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FEATURE ARTICLE
PACKING A SUPERPUNCH
Immunotherapy: The Next Frontier

Cell Support

Many cancer treatments are classified as immunotherapy, but most fall into the four following categories.

Q What are monoclonal antibodies (immune checkpoint inhibitors)?

A Researchers have developed monoclonal antibodies that target immune cells (lymphocytes).

These antibodies seek out specific proteins on lymphocytes (immune checkpoints) that regulate the lymphocyte activity. After activation, the lymphocytes can then attack cancer cells.

Q What is adoptive cell therapy?

A Adoptive cell therapy differs from monoclonal antibodies in that the lymphocytes are directly harvested from the patient's tumor and multiplied in a lab. These cells can be modified, augmented, and then administered to the patient as a form of immune cellular therapy against the cancer.

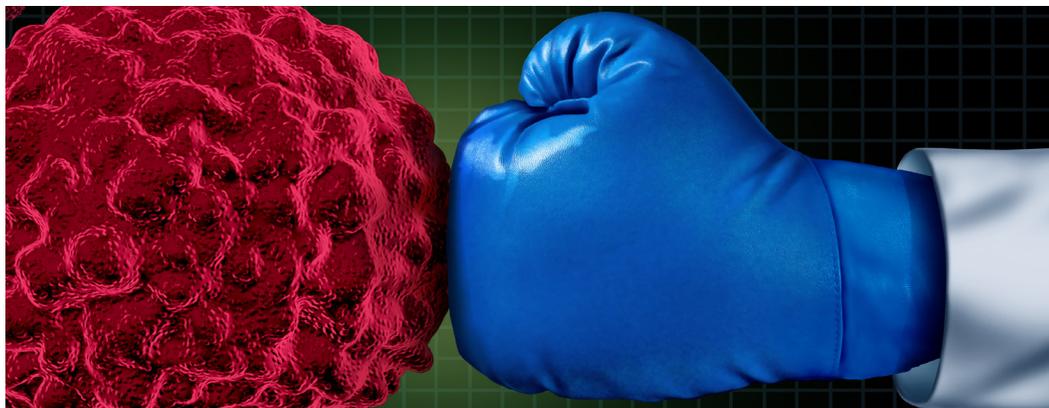
Q What are cancer vaccines?

A Vaccines are another form of immunotherapy, and many are in development. Peptide vaccines are based on stimulating an immune response against a protein commonly present on certain cancer cells. Dendritic cell vaccines are a type of cell-based therapy and require removal of the cells which present proteins to the immune system (called dendritic cells). These extracted dendritic cells can then be activated and programmed to recognize cancer cells based on common cancer proteins.

Q What are non-specific immunotherapies (cytokines)?

A Some immunotherapy drugs and proteins don't target cancer cells specifically, but instead boost the immune system, leading it to a better response to cancer cells. The cytokines (interleukins and interferons) are capable of activating a broad array of immune cells with the potential benefit of fighting infections or cancer.

Immunotherapy: The Next Frontier



The human body is incredibly effective at fighting disease . . . except when the disease is cancer. Thanks to recent discoveries, Texas Oncology physicians are increasingly turning to immunotherapy, transforming the immune system from Clark Kent to Superman®.

“Immunotherapy is one of the next great frontiers in cancer care,” said Dr. Lance Cowey, M.D., a medical oncologist at Texas Oncology–Baylor Charles A. Sammons Cancer Center. “It could rank with radiation therapy and chemotherapy as the next great advancement in cancer care. Recent discoveries have been game changers in the way we look at immunotherapy to treat cancer.”

Patients treated with immunotherapy are given drugs that enhance the immune system; in effect giving it a booster shot and allowing it to pack a superpunch. The growth of cancer cells is slowed or stopped entirely and the cancer cannot spread as a result.

First-generation immunotherapy treatments are non-cancer type specific. Patients are injected with additional interleukins or interferons, which the body makes naturally, to help the immune system cells grow and divide more quickly, and resist infection and cancer. This is an effective treatment for some cancers.

