A Baylor Charles A. Sammons Cancer Center Publication on Oncology Innovations

SPRING 2018 | VOLUME 7 | ISSUE 01

CANCER UPDATES

Feature Article

STROKE BY STROKE, SWIM ACROSS AMERICA BENEFITS INNOVATIVE CLINICAL TRIALS CENTER

AT BAYLOR CHARLES A. SAMMONS CANCER CENTER AT DALLAS

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FROM THE MEDICAL

DIRECTOR

Just Keep Swimming

Dory from the movie "Finding Nemo"

In the 3D-animated film "Finding Nemo," Dory utters a phrase that not only summarizes her outlook on life, it also captures the essence of the film; "When life gets you down, you know what you gotta do, just keep swimming."

As a former competitive swimmer, I can relate to this quote. During difficult times, the water was cathartic. I used it to relieve stress and refocus my efforts on what was truly important for me, my future and the future of those around me. I am sure you can relate to difficult times and what approaches you used to keep from drowning in life's choppy waters.

In this issue of *Cancer Updates*, we recognize and celebrate the long-standing and fruitful relationship that Baylor Charles A. Sammons Cancer Center at Baylor University Medical Center, part of Baylor Scott & White Health, has had with Swim Across America (SAA), a philanthropic organization that has donated more than $65 million nationally to cancer research. Locally, SAA Dallas has funded more than $2.1 million of research through the Swim Across America Innovative Clinical Trials Center at Baylor Dallas.

In this issue, you'll learn about SAA grants that helped investigators:

- Study ways to enhance identification of biomarkers for pancreatic cancers
- Study the benefits of dendritic cell vaccination in patients with triple negative breast cancer
- Expand the opportunities to treat multiple myeloma by studying the molecular mechanisms of regulatory elements of the disease

These preliminary studies are critical to laying the groundwork for expanded funding to conduct more extensive research in these areas. Swim Across America is playing a vital role in cancer research funding across the country and here at home through the SAA Integrated Clinical Trials Center. We look forward to a continued beneficial relationship with SAA, one that will further our mission to expand opportunities to diagnose and treat a variety of cancers.

Carlos Becerra, MD
Interim Chief of Oncology, Baylor Scott & White Health – North Texas
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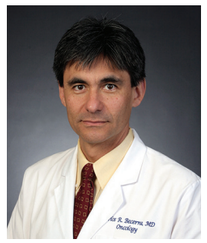


Feature Article

STROKE BY STROKE, SWIM ACROSS AMERICA BENEFITS INNOVATIVE CLINICAL TRIALS CENTER

AT BAYLOR CHARLES A. SAMMONS CANCER CENTER AT DALLAS

In 1975, 12-year-old Jeff Keith from Fairfield, CT, lost his right leg to cancer. Ten years later, he and friend Matt Vossler staged the first Run Across America raising $1 million for cancer research. Keith went on to graduate school and Vossler wanted to continue raising money for research but knew another run across the U.S. wouldn't be feasible. Childhood friends Vossler, Keith and Hugh Curran took to water, creating the first open water fundraising event for cancer. That first swim event—Making Waves to Fight Cancer—evolved into Swim Across America (SAA), a 30-year-old 501c3 nonprofit organization supported by more than 120 Olympians. True to its name, SAA holds dozens of community-oriented open water swims and pool swims from coast to coast to raise funds for local beneficiaries supporting cancer research, prevention and treatment. In fact, the national SAA just announced that Merck, an international health care company, donated $3 million to SAA. Jill DeSimone, senior vice president of U.S. Oncology at Merck, stated, "Swim Across America has created a program that has inspired thousands of Americans, including many Merck employees, to participate in its benefit swims with the proceeds funding cancer research and clinical trials. We know this contribution will help SAA do even more to fight cancer."

On June 11, 2011, SAA-Dallas was created and its first swim event was at Lake Ray Hubbard at the Harbor in Rockwall, Texas. The inaugural swim raised more than $350,000 to benefit the new Innovative Clinical Trials Center (ICTC) at Baylor Charles A. Sammons Cancer Center at Dallas. In 6 years, SAA-Dallas has raised $2 million for the ICTC. Recognizing the importance of the relationship between SAA and Baylor Sammons Cancer Center at Dallas, the ICTC was renamed the Swim Across America Innovative Clinical Trials Center.

Among the swimmers at the inaugural event was Carlos Becerra, MD, medical director of the ICTC and a Masters swimmer. Dr. Becerra was joined by a team of colleagues, coworkers and friends.

Participants in SAA are motivated by a desire to make a meaningful impact in the fight against cancer through their love of swimming. SAA events unite beginning swimmers, recreational swimmers, competitive swimmers, Masters swimmers, Olympians, kayakers, boaters and thousands of volunteers, all committed to finding a cure for cancer. The SAA scoreboard doesn't tally how fast participants swim; it records how much money swimmers raise to fight cancer. In three decades, SAA has raised more than $70 million for cancer research, prevention and treatment.

Baylor Sammons Cancer Center's ICTC is among an elite group of beneficiaries, such as Memorial Sloan-Kettering Cancer Center, Dana Farber Cancer Institute, Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, and the University of California, San Francisco Children's Hospital, that are supported by SAA benefit swims.

According to Daniel Watters, a 1988 Olympian who was part of the inaugural SAA-Dallas organizing committee, SAA chose to support the ICTC at Baylor Sammons Cancer Center after an intensive search looking for the best of the best in terms of cancer research and treatment in North Texas.

"Our niche is funding early stage research and clinical trials that show promise of breakthrough diagnosis and treatment," said Rob Butcher, SAA's chief executive officer. "We are like an angel investor that provides seed money for investigative research so that Dr. Becerra and his team can pilot ideas and collect data that supports hospitals like Baylor Dallas to obtain additional funding from government, commercial, and other sources to expand their research. The desired outcome is that SAA grant dollars will speed up new investment and breakthroughs in how we fight cancer."

Ryan Berube, Olympic gold medal winner who anchored the U.S. men's team in the 4 × 200 freestyle relay at the 1996 Summer Games in Atlanta, Georgia, is the SAA-Dallas cochair. "I have swum in all of the SAA-Dallas events and last year I stepped into the cochair role," said Berube. "The money raised from the six

SAA events in Dallas has been used to fund cancer research in Dallas at the Baylor Sammons Cancer Center ICTC. Our goal is to make a material difference in cancer survival rates. Dr. Becerra and his colleagues have done some magnificent work in pancreatic cancer thanks to SAA funding. We've started to see some impact in the last 2 or 3 years from clinical trials that have gone from phase 1 to phase 2 thanks to additional funding gained by ICTC researchers as a result of their original pilot studies funded by SAA."

The SAA-ICTC consolidates all oncology phase I clinical trials from Baylor University Medical Center, part of Baylor Scott & White Health. Baylor Dallas researchers and their academic and clinical research sponsors are now in one 6376-square-foot facility. These trials offer opportunities for patients to participate in the newest investigative therapies being developed in cancer, therapies that may be the last line of hope for many individuals. At the same time, phase I trials are an essential component in bringing new treatments from the bench to the bedside. The SAA-ICTC is dedicated to providing access to experimental treatments only available in a few centers around the world, including immunotherapeutic options such as cancer vaccines from the Baylor Institute for Immunology Research and pharmaceutical agents selected for specific molecular targets.

