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Feature Article

BAYLOR UNIVERSITY MEDICAL CENTER AT DALLAS AND BAYLOR INSTITUTE FOR IMMUNOLOGY RESEARCH (BIIR) ARE

CREATING NEW IMMUNE THERAPIES AGAINST CANCER

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FROM THE MEDICAL

DIRECTOR

> There's only one basic principle of self-defense—you must apply the most effective weapon, as soon as possible, to the most vulnerable target.
>
> Bruce Lee

In this issue, we focus on utilizing our body's own defense, our immune system, in the battle against cancer. The American Society of Clinical Oncology named immunotherapy the "advance of the year" for 2016. In essence, we are engaging the weapons within to fight the enemy within.

Our arsenal in this battle is growing rapidly. With the Baylor Institute for Immunology Research (BIIR), we have been studying dendritic cell cancer treatment vaccines for over 15 years. Building on the lessons learned with the early dendritic cell melanoma trials, we have recently completed a trial in advanced breast cancer and are accruing patients with pancreatic cancer. BIIR researchers are now developing the next generation of "dendritic cell-engaging" vaccines that will obviate the need for *ex vivo* dendritic cell manipulation, allowing the process to occur within the body.

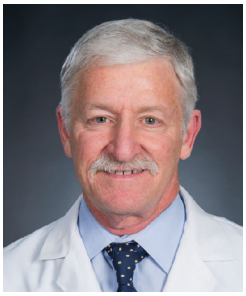
Checkpoint inhibitors have rapidly moved from clinical trials to approved agents, with applications in melanoma, non–small cell lung cancer, renal cell carcinoma and Hodgkin's disease, with more indications accruing rapidly. Antibody therapy, both "naked" and "load-bearing," has been part of our therapeutic arsenal since the approval of rituximab almost 20 years ago.

We have just begun to explore the potential of chimeric antigen receptor T-cell (CAR T-cell) therapies. At Baylor University Medical Center at Dallas, we now have clinical trials using chimeric antigen receptor T-cells (CAR T-cells) in acute lymphoblastic leukemia, mantle cell lymphoma and pancreatic cancer. With all of these new immune approaches to cancer treatment, we would be remiss to forget one of the first immunotherapy approaches to result in cancer cures—allogeneic hematopoietic stem cell transplantation.

So as we look to find new approaches to combat cancer, we must look within, for the answer may be closer than we thought.

Alan M. Miller, MD, PhD
Chief of Oncology, Baylor Scott & White Health – North Texas
Medical Director, Baylor Charles A. Sammons Cancer Center at Dallas

Effective March 1, 2017, Dr. Miller is no longer with Baylor Scott & White Health. Carlos Becerra, MD is now serving as the interim chief of oncology.



Feature Article

BAYLOR UNIVERSITY MEDICAL CENTER AT DALLAS AND BIIR ARE

CREATING NEW IMMUNE THERAPIES AGAINST CANCER

In many ways, the Baylor Charles A. Sammons Cancer Center at Dallas is at the forefront of cancer research innovation. "Precision medicine" through genomic-based cancer therapies, mentioned in last year's presidential State of the Union message, has been part of the discussion and practice at Baylor University Medical Center at Dallas for more than five years. And the national "Cancer MoonShot" announced in January, which seeks to beat cancer through the development of immune therapies, is something Baylor University Medical Center at Dallas and Baylor Institute for Immunology Research (BIIR) have successfully pursued for more than 20 years. Clearly, Baylor Dallas and BIIR are well-positioned to continue and enhance their national footprint in the fight against cancer.

"Immune approaches to cancer are the central point of the president's moonshot," said Alan M. Miller, MD, PhD, chief of oncology for Baylor Scott & White Health – North Texas, and medical director of the Baylor Charles A. Sammons Cancer Center at Dallas. "Between genomic-directed therapies and immune therapies, that is where we are going in cancer treatment."

Immune therapies aim to unlock the power of the human immune system, unleashing it to seek and destroy cancer cells (Figure 1). These types of therapies are:

- Immune vaccines, which retrain lymphocytes, called T-cells, to attack cancer.
- Chimeric antigen receptor T-cell (CAR T-cell)— T-Cells removed from a patient or donor and engineered in the laboratory to produce CARs on the cell surface which provide the immune system with a new way to recognize and kill cancer.
- Immune checkpoint inhibitors, which uncloak cancer cells, enabling the immune system to resume its job of clearing the body of disease.

Dr. Miller believes the immune therapy approaches have far-reaching possibilities, and Baylor University Medical Center at Dallas is playing a significant role in their development and implementation to fulfill unmet medical needs, especially for patients with advanced and difficult-to-treat cancers.

"Frankly, in many ways, immune therapies are going to eclipse genomic-targeted therapies because they have so much broader implications," he said. "With the immune therapies, once you awaken the immune system to recognize the cancer, that immune surveillance can continue forever."

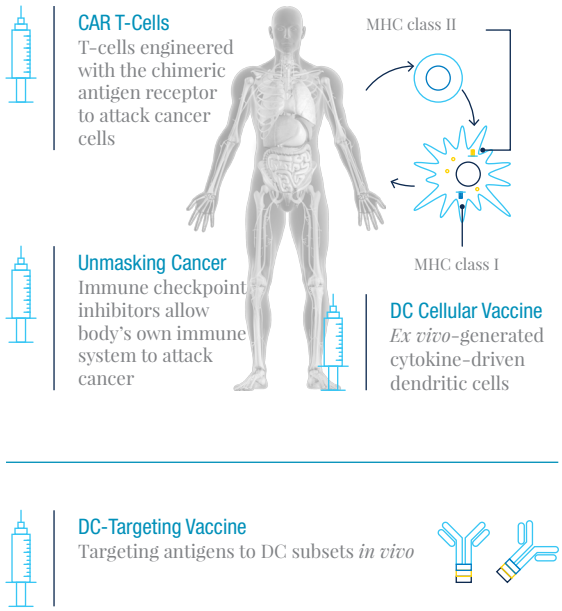


Figure 1. Cancer Immunotherapy Adapted by permission from Macmillan Publishers Ltd: *Nature Reviews Cancer* (12:265-277), 2012.

Broad Approach vs. Narrow Approach

In precision medicine, DNA or RNA is sequenced and analyzed to identify specific gene mutations based on the individual patient's molecular tumor profile. These mutations cause the growth of tumor cells due to an increase or decrease in protein expression. Therefore, specific treatments can be targeted toward these changes in a patient's cancer. But, there are many avenues in cell signaling pathways, and cancer can eventually find another way around a pathway blocked by therapy, thereby circumventing the actions of these targeted drugs and enabling the disease to progress.

"In genomic-targeted therapy, you have to develop a different therapy for each type of cancer," Dr. Miller said. "But when you're talking about things like checkpoint inhibitors, you're starting to talk about things that can apply over a very broad range of cancers." For example, a checkpoint inhibitor such as the drug pembrolizumab can be active against multiple types of cancer, including solid tumor lung, breast and colon cancers, as well as lymphatic system tumors, including Hodgkin's disease.

For more than 20 years, Baylor University Medical Center at Dallas and BIIR have been successful, in a limited percentage of patients, in using the dendritic cells of the immune system to formulate vaccines that fend off melanoma, the deadliest form of skin cancer, with several long-term survivors.

"If you look at their melanoma tumors, they never get any bigger. You can biopsy them, and they actually may have cancer in them, but it's held in check, and without repeated therapy," Dr. Miller said. "The immune system continues to recognize them and hold them in check."

Now, dendritic cell technology is accelerating at Baylor University Medical Center at Dallas and BIIR, with therapies aimed at breast, pancreatic and brain cancers. Checkpoint inhibitors are providing new advances in the treatment of melanoma and lung cancer, and chimeric antigen receptor T-cells (CAR T-cells) are providing new alternatives in cancer therapy, especially for patients with blood cancers such as leukemia and lymphoma (see details in this issue).

A Record of Accomplishments

Baylor University Medical Center at Dallas has a rich history of immune therapy innovation, especially in the area of dendritic cell research, as shown in the seminal work of the team at BIIR. Their novel treatments for colleague and mentor, Ralph M. Steinman, MD, helped him fight his pancreatic cancer for 4½ years, far beyond the median survival for this disease.

It was the late Dr. Steinman who coined the term "dendritic cells" in 1973. In 2011, Dr. Steinman was awarded the Nobel Prize for his discovery of the dendritic cell and its role in adaptive immunity. BIIR's oncology vaccine research facility is named after him: the Ralph M. Steinman Center for Cancer Vaccines at BIIR in Dallas.

NATIONAL 'CANCER MOONSHOT'

Ultimately, the aim of the 'moonshot' is to win the war on cancer—to get to a point in the very near future when we are managing cancer the same way we might manage any chronic disease. . .When we can finally stop the toxic therapies, such as chemotherapy and radiation that decimate the immune system, and instead, rally the full power of the immune system and the body's natural killer cells to fight off the cancer the way they were designed to do, the patient is not only surviving the diagnosis, but living—even thriving—with cancer.

