Department of Investigational Cancer Therapeutics

Phase I Clinical Trials

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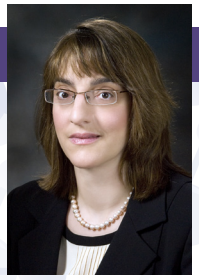
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Making Cancer History®



FROM THE CHAIR

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

I was delighted and honored to be appointed the Chair of The Department of Investigational Cancer Therapeutics at University of Texas MD Anderson Cancer Center in June 2013. The faculty and staff in the department are unparalleled in their experience and commitment to early drug development and research-driven compassionate patient care. The Phase I program at MD Anderson is one of the largest in the world. From September 2012 to August 2013, we saw 1,756 new patients or consults with both common and rare tumor types and enrolled 1,007 patients into therapeutic clinical trials.

This is very exciting era in oncology.

With the increasing availability of molecular profiling as well as a large portfolio of novel molecularly-targeted therapies, the upcoming years will likely be transformative in cancer care. The Department of Investigational Cancer Therapeutics trials have included a broad array of agents, including signal transduction inhibitors, novel nanoparticles, immunologic agents, vaccines, epigenetic modulators, and proteasome inhibitors. We are working hard to stay at the forefront of drug development, by bringing in all novel therapeutic options to our patients. Our goal is to deliver truly personalized treatment, by having a large portfolio of treatment options, and being able to offer all patients specific molecularly targeted therapies targeting the oncologic alterations that are "drivers" of their own tumors.

With the rapid evolution in next generation sequencing, there has been a growing interest in genomically-informed therapy. We are working closely with the MD Anderson Cancer Center Khalifa Institute of Personalized Cancer Therapy to make genomic testing possible for all patients with advanced disease who are considering enrollment on clinical trials.

Our Department has led the way in genomically-informed therapies offered in the Phase I setting. Our early studies have suggested that matching patients to trials targeting the genomic alterations in their tumors may indeed demonstrate improved clinical benefit. In this issue, we highlight clinical benefit from a molecularly matched combination therapy trial in our response highlight corner. As the Food and Drug Administration is starting to consider genotype-selected trials as a path for registration, our Department is well positioned to spearhead such trials, and rapidly determine the clinical benefit of targeting each aberration across many tumor types.

There is a growing interest in delivering genomically informed therapy earlier in the treatment course for advanced disease. We therefore have also activated several Phase II clinical trials that are genotype-selected but histology independent. Thus patients with tumors bearing genomic alterations with many tumor types, including rarer tumor types, will be able to enroll onto these trials. Our clinical trial portfolio includes trials for common alterations such as alterations in PIK3CA, B-Raf, and K-Ras as well as rarer genomic alterations and trials for rarer tumors. On page three we present a clinical trial with bromodomain extra-terminal (BET) inhibitors for NUT midline carcinoma, a rare cancer that arises in the midline and is characterized by a NUT gene translocation that generates a fusion protein with BET proteins. As more therapeutic options become available, we will become more aware of rarer tumor types with clear molecular drivers, and even common tumors will be thought of smaller molecular subtypes.

The biomedical literature is expanding at a daunting rate making it difficult for the practicing oncologists to be able to survey all that is known about an individual gene. Furthermore each specific mutation may have a different impact on protein function, and therapeutic sensitivity. We are thus working closely with the scientists in the MD Anderson Institute for Personalized Cancer Therapy Decision Support Team, the Department of Biomedical Informatics at MD Anderson, and with the University Texas School of Biomedical Informatics through a collaboration funded by the National Cancer Institute. We are actively building a knowledgebase and tools to help guide treatment options in order to prioritize multiple genomic alterations seen, and to select the optimal standard of care or investigational therapy for each individual patient.

It is clear that we all need to work together as a team to deliver the best care to our patients. I would be happy to chat with you in general about genomically-informed therapy or about specific genomic alterations, or about specific patients. I am usually accessible by email: ferric@ mdanderson.org.