> The money raised from the six SAA events in Dallas has been used to fund cancer research in Dallas at the Baylor Sammons Cancer Center ICTC. Our goal is to make a material difference in cancer survival rates. Dr. Becerra and his colleagues have done some magnificent work in pancreatic cancer thanks to SAA funding. We've started to see some impact in the last 2 or 3 years from clinical trials that have gone from phase 1 to phase 2 thanks to additional funding gained by ICTC researchers as a result of their original pilot studies funded by SAA.
>
> **Ryan Berube**
> Olympic gold medal winner and SAA-Dallas cochair

BAYLOR UNIVERSITY MEDICAL CENTER AND BIIR

STUDY DEMONSTRATES BENEFITS OF DENDRITIC CELL VACCINE FOR WOMEN WITH TRIPLE-NEGATIVE BREAST CANCER

It is well known that women with triple-negative breast cancer (TNBC) have higher pathologic complete responses (pCRs) after preoperative chemotherapy than women with other types of breast cancer. This increased pCR translates into a greater disease-free survival than in women with only a partial response to chemotherapy. However, for those women with TNBC who do not attain pCR after treatment, there is a greater risk of cancer recurrence and decreased overall survival compared with non-TNBC patients who do not achieve a pCR. Therefore, it is important to increase the pCR rate in women with TNBC who are positive for estrogen receptor and negative for human epidermal growth factor receptor after neoadjuvant therapy. Immunotherapy is an attractive strategy to treat human breast cancers because the immune system can be a factor not only in the development of a tumor, but also in its elimination. Interestingly, some studies demonstrated that enhancing the immune system in women with breast cancer may augment the cytotoxic effects of standard chemotherapies.

Joyce O'Shaughnessy, MD, an oncologist on the medical staff of Baylor University Medical Center, was a chief investigator for a study that examined the safety and initial clinical efficacy of a personalized dendritic cell (DC) vaccine for use in TNBC patients. The research was conducted at Baylor University Medical Center. Collaborators include the Baylor Institute for Immunology Research (BIIR) and the Jackson Laboratory in Farmington, Connecticut. Vaccination of patients against their tumor-specific antigens promotes immune responses. However, the question is whether the immune responses induced by vaccination successfully fight and defeat cancer.

DCs are antigen-presenting cells that can take up, process and present antigens found in the body to T cells of the immune system. One group of these T cells is CD8+ cytotoxic lymphocytes, which are thought to be the main drivers of antitumor immunity. DCs with antigens cause the differentiation of these antigen-specific CD8+ T cells into effector T cells, which are thought to eliminate cancer cells. In addition to these effector T cells, the DCs induce cells involved in protective T-cell immunity (tumor-specific memory T cells that respond when the tumor relapses). Knowing these traits of DCs, BIIR developed a DC vaccine optimized for CD8+ (cytotoxic) T cells (effector) and tumor-specific memory responses. This vaccine approach has been used successfully in clinical trials for melanoma and HIV.

With this in mind, Dr. O'Shaughnessy collaborated with Karolina Palucka, MD, PhD, an immunologist who was formerly employed by BSWRI ."Ten patients with locally advanced TNBC were chosen for the trial," Dr. O'Shaughnessy said. "The patients received standard preoperative dose-dense doxorubicin/cyclophosphamide chemotherapy followed by paclitaxel and carboplatin chemotherapy, combined with antigen-loaded [antigens found to be overexpressed in TNBC (cyclin B1) and Wilms tumor protein (WT1) along with control viral antigens: cytomegalovirus, Epstein-Barr virus, and influenza virus] autologous monocyte-derived DC vaccinations administered intratumorally and subcutaneously. This approach capitalizes on the unique capacity of DCs to prime lymphocytes and to regulate and maintain immune responses. Only DCs can prime naïve T cells. This feature is essential to successful vaccination, as it might allow generation of a 'new' immune response, possibly not compromised by the cancer."

The DC vaccines were given at four time points before definitive surgery and three times after surgery, both before and after radiation therapy ("booster" vaccines). Biopsies were collected before treatment, before the fourth cycle of doxorubicin/cyclophosphamide (after two vaccinations), and at the time of surgery for those patients with residual disease. These samples were analyzed for the types of immune cell infiltrate and the degree of infiltration. Blood was collected at various time points before and after treatment so the patient's immune system could be monitored during vaccination.

Promising results for patients with TNBC

All patients have completed treatment and are in the follow-up phase of the study. All study enrollees received the four vaccinations during preoperative chemotherapy, and 8 of the 10 women received all seven vaccinations. At the time of definitive surgery, four patients achieved a pCR, three patients had macroscopic residual disease in the breast and axillary lymph nodes, and three patients had residual cancer burden scores of 1 (minimal residual disease).

Since this was a phase I clinical trial, the adverse events during vaccine therapy were investigated. Investigators found that the incidence and grade of chemotherapy-related adverse events were not greater than would be expected with chemotherapy alone. At this phase of the study, the researchers concluded that vaccine preparation and administration were feasible and safe in the outpatient oncology setting. They also found that a combination of intratumoral and subcutaneous administration of an autologous DC vaccine given during neoadjuvant chemotherapy in TNBC patients is safe.

The study was funded through a grant awarded by Baylor Charles A. Sammons Cancer Center's Swim Across America Innovative Clinical Trials Center at Baylor Dallas and by the Baylor Health Care System Foundation Amy T. Selkirk Fund.

BAYLOR CHARLES A. SAMMONS CANCER CENTER'S SWIM ACROSS AMERICA INNOVATIVE CLINICAL TRIALS CENTER AT BAYLOR UNIVERSITY MEDICAL CENTER

PANCREATIC CANCER: EARLY STUDIES IN DETECTION AND TREATMENT

Pancreatic adenocarcinoma (PDAC), the most common type of pancreatic cancer, is the fourth leading cause of cancer-related death in the United States. It is an extremely slow-growing tumor. PDAC normally remains undetectable until late in the disease process, due in part to the physical location of the pancreas. It is situated behind the stomach at the back of the retroperitoneal space, overlaying the aorta, vena cava, and spine, deep inside the body. Because of the location of the pancreas, a computed tomography or magnetic resonance imaging scan is typically needed to detect a lesion, so it may not be discovered until the patient develop symptoms. PDACs located in the head of the pancreas may obstruct the bile duct, resulting in jaundice. Approximately 80 percent of PDAC cases present with this painless jaundice. When the lesion is located in the body or tail of the pancreas, however, the first symptom is likely to be pain associated with invasion of the spleen or stomach, occurring much later in the course of the disease.

Surgery is the only potentially curative treatment for PDAC. But due to the late stage at diagnosis, many patients will not be good candidates for surgery. Tumor staging, based on evidence of peritoneal or hepatic metastases and radiological findings of blood vessel involvement, classifies tumors as resectable, borderline resectable or nonresectable. By these criteria, only 25 to 30 percent of tumors are considered operable or resectable at diagnosis. Thus, treatment with curative intent is very difficult for most patients. Two main areas of research, then, are efforts to increase earlier detection and improve treatment.

Pinpointing biomarkers to improve detection, treatment and monitoring of pancreatic cancer

Biomarkers are any measurable biological molecule that can be found in the tumor, blood or other bodily fluids that signals an abnormal process, such as cancer. Measurement of biomarkers in blood is considered a less invasive method to detect cancer at an early state, measure relapse of disease or determine optimum treatment for a patient. A number of different classes of biomarkers have been studied. Two translational studies funded by the Baylor Charles A. Sammons Cancer Center's Swim Across America Innovative Clinical Trials Center (SAA-ICTC) at Baylor University Medical Center are focused on identifying more precise biomarkers for the early detection, disease monitoring and optimum treatment for pancreatic cancer. These studies utilize two types of analysis—cell-free circulating tumor-specific DNA analysis (ctDNA) and microRNA (miRNA) analysis—looking for the presence of these biomarkers in the blood of patients with pancreatic tumors.

ctDNA analysis for personalized monitoring of pancreatic cancer

Scott Celinski, MD, codirector of the Baylor Pancreatic Cancer Research and Treatment Center and lead investigator, and Muhammed Murtaza, MD, PhD, codirector of the Translational Genomics Research Institute (TGen) Center for Noninvasive Diagnostics and coinvestigator, launched a pilot study to test whether ctDNA in plasma can be used as a personalized biomarker of tumor burden in patients with PDAC. Researchers had previously shown that ctDNA may be useful for monitoring tumor burden and disease progression in a multitude of solid cancers.