Cancer MoonShot 2020, which aims to bring together government, pharmaceutical and biotechnology companies, academic centers, and community oncologists to find vaccine-based immunotherapies against cancer.

Expanding the Armamentarium

In the future, Dr. Miller believes that immunotherapy and genomic therapies will be used in combination, either in sequence or simultaneously, to treat cancer. For him, they are two more legs of what is now a five-legged stool of available cancer therapies: immunotherapy and genomic therapy, in addition to surgery, radiation and chemotherapy.

"Just the same way we started using surgery, radiation and chemo as individual modalities—and then found out that in many cases we can get the most benefit out of using them in combinations—I believe we'll see that same combination with targeted genomic therapies and immune therapies," Dr. Miller said.

BAYLOR UNIVERSITY MEDICAL CENTER AT DALLAS AND BIIR

GET GLOBAL IN DEVELOPMENT OF CANCER VACCINES

Dendritic cells are keys to the immune system and vaccine development.

Since the inception of Baylor Institute for Immunology Research (BIIR) by founding director Jacques Banchereau, PhD, in 1996, BIIR has been at the forefront of developing vaccines to treat cancer.

Preventive vaccines aim to stop infection from exposure to pathogens, such as viruses, parasites, bacteria, allergens and fungal infections—diseases with specific causes that originate outside the body. In contrast, cancer vaccines are therapies designed to combat tumors that form from genetic mutations inside the body.

"We have been one of the leading sites for the study of a particular type of immune cell called the dendritic cell," said Gerard Zurawski, PhD, director of the Center for Biotechnology and co-director of BIIR. Dendritic cells, a key component of the immune system, are essential in cancer vaccines because of their capacity to capture, process and present antigens to T-cells, which in turn attack the cancer.

> We've discovered over many years that dendritic cells are master regulators of the immune system.
>
> Gerard Zurawski, PhD
> Director of the Center for Biotechnology and Co-Director of BIIR

Dendritic cells are found throughout the body, acting as sentinels against disease. They have surface receptors that recognize particular components of infectious disease-causing organisms as well as receptors that receive immune signals. These receptors identify organisms and process them so they can be presented to the rest of the immune system.

"Master Regulators of the Immune System"

"We've discovered over many years that dendritic cells are master regulators of the immune system," Dr. Zurawski said. "They orchestrate the types of immune responses that need to happen, based on the nature of the insult to the body. The immune system has evolved to deal with all sorts of things that are constantly challenging us."

Cancer cells can produce proteins that can overwhelm or trick the immune system, allowing the cancer to spread. Cancer can inhibit the ability of dendritic cells, an important link between the innate and adaptive immune response, in mounting a primary defense against the cancer. BIIR's cancer vaccines are based on the discovery that it is possible to extract blood from a patient, tease out the dendritic cells, sensitize them to tumor-specific antigens and then inject them back into that same patient to elicit a cellular response, essentially teaching T-cells to kill the cancer. This is the basis of dendritic cellular therapy.

The advantages of using dendritic cells to create cancer vaccines are that they are easy to administer through simple injections and have few significant side effects. The disadvantages are that the therapy is made specifically for each patient, must be manufactured in a tightly regulated Good Manufacturing Practice production facility for safety, is expensive and has limited application.

"It has to go back to exactly the same patient from whom you took the blood to modify the dendritic cells," Dr. Zurawski said. "Otherwise, you'd have a rejection of the cells that you transplanted. It's a patient-specific therapy."

In BIIR's early melanoma vaccines, 10 to 20 percent of patients had excellent results in combating the cancer. The vaccines were extremely effective and long-lasting. But the success rate was not high enough to warrant commercialization. For most patients, the cancer still found ways to escape the immune response.

New Discoveries Leading to Innovative Therapies

In recent years, studies have brought about an increased understanding of dendritic cell biology, including the existence of distinct subsets with specific functions and the distinct molecular mechanisms that dendritic cells use to regulate the immune response.

Now, a new generation of dendritic cell-based drugs is being developed that can stimulate a broader array of immune responses. This new approach is known as dendritic cell targeting.

BIIR researchers have found that fusing antibodies with tumor cell–specific antigens produces a vaccine with broader applications, at lower cost, and available to a wide range of patients.

"You can take a monoclonal antibody that recognizes particular receptors on the surface of dendritic cells and link that antibody with a tumor-associated antigen," Dr. Zurawski said. "It's a way of delivering the antigen very specifically to the dendritic cell, which can then uptake, process and present the antigen on the cell surface. With the right receptor and the right antibody, the dendritic cells can be activated against the tumor. This approach may also be a valuable new tool for preventive vaccines against infection. By changing the antigen that is attached to the antibody, we can activate the dendritic cells against disease-causing organisms like traditional vaccines do."

BIIR has been refining this technology for more than a decade, with support from the National Institutes of Health, and is preparing to take this approach to Baylor University Medical Center at Dallas clinical trials for vaccines against head and neck cancer, breast cancer, pancreatic cancer and potentially more types of cancer.

BAYLOR INSTITUTE FOR IMMUNOLOGY RESEARCH IS

DEVELOPING A VACCINE TO PREVENT CANCER IN PATIENTS INFECTED WITH HPV

HPV vaccine would be BIIR's first commercially available drug based on dendritic cell targeting.

79M

Americans are estimated to be infected by HPV according to the CDC.

Since 2006, vaccines have been available in the US for preteens to prevent infection from the sexually transmitted human papillomavirus (HPV), which causes most cervical cancers as well as some cancers of the vagina, vulva, penis, anus, rectum and throat.

But what about those who already are infected by HPV? The US Centers for Disease Control and Prevention (CDC) estimated that 79 million Americans, nearly 1 out of 4, are infected by HPV and that HPV causes nearly 39,000 new cases of cancer each year.

The Baylor Institute for Immunology Research (BIIR) is working on its first commercially available dendritic cell-targeting vaccine, one specifically designed to prevent cancer in those who are infected by HPV. Gerard Zurawski, PhD, co-director of BIIR, estimated that this potentially life-saving vaccine could be ready for early phase clinical trials sometime in 2017.

This vaccine is based on discoveries associated with a receptor called CD40, which is found on the surface of dendritic cells. Dendritic cells are key orchestrators of the human immune system, able to instruct T-cells to kill cancer.

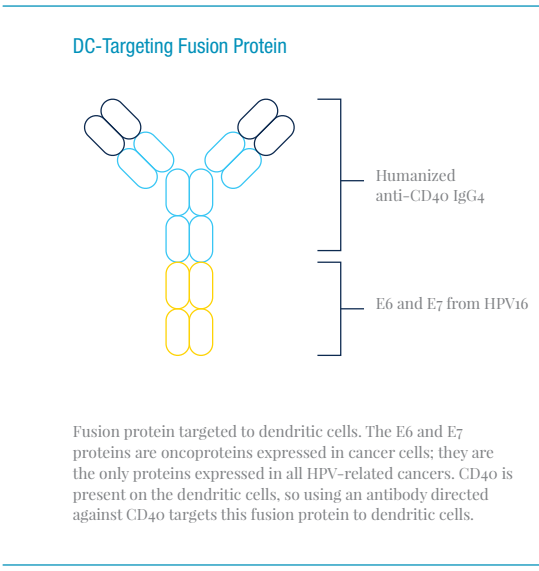
"We've constructed a dendritic cell-targeting vaccine that is composed of an antibody recognizing CD40 that is directly linked to two HPV proteins, called E6 and E7. The hope is that the activated dendritic cells then instruct T-cells in patients to control the cancerous cells," Dr. Zurawski said (Figure 2).

According to a BIIR-led study published online August 2, 2016, in *Cancer Immunology Research*, "These data suggest that CD40-targeting vaccines for HPV-associated malignancies can provide a highly immunogenic platform with a strong likelihood of clinical benefit." This work was led by SangKon Oh, PhD, an investigator at BIIR.

Dr. Zurawski, one of the authors of the study, said HPV typically starts as a mild infection. "But the virus can remain latent. In a significant number of cases, the virus has the ability, over time, to cause some cells that are infected to become cancerous," he said.

According to the CDC, HPV is thought to be responsible for more than 90 percent of anal and cervical cancers, about 70 percent of vaginal and vulvar cancers, and more than 60 percent of penile cancers. Cancers of the head and neck are often caused by tobacco and alcohol. However, according to the CDC, recent studies show that about 70 percent of cancers of the oropharynx may be linked to HPV and that many cancers of the oropharynx may be caused by a combination of tobacco, alcohol and HPV.

"CD40 is a potent activating receptor on the dendritic cells that gets the T-cells really excited, and in some cases, proliferating," Dr. Zurawski said. "Studies at BIIR have found that activation of the CD40 receptor is particularly good at programming a kind of immune response that gets a type of T-cell called cytotoxic lymphocytes, or CD8 T-cells, expanded in an antigen-specific manner."



Fusion protein targeted to dendritic cells. The E6 and E7 proteins are oncoproteins expressed in cancer cells; they are the only proteins expressed in all HPV-related cancers. CD40 is present on the dendritic cells, so using an antibody directed against CD40 targets this fusion protein to dendritic cells.

