Department of Investigational Cancer Therapeutics

Phase I Clinical Trials

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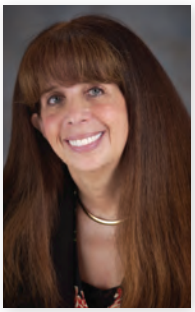
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Making Cancer History®

Complementary and Alternative Therapies:

Bringing Potent Anti-Cancer Properties or Unknown Adverse Drug Interactions to the Clinic?

FROM THE CHAIR



Razelle Kurzrock, MD
Chair, Department of Investigational Cancer Therapeutics

About half of all anti-cancer drugs introduced since the 1940s are natural products or medicines derived from natural products, according to David Newman, DPhil and Gordon Cragg, DPhil of the Natural Products Branch of the National Cancer Institute's Developmental Therapeutics Program *[Journal of Natural Products 2007;70:461-77].* A particularly potent example is paclitaxel, which came from the bark of the Pacific Yew tree. Despite the proven efficacy of pharmaceutical agents derived from nature, Dr. Newman notes that few American companies are investigating natural products as potential sources of potent drugs. However, many cancer patients are trying natural products with putative anti-cancer properties on their own, without the knowledge or supervision of their physicians. Because we frequently find that patients enrolling in Phase I clinical trials in our Clinical Center for Targeted Therapy are also using such complementary and alternative medicine (CAM) products, we decided to do a formal survey of CAM use in our clinic.

Maitake mushroom

Bench to Bedside & Back

Survey Reveals Potential CAM Use Among Patients on Phase I Clinical Trials

An abundance of surveys have revealed a high prevalence of the use of unconventional medical practices, dubbed CAM by the NIH National Center for Complementary and Alternative Medicine (NCCAM), in a variety of populations, including cancer patients. These often include nutraceuticals, herbal formulas, mushrooms, spices, and other biologically active natural products. Because many of these CAM agents may have unknown pharmacologic effects or interactions with experimental drugs prescribed in Phase I clinical trials, Aung Naing, MD, above, assistant professor in Investigational Cancer Therapeutics, and colleagues conducted an anonymous written survey of CAM usage in 309 patients with advanced malignancies seen in the Clinical Center for Targeted Therapy for enrollment in a Phase I clinical trial *[Cancer;Epub: April 28, 2011].* Patients were asked about the use of both pharmacologic (e.g., any oral, topical, or intravenous agent) and nonpharmacologic (e.g., acupuncture, massage, meditation) CAM. Forty percent of patients reported using pharmacologic CAM. The most frequently endorsed reasons for using CAM in general were to do everything possible to fight their cancer and to improve their immune systems, and only five percent reported experiencing any side effects. Less than a quarter of patients failed to fully disclose their CAM use to their physicians, and a physician recommended their CAM use in 22 percent of cases, but the extent to which this nondisclosure referred to pharmacologic vs. nonpharmacologic modalities is unknown.

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Why MD Anderson?

- We are ranked #1 nationwide in cancer care by U.S. News & World Report.
- We lead the way nationally in National Cancer Institute grant awards dollars, receiving nearly $200 million annually.
- We have 12 specialized Programs of Research Excellence (SPORE) awards from the National Institutes of Health, more than any other institution in the country.
- We see 105,219 cancer patients per year, 32,380 of them new patients.
- Nearly 10,000 patients are on therapeutic clinical trials.

Given the high prevalence of CAM use among cancer patients, we recommend encouraging open communication regarding CAM between patients and healthcare providers, especially when experimental therapies are also being administered, because the effects of conventional treatment for cancer can be masked or distorted by CAM use, and failure to engage in effective communication could result in unwanted outcomes. There is an urgent need to educate cancer patients and physicians about CAM usage and possible interactions with prescribed medications. At MD Anderson, patients using CAM can be referred for a consult with Richard Lee, MD, medical director of the Integrative Medicine Center, to prevent potentially adverse interactions with prescribed drugs.

