Department of Investigational Cancer Therapeutics

Phase I Clinical Trials

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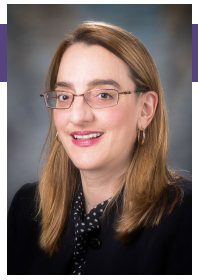

FROM THE CHAIR

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

I am really very proud of what we accomplished this year in the Department of Investigational Cancer Therapeutics on all fronts, especially in patient care and state-of-the-art research.

In fiscal year 2014, we recorded 2,034 new patients and consults. Our research-driven patient care is increasingly focused on understanding each patient's needs and expectations so we can personalize treatment choices and optimize opportunities for participating in innovative trials. We are actively working to increase patient satisfaction by initiatives such as decreasing patient wait times and improving our communication with patients and their families, as well as our consulting physicians.

Over the past year we dramatically expanded our clinical trial portfolio, and now offer a large variety of trials to our patients. Our investigations include first-in-human studies of exciting new agents, new combination therapies of novel agents paired with standard-of-care options, and novel/novel combination therapies. We are testing innovative targeted therapies (small molecule inhibitors as well as antibodies), antibody-drug conjugates, and immunotherapies, unique combinations as well as different delivery approaches to chemotherapeutics, and many others.

Precision medicine has come to the forefront in the national healthcare agenda. The Department of Investigational Cancer Therapeutics has always been a leader in implementing precision oncology. More recently, we have been working closely with the directors of the Khalifa Bin Zayed Al Nahyan Institute for Personalized Cancer Therapy (IPCT) – John Mendelsohn, MD, and Gordon Mills, MD, PhD, and Kenna Shaw, PhD – to offer genomic testing to all patients interested in genomically informed trials and to increase awareness of relevant trials across The University of Texas MD Anderson Cancer Center. Further, we are testing the concept of genomic medicine in an innovative randomized trial, IMPACT II, led by Apostolia Tsimberidou, MD, PhD, and described later in this newsletter.

Although Phase I trials remain one of our key missions, we have made a major effort to expand our clinical trial portfolio of genomically selected Phase I expansions as well as genomically selected multi-histology or histology-agnostic Phase II trials. For this purpose we not only recruited several industry-sponsored basket trials, but we also designed novel investigator-initiated basket trials, as described in this newsletter. We have activated several new trials for patients with a variety of genomic alterations including alterations in AKT1, ALK, BRAF, BRCA1 and 2, EGFR, FGFR, HER2, IDH1 and 2, MET, NTRK, SMO and PTCH, PIK3CA, PTEN, and several others. We are continuously striving to have at least one genomically matched trial option for each actionable alteration and for every patient.

We have the unique support of the IPCT Precision Oncology Decision Support team. This team of research scientists focuses on molecular oncology and genomic medicine, attends our weekly treatment planning conference, and assists us in interpreting the functional impact of genomic alterations and determining potential actionability of specific mutations found. We have made a significant amount of our genomics knowledge base publicly available through our precision oncology website: personalizedcancertherapy.org. We hope that this will help oncologists throughout the world determine the therapeutic implications of each genomic alteration and discover potential trial options. We always welcome questions as well as patient referrals.

During the next few years, we will be increasingly transitioning to novel combination therapies based on strong preclinical rationale generated in our labs. We have built a strong basic and translational research program and have positioned ourselves to perform co-clinical trials. We also have been successful in securing significant peer-reviewed funding this year, and now investigators in our group have research funding from the NIH and the Department of Defense, as well as major organizations such as the Komen Foundation and the Sidney Kimmel Foundation.

The Department of Investigational Cancer Therapeutics is entering a new era of clinical and academic excellence in delivering research-driven patient care. We are grateful for the support of our referring oncologists. But most importantly, we are grateful for the honor and privilege to serve our patients.

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Era of basket trials targets genomic alterations across multiple tumor types – by Parvathy Hariharan

With huge advances in personalized cancer therapy, oncologists are looking beyond treating each organ or disease site to instead target each tumor's genomic alterations irrespective of its location in the body. Symbolic of this evolving molecular approach to medicine, Investigational Cancer Therapeutics (ICT) faculty are conducting basket trials, which are biomarker-directed clinical trials for many types of malignancies that exhibit the same molecular aberrations. While the concept of genetically matching tumor and therapy is not new, basket trials are particularly important for patients with rare mutations in rare cancers. "Basket trials fulfill a critical need to explore the utility of drugs in an abnormality that we think is compelling," says Funda Meric-Bernstam, MD, chair of the ICT department and medical director of the Institute for Personalized Cancer Therapy (IPCT). "Since they are designed with high thresholds for response assessments, we can make early decisions about go/no go if this is a worthwhile molecular target to pursue."

