients with Advanced Malignancies	Anti-PD1 IgG4 antibody	Aung Naing, MD	≥18	Yes, if asymptomatic and off steroids within 2 weeks of study enrollment.
2015-0033	A Phase I Open-label, Multicenter Study to Assess the Safety, Tolerability and Pharmacokinetics of Orally Administered CUDC-907, an HDAC and PI3K Inhibitor, in Subjects with Advanced/Relapsed Solid Tumors	HDAC and PI3K inhibitor	Sarina Piha-Paul, MD	≥18	Stable or improving CNS disease that is not under active treatment after receipt of adequate therapy is allowed.
2014-1054	A Phase I, Open-label, Dose-escalation, Dose-finding Study Evaluating the Safety and Pharmacokinetics of SM04755 in Subjects with Advanced Colorectal, Gastric, Hepatic, or Pancreatic Cancer	Wnt inhibitor	Sarina Piha-Paul, MD	≥18	No
2014-1052	A Phase I Study of MEDI4736 (Anti-PD-L1 Antibody) in Combination with Tremelimumab (Anti-CTLA4 Antibody) in Subjects with Advanced Solid Tumors	Anti-PD-L1 and anti-CTLA4 antibodies	Aung Naing, MD	≥18	Yes, if treated and stable at least 6 weeks with no corticosteroid use at least 14 days prior to first dose.
2014-1045	A Phase I, Gene Alteration-based, Open-label, Multicenter Study of Oral Debio 1347 (CH5183284) in Patients with Advanced Solid Malignancies, whose Tumors Have an Alteration of the FGFR 1, 2 or 3 Genes	FGFR inhibitor	Funda Meric-Bernstam, MD	≥18	Yes, if asymptomatic and stable on recent imaging with no active treatment in last 6 months.
2014-1022	An Open-label, Phase I, Dose-escalation Trial to Evaluate the Safety, Tolerability, Maximum Tolerated Dose, Pharmacokinetics, and Pharmacodynamics of the Anti-FGFR2 Antibody-drug Conjugate BAY 1187982 in Subjects with Advanced Solid Tumors Known to Express FGFR2	Anti-FGFR2 antibody-drug conjugate	Funda Meric-Bernstam, MD	≥18	Yes, if asymptomatic longer than 3 months from end of previous therapy and before first dose of study drug.
2014-1005	A Phase I/Ib Study of MGCD516 in Patients with Advanced Solid Tumor Malignancies	MET, AxI, VEGFR, PDGFR, KIT, FLT3, Trk, RET, DDR2 and Eph inhibitor	Shumei Kato, MD	≥18	Yes, if stable and off steroid at least 2 weeks prior to drug administration and at least 4 weeks since cranial radiation.
2014-0999	A Phase I, Multicenter, Open-label Dose-escalation and Expansion Study of PCA062, Administered Intravenously in Adult Patients with pCAD-positive Tumors	Antibody-drug conjugate targeting P-cadherin	Vivek Subbiah, MD	≥18	No
2014-0891	A Phase I Study of KBP-5209 in Patients with Advanced Solid Tumors	EGFR, HER2 and HER4 inhibitor	Sarina Piha-Paul, MD	≥18	Yes, if asymptomatic and patients have completed radiotherapy or surgery for CNS mets at least 2 weeks prior to study entry. If steroids are used, patients must have been on stable dose for at least 2 week prior to signing consent.
2014-0878	A Multicenter Phase Ia/Ib Ascending-dose Study of DCC-2701 to Assess Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics in Patients with Advanced Solid Tumors	MET, TIE2, VEGFR2, TRK kinase inhibitor	Sapna Patel, MD; Filip Janku, MD, PhD	≥18	Yes, if stable and off anticonvulsants or corticosteroids at least 3 months prior to start of treatment.
2014-0809	A Phase I, Open-label, Dose-escalation Study of Immunoconjugate L-DOS47 in Combination with Standard Doublet Therapy of Pemetrexed/Carboplatin in Patients with Stage IV (TNM M1a and M1b) Recurrent or Metastatic Non-Squamous Non-Small Cell Lung Cancer	AFAIKL2 antibody	Sarina Piha-Paul, MD	≥18	No
2014-0763	A Phase I Study of Mogamulizumab (KW-0761) in Combination with MEDI4736 and Mogamulizumab in Combination with Tremelimumab in Subjects with Advanced Solid Tumors	Anti-CCR4 antibody combined with anti-PD1 and anti CTLA4 antibody	David Hong, MD	≥18	Yes, brain mets allowed if asymptomatic, clinically stable and have not received corticosteroids or anti-convulsants for at least 28 days prior to screening.