To date, the pilot study has enrolled more than 10 patients with PDAC since December 2010. For each patient, serial plasma samples have been collected pre- and postoperatively, along with samples from the resected tumor specimen for genomic analyses. Based on tumor analysis, the researchers develop molecular assays specific to each patient's cancer for personalized monitoring of tumor burden. The goal of the study is to follow each patient longitudinally to determine if these plasma ctDNAs correlate with the presence of the tumor and if there is a drop in the patient- and PDAC-specific biomarkers after removal of the tumor. If ctDNAs do track with the presence or absence of tumor, then they will follow these ctDNAs to see if they change at the time of cancer relapse. Researchers hope that select ctDNAs will allow them to track tumor burden in real time, as the documented half-life in other cancer types is less than 2 hours. They continue to collect plasma and urine samples from the enrolled patients. If initial findings are encouraging, the goal is to pursue extramural grant sources to expand analysis with a larger set of patients.

"So far, we have made progress in two aspects: clinical accrual and technology development," Dr. Murtaza said. "Together with additional support from other grants, we are developing a novel method for personalized ctDNA monitoring to target multiple cancer mutations from each patient's tumor simultaneously. This will enable greater sensitivity and precision in liquid biopsy tests. We are in the final stages of optimizing this method and hope to test its clinical relevance in this pancreatic cancer study shortly."

"Cell-free DNA fragments contributed by a tumor into blood can be measured using molecular analysis for cancer-specific somatic mutations," Dr. Murtaza explained. "ctDNA is therefore an inherently cancer-specific biomarker for solid cancers such as pancreatic cancer. Potential applications of ctDNA analysis include personalized monitoring of tumor burden to detect treatment response, tumor dynamics, minimal residual disease, and relapse, as well as minimally invasive serial investigation of the cancer genome for molecular stratification and tracking subclonal evolution."

During the pilot study, investigators are exploring if personalized ctDNA tracking can be used for assessment of postoperative residual disease, early detection of systemic relapse and disease progression, and rational and informed selection and scheduling of adjuvant chemotherapy.

Next-generation sequencing for detection of miRNA biomarkers for pancreatic cancer

Spurred by the dismal 5-year survival rate for pancreatic cancer patients, Ajay Goel, PhD, investigator and director of the Center for Gastrointestinal Research and director of the Center for Translational Genomics and Oncology at Baylor University Medical Center, launched a study to develop another type of tumor-associated nucleic acid in circulation as a biomarker for PDAC miRNAs. Utilizing the same patient samples as in the study of Drs. Murtaza and Celinski, along with the same patient tracking goals, Dr. Goel used innovative strategies that included next-generation sequencing for genome-wide discovery of highly specific miRNAs in both tissue and serum.

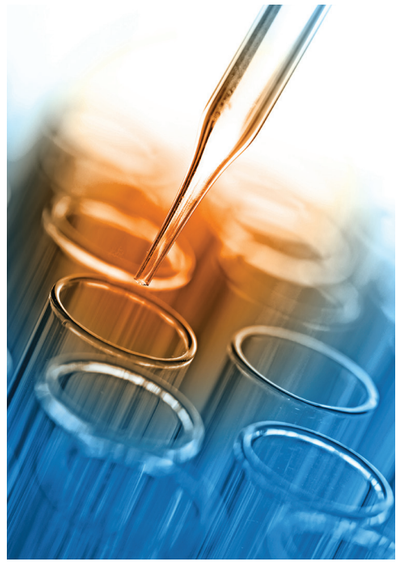
Researchers had previously shown that circulating miRNAs (~22 nucleotides in length) may be useful for monitoring tumor burden and disease progression in a multitude of solid cancers. Small noncoding RNAs, miRNAs, play a pivotal role in the regulation of genes known to be involved in the development of cancer. Accumulating evidence suggests that miRNAs are implicated in the tumorigenesis of every human cancer, including PDAC. As biomarkers, miRNAs are more robust than messenger RNAs, being less prone to degradation in tissues, blood, stool and other bodily fluids.

RNA sequencing has been completed on a small group of healthy volunteers and patients with PDAC. In addition, the research team has identified a panel of miRNAs that can be detected in blood for early detection of PDAC. These initial results were recently presented at the American Gastroenterological Association's annual Digestive Disease Week. The presentation received "Abstract of Distinction" honors. Dr. Goel said the findings are being compiled in anticipation of publication in a scientific journal.

"This study combined recent advances into two areas of circulating biomarkers, ctDNA and miRNAs," explained Dr. Goel. "It leveraged the unique strengths of the exclusive tumor specificity of somatic mutations in ctDNA and the functional insights provided by miRNAs. Our goal was to combine these approaches to identify a set of biomarkers that can sensitively detect early pancreatic cancer while providing specificity for invasive cancer and reducing false-positives from precancerous lesions or nonmalignant pancreatic disease."

Unlike glycoprotein biomarkers, tumor-associated nucleic acids in circulation represent cancer activity exclusively and rely on specific markers for tumor cells such as somatic mutations. Overall, combining the tumor specificity of ctDNA and the functional insight of circulating miRNAs can provide an accurate and informative biomarker for detection, prognosis, and monitoring of pancreatic cancer and for distinguishing PDAC at early stages of development.

Plans for the future for biomarker studies

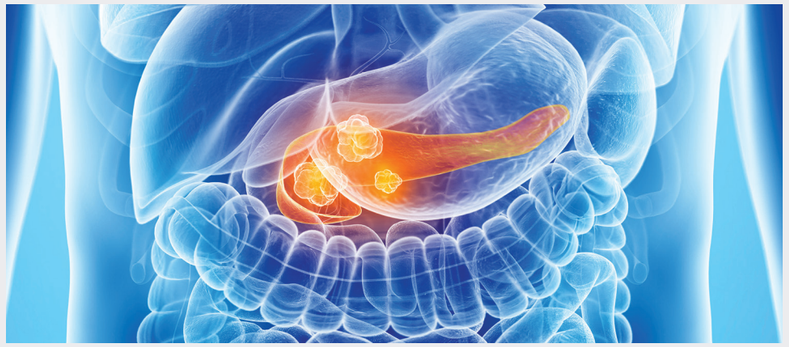


It is well known that assessing treatment response and detecting relapse after surgery in patients with pancreatic cancer is challenging. With development of biomarkers specific for PDAC that can be used for liquid biopsies and disease monitoring, the goal of these studies is to optimize treatment schedules for individual patients with early stage pancreatic cancer. For example, for patients who receive neoadjuvant chemotherapy, investigators may be able to assess within a few weeks whether the patients are benefiting from this treatment or if they would be better off proceeding to surgery right away. Similarly, after patients undergo surgery, they can be monitored for cancer recurrence weeks or months earlier than imaging, potentially improving their outcomes with more timely treatment. Researchers anticipate having preliminary results from the study by 2018.

Dr. Goel and Dr. Murtaza agree that funding preliminary clinical translational studies and the setup of well-annotated patient cohorts is critical to the success of their work. Without the support of organizations like SAA, they said, it would be nearly impossible to pursue novel ideas in translational genomics because it is difficult to secure extramural peer-reviewed funding from sources like the National Institutes for Health without demonstrating preliminary results and having existing clinical cohorts and resources.

A PILOT STUDY INVESTIGATING THE SAFETY OF ANAKINRA COMBINED WITH STANDARD CHEMOTHERAPY REGIMENS IN PATIENTS WITH METASTATIC PANCREATIC DUCTAL ADENOCARCINOMA

Patients with chronic pancreatitis have a greater risk of developing PDAC. In pancreatitis, the pancreas is inflamed, due to the release of digestive enzymes that are normally stored in the pancreas. These digestive enzymes are activated in pancreatitis and attempt to digest the organ, causing inflammation. The presence of inflammation appears to be the key to this increased risk of cancer. Formation of pancreatic cancer is associated with a stromal desmoplastic reaction that causes a dense stroma to surround the cancer cells, making them less responsive to conventional chemotherapies. Inflammation promoting pancreatic cancer



can come from many avenues, including from the interaction between the cancer cells and stroma. A number of studies have shown that secretion of interleukin (IL)-1β, a key mediator of inflammation, from cells in the stroma can confer chemoresistance to PDAC cells *in vitro*. Based on these and other studies, Carlos Becerra, MD, medical director of the SAA-ICTC at Baylor Sammons Cancer Center at Dallas, initiated a study to evaluate the safety of a drug called anakinra in combination with standard chemotherapy regimens in patients with PDAC. Anakinra (Kineret®) is a Food and Drug Administration–approved drug for treatment of adults with moderate to severe rheumatoid arthritis. Anakinra blocks the inflammatory action of IL-1β binding with the IL-1 receptor and prevents IL-1β from activating inflammatory pathways. Because anakinra has been deemed safe, even for treatment of neonates, the study investigated the safety and efficacy of anakinra treatment of metastatic patients with PDAC.