Clinical Trials Combine CAM Agents with Conventional Drugs to Detect Possible Interactions

To determine whether and how natural products reported to have anti-cancer properties, such as curcumin or mushroom formulas, might interact with FDA-approved anti-cancer drugs, Siquing Fu, MD, left, assistant professor in Investigational Cancer Therapeutics, is conducting clinical studies of these products in combination with FDA-approved anti-cancer drugs. This interaction may be synergistic to enhance response, interfere with the mechanism of action of the approved drugs, increase toxicity, or have no effect at all, said Dr. Fu. He is currently principal investigator of one recently opened clinical trial combining the epigenetic agent azacytidine with the anti-angiogenic and immunomodulatory agent lenalidomide, and *grifola frondosa,* a mushroom. Currently on hold, two other clinical trials combine curcumin, found in previous studies to have many anti-cancer properties, with the anti-oxidant isoquercitrin in one study and vorinostat, a histone deacetylase (HDAC) inhibitor plus sorafenib, a multikinase inhibitor, in another.

Dr. Fu selects natural products to study by looking at epidemiologic studies, often starting with a significant association found between frequent ingestion of a substance in a country's diet and a much lower than expected incidence of some type of cancer; case series of patients with unexpected marked tumor regressions found to be taking an undisclosed CAM product such as a traditional Chinese medicine remedy; and studies conducted in the laboratory demonstrating potent anti-cancer properties. For example, three patients with advanced hepatocellular carcinoma who were not responding to conventional treatment had dramatic liver mass reductions after using Chinese herbal formulas such as Ling Zhi *[Journal of Clinical Oncology 2011;29:e288-91].* Prepared from an edible mushroom, Ling Zhi proved to have anticancer activity in vitro and in mouse models of cancer. Bharat Aggarwal, MD, professor in Experimental Therapeutics, has published numerous studies about the many potent anti-cancer properties of the spice curcumin as well as new nanoparticle delivery systems developed to enhance its bioavailability *[Biochemical Pharmacology 2010;8:1833-43].*

Clinical studies conducted in our department have also demonstrated that CAM may have antitumor properties and other beneficial effects. As part of a Phase II study, we previously reported two patients who benefitted from use of oral curcumin. One patient exhibited more than 70 percent tumor reduction, albeit short-lived. The other patient had durable minor tumor reduction lasting 2.5 years—a remarkable feat for advanced pancreatic cancer. We hope response rates to this agent will increase with enhanced absorption of the liposomal form of the agent. However, despite the proven safety and lack of toxicity of the curcumin used in these studies, future clinical trials that include curcumin are meeting regulatory hurdles that are difficult to overcome.

Thus, our biggest challenge in conducting studies with CAM is not discovering potential products to investigate, but getting regulatory approval to administer to cancer patients a mushroom or spice that is normally regulated as a food product. Once the food-regulated product such as curcumin is to be used in the clinic, an Investigational New Drug (IND) application must be filed as if it were a drug, and the labeling of the product used in the study must be changed to conform to IND requirements before it can be given to patients. We are currently working hard to meet these regulatory requirements so that these natural products can be studied scientifically, using the same methods used to test any pharmaceutical agent.

curcumin from the spice turmeric

Triplet Targeting mTOR and Angiogenesis Sends Aggressive Metaplastic Breast Cancer into Complete Remission

Laurie Dragon had to make a second home in Houston for eight months when her oncologist in Georgia discovered that her rare form of breast cancer—a high-grade, triple negative, metastatic, sarcomatous type of metaplastic breast cancer—had returned after 15 months in remission. But she looks forward to her semi-annual return visits to MD Anderson's Clinical Center for Targeted Therapy (CCTT) now that she has had a lasting complete response to a Phase I clinical trial of the triple drug combination DAT. The drug regimen DAT consists of the cytotoxic agent liposomal doxorubicin, the anti-angiogenic agent bevacizumab, and temsirolimus, an mTOR inhibitor that also targets VEGF for an enhanced anti-angiogenic effect. Stacy Moulder, MD, right, assistant professor in the Departments of Breast Medical Oncology and Investigational Cancer Therapeutics, is Dragon's oncologist and principal investigator of the trial, and Thorunn Helgason is the senior clinical study coordinator.

