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AACR 2020 – Gracell validates a novel Car-T target

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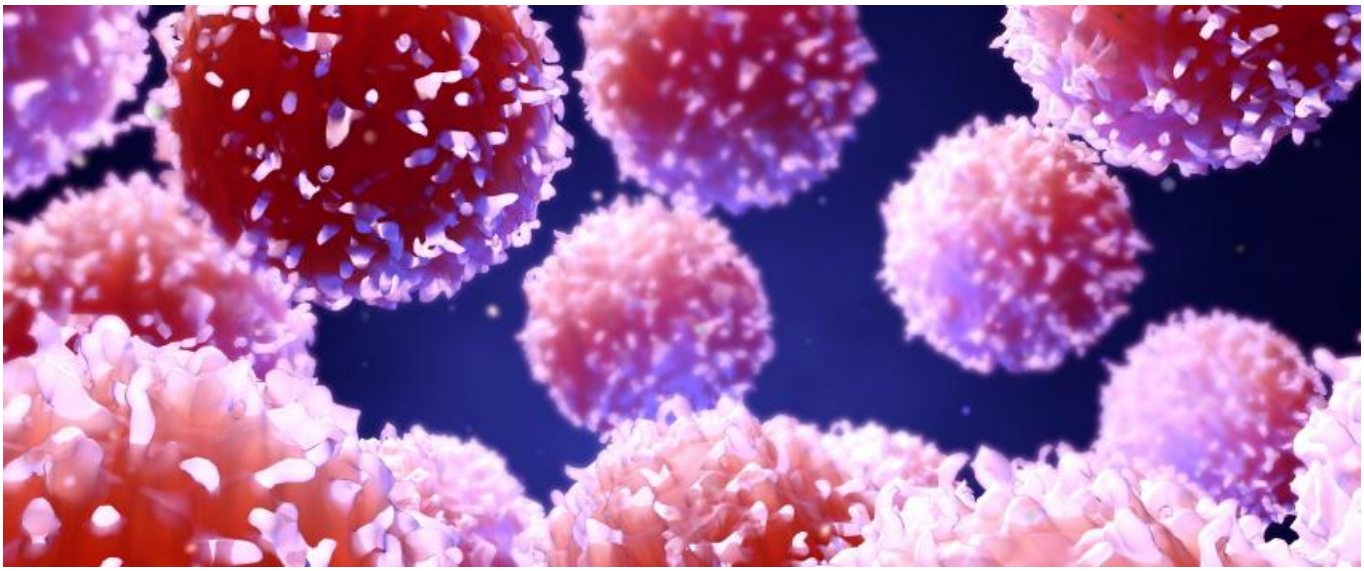


The Chinese group sees responses in all five subjects treated with its allogeneic anti-CD7 Car-T therapy.

Haematological cancers originating at T cells are relatively rare but highly intractable. Now the private Chinese group Gracell looks to have made a breakthrough with an allogeneic Car-T therapy – and not only that, but its antigen of choice, CD7, is one that had fallen by the wayside after antibody approaches against it disappointed.

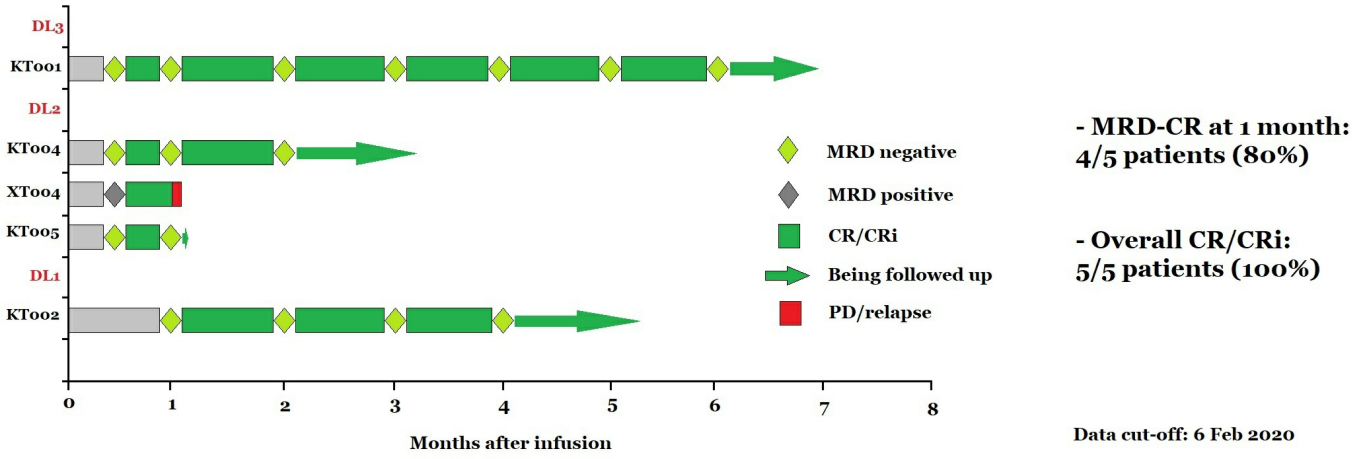
Data presented at the AACR meeting today show that all five T-cell leukaemia subjects treated with Gracell's anti-CD7 Car, GC027, went into remission, and though one relapsed quickly the rest of the remissions remain deep. These are the first clinical data for an anti-CD7 Car, and should be of interest to the private US group Wugen, which is following a very similar approach.