Basket studies can be expansions of Phase I studies, or Phase II studies of new drugs or drugs approved for other tumor types. They are largely cancer-type agnostic, but not completely so, in that they allow for some types of tumors in which a drug seems promising, but not in others in which evidence shows that it will not be useful. For instance, BRAF inhibitors show a high response rate as single agents in melanomas with the BRAF V600E mutation, but not in colorectal cancers with the same mutation in the absence of combination therapy. Patients are enrolled in different cohorts of these signal-seeking studies, which are adaptively designed to shut down non-responding arms and expand responding arms. Before their advent, it was tough for patients with "actionable" mutations in rare cancers to access expensive targeted therapies without a clinical trial showing that the drug worked for their disease.

The critical challenge in conducting basket trials, however, is in accruing patients. A trial on patients with rare mutations in rare tumors means studying a subset of an already small population. Take this example from Vivek Subbiah, MD, an assistant professor of ICT who is leading a basket trial of a BRAF inhibitor: While lung cancers are common, and BRAF mutations are prevalent in melanomas, the combination of BRAF mutations in lung cancer is rare enough to be called an orphan disease. "If less than 2% of patients with lung cancer have this mutation, it is going to be tough getting them on the trials. And patients on these trials have to be monitored closely. So they should be either living geographically close by or be able to commute back and forth to MD Anderson."

Given their nature, it is easiest to conduct basket trials in a center where patients regularly undergo genetic testing. At MD Anderson, patients are offered participation on multiple testing protocols. Offered by the IPCT, the Clearinghouse protocol is an assay that tests a panel of 50 genes; more than 5,000 patients have been tested to date. An expanded research testing protocol called CMS400 analyzes a 409-gene panel. The ICT department collaborated with Foundation Medicine to enable testing for the IMPACT2 study. ICT faculty are also participating in NCI-MATCH, an NCI-sponsored protocol that will use an expanded profiling platform called Oncomine for testing and matching, led at MD Anderson by Cathy Eng, MD, professor of Gastrointestinal Medical Oncology. Savvy patients are also walking in with genomic profiling reports from a variety of organizations.

Photo by Denise De La Cruz

Sarina Piha-Paul, MD, Funda Meric-Bernstam, MD, and Vivek Subbiah, MD, coordinate basket trials from MD Anderson's centralized ICT department.

With MD Anderson's leadership as one of the nation's best cancer centers and ICT's history of initiating studies of novel therapies, accruing rare patient populations is easier here, Meric-Bernstam says. She credits the resources provided by both institutional and philanthropic funds for enabling faculty to do more investigator-initiated studies. Over the past year, ICT has made clinical trials available for over 40 genetic alterations, a commitment to genomic medicine that has paid off by generating greater national interest in conducting such trials at MD Anderson and consequently giving our patients more treatment options. To enable quick communication about trial eligibility and availability, the IPCT has enabled an email alert system for patients tested with the Clearinghouse protocol. The treating physician receives an email listing the patient's mutations, relevant clinical trials, their principal investigators, and the pager numbers of the research coordinators. "We really want to make it easy for physicians," Meric-Bernstam says. MD Anderson is the highest accruer of patients among all centers for most basket trials ICT investigators have participated in—a testament to both the rarity of the patients and the reach of the institution.

Conducting a basket trial across several tumor types is easier and more efficient in a centralized location like the ICT department. Pooling data from different arms lends statistical power to show evidence of meaningful benefit

••• basket trials continued on page 4

From the desk of our department administrator

Tandy Tipps, PhD

Fiscal year 2014 was very productive and impactful for ICT. We increased the number of sponsored and investigator-initiated clinical trials to provide more treatment options for our patients. We launched a department-wide sustainability initiative, and challenged our team members to find ways to decrease costs on office supplies and electricity usage while also decreasing our carbon footprint. The department saved over $30,000. This initiative showed us areas that we will work on for sustainability in FY 2015 as well as maintaining what we accomplished in FY 2014. We also launched a more extensive and robust community outreach program that incorporates the participation of Mandarin and Spanish bilingual team members and subsequently produced bilingual materials.

