**Biotech Innovations**

**Moderna’s mRNA Vaccine for Seasonal Flu Enters Clinical Trials**

Moderna Inc, maker of the COVID-19 vaccine mRNA-1273, is betting that its genetic platform will translate to the seasonal flu. In July, the company announced that the first participants had been dosed in a phase 1 and 2 clinical trial of its quadrivalent influenza candidate, mRNA-1010. The study involving approximately 180 healthy US adults was fully enrolled as of early September.

The trial will evaluate the safety and immunogenicity of 3 dose levels of mRNA-1010, which contains genetic instructions for cells to produce the hemagglutinin surface proteins from 4 flu strains recommended by the World Health Organization.

The company is also testing mRNA-1345, an experimental vaccine against respiratory syncytial virus (RSV), with a global phase 2 and 3 study involving about 34 000 participants set to launch by the end of the year. The US Food and Drug Administration granted mRNA-1345 fast-track designation in August. There’s currently no approved RSV vaccine.

The candidates are part of Moderna’s larger strategy to develop combination mRNA vaccines against respiratory viruses including SARS-CoV-2, influenza, and RSV. A COVID-19 and seasonal flu combination vaccine is already in the works.

“Our vision is to develop an mRNA combination vaccine so that people can get one shot each fall for high efficacy protection against the most problematic respiratory viruses,” Stéphane Bancel, Moderna’s chief executive officer, said in a statement.

**India’s New COVID-19 DNA Vaccine for Adolescents and Adults Is a First**

In August, the government of India granted Emergency Use Authorization to a COVID-19 DNA vaccine. Pharmaceutical firm Zydus Cadila, in partnership with India’s Department of Biotechnology, developed the 3-dose intradermal vaccine, called ZyCoV-D, which is authorized there for use in people aged 12 years or older. The endorsement marks the first clinical use of a DNA vaccine in humans.

Ahmedabad-based Zydus in July announced interim results from a phase 3 trial involving more than 28 000 volunteers. ZyCoV-D was 67% effective against symptomatic infections. No severe cases or COVID-19 deaths occurred among vaccinated individuals after the second dose and no moderate cases occurred after the third dose. The doses are given 28 days apart.

The vaccine contains plasmid DNA, circular strands of genetic material that enter the host cells’ nuclei, where they’re converted into messenger RNA (mRNA). The mRNA then travels out of the nuclei into the cytoplasm and is translated into the SARS-CoV-2 spike protein, as in now-familiar mRNA vaccines.

No severe adverse events or deaths occurred among adults in a phase 1 trial. Tolerability was similar for adults and about 1000 adolescents enrolled in the phase 3 trial, according to the company.

A painless, needle-free injector delivers the vaccine in a narrow fluid stream into the skin. Although it’s stored in colder temperatures, ZyCoV-D is stable at 77 °F for at least 3 months, which may reduce wasted doses. A 2-dose regimen also is being evaluated.

Ten other DNA vaccines are in clinical development against the novel coronavirus, according to the World Health Organization’s COVID-19 vaccine tracker. Pennsylvania-based INOVIO is initiating a phase 3 trial of INO-4800, its plasmid DNA vaccine candidate against SARS-CoV-2. According to the company’s projections, INO-4800 should be stable at room temperature for more than a year.

**Vaccine-Induced SARS-CoV-2 Antibodies in Inflammatory Diseases**

The good news: about 9 out of 10 patients with a chronic inflammatory disease (CID) produced antibodies against SARS-CoV-2 after full vaccination in a recent study. The not-so-good news: their antibody levels were about a third as strong as those observed in a group of volunteers without CIDs.

Researchers studied 133 patients with an average age of 46 years who were taking at least 1 immunosuppressive medication for conditions including inflammatory bowel disease, rheumatoid arthritis, spondyloarthritis, lupus, and multiple sclerosis. About 89% of them developed SARS-CoV-2 antibodies after receiving 2 doses of the Pfizer-BioNTech or Moderna vaccines, but their levels were lower than those observed in a group of 53 healthy participants.

Only 65% of patients with CIDs who used glucocorticoids and 60% of those who used B cell-depleting therapies developed antibodies. The researchers drew no conclusions about immune responses associated with the use of tumor necrosis factor inhibitors (TNFis), Janus kinase inhibitors (JAKis), and antimetabolites like methotrexate.

However, some of the participants—particularly those using TNFis and JAKis—produced similar antibody titers against the virus’s spike protein as individuals who recovered quickly from COVID-19 in other studies. These levels may therefore “provide sufficient humoral protection,” the study’s authors wrote in the Annals of Internal Medicine.

The researchers cautioned that the findings are preliminary and require confirmation in a larger study. Next, they plan to measure antibody responses again after study participants with CIDs receive a third vaccine dose, per recommendations for people with moderately to severely compromised immune systems. — Jennifer Abbasi

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

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