Gracell's data are all the more remarkable because in its study the healthy volunteer-derived GC027 cells were dosed only once, and had fairly limited persistence. Nevertheless, the Car-T cells expanded robustly within two weeks in four of the five subjects, leading to MRD-negative (a very stringent criterion) complete remissions.

Three of these subjects remained in CR three to six months later, said Gracell's Xinxin Wang, presenting the data today; the fourth subject remains MRD-negative just over a month after infusion. Meanwhile, the fifth patient went into an MRD-positive CR at two weeks, but their leukaemia relapsed by the four-week time point.

On the toxicity side, all five subjects experienced serious cytokine release syndrome, one at grade 4, though none had neurotoxicity or graft-versus-host disease.

The study's discussant, Dr Yvonne Chen of University of California, Los Angeles, put the toxicity down to the relatively high doses of Car-T cells used. Also, Gracell said it had used an "enhanced" lymphodepleting Flu/Cy regimen to ensure Car-T cell engraftment.



Adapted from Gracell & AACR.

Only one other company, China's Persongen, is known to be in the clinic with a CD7-directed cell therapy, though it is unclear whether this is an autologous or allogeneic project. In the US Baylor College has listed a phase I trial of an autologous anti-CD7 Car, but this is not planned to start for another year.

The most relevant competitor for Gracell is perhaps Wugen, a venture-backed company founded two years ago in California and still operating in stealth mode. This group is also working on an allogeneic Car, licensed from Washington University and coded WU CART 007, which like GC027 uses Crispr editing.

Anti-CD7 Car-T therapy approaches				
Project	**Properties**	**Company/institution**	**Trial ID**	**Status**
GC027 Truucar	Allogeneic, TCRα & CD7 knockout by Crispr	Gracell	NCT04264078	First human data AACR 2020
CD7 Car-T cells	?	Persongen	NCT04004637	Phase I started Jun 2019
CD7-specific Car-T cells	Autologous or donor-derived	Shenzhen Geno-Immune	NCT04033302	Phase I started Sep 2019
CD7.CAR/28zeta Car-T cells	Autologous, CD7 knockout by Crispr	Baylor College	NCT03690011	Phase I starts Mar 2021
WU CART 007	Allogeneic, TCRα & CD7 knockout by Crispr	Wugen	None	Preclinical
Source: clinicaltrials.gov.				

One of the problems of using Car-T to target T-cell malignancies is that the antigen of choice will by definition be present on the target cells as well as on the Car-T cells. Thus the Car-T cells are liable to target and destroy each other, in a phenomenon known as fratricide.

To avoid this Gracell uses Crispr to edit out the CD7 antigen on GC027. However, manufacturing is not straightforward, as Crispr knockout is a separate step to knocking in the Car construct, which is done using a traditional lentivirus. Dr Chen also cautioned that long-term durability of GC027 had yet to be determined.

For now the company is studying GC027 in T-cell ALL, though T-cell lymphoma is another logical indication, and this is being targeted by other groups. Another approach to treating T-cell lymphoma using Car-T therapy is being taken by Autolus through its Auto4 and Auto5 projects.

A separate Gracell technology claims to use a one-day manufacturing process. This