Figure 2. Targeting CD40 for HPV-Related Cancer

Adapted from *Cancer Immunology Research* 2016 Oct;4(10):823-834

While this vaccine is currently in preclinical testing at Baylor University Medical Center at Dallas for head and neck cancer, this technology holds the promise of benefiting patients with other types of cancer as well. According to the paper in *Cancer Immunology Research*, "Data from this study strongly support the development of CD40-targeting vaccines for other cancers in the future."

Dr. Zurawski expects to start production soon of the HPV vaccine that will be administered to humans. Vaccine manufacturing will be performed by the Baylor Scott & White Health production facility in Temple, Texas, part of the Scott & White Cancer Institute.

Baylor Scott & White Research Institute (BSWRI) is contracting with Charles River Laboratories in Scotland to perform preclinical safety studies and has licensed the intellectual property to BSWRI-owned Denceptor Therapeutics Limited in Cambridge, England. Denceptor will generate investments to fund this and possibly other dendritic cell-targeting vaccines to address other types of cancer.

"We anticipate that this will bring new cancer clinical trials with dendritic cell-targeting vaccines to Baylor University Medical Center," Dr. Zurawski said. "The idea of the company [Denceptor] is to provide money to allow development of early phase clinical trials of a number of different dendritic cell-targeting vaccine approaches."

If those trials are successful, he said, BSWRI and Denceptor should be able to attract pharmaceutical partners that would enable later-phase clinical trials. These trials hopefully would lead to approval by the US Food and Drug Administration and eventual commercialization.

"The next cancer types being considered for similar dendritic cell-targeting vaccines are breast cancer and pancreatic cancer," Dr. Zurawski said.

FOR THE FIRST TIME

DENDRITIC CELL VACCINE IS USED IN PATIENTS WITH LIFE-THREATENING TRIPLE-NEGATIVE BREAST CANCER

Fort Worth's vibrant Amy T. Selkirk put up a valiant one-year struggle against triple-negative breast cancer (TNBC), the most aggressive form of breast cancer. But in 2012, she died of this disease. Because of Amy's courageous battle, her husband, Bruce Selkirk, raised more than $1 million in Amy's name for the nation's first locally advanced TNBC vaccine clinical trial at Baylor University Medical Center at Dallas.

Joyce O'Shaughnessy, MD, Celebrating Women Chair of Breast Cancer Research at Baylor University Medical Center at Dallas said, "I really felt we should try to improve the immune system in these women against their triple-negative breast cancer." Dr. O'Shaughnessy's weapon of choice was a cancer vaccine that works to reignite the immune system by reprogramming dendritic cells.

"There are many ways to come at immunotherapy. Baylor has been an innovative leader—one of the few centers in the country—that has focused on dendritic cells and their function in immune therapy," said Dr. O'Shaughnessy, who is also co-director of the Baylor University Medical Center at Dallas – TGen Women's Cancer Study Group. "We decided to leverage what is here on the Baylor University Medical Center campus and bring that dendritic vaccine expertise to triple-negative breast cancer patients."

Ten women were enrolled in this clinical trial of TNBC, so called because patients with this subtype of breast cancer do not have receptors for estrogen, progesterone or the HER2 gene and, therefore, do not respond to treatments based on estrogen, progesterone or HER2. The goal was to create personalized vaccines using each patient's own immune cells.

> Baylor has been an innovative leader—one of the few centers in the country—that has focused on dendritic cells and their function in immune therapy.
>
> Joyce O'Shaughnessy, MD
> Celebrating Women Chair of Breast Cancer Research

All the patients simultaneously received standard-of-care chemotherapy to help shrink their tumor prior to surgery. From the outset, Dr. O'Shaughnessy believed it was important to introduce the vaccine while patients were still in a potentially curative setting, before the cancer became metastatic and spread to other parts of their bodies.

"We're trying to innovate. We're trying to push the field forward. We're trying to do something for this cancer that has such a great unmet medical need," she said.

The first of these women on the study, "Safety study of chemotherapy combined with dendritic cell vaccine to treat breast cancer," was dosed in December 2013. Since then, two have died from disease recurrence. "The other eight remain without any detectable disease," Dr. O'Shaughnessy said.

"These patients all had very high risk of dying from triple-negative breast cancer without effective therapy," she said. "The whole idea is to wake up these dendritic cells, which basically are not functioning. Their immune system was not working to kill off this cancer."

Genomic-driven targeted therapies can also help TNBC patients, but these cancers are often driven by multiple mutations. What if there are other mutations ready to step to the plate and take over? "When we think about targeted therapies, we think about a drug targeted against one mutation or one driving [cellular] pathway in the cancer," Dr. O'Shaughnessy said.

"That's the beauty of an immunotherapy. If you can get the immune system stimulated against the cancer, it will just kill it, regardless of how many mutations there are."

Still, she is not ready to talk about this clinical trial as promising just yet. She had hoped that more of the women in the study would have registered a pathological complete response (PCR), meaning no cancer in their breast or lymph nodes, prior to surgery. As it was, approximately half recorded a PCR, about the same as standard chemotherapy.

One outstanding question is whether the dendritic cell therapy activated the immune system and either held off or eradicated any residual microscopic disease. As she waits to see if the eight women in the study will remain free of cancer for at least three years, Dr. O'Shaughnessy is hopeful that the vaccine will continue to act as a maintenance drug.

This study was funded by the Amy T. Selkirk Fund for Breast Cancer Immunotherapy, part of Baylor Health Care System Foundation.

"PANCVAX" CLINICAL TRIAL IS

FIRST STUDY OF DENDRITIC CELL VACCINE IN PANCREATIC CANCER PATIENTS

AT BAYLOR UNIVERSITY MEDICAL CENTER AT DALLAS

Patients receive a combination of chemotherapy and cancer vaccine in an effort to spur their immune system into fighting the cancer

This year, pancreatic cancer will eclipse breast cancer to become the nation's third-leading cause of cancer-related death. Patients with lung, colorectal and breast cancer—the other leading causes of cancer mortality—all have benefited from new treatments, leaving the number who die from these cancers relatively stable over the past five years. But the number of patients who die of pancreatic cancer has increased more than 10 percent during that same period, and the disease now accounts for nearly 42,000 deaths annually. Most die within the first year of diagnosis, with fewer than 10 percent surviving more than five years.

Carlos Becerra, MD, medical director of Baylor University Medical Center's Innovative Clinical Trials Center and interim deputy chief of oncology for Baylor University Medical Center at Dallas, said that clearly new treatments are needed for this most aggressive of cancers.

The high mortality rate in pancreatic cancer is due largely to the lack of method for early detection; most patients have advanced disease by the time they are diagnosed. One avenue of hope is a Baylor University Medical Center at Dallas clinical trial, which for the first time uses a dendritic cell vaccine in an effort to mobilize the patient's own immune system to combat pancreatic cancer.

The study, "Dendritic cell vaccine and chemotherapy for patients with pancreatic cancer," or PancVax, is a single center exploratory safety trial that is evaluating the effectiveness and safety of combining a cancer vaccine with chemotherapy, including the standard-of-care treatments of FOLFIRINOX or the combination of gemcitabine plus nab-paclitaxel.

"We want to determine if we can elicit an immune response," said Dr. Becerra, whose study is based on a storied history at Baylor University Medical Center at Dallas. It was prompted by the early efforts of staff at the Baylor Institute of Immunology Research (BIIR); they used dendritic cell therapy to lengthen the survival of Dr. Ralph Steinman, who developed pancreatic cancer. He was the Nobel Prize laureate who discovered the dendritic cell and its role in adaptive immunity. In addition, the world's first cancer vaccine against melanoma was pioneered at BIIR.

Step-by-Step Study Enrolling Pancreatic Cancer Patients

The PancVax study has taken years of planning and regulatory approvals. The first patient in the study was enrolled in late 2015. Although the study is planned to accrue as many as 20 patients, the US Food and Drug Administration has required treating the first three patients one at a time, sequentially, with each completing the vaccination treatment (a series of six injections), which will provide both an added margin of safety and a slower start to the trial. Two patients have completed six vaccines and one is currently under treatment.

The blood cells needed to make the dendritic cells are collected by apheresis. A minimum of 10,000 dendritic cells are needed from each patient to produce a sufficient vaccine. The dendritic cells are transfected with two antigens: mesothelin, a protein found on normal mesothelial cells lining the pleura, pericardium, and peritoneum and overexpressed in a number of tumors including pancreatic adenocarcinoma; and Wilms' tumor protein, found in Wilms' tumors of the kidney and many other cancers, including pancreatic adenocarcinoma.

"Those dendritic cells will then educate the T-cells to go and attack the cancer," Dr. Becerra said.

The vaccine is specific to each patient by using their own cells to make the vaccine, thus minimizing the risk of rejection or other potential complications. So far, there have been no significant side effects, he said. "Our hope is that the immune system will take over and control the cancer, and the patients can live longer," Dr. Becerra said.

