Neoadjuvant clinical trials: a new paradigm for melanoma treatment

By Michael A. Davies, M.D., Ph.D., Deputy Chair and Associate Professor, Melanoma Medical Oncology

The treatment of melanoma patients with distant metastases, which is also called stage IV disease, has changed dramatically in recent years. After many years of little progress, we are now in the midst of a transformative era in which advances are being made on a regular basis. Six new medications and one combination therapy regimen were approved by the U.S. Food and Drug Administration for the treatment of stage IV melanoma between 2011 and the end of 2014.

These new medications represent a tremendous advance for patients with the most advanced form of melanoma. However, they also present a key opportunity to see if these same medications can be used to improve outcomes in patients with earlier stages of disease.

Surgery remains the mainstay of treatment for patients who present with melanoma in the skin and/or in nearby (“regional”) lymph nodes. Unfortunately, many of these melanomas will recur, either in the same area as the initial surgery or in distant sites in the body.

Systemic treatment after surgery, which is called adjuvant therapy, is given in high-risk patients to reduce the risk of such recurrences. Two different forms of interferon, a cytokine that our bodies normally make when we are fighting the flu, are the only currently approved adjuvant treatments for melanoma.

Treating patients with systemic therapy prior to surgery is a standard practice in many other cancers, such as breast cancer. This approach, which is known as neoadjuvant therapy, can not only reduce the risk of cancer recurrence, but it may also make surgery much easier for the patients if the size of the tumor(s) is reduced. Giving treatment prior to surgery also allows physicians to determine if a treatment is working. This information can let us know whether it makes sense to continue giving the same treatment after surgery, or whether a different treatment should be used to further reduce the chance of relapse.

Historically, a neoadjuvant treatment for melanoma patients undergoing surgery has not been feasible due to a lack of treatments with high response rates. However, due to the development of more effective therapies, we are now opening clinical trials at The University of Texas MD Anderson Cancer Center to test this approach. The initial trials are for melanoma patients with spread of the cancer to the regional lymph nodes (stage III disease).

Dr. Jennifer Wargo, Assistant Professor in Surgical Oncology, is leading a randomized clinical trial in which one-third of patients will undergo standard surgical treatment, and two-thirds of patients will receive neoadjuvant treatment with the targeted therapies dabrafenib (BRAF inhibitor) and trametinib (MEK inhibitor). This trial is open to patients with a Braf mutation, which occurs in ~50% of melanomas of the skin.

In the coming months, Dr. Rodabe Amaria, Assistant Professor in Melanoma Medical Oncology, will lead a randomized clinical trial of neoadjuvant immunotherapy. In this trial, half of the patients will be treated with single-agent nivolumab (PD1 blocking antibody), and half of the patients will be treated with nivolumab in combination with ipilimumab (CTLA4 blocking antibody). This trial will be open to patients with and without Braf mutations.

For patients who have already undergone surgery to remove the lymph nodes, Dr. Sapna Patel, Assistant Professor in Melanoma Medical Oncology, will lead a randomized clinical trial of adjuvant therapy with pembrolizumab versus the current standard of care, interferon. This trial will also be open to patients with and without Braf mutations.

As part of our MD Anderson Melanoma Moon Shot, our team of clinicians and scientists will also work together to study blood and tumors that are collected from patients as a part of these trials. These research studies are designed to improve our ability to predict future patients who will benefit from each of these treatments, and to develop new therapies that are even more effective.

Overall, these exciting clinical trials have the chance to set a new paradigm for the treatment of many melanoma patients, and to lead to more effective, personalized treatments for this disease. To learn more about the MD Anderson Melanoma Moon Shot, visit the website at http://bit.ly/104jyas
The latest news in cancer research, including presentations representing the cutting-edge work of MD Anderson Cancer Center melanoma researchers, attracted more than 25,000 oncology professionals from around the world to the 51st Annual Meeting of the American Society of Clinical Oncology (ASCO), May 29-June 2, 2015 in Chicago.

The 2015 ASCO Annual Meeting focused on the theme of Innovation and Illumination, noting the potential for integrating cancer science and health information technology to achieve more rapid improvements in patient care. Numerous abstracts submitted by MD Anderson researchers, describing early findings from melanoma studies, were selected for presentation at the prestigious meeting.

