New immunotherapy piggybacks off polio vaccine to treat cancer

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December 17, 2020 -- As if we needed another reason to get vaccinated, researchers have developed a technology that leverages the polio vaccine to help treat cancer for those who develop the disease later in life. The technology, conceived at Duke University and developed by Istari Oncology, uses antigens produced by the polio vaccine to trigger the immune system to eat away at targeted cancer cells.

Istari is a company that was spun out of Duke University Tisch Brain Tumor Center and is focused on developing novel immunotherapies for solid tumors, according to Matthew Stober, president and CEO of Istari and Dr. Garrett Nichols, chief medical officer of Istari Oncology, who recently spoke with The Science Advisory Board.

Why solid tumors?

Matt Stober, president and CEO of Istari Oncology.

Checkpoint inhibitors are a type of cancer immunotherapy that target key regulators of the immune system, which are often stimulated by cancers as a means of escaping host immune responses. However, only about one-third of cancer patients respond to checkpoint inhibitor therapies.

This has resulted in a group of patients representing high unmet need for second-line therapies for the treatment of resistant tumors. Some of the most aggressive cancers fall into these recurrent categories, including melanoma (skin cancer) and glioblastoma multiforme (GBM; brain cancer).

Targeting solid tumors with poliovirus

Based on foundational research conducted by Duke University researcher Dr. Matthias Gromeier, the PVSRIPO technology platform is uniquely positioned to target previously untreated and treatment-resistant tumors by leveraging an unexpected source, the polio vaccine. PVSRIPO is a new kind of viral immunotherapy based on the Sabin type 1 polio vaccine.

The Sabin type 1 polio virus is a live attenuated (weakened) version of the poliovirus first used in vaccination efforts against poliomyelitis, a deadly infection affecting the central nervous system. Gromeier sought to further attenuate the virus to make it even safer for therapeutic use.

To accomplish this, he substituted the internal ribosomal entry site cassette of poliovirus, which is essential for viral replication, with sequences from a human rhinovirus. The result of this

substitution is PVSRIPO, a fully validated neuro-incompetent virus unable to infect healthy human cells.

What do poliovirus and cancer have in common?

The answer is in the poliovirus receptor, CD155. The wild poliovirus uses this molecule to enter the anterior motor neurons, where it causes polio disease. But interestingly, this glycoprotein is also expressed on nearly all solid cancer cells, as well as key cells in the immune system. In many treatment-resistant cancers, CD155 is associated with increased tumor migration and invasiveness, and also poor patient prognosis, according to Nichols.

For those individuals who have previously received the polio vaccine (nearly everyone in the U.S. and over 85% of the global population), administration of PVSRIPO therapy directly into tumors will kill CD155-expressing cancer cells, but also stimulate antitumor immune responses to poliovirus in order to clear cancer cells. Upon entry into cancer cells, PVSRIPO causes antigen-specific T-cell mediated immunity, which is augmented by anti-poliovirus-specific memory CD4+ T-cell recall.

The PVSRIPO therapy is administered directly into the tumor. The virus is administered at 50,000,000 particles for glioblastoma and up to 100,000,000 for melanoma.

"In GBM, it's generally just one infusion of therapy and then we monitor the patient," explained Nichols. "Over a period of months, the virus will summon an immune response to the tumor. The tumor becomes inflamed and then the tumor contracts."

Synergies with checkpoint inhibitors

PVSRIPO is being developed initially as a second-line treatment for patients who do not respond to checkpoint inhibitor therapies, Stober and Nichols explained. However, the company is either conducting or planning clinical trials evaluating the effectiveness of PVSRIPO in combination with checkpoint inhibitors in melanoma (LUMINOS-102; planned) and glioblastoma (LUMINOS-101; recruiting).

Dr. Garrett Nichols, chief medical officer of Istari Oncology.

In a phase I glioblastoma trial, the Istari team has already demonstrated prolonged overall survival of 21% at 36 months among patients treated with PVSRIPO. In the phase I melanoma trial, 67% of heavily pretreated patients achieved a response to PVSRIPO with only three injections.

Beyond melanoma and glioblastoma, Istari is planning to initiate a basket trial in the second half of 2021 to explore the use of PVSRIPO in bladder, head and neck, esophageal, and gastric cancers.

"Our mission is to harness the patient's own immune system to target and sustain the lethal response to cancer," Stober said.
Given the high safety profile of the PVSRIPO platform, the team believes that they can transform the immunotherapy space with improved treatment options and better quality of life for patients.