Biotech Innovations

CAR Natural Killer Cell Therapy Safe and Effective in First Trial

A variation on chimeric antigen receptor (CAR) T-cell therapy that instead modifies natural killer (NK) immune cells appeared to be safe and effective in an ongoing phase 1 and 2 trial of patients with CD19-positive blood cancers.

CAR NK-cell therapy could be easier to manufacture and less toxic than its T-cell–based counterpart. As with CAR T-cell therapy, NK cells are modified to express an anti-CD19 CAR. But the new technique uses donor cells from umbilical cord blood, which opens the door to an off-the-shelf product that could be administered to more than 1 patient. The engineered cells also express the cytokine interleukin 15 to enhance their expansion and persistence in the body and a "safety switch" enzyme called inducible caspase 9.

The trial, reported in the *New England Journal of Medicine*, involved 11 patients with relapsed or refractory non-Hodgkin lymphoma or chronic lymphocytic leukemia who underwent lymphodepleting chemotherapy before treatment. Within 30 days of a single infusion of CAR-NK therapy, 8 patients responded, with 7 of them experiencing complete remission at a median follow-up of 13.8 months. The CAR-NK cells were still present in patients' bodies at low levels at least a year after the infusion.

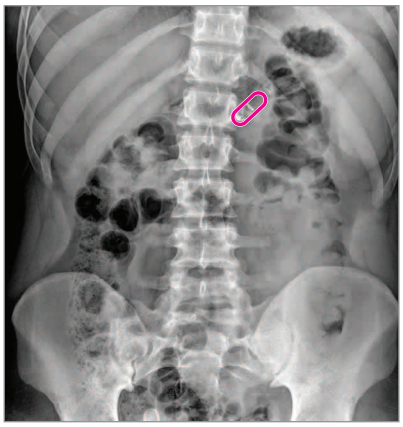
The therapy's safety profile was also promising. No patients experienced cytokine release syndrome or neurotoxicity, common CAR-T therapy adverse effects. "We believe that perhaps this could be related to differences in the inflammatory proteins that T cells and NK cells produce when they encounter their target," the study's senior author, Katy Rezvani MD, PhD, of the MD Anderson Cancer Center in Houston, said in an email. Graft-vs-host disease also didn't occur, despite the use of donor cells.

The trial will eventually test the treatment in 60 patients, with final results available in 3 years, Rezvani said. The researchers are now working with a commercial partner, Takeda Pharmaceutical, to develop a large multicenter study needed for regulatory approval.

Meanwhile, National Cancer Institute researchers and colleagues writing in *Nature Medicine* described a potentially less toxic CAR T-cell therapy using a new anti-CD19 CAR design. In a phase 1 trial involving 20 participants with B-cell lymphoma, just 5% of patients who received the investigational therapy experienced severe neurologic toxicity, compared with 50% of patients who received treatment with the CAR in axicabtagene ciloleucel (Yescarta).

Oral Injections Tested in Proof-of-Concept Trial

A microneedle-containing pill safely injected an oral version of a biologic drug directly into the intestinal wall in a first-in-human phase 1 trial, Rani Therapeutics recently announced. The drug, octreotide, is a subcutaneous injection used to treat acromegaly and neuroendocrine disorders. The San Jose–based startup is also developing orally administered injections for diabetes, rheumatoid arthritis, and cardiovascular disease biologics, among others.



Rani Therapeutics

In the study, 52 healthy adults tested the octreotide-loaded capsule, while another 6 received an intravenous injection of the drug. The pill was well tolerated, caused no serious adverse events, and had a high bioavailability that a spokesperson said was comparable with the standard drug.

The so-called RaniPill is a capsule that passes intact through the stomach to the small intestine, where its coating dissolves. A tiny balloon then deploys, pushing a dissolvable, drug-filled microneedle into the intestinal wall. Because the intestines have no sharp pain receptors, the company said the approach is painless. The capsule's remnants pass in the stool within a few days.

In an email, Mir Imran, Rani Therapeutics' founder and chief executive officer, said the pill has the potential to revolutionize the biologics market if its safety and effectiveness can be further demonstrated. Most biologics today are injected, which the company says affects patient adherence.

23andMe Develops First Drug Compound Using Consumer Data

Direct-to-consumer genetic testing company 23andMe has developed an antibody aimed at treating inflammatory skin conditions. The DNA testing and research outfit licensed the compound to Barcelona-based pharmaceutical firm Almirall in January, its first such deal for a drug compound developed in-house using consumer data.

The company said that more than 80% of its over 10 million customers have consented to their deidentified genetic and phenotypic information being used for drug discovery and other research, and that each individual's data are used in 200 studies on average.

In this case, that research helped to pinpoint targets for an immunodermatology candidate. The compound is a bispecific monoclonal antibody that blocks the IL-36 cytokine family, which is associated with autoimmune and inflammatory diseases, including skin conditions like psoriasis. Skin health–focused Almirall plans to conduct clinical trials building on 23andMe's preclinical research.

More drug candidates will likely follow. The genetic testing company has research programs across several therapeutic areas, including oncology and respiratory and cardiovascular diseases, a spokesperson said in an email. In 2018 it announced a drug research and development partnership with pharmaceutical giant GlaxoSmithKline plc. **– Jennifer Abbasi**

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