On May 30, Melanoma Medical Oncology Deputy Chair and Associate Professor Michael A. Davies, M.D., Ph.D., an acclaimed targeted therapy expert, served as an invited discussant in the Melanoma and Skin Cancers oral abstract session, presenting “Response and Resistance with BRAF/MEK Inhibition.”

ASCO Science of Oncology Award recipient and Immunology Chair James P. Allison, Ph.D., who pioneered the checkpoint blockade strategy that led to the development of ipilimumab, presented the award lecture, “Immune Checkpoint Blockade in Cancer Therapy: New Insights, Opportunities, and Prospects for a Cure” in the meeting’s plenary session May 31.

Presentations in the Melanoma/Skin Cancers Poster Session June 1 included the following:

Dr. Davies presented “Demographics, tumor characteristics, and clinical outcomes associated with somatic mutations in 201 cancer-related genes in advanced melanoma patients (pts).” Dr. Davies further served as senior author of a poster presented by Baylor College of Medicine medical resident Jan Kemnade, M.D., Ph.D., “Identification of potentially actionable mutations in RTKs in melanoma detected by next generation sequencing (NGS).”

MD Anderson Surgical Oncology Assistant Professor Jennifer Wargo, M.D., presented the poster, “Neoadjuvant BRAF (dabrafenib) and MEK (trametinib) inhibition for high-risk resectable stage III and IV melanoma.”

Melanoma postdoctoral fellow Junna Oba, M.D., presented the poster, “A global genomic and small molecule inhibitor interrogation of KIT mutant melanoma to reveal underlying biology and novel molecular targets,” whose senior author was Melanoma Assistant Professor Scott Eric Woodman, M.D., Ph.D.

Dr. Woodman also served as senior author of a poster presented by Melanoma senior research programmer Jason Roszik, Ph.D., “A novel algorithm applicable to cancer next-generation sequencing panels to predict total tumor mutation load and correlation with clinical outcomes in melanoma.”

Melanoma Assistant Professor Adi Diab, M.D., presented “Phase I trial of the CKK 4/6 inhibitor, P1446A-05 (voruciclib) in combination with the BRAF inhibitor (BRAFi), vemurafenib in advanced, BRAF-mutant melanoma.”

The posters presented by Dr. Davies, Dr. Wargo, Dr. Oba, and Dr. Roszik were supported by the philanthropic contributions to the MD Anderson Melanoma Moon Shots Program.

Founded in 1964, ASCO is the world’s leading professional organization representing physicians who care for people with cancer. The society, which has more than 35,000 members, is committed to improving cancer care through scientific meetings, educational programs and peer-reviewed journals.
Dr. Wen-Jen Hwu becomes 1st patient care award recipient

MD Anderson’s Melanoma Medical Oncology and Research team is dedicated to helping our patients get the best treatment possible. Gifts from individuals provide a significant portion of the funding needed to get new laboratory and clinical research off the ground. To donate by mail to our melanoma research efforts, please send a check made out to “MD Anderson Cancer Center” specifying “Melanoma Vaccines” in the memo line to: Dr. Patrick Hwu, Chair, Melanoma Medical Oncology Department, MD Anderson Cancer Center, 1515 Holcombe Blvd., unit 430, Houston, TX 77030.

Dr. Patrick Hwu appointed Cancer Medicine Division head

Patrick Hwu, M.D., chair of the Melanoma Medical Oncology and Sarcoma Medical Oncology Departments at MD Anderson Cancer Center, became Head of the Division of Cancer Medicine (DoCM), the largest in the institution, effective March 4, 2015.

Dr. Hwu was selected from a slate of exceptional candidates after a “rigorous and extraordinarily competitive national search,” according to the announcement by Ethan Dmitrovsky, M.D., MD Anderson provost and executive vice president; Thomas Buchholz, M.D., executive vice president and physician-in-chief; and Thomas Burke, M.D., executive vice president, MD Anderson Cancer Network.

“Dr. Hwu is an internationally respected physician-scientist who has 25 years of experience in the fields of tumor immunology, targeted therapies and translational studies,” they noted. “He also is a seasoned leader who remarkably, in addition to chairing two departments, has served as Co-director of our Center for Cancer Immunology Research, Co-director of our immunotherapy platform, Co-leader of our CCG melanoma program and one of the leaders of the Melanoma SPORE. He has accomplished all this with a deep commitment to mentorship and to the highest standards of clinical excellence.”