RESPONSE HIGHLIGHT

Patient with Metastatic Melanoma Has Durable Response to Combination BRAF/MEK Inhibitor Therapy

– by Christel Bastida, PhD

At first, Sherrie Barefield thought she had a breast lump. After rushing to see her gynecologist, she was told that she did not have a breast cancer, but she did have an enlarged lymph node. The node was biopsied, the result inconclusive. However, after a node was removed, Mrs. Barefield was found to have metastatic melanoma, despite the lack of visible tumor on the skin itself.

While her oncologist felt she had only months to live, Sherrie weighed her options. Then she got a phone call from her sister, who had been researching treatment options online all night. "You're going to MD Anderson," she said. Living in Georgia, Sherrie had never heard of MD Anderson, but was ready to learn about her options.

Mrs. Barefield was first seen by Dr. Papadopoulos in the Melanoma Medical Oncology Department at MD Anderson. She started a combination treatment designed to inhibit the survival and division of cancer cells. Unfortunately, Sherrie experienced several side effects on the regimen. During an appointment, Dr. Papadopoulos said, "I have good news and I have bad news."

Unfortunately, the melanoma was progressing. Dr. Papadopoulos gave her a list of all of the possible treatments she could choose. Among her options was Dr. Gerald Falchook's clinical trial in the Department of Investigational Cancer Therapeutics at MD Anderson that was showing promise in patients with BRAF mutations. There was a spot open on the targeted therapy trial, and Mrs. Barefield decided to go for it.

The first treatment in our department also resulted in side effects and progression. Mrs. Barefield was ready to try a new therapy and had her family's support to help her through it. Dr. Aung Naing treated her with an orally active BRAF inhibitor in combination with a MEK inhibitor. Sherrie's cancer was responsive and her tumors soon shrank. In the following weeks, Mrs. Barefield continued treatment with the help of her family especially her husband, her sister, and her sister-in-law.

On her current treatment, Sherrie has experienced minimal side effects thus far. In fact, she feels great. "People say I don't even look sick. Sometimes I even forget I'm sick. I feel fine!" she enthused.

Mrs. Barefield comes in for checkups and to get her medicine once a month. Some of her laboratory work is done at a hospital close to home. She never travels to MD Anderson alone; she is always accompanied by a member of her family so that she has someone with her when she gets any news, good or bad.

Sherrie and her family have been impressed by the helpfulness and caring attitude of those treating her and also other staff around MD Anderson Cancer Center. People who are diagnosed with cancer sometimes contact her when they want to learn more about MD Anderson and their treatment options, and Sherrie has only wonderful things to say about her treatment here.

Sherrie's new treatment regimen has allowed her to continue living her normal life, and celebrate the holidays unaffected by cancer treatment toxicity. She is looking forward to more time with her family and friends this year.

From the desk of our department administrator

Tandy Tipps, PhD

As we continue to develop our existing relationships both inside and outside of MD Anderson, I would like to acknowledge the contributions of our faculty and staff. Your efforts allow our phase I program to be a place patients turn to for novel treatments for cancer, including malignancies that are rare, late-stage, metastatic, and heavily pretreated.

The anti-tumor activity and minimal side effects seen in patients in our care are a testament to the excellence of the people who work every day to treat our patients. In addition, those who design our studies, analyze data, write protocols, and publish our work are crucial to our performing clinical trials, and carry our message to a wider community. Administrators, your detailed and courteous work ethic keep our department going on a daily basis.

Indeed, the excellent treatment our patients receive here enables our development of relationships with contract research organizations, and pipeline collaborations with pharmaceutical and biotechnology companies; thus, enabling more treatment opportunities for our patients. Further, our relationships involving gene screening with IPCT and our focus on Moonshot goals to advance the treatment of cancer, particularly triple negative breast cancer, are continuing to grow. All of these relationships, in turn, allow us to continue to provide the newest and most promising agents to our patients.

I look forward to assisting in nurturing our current relationships. If you are interested in collaborating with ICT and having ICT as a site for your clinical trial, please do not hesitate to contact me at TRTipps@mdanderson.org.

