MEDICINE

Support for risky cancer therapy

Advisers give go-ahead as US regulators mull approval of genetically engineered treatment.

BY HEIDI LEDFORD

External advisers to the US Food and Drug Administration (FDA) have thrown their support behind a therapy that genetically engineers a patient's own immune cells to target and destroy cancers.

In a unanimous vote on 12 July, the panel determined that the benefits of CAR-T therapy outweigh its risks. The vote comes as the agency considers whether to issue its first approval of such a treatment — a drug called tisagenlecleucel manufactured by Novartis of Basel, Switzerland.

Novartis is seeking approval to use tisagenlecleucel to treat children and young adults who have a form of acute leukaemia, and who have not responded sufficiently to previous treatment or have relapsed since that treatment.

Studies have shown that CAR-T therapies can produce lasting remissions in such cases. In one key trial of tisagenlecleucel, which started in 2015, 52 out of 63 participants experienced overall remission. The unpublished trial had no control group, so investigators cannot say with certainty how much effect the treatment had. But many participants of such trials have remained cancer-free for months or years.

"This is a major advance, and is ushering in a new era," said panel member Malcolm Smith, a paediatric oncologist at the US National Institutes of Health in Bethesda, Maryland.

But the therapy poses serious risks. During the 2015 tisagenlecleucel trial, 47% of participants experienced an extreme inflammatory reaction known as cytokine release syndrome. This is characterized by symptoms such as high fevers and organ failure, and can be fatal. Novartis says that trial clinicians managed the reaction successfully in all cases.

By contrast, over the past year some other CAR-T trials have reported the deaths of several participants from severe brain swelling.

CAR-T therapies also present a gnarly regulatory challenge for the FDA: how to assure the potency and purity of a complex, living drug that must be made afresh for each recipient.

To generate a batch of tisagenlecleucel, technicians purify a sample of white blood cells from a patient. They then use a virus to insert into the T cells genes for a cellular receptor — called a chimaeric antigen receptor — that will recognize leukaemia cells. The cells are grown in culture and then reintroduced into the patient. It takes about 22 days to manufacture each person's treatment.

Little is known about any long-term toxic effects of the therapy. But the young patients who would receive it have few alternatives, and those alternatives carry risks of their own, said Bruce Roth, an oncologist at Washington University School of Medicine in St Louis, Missouri, and chair of the FDA advisory panel.

"Although I have some concerns about late toxicity, you have to be a long-term survivor to be concerned about late toxicity," he said. "And I think that's what this drug gets us." The FDA is not obligated to follow the recommendations of its advisers, but it often does. ■