Immunotherapy Network Launches First Trial

**NCI–industry–academia partnership aims to advance the development of effective therapies**

When clinical trial number NCT01456585 opened in June, it held a unique distinction: The phase I study of a CD40-targeting compound in patients with operable pancreatic cancer is the first led by the Cancer Immunotherapy Trials Network (CITN). Established by the National Cancer Institute (NCI) to accelerate the development of promising immunotherapeutic agents, the CITN includes 28 prominent research institutions in the United States and Canada.

“I’m really excited about what this represents—a true assembly of experts,” says Robert Vonderheide, MD, DPhil, a medical oncologist at the Abramson Cancer Center of the University of Pennsylvania (UPenn), a CITN site. He notes that biotech and pharmaceutical companies are contributing experimental drugs, financial support, and expertise in trial design to the CITN.

The network grew out of an NCI workshop on immunotherapies in 2007. “Immunotherapeutic agents had been invented and proven effective in the lab at accelerating an immune response,” says Martin “Mac” Cheever, MD, principal investigator of the CITN, based at the Fred Hutchinson Cancer Research Center in Seattle. “We wanted to know what agents might benefit patients if we could learn how to use them.”

Workshop attendees chose 20 agents for further study. The agents all had the potential to treat multiple types of cancer, had proven effective physiologically, were not widely available for testing, and were not likely to be approved for commercial use in the near future. NCI would then help procure the agents or manufacture them for researchers’ use.

However, individual cancer centers and research facilities did not have the expertise and experience needed to adequately test the agents. “The feeling was that we needed a network of institutions to formulate the best trials and develop standard methodologies for monitoring responses,” recalls NCI’s William Merritt, PhD, program director for the CITN.

In 2010, following an initial $3-million investment, NCI awarded a $14-million, 5-year grant to Fred Hutchinson to create the infrastructure for collaboration, support an operations and statistics center, and implement early-phase trials. Fred Hutchinson provided an additional $3 million. Following a competitive application process to select member institutions, the CITN was formally established in 2011.

**SUCCESSES DRIVE INTEREST**

In 2010, the U.S. Food and Drug Administration (FDA) approved sipuleucel-T (Provenge; Dendreon), the first immune system–stimulating cancer therapy, for advanced prostate cancer. It involves obtaining a patient’s immune cells, exposing them to a prostate cancer–associated antigen, and then injecting them back into the patient.

Attention to immunotherapies really began to soar last year, when the FDA approved ipilimumab (Yervoy; Bristol-Myers Squibb) for metastatic melanoma. (It blocks cytotoxic T-lymphocyte antigen that otherwise may inhibit T cells.)

“It was as if a dam burst,” explains Vonderheide, co-principal investigator for the CITN at UPenn.

Interest in immunotherapy is also rising as researchers turn to combination therapies in the hopes of preventing drug resistance and metastasis. Dendreon, for example, will provide funding to the CITN for a study later this year that will combine sipuleucel-T with a T-cell growth factor involved in maintaining normal T-cell number, interleukin-7 [IL-7 (Cytheris)], in patients with advanced prostate cancer.

“It can be hard for investigators to get access to other agents and hard to get companies to cooperate. The CITN has set up the infrastructure to make that happen,” notes Dendreon’s Mark Frohlich, MD, the company’s chief medical officer.

“The CITN provides us access to prominent investigators with experience in immunotherapy as well as a cost-effective way for us to get information about how our therapy works in combination with other biologic agents,” adds Frohlich.

Similarly, Pfizer will learn more about its investigational dendritic cell–activating monoclonal antibody CP-870,893, which targets CD40, in the CITN’s first trial. Led by Vonderheide, the trial will assess CP-870,893 in combination with chemotherapy in patients with pancreatic cancer.

CP-870,893 was developed years ago and tested in melanoma, says Pfizer’s James Merson, PhD, a senior vice president and head of Vaccine Research West in La Jolla, CA. Initial results weren’t compelling, and with numerous immune modulators in the company’s portfolio and limited resources to study them, partnering with the CITN made good business sense, he says. More importantly, “we want to make sure that a potential benefit for patients is not blocked.”

Says NCI’s Howard Streicher, MD, CITN project scientist: “If the network weren’t there, these studies would not be possible.” – Suzanne Rose

**CITN TRIALS ON THE HORIZON**

CITN investigators plan to test these agents against various cancers in clinical trials, in the order listed, over the next 5 years:

- CP-870,893, a dendritic cell-activating monoclonal antibody, in prostate cancer
- IL-15, a T-cell and natural killer cell growth factor, in lung, head and neck, and renal cancers, and melanoma
- IL-7, a T-cell growth factor, in prostate cancer and melanoma
- IDO (indoleamine 2,3-dioxygenase) inhibitors, for the inhibition of immunosuppressive enzyme IDO in melanoma and ovarian cancer
- P173-ligand, a dendritic cell growth factor, in melanoma.
CANCER DISCOVERY

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