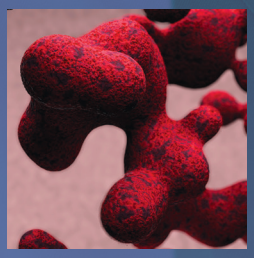
Researchers are now in the process of analyzing test samples from the initial patients in the trial, and plans are for more patients to accrue in the coming year. The study is funded through the Cancer Prevention and Research Institute of Texas, which the voters of Texas approved in 2007, authorizing the state to issue $3 billion in bonds to fund groundbreaking cancer research and prevention programs and services for cancer patients.

For information about enrolling in PancVax or other cancer clinical trials at Baylor University Medical Center at Dallas, please contact the office of Clinical Oncology Research Coordination at 214.818.8472.

VACCINE-BASED CLINICAL TRIALS AIM TO

ATTACK DIFFICULT-TO-TREAT GLIOBLASTOMA BRAIN TUMORS

AT BAYLOR UNIVERSITY MEDICAL CENTER AT DALLAS



Brain tumors are unlike any other cancer. They strike at the organ that allows us to think and control our bodies in a way that other cancers do not. They are also highly resistant to standard treatments.

Only a limited number of anticancer drugs can get into the brain. To get to the tumor cells, you must use drugs that can penetrate the protective blood vessels that make up the blood-brain barrier.

"Our brain was designed, evolutionarily, to keep poisons out, and so only the drugs that are small molecularly, or fat soluble, get into the brain," said Karen Fink, MD, PhD, medical director of neuro-oncology at Baylor University Medical Center at Dallas, and principal investigator at Baylor Scott & White Research Institute. As a result, only a handful of drugs have been approved for use against glioblastoma multiforme (GBM), an extremely aggressive and deadly type of cancer that makes up the majority of primary brain tumors.

Current standard-of-care treatment for GBM includes the surgical removal of as much of the tumor as possible without removing too much vital brain tissue, followed by radiation and chemotherapy using temozolomide. This treatment regimen typically achieves a median survival of 14.6 months. Unfortunately, recurrence of GBM is virtually assured, because surgery cannot remove all of the cancer cells since they are highly invasive and aggressively disperse into surrounding brain tissue. Recurring GBM tumors usually appear within a few centimeters of the resected tumor.

"There are infiltrating tumor cells even in brain tissue that appear perfectly normal," Dr. Fink said. "There's almost always microscopic tumor left, and we have limited treatments for tumors that recur."

The short list of drugs approved for recurring GBM includes temozolomide, carboplatin, irinotecan, bevacizumab and lomustine.

"We're always looking for better therapeutics, because the results of these drugs are disappointing for patients with recurrent GBM," said Dr. Fink, noting that median survival for recurring GBM is only 6 months.

New clinical trials using vaccines for glioblastoma at Baylor University Medical Center at Dallas

Now, using immune therapies, several clinical trials have recently started at Baylor University Medical Center at Dallas and are providing new opportunities for patients with brain cancer. "The hope is, by giving vaccines, we can harness the immune system to attack glioblastoma. In the past, the immune system has not been felt to play much of a role in fighting glioblastoma, but more recently we have realized that we may be able to rev up the immune system by giving it a target to recognize," said Dr. Fink. "The vaccine trials we have open at Baylor University Medical Center try to get the patient's immune system to recognize and kill the tumor cells and to provide protection against tumor recurrence.

> The hope is, by giving vaccines, we can harness the immune system to attack glioblastoma.
>
> Karen Fink, MD, PhD
> Medical Director of Neuro-oncology

"After a vaccine, the immune system can seek out and destroy brain tumor cells that we can't even necessarily see on scans or at surgery. The body itself should help eliminate those abnormal cells," said Dr. Fink.

One clinical trial that began this year involves a vaccine called ICT-121 for GBM patients with recurrent tumors. The treatment primes the patient's immune system to recognize CD-133, which is a marker that is present on many hematopoietic and progenitor stem cells, including many cancer stem cells. The presence of CD-133 on cancer cells is associated with resistance to chemotherapy and survival of the cancer cells.

"Stem cells are the cells within our body that rejuvenate and regenerate our tissues. They're pretty rare. But in glioblastomas, they are the cells that are more resistant to chemotherapy, and they are the ones that we think lead the glioblastoma to keep recurring," Dr. Fink said.

Dendritic cells are removed from the blood of a patient, then sensitized, or pulsed, with CD-133. These activated dendritic cells are then given back to the patient as a series of vaccine injections—once a week for a month, and then once every two months. "The CD-133–sensitized dendritic cells recognize the GBM stem cells and recruit the rest of the immune system to destroy those stem cells, which is how we hope to eradicate the glioblastoma," Dr. Fink said.

About 100 patients will be enrolled nationwide in this clinical trial, including patients at Baylor University Medical Center at Dallas. Like other brain cancer clinical trials, this study involves multiple sites so that a sufficient number of patients with this rare disease can be analyzed and enough evidence can be collected to make valid conclusions.

Patients in this clinical trial may not have been on the drug bevacizumab (Avastin®) and cannot be receiving a steroid dose more than four milligrams per day.

Phase 3 Clinical Trial Vaccine Aimed at Newly Diagnosed Patients

Another brain cancer clinical trial, a phase 3 study called ICT-107, began in September at Baylor University Medical Center at Dallas as a frontline treatment against GBM tumors. This clinical trial also uses a patient's dendritic cells but sensitizes them against six different tumor antigens. "The idea is, if you expose the dendritic cells to more antigens, they're more likely to be more effective when they're put back into the body," Dr. Fink said. Phase 2 testing, which was also conducted at Baylor University Medical Center at Dallas, showed that this vaccine was well-tolerated by patients.

Both the ITC-121 and ITC-107 clinical trials are complicated by a requirement that patients have a particular blood subtype known as HLA-A2, which correlates with a particular immune response. This subtype is found in about 30 percent to 40 percent of the populace.

"We've made strides against brain cancer in the last couple of decades, and people are living longer," Dr. Fink said. "We have hope that these new immune system vaccines will be more effective against GBM and will provide another weapon to aim at these aggressive tumors."

CLINICAL TRIALS USING CAR T-CELLS START TO TREAT BLOOD CANCERS ALL AND MCL

AT BAYLOR UNIVERSITY MEDICAL CENTER AT DALLAS

Beyond vaccines, beyond checkpoint inhibitors, chimeric antigen receptor T-cells (CAR T-cells) are the latest form of cancer therapies aimed at re-establishing the body's immune response to tumors. Like the Chimera of Greek mythology, a hybrid creature composed of more than one animal, CAR T-cells are molecules engineered in the laboratory using a hybrid of proteins grafted onto a patient's T-cells. The hybrid assembly allows the CAR T-cells to carry out multiple specific functions.

This engineering allows CAR T-cells to recognize specific proteins, or antigens, present on the surface of targeted cancer cells, allowing the CAR T-cells to become activated and destroy the tumor (Figure 3). "CAR T-cells are among the most promising approaches to fighting cancer, especially blood cancers, through the development of adoptive cell transfer therapies," said Yair Levy, MD, medical director of hematologic malignancy clinical research at Baylor University Medical Center at Dallas. "They represent a dynamic new line of therapies for blood cancers that have repeatedly relapsed after intensive chemotherapy or have simply failed to respond to standard therapies," Dr. Levy said.

> With the tools of molecular biology, we can create lymphocytes with properties that never existed before in the course of evolution.
>
> Yair Levy, MD
> Medical Director of Hematologic Malignancy Clinical Research

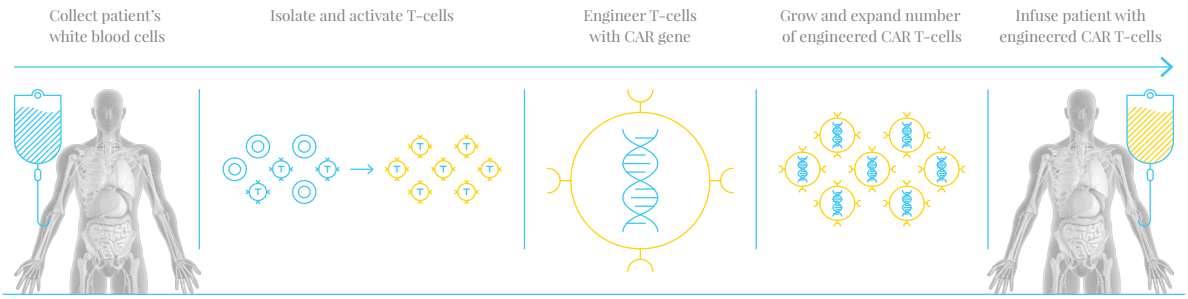


Figure 3. Engineering of patient-specific CAR T-cells

Other cancer immune therapies, such as vaccines derived from a patient's dendritic cells or checkpoint inhibitors that bypass the immune system's natural throttles, rely on reawakening the body's own immune system to seek out and destroy cancer. In contrast, CAR T-cells involve adoptive transfer of effector cells made outside the body, which identify and are targeted specifically against the cancer cells. They may propagate, expand and persist once they are injected into the patient.