Recent advances have focused on fighting cancer more specifically. Every day, foreign pathogens like bacteria or viruses invade the body and cause disease. To fight these, the immune system makes antibodies which bind to specific antigens within the foreign cells and eliminate them.

New immunotherapy drugs work similarly. Antibodies are designed and created in a lab

to target specific antigens in cancers. Once they're injected into a patient, the antibodies are on a seek and destroy mission. The upside is healthy cells are not affected since they don't contain the targeted antigens.

Vaccines are a third form of immunotherapy. Physicians remove immune cells and create a vaccine specific to a patient and their cancer. The vaccines may boost the immune response. They can also help prevent recurrence since the immune system has a “memory” of how it fought diseases in the past.

Cowey is excited about the prospects for immunotherapy for many cancer types. “There is still a lot of work to do, but research is constantly evolving,” he noted. “We recently discovered lung cancer was responsive to some immunotherapies. That rocked everyone's world because it had previously been considered a non-responsive cancer. As a result, we're looking at many other non-responsive cancers to determine if immunotherapy may now be effective.”

Cowey encourages patients to speak with their doctor about whether immunotherapy is an effective, appropriate treatment option for their cancer. 



Lance Cowey, M.D.

Medical Oncologist,
Texas Oncology–Baylor Charles A.
Sammons Cancer Center

Treatment Breakthroughs Spur Domino Effect



For years, patients diagnosed with late stage melanoma had little reason for hope. No new treatments had become available for more than a decade. But then, 2011 was a breakthrough year for melanoma treatments, when two drugs made huge strides in treating the disease. Now, Texas Oncology researchers are looking at the long-term effectiveness of one of the immunotherapy treatments, paving the way for other new, promising alternatives to reach patients.

“Breakthroughs in cancer treatment lead to others,” said Debra Patt, M.D., a medical oncologist at Texas Oncology–Austin Central. “It’s exciting to see the groundbreaking research we’re doing at Texas Oncology result in more treatments

being evaluated through clinical trials, approved by the FDA and being used to help our cancer patients.”

Ipilimumab received FDA approval as a treatment for Stage III and Stage IV melanoma that can’t be removed by surgery or has spread to other parts of the body. It doesn’t kill melanoma cells directly. Instead, it helps increase immune system activity so that the immune system can kill cancer cells.

Patt, lead investigator, and other Texas Oncology researchers recently participated in an important nationwide research study that aimed to provide a more precise estimate of long-term survival rates for patients with advanced or metastatic melanoma treated with ipilimumab. Researchers analyzed 1,861 melanoma patients who received the drug during treatment and ultimately confirmed evidence supporting its effectiveness. The study was the largest of its kind to date.

“We saw that a large percentage of patients lived beyond the prescribed range, and that gives patients and physicians great hope,” said Patt.

After ipilimumab received FDA approval, two additional similar treatments have been approved. Ipilimumab is also currently undergoing clinical trials for the treatment of certain lung, head and neck, bladder, and prostate cancers.

“Texas Oncology’s participation in cancer research, like this study, allows patients access to exciting new clinical trials and novel therapies in their own communities,” Patt said. 



Debra Patt, M.D., M.P.H., M.B.A.
Medical Oncologist,
Texas Oncology–Austin Central

Continuing Immunotherapy Research is Essential



Joseph Fay, M.D.
Medical Oncologist,
Texas Oncology–Baylor Charles A. Sammons
Cancer Center Blood and Marrow Transplant

“Immunotherapy is the path for future cancer treatment,” said Joseph Fay, M.D., medical oncologist at Texas Oncology–Baylor Charles A. Sammons Cancer Center Blood and Marrow Transplant. “It will become the standard treatment option and lead to the eradication of the disease altogether. In this generation, we’ve seen polio and other deadly infectious diseases eradicated using vaccines and immune system responses.

“Although the data aren’t conclusive, it appears that immunotherapy is already curing some cancers, such as melanoma and certain hematological malignancies. It suggests treatment like chemotherapy reduces the number of cancer cells, and then the immune system takes over to kill the remaining cells and prevent more from developing.”