Further, as a component in our continued efforts to give back and positively impact the lives of others, ICT participated in the Fall Festival and Adopt-A-Family events. The department raised over $1,200 to provide a game booth with prizes and candy for the Fall Festival, an event for children who are patients during Halloween, and almost $2,500 for Adopt-A-Family.

I look forward to all the positive endeavors that we will embark upon that will continue to benefit the lives of our patients and their families.

Not your bread-and-butter oncology

Next-generation sequencing study helping to advance targeted therapy clinical trials

Traditionally, molecular diagnostic testing in solid tumors has lagged far behind that for leukemias, but researchers are gaining ground through Cancer Mutation Scan 400 (CMS400), a next-generation sequencing (NGS) platform that examines nearly the entire exome for 409 genes.

Principal investigator Russell Broaddus, MD, PhD, professor of Pathology and medical director of Solid Tumor Molecular Diagnostics in the Division of Pathology and Laboratory Medicine, likens progress to that of human evolution. "What we're hoping is that this clinical protocol pushes solid tumor testing more along the evolutionary line," he said. "In a relatively short period of time, about 20 years, we've really come a long way in solid tumor molecular diagnostics."

CMS400 can identify 409 mutations, eight times more than the previous standard CMS50 test. "The CMS50 approach works well for bread-and-butter oncology issues," or common cancers for which there are known treatments, Broaddus said. However, "there are a lot of not bread-and-butter oncologic issues where standard therapeutic approaches have failed."

The CMS400 protocol, sponsored by the MD Anderson Provost's Office, will continue for the next several months to enroll patients with advanced solid tumors. The two major facets of the protocol are to determine if an expanded NGS platform is clinically useful and to enroll patients on an appropriate targeted therapy trial when actionable mutations are detected. An actionable mutation for this trial is defined as one that can be therapeutically targeted in a clinical trial available at MD Anderson.

Included in the first 200 patients analyzed is a subset of patients who have multiple actionable genes. So far, CMS400 is identifying more potential targets, including many variants of unknown functional significance, or VUSs, than CMS50. "Further study of these VUSs is a tremendous opportunity for scientific advances," Broaddus said.

Patients with mutations in genes that are potentially actionable have access to a decision support team in the Institute for Personalized Cancer Therapy (IPCT) that can help evaluate each mutation found to determine whether there is scientific data to support a recommendation of a targeted therapy specific to that patient. Kenna Shaw, PhD, Executive Director of the IPCT, suggests that such a support system is necessary to "ensure that use of molecular testing data to inform care decisions is consistent and effective so we can improve how genomics informs patient care" at MD Anderson. Other co-principal investigators for this protocol are Scott Kopetz, MD, PhD, associate professor of Gastrointestinal Medical Oncology, and Jack Lee, PhD, professor of Biostatistics.

The spectrum of tumor types and organ sites examined so far include colorectal, head and neck, breast, and lung, and a fair number of rare cancer types such as sarcoma. In addition to analyzing 409 mutations, CMS400 can detect gene amplifications, although it wasn't specifically designed to do so. This is important, as there are currently about 20 clinical trials enrolling patients on amplifications.

By Claire Blondeau

Hope is on the horizon for cMET inhibitors

Overexpressed in many solid tumors, the cMET proto-oncogene is considered a promising target for drug development. The cMET and its associated ligand—the hepatocyte growth factor (HGF)—act as a receptor tyrosine kinase and trigger many cellular growth pathways in aggressive cancers.

David Hong, MD, associate professor and deputy chair of Investigational Cancer Therapeutics, leads eight clinical protocols—five of them currently recruiting patients—on drugs directly inhibiting the cMET receptor. "We clearly know that cMET gene amplification is associated with poor prognosis," he said. "It may have a role in epithelial-mesenchymal transition; it may have a role in drug resistance. It's also closely tied to the epidermal growth factor receptor (EGFR), whose interaction with cMET is important."

In a study published in Clinical Cancer Research in 2014, Hong and his colleagues analyzed more than 1,000 patients with advanced solid tumors over a period of two years to learn that patients with the amplified cMET gene—while making up only 2.6% of the study population—had tumors with higher histological grading and a greater number of metastases. These patients frequently had mutated BRAF oncogenes and losses in tumor-suppressing PTEN genes but showed variable responses to targeted therapies, suggesting a need for deeper insights into the biology of this oncogene.