"With the tools of molecular biology, we can create lymphocytes with properties that never existed before in the course of evolution," Dr. Levy said. "Some CAR T-cells have shown results that are nothing short of spectacular."

Beginning of New Chimeric Antigen Receptor T-cell (CAR T-cell) Clinical Trials at Baylor University Medical Center at Dallas

On September 1, Baylor University Medical Center at Dallas began clinical trials involving CAR T-cells targeted at acute lymphoblastic leukemia (ALL) and mantle cell lymphoma (MCL). Houston Holmes, MD, the hematologist on the medical staff at Baylor University Medical Center at Dallas, serves as principal investigator for these studies.

ALL is a cancer that starts from immature forms of white blood cells called lymphocytes in the bone marrow, where new blood cells are made. Acute leukemia invades the blood quickly and can involve the lymph nodes, liver, spleen, brain and spinal cord. MCL is another lymphoid cancer considered treatable, but incurable, with standard therapies. It initially responds to most treatments, but when it recurs, it is quite difficult to treat.

Both ALL and MCL are B-cell malignancies that express an antigen called CD19. CAR T-cells in these clinical trials are modified lymphocytes with artificial T-cell receptors specifically engineered to target cancer cells that produce CD19.

How Chimeric Antigen Receptor T-cells (CAR T-cells) Work Against the Cancer

Cancer cells produce antigens that can mediate the normal response of a patient's immune system, allowing the tumor to progressively grow. Unlike acute infections, cancer growth is initially hidden to the immune system, as T-cells are restrained by mechanisms that limit the immune response to the tumors. "Although the body's own T-cells are aware of the cancer, they do not activate an antitumor response; they are tolerant," explained Dr. Levy.

T-cells need a secondary stimulation to be activated against the cancer. In the engineering of CAR T-cells, the T-cells are modified with artificial T-cell receptors, producing a second costimulatory signal that activates them against the cancer.

"We can take antibodies, manipulate them molecularly, insert them into T-cell lymphocytes and give them a new recognition that they never had before, a recognition based on an antibody," Dr. Levy said. The CAR T-cells pursue cancer cells that contain specificity to the receptor that was grafted, such as CD19. "CAR T-cells offer a targeted approach to cancer treatment, and especially in blood cancers," Dr. Levy said. "These are antibodies that can recognize molecules on blood cancers and therefore specifically target them."

IMMUNE CHECKPOINT INHIBITORS

MAKE PROGRESS AGAINST SKIN CANCER AND LUNG CANCER

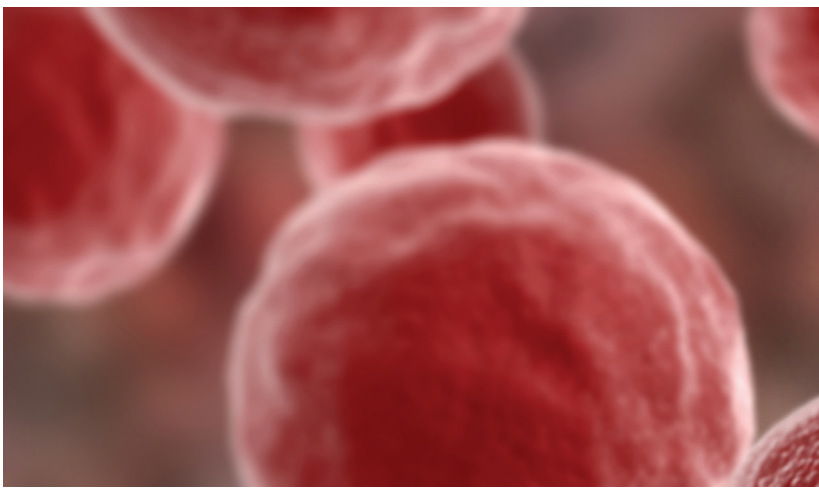
Baylor University Medical Center at Dallas leads the way with important study contributions.

Throughout our lives, the miracle that is our human immune system protects us from harm. Without any effort on our part, the immune system is on constant alert, scanning our bodies for anything out of the ordinary and potentially dangerous, such as viral, bacterial and fungal infections—and, yes, even cancer.

"We've known for many decades that the immune system plays a role in cancer surveillance," said Lance Cowey, MD, a medical oncologist on the medical staff and co-medical director of Baylor University Medical Center's Skin Malignancy Research and Treatment Center. "But identifying and overcoming the barriers of the immune function against cancer has been a problem."

On its own, the immune system can be an imperfect defense against cancer. The problem is that cancer cells can be "smart." They can disguise or cloak themselves from the immune system.

The cancer takes advantage of a specific part of our immune system that also protects us: immune checkpoints.



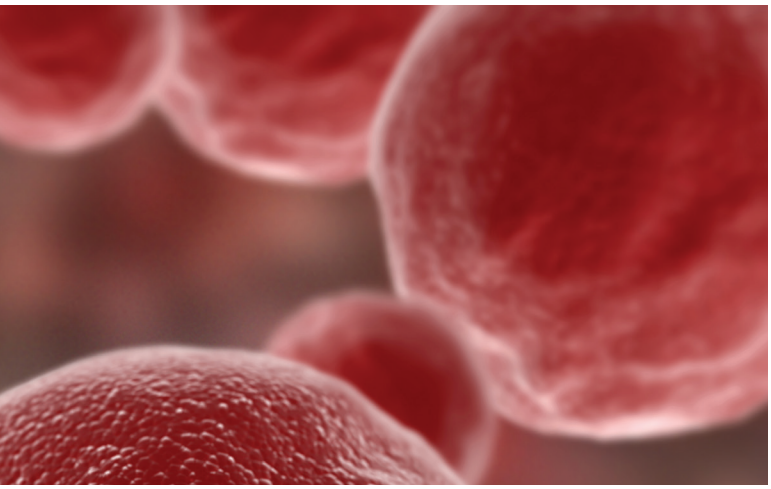
"It's similar to how your coffee maker has an automatic off-switch," explained Dr. Cowey. "Immune checkpoints prevent overactive immune cell function. It's a way the immune cells autoregulate themselves. After activation, the immune cells can then be deactivated so that we don't have persistent immune activation for longer than what is needed."

Once infections are cleared from the body, usually within a few weeks, immune checkpoints tell the immune system to stand down, to flip the off-switch. They keep the immune system from rampaging out of control and attacking healthy cells. But cancer can play a trick on the immune checkpoints by sending out signals that tell the immune system, "These aren't the cancer cells you're looking for."

"The cancer cells take advantage of the immune checkpoints. They take advantage of the off-switches to circumvent normal immune activity against the cancer," Dr. Cowey said. Thus, the cancer hides in plain sight, suddenly invisible to the immune system and free to do what cancer does: uncontrollably grow, divide and spread.

What are Immune Checkpoint Inhibitors?

In just the last few years, cancer researchers have discovered a new set of drugs that allow the immune system to uncloak cancer cells. These drugs are called immune checkpoint inhibitors. And they do exactly that. They inhibit the immune checkpoints, enabling the immune system to once again see, attack and kill the cancer cells (Figure 4). "The immune cells are already primed to recognize the cancer. They've already got the scent. All we're doing is releasing the hounds to attack the cancer," Dr. Cowey said.



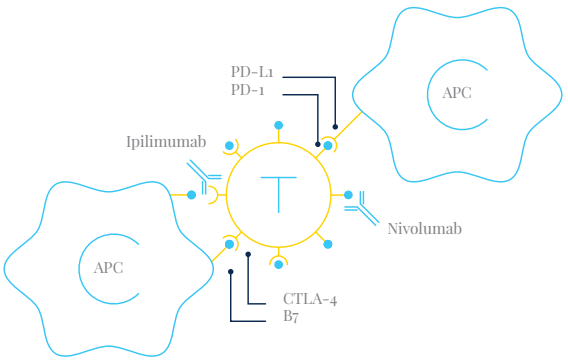


Figure 4. Site of action for checkpoint inhibitors

Adapted by permission from Macmillan Publishers Ltd: *Nature Reviews Urology* (13:421-431), 2016.

Melanoma Study Led to FDA Approval

Baylor University Medical Center at Dallas (BUMC) has been a leader in developing immune checkpoint inhibitors. Led by Dr. Cowey, BUMC was one of the largest among 137 centers worldwide that tested 945 advanced inoperable melanoma skin cancer patients with a combination of two checkpoint inhibitors called nivolumab and ipilimumab. This combination of drugs, documented by Dr. Cowey and other researchers in the July 2015 issue of *The New England Journal of Medicine**, was approved by the US Food and Drug Administration in September 2015 for treatment of advanced melanoma.

Both of these checkpoint inhibitors are monoclonal antibodies. Nivolumab (Opdivo®) binds to the immune checkpoint protein known as PD-1 (programmed death protein 1). Ipilimumab (Yervoy®) binds to the immune checkpoint protein known as CTLA-4 (cytotoxic T-lymphocyte–associated protein 4). "Identification of the immune checkpoints PD-1 and CTLA-4 have been breakthroughs, as they have been important targets for activating the immune system to have an anticancer effect," Dr. Cowey said.