A pioneer in immunotherapy, Fay has served as principal investigator for more than 80 clinical trials, including several current National Cancer Institute clinical trials of dendritic cell biology and immunotherapy.



HOW DOES IPILIMUMAB WORK?

A group of immune system cells called T-cells can recognize and destroy cancer cells. There is also a mechanism in the immune system that interrupts T-cells from this destruction. Ipilimumab works with the body’s immune system to turn off this mechanism, allowing T-cells to continue fighting cancer cells.

About Texas Oncology

As an independent oncology practice, Texas Oncology is comprised of more than 375 physicians and more than 150 sites of service throughout Texas and southeastern Oklahoma and is a pioneer in community-based cancer care. Patients are treated with today's most advanced, effective cancer technologies and treatments, and have the opportunity to take part in some of the most promising clinical trials in the nation for new drugs and treatments for a broad range of cancers, near the critical support of family and friends.

Texas Breast Specialists, Texas Oncology Surgical Specialists, and Texas Urology Specialists are a part of **Texas Oncology**.

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faces of IMMUNOTHERAPY

After a Stage IV melanoma diagnosis and conventional therapies provided little progress against her disease, Kathie turned to a Phase III clinical trial for ipilimumab. One year ago, De Gracia's tests detected no cancer.



Kathie De Gracia, Addison

“I'm a huge proponent of immunotherapy. I'm fortunate to be alive today, thanks to Texas Oncology's research and new treatment developments. Together, Dr. Cowey and I fought my cancer in different ways. I wouldn't have received the same outstanding treatment anywhere else.”

Children's Cancer Vaccine Has Exciting Potential

Texas Oncology is using immunotherapy to treat its smallest – and often most vulnerable – patients. A clinical trial of an innovative vaccine is underway that could be a lifesaving breakthrough for pediatric patients with Ewing sarcoma, a rare bone cancer.

“We're looking at the immune system response against cancer cells and their impact on further growth of tumors,” said Maurizio Ghisoli, M.D., a pediatric oncologist at Texas Oncology–Medical City Dallas Pediatric Hematology-Oncology. **“Much like with the measles or other vaccines, after activation, the immune system memorizes its response against cancer antigens and then polices growth of new cancer cells.”**

Ewing sarcoma is an aggressive bone and soft tissue cancer, primarily affecting children and adolescents. While it accounts for about 3 percent of all childhood cancers, two-thirds of the patients diagnosed with it will not survive with current treatments.

Ghisoli is the lead investigator for a Phase I personalized vaccine clinical trial that aims to combat the genetic characteristics of each child's cancer. “Mary Crowley Cancer Research Center researchers have developed a technology that led us to turn off the cancer cell signal that blocks the immune system activation and in turn fights cancer,” said Ghisoli. “With this technology, and our knowledge of how

the immune system works, we believed we could treat patients with Ewing sarcoma and other solid tumors.”

Physicians surgically remove cancer tissue from the patient and use it to develop a whole-cell personalized vaccine. The vaccine, customized to the specific antigenic makeup of the patient's cancer, is then injected under the patient's skin every month over a four to 12 month period.

The vaccine trains the immune system to recognize tumor cells and boosts the immune system so that it produces more cancer-fighting cells. The patient is closely monitored to measure the *in-vitro* immune system's response.

“In the Phase I trial, we've proven the vaccine is safe and this technology is feasible for the pediatric population,” Ghisoli said. “All 17 patients tested that received the vaccine had a seroconversion of the ELISPOT (an *in-vitro* test used to measure immune response against specific antigens). We've seen several patients whose cancer hasn't progressed in 18 months, and although we are still in an early phase in our research, that's very promising. It's offering great benefit with minimal side effects.”

With these encouraging results, the team is exploring initiation of a randomized, multicenter Phase IIb trial upon FDA approval. 



Maurizio Ghisoli, M.D.
Pediatric Hematology-Oncology,
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