However, while many drug companies continue to develop cMET inhibitors, either as monoclonal antibodies or tyrosine kinase inhibitors, these drugs have not seen many recent successes. In March 2014, the phase III METLung trial of the cMET antibody onartuzumab in combination with the EGFR inhibitor erlotinib in patients with advanced non-small cell lung cancer was stopped due to insufficient clinical efficacy, despite positive reports from the earlier phase II trial. In November 2014, Phase III trials of the anti-HGF antibody rilotumumab in advanced gastric cancer were halted following safety concerns. While Hong acknowledged that these results are disappointing, he emphasized that deeper subset analyses to define specific levels of cMET amplification are critical to identify biomarkers of benefit. He cited the example of the successful phase I study of crizotinib—a drug that inhibits cMET/HGF, the anaplastic lymphoma kinase (ALK), and the ROS1 oncogene—in non-small cell lung cancer that showed enhanced drug efficacy in tumors with the highest cMET amplification. This study categorized cMET amplification in tumors into three groups—low, intermediate, and high—as measured by visualizing the number of gene copies in the tumors by fluorescent in situ hybridization (FISH) instead of immunohistochemical analyses that only indicate protein overexpression. "The criteria as to how cMET amplification can be defined is fairly loose and hasn't been fixed," he said.

In his own experience with multiple cMET inhibitors, Hong thinks there is hope yet. "There does seem to be a subset of patients who benefit. And it appears to correlate with very high amplification of cMET, even though that population may be very small," he stated. "We don't fully understand all of the reasons for that. There may be other concomitant pathways or the absence of concomitant pathways in these patients that maybe of prognostic value." He said that patients in his trial on the cMET tyrosine kinase inhibitor AMG337 in gastric and esophageal cancer showed a preliminary response rate of 50%. All of these patients had cMET amplification, but the responders tended to have higher amplification. The team is looking forward to expanding the trial to other tumor subtypes, including clear cell sarcoma, and is analyzing additional biomarkers of interest.

Hong envisions that cMET inhibitors can be best used clinically by tailoring their effects to benefit patients by a couple of different strategies. One is to narrow the population to truly identify patients who benefit by developing clinical biomarkers. The other is to find the most synergistic drug for combination therapy, such as EGFR inhibitors. Considering that cMET is often overexpressed following resistance to EGFR inhibitors, he stated that these studies need to consider many different factors. "There may be more to it than just combining the two, even the timing of these two drugs in combination," he said. "We still need to figure out a lot of things."

By Parvathy Hariharan

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IMPACT 2 aims to transform cancer treatment

Researchers seek to determine whether patients treated with a targeted therapy selected on the basis of mutational analysis of the tumor have longer progression-free survival than those whose treatment is not selected based on alteration analysis.

The Initiative for Molecular Profiling and Advanced Cancer Therapy (IMPACT) 2 trial is a large-scale, randomized Phase II study that assigns precision treatment to patients after profiling the molecular makeup of their metastatic cancers. This study builds upon the results of the first IMPACT protocol, which found that in patients with one molecular alteration, the clinical outcomes were significantly higher in patients treated with matched targeted therapy compared to those treated with non-matched therapy.

"If the results of the first IMPACT trial are confirmed and we demonstrate that therapy targeting molecular alterations–that is, precision medicine–is superior to the standard approach, then the treatment of cancer will be transformed," said principal investigator Apostolia Tsimberidou, MD, PhD, associate professor of Investigational Cancer Therapeutics.

Opportunity for patients to receive targeted therapies

IMPACT 2, which was activated in May 2014 (ClinicalTrials.gov identifier: NCT02152254), seeks to enroll approximately 1,400 patients with metastatic cancer (any tumor type) who have received up to three prior therapies. Patients will undergo tumor biopsy followed by molecular profiling via a comprehensive genomic profiling assay, provided by the Massachusetts-based company Foundation Medicine, which can identify 315 cancer-related genes and 28 other genes often rearranged in cancer.

Advances in biomarker identification

A tumor board that consists of investigators from each participating department establishes the ordered list of alterations and ordered list of trials and drugs that may depend on organ site. The board uses a standardized treatment algorithm that is updated weekly based on the available clinical trials that are actively recruiting patients.

Since joining MD Anderson in 1998, Tsimberidou's quest has been to recast cancer treatment from one-size-fits-all to personalized medicine. She has designed more than 20 clinical trials. She is widely published and is a frequent keynote speaker at national and international conferences and academic institutions, and her work has been extensively covered by the mass media.