Diagnosed in 2007, Dragon initially received standard treatment in Savannah, Georgia of right lumpectomy, adjuvant docetaxel and cyclophosphamide, then radiation to the breast. When a follow-up visit 15 months later revealed biopsy-proven metastatic disease, Dragon's family recommended she go to MD Anderson, where a family member had reported a past positive experience. Dragon initially saw Dr. Daniel Booser in October 2009 in the Breast Center, who referred her to the CCTT for evaluation for possible enrollment in a Phase I clinical trial. "Standard chemotherapy wasn't working, so I wanted to try something new that might work," Dragon commented. "I thought, if I'm going to have treatment, I might as well try something different." After 6 cycles of DAT, then discontinuation of bevacizumab due to proteinuria and grade 2 peripheral edema, a complete response to treatment was confirmed. After eight cycles of treatment, she discontinued protocol therapy and was started on maintenance therapy with intravenous temsirolimus. Dragon has remained disease-free on maintenance therapy and in December 2010, temsirolimus was discontinued and she started a similar medication, everolimus, an oral mTOR inhibitor. "So many patients don't do well with this type of breast cancer, then in walks Laurie Dragon. I get teary when I think about her," said Dr. Moulder as she gave Dragon a hug.

Dragon expressed feeling pleasantly surprised at how differently she has been treated at MD Anderson by all staff and her care team compared with at other hospitals she had attended. "I always look forward to coming back and seeing them. Everyone is very caring, and the attention to treatment procedures is very meticulous," she said. "Dr. Moulder herself called me one night at 10 PM when a blood clot was found in my arm. Her husband added, "They always answered all of our questions and took the time to explain things in laymen's terms—all the procedures and what to expect."

"Dr. Moulder saved my life," said Dragon. "And my family has been very supportive. My kids visited when I lived in Houston for eight months." Her husband added, "I made sure someone was with her at all times. When I couldn't be here, my daughter or sister came. I didn't want her to be alone while she was having treatment." Dragon continued, "I also received lots of community support. Now I have no limits on my activities; I can do anything I want. I work in the yard and garden. I just got a bicycle and I ride that a lot. We have three grown children and nine grandchildren, and we enjoy a lot of family gatherings. " Dragon's advice to anyone thinking of trying an experimental treatment or enrolling in a clinical trial? "Just do it!"

DAT Interrupts Cancer Stem Cell Signaling in Metaplastic Breast Cancer

Metaplastic breast cancer is typically negative for estrogen and progesterone receptors as well as for HER2/neu, but is rich in epithelial to mesenchymal transition (EMT) and cancer stem cell characteristics. These features make it particularly prone to metastasis and resistant to treatment. The DAT regimen was selected for Dragon based on this breast cancer subtype's propensity to carry mutations in PI3K and high activation of components of the PI3K/mTOR pathway, PTEN loss, and high levels of angiogenesis and expression of VEGF and *HIF-1α*. In a case series of five patients treated on the DAT regimen *[Moulder, Moroney, Helgason, Wheler, Booser, Albarracin, Morrow, Koenig, Kurzrock, Journal of Clinical Oncology 2011;29:epub Apr 11],* Dragon had a complete response, yet no *PI3K* mutation or *PTEN* loss was detected in her tumor. Drs. Moulder, Moroney, and Kurzrock surmised that pathway activation might be a better predictor of response for this breast cancer subtype than the mutation analysis that was done on her tumor specimen. Furthermore, because the mutation analysis for PI3K fails to detect about 30 percent of mutations, it is possible that this mutation was missed. In addition, she may have responded to the enhanced anti-angiogenesis conferred by the *mTOR* inhibitor in combination with bevacizumab, which reduces levels of both *HIF-1α* and *VEGF.* This combination could enhance inhibition of the paracrine signaling between cancer stem cells and tumor vasculature, disrupting the vascular niche that is crucial to the viability of cancer stem cells, Dr. Moulder explained. Most importantly, Dr. Moulder and colleagues believe that metaplastic breast cancer can serve as a surrogate for cancer stem cell response in the clinical development of therapies targeted to cancer stem cells.