"These drugs have been especially effective in combating melanoma. The combination of ipilimumab and nivolumab has set the highest standard in terms of efficacy in regards to response rate and progression-free survival, compared to other therapies," Dr. Cowey said.

Next-generation trials are already under way to challenge these standards and hopefully improve tolerability. Dr. Cowey is accruing patients to several next-generation combination studies evaluating checkpoint inhibitors in combination with other immune modulators, viral therapy and genetic-targeted therapy.

Checkpoint Inhibitors for Non-Small Cell Lung Cancer

Lung cancer, by far the single greatest cause of cancer-related death, is also one of the more difficult cancers to treat. More than 162,000 Americans will die of this cancer this year. Of the different types of lung cancer, non-small cell lung cancer (NSCLC) is responsible for more than four of every five cases of lung cancer.

"NSCLC tumors are very aggressive and often inoperable by the time they are diagnosed," said Kartik Konduri, MD, co-medical director of the Baylor University Medical Center Chest Cancer Research and Treatment Center. "By the time we usually find the cancer, it is already far advanced," said Dr. Konduri, noting that patients 20 to 30 years ago generally died within six to eight months of diagnosis.

Breakthroughs in recent years have nearly doubled that median survival to 15 to 18 months, thanks to new discoveries including mutations/rearrangements in the EGFR and ALK genes, respectively. These tumors respond well to oral tyrosine kinase inhibitors as a first-line therapy for NSCLC. But what treatments do we have for patients with NSCLC who don't have mutations or other changes in the EGFR or ALK genes in their tumors?

Dr. Konduri is the principal investigator at Baylor University Medical Center at Dallas in a multisite clinical trial known as CheckMate 370. Started in November 2015, this multiyear study could enroll as many as 1,950 patients who are being prescribed combinations of various chemotherapies, followed by the immune checkpoint inhibitor nivolumab.

Patients whose NSCLC tumors have not progressed after first-line standard-of-care treatments are among those eligible for this randomized clinical trial, in which nivolumab is employed as a maintenance drug. Patients start with chemotherapy, then transition to stay on maintenance chemotherapy, move to an immunotherapy or use a combination of chemotherapy and immunotherapy.

> Checkpoint inhibitors are promising drugs. They have opened up a new avenue for therapy. It's a new way of treating patients in oncology. In lung cancer, which is a difficult cancer to treat, it gives more hope for our patients.
>
> Kartik Konduri, MD
> Co-Medical Director, Chest Cancer Research and Treatment Center

"The checkpoint inhibitors block the signals from the tumor that prevent the immune system from attacking it," Dr. Konduri said. "When the cloaking signal from the cancer is blocked, the inhibitory effect on the immune system is removed, and the immune system can rev up and recognize tumor antigens, attack the tumor cells and kill them. These types of trials open up possibilities to find out if these drugs could be used in the frontline setting (or in other settings, for example, after radiation for stage III cancer) in the treatment of lung cancer."

**N Engl J Med. 2015 Jul 2;373(1):23-34.*

For information about enrolling in CheckMate 370 or other cancer clinical trials at Baylor University Medical Center at Dallas, please contact the office of Clinical Oncology Research Coordination at 214.818.8472.

May 2, 2016 - Oct. 13, 2016

RECENT PUBLICATIONS

FROM BAYLOR CHARLES A. SAMMONS CANCER CENTER

Boland CR, Goel A. Prognostic Subgroups among Patients with Stage II Colon Cancer. N Engl J Med. 2016;374(3):277-278.

Bono P, Oudard S, Bodrogi I, Hutson TE, Escudier B, Machiels JP, Thompson JA, Figlin RA, Ravaud A, Basaran M, Porta C, Bracarda S, Brechenmacher T, Lin C, Voi M, Grunwald V, Motzer RJ. Outcomes in Patients With Metastatic Renal Cell Carcinoma Who Develop Everolimus-Related Hyperglycemia and Hypercholesterolemia: Combined Subgroup Analyses of the RECORD-1 and REACT Trials. Clin Genitourin Cancer. 2016 Oct;14(5):406-414.

Bunnell AE, Garby CA, Pearson EJ, Walker SA, Panos LE, Blum JL. The Clinical Utility of Next Generation Sequencing Results in a Community-Based Hereditary Cancer Risk Program. J Genet Couns. 2016 Jun 9. [Epub ahead of print]

Campbell JA, Krause JR. Acute promyelocytic leukemia after renal transplant and filgrastim treatment for neutropenia. Proc (Bayl Univ Med Cent). 2016 Oct;29(4):396-398.

Campa M, Mansouri B, Wilcox B, Griffin JR. Radiation-induced localized bullous pemphigoid in a patient with breast carcinoma. Dermatol Online J. 2016 Jan 15;22(1).

Cass I, Duska LR, Blank SV, Cheng G, duPont NC, Frederick PJ, Hill EK, Matthews CM, Pua TL, Rath KS, Ruskin R, Thaker PH, Berchuck A, Gostout BS, Kushner DM, Fowler JM. Stress and burnout among gynecologic oncologists: A Society of Gynecologic Oncology Evidence-based Review and Recommendations. Gynecol Oncol. 2016 Nov;143(2):421-427.

Chari A, Htut M, Zonder JA, Fay JW, Jakubowiak AJ, Levy JB, Lau K, Burt SM, Tunquist BJ, Hilder BW, Rush SA, Walker DH, Ptaszynski M, Kaufman JL. A phase 1 dose-escalation study of filanesib plus bortezomib and dexamethasone in patients with recurrent/refractory multiple myeloma. Cancer. 2016 Nov 15;122(21):3327-3335.

Cheng YL, Jordan L, Chen HS, Kang D, Oxford L, Plemons J, Parks H, Rees T. Chronic periodontitis can affect the levels of potential oral cancer salivary mRNA biomarkers. J Periodontal Res. 2016 Aug 23. doi: 10.1111/jre.12407. [Epub ahead of print]

Choueiri TK, Escudier B, Powles T, Tannir NM, Mainwaring PN, Rini BI, Hammers HJ, Donskov F, Roth BJ, Peltola K, Lee JL, Heng DY, Schmidinger M, Agarwal N, Sternberg CN, McDermott DF, Aftab DT, Hessel C, Scheffold C, Schwab G, Hutson TE, Pal S, Motzer RJ; METEOR investigators. Cabozantinib versus everolimus in advanced renal cell carcinoma (METEOR): final results from a randomised, open-label, phase 3 trial. Lancet Oncol. 2016 Jul;17(7):917-27.

Cizenski J, Griffin J, Menter A. Image Gallery: Cutaneous T-cell lymphoma mimicking a gyrate erythema. Br J Dermatol. 2016 May;174(5):e42.

Colbert GB, Vankawala P, Kuperman MB, Mennel RG. Mammary-type myofibroblastoma with the nephrotic syndrome. Proc (Bayl Univ Med Cent). 2016 Jul;29(3):318-20.

Cortés J, Rugo HS, Twelves C, Awada A, Perez EA, Im SA, Zhao C, Hoch U, Tomkinson D, Buchanan J, Tagliaferri M, Hannah A, O'Shaughnessy J. Safety and tolerability of etirinotecan pegol in advanced breast cancer: analysis of the randomized, phase 3 BEACON trial. Springerplus. 2016 Jul 8;5(1):1033.

Ghosh P, Tie J, Muranyi A, Singh S, Brunhoeber P, Leith K, Bowermaster R, Liao Z, Zhu Y, LaFleur B, Tran B, Desai J, Jones I, Croxford M, Jover R, Goel A, Waring P, Hu S, Teichgraber V, Rohr UP, Ridder R, Shanmugam K, Gibbs P. Girdin (GIV) Expression as a Prognostic Marker of Recurrence in Mismatch Repair-Proficient Stage II Colon Cancer. Clin Cancer Res. 2016 Jul 15;22(14):3488-98.

Glasgow SC, Morris AM, Baxter NN, Fleshman JW, Alavi KS, Luchtefeld MA, Monson JR, Chang GJ, Temple LK. Development of The American Society of Colon and Rectal Surgeons' Rectal Cancer Surgery Checklist. Dis Colon Rectum. 2016 Jul;59(7):601-6

Habib JG, O'Shaughnessy JA. The hedgehog pathway in triple-negative breast cancer. Cancer Med. 2016 Aug 18. doi: 10.1002/cam4.833. [Epub ahead of print]

Hashimoto Y, Zumwalt TJ, Goel A. DNA methylation patterns as noninvasive biomarkers and targets of epigenetic therapies in colorectal cancer. Epigenomics. 2016 May;8(5):685-703.

Haskins IN, Fleshman JW, Amdur RL, Agarwal S. The impact of bowel preparation on the severity of anastomotic leak in colon cancer patients. J Surg Oncol. 2016 Sep 16. doi: 10.1002/jso.24426. [Epub ahead of print]

Hicks DA, Galimanis CE, Webb PG, Spillman MA, Behbakht K, Neville MC, Baumgartner HK. Claudin-4 activity in ovarian tumor cell apoptosis resistance and migration. BMC Cancer. 2016 Oct 11;16(1):788.