In addition to evaluating drug safety, the study collected preliminary immune modulation and clinical activity information, as well as information on overall survival and serious adverse events related to the study drug. A total of 16 patients with metastatic PDAC were treated with a standard regimen of chemotherapy (modified FOLFIRINOX), administered every 2 weeks. During this treatment, patients received anakinra, given as a daily self-administered subcutaneous injection, for 2 months. Most patients' tumors regressed or stopped growing. In one patient, the pancreas tumor shrunk in half, decreasing from 27.5 mm to 13.3 mm after treatment with FOLFIRINOX plus anakinra, and two small lung metastases became undetectable. Of the 14 patients who completed the study, the median overall survival was 16.7 months. The range was 1.2 months for one patient who did not respond to treatment to almost 4 years for another patient.

One advantage to using anakinra in combination with the modified FOLFIRINOX regimen was that there were few additional toxicities than with the chemotherapy alone. The main reported toxicity was neutropenia. This side effect can be lessened by giving the patient a drug to stimulate the bone marrow to produce more white blood cells, thereby counteracting the effect of anakinra.

This study has been completed and investigators are excited about the results. Investigators were encouraged by the positive effects of anakinra on participants' quality of life. One benefit was an unexpected analgesic effect during its use, which resulted in a decrease in narcotic utilization. Decreased use of narcotics allows patients to be present and interact with their family and friends, preserving their quality of life for a longer period of time. "Maintaining patient health is a key to treating this disease. For a patient to withstand chemotherapy, proper nutrition, not losing weight, and a good attitude are vital for survival," explained Dr. Becerra. "We need to do further testing of anakinra in order to develop better treatment options for PDAC."

As a follow up to this study, a second study was designed to test the efficacy of combining anakinra with a three-drug chemotherapy regimen of gemcitabine, nab-paclitaxel (Abraxane®), and cisplatin in patients with metastatic or potentially resectable pancreatic cancers (the AGAP trial). The hypothesis is that there are many PDAC patients with undetected BRCA1/2 mutations, and the addition of cisplatin should result in a better tumor response in these patients. Moreover, whatever the mutation status of the patient, adding anakinra should do two things. First, it should decrease the amount of stroma in the tumor, enhancing the access of therapeutic drugs to tumor cells. Second, it should maintain or increase the well-being of PDAC patients while they are undergoing chemotherapy, thereby making them better able to tolerate these life-saving treatments. This trial is ongoing, and preliminary results reveal a high disease control rate. None of this could have been accomplished without seed funding from SAA for the first clinical trial with PDAC patients being treated with FOLFIRINOX and anakinra.

NIH U01 Grant

With the agreement between Baylor Dallas and TGen and the merger of Baylor Health Care System and Scott & White Healthcare have come greater cooperation, not only between Baylor Dallas and TGen but between institutions within the Baylor Scott & White Health system. One such collaboration has been in the area of pancreatic cancer. Baylor Dallas holds twice-monthly pancreas multidisciplinary tumor conferences where medical, surgical, and radiation oncologists, along with radiologists, pathologists, and others within the patient care team, meet and discuss care of patients with pancreatic cancer, as well as patients with other pancreatic neoplasms that have the potential to lead to cancer.

Daniel Von Hoff, MD, FACP, an expert in the area of pancreatic cancer and clinical trials, attends these conferences every 2 months. Additionally, physicians from Scott & White Medical Center – Temple hospital participate by videoconference, presenting their own patients and joining the discussion on the care of patients. As a logical outgrowth of this work, Drs. Von Hoff and Goel submitted a proposal to the National Institutes for Health for the discovery of biomarkers for pancreatic cancer.

This grant, entitled "Noncoding RNA Biomarkers for Noninvasive and Early Detection of Pancreatic Cancer," was recently funded. This UO1 grant—a research project cooperative agreement—involves multiple sites. In addition to Baylor Dallas and TGen, the group includes Scott & White – Temple, Honor Health and the University of Arizona. Researchers are international, including individuals from Samsung University in Korea and Nagoya University in Japan, as well as the Medical College of Wisconsin, Hoag Hospital, University of Southern California and the Ochsner Clinic in New Orleans. All of these sites will be collecting tumor and blood samples from pancreatic tumors and other pancreatic neoplasms, such as dysplasia and cysts, to better develop biomarkers for pancreatic cancer.

THE ROLE OF REGULATORY ELEMENTS IN CONTROLLING DRIVER GENE EXPRESSION IN MULTIPLE MYELOMA

BAYLOR INSTITUTE FOR IMMUNOLOGY RESEARCH AND BAYLOR SAMMONS CANCER CENTER AT BAYLOR UNIVERSITY MEDICAL CENTER

Multiple myeloma (MM) is a neoplastic disorder of plasma cells. It is characterized by a number of features including destruction of bone, renal failure, anemia, hypercalcemia and infections; however, early in the course of the disease, the patient may not experience any of these symptoms. With the introduction of newer systemic agents such as proteasome inhibitors and immunomodulatory therapies, patients with MM can return to a near-typical lifestyle. Advances in treatment along with enhancements in autologous and allogeneic stem cell transplantations have resulted in improved patient outcomes; however, this disease is still not curable, with a 5-year survival rate of less than 50 percent. About 13,000 Americans are expected to die from the disease this year. Thus, new treatment strategies are needed to improve the prognosis for MM.

> Drugs that target the transcriptional process show promising anti-myeloma activity.
>
> Yin C. Lin, PhD
> Baylor Institute for Immunology Research and the Baylor Sammons Cancer Center at Baylor University Medical Center

With funding from Swim Across America, Yin C. Lin, PhD, a member of the Baylor Institute for Immunology Research and the Baylor Sammons Cancer Center at Baylor University Medical Center, is conducting a study that may suggest innovative approaches for treatment of MM. His goal is to identify regulatory elements that control expression of driver genes in MM.

Driver genes

Cancerous cells typically contain a large number of somatic mutations that accumulate more as a function of time than a neoplastic process. Only a few of these mutations confer a direct or indirect selective growth advantage to the tumor cell. Thus, these are considered mutations in genes that "drive" the neoplastic process, while those with little or no contribution to cancer progression are considered "passengers." In certain contexts such as resistant or recurrent disease, passenger mutations may transform into driver mutations.

About 140 driver genes have been identified in the human genome across a variety of cancer types. These genes tend to fall into one of two categories: oncogenes or tumor suppressors. Gene mutation can result in gain or loss of function of the biochemical activity of the protein, while epigenetic modification of these genes, as a result of DNA methylation, histone modifications, and the effect of noncoding RNAs, can result in aberrant gene expression.

The role of regulatory elements in driver gene expression

Much research has been conducted pertaining to the different transcriptional profiles and genetic changes that characterize the various types of MM. However, less is understood about regulatory elements found in the driver genes that control their transcription. This is the area Dr. Lin has pursued: studying enhancers and long noncoding RNAs (lncRNAs) and how they regulate expression of driver genes in MM.

Enhancers are short sequences of DNA, normally upstream of the start site of the transcription of the gene that activate target gene expression through binding to specific transcription factors. These enhancers are normally a few hundred base pairs in length. When bound by transcription factors (TFs), they may be occupied by multiple TFs at the same time. Often a number of TFs work together to enhance target gene expression. When there are multiple enhancer regions bound by an assortment of TFs that control genes vital for specifying the identity of a cell, such as conferring identity of a pancreas cell versus a cancerous pancreas cell, these regions are termed *super-enhancers*.

This study has focused on understanding super-enhancers and their role in the development of MM.