Dr. Moulder and co-investigators are currently pursuing a nationwide, multicenter Phase II clinical trial of this promising regimen, which will enable the recruitment of enough patients with this rare tumor subtype to assess its efficacy.

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Did You Know That in Fiscal Year 2010...

- There were 118 Phase I clinical trials on the program's priority list?
- 1,182 patients were enrolled in Phase I trials?
- The Clinical Center for Targeted Therapy had 13,677 patient visits—4,991 more than in 2009?
- The department received more than $10 million in peer-reviewed and sponsored research?
- This became the largest program in the world expediting the development of early phase clinical trials of new cancer therapeutic agents?

The goals for Phase I trials in the next couple years are to:

- Move the program toward personalized therapy, fingerprinting patients to predict potential response, and identify preliminary subsets of responsive patients to use as a foundation for Phase II studies.
- Enhance the capacity of Phase I studies to serve as a conduit to Phase II efficacy studies, especially for uncommon tumors, so that early evidence of response can be quickly translated into new treatment.
- Have a large number of high-impact studies, aiming to investigate "the best molecules in the nation."
- Emphasize strongly the quality of patient care, keeping in mind that the patient must always come first, not the study.
- Continue to foster team work and a collaborative atmosphere both within the program and in its interactions with other investigators throughout the institution, so that the ultimate goal of bringing new therapies to cancer patients can be met.
- Further develop the Phase I infrastructure, from faculty to research nurses, coordinators and other personnel, in order to maximize program growth and excellence.

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Active Phase I Program Protocols