The announcement cited Dr. Hwu’s impressive academic credentials, scientific and clinical contributions, and his many achievements since he joined the MD Anderson faculty in 2003 as inaugural chair of the Melanoma Medical Oncology Department, including his endowed position as the Sheikh Mohamed Bin Zayed Al Nahyan Distinguished Chair in Cancer Research.

The division, which numbers more than 2,800 employees (including 366 faculty members), encompasses 15 academic medical oncology departments, 10 cancer treatment centers, and an accredited Hematology/Oncology fellowship program.

Gifts fuel MD Anderson melanoma mission: How to help

MD Anderson Melanoma Medical Oncology and Research team is dedicated to helping our patients get the best treatment possible. Gifts from individuals provide a significant portion of the funding needed to get new laboratory and clinical research off the ground. To donate by mail to our melanoma research efforts, please send a check made out to “MD Anderson Cancer Center” specifying “Melanoma Vaccines” in the memo line to: Dr. Patrick Hwu, Chair, Melanoma Medical Oncology Department, MD Anderson Cancer Center, 1515 Holcombe Blvd., unit 430, Houston, TX 77030.
Current Clinical Trials in Melanoma Medical Oncology

For more information on these trials, call the toll-free AskMDAnderson number, 1-877-632-6789. The print version of this list was up to date as of our July 1, 2015 copy deadline. To see all the Melanoma Department clinical trials that are current at any given time, visit the MD Anderson Melanoma Clinical Trials website page at http://bit.ly/1bBxR4l

Neoadjuvant

Neoadjuvant and Adjuvant Dabrafenib and Trametinib Compared to Upfront Surgery in Patients with Clinical Stage III or Oligometastatic Stage IV Melanoma (Combi-Neo) (2014-0409) (NCT02231775)
Principal Investigator: Jennifer Wargo, M.D.
Co-Principal Investigator: Rodabe Amaria, M.D.
The goal of this clinical research study is to compare receiving the combination of dabrafenib and trametinib before surgery to having surgery alone in patients with melanoma. The safety of the study drug combination will also be studied.

Principal Investigator: Sapna Patel, M.D.
The goal of this clinical research study is to learn about the safety of giving LPV7, polyICLC, resiquimod, and montanide ISA 51 to patients with melanoma. Researchers also want to learn if the study drugs cause any changes in the immune system.

Chemotherapy-Naïve Patients (no previous chemotherapy)

Lymphodepletion Plus Adoptive Cell Transfer with TGF-beta Resistant (DNRII) and NGFR Transduced T-Cells Followed by High-Dose Interleukin-2 in Patients with Metastatic Melanoma (2012-0758) (NCT01955460)
Principal Investigator: Patrick Hwu, M.D.
The goal of this clinical research study is to find the highest tolerable dose of T-cells injected with the genes TGF-DNR and NGFR that can be given in combination with chemotherapy (cyclophosphamide and fludarabine) and aldesleukin to patients with metastatic melanoma. This study involves gene therapy. T-cells are types of white blood cells that help your body fight infections. They may recognize and kill melanoma cells. Researchers want to grow your T-cells in a laboratory, inject them with TGF-DNR and NGFR genes which may help them recognize tumors and then give them back to you by vein. This may help to control melanoma. Cyclophosphamide is designed to block cancer cells from dividing, which may slow or stop their growth and spread throughout the body. This may cause the cancer cells to die. Fludarabine is designed to interfere with the DNA (genetic material) of cancer cells, which may cause the cancer cells to die. Aldesleukin is designed to block the activity of cells that may decrease the immune system’s ability to fight cancer.

A Phase I/II Study of Lymphodepletion Plus Adoptive Cell Transfer with T-Cells Transduced with CXCR2 and NGFR Followed by High-Dose Interleukin-2 in Patients with Metastatic Melanoma (2009-0471) (NCT01740557)
Principal Investigator: Patrick Hwu, M.D.
The goal of this clinical research study is to learn the side effects of T-cells injected with CXCR2 and NGFR when given in combination with chemotherapy (cyclophosphamide and fludarabine) and aldesleukin to patients with metastatic melanoma in an attempt to allow them to better localize the tumor. The safety of this combination will also be studied.