By Claire Blondeau

Basket Trials continued from page 2

to warrant use of those drugs in rare tumor types that would be otherwise neglected. The structure of basket studies can also be a learning experience for companies with potential implications for future trials with more patients. Faculty members also predict a growing interest in basket trials as our knowledge of predictive biomarkers continues to expand. Meric-Bernstam envisions that their evolving landscape will explore combinations of multiple agents.

Sarina Piha-Paul, MD, an assistant professor of ICT who leads seven such studies, agrees that the biggest benefit of basket trials is demonstrating the rationale behind targeted therapy that will eventually enable widespread genomic testing. "The responsibility to prove that it's appropriate to target therapies to tumor genetics falls on us," she says. "We have to continue doing this work in order to push the field of cancer research forward."

Active Phase I Program Protocols
March 2015

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ADVANCED CANCERS

Protocol #	Title	Mechanism of Action	Principal Investigator	Age Requirement	Stable CNS metastases allowed?
2008-0384	A Phase I Trial of Doxil, Bevacizumab and Temsirolimus	Anthracycline antibiotic, monoclonal antibody, and mTOR inhibitor	Daniel Karp, MD	≥ 15	Yes
2009-0583	A Phase I Open-Label, Non-Randomized, Dose-Escalation First-in-Human Trial to Investigate the cMET Kinase Inhibitor EMD 1214063 Under Two Different Regimens in Subjects with Advanced Solid Tumors	cMET inhibitor	David Hong, MD	≥18	Yes
2009-0729	A Phase I Trial of Sirolimus (mTOR inhibitor) and Vorinostat (Histone Deacetylase Inhibitor) in Patients with Advanced Cancer	mTOR inhibitor combined with histone deacetylase inhibitor	Filip Janku, MD, PhD	≥ 15	Yes
2009-0855	Phase I Study of Combination of Nab-paclitaxel, Gemcitabine, and Bevacizumab in Advanced Malignancies	Recombinant monoclonal antibody, nanoparticle albumin-bound paclitaxel, chemotherapy agent	David Hong, MD	≥ 15	Yes
2010-0413	A Phase I Clinical Trial of Hepatic Arterial Infusion of Oxaliplatin, Oral Capecitabine With or Without Systemic Bevacizumab for Patients with Advanced Cancer Metastatic to the Liver	Regional (hepatic) chemotherapy with DNA synthesis inhibitor, with or without VEGF inhibitor	Apostolia Tsimberidou, MD, PhD	≥ 18	Yes
2010-0486	Phase I Trial of Bevacizumab and Temsirolimus in Combination with 1) Carboplatin, 2) Paclitaxel, 3) Sorafenib for the Treatment of Advanced Cancer	Anti-VEGF monoclonal antibody and mTOR inhibitor combined with alkylating agent, mitotic inhibitor, or RAF kinase/VEGFR inhibitor	Shannon Westin, MD	≥ 15	Yes
2010-0504	Hormone Receptor Positive Disease Across Solid Tumor Types: A Phase I Study of Single-Agent Hormone Blockade and Combination Approaches with Targeted Agents Selected to Provide Synergy and Overcome Resistance	Hormone blocker	Jennifer Wheler, MD	≥ 18	Yes