In contrast to enhancers, lncRNAs are molecules of RNA that are more than 200 nucleotides in length and thought not to encode proteins. Although lncRNAs make up most of the human transcriptome, much less is known about their function. More evidence is pointing to them being part of a regulatory network working with TFs in enhancing or inhibiting gene-specific expression and the basal transcription machinery. Nevertheless, only a small percentage of lncRNAs have been characterized. Interestingly, a number of lncRNAs have been shown to be overexpressed in various cancers, and their aberrant expression has been shown to be associated with specific forms of cancer.

"Drugs that target the transcriptional process show promising anti-myeloma activity," explained Dr. Lin. "A continued improvement in our understanding of multiple myeloma at the molecular level not only identifies novel diagnostic markers and targets for therapeutic intervention, but also justifies the study of transcriptional regulation and the factors that are involved in this process."

In the current study, samples were collected from 27 treatment-naïve MM patients. The goal was to identify a core set of TFs that drives the aberrant gene expression program and defines the connectivity among these TFs. Additionally, researchers focused on identifying the potential roles of lncRNAs, which are overexpressed in MM, and their interaction with the TFs.

"By identifying active regulatory elements, TF footprints, and changes to the chromatin states in primary myeloma cells, we identified a set of transcriptional regulators that is important to the dysregulated myeloma gene expression program and distinct functional genomic regions that are specific to this disease," said Dr. Lin. "A set of TFs was predominantly regulated by super-enhancers in different MM patients, and these TFs were highly interconnected in a TF regulatory network. Distinct enhancer regions controlled the gene expression of signaling and adhesion molecules, the latter of which are known to associate with the disease. Our findings reveal potential therapeutic targets at the level of transcriptional control."

The study has had other findings as well:

- Interferon regulatory factor, E26 transformation-specific family TF, E-protein TF, and activator protein-1 TF family members of the active enhancer repertoire drive gene expression in myeloma.
- Recurring super-enhancers are associated with oncogenes and TF genes across samples from primary myeloma patients.
- Heterochromatin regions in B cells become accessible in myeloma and are associated with lncRNA expression and activation of the cyclic AMP pathway.
- The network building blocks change in myeloma.
- Employing an integrative approach leads to a better understanding of the TF regulatory network present in myeloma.

"Targeting TFs in MM shows promising anti-tumor activity," explained Dr. Lin. "Previous research has shown that two TFs, Ikaros and interferon regulatory factor-4, can be targeted. Lenalidomide, a drug that has been used as a standard therapy in MM, causes the degradation of Ikaros,

which results in death of tumor cells. Despite a wide spectrum of genetic heterogeneity among MM patient-derived cell lines, reducing interferon regulatory factor-4 activity results in death of all of these cell lines (but not in cell lines of other cancers). Our research identified more TFs in the myeloma network that previously were underappreciated. As a result of this study, we have a better understanding of how these factors work together. We have furthered the work aimed at targeting TFs by identifying not just interferon regulatory factor-4 and Ikaros, but also other TFs that might be targeted to provide effective treatment of MM."

Nov., 2017 - Feb. 12, 2018

RECENT PUBLICATIONS

FROM BAYLOR CHARLES A. SAMMONS CANCER CENTER

Alsahhar JS, Idriss R, Bahirwani R. A Rare Case of Cutaneous Metastases Secondary to Hepatocellular Carcinoma. 2018 Jan 15. *Clin Gastroenterol Hepatol.* pii: S1542-3565(18)30033-8. doi: 10.1016/j.cgh.2018.01.009. [Epub ahead of print]

Althans AR, Brady JT, Times ML, Keller DS, Harvey AR, Kelly ME, Patel ND, Steele SR. Colorectal Cancer Safety Net: Is It Catching Patients Appropriately? *Dis Colon Rectum.* 2018 Jan;61(1):115-123.

Antonia SJ, Villegas A, Daniel D, Vicente D, Murakami S, Hui R, Yokoi T, Chiappori A, Lee KH, de Wit M, Cho BC, Bourhaba M, Quantin X, Tokito T, Mekhail T, Planchard D, Kim YC, Karapetis CS, Hiret S, Ostoros G, Kubota K, Gray JE, Paz-Ares L, de Castro Carpeño J, Wadsworth C, Melillo G, Jiang H, Huang Y, Dennis PA, Özgüroğlu M; PACIFIC Investigators.Durvalumab after Chemoradiotherapy in Stage III Non-Small-Cell Lung Cancer (Konduri K). *N Engl J Med.* 2017 Nov 16;377(20):1919-1929.

Augestad KM, Keller DS, Bakaki PM, Rose J, Koroukian SM, Øresland T, Delaney CP. The impact of rectal cancer tumor height on recurrence rates and metastatic location: A competing risk analysis of a national database. *Cancer Epidemiol.* 2018 Jan 30;53:56-64.

Block TM, Alter H, Brown N, Brownstein A, Brosgart C, Chang KM, Chen PJ, Cohen C, El-Serag H, Feld J, Gish R, Glenn J, Greten TF, Guo JT, Hoshida Y, Kowdley KV, Li W, Lok AS, McMahon B, Mehta A, Perrillo R, Rice CM, Rinaudo J, Schinazi RF, Shetty K. Research priorities for the discovery of a cure for chronic hepatitis B: Report of a workshop. *Antiviral Res.* 2017 Dec 14;150:93-100.

Blum JL, Robert N, Andersen J, Favret A, Ward P, Osborne C, Pippen J. Use of Biomarkers to Guide Decisions on Adjuvant Systemic Therapy in Early-Stage Invasive Breast Cancer. *J Clin Oncol.* 2018 Feb 1;36(4):428-429.

Charlton M, Levitsky J, Aqel B, O'Grady J, Hemibach J, Rinella M, Ghabril M, Thomason R, Burra P, Little EC, Berenguer M, Shaked A, Trotter J, Roberts J, Rodriguez-Davalos M, Rela M, Pomfret E, Saliba F. International Liver Transplant Society Consensus Statement on IMMUNOSUPPRESSION IN LIVER TRANSPLANT RECIPIENTS. *Transplantation.* 2018 Feb 26. doi: 10.1097/TP.0000000000002147. [Epub ahead of print].

Choi S, Cui C, Luo Y, Kim SH, Ko JK, Huo X, Ma J, Fu LW, Souza RF, Korichneva I, Pan Z. Selective inhibitory effects of zinc on cell proliferation in esophageal squamous cell carcinoma through Orai1. *FASEB J.* 2018 Jan;32(1):404-416.

Chung JH, Pavlick D, Hartmaier R, Schrock AB, Young L, Forcier B, Ye P, Levin MK, Burris H, Gay LM, Hoffman AD, Stephens PJ, Frampton GM, Lipson DM, Nguyen DM, Ganesan S, Park BH, Vahdat LT, Leyland-Jones B, Mughal TI, Pusztai L, O'Shaughnessy J, Miller VA, Ross JS, Ali SM. Hybrid capture-based genomic profiling of circulating tumor DNA from patients with estrogen receptor-positive metastatic breast cancer. *Ann Oncol.* 2017 Nov 1;28(11):2866-2873.

Condorelli R, Spring L, O'Shaughnessy J, Lacroix L, Bailleux C, Scott V, Dubois J, Nagy RJ, Lanman RB, Iafrate AJ, Andre F, Bardia A. Polyclonal RB1 mutations and acquired resistance to CDK 4/6 inhibitors in patients with metastatic breast cancer. *Ann Oncol.* 2017 Dec 11. doi: 10.1093/annonc/mdx784. [Epub ahead of print]

Cowey CL, Liu FX, Black-Shinn J, Stevinson K, Boyd M, Frytak JR, Ebbinghaus SW. Pembrolizumab Utilization and Outcomes for Advanced Melanoma in US Community Oncology Practices. *J Immunother.* 2018 Feb/Mar;41(2):86-95.

Expert Panel on Gastrointestinal Imaging: Horowitz JM, Kamel IR, Arif-Tiwari H, Asrani SK, Hindman NM, Kaur H, McNamara MM, Noto RB, Qayyum A, Lalani T. ACR Appropriateness Criteria® Chronic Liver Disease. *J Am Coll Radiol.* 2017 Nov;14(11S):S391-S405.

