Research

Bolt Bio preps clinical trials of immune-stimulating cancer drug in stubborn solid tumors

by Arlene Weintraub | Nov 11, 2019 9:36am

Bolt Biotherapeutics is developing drug conjugates that connect antibodies to agents that stimulate the immune system to attack cancer rather than to compounds that directly poison cancer cells. (PDPics/Pixabay)

One of the first immune-stimulating cancer drugs, prostate cancer vaccine Provenge, never quite lived up to expectations, but the scientist whose work led to the development of the product remains committed to immuno-oncology. He's Edgar Engleman, M.D., professor of medicine and pathology at Stanford University. Now, his latest creation, backed by $70 million in venture funding, is moving closer to the clinic.

In animal studies, the drug, which targets the tumor marker HER2, eradicated large tumors, according to a presentation at the Society for Immunotherapy of Cancer (SITC) annual meeting in Maryland. The drug also protected the animals from the development of new tumors, the company said.

The studies help define the mechanism by which Bolt's technology "is able to eliminate these hard to treat solid tumors, while generating immunological memory to suppress recurrence," said the company's senior vice president of research, David Dornan, Ph.D., in a statement.

Bolt has been picking up steam since the start of the year, when the company raised $54 million in a series B financing. Its backers include Novo Holdings, Vivo Capital, Nan Fung Life Sciences and Pivotal bioVenture Partners.

At the American Association for Cancer Research (AACR) conference in April, Bolt released preclinical data showing that its ISAC could kill human HER2-positive tumor models that had previously been treated with Herceptin, the pioneering Genentech drug that is now the standard of care for these stubborn cancers.

In animal trials also presented at the AACR conference, Bolt's therapy was used to clear HER2-positive tumors (PDF). When the same animals were presented with HER2-negative tumors, the new cancers did not grow—proof, the company said at the time, that the animals had gained "immunological memory" that protected them over the long run.

During the recent SITC meeting, Bolt's scientists explained that they measured immunologic memory by tracking tumor growth after the animals had been treated with the ISAC. To confirm that the immune system was retaining the ability to fight the cancer, they eliminated CD4 and CD8 T cells, after which tumors started growing again.

RELATED: AstraZeneca and Daiichi get Q2 2020 PDUFA date for breast cancer ADC

Antibody-drug conjugates (ADCs) are well established in oncology and continue to be a major focus of R&D. AstraZeneca and Daiichi Sankyo are awaiting the FDA's verdict on their HER2-targeting ADC, which is a humanized HER2 antibody connected to a payload that delivers chemotherapy directly to cancer cells.

Astellas and Seattle Genetics are working on an ADC that targets a protein commonly found in solid tumors, Nectin-4, and that works by disrupting the infrastructure of cancer cells. They recently posted positive phase 1 trial results in patients with urothelial cancer who were treated with the drug along with Merck's PD-1 inhibitor Keytruda.

Bolt's approach is different, because its ISAC technology is based around the idea of connecting antibodies to agents that stimulate the immune system to attack the cancer rather than to compounds that directly poison cancer cells. And it's designed to be able to be used as a solo therapy.

Bolt will include patients with solid tumors in the phase 1 trial. CEO Randall Schatzman, Ph.D., said that the trial would begin next year and will test the ISAC as a monotherapy. "While much progress has been made in cancer immunotherapy, there still remains a significant need for single-agent therapies that can impact well-established tumors and provide durable efficacy in tumors that are refractory to standard of care therapies," Schatzman said in the statement.