2010-0588	A Phase I Trial of Sirolimus (mTOR Inhibitor) or Vorinostat (HDAC Inhibitor) in Combination with Hydroxychloroquine (Autophagy Inhibitor) in Patients with Advanced Malignancies	mTOR, HDAC inhibitors combined with autophagy inhibitor	Filip Janku, MD, PhD	≥ 18	Yes
2010-0671	A Phase I, First-in-Human Study Evaluating the Safety, Tolerability, and Pharmacokinetics of AMG 337 in Adult Subjects with Advanced Solid Tumors	cMET inhibitor	David Hong, MD	≥ 18	Yes
2011-0051	A Phase I Study of Pazopanib and Vorinostat in Patients with Advanced Malignancies	Angiogenesis inhibitor combined with a HDAC inhibitor	Siqing Fu, MD, PhD	≥ 18	Yes
2011-0530	A Phase I Study Determining the Safety and Tolerability of Combination Therapy with Pazopanib, a VEGFR/PDGFR/ Raf with MEK inhibitor Inhibitor, and GSK1120212, a MEK Inhibitor, in Advanced Solid tumors Enriched with Patients with Advanced Differentiated Thyroid Cancer	VEGFR/PDGFR/Raf inhibitor combined	Siqing Fu, MD, PhD	≥ 18	Yes
2011-0686	A Phase I, Open-Label, Dose Escalation Study or Oral LGK974 in Patients with Malignancies Dependent on Wnt Ligands	Wnt pathway inhibitor	Filip Janku, MD, PhD	≥ 18	Yes CNS met but no CNS primary
2011-0916	A Phase I Dose-Escalation Study of Erlotinib in Combination with Pralatrexate in Subjects with Advanced Cancer	EGFR inhibitor combined with dihydrofolate reductase (DHFR) inhibitor	Jennifer Wheler, MD	≥ 15	Yes
2011-0923	Phase I Study of Temsirolimus in Combination with Metformin in Patients with Advanced Cancers	mTOR inhibitors	Aung Naing, MD	≥ 15	Yes
2011-0953	A Phase 1 Trial of Vandetanib (a multi-kinase inhibitor of EGFR, VEGFR and RET inhibitor) in Combination with Everolimus (an mTOR inhibitor) in Advanced Cancer	EGFR/VEGFR/RET inhibitor and mTOR inhibitor	Vivek Subbiah, MD	≥ 15	Yes
2011-1043	A Phase I Trial of Anakinra (IL-1 receptor antagonist) or Denosumab (anti-RANKL monoclonal antibody) in Combination with Everolimus (mTOR inhibitor) in Patients with Advanced Malignancies	IL-1R antagonist or anti-RANKL monoclonal antibody combined with mTOR inhibitor	Filip Janku, MD, PhD	≥ 15	Yes
2011-1159	A Phase 1, Multicenter, Open-label Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of MEDI0639 in Adult Subjects with Advanced Solid Tumors	Monoclonal antibody as notch inhibitor	Aung Naing, MD	≥ 18	No
2011-1183	A Phase I Trial of Sorafenib (CRAF, BRAF, KIT, RET, VEGFR, PDGFR Inhibitor) or Crizotinib (MET, ALK, ROS1 inhibitor) in Combination with Vemurafenib (BRAF Inhibitor) in Patients with Advanced Malignancies	BRAF inhibitor combined with CRAF, BRAF, KIT, RET, VEGFR, PDGFR inhibitor	Filip Janku, MD, PhD	≥ 18	Yes
2012-0061	A Phase I Trial of Bevacizumab, Temsirolimus Alone and in Combination with Valproic Acid or Cetuximab in Patients with Advanced Malignancy and Other Indications	Anti-VEGF monoclonal antibody and mTOR inhibitor combined with histone deacetylase inhibitor or EGFR inhibitor	Sarina Piha-Paul, MD	≥ 15	Yes