Goel A. IGF-1R: SUMO-ing its weight in chemoresistant colorectal cancer. *Br J Cancer.* 2017 Dec 5;117(12):1733-1735.

Goel A. Utilizing biomarkers in colorectal cancer: an interview with Ajay Goel. *Future Oncol.* 2017 Dec;13(28):2511-2514

Goyal NG, Levine BJ, Van Zee KJ, Naftalis E, Avis NE. Trajectories of quality of life following breast cancer diagnosis. *Breast Cancer Res Treat.* 2018 Jan 24. doi: 10.1007/s10549-018-4677-2. [Epub ahead of print]

Gupta N, Konda V, Siddiqui U. Gastric cardia lesion with abnormal volumetric laser endomicroscopy imaging. *Gastrointest Endosc.* 2018 Feb;87(2):610-612.

Hallmeyer S, Gonzalez R, Lawson DH, Cranmer LD, Linette GP, Puzanov I, Taback B, Cowey CL, Ribas A, Daniels GA, Moore T, Gibney GT, Tawbi H, Whitman E, Lee G, Mun Y, Liu S, Hamid O. Vemurafenib treatment for patients with locally advanced, unresectable stage IIIC or metastatic melanoma and activating exon 15 BRAF mutations other than V600E. *Melanoma Res.* 2017 Dec;27(6):585-590.

Han J, Jackson D, Holm J, Turner K, Ashcraft P, Wang X, Cook B, Arning E, Genta RM, Venuprasad K, Souza RF, Sweetman L, Theiss AL. Elevated d-2-hydroxyglutarate during colitis drives progression to colorectal cancer. *Proc Natl Acad Sci U S A.* 2018 Jan 16 Jan 30;115(5):1057-1062.

Huo X, Zhang X, Yu C, Cheng E, Zhang Q, Dunbar KB, Pham TH, Lynch JP, Wang DH, Bresalier RS, Spechler SJ, Souza RF. Aspirin prevents NF-κB activation and CDX2 expression stimulated by acid and bile salts in oesophageal squamous cells of patients with Barrett's oesophagus. *Gut.* 2018 Apr;67(4):606-615.

Jiao X, Pulgar S, Boyd M, Braiteh F, Mirakhur B, Pitman Lowenthal S, Fox P, Frytak J, Cox D, Paulson AS. Treatment Patterns and Clinical Outcomes in Patients With Metastatic Gastroenteropancreatic Neuroendocrine Tumors Treated in the Community Practice Setting in the United States. *Pancreas.* 2018 Feb;47(2):173-182.

Joshi HM, Keller DS, Chand M. Utilization of Indocyanine green to demonstrate lymphatic mapping in colon cancer. *J Surg Oncol.* 2017 Dec;116(8):1005-1007.

Ko KP, Kim SJ, Huzarski T, Gronwald J, Lubinski J, Lynch HT, Armel S, Park SK, Karlan B, Singer CF, Neuhausen SL, Narod SA, Kotsopoulos J; and the Hereditary Breast Cancer Clinical Study Group (Blum JL). The association between smoking and cancer incidence in BRCA1 and BRCA2 mutation carriers. *Int J Cancer.* 2018 Jan 13. doi: 10.1002/ijc.31257. [Epub ahead of print]

Konda VJA, Spechler SJ. Endoscopic eradication therapy and the test of time. *Gastrointest Endosc.* 2018 Jan;87(1):85-87.

Loibl S, O'Shaughnessy J, Untch M, Sikov WM, Rugo HS, McKee MD, Huober J, Golshan M, von Minckwitz G, Maag D, Sullivan D, Wolmark N, McIntyre K, Ponce Lorenzo JJ, Metzger Filho O, Rastogi P, Symmans WF, Liu X, Geyer CE Jr. Addition of the PARP inhibitor veliparib plus carboplatin or carboplatin alone to standard neoadjuvant chemotherapy in triple-negative breast cancer (BrighTNess): a randomised, phase 3 trial. *Lancet Oncol.* 2018 Feb 28. pii: S1470-2045(18)30111-6. doi: 10.1016/S1470-2045(18)30111-6. [Epub ahead of print]

Mazharuddin S, Chattopadhyay A, Levy MY, Redner RL. IRF2BP2-RARA t(1;17)(q42.3;q21.2) APL blasts differentiate in response to all-trans retinoic acid. *Leuk Lymphoma.* 2018 Jan 19:1-4.

Miles D, Cameron D, Hilton M, Garcia J, O'Shaughnessy J. Overall survival in MERiDiAN, a double-blind placebo-controlled randomised phase III trial evaluating first-line bevacizumab plus paclitaxel for HER2-negative metastatic breast cancer. *Eur J Cancer.* 2018 Feb;90:153-155.

Morikawa T, Inada R, Nagasaka T, Mori Y, Kishimoto H, Kawai T, Umeda Y, Mishima H, Goel A, Fujiwara T.BRAF V600E mutation is a predictive indicator of upfront chemotherapy for stage IV colorectal cancer. *Oncol Lett.* 2018 Feb;15(2):2195-2201.

Myers RM, Hill BT, Shaw BE, Kim S, Millard HR, Battiwalla M, Majhail NS, Buchbinder D, Lazarus HM, Savani BN, Flowers MED, D'Souza A, Ehrhardt MJ, Langston A, Yared JA, Hayashi RJ, Daly A, Olsson RF, Inamoto Y, Malone AK, DeFilipp Z, Margossian SP, Warwick AB, Jaglowski S, Beitinjaneh A, Fung H, Kasow KA, Marks DI, Reynolds J, Stockerl-Goldstein K, Wirk B, Wood WA, Hamadani M, Satwani P. Long-term outcomes among 2-year survivors of autologous hematopoietic cell transplantation for Hodgkin and diffuse large b-cell lymphoma. *Cancer.* 2018 Feb 15;124(4):816-825

O'Shaughnessy J, Petrakova K, Sonke GS, Conte P, Arteaga CL, Cameron DA, Hart LL, Villanueva C, Jakobsen E, Beck JT, Lindquist D, Souami F, Mondal S, Germa C, Hortobagyi GN. Ribociclib plus letrozole versus letrozole alone in patients with de novo HR+, HER2- advanced breast cancer in the randomized MONALEESA-2 trial. *Breast Cancer Res Treat.* 2018 Feb;168(1):127-134

Osborne C, Challagalla JD, Eisenbeis CF, Holmes FA, Neubauer MA, Koutrelakos NW, Taboada CA, Vukelja SJ, Wilks ST, Allison MA, Reddy P, Sedlacek S, Wang Y, Asmar L, O'Shaughnessy J. Ixabepilone and Carboplatin for Hormone Receptor Positive/HER2-neu Negative and Triple Negative Metastatic Breast Cancer. *Clin Breast Cancer.* 2018 Feb;18(1):e89-e95.

Paulson AS, Hess LM, Liepa AM, Cui ZL, Aguilar KM, Clark J, Schelman W. Ramucirumab for the treatment of patients with gastric or gastroesophageal junction cancer in community oncology practices. *Gastric Cancer.* 2018 Feb 3. doi: 10.1007/s10120-018-0796-z. [Epub ahead of print]

Sarkar S, O'Connell MR, Okugawa Y, Lee BS, Toiyama Y, Kusunoki M, Daboval RD, Goel A, Singh P. FOXD3 Regulates CSC Marker, DCLK1-S, and Invasive Potential: Prognostic Implications in Colon Cancer. *Mol Cancer Res.* 2017 Dec;15(12):1678-1691.

Schadendorf D, Wolchok JD, Hodi FS, Chiarion-Sileni V, Gonzalez R, Rutkowski P, Grob JJ, Cowey CL, Lao CD, Chesney J, Robert C, Grossmann K, McDermott D, Walker D, Bhore R, Larkin J, Postow MA. Efficacy and Safety Outcomes in Patients With Advanced Melanoma Who Discontinued Treatment With Nivolumab and Ipilimumab Because of Adverse Events: A Pooled Analysis of Randomized Phase II and III Trials. *J Clin Oncol.* 2017 Dec 1;35(34):3807-3814.