Study uses BET inhibitor for NUT midline carcinomas and other malignancies

– by Christel Bastida, PhD

As a faculty member in the Department of Investigational Cancer Therapeutics, Dr. Sarina Piha-Paul designs and conducts phase I clinical trials involving new agents targeted to mutations which are particular to a patient's malignancy. Dr. Piha-Paul recently activated a pharmaceutically sponsored, multi-center trial for patients with nuclear protein in testis (NUT) midline carcinomas.

NUT midline carcinoma (NMC) is a rare cancer that usually arises in the midline and is characterized by a NUT gene translocation that generates a fusion protein with bromodomain extra-terminal (BET) proteins. Bromodomains are small protein domains found in a variety of proteins that recognize and bind to acetylated histone tails. This binding affects chromatin structure, and thereby regulates epigenetically controlled processes including gene transcription and mRNA elongation. In this study, Dr. Piha Paul will be using an orally bioavailable small molecule BET inhibitor which is thought to result in inhibition of expression of the translocated NUT gene seen in NMC.

As a newly described disease without specific histology, NMC is often undiagnosed, or mistaken for other entities, including thymic carcinoma, squamous cell carcinoma of the head and neck, lung carcinoma, and Ewing sarcoma. NMC may occur in multiple organ sites and is histologically indistinguishable from other undifferentiated squamous cell carcinomas. NMC is a very aggressive disease that is resistant to therapy and has a median life expectancy of approximately 6.7 months.

According to Dr. Piha-Paul, "What's great about this study is that we can draw attention to a type of cancer that is newly identified and very aggressive." She further explains, "While this type of malignancy is thought to be rare, the actual incidence of NUT midline carcinomas is obscured by the fact that patients are not routinely tested for NUT gene translocations." Patients with poorly differentiated or undifferentiated carcinoma of the upper-aerodigestive tract that are negative on testing for human papilloma virus (HPV) and Epstein-Barr virus (EBV) and are positive for p16, may be appropriate for further testing to determine if they have NMC. NMC is diagnosed by ectopic expression of NUT protein as determined by immunohistochemistry (IHC) and/or detection of NUT gene translocation as determined by fluorescence in-situ hybridization (FISH).

Indeed, the aggressiveness of NUT midline carcinomas and lack of standard treatment for patients with this malignancy have a significant unmet medical need for more effective therapy. Further, recent studies using BET inhibitors in tumor types other than NMC such as colon cancer, neuroblastoma, small cell lung cancer and N-MYC driven cancers (e.g. non-small cell lung cancer) show promise, suggesting that this drug may be efficacious in several tumor types.

BRAF inhibitor and MEK inhibitor combination tested in Phase I trials in ICT now approved by FDA

Recently, the combination of BRAF inhibitor dabrafenib and MEK inhibitor trametinib received accelerated FDA approval for patients with unresectable or metastatic melanoma who have a BRAF V600E or V600K mutation. Preliminary analysis showed greater efficacy with the combination compared to dabrafenib monotherapy in a phase III study. The improved efficacy endpoints included: (1) increase in response rate from 54% to 76%, and (2) increase in response duration from 5.6 months to 10.5 months.

Dabrafenib and trametinib were previously approved in May 2013 separately as a single agents for treatment of BRAF V600E or V600K mutant unresectable or metastatic melanoma. Dabrafenib is a selective BRAF inhibitor and trametinib is a MEK1/2 inhibitor. Both agents target the RAS/RAF/MEK/ERK pathway.

The phase 3 trial was initiated after promising results were observed in the phase 1 study (led by Dr. Falchook in ICT) and the randomized phase 2 study (led by Dr. Kevin Kim in the Dept. of Melanoma), which was published in the New England Journal of Medicine in October 2012. Previous preclinical studies had demonstrated that the combination would be more effective than either drug alone.

Dr. Falchook had this to say of all who contributed to our phase I trial of the combination: "Our work in the phase 1 trial made it possible for this drug combination to proceed to ground-breaking phase 2 and phase 3 trials. Each of you has contributed to this success, directly or indirectly, and your efforts have made a difference. Thousands of patients will benefit from this new treatment. Your dedication is helping to develop better and less toxic treatments for cancer patients. I am proud to work with all of you. Thank you for everything that you do."