BRF117277: A Phase II, Open-Label, Multicentre Study of Dabrafenib plus Trametinib in Subjects with BRAF Mutation-Positive Melanoma that Has Metastasized to the Brain (2013-1020) (NCT02039947)
Principal Investigator: Michael Davies, M.D., Ph.D.
The goal of this clinical research study is to learn if the combination of dabrafenib and trametinib can help to control the disease. The safety of this combination will also be studied.

IPI-Biochemotherapy for Chemonaive Patients with Metastatic Melanoma (2011-0073) (NCT01409174)
Principal Investigator: Rodabe Amaria, M.D.
The goal of the Phase I part of this clinical research study is to find the highest tolerable dose of the drug Yervoy (ipilimumab) that can be given with the drugs Temodar (temozolomide), Intron-A (interferon alfa-2b), Proleukin (aldesleukin, IL-2), and Platirol (cisplatin) to patients with metastatic melanoma. The safety of this combination will also be studied in Phase I. The goal of Phase II is to learn if this combination can help to control metastatic melanoma. Ipilimumab, interferon alfa-2b, and aldesleukin are designed to block the activity of cells that decrease the immune system's ability to fight cancer. Temozolomide is designed to stop cancer cells from making new DNA (the genetic material of cells). This may stop the cancer cells from dividing into new cells. Cisplatin is designed to poison the cancer cells, which may cause them to die.

Phase II Study of Abraxane Plus Ipilimumab in Patients with Metastatic Melanoma (2011-1157) (NCT01827711)
Principal Investigator: Adi Diab, M.D.
The goal of this clinical research study is to learn if the combination of ipilimumab and ABI-007 (abraxane) can help to control metastatic melanoma. The safety of this drug combination will also be studied. Ipilimumab is designed to increase the immune system’s ability to fight cancer. ABI-007 is designed to stop cancer cells from making new DNA (the genetic material of cells.) This may stop the cancer cells from dividing into new cells.

Patients with Previous Chemotherapy

An Open-Label, Multicentre, Corollary Study of Pre-Operative Therapy with Dabrafenib and the Combination of Dabrafenib with Trametinib in Subjects with BRAF Mutation-Positive Metastatic Melanoma to the Brain (2012-0208) (NCT01978236)
Principal Investigator: Michael Davies, M.D., Ph.D.
The goal of this clinical research study is to find the highest tolerable dose of MPDL3280A that can be given in combination with vemurafenib (Zelboraf) to patients with locally advanced or metastatic melanoma that has a BRAF mutation. The safety of the drug combination will also be studied. MPDL3280A is designed to help the immune system recognize the tumors and may help stop their growth. Vemurafenib is designed to block the BRAF gene mutation. This mutation causes cancer cells to grow and multiply. By blocking this mutation, the drug may kill the cancer cells with the mutation and/or stop the tumor from growing.

Expanded Access Program with Nivolumab (BMS-936558) in Combination with Ipilimumab (Yervoy) in Anti-CTLA-4 Treatment-Naive Subjects with Unresectable or Metastatic Melanoma (2014-0639) (NCT02198249)
Principal Investigator: Sapna Patel, M.D.
The goal of this clinical research study is to provide access to nivolumab, given in combination with Yervoy™ (ipilimumab), to patients with metastatic or unresectable melanoma. Researchers also want to learn if this drug combination can help to control the disease. Lab research will be done that may benefit future patients.

An Open-Label, Multicenter, Dose-Escalation, Phase 1b/2 Study of the Safety, Efficacy, Pharmacodynamics, and Pharmacokinetics of RTA 408 in Combination with Ipilimumab in the Treatment of Patients with Unresectable or Metastatic Melanoma (2014-0613) (NCT02259231)
Principal Investigator: Sapna Patel, M.D.
The goal of Part 1 of this clinical research study is to find the highest tolerated dose of RTA 408 that can be given with ipilimumab to patients with unresectable or metastatic melanoma. The safety of this drug combination will also be studied. The goal of Part 2 of this study is to learn if giving RTA 408 with ipilimumab can help to control unresectable or metastatic melanoma.
A Phase I/II Clinical Trial to Study the Safety and Tolerability of MK-3475 Plus Pegylated Interferon alfa-2b (PEG-IFN) and MK-3475 Plus Iplimumab (IPI) in Subjects with Advanced Melanoma (MEL) and Renal Cell Carcinoma (RCC) (Keynote 029) (2014-0032) (NCT02089685)

Principal Investigator: Wen-Jen Hwu, M.D., Ph.D.

