TREND WATCH

Actinium partners with UC Davis on gene therapy for HIV-related lymphoma

January 28, 2020

ADD TOPIC TO EMAIL ALERTS

Mehrdad Abedi

Actinium Pharmaceuticals has forged an agreement with University of California, Davis for the use of its proprietary CD45 antibody radiation-conjugate, apamistamab-I-131, in the institution's ongoing phase 1/phase 2 clinical trial of stem cell gene therapy for patients with HIV-related lymphoma.

Apamistamab-I-131 (Iomab-B, Actinium Pharmaceuticals) will replace the chemotherapy conditioning used in the gene therapy trial, which will be the first of its kind to incorporate antibody radiation-conjugate (ARC)-based conditioning, according to the manufacturer. The overall goal of the collaboration is to develop an anti-HIV stem cell gene therapy that will simultaneously treat HIV-related lymphoma and develop immune cells that are resistant to HIV in a population of patients with relapsed or refractory HIV-related lymphoma.

"Patients with HIV-related lymphoma face a dismal prognosis with few viable therapeutic options as they battle both cancer and HIV," **Mehrdad Abedi, MD,** professor of hematology and oncology at UC Davis Comprehensive Cancer Center and the study's primary investigator, told Healio.

"The compromised state of these patients limits our ability to fully address their cancer or HIV, given the toxicities of current therapies," he added. "We envisioned a future where a single treatment of our stem cell gene therapy can cure patients of their lymphoma and leave the patient with a new immune system that can fight, be resistant to and prevent the mutation of HIV."

Overcoming current treatment limitations

There are several limitations to current HIV treatment, as Abedi outlined.

Patients with HIV must take a combination of drugs daily for the rest of their lives to control the virus. If not taken regularly, HIV becomes resistant to the drugs and continues to destroy immune cells.

Production of the anti-HIV stem cell gene therapy entails genetically modifying autologous stem cells with a combination of three anti-HIV genes. Before receiving the gene therapy at UC Davis, patients must undergo conditioning, which involves depletion of their stem cells to enable the new anti-HIV cells to engraft and re-establish a healthy blood and immune system.

“Currently, conditioning is accomplished with nontargeted chemotherapy and/or external radiation that can be too toxic for these compromised patients or not deplete all of their stem cells, which can lead to persistence of HIV reservoirs despite the gene therapy,” Abedi explained. “Pending regulatory approval, we are planning to add Actinium’s ARC-targeted conditioning technology to address the limitations of current conditioning regimens. Actinium’s ARC can not only selectively deplete stem cells by targeting a marker on their surface called CD45, but also lymphoma cancer cells, which also express the CD45 protein on their surface.”

The excitement behind gene therapy lies in its hypothesized ability to cure diseases with a single treatment, according to Abedi.

“It is amazing to see how rapidly this field is advancing across many disease indications previously thought to be untreatable and certainly not curable,” he told Healio. “To have a revolutionary technology like gene therapy be reliant on decades-old chemotherapies seems incredibly counterintuitive. Therefore, it is exciting to see new conditioning regimens emerge that can be used safely, predictably and reliably.”

Abedi said that in previous clinical trials, all patients who received the CD45 ARC were able to tolerate a successful stem cell transplant.

“This gave us strong interest to begin using an ARC-targeted conditioning regimen with our stem cell gene therapy,” he said.

“Our focus is on improving patient outcomes and we have a long-term vision of curing patients of their lymphoma and HIV,” Abedi explained. He added that investigators will initially study the use of apamistamab-I-131 among six patients, with plans to expand the study if the results are promising.

“We will be able to evaluate clinical signals such as the ability to receive a transplant, transplant engraftment and whether the transplant eliminated their lymphoma in just a few months after the transplant,” Abedi said. “We will also evaluate the presence of

the anti-HIV genes and if the genes have created an HIV-resistant immune system."

Generating proof of concept


Dale Ludwig

Terms of the deal between Actinium and UC Davis, including its duration, had not been made available by the time of reporting. The initial focus of the agreement is to generate a clinical proof of concept for the use of Actinium's ARC conditioning technology in concert with UC Davis' anti-HIV stem cell therapy, according to **Dale Ludwig, PhD,** chief scientific officer at Actinium.

"Based on established clinical proof of concept with our apamistamab-I-131 ARC for targeted conditioning, including in patients with lymphoma, we are confident the initial phase of this collaboration will be successful and we are excited by the prospect of further expanding the scope of this important work," he told Healio.

Ludwig asserted that apamistamab-I-131 has numerous advantages over current chemotherapy-based conditioning due to its antitumor activity, reduced toxicity and effectiveness in conditioning for transplantation.

"Supported by extensive clinical investigation in 12 trials and over 300 patients, a single therapeutic dose of apamistamab-I-131 is sufficient for conditioning, and due to its dual activity, even a patient with active disease could expect to receive therapy within 2 weeks, which is anticipated to lead to better outcomes compared with chemotherapy, external beam radiation, or exploratory approaches such as naked antibodies or antibody-drug conjugates," he said. "Given the potential of this ARC-targeted conditioning technology for bone marrow transplant, we are grateful to Dr. Abedi for the opportunity to advance the Iomab-ACT program into the promising field of gene stem cell therapy." – *by Drew Amorosi*

For more information:

Mehrdad Abedi, MD, and **Joseph Anderson, PhD, MAS,** can be reached at UC Davis Comprehensive Cancer Center, 2279 45th St., Sacramento, CA 95817.

Dale Ludwig, PhD, can be reached at dludwig@actiniumpharma.com.

Disclosures: Ludwig reports employment by Actinium Pharmaceuticals. Abedi and Anderson report no relevant financial disclosures.