Shiao SPK, Grayson J, Yu CH, Wasek B, Bottiglieri T. Gene Environment Interactions and Predictors of Colorectal Cancer in Family-Based, Multi-Ethnic Groups. *J Pers Med.* 2018 Feb 16;8(1).

Sonohara F, Gao F, Iwata N, Kanda M, Koike M, Takahashi N, Yamada Y, Kodera Y, Wang X, Goel A. Genome-wide Discovery of a Novel Gene-expression Signature for the Identification of Lymph Node Metastasis in Esophageal Squamous Cell Carcinoma. *Ann Surg.* 2017 Dec 12. doi: 10.1097/SLA.0000000000002622. [Epub ahead of print]

Souza RF, Spechler SJ. Oesophagus: A new candidate for the progenitor cell of Barrett metaplasia. *Nat Rev Gastroenterol Hepatol.* 2018 Jan;15(1):7-8.

Strasser-Weippl K, Sudan G, Ramjeesingh R, Shepherd LE, O'Shaughnessy J, Parulekar WR, Liedke PER, Chen BE, Goss PE. Outcomes in women with invasive ductal or invasive lobular early stage breast cancer treated with anastrozole or exemestane in CCTG (NCIC CTG) MA.27. *Eur J Cancer.* 2017 Dec 20;90:19-25.

Stupp R, Taillibert S, Kanner A, Read W, Steinberg DM, Lhermitte B, Toms S, Idbaih A, Ahluwalia MS, Fink K, Di Meco F, Lieberman F, Zhu JJ, Stragliotto G, Tran DD, Brem S, Hottinger AF, Kirson ED, Lavy-Shahaf G, Weinberg U, Kim CY, Paek SH, Nicholas G, Burna J, Hirte H, Weller M, Palti Y, Hegi ME, Ram Z. Effect of Tumor-Treating Fields Plus Maintenance Temozolomide vs Maintenance Temozolomide Alone on Survival in Patients With Glioblastoma: A Randomized Clinical Trial. *JAMA.* 2017 Dec 19;318(23):2306-2316.

Takehara Y, Nagasaka T, Nyuya A, Haruma T, Haraga J, Mori Y, Nakamura K, Fujiwara T, Boland CR, Goel A. Accuracy of four mononucleotide-repeat markers for the identification of DNA mismatch-repair deficiency in solid tumors. *J Transl Med.* 2018 Jan 12;16(1):5.

Toden S, Ravindranathan P, Gu J, Cardenas J, Yuchang M, Goel A. Oligomeric proanthocyanidins (OPCs) target cancer stem-like cells and suppress tumor organoid formation in colorectal cancer. *Sci Rep.* 2018 Feb 20;8(1):3335.

Toiyama Y, Okugawa Y, Tanaka K, Araki T, Uchida K, Hishida A, Uchino M, Ikeuchi H, Hirota S, Kusunoki M, Boland CR, Goel A. A Panel of Methylated MicroRNA Biomarkers for Identifying High-Risk Patients with Ulcerative Colitis-associated Colorectal Cancer. *Gastroenterology.* 2017 Dec;153(6):1634-1646.

Traina TA, Miller K, Yardley DA, Eakle J, Schwartzberg LS, O'Shaughnessy J, Gradishar W, Schmid P, Winer E, Kelly C, Nanda R, Gucalp A, Awada A, Garcia-Estevez L, Trudeau ME, Steinberg J, Uppal H, Tudor IC, Peterson A, Cortes J. Enzalutamide for the Treatment of Androgen Receptor-Expressing Triple-Negative Breast Cancer. *J Clin Oncol.* 2018 Jan 26:JCO2016713495. doi: 10.1200/JCO.2016.71.3495. [Epub ahead of print]

Trotter JF. Pro: Direct-acting agents are associated with occurrence and recurrence of hepatocellular carcinoma. *Liver Transpl.* 2017 Dec;23(12):1593-1595.

Vedeld HM, Goel A, Lind GE. Epigenetic biomarkers in gastrointestinal cancers: The current state and clinical perspectives. *Semin Cancer Biol.* 2017 Dec 15. pii: S1044-579X(17)30181-5. doi: 10.1016/j.semcancer.2017.12.004. [Epub ahead of print]

Voss MH, Hussain A, Vogelzang N, Lee JL, Keam B, Rha SY, Vaishampayan U, Harris WB, Richey S, Randall JM, Shaffer D, Cohn A, Crowell T, Li J, Senderowicz A, Stone E, Figlin R, Motzer RJ, Haas NB, Hutson T. A randomized phase 2 trial of CRLX101 in combination with bevacizumab versus standard of care in patients with advanced renal cell carcinoma. *Ann Oncol.* 2017 Nov 1;28(11):2754-2760.

Webb HR, Latifi HR, Griffeth LK. Utility of whole-body (head-to-toe) PET/CT in the evaluation of melanoma and sarcoma patients. *Nucl Med Commun.* 2018 Jan;39(1):68-73.

Weber J, Mandala M, Del Vecchio M, Gogas HJ, Arance AM, Cowey CL, Dalle S, Schenker M, Chiarion-Sileni V, Marquez-Rodas I, Grob JJ, Butler MO, Middleton MR, Maio M, Atkinson V, Queirolo P, Gonzalez R, Kudchadkar RR, Smylie M, Meyer N, Mortier L, Atkins MB, Long GV, Bhatia S, Lebbé C, Rutkowski P, Yokota K, Yamazaki N, Kim TM, de Pril V, Sabater J, Qureshi A, Larkin J, Ascierto PA; CheckMate 238 Collaborators. Adjuvant Nivolumab versus Ipilimumab in Resected Stage III or IV Melanoma. *N Engl J Med.* 2017 Nov 9;377(19):1824-1835.

Weng W, Liu N, Toiyama Y, Kusunoki M, Nagasaka T, Fujiwara T, Wei Q, Qin H, Lin H, Ma Y, Goel A.Novel evidence for a PIWI-interacting RNA (piRNA) as an oncogenic mediator of disease progression, and a potential prognostic biomarker in colorectal cancer. *Mol Cancer.* 2018 Jan 30;17(1):16.

Wilder EG, Frieder J, Sulhan S, Michel P, Cizenski JD, Wright JM, Menter MA. Spectrum of orocutaneous disease associations: Genodermatoses and inflammatory conditions. *J Am Acad Dermatol.* 2017 Nov;77(5):809-830.

Yamada A, Yu P, Lin W, Okugawa Y, Boland CR, Goel A. A RNA-Sequencing approach for the identification of novel long non-coding RNA biomarkers in colorectal cancer. *Sci Rep.* 2018 Jan 12;8(1):575.

Yang Q, Lin W, Liu Z, Zhu J, Huang N, Cui Z, Han Z, Pan Q, Goel A, Sun F. RAP80 is an independent prognosis biomarker for the outcome of patients with esophageal squamous cell carcinoma. *Cell Death Dis.* 2018 Feb 2;9(2):146.