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 8:00 a.m. to 8:30 a.m. in the Rotary House, first floor conference rooms A/B/C.

Emailing the patient's name and record number to Ly M. Nguyen, senior study coordinator, by noon Tuesday is recommended, but not mandatory, to add a case to the meeting agenda.

Protocol #	Title	Mechanism of Action	Principal Investigator	Age Requirement	Stable CNS metastases allowed?
2012-0119	An Open-Label, Phase II Study of Vemurafenib in Patients with BRAF V600 Mutation-Positive Cancers	BRAF inhibitor	Vivek Subbiah, MD	≥ 18	Yes
2012-0153	A Phase I Dose-Escalation Study of the BRAF Inhibitor Vemurafenib (Zelboraf) in Combination with the mTOR Inhibitor Everolimus (Afinitor) in Subjects with Advanced Cancer	BRAF inhibitor combined with mTOR inhibitor	Vivek Subbiah, MD		
2012-0256	Initial Phase I Study of WT2725 Dosing Emulsion in Patients with Advanced Solid Malignancies	Wilms' tumor gene product 1 (WT1) antigen peptide	Siqing Fu, MD, PhD	≥ 18	Yes
2012-0394	Phase I Study of the Combination of Vemurafenib with Carboplatin and Paclitaxel in Patients with Advanced Malignancy	BRAF inhibitor with alkylating agent and antimitotic agent	Filip Janku, MD, PhD	≥ 15	Yes
2012-0423	A Phase I Trial of GSK2118436 (BRAFi) and Pazopanib in Patients with BRAF-Mutated Advanced Malignant Tumors	BRAF inhibitor combined with anti-angiogenesis agent	Filip Janku, MD, PhD	≥ 18	Yes
2012-0533	Phase 1 Trial of ADI PEG 20 plus Cisplatin in Patients with Metastatic Melanoma or other Argininosuccinate Synthetase (ASS) Deficient Advanced Solid Malignancies	Pegylated arginine deiminase (alkylating agent) plus chemotherapy	Siqing Fu, MD, PhD	≥ 18	Yes
2012-0721	A Phase I Trial of Dasatinib in Combination with Crizotinib in Patients with Advanced Malignancies	BCR-ABL, c-KIT, EPHA2 and PDGFRβ inhibitor combined with ALK, c-MET, and ROS1 receptor tyrosine kinase inhibitor	David Hong, MD	≥ 18	Yes
2012-0748	A Phase I Trial of Vemurafenib in Combination with Cetuximab and Irinotecan in Patients with BRAF (V600E) Mutant Advanced Solid Malignancies	BRAF inhibitor + EGFR inhibitor and DNA topoisomerase I inhibitor	David Hong, MD	≥ 18	Yes
2012-0784	A Phase I Trial of Ipilimumab (Immunotherapy) and Imatinib Mesylate (c-Kit inhibitor) in Patients with Advanced Malignancies	Anti CTLA-4 antibody combined with tyrosine kinase inhibitor	David Hong, MD	≥ 15	Yes
2012-0795	A Phase I Trial of Ipilimumab (anti CTLA-4 antibody) in Combination with Lenalidomide (IMiD) in Patients with Advanced Malignancies	Anti CTLA-4 antibody combined with antiangiogenesis agent	Filip Janku, MD, PhD	≥ 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
2013-0372	A Phase I Pharmacokinetics Study of Oral MLN9708 in Patients with Advanced Solid Tumors or Hematologic Malignancies with Varying Degrees of Liver Dysfunction	Proteasome inhibitor	Siqing Fu, MD, PhD	≥ 18	Yes
2013-0466	A Phase 1 Dose-Escalation and Pharmacokinetic Study of NC-4016 in Patients With Advanced Solid Tumors or Lymphoma	Polymeric micellar nanoparticle of oxaliplatin metabolite	Vivek Subbiah, 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	No
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, PhD	≥ 18	Yes
2013-0574	Phase 1 Dose-Escalation, Safety, Pharmacokinetic and Pharmacodynamic Study of BVD-523 in Patients with Advanced Malignancies	ERK inhibitor	Filip Janku, MD, PhD	≥ 18	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
2013-0633	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 1A: ≥ 16 Part 1B: 12 - 15 Part 2 (expansion): ≥ 16, then 12 - 15 once	No brain primaries but allows brain mets
2013-0684	A Multicenter Phase I Study of MRX34, MicroRNA miR-RX34 Liposomal Injection	Micro ribonucleic acid	David Hong, MD	≥ 18	Yes
2013-0813	A Phase Ib Open-Label, Multi-Center, 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
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
2013-0918	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	Siqing Fu, MD, PhD	≥ 18	Yes if stable
2014-0069	A Dose-Finding Phase 1 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 2 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
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 (Viju Bhadkamkar)	Apostolia Tsimberidou, MD, PhD	≥ 18	No
2014-0512	A Phase 1/2A, 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	Jennifer Wheler, MD	≥ 18	Yes, if asymptomatic and off anticonvulsants or steroids for at least 2 weeks