Mrs. Barefield, our highlighted patient on page 2, is just one example of a patient whose life was changed as a result of the work of many basic and clinical cancer researchers working together toward the common goal of making cancer history.

– by Christel Bastida, PhD

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Advance Practice Nurse Tiffiny Jackson Excels in Patient Education – by Christel Bastida, PhD

In the clinic, Tiffiny Jackson, an Advance Practice Nurse in the department of Investigational Cancer Therapeutics, is constantly in motion. "I help manage patient symptoms, coordinate getting patients on trials, and assist in getting financial approval for individuals to get on study," says the mid-level provider. Most of the week Tiffiny sees patients, coordinating their care with their physicians.

However, her work in the clinic is just one part of what Ms. Jackson's role in our department. Tiffiny also secured funding from Volunteer Endowment for Patient Support (VPES) fund to produce a patient educational DVD to educate patients and their families on the participation in Phase I clinical trials in the Department of Investigational Cancer Therapeutics.

The video titled "Access to Hope" is shown to potential patients that may enroll in our clinical trials, and is also helpful to patients outside of our department as well. Those interested in participating in clinical trials can benefit from the information provided in the video.

Community outreach is another component of what Tiffiny does to reach out to patients. Tiffiny often speaks to church groups about early detection and clinical trials. "I talk about screenings to community groups, and I talk about clinical trials to patient groups," says Tiffiny, "I really enjoy educating patients about our trials and what we do here in ICT."

Beyond her role in Investigational Cancer Therapeutics, Tiffiny also participates in international efforts to improve access to healthcare. Last year Tiffiny took part in Eucharia Iwuanyanwu's Africa Cancer Care Inc. group to provide medical care for people who would not otherwise have access to care in Nigeria. On the medical mission, the group of provided cancer screenings and basic medical services to patients in Nigeria.

Tiffiny is one of the many great people we have in our department whose interest in quality patient care extends well beyond their role at work.

If you know of patient groups who would like to get more information about clinical trials, please feel free to email Tiffiny at tljackson@mdanderson.org. She would be happy speak to groups about clinical trials, and studies in our department.

To view the video, please visit the MD Anderson website at mdanderson.org, search for "Investigational Cancer Therapeutics." The video is in the bottom right corner of our departmental website.

