CAR T-Cell Therapy Shows Early Promise for Gastrointestinal Cancer

In an ongoing phase 1 trial, an investigational immunotherapy showed promise for treating gastric and pancreatic cancers that lack effective treatment and generally have a poor prognosis, according to an interim analysis reported in *Nature Medicine*.

The therapy, called CT041, uses chimeric antigen receptor (CAR) T cells targeting Claudin18.2 (CLDN18.2), a protein that tightly joins gastric epithelial cells and is expressed by about 60% of gastric cancers. The interim analysis assessed 37 patients previously treated for various CLDN18.2-positive digestive system cancers. They received 1 of 3 CT041 doses in a dose-escalation and de-escalation phase followed by a dose-expansion phase.

Of 36 patients with measurable target lesions, 30, or 83.3%, showed tumor regression. The overall response rate (ORR) and disease control rate (DCR) reached 48.6% and 73%, respectively. The 6-month duration of response rate was 44.8%. In patients with gastric cancers, the ORR and DCR reached 57.1% and 75%, respectively, and the 6-month overall survival rate was 81.2%.

The most frequent grade 3 or higher adverse events were preconditioning-related hematologic toxicities among all 37 patients, who recovered in a median of 4 to 9 days. In addition, 35 of 37 patients had grade 1 or 2 cytokine release syndrome, lasting a median of 6 days. No patient experienced a dose-limiting toxic effect within 28 days after the first infusion.

"These initial results suggest that CT041 has promising efficacy with an acceptable safety profile in patients with heavily pretreated, CLDN18.2-positive digestive system cancers, particularly in those with gastric cancers," the authors wrote.

Maternal RSV Vaccine Could Protect Infants, Interim Analysis Suggests

In investigational protein-based maternal vaccine for respiratory syncytial virus (RSV) elicited neutralizing antibodies among pregnant women, and these antibodies were transferred to their infants before birth, according to a planned interim analysis of an ongoing phase 2b randomized trial reported in the *New England Journal of Medicine*.

The vaccine candidate, called RSVpreF, targets the virus’ prefusion F protein. Though not an efficacy trial, a post hoc analysis suggested that vaccination with RSVpreF during pregnancy may prevent medically attended and severe RSV-associated lower respiratory tract illnesses in infants, according to the authors.

The study involved 327 pregnant women who at 24 through 36 weeks’ gestation received a 120-μg or 240-μg vaccine dose with or without an aluminum hydroxide adjuvant and 79 pregnant women who received placebo. Maternal adverse events included mild to moderate injection site pain with no serious vaccine-related adverse events.

Of 405 infants in 4 treated groups, 3 developed medically attended RSV-associated lower respiratory tract illness, with 1 severe case, compared with 5 illnesses with 3 severe cases among 103 infants in the placebo group. That translated to an efficacy of 84.7% against medically attended and 91.5% against severe RSV-related lower respiratory tract illness, though the confidence intervals were wide. No infant vaccine-related adverse events were reported through the interim analysis at 5 months.

“These serologic and initial efficacy data suggest that maternal vaccination with RSVpreF vaccine during pregnancy has the potential to protect infants from RSV infection well into their first 6 months of life,” the authors wrote.

The monoclonal antibody therapy palivizumab is currently approved for preventing RSV but its use is restricted to specific high-risk infants. If approved following an ongoing phase 3 trial of the nonaluminum formulation, RSVpreF may become the first widely available preventive treatment for RSV-related illness in infants.

Urine Test Detects SARS-CoV-2 Antibodies

An experimental test detects SARS-CoV-2 antibodies in urine, researchers recently reported in a preliminary study in *Science Advances*. If further validated, the new test could be a safe, noninvasive tool to identify resolving or prior infections.

The analysis involved 209 urine samples paired with 187 serum samples simultaneously collected from 139 patients with SARS-CoV-2 infection confirmed by polymerase chain reaction testing. Negative controls included 30 samples collected before the COVID-19 pandemic or from patients without symptoms.

The urine-based enzyme-linked immunosorbent assay (ELISA) test demonstrated 94% sensitivity and 100% specificity for detecting the SARS-CoV-2 nucleocapsid protein in patient samples, with a positive predictive value of 1.0 and a negative predictive value of 0.79. In comparison, a previously validated serum-based ELISA test demonstrated 88% sensitivity and 100% specificity, with a positive predictive value of 1.0 and a negative predictive value of 0.70.

COVID-19 mRNA vaccines induce antibodies to the SARS-CoV-2 spike protein, whereas infected patients also generate antibodies to SARS-CoV-2 nucleocapsid, envelope, and membrane proteins. As a result, the new test could potentially distinguish between patients who have received mRNA vaccines but were not infected and those who have been infected.

However, the assay was not tested against urine samples from patients with respiratory infections caused by different coronaviruses, so the researchers cautioned that cross-reactivity with other human coronaviruses can’t be ruled out.

— Howard D. Larkin

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