SOLID TUMORS

Protocol #	Title	Mechanism of Action	Principal Investigator	Age Requirement	Stable CNS metastases allowed?
2009-0716	Phase I Safety and Pharmacokinetic Study of QBI-139 Injection Administered by Weekly Intravenous Infusion in Patients with Refractory Malignancies	Ribonuclease protein antagonist	Jennifer Wheler, MD	≥ 18	Yes
2010-0700	Aerosol Interleukin-2 for Pulmonary Metastases	Aerosol IL-2	Aung Naing, MD	≥ 15	Yes
2010-0801	A Rollover Study to Provide Continued Treatment with GSK2118436 to Subjects with BRAF Mutation-Positive Tumors	BRAF inhibitor	Sarina Piha-Paul, MD	≥ 18	Yes
2011-1009	An Open Label Phase I Dose Escalation Study to Evaluate the the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Maximum Tolerated Dose of the Anti-mesothelin antibody Drug Conjugate BAY 94-9343 in Subjects with Advanced Solid Tumors	Anti-mesothelin antibody conjugate	George Blumenschein, MD	≥ 18	Yes
2012-0186	A Phase I Open-Label Study to Assess the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of BAX69 in Subjects with Malignant Solid Tumors	Anti-macrophage migration inhibitory factor antibody	Apostolia Tsimberidou, MD, PhD	≥ 18	No
2012-0741	Open-Label Dose-Escalation Trial to Evaluate the Safety, Pharmacokinetics, and Pharmacodynamics of Daily Oral MGCD265 Administered without Interruption to Subjects with Advanced Malignancies	c-MET, VEGFR-1,-2,-3, and tyrosine kinase inhibitor	Jennifer Wheler, MD	≥ 18	Yes
2012-0952	Phase I Dose Escalation of Monthly Intravenous Ra-223 Dichloride in Osteosarcoma	Targeted radiopharmaceutical emitting alpha radiation	Vivek Subbiah, MD	≥ 15	Yes
2012-0985	A Phase I Open-Label Dose Escalation Study with Expansion to Assess the Safety and Tolerability of INC280 in Patients with c-MET Dependent Advanced Solid Tumors	cMet inhibitor	David Hong, MD	≥ 18	Yes
2013-0160	A Phase I/II Clinical Trial Evaluating DCVax-Direct, Autologous Activated Dendritic Cells for Intratumoral Injection, in Patients with Solid Tumors	Autologous dendritic cells activated with BCG and IFNγ for intratumoral injection	Vivek Subbiah, MD	≥ 18 ≤ 75	Yes brain primary but no brain mets
2013-0180	Phase 1 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
2013-0346	A Phase Ia/b Non-randomized, Dose Escalation Study of the the Safety, Pharmacokinetics, and Pharmacodynamics of Sterile Compound 31510 (Ubidecarenone, USP) Nanosuspension for Infection Administered Intravenously to Patients with Solid Tumors	Oligonucleotide STAT3 inhibitor	Siqing Fu, MD, PhD	≥ 18	Yes
2013-0549	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
2013-0638	A Phase 1b/2 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
2013-0665	Phase I Study of MLN0128 in Combination with Aflibercept in Patients with Advanced Cancers	mTOR inhibitor and VEGF inhibitor	Aung Naing, MD	≥ 18	Yes
2013-0699	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
2013-0866	A Phase 1, Multi-Center, Open-label Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of AMP-514 in Subjects with Advanced Solid Malignancies	Anti-PD-L1 antibody	Aung Naing, MD	≥ 18	No
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
2013-0961	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
2013-0969	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
2013-1008	A Phase IB Study of MK-3475 in Subjects with Select Advanced Solid Tumors	PD-1 inhibitor	Sarina Piha-Paul, MD	≥ 18	Yes if stable
2013-1031	Phase I Trial of ADI-PEG 20 plus Doxorubicin in Patients with HER2 Negative Metastatic Breast Cancer or Advanced Solid Tumor	Pegylated arginine deaminase (alkylating agent) plus chemotherapy	Siqing Fu, MD, PhD	≥ 18	Yes
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
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	Jennifer Wheler, MD	≥ 18	Yes, if clinically stable for 3 weeks and off corticosteroids or anticonvulsants
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

Protocol #	Title	Mechanism of Action	Principal Investigator	Age Requirement	Stable CNS metastases allowed?
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, and 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
2014-0193	A Phase 1b 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
2014-0338	A Phase I Study of LY3164530, a Bispecific Antibody Targeting MET and EGFR in Patients with Advanced or Metastatic Cancer	MET/EGFR inhibitor	David Hong, MD	≥ 18	No
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
2014-0459	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
2014-0495	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 IL-10	Aung Naing, MD	≥ 18	No
2014-0569	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 anti-convulsives with no LMD
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.
2014-0669	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
2014-0689	Modular Phase II Study to Link Targeted Therapy to Patients with Pathway Activated Tumors: Module 8 – LEE011 for Patients with CDK4/6 Pathway Activated Tumors	CDK4/6 inhibitor	Vivek Subbiah, MD	≥ 18	Yes, if clinically stable with no steroids or anticonvulsants and > 4 weeks from prior tx and no leptomeningeal involvement
2014-0733	A Phase 1, Open-Label, Dose Escalation, Multi-Center Study of ACT-PFK-158, 2HCl in Patients with Advanced Solid Malignancies	PFKFB3 inhibitor	Siqing Fu, MD, PhD	≥ 18	No
2014-0753	A Phase 1/2 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
2014-0763	Phase 1 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-PD-1 and anti CTLA-4 antibody	David Hong, MD	≥ 18	Yes, brain mets allowed if asymptomatic, clinically stable and have not received corticosteroids or anticonvulsants for 28 days prior to screening
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
2014-0878	A Multicenter Phase Ia/1b 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