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Protocol	Principal Investigator	Drug Mechanisms	Diseases	Comment
BAY 73-4506	George Blumenschein, Jr., MD	Multi-kinase (raf, VEGFR, PDGFR) inhibitor	Advanced cancer	
GSK1120212 and 1) docetaxel 2) erlotinib 3) pemetrexed 4) pemetrexed and carboplatin or 5) nab-paclitaxel	George Blumenschein, Jr., MD	MEK inhibitor combined with chemotherapy	Solid tumors	Allows CNS metastases
*Azacytidine and valproic acid + carboplatin	Gerald Falchook, MD	Histone deacetylase inhibitor, hypomethylating agent, and chemotherapeutic agent	Ovarian cancer	
Bevacizumab and bortezomib	Gerald Falchook, MD	Anti-angiogenic agent and proteasome inhibitor	Advanced cancer	Allows children any age and CNS metastases
Bevacizumab and 1) sunitinib 2) sorafenib 3) erlotinib and cetuximab 4) trastuzumab and lapatinib	Gerald Falchook, MD	Anti-angiogenic agent and multi-kinase inhibitor, EGFR inhibitor, HER2 inhibitor	Advanced cancer	Allows children any age and CNS metastases
GSK 2118436	Gerald Falchook, MD	BRAF inhibitor	Solid tumors	
MLN8237	Gerald Falchook, MD	Aurora kinase inhibitor	Solid tumors	Allows CNS metastases
MLN8237 (enteric coated tablet)	Gerald Falchook, MD	Aurora kinase inhibitor	Solid tumors	Allows CNS metastases
EMD1214063	Gerald Falchook, MD	cMET inhibitor	Advanced cancer	Allows CNS metastases
GSK 1120212	Gerald Falchook, MD	MEK inhibitor	Advanced cancer	Allows CNS metastases
MLN8237 and paclitaxel	Gerald Falchook, MD	Aurora kinase inhibitor	Solid tumors	Allows CNS metastases
EMD1204831	Gerald Falchook, MD	c-MET inhibitor	Solid tumors	Allows CNS metastases
GSK2118436 and GSK1120212	Gerald Falchook, MD	MEK and BRAF inhibitors	Solid tumors	Allows CNS metastases
Trientine and carboplatin	Siqing Fu, MD, PhD	Chelating agent and alkylating agent	Advanced cancer	Allows children any age and CNS metastases
CUDC-101	Siqing Fu, MD, PhD	HDAC/EGFR/Her2 inhibitor	Solid tumors	Allows CNS metastases
Pazopanib and vorinostat	Siqing Fu, MD, PhD	Angiogenesis inhibitor and HDAC inhibitor	Advanced cancer	Allows brain primary and CNS metastases
MK-2206 and paclitaxel	Ana Gonzalez-Angulo, MD	AKT inhibitor combined with microtubule inhibitor	Advanced cancer	Allows brain primary and CNS metastases
BYL719	Ana Gonzalez-Angulo, MD	PI3K inhibitor	Advanced cancer	
*Tipifarnib and sorafenib	David Hong, MD	Combines farnesyltransferase inhibitor (tipifarnib) with raf kinase/ VEGFR inhibitor (sorafenib)	Advanced cancer	
E7080	David Hong, MD	Angiogenesis inhibitor	Advanced cancer	
*Gemcitabine and dasatinib	David Hong, MD	Src inhibitor and anti-metabolite	Solid tumors	Allows CNS metastases
AZD2171 and bevacizumab	David Hong, MD	VEGF inhibitor	Advanced cancer	Allows CNS metastases
*PBI-05204	David Hong, MD	Cytotoxic agent	Advanced cancer	
*BIIB028	David Hong, MD	Hsp90 inhibitor	Solid tumors	
AMG 208	David Hong, MD	c-MET inhibitor	Solid tumors	
*PX866	David Hong, MD	PI3K inhibitor	Solid tumors	
MABp1	David Hong, MD	IL-1α inhibitor (human monoclonal antibody)	Advanced cancer	Allows CNS metastases
Nab-paclitaxel, gemcitabine, bevacizumab	David Hong, MD	Recombinant monoclonal antibody, nanoparticle albumin-bound paclitaxel, chemotherapy agent	Advanced cancer	Allows children any age and CNS metastases
LY2606368	David Hong, MD	CHK1 inhibitor	Advanced cancer	
ABT 348 monotherapy or ABT 348 and 1) carboplatin and gemcitabine or 2) docetaxel ABT 348 BID dosing	David Hong, MD	Aurora kinase inhibitor and VEGF inhibitor combined with alkylating agent/chemotherapy or antimitotic agent	Advanced cancer	

* Closed to new patient entry

Continued on next page

TREATMENT PLANNING CONFERENCE

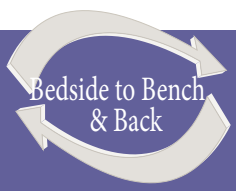
Referring physicians and nurses who want to present patients for possible phase I clinical trial inclusion are invited to attend the weekly treatment planning conference held every Wednesday from 9:00 a.m. to 9:30 a.m. in the Rotary House, first floor conference rooms A/B/C.

Emailing the patient's name and record number to Kristie Lawhorn, RN, research nurse supervisor, by noon Tuesday is recommended, but not mandatory, to add a case to the meeting agenda.