2014-0753	A Phase I/II Study Exploring the Safety, Tolerability, and Efficacy of INCB024360 in Combination with MEDI4736 in Subjects with Selected Advanced Solid Tumors	Enzyme indoleamine 2, 3-dioxygenase 1 (IDO1) inhibitor combined with PD-L1 antagonist	Aung Naing, MD	≥18	Yes, if treated and clinically stable and off steroids for at least 2 weeks.
2014-0733	A Phase I, Open-label, Dose-escalation, Multicenter Study of ACT-PFK-158, 2HCl in Patients with Advanced Solid Malignancies	PFKFB3 inhibitor	Siqing Fu, MD, PhD	≥18	No
2014-0669	A Modular Phase II Study to Link Targeted Therapy to Patients with Pathway-activated Tumors: Module 7- Ceritinib (LDK378) for Patients whose Tumors Have Aberrations in ALK or ROS1	ALK inhibitor	Vivek Subbiah, MD	≥18	Yes, if neurologically stable and off steroids within 2 weeks prior to study entry.
2014-0605	A Phase I Study of Glutaminase Inhibitor CB-839 in Advanced Solid Tumors	Glutaminase inhibitor	Funda Meric-Bernstam, MD	≥18	Yes, if no active CNS disease at least 4 weeks prior to therapy, stable lesions without steroids at least 3 weeks prior to first dose.
2014-0569	A Modular Phase II Study to Link Targeted Therapy to Patients with Pathway-activated Tumors: Module 6-BGJ398 for Patients with Tumors with FGFR Genetic Alterations	FGFR kinase inhibitor	Sarina Piha-Paul, MD	≥18	Yes, if 4 weeks from prior therapy, clinically table at the time of study entry, off steroids or anticonvulsants with no LMD.
2014-0495	A Phase I, Open-label Dose-escalation First-in-human Study to Evaluate the Tolerability, Safety, Maximum Tolerated Dose, and Pharmacokinetics of AM0010 in Patients with Advanced Solid Tumors	Pegylated recombinant IL10	Aung Naing, MD	≥18	No

Continued

Protocol #	Title	Mechanism of Action	Principal Investigator	Age Requirement	Stable CNS Metastases Allowed?
2014-0459	MY Pathway: An Open-label Phase IIa Study Evaluating Trastuzumab/Pertuzumab, Erlotinib, Vemurafenib, and Vismodegib in Patients who Have Advanced Solid Tumors with Mutations or Gene Expression Abnormalities Predictive of Response to One of These Agents	HER2, EGFR, BRAF and hedgehog pathway inhibitors	Funda Meric-Bernstam, MD	≥18	Yes, with minimal neurologic symptoms, evidence of stable disease (for at least 1 month) or response on follow-up scan, and require no corticosteroid therapy.
2014-0384	A Phase I Dose-escalation Study of LY2940680 in Patients with Advanced Cancer	Hedgehog pathway inhibitor	David Hong, MD	≥18	Yes, if clinically stable for ≥60 days and off steroids and/or anticonvulsants.
2014-0338	A Phase I Study of LY3164530, a Bispecific Antibody Targeting MET and EGFR, in Patients with Advanced or Metastatic Cancer	EGFR/MET inhibitor	David Hong, MD	≥18	Yes, if asymptomatic for at least 28 days and not receiving corticosteroids and/or anticonvulsants.
2014-0193	A Phase Ib Trial of LY2606368 in Combination with Cisplatin or Cetuximab in Advanced and/or Metastatic Tumors	CHK1 inhibitor + chemo or anti-EGFR monoclonal antibody	David Hong, MD	≥18	Yes, if clinically stable and off corticosteroids
2014-0160	A Phase I, Open-label, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics and Preliminary Anti-tumor Activity of Ascending Doses of AZD5363 under Adaptable Dosing Schedules in Patients with Advanced Solid Malignancies	AKT inhibitor	Shannon Westin, MD; Funda Meric-Bernstam, MD	≥18	Yes, if asymptomatic, treated and stable and not requiring steroids for at least 4 weeks prior to start of study treatment.