Active Phase I Program Protocols

March 2014

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
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Protocol #	Title	Mechanism of Action	Principal Investigator	Age Requirement	Stable CNS metastases allowed?	Lymphoma and myeloma allowed?
2008-0384	A Phase I Trial of Doxil, Bevacizumab and Temsirolimus	Anthracycline antibiotic, Monoclonal antibody, and mTOR inhibitor	Daniel Karp, MD	≥12	Yes	Yes
2009-0410	A multi-arm Phase I trial of hepatic arterial infusion of irinotecan with 1) systemic bevacizumab and cetuximab 2) systemic bevacizumab and oxaliplatin 3) systemic bevacizumab in patients with advanced solid tumors metastatic to the liver	Regional (hepatic) and systemic chemotherapy	Apostolia Tsimberidou, MD, PhD	No age limit	Yes	Yes
2009-0521	A Phase I Trial of Dasatinib (Src Inhibitor), Bevacizumab (anti-VEGF monoclonal antibody) and metronomic Paclitaxel in Patients Advanced Malignancies	Src inhibitor combined with anti-VEGF monoclonal antibody and microtubule inhibitor	Filip Janku, MD, PhD	No age limit	Yes	Yes
2009-0583	A Phase I Open-Label, Non-Randomized, Dose-Escalation First-in-Man Trial to Investigate the cMet Kinase Inhibitor EMD 1214063 Under Two Different Regimens in Subjects with Advanced Solid Tumors	cMET inhibitor	Gerald Falchook, MD	≥18	Yes	Yes
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	No
2009-0741	A Phase I Study of Hepatic Arterial Infusion of Abraxane in Combination with Gemcitabine and Bevacizumab for Patients with Advanced Cancers Metastatic to the Liver	Antimicrotubule agent with a nucleoside analog and anti-VEGF monoclonal	Apostolia Tsimberidou, MD, PhD	No age limit	Yes	Yes
2009-0743	A Phase I Trial of Lapatinib in Combination with 1) Sirolimus or 2) Metformin in Advanced Cancer	Tyrosine kinase inhibitor combined with mTOR inhibitor or antihyperglycemic agent	Filip Janku, MD, PhD	No age limit	Yes	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	No age limit	Yes	Yes
2009-0904	A Phase I Study of LY2606368 in Patients with Advanced Cancer	CHK1 inhibitor	David Hong, MD	≥ 18	Yes	Yes
2010-0108	A Phase I Study of Lenalidomide in Combination with Bevacizumab, Sorafenib, Temsirolimus, or 5-Fluorouracil, Leucovorin, Oxaliplatin (FOLFOX) in Patients with Advanced Cancers	Antiangiogenic agent combined with VEGF or tyrosine kinase or mTOR inhibitors or chemotherapy regimen	Apostolia Tsimberidou, MD, PhD	≥ 18	Yes	Yes
2010-0245	Phase Ib Dose Escalation and Biomarker Study of MK-2206 in Combination with Standard Doses of Weekly Paclitaxel in Patients with Locally Advanced or Metastatic Solid Tumors with an Expansion in Advanced Breast Cancer	AKT inhibitor combined with microtubule inhibitor	Stacy Moulder, MD	≥ 18	Yes	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	Yes
2010-0449	A Phase Ia, Multicenter, Open-Label Dose Escalation Study of Oral BYL719, in Adult Patients with Advanced Solid Malignancies, whose Tumors have a Mutation of the PIK3CA Gene	PI3K inhibitor	Filip Janku, MD, PhD	≥ 18	Yes	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 VEGFR inhibitor	anti-VEGF monoclonal antibody and mTOR inhibitor combined with alkylating agent, mitotic inhibitor, or RAF kinase/	Shannon Westin, MD	No age limit	Yes	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	Yes