The goal of this clinical research study is to find the highest tolerable dose of MK-3475 that can be given in combination with pegylated interferon alfa-2b (PEG-IFN). The safety of these drug combinations will also be studied.

Lymphodepletion Plus Adoptive Cell Transfer with TGF-beta Resistant (DNRII) and NGFR Transduced T-Cells Followed by High-Dose Interleukin-2 in Patients with Metastatic Melanoma (2012-0758) (NCT01955460)

Principal Investigator: Patrick Hwu, M.D.

The goal of this clinical research study is to find the highest tolerable dose of T-cells injected with the genes TGFb-DNR and NGFR that can be given in combination with chemotherapy (cytrophosphamide and fludarabine) and aldesleukin to patients with metastatic melanoma. This study involves gene therapy. T-cells are types of white blood cells that help your body fight infections. They may recognize and kill melanoma cells. Researchers want to grow your T-cells in a laboratory, inject them with TGFb-DNR and NGFR genes which may help them recognize tumor cells, and then give them back to you by vein. This may help to control melanoma. Cyclophosphamide is designed to block cancer cells from dividing, which may slow or stop their growth and spread throughout the body. This may cause the cancer cells to die. Fludarabine is designed to interfere with the DNA (genetic material) of cancer cells, which may cause the cancer cells to die. Aldesleukin is designed to block the activity of cells that may decrease the immune system’s ability to fight cancer.

A Phase I/II Study of Lymphodepletion Plus Adoptive Cell Transfer with T-Cells Transduced with CXC2R and NGFR Followed by High-Dose Interleukin-2 in Patients with Metastatic Melanoma (2009-0471) (NCT01740557)

Principal Investigator: Patrick Hwu, M.D.

The goal of this clinical research study is to learn the side effects of T-cells injected with CXC2R and NGFR when given in combination with chemotherapy (cytrophosphamide and fludarabine) and aldesleukin to patients with metastatic melanoma in an attempt to allow them to better localize the tumor. The safety of this combination will also be studied.

BRF117277: A Phase II, Open-Label, Multicentre Study of Dabrafenib plus Trametinib in Subjects with BRAF Mutation-Positive Melanoma that Has Metastasized to the Brain (2013-1020) (NCT02039947)

Principal Investigator: Michael Davies, M.D., Ph.D.

The goal of this clinical research study is to learn if the combination of dabrafenib and trametinib can help to control BRAF V600 positive melanoma that has spread to the brain. The safety of the study drugs will also be studied.

T-Cells +/- Dendritic Cells (2004-0069) Phase II (NCT00338377)

Principal Investigator: Patrick Hwu, M.D.

In this study, T-cells capable of recognizing and killing melanoma will be isolated from tumor biopsies and expanded in the laboratory. The T-cells will then be reinfused into the patients with or without dendritic cells, which are immune cells capable of potently activating T-cells. This study is for patients with a good performance status, with measurable metastatic melanoma, and a site that can easily be biopsied.

Activation of pDCs at tumor and vaccine sites with TLR agonist (2008-0416) Phase II (NCT00960752)

Principal Investigators: Patrick Hwu, M.D. and Richard Royal, M.D.

In this study, we are combining vaccines with a novel agent called resiquimod that can further stimulate the immune system. For patients with metastatic melanoma with measurable disease, Stage III (in transit lesions) or Stage IV (M1A). Patients must be at least 18 years old, have uncontrolled stage IIIC (in transit lesions) or Stage IV (M1A) melanoma, and a site that can be biopsied. The safety and level of effectiveness of the study drug combination will also be studied.
Selected Presentations

In addition to their outstanding representation at the ASCO Annual Meeting this year, our faculty were invited to participate in these international meetings during the first half of 2015:

MD Anderson Cancer Medicine Division Head and Melanoma Medical Oncology Chair Patrick Hwu, M.D., and Surgical Oncology Assistant Professor Jennifer Wargo, M.D., gave invited presentations at the American Association for Cancer Research (AACR) Annual Meeting 2015, held April 18-22 in Philadelphia. Dr. Hwu presented “Molecular correlates to clinical benefit from T cell adoptive transfer” in a Biomarkers for Immunotherapy Response session, “Recent Advances in Diagnostics and Therapeutics Research.”

