First mRNA HIV Vaccine Clinical Trial Launches

Moderna Inc is setting its sights on HIV. The biotech firm, along with nonprofit partner IAVI, the International AIDS Vaccine Initiative, announced in late January that researchers had administered the first doses of an investigational mRNA HIV vaccine to volunteers in a phase 1 clinical trial. The vaccine candidate uses prime and boost antigens to induce specific B-cell responses that ideally will lead to the development of broadly neutralizing HIV antibodies. Scientists at IAVI and Scripps Research developed the vaccine antigens as proteins. They previously tested the prime antigen in an adjuvanted protein-based vaccine, which induced the desired B-cell response among 97% of trial participants.

With Moderna’s mRNA platform—the same approach behind the company’s COVID-19 vaccine mRNA-1273—the vaccine carries genetic instructions for human cells to produce HIV surface proteins. The technology allows for rapid vaccine development and testing. The prime-boost combination tested in the current trial could be the first in a vaccine series that induces a range of broadly neutralizing antibodies.

“The COVID-19 pandemic really demonstrated the success of mRNA vaccines and so the path from discussing its application for HIV to a Phase 1 clinical trial happened at an accelerated pace,” David Diemert, MD, of the George Washington University School of Medicine and Health Sciences, where the first doses were administered, said in a statement.

The trial, taking place at 4 US clinical sites, will monitor safety and measure immune responses among 56 healthy HIV-negative adults.

Patients With Complete Paralysis Walk With Spinal Cord Implant

A newly developed epidural electrical stimulation (EES) system described in Nature Medicine helped 3 individuals with severe spinal cord injuries regain trunk and leg motor function in an ongoing clinical trial. The patients with complete sensorimotor paralysis were able to perform activities such as stepping on a treadmill independently the first day of treatment, although they did not regain natural movements.

The system includes an electrode paddle lead implanted directly on the spinal cord. Paddle leads that previously were used to deliver EES were designed for pain relief, with electrodes arranged to target the dorsal column rather than the dorsal roots involved in leg and lower-trunk movements.

Researchers designed and fabricated a larger paddle lead with optimally placed electrodes that target the sacral, lumbar, and low-thoracic dorsal roots. “Our breakthrough here is the longer, wider implanted leads with electrodes arranged in a way that corresponds exactly to the spinal nerve roots,” Jocelyne Bloch, MD, of the Lausanne University Hospital in Switzerland, said in a statement. “That gives us precise control over the neurons regulating specific muscles.”

After a 5-month training program, the individuals improved their gait patterns and their ability to bear weight, allowing them to stand independently and walk outside the laboratory with a front-wheel walker while using the EES system.

With the electrical stimulation, their real-world activities expanded to include riding a recumbent bike, paddling a canoe on a lake, and having a drink while standing at a bar. One participant regained the ability to climb stairs. To use the system while out in the community, the patients remotely select an activity on a tablet device, which relays the information to a pacemaker implanted in the abdomen. The pacemaker then sends signals to the paddle lead.

Bloch and her collaborators are also planning clinical trials to test brain-controlled spinal cord stimulation and an intervention that combines the new EES system with pharmacological neuromodulation.

Decade-Long CLL Remission After CAR T-Cell Therapy Reported

More than 10 years after 2 patients with end-stage chronic lymphocytic leukemia (CLL) received tisagenlecleucel, an anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, a group of highly activated CAR T cells were still proliferating in their blood, keeping the cancer at bay. Researchers reported the finding—the longest known CLL remission after CAR T-cell therapy—in Nature. The patients received an infusion of genetically engineered autologous T cells as part of a phase I clinical trial in 2010. Their CAR T-cell populations evolved over time, shifting from predominantly CD8+ killer T cells to mainly CD4+ T cells with cytotoxic characteristics. The cells remained functionally active and not exhausted, a key component for maintaining remission with CAR T-cell therapy.

Identifying and characterizing the CAR T-cell populations provides “novel insight into the CAR T cell characteristics associated with anti-cancer response and long-term remission in leukaemia,” the authors wrote.

The US Food and Drug Administration approved the immunotherapy, marketed as Kymriah, in 2017 for certain pediatric and young adult patients with acute lymphoblastic leukemia, or ALL. It’s now also approved for some adults with large B-cell lymphoma. Only a small subset of patients with CLL benefit from CAR T-cell therapy, although researchers are working on innovations to address this. — Jennifer Abbasi

Note: Source references are available through embedded hyperlinks in the article text online.