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CURRENT CLINICAL TRIALS

Site	Study ID	Location	Principal Investigator	Study title
Breast	16097	Texas Oncology-Dallas	Joyce A. O'Shaughnessy, MD	Phase 2 Study of the Safety, Efficacy, and Pharmacokinetics of G1T28 in Patients with Metastatic Triple-Negative Breast Cancer Receiving Gemcitabine and Carboplatin Chemotherapy (G1T28-04)
	14192	Texas Oncology-Dallas	Cynthia Osborne, MD	Phase I Multicenter, Open Label, Two Part Dose Escalation Study of RAD1901 in Post Menopausal Women with Advanced Estrogen Receptor Positive and HER2 Negative Breast Cancer
	16208	Texas Oncology-Dallas	Joyce A. O'Shaughnessy, MD	A Study of Pembrolizumab (MK-3475) Plus Chemotherapy vs Placebo Plus Chemotherapy as Neoadjuvant Therapy and Pembrolizumab vs Placebo as Adjuvant Therapy in Participants With Triple Negative Breast Cancer (TNBC) (MK-3475-522/KEYNOTE-522)
	16104	Texas Oncology-Dallas	Joyce A. O'Shaughnessy, MD	A Phase I, Open Label, Dose Escalation Study to Evaluate the Safety and Tolerability of SGN-LIV-1 in Patients with Metastatic Breast Cancer
Breast and Solid Tumor or NHL	12220	Texas Oncology-Dallas	Carlos H.R. Becerra, MD	A Dose Escalation Study Evaluating the Safety and Tolerability of GDC-0032 in Patients With Locally Advanced or Metastatic Solid Tumors or Non-Hodgkin's Lymphoma (NHL) and in Combination with Endocrine Therapy in Patients with Locally Advanced or Metastatic Hormone Receptor positive Breast Cancer
Chest	15183	Texas Oncology-Dallas	Carlos H.R. Becerra, MD	Phase 2, Fast Real-time Assessment of Combination Therapies in Immuno-ONcology Study in Subjects with Advanced Non-small Cell Lung Cancer (FRACTION-Lung)
GI	13195	Texas Oncology-Dallas	Carlos H.R. Becerra, MD	A Phase I/II Study of CX-4945 in Combination with Gemcitabine plus Cisplatin in the Frontline Treatment of Patients with Cholangiocarcinoma
	T0-1711	Texas Oncology-Dallas	Carlos H.R. Becerra, MD	A Multicenter, Double Blind, Randomized, Placebo Controlled Study of Varlitinib Plus Capecitabine Versus Placebo Plus Capecitabine in Patients with Advanced or Metastatic Biliary Tract Cancer as Second Line Systemic Therapy
	16066	Texas Oncology-Dallas	A. Scott Paulson, MD	A Phase 2, Open-Label, Single Arm, Multicenter Study to Evaluate the Efficacy and Safety of INCB054828 in Subjects with Advanced/ Metastatic or Surgically Unresectable Cholangiocarcinoma Including FGFR2 Translocations Who Failed Previous Therapy
	016-137	Baylor Dallas	Carlos H.R. Becerra, MD	A Feasibility and Safety Study of a PSCA-Specific Chimeric Antigen Receptor Engineered T Cells (BPX-601) in Subjects with Non-Resectable Pancreatic Cancer
GU	15228	Texas Oncology-Dallas	C. Lance Cowey, MD	A Phase 2, Open-label, Single Agent, Multi-Center Study to Evaluate the Efficacy and Safety of a Pan-FGFR Tyrosine Kinase Inhibitor INCB054828 in Patients with Metastatic or Surgically Unresectable Urothelial Carcinoma Harboring FGF/FGFR Alterations
	16177	Texas Oncology-Dallas	Thomas E. Hutson, DO, PharmD	Phase 3b/4 Safety Trial Of Nivolumab Combined with Ipilimumab in Subjects with Previously Untreated, Advanced or Metastatic RCC
	T01644	Texas Oncology-Dallas	Thomas E. Hutson, DO, PharmD	A Single-Arm, Multicenter, Phase 2 Trial to Evaluate Efficacy and Safety of Lenvatinib in Combination with Everolimus in Subjects with Unresectable Advanced or Metastatic Non-Clear Cell Renal Cell Carcinoma (nccRCC) Who Have Not Received Any Chemotherapy for Advanced Disease (E7080-M001-221)

Head & Neck	017-075	Baylor Dallas	Eric Nadler, MD, MPP	A Multicentre, Randomized, Open-Label, Phase III Clinical Trial Of Gemcitabine And Carboplatin Followed By Epstein-Barr Virus-Specific Autologous Cytotoxic T Lymphocytes Versus Gemcitabine And Carboplatin As First Line Treatment For Advanced Nasopharyngeal Carcinoma Patients
Hematologic Malignancies	017-012	Baylor Dallas	M. Yair Levy, MD	A Phase 3 Randomized, Controlled, Ope-Label Study of Selinexor, Bortezomib, and Dexamethasone (SVD) Versus Bortezomib and Dexamthasone (VD) in Patients with Relapsed or Refractory Multiple Myeloma (RRMM)
	017-040	Baylor Dallas	Luis A. Pineiro, MD	An Open-Label, Dose-Finding Study of Vedolizumab IV for Treatment of Steroid-Refractory Acute Intestinal Graft-Versus-Host Disease (GvHD) in Patients who Have Undergone Allogeneic Hematopoietic Stem Cell Transplantation (allo-HSCT)
	017-108	Baylor Dallas	M. Yair Levy, MD	A Phase 1-2 Dose-Escalation and Cohort-Expansion Study of Oral eFT508 in Subjects with Hematological Malignancies
	017-142	Baylor Dallas	Micah Burch, MD	A Double-blind, Double-dummy Phase 2 Randomized Study to Evaluate the Efficacy and Safety of Ruxolitinib (INCB018424) versus Anagrelide in Subjects with Essential Thrombocythemia (ET) who are Resistant or Intolerant to Hydroxyurea (HU)
	017-127	Baylor Dallas	Andrew R. Whiteley, MD	A Phase 3, Multicenter, Randomized, Open-Label Study of Guadecitabine (SGI-110) versus Treatment Choice in Adults with Previously Treated Acute Myeloid Leukemia
	017-092	Baylor Dallas	Jana Reynolds, MD	A Phase 3, Multicenter, Double-Blind, Randomized, Placebo-Controlled Study of AG-120 in Combination with Azacitidine in Subjects ≥ 18 Years of Age with Previously Untreated and Relapsed Acute Myeloid Leukemia with an IDH1 Mutation Who Are Candidates for Non-intensive Therapy
Melanoma	017-088	Baylor Dallas	C. Lance Cowey, MD	Phase Lb, Open-Label, Multicenter, Global Study Designed to Evaluate the Preliminary Efficacy, Safety and Pharmacokinetics of Atezolizumab and Cobimetinib When Given to Patients with BRAFV600-WT Metastatic or Unresectable Locally Advanced Melanoma Who Have Progressed on a Prior Anti-PD-1 Therapy
	T01702	Texas Oncology-Dallas	C. Lance Cowey, MD	A Phase 3, Randomized Study of Adjuvant Immunotherapy with Nivolumab Combined with Ipilimumab Versus Ipilimumab or Nivolumab Monotherapy after Complete Resection of Stage IIIb/c/d or Stage IV Melanoma
	T0-1656	Texas Oncology-Dallas	Carlos H.R. Becerra, MD	An Open Label, Phase Ib, Multi-Arm Study to Evaluate the Safety, Tolerability and Pharmacodynamics of Investigational Treatments in Combination with Standard of Care Immune Checkpoint Inhibitors in Patients with Advanced Melanoma
Neuro-oncology	017-046	Baylor Dallas	Karen Fink, MD, PhD	A Randomized, Placebo Controlled Phase 2b/3 Study of ABT-414 in Subjects with Newly Diagnosed Giloblastoma Multiforme (GBM) with Epidermal Growth Factor Receptor (EGFR) Amplification
Multiple Indications	16041	Texas Oncology-Dallas	Carlos H.R. Becerra, MD	An Open-label Phase 2 Multi-cohort Trial of Nivolumab in Advanced or Metastatic Malignancies: Thyroid, Uterine, Testicular, Penile, NON-LUNG Small Cell, Nasopharyngeal, Mesothelioma (primary abdominal), Merkel Cell. Lynch Syndrome Associated Cancers (excluding HNPCC), Histiocytosis, Vulvar
Solid Tumors	17139	Texas Oncology-Dallas	Carlos H.R. Becerra, MD	A Multi-Center, Open-Label, Clinical Pharmacology Study for Idasanutlin, an Mdm2 Antagonist with a Hybrid Randomized/Sequential, Single-Dose, 4-Period Crossover Design to Investigate the Bioequivalence or Relative Bioavailability of Three New Idasanutlin Tablet Variants Following Oral Administration in Patients with Solid Tumors
	T01449	Texas Oncology-Dallas	Carlos H.R. Becerra, MD	Phase I, Open Label Study to Evaluate the Safety, Tolerability and Pharmacokinetics of TAS-102 in Patients with Locally Advanced Solid Tumors and Varying Degrees of Renal Impairment

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Yi-Zarn Wang, DDS, MD, FACS	Surgical Oncology
Katerina Wells, MD, MPH	Colon and Rectal Surgery

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