Protocol	Principal Investigator	Drug Mechanisms	Diseases	Comment
Sirolimus and cetuximab	Filip Janku, MD, PhD	mTOR inhibitor, anti-EGFR monoclonal antibody	Advanced cancer	Allows children and CNS metastases
Lapatinib and 1) sirolimus or 2) metformin	Filip Janku, MD, PhD	Tyrosine kinase inhibitor combined with mTOR inhibitor or antihyperglycemic agent	Advanced cancer	Allows children any age and CNS metastases
Hydroxychloroquine and 1) sirolimus or 2) vorinostat	Filip Janku, MD, PhD	Autophagy, mTOR, and HDAC inhibitors	Advanced cancer	Allows CNS metastases
Olanzapine	Razelle Kurzrock, MD	Atypical neuroleptic	Advanced cancer with cachexia	
*R7112	Razelle Kurzrock, MD	MDM2 antagonist	Advanced cancer	
*NPI-0052	Razelle Kurzrock, MD	Proteosome inhibitor	Advanced cancer	No CNS metastases
Doxil, gemcitabine, and Velcade	Razelle Kurzrock, MD	Chemotherapy with proteosome inhibitor	Advanced cancer	Allows children any age and CNS metastases
*AMG655	Razelle Kurzrock, MD	Activating peptide against death receptor (DR5)	Advanced cancer	No CNS metastases
*PRO 1762 (TRAIL)	Razelle Kurzrock, MD	Tumor necrosis-related, apoptosis-inducing ligand	Solid tumors, non-Hodgkins lymphoma	
CNTO 328 rollover	Razelle Kurzrock, MD	Antibody against interleukin-6	Castleman's disease, lymphoid tumors, myeloma	No CNS metastases
Curcumin	Razelle Kurzrock, MD	Plant-derived NFκB inhibitor	Pancreatic cancer	Phase II
Hepatic arterial infusion with abraxane	Razelle Kurzrock, MD	Anti-microtubule agent	Solid tumors	
Doxil, bevacizumab, temsirolimus	Razelle Kurzrock, MD	Anthracycline antibiotic, monoclonal antibody, and mTOR inhibitor	Advanced cancer	Allows children and CNS metastases
Temsirolimus, topotecan, and bortezomib	Razelle Kurzrock, MD	mTOR inhibitor, combined with topoisomerase and proteosome inhibitors	Advanced cancer	Allows children and CNS metastases
*CNTO328	Razelle Kurzrock, MD	IL-6 monoclonal antibody	Solid tumors	
Torisel and PI3 kinase mutations	Razelle Kurzrock, MD	mTOR inhibitor	Advanced cancer	
XL-184 randomized discontinuation	Razelle Kurzrock, MD	MET/RET/VEGFR inhibitor	Advanced cancer	
GSK 2126458	Razelle Kurzrock, MD	PI3K inhibitor	Advanced cancer	Allows CNS metastases
Dasatinib, bevacizumab, paclitaxel	Razelle Kurzrock, MD	Src inhibitor combined with anti-VEGF monoclonal antibody and microtubule inhibitor	Advanced cancer	Liver predominant disease. Allows children any age and CNS metastases
Docetaxel and sirolimus	Razelle Kurzrock, MD	Antimitotic agent and mTOR inhibitor	Advanced cancer	Allows children any age and CNS metastases
Sirolimus and vorinostat	Razelle Kurzrock, MD	mTOR inhibitor combined with histone deacetylase inhibitor	Advanced cancer	Allows children any age and CNS metastases
BKM120 and GSK1120212	Razelle Kurzrock, MD	PI3K and MEK inhibitors	Advanced cancer	Allows CNS metastases
GSK1120212 and GSK2141795	Razelle Kurzrock, MD	MEK and AKT inhibitors	Solid tumor	Allows CNS metastases
Temsirolimus	Razelle Kurzrock, MD	mTOR inhibitor	Advanced cancer	Allows brain primary and CNS metastases
MK-4827 and temozolomide	Razelle Kurzrock, MD	PARP inhibitor and alkylating agent	Advanced cancer	Allows brain primary and CNS metastases
MK-8669 and MK-2206 or MK-0752	Razelle Kurzrock, MD	mTOR and AKT inhibitors or mTOR and notch inhibitor	Advanced cancer	Allows brain primary and CNS metastases
*KX2-391	Aung Naing, MD	Src kinase inhibitor	Advanced cancer	Allows CNS metastases
Valproic acid and 1) sorafenib 2) Sutent 3) dasatinib 4) erlotinib 5) lapatinib or 6) lenalidomide	Aung Naing, MD	HDAC inhibitor Combined with targeted agents	Solid tumors	
*TAS106 and carboplatin	Aung Naing, MD	RNA polymerase inhibitor	Solid tumors	
IMC-A12 and CCI-779	Aung Naing, MD	IGF-1R and mTOR inhibitors	Advanced cancer	Allows children age 16 or older and CNS metastases
MSC1936369B and temsirolimus	Aung Naing, MD	MEK and mTOR inhibitors	Advanced cancer	Allows brain primary and CNS metastases
Bevacizumab and temsirolimus	Sarina Piha-Paul, MD	Monoclonal antibody and mTOR inhibitor	Advanced cancer	Allows children any age
GDC-0449	Sarina Piha-Paul, MD	Hedgehog pathway inhibitor /drug interaction study	Advanced cancer	
IP oxaliplatin and paclitaxel plus IV paclitaxel and bevacizumab	Apostolia Tsimberidou, MD, PhD	Regional (intraperitoneal) therapy	Advanced cancer	Allows children any age and CNS metastases
Hepatic arterial infusion of cisplatinum with IV Doxil	Apostolia Tsimberidou, MD, PhD	Cytotoxic, combined regional and systemic chemotherapy	Advanced cancer	Liver predominant disease. Allows children any age and CNS metastases