Dr. Wargo presented “Therapeutic targeting and monitoring tumor immunity in melanoma” in an AACR educational session. She also presented “Immune effects of targeted therapy and implications for combination strategies” in the Dharma Master Jiantai Symposium in Targeted Therapy: “How to Combine Targeted Therapy with Immunotherapy.”

Melanoma Medical Oncology Assistant Professor Adi Diab, M.D., was awarded a Certificate of Honor at the First Annual Immuno-Oncology Young Investigators’ Forum, April 30-May 3, 2015 in Chicago. Dr. Diab was among a number of researchers from institutions across the nation, including his department colleagues Dr. Isabella C. Glitza and Dr. Dae Won Kim, whose abstracts were chosen for presentation at the meeting.

Dr. Diab’s high-ranking clinical presentation was entitled “Phase I/II Safety and Efficacy Study of Intratumoral TLR7/8 Agonist and CD40 Ligand in Combination with Systemic Ipilimumab or Pembrolizumab in Patients with Metastatic Melanoma.” Melanoma Associate Professor Willem Overwijk, Ph.D., served as moderator of two sessions of the program, which was co-chaired by MD Anderson Immunology Chair James Allison, Ph.D.

Elizabeth A. Grimm, Ph.D., professor in the Department of Melanoma Medical Oncology and deputy head for research affairs in the Division of Cancer Medicine, served as moderator of the “SBRT Primer-SAM” session May 2, 2015 at the 97th Annual Meeting of the American Radium Society, held May 2-5 in Kauai, Hawaii.

On June 18, 2015, at the International Society of Ocular Oncology Meeting (ISOO 2015) in Paris, Melanoma Assistant Professor Scott Eric Woodman, M.D., Ph.D., joined MD Anderson Ophthalmic Plastic Surgery Professor Bita Esmaeili, M.D., to provide an update on the uveal melanoma Texas Cancer Genome Atlas (TCGA) project. The previous month, Dr. Woodman had been named third co-chair of the TCGA Uveal Melanoma Analysis Working Group. A National Institutes of Health research program, TCGA, which is part of the Center for Cancer Genomics at the National Cancer Institute, has helped set the standards for characterizing the genomic underpinnings of dozens of cancers on a large scale.

TCGA researchers currently are mapping the genetic changes in 20 cancers selected for study based on criteria including poor prognosis, overall public health impact, and availability of human tumor and matched-normal tissue samples that meet TCGA standards for patient consent, quality and quantity. Analysis is under way in 13 Analysis Working Groups ranging from cervical cancer to uveal melanoma, the most common primary eye cancer in adults, which develops from melanocytes (melanin pigment containing cells) of the uvea, the middle layer of the eye.

Melanoma Associate Professor Suhendan Ekmeckioglu, Ph.D., presented “Novel therapeutic approaches by targeting CD74 expression in melanoma” in the Melanoma Targeted Drugs Symposium June 21, 2015 at the EACR-AACR-SIC Special Conference on Anticancer Drug Action and Drug Resistance: from Cancer Biology to the Clinic, June 20-23 in Florence, Italy.
highly motivated MD Anderson Melanoma Medical Oncology investigator, armed with an intriguing back story of fighting cancer and an enterprising new research proposal, was recently selected to receive the Melanoma Research Alliance’s coveted Young Investigator Award.

The three-year award, effective May 1, 2015, consists of a grant totaling $225,000 to fund the research work of \textit{Vashisht Yennu Nanda, Ph.D.}, as principal investigator of a project entitled “A novel mitochondrial inhibitor to overcome resistance to MAPK inhibition.”

Dr. Yennu Nanda’s laboratory-based research in our department is focused on understanding the molecular drivers of melanoma growth and metastasis, and using that knowledge to identify molecular diagnostic markers and therapeutic targets. He has continued to pursue an adventurous path since joining MD Anderson Cancer Center in 2000 after obtaining his Ph.D. in biochemistry from the University of Hyderabad in India.