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 8:00 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?	Lymphoma and myeloma allowed?
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	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	c-Met inhibitor	David Hong, MD	≥ 18	Yes	Yes
2010-0700	Aerosol Interleukin-2 for Pulmonary Metastases	IL-2	Aung Naing, MD	≥ 12	Yes	No
2010-0801	A Rollover Study to Provide Continued Treatment with GSK2118436 to Subjects with BRAF Mutation-Positive Tumors	BRAF inhibitor	Gerald Falchook, MD	≥ 18	Yes	No
2010-0857	Phase I Parallel Protocol of MK-8669 (Ridaforolimus) + MK-2206 and MK-8669 (Ridaforolimuus) + MK-0752 Doublets (MK-MK) in Patients with Advanced Cancer	mTOR inhibitor with AKT inhibitor or Notch inhibitor	Sarina Piha-Paul, MD	≥ 18	Yes	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	Yes
2011-0322	Phase I Combination of Pazopanib and Everolimus in PI3KCA Mutation Postive/PTEN Loss Patients with Advanced Solid tumors Refractory to Standard Therapy	Angiogenesis inhibitor combined with PI3K inhibitor	Jennifer Wheler, MD	+ ≥ 16	Yes	Yes
2011-0399	A Phase I Study of BAY 80-6946 (phosphatidylinositol 3'-kinase inhibitor) in Combination with Paclitaxel in Subjects with Advanced Solid Malignancy	PI3K inhibitor combined with microtubule inhibitor	Jennifer Wheler, MD	≥ 18	No	Yes
2011-0530	A Phase I Study Determining the Safety and Tolerability of Combation Therapy with Pazopanib, a VEGFR/PDGFR/ Raf Inhibitor, and GSK1120212, a MEK Inhibitor, in Advanced Solid tumors Enriched with Patients with Advanced Differentiated Thyroid Cancer	VEGFR/PDGFR/Raf inhibitor combined with MEK inhibitor	Ralph Zinner, MD	≥ 18	Yes	Yes
2011-0554	A Phase II, Open-Label, Single-Arm Study of Brentuximab Vedotin in Patients with CD30-Positive Nonlymphomatous Malignancies	Antimicrotubule CD30 antibody with protease-cleavable linker	Jennifer Wheler, MD	≥ 12	Yes	No
2011-0682	A Phase I Sudy to Evaluate the Safety and Tolerability and Pharmacokinetic/Pharmacodynamics of MK-8242 in Patients with Advanced Solid Tumors	HDM2 inhibitor	David Hong, MD	≥ 18	No	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	Yes
2011-0874	A Phase I, Open-label Dose Escalation Study of the VEGF-C Human Monoclonal Antibody VGX-100 Administered by Intravenous Infusion alone and Co-Administered with Bevacizumab in Adult Patients with Advanced or Metastatic Solid Tumors	VEGF monoclonal antibodies	Gerald Falchook, MD	≥ 18	Yes	Yes
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	No age limit	Yes	Yes
2011-0923	Phase I Study of Temsirolimus in Combination with Metformin in Patients with Advanced Cancers	mTOR inhibitors	Aung Naing, MD	≥ 14	Yes	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	No age limit	Yes	Yes
2011-1009	An Open Label Phase I Dose Escalation Study to Evaluate 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	Ant-mesothelin antibody conjugate	George Blumenschein, Jr, MD	≥ 18	Yes	No
2011-1043	A Phase I Trial of Anakinra (IL-1 receptor antagonist), Denosumab (anti-RANKL monoclonal antibody) or Crizotinib (MET, ALK inhibitor) in Combation with Everolimus (mTOR inhibitor) in Patients with Advanced Malignancies	IL-1R antagonist, anti-RANKL monoclonal antibody, or MET/ALK inhibitor combined with mTOR inhibitor	Filip Janku, MD, PhD	No age limit	Yes	Yes
2011-1054	A Phase I Study of ISIS 481464, an Antisense Oligonucleotide Inhibitor of STAT3, Administered to Patients with Advanced Cancers	Oligonucleotide STAT3 inhibitor	David Hong, MD	≥ 18	No	Yes
2011-1142	A Phase I Trial of Pazopanib or Pemetrexed in Combination with Crizotinib in Patients with Advanced Malignancies	Angiogenesis inhibitor or chemotherapy combined with ALK inhibitor	Ralph Zinner, MD	≥ 13	Yes	Yes
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	Yes