Protocol	Principal Investigator	Drug Mechanisms	Diseases	Comment
Hepatic arterial infusion of oxaliplatin and 1) hepatic arterial infusion of fluorouracil with bevacizumab 2) systemic fluorouracil, leucovorin, bevacizumab, and cetuximab 3) bevacizumab or 4) bevacizumab and cetuximab	Apostolia Tsimberidou, MD, PhD	Regional (hepatic) chemotherapy with Avastin	Advanced cancer	Liver predominant disease. Allows children any age and CNS metastases
Hepatic arterial infusion of irinotecan and 1) bevacizumab 2) bevacizumab and oxaliplatin 3) bevacizumab and cetuximab	Apostolia Tsimberidou, MD, PhD	Regional (hepatic) and systemic chemotherapy	Advanced cancer	Liver predominant disease. Allows children any age and CNS metastases
5-azacytidine and oxaliplatin	Apostolia Tsimberidou, MD, PhD	Hypomethylating agent (azacytidine) and platinum compound (oxaliplatin)	Advanced cancer	
Hepatic arterial infusion of abraxane and IV gemcitabine and bevacizumab	Apostolia Tsimberidou, MD, PhD	Antimicrotubule agent with a nucleoside analog and anti-VEGF monoclonal antibody	Advanced cancer	Liver predominant disease. Allows CNS metastases
Bendamustine and bevacizumab	Apostolia Tsimberidou, MD, PhD	Cytotoxic alkylating agent, anti-VEGF monoclonal antibody	Advanced cancer	Allows children age 13 or older and CNS metastases
Lenalidomide with 1) bevacizumab 2) sorafenib 3) temsirolimus or 4) FOLFOX	Apostolia Tsimberidou, MD, PhD	Antiangiogenic agent, VEGF or tyrosine kinase or mTOR inhibitors or chemotherapy regimen	Advanced cancer	Allows CNS metastases
Hepatic arterial infusion of oxaliplatin with 1) capecitabine and bevacizumab or 2) capecitabine	Apostolia Tsimberidou, MD, PhD	Regional (hepatic) chemotherapy with DNA synthesis inhibitor, with or without VEGF inhibitor	Advanced cancer	Liver predominant disease.
Bevacizumab and temsirolimus and 1) carboplatin 2) paclitaxel or 3) sorafenib	Shannon Westin, MD	anti-VEGF monoclonal antibody and mTOR inhibitor combined with alkylating agent, mitotic inhibitor, or RAF kinase/VEGFR inhibitor	Advanced cancer	Allows children any age and CNS metastases
Valproic acid and bevacizumab	Jennifer Wheler, MD	Oral histone deacetylase inhibitor combined with monoclonal antibody against VEGF	Advanced cancer	Allows children any age
XL147 + Taxol/carboplatin	Jennifer Wheler, MD	PI3K inhibitor	Advanced cancer	
*R4733	Jennifer Wheler, MD	Gamma secretase	Solid tumors	
EGFR mutation (umbrella protocol)	Jennifer Wheler, MD	Screening for EGFR mutations	Advanced cancer	
Erlotinib + cetuximab (companion to EGFR mutation umbrella protocol)	Jennifer Wheler, MD	EGFR inhibitor and monoclonal antibody	Advanced cancer	
Erlotinib + bortezomib (companion to EGFR mutation umbrella protocol)	Jennifer Wheler, MD	EGFR inhibitor and proteasome inhibitor	Advanced cancer	
Erlotinib + dasatinib (companion to EGFR mutation umbrella protocol)	Jennifer Wheler, MD	EGFR inhibitor and anti-metabolite	Advanced cancer	
QBI-139	Jennifer Wheler, MD	ribonuclease protein antagonist	Solid tumors	
*GSK2141795	Jennifer Wheler, MD	AKT inhibitor	Advanced cancer	Allows CNS metastases
Anastrozole monotherapy or anastrozole and 1) bevacizumab 2) everolimus 3) sorafenib or 4) erlotinib	Jennifer Wheler, MD	Hormone blocker	Advanced cancer	Allows children any age and CNS metastases