“After acquiring a Ph.D. in cancer drug development in a medicinal chemistry setting, I decided to pursue an academic career in cancer therapy research in a molecular biology setting,” Dr. Yennu Nanda explained. “Being a world-renowned institute for cancer research, MD Anderson was the first choice for me to apply for a postdoctoral fellowship, which I pursued with the help of a U.S. Army Department of Defense postdoctoral award in the Department of Molecular and Cellular Oncology.” In that position, he was able to extend his graduate training in making anticancer chemicals with figuring out the molecular mechanisms of action of anticancer drugs, he said.

“One of my most frustrating observations during my postdoctoral training was that while most cancer cells die in response to anticancer drugs, there are usually some cells left behind that do not seem to be hurt by these drugs,” Dr. Yennu Nanda recalled. That’s also the most frustrating observation in the clinical treatment of cancer patients, where resistance to various treatments is almost universal after an initial response, he noted.

“In 2008, \textit{Dr. Michael Davies} had started a research project in the Department of Melanoma Medical Oncology to understand such resistance at the molecular level, and invited me to work with him on this research as an Instructor, which I accepted;” he recounted. This work identified key mechanisms of resistance of melanoma cells to inhibitors that target the MAPK pathway in oncogenic BRAF mutant tumors, and a mechanism to counteract this resistance, leading to a high-impact publication in \textit{Cancer Research}.

Asked what he regarded as his most significant research accomplishment since arriving in our department, Dr. Yennu Nanda cited the elucidation of mitochondrial oxidative phosphorylation as an important mechanism of resistance to MAPK pathway targeted therapies, and finding a novel method to counteract this resistance. This finding has strong potential for clinical implementation.

Dr. Yennu Nanda then cited another accomplishment of equal value in a different area: “mentoring junior investigators to help them find unique paths to pursue careers in cancer research.”

“It will take an army to cure this disease,” Dr. Yennu Nanda observed. “Being in a position to influence fresh talent to gather their wits against cancer gives me a great sense of pride as an academic researcher, and is the most motivating aspect of my job.”

\textbf{AIM for the CURE Walk slated for September}

Join us for our 2015 AIM for the CURE Melanoma Walk and Fun Run, scheduled for Saturday evening, Sept. 26 at MD Anderson Cancer Center in Houston.

AIM at Melanoma and MD Anderson are partnering again this year to sponsor the annual 5-K walk and fun run, which benefits melanoma research at MD Anderson. This year’s event offers a special attraction: the walk will be emceed by popular ABC-TV Good Morning America anchor \textit{Robin Roberts}.

Melanoma Medical Oncology Deputy Chair \textit{Michael A. Davies, M.D., Ph.D.}, and AIM cofounder \textit{Jean Schlipmann} are scheduled speakers. Free skin cancer screening examinations will take place from 6-9 p.m., and there will be plenty of entertainment, including live music.

The meeting place will be in the Mays Clinic valet area on the MD Anderson campus. Free parking is available in the nearby Pressler garage. Registration sign-in opens at 6 p.m., with the opening ceremony at 7:15 p.m. The walk/run will start at 8 p.m. Further information, including online registration, is available on the AIM at Melanoma website, www.aimatmelanoma.org.
Grateful patient spurs Melanoma nurse’s honor

Melanoma Medical Oncology Professor Wen-Jen Hwu, M.D., Ph.D., has had all kinds of experiences during her decades of clinical practice, but it was a first even for her when one of her patients gave her instructions, rather than the other way around.

When Dr. Hwu entered the examining room where he was waiting, the patient handed her a copy of the Houston Chronicle, showed her the page describing its 2015 “Salute to Nurses” program and campaign to recognize Houston’s top 150 nurses, and told her: “You need to nominate Karen.” He was referring to Medical Oncology Research Nurse Karen Mae Perdon, R.N., whom he had come to know and appreciate as a patient participating in a clinical trial led by Dr. Hwu.

Dr. Hwu was delighted to oblige her patient by filling out the newspaper form nominating Ms. Perdon, describing her as “one of the hardest-working and most productive” individuals with whom she’d ever worked – high praise indeed from Dr. Hwu, who is well known for those traits.

In April, Ms. Perdon received an email from an MD Anderson official that she had been selected as one of the Chronicle’s “Top 150 Nurses in Houston.”