Hortobagyi GN, Stemmer SM, Burris HA, Yap YS, Sonke GS, Paluch-Shimon S, Campone M, Blackwell KL, André F, Winer EP, Janni W, Verma S, Conte P, Arteaga CL, Cameron DA, Petrakova K, Hart LL, Villanueva C, Chan A, Jakobsen E, Nusch A, Burdaeva O, Grischke EM, Alba E, Wist E, Marschner N, Favret AM, Yardley D, Bachelot T, Tseng LM, Blau S, Xuan F, Souami F, Miller M, Germa C, Hirawat

S, O'Shaughnessy J. Ribociclib as First-Line Therapy for HR-Positive, Advanced Breast Cancer. N Engl J Med. 2016 Oct 7.

Imaoka H, Toiyama Y, Fujikawa H, Hiro J, Saigusa S, Tanaka K, Inoue Y, Mohri Y, Mori T, Kato T, Toden S, Goel A, Kusunoki M. Circulating microRNA-1290 as a novel diagnostic and prognostic biomarker in human colorectal cancer. Ann Oncol. 2016 Oct;27(10):1879-86.

Kathania M, Khare P, Zeng M, Cantarel B, Zhang H, Ueno H, Venuprasad K. Itch inhibits IL-17-mediated colon inflammation and tumorigenesis by ROR-γt ubiquitination. Nat Immunol. 2016 Aug;17(8):997-1004.

Keller DS, Parikh N, Senagore AJ. Predicting opportunities to increase utilization of laparoscopy for colon cancer. Surg Endosc. 2016 Aug 29. [Epub ahead of print]

Kim TW, Hong S, Lin Y, Murat E, Joo H, Kim T, Pascual V, Liu YJ. Transcriptional Repression of IFN Regulatory Factor 7 by MYC Is Critical for Type I IFN Production in Human Plasmacytoid Dendritic Cells. J Immunol. 2016 Oct 15;197(8):3348-3359.

Kinney MH, Knox SM. Operative management of dermatofibrosarcoma protuberans of the breast. Proc (Bayl Univ Med Cent). 2016 Jul;29(3):315-7.

Klein J, Gonzalez SA, Fischbach BV, Yango AF, Rajagopal A, Rice KM, Saim M, Barri YM, Melton LB, Klintmalm GB, Chandrakantan A. Routine Ultrasonography Surveillance of Native Kidneys for Renal Cell Carcinoma in Kidney Transplant Candidates. Clin Transplant. 2016 Aug;30(8):946-53.

Lazaryan A, Wang T, Spellman SR, Wang HL, Pidala J, Nishihori T, Askar M, Olsson R, Oudshoorn M, Abdel-Azim H, Yong A, Gandhi M, Dandoy C, Savani B, Hale G, Page K, Bitan M, Reshef R, Drobyski W, Marsh SG, Schultz K, Müller CR, Fernandez-Viña MA, Verneris MR, Horowitz MM, Arora M, Weisdorf DJ, Lee SJ. Human leukocyte antigen supertype matching after myeloablative hematopoietic cell transplantation with 7/8 matched unrelated donor allografts: A report from the Center for International Blood and Marrow Transplant Research. Haematologica. 2016 Oct;101(10):1267-1274.

Li W, O'Shaughnessy JA, Hayes DF, Campone M, Bondarenko I, Zbarskaya I, Brain E, Stenina M, Ivanova O, Graas MP, Neven P, Ricci DS, Griffin TW, Kheoh T, Yu MK, Gormley M, Martin J, Schaffer M, Zelinsky K, De Porre P, Johnston SR. Biomarker Associations with Efficacy of Abiraterone Acetate and Exemestane in Postmenopausal Patients with Estrogen Receptor-Positive Metastatic Breast Cancer. Clin Cancer Res. 2016 Dec 15;22(24):6002-6009.

Lowery JT, Ahnen DJ, Schroy PC 3rd, Hampel H, Baxter N, Boland CR, Burt RW, Butterly L, Doerr M, Doroshenk M, Feero WG, Henrikson N, Ladabaum U, Lieberman D, McFarland EG, Peterson SK, Raymond M, Samadder NJ, Syngal S, Weber TK, Zauber AG, Smith R. Understanding the contribution of family history to colorectal cancer risk and its clinical implications: A state-of-the-science review. Cancer. 2016 Sep 1;122(17):2633-45.

Mitsui H, Kiecker F, Shemer A, Cannizzaro MV, Wang CQ, Gulati N, Ohmatsu H, Shah KR, Gilleaudeau P, Sullivan-Whalen M, Cueto I, McNutt NS, Suárez-Fariñas M, Krueger JG Discrimination of dysplastic nevi from common melanocytic nevi by cellular and molecular criteria. J Invest Dermatol. 2016 Oct;136(10):2030-40.

Moreno-Ortiz JM, Ayala-Madrigal Mde L, Corona-Rivera JR, Centeno-Flores M, Maciel-Gutiérrez V, Franco-Topete RA, Armendáriz-Borunda J, Hotchkiss E, Pérez-Carbonell L, Rhees J, Boland CR, Gutiérrez-Angulo M. Novel Mutations in MLH1 and MSH2 Genes in Mexican Patients with Lynch Syndrome. Gastroenterol Res Pract. 2016;2016:5278024.

Peterson DE, O'Shaughnessy JA, Rugo HS, Elad S, Schubert MM, Viet CT, Campbell-Baird C, Hronek J, Seery V, Divers J, Glaspy J, Schmidt BL, Meiller TF. Oral mucosal injury caused by mammalian target of rapamycin inhibitors: emerging perspectives on pathobiology and impact on clinical practice. Cancer Med. 2016 Aug;5(8):1897-907

Pichler M, Stiegelbauer V, Vychytilova-Faltejskova P, Ivan C, Ling H, Winter E, Zhang X, Goblirsch M, Wulf-Goldenberg A, Ohtsuka M, Haybaeck J, Svoboda M, Gerger A, Okugawa Y, Hoefler G, Goel A, Slaby O, Calin GA. Genome-wide microRNA analysis identifies miR-188-3p as novel prognostic marker and molecular factor involved in colorectal carcinogenesis. Clin Cancer Res. 2016 Sep 6. pii: clincanres.0497.2016. [Epub ahead of print]

Raudonis BM, Kelley IH, Rowe N, Ellis J. A Pilot Study of Proinflammatory Cytokines and Fatigue in Women With Breast Cancer During Chemotherapy. Cancer Nurs. 2016 Jun 27. [Epub ahead of print]

Roy A, Mahasittiwat P, Weiner AA, Hunt SR, Mutch MG, Birnbaum EH, Kodner IJ, Read TE, Fleshman JW, Olsen JR, Myerson RJ, Parikh PJ. Preoperative short-course radiation therapy for rectal cancer provides excellent disease control and toxicity: Results from a single US institution. Pract Radiat Oncol. 2017 Jan - Feb;7(1):e51-e58.

Sapisochin G, Facciuto M, Rubbia-Brandt L, Marti J, Mehta N, Yao F, Vibert E, Cherqui D, Grant DR, Hernandez-Alejandro R, Dale C, Cucchetti A, Pinna A, Hwang S, Lee S, Agopian V, Busuttil R, Rizvi S, Heimbach J, Montenovo M, Reyes J, Cesaretti M, Soubrane O, Reichman T, Seal J, Tw Kim P, Klintmalm G, Sposito C, Mazzaferro V, Dutkowski P, Clavien PA, Toso C, Majno P, Kneteman N, Saunders C, Bruix J; iCCAInternational Consortium. Liver transplantation for "very early" intrahepatic cholangiocarcinoma. international retrospective study supporting a prospective assessment. Hepatology. 2016 Oct;64(4):1178-88.

Sarantopoulos J, Goel S, Chung V, Munster P, Pant S, Patel MR, Infante J, Tawbi H, Becerra C, Bruce J, Kabbinavar F, Lockhart AC, Tan E, Yang S, Carlson G, Scott JW, Sharma S. Randomized phase 1

crossover study assessing the bioequivalence of capsule and tablet formulations of dovitinib (TKI258) in patients with advanced solid tumors. Cancer Chemother Pharmacol. 2016 Sep 28. [Epub ahead of print]

Schmitt N, Liu Y, Bentebibel SE, Ueno H. Molecular Mechanisms Regulating T Helper 1 versus T Follicular Helper Cell Differentiation in Humans. Cell Rep. 2016 Jul 26;16(4):1082-95

Shigeyasu K, Okugawa Y, Toden S, Boland CR, Goel A. Exportin-5 functions as an oncogene and a potential therapeutic target in colorectal cancer. Clin Cancer Res. 2016 Aug 23. pii: clincanres.1023.2016. [Epub ahead of print]

Shirley BM, Kang DR, Sakamoto AH. Malignant Solitary Fibrous Tumor of the Scalp. J Maxillofac Oral Surg. 2016 Jul;15(Suppl 2):245-8.