2014-0137	An Open-label Phase I Dose-escalation Study to Evaluate the Safety, Tolerability, Maximum Tolerated Dose, Pharmacokinetics, and Pharmacodynamics of the Anti-C4.4a Antibody-drug Conjugate BAY 1129980 in Subjects with Advanced Solid Tumors Known to Express C4.4a	Anti-C4.4a antibody-drug conjugate	Vivek Subbiah, MD	≥18	Yes, if clinically stable and off corticosteroids or anticonvulsants for 1 month prior to screening.
2014-0119	Combination Treatment with Everolimus, Letrozole and Trastuzumab in Hormone Receptor and HER2/neu-positive Patients with Advanced Metastatic Breast Cancer and other Solid Tumors: Evaluating Synergy and Overcoming Resistance	mTOR inhibitor combined with aromatase inhibitor and HER-2 monoclonal antibody	Filip Janku, MD, PhD	≥18	Yes, if clinically stable for 3 weeks and off corticosteroids or anticonvulsants.
2014-0066	A Phase I, Open-label, Dose-escalation Study Evaluating the Safety, Pharmacokinetics, and Clinical Effects of Intravenously Administered PT-112 Injection in Subjects with Advanced Solid Tumors	Phosphorylated platinum	Daniel Karp, MD	≥18	Yes
2013-1031	Phase I Trial of ADI-PEG 20 plus Doxorubicin in Patients with HER2-negative Metastatic Breast Cancer or Advanced Solid Tumors	Pegylated arginine deaminase (alkylating agent) plus chemotherapy	Siqing Fu, MD, PhD	≥18	Yes
2013-0969	A Phase I Study of PF-06647263 in Advanced Solid Tumors	Anti-Efrin-A4 antibody-drug conjugate	David Hong, MD	≥18	Yes, if stable and don't require steroids.
2013-0961	A Phase II Study of the PARP Inhibitor BMN673 in Advanced Cancer Patients with Somatic Alterations in BRCA1/2 or a Homologous Recombination Defect	PARP inhibitor	Sarina Piha-Paul, MD	≥18	Yes, if stable.
2013-0904	An Open-label, Phase II Study of Neratinib in Patients with Solid Tumors with Somatic Human Epidermal Growth Factor Receptor (EGFR, HER2, HER3) Mutations or EGFR Gene Amplification	HER inhibitor	Sarina Piha-Paul, MD	≥18	Yes
2013-0699	A First-in-human, Dose-escalating Safety Study of Tissue Factor Specific Antibody-drug Conjugate (HuMax-TF-ADC) in Patients with Locally Advanced and/or Metastatic Solid Tumors Known to Express Tissue Factor	Human monoclonal antibody to tissue factor conjugated to a microtubule inhibitor	David Hong, MD	≥18	No
2013-0665	A Phase I Study of MLN0128 in Combination with Aflibercept in Patients with Advanced Cancers	mTOR inhibitor and VEGF inhibitor	Aung Naing, MD	≥18	Yes
2013-0638	A Phase Ib/II Dose-escalation and Expansion Trial of NC-6004 (Nanoparticle Cisplatin) plus Gemcitabine in Patients with Advanced Solid Tumors or Non-Small Cell Lung Cancer	Polymeric micelle containing cisplatin as an active moiety	Vivek Subbiah, MD	≥18	No brain primaries but allows brain mets.
2013-0549	A Phase I Safety Study of Intratumoral Injection of Clostridium Novyi-NT Spores in Patients with Treatment-refractory Solid Tumor Malignancies	C. novyi-NT lyses tumor cells in hypoxic tumor cores	Filip Janku, MD, PhD	≥18	No
2013-0346	A Phase Ia/b Non-randomized, Dose-escalation Study of the Safety, Pharmacokinetics, and Pharmacodynamics of Sterile Compound 31510 (Ubidecarenone, USP) Nanosuspension for Infection Administered Intravenously to Patients with Solid Tumors	Oligonucleotide STAT3 inhibitor	Vivek Subbiah, MD	≥18	Yes
2013-0180	A Phase I Study of the Safety and Tolerability of ATR-101 in Adrenocortical Carcinoma	Achiral, lipophilic Acyl-CoA: cholesterol acyltransferase (ACAT) inhibitor	Aung Naing, MD	≥18	Yes, brain primary but no brain mets.
2013-0064	A Phase I, Open-label, Dose-escalation Study to Assess Safety and Tolerability of SOR-C13 in Subjects with Advanced Solid Tumors Commonly Known to Express the TRPV6 Ion Channel	13-mer synthetic peptide	Siqing Fu, MD, PhD	≥18	No