Protocol #	Title	Mechanism of Action	Principal Investigator	Age Requirement	Stable CNS metastases allowed?	Lymphoma and myeloma allowed?
2012-0023	Open-Label, Phase I Study of LOR-253 HCl in Patients with Advanced or Metastatic Solid Tumours	KLF-4 stimulator and angiogenesis inhibitor	Jennifer Wheler, MD	≥ 18	No	Yes
2012-0061	A Phase I Trial of Bevacizumab, Temsirolimus Alone and in Combination with Valproic Acid or Cetuximab in Patients with Advanced Malignancy	Anti-VEGF monoclonal antibody and mTOR inhibitor combined with histone deacetylase inhibitor or EGFR inhibitor	Sarina Piha-Paul, MD	No age limit	Yes	Yes
2012-0119	An Open-Label,Pphase II Study of Vemurafenib in Patients with BRAF V600 Mutation-Positive Cancers	BRAF inhibitor	Vivek Subbiah, MD	≥ 18	Yes	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	No age limit	Yes	Yes
2012-0186	A Phase I Open-Label Study to Assess the Safety, Tolerability, Pharmacokientics, and Pharmacodynamics of BAX69 in Subjects with Malignant Solid Tumors	Anti-macrophage migration inhibitory factor antibody	Apostolia Tsimberidou, MD, PhD	≥ 18	No	No
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	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	Gerald Falchook, MD	≥ 12	Yes	Yes
2012-0401	Phase 1 Study of Anti-TGFBetaRII Monoclonal Antibody IMC-TR1 (LY3022859) in Patients With Advanced Solid Tumors That Have Failed Standard Therapy or for Which No Standard is Available	TGFßII monoclonal antibody	David Hong, MD	≥ 18	Yes	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	Yes
2012-0533	Phase 1 Trial of ADI-PEG 20 plus Cisplatin in Patients with Metastatic Melanoma or other Argininousccinate Synthetase (ASS) Deficient Advanced Solid Malignancies	Pegylated arginine deiminase (alkylating agent) plus chemotherapy	Siqing Fu, MD, PhD	≥ 18	Yes	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,	David Hong, MD/ Denis Fontes Jardim, MD	≥ 18	Yes	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/ Hazem El-Osta, MD	≥ 18	Yes	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	Yes
2012-0795	A Phase I Trial of Ipilimumab (anti CTLA-4 antribody) in Combination with Lenalidomide (IMiD) in Patients with Advanced Malignancies	Anti CTLA-4 antibody combined with antiangiogenesis agent	Filip Janku, MD, PhD	≥ 18	Yes	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	No
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	No
2012-1160	A Phase Ib, Open-Label, Multi-Center, Dose Escalation and Expansion Study for an Orally Administered Combiation of BKM120 Plus MEK162 in Adult Patients with Selected Advanced Solid Tumors	PI3K inhibitor combined with MEK inhibitor	Filip Janku, MD, PhD	≥ 18	Yes	Yes
2013-0064	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	No
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	No	No
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	Yes

Continued

Protocol #	Title	Mechanism of Action	Principal Investigator	Age Requirement	Stable CNS metastases allowed?	Lymphoma and myeloma allowed?
2013-0257	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 and ≤ 75	Yes	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 Administrered Intravenously to Patients with Solid Tumors	Oligonucleotide STAT3 inhibitor	Ralph Zinner, MD	≥ 18	Yes	No
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	Gerald Falchook, MD	≥ 18	Yes	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	Yes
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	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	No
2013-0574	Phase 1 Dose-Escalation, Safety, Pharmacokinetic and Pharmacodynamic Study of BVD-523 in Patients with Advanced Malignances	ERK inhibitor	Filip Janku, MD, PhD	≥ 18	Yes	Yes
2013-0616	A Phase I Study of LY3009120 in Patients with Advanced or Metastatic Cancer	Raf/Ras/MEK/ERK inhibitor	David Hong, MD	≥ 18	Yes	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	Part 1A: ≥ 16 Part 1B: 12 - 15 Part 2 (expansion): ≥ 16, then 12 - 15 once Part 1B has been completed	Yes	Yes
2013-0682	Modular Phase II Study to Link Targeted Therapy to Patients with Pathway Activated Tumors: Module 1 - BKM120 for Patients with PI3K-Activated Tumors	PI3K inhibitor	Sarina Piha-Paul, MD	≥ 18	Yes	Yes
2013-0684	A Multicenter Phase I Study of MRX34, MicroRNA miR-RX34 Liposomal Injection	Micro ribonucleic acid	David Hong, MD	≥ 18	Yes	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 + PI3K inhibitor	Filip Janku, MD, PhD Yes		≥ 18	Yes
2013-0865	Modular phase II study to link targeted therapy to patients with pathway activated tumors: Module 2 - Dovitinib for patients with tumor pathway activations inhibited by dovitinib including tumors with mutations or translocations of FGFR, PDGFR, VEGF, cKIT, FLT3, CSFR1, Trk and RET	Multikinase inhibitor of FGFR, PDGFR, VEGF, cKIT, FLT3, CSFR1, Trk and RET	Sarina Piha-Paul, MD	≥ 18	No	Yes
2013-0904	An Open-Label, Phase 2 Study of Neratinib in Patients with Solid Tumors with Somatic Human Epidermal Growth Factor Receptor (EGFR, HER2, HER3) Mutations or EGFR Gene Amplification	Pan-HER inhibitor	Sarina Piha-Paul, MD	≥ 18	Yes	No