Shu CA, Pike MC, Jotwani AR, Friebel TM, Soslow RA, Levine DA, Nathanson KL, Konner JA, Arnold AG, Bogomolniy F, Dao F, Olvera N, Bancroft EK, Goldfrank DJ, Stadler ZK, Robson ME, Brown CL, Leitao MM Jr, Abu-Rustum NR, Aghajanian CA, Blum JL, Neuhausen SL, Garber JE, Daly MB, Isaacs C, Eeles RA, Ganz PA, Barakat RR, Offit K, Domchek SM, Rebbeck TR, Kauff ND. Uterine Cancer After Risk-Reducing Salpingo-oophorectomy Without Hysterectomy in Women With BRCA Mutations. JAMA Oncol. 2016 Nov 1;2(11):1434-1440.

Sternberg C, Armstrong A, Pili R, Ng S, Huddart R, Agarwal N, Khvorostenko D, Lyulko O, Brize A, Vogelzang N, Delva R, Harza M, Thanos A, James N, Werbrouck P, Bögemann M, Hutson T, Milecki P, Chowdhury S, Gallardo E, Schwartsmann G, Pouget JC, Baton F, Nederman T, Tuvesson H, Carducci M. Randomized, Double-Blind, Placebo-Controlled Phase III Study of Tasquinimod in Men With Metastatic Castration-Resistant Prostate Cancer. J Clin Oncol. 2016 Aug 1;34(22):2636-43.

Thompson PA, Ashbeck EL, Roe DJ, Fales L, Buckmeier J, Wang F, Bhattacharyya A, Hsu CH, Chow HH, Ahnen DJ, Boland CR, Heigh RI, Fay DE, Hamilton SR, Jacobs ET, Martinez ME, Alberts DS, Lance P. Selenium Supplementation for Prevention of Colorectal Adenomas and Risk of Associated Type 2 Diabetes. J Natl Cancer Inst. 2016 Aug 16;108(12).

Thompson PA, Ashbeck EL, Roe DJ, Fales L, Buckmeier J, Wang F, Bhattacharyya A, Hsu CH, Chow SH, Ahnen DJ, Boland CR, Heigh RI, Fay DE, Hamilton SR, Jacobs ET, Martinez EM, Alberts DS, Lance P. Celecoxib for the Prevention of Colorectal Adenomas: Results of a Suspended Randomized Controlled Trial. J Natl Cancer Inst. 2016 Aug 16;108(12).

Trotter JF. Editorial for neuroendocrine tumor for liver transplant. Am J Transplant. 2016 Jun 19. doi: 10.1111/ajt.13924. [Epub ahead of print]

Vogelzang NJ, Fizazi K, Burke JM, De Wit R, Bellmunt J, Hutson TE, Crane E, Berry WR, Doner K, Hainsworth JD, Wiechno PJ, Liu K, Waldman MF, Gandhi A, Barton D, Jungnelius U, Fandi A, Sternberg CN, Petrylak DP. Circulating Tumor Cells in a Phase 3 Study of Docetaxel and Prednisone with or without Lenalidomide in Metastatic Castration-resistant Prostate Cancer. Eur Urol. 2017 Feb;71(2):168-171.

Waller A, Findeis S, Lee MJ. Familial Adenomatous Polyposis. J Pediatr Genet. 2016 Jun;5(2):78-83.

Weng W, Okugawa Y, Toden S, Toiyama Y, Kusunoki M, Goel A. FOXM1 and FOXQ1 are promising prognostic biomarkers and novel targets of tumor suppressive miR-342 in human colorectal cancer. Clin Cancer Res. 2016 Oct 1;22(19):4947-4957.

Yardley DA, Reeves J, Dees EC, Osborne C, Paul D, Ademuyiwa F, Soliman H, Guthrie T, Andersen J, Krekow L, Choksi J, Daniel B, Danso M, Favret A, Oommen S, Brufsky A, Bromund JL, Lin Y, Ibrahim AB, Richards PD. Ramucirumab With Eribulin Versus Eribulin in Locally Recurrent or Metastatic Breast Cancer Previously Treated With Anthracycline and Taxane Therapy: A Multicenter, Randomized, Phase II Study. Clin Breast Cancer. 2016 Dec;16(6):471-479.

Yin W, Duluc D, Joo H, Xue Y, Gu C, Wang Z, Wang L, Ouedraogo R, Oxford L, Clark A, Parikh F, Kim-Schulze S, Thompson-Snipes L, Lee SY, Beauregard C, Woo JH, Zurawski S, Sikora AG, Zurawski G, Oh S. Therapeutic HPV cancer vaccine targeted to CD40 elicits effective CD8+ T-cell immunity. Cancer Immunol Res. 2016 Oct;4(10):823-834.

Zaydfudim VM, Vachharajani N, Klintmalm GB, Jarnagin WR, Hemming AW, Doyle MB, Cavaness KM, Chapman WC, Nagorney DM. Liver Resection and Transplantation for Patients With Hepatocellular Carcinoma Beyond Milan Criteria. Ann Surg. 2016 Oct;264(4):650-8.

BAYLOR CHARLES A. SAMMONS CANCER CENTER

CURRENT CLINICAL TRIALS

Site	Study ID	Location	Principal Investigator
Breast	016-143	BUMC	Joyce A. O'Shaughnessy, MD
Chest	T01623	Texas Oncology-Dallas	Kartik Konduri, MD
GU	15197	Texas Oncology-Dallas	Thomas E. Hutson, DO
Hematologic Malignancies	016-024	BUMC	Micah Burch, MD
	016-068	BUMC	Joseph Fay, MD
	016-048	BUMC	Joseph Fay, MD
	016-059	BUMC	Houston Holmes, MD
	016-024	BUMC	M. Yair Levy, MD
	016-077	BUMC	M. Yair Levy, MD
	016-144	BUMC	M. Yair Levy, MD
Liver	15190	Texas Oncology-Dallas	A. Scott Paulson, MD
Neuro-oncology	016-130	BUMC	Karen Fink, MD, PhD
Solid Tumors	15215	Texas Oncology-Dallas	Carlos H. Roberto Becerra, MD
	T01608	Texas Oncology-Dallas	Carlos H. Roberto Becerra, MD

Study Title

Neratinib Treatment in Patients with Chemotherapy-Refractory Metastic Breast Cancer

A Phase II Single-arm Trial to Investigate Tepotinib in Stage IIIB/IV Adenocarcinoma of the Lung with MET Exon 14 (METex14) Skipping Alterations After Failure of at Least One Prior Active Therapy, Including a Platinum-doublet-containing Regimen

A Phase 3, Multinational, Randomized, Open-label, Parallel-arm Study of Avelumab (msb0010718c) in Combination with Axitinib (Inlyta(Registered)) Versus Sunitinib (Sutent(Registered)) Monotherapy in the First-line Treatment of Patients with Advanced Renal Cell Carcinoma

Open-Label, Phase 2 Study to Evaluate the Efficacy and Safety of CUDC-907 with and without Rituximab in Patients with Relapsed/Refractory MYC-Altered Diffuse Large B-Cell Lymphoma

Clinical-grade Molecular Profiling of Patients with Multiple Myeloma and Related Plasma Cell Malignancies (MMRF-002)

Phase II Multicenter Trial of Single Autologous Hematopoietic Cell Transplant Followed by Lenalidomide Maintenance for Multiple Myeloma with or without Vaccination with Dendritic Cell /Myeloma Fusions

A Phase 1/2 Multi-Center Study Evaluating the Safety and Efficacy of KTE-C19 in Adult Subjects with Relapsed/Refractory B-precursor Acute Lymphoblastic Leukemia (r/r ALL)

A Phase I Dose Escalation Study of Immunotherapy with IMMU-114 in Patients with Non-Hodgkin's Lymphoma (NHL) and Chronic Lymphocytic Leukemia (CLL)

A Two-Stage Blinded Study to Assess Accelerometry-Tracked Pre-Treatment Physical Activity as Surrogate Indicator of Clinical Performance Status

A Randomized, Phase II Study of CX-01 Combined with Standard Induction Therapy for Newly Diagnosed Acute Myeloid Leukemia

A Phase II Study of Pembrolizumab (MK-3475) as Monotherapy in Subjects with Previously Systemically Treated Advanced Hepatocellular Carcinoma (KEYNOTE-224)

A Phase 3, Randomized, Open-Label Study to Evaluate the Efficacy and Safety of Eflornithine with Lomustine Compared to Lomustine Alone in Patients with Anaplastic Astrocytoma that Progress/Recur After Irradiation and Adjuvant Temozolomide Chemotherapy

An Open-Label, First-in-Human Study of the Safety, Tolerability, and Pharmacokinetics of VX-970 in Combination With Cytotoxic Chemotherapy in Subjects with Advanced Solid Tumors

A Phase 1, Open-Label Dose Escalation First-in-Human Study to Evaluate the Tolerability, Safety, Maximum Tolerated Dose, Preliminary Clinical Activity and Pharmacokinetics of AM0010 in Patients with Advanced Solid Tumors

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