* Closed to new patient entry



Upcoming Phase I Program Protocols

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Protocol	Principal Investigator	Drug Mechanisms	Diseases	Comment
GSK 1120212 rollover	Gerald Falchook, MD	MEK inhibitor	Advanced cancer	Allows CNS metastases
GSK2118436 or GSK2118436/ GSK1120212 BRAF or BRAF/MEK rollover	Gerald Falchook, MD	MEK and BRAF inhibitors	Solid tumors	Allows CNS metastases
Curcumin, vorinostat, and sorafenib	Siqing Fu, MD, PhD	Natural plant-derived NFκB inhibitor, histone deacetylase inhibitor and VEGF inhibitor	Advanced cancer	Allows CNS metastases
Azacytidine, lenalidomide, grifola frondosa	Siqing Fu, MD, PhD	Hypomethylating agent, antiangiogenesis, and maitake mushroom	Advanced cancer	Allows children any age and CNS metastases
Nano-curcumin and/or resveratrol	Siqing Fu, MD, PhD	Natural plant-derived NFkB inhibitor and anticancer agent	Advanced cancer	Allows children any age and CNS metastases
AMG655 rollover	David Hong, MD	Activating peptide against death receptor (DR5)	Advanced cancer	No CNS metastases
BEZ235 and MEK162	Filip Janku, MD, PhD	PI3K and MEK inhibitors	Advanced cancer	Allows CNS metastases
Cetuximab and SIR-Spheres	Razelle Kurzrock, MD	EGFR inhibitor and Yttrium microspheres	Advanced cancer	Allows children any age, brain primary and CNS metastases
Pazopanib and GSK1120212	Razelle Kurzrock, MD	VEGFR/PDGFR/Raf and MEK inhibitors	Advanced cancer	Allows CNS metastases
IL-2 aerosol	Aung Naing, MD	Anti-interleukin-2 aerosol	Advanced cancer with pulmonary metastases	Allows children any age, brain primary and CNS metastases
OSI-906 and AZD6244	Sarina Piha-Paul, MD	IGFR and RAS/RAF/MEK/ERK inhibitors	Advanced cancer	Allows children any age and CNS metastases
BAY-80-6946 and paclitaxel	Jennifer Wheler, MD	PI3K and microtubule inhibitors	Advanced cancer	
Brentuximab Vedotin	Jennifer Wheler, MD	CD-30 antibody	Solid tumors	Allows CNS metastases
MGCD265 and 1) erlotinib or 2) docetaxel	Jennifer Wheler, MD	VEGF/MET and EGFR inhibitors or VEGF/MET inhibitor and antimitotic agent	Advanced cancer	
Pazopanib and everolimus	Jennifer Wheler, MD	Angiogenesis and PI3K inhibitors	Advanced cancer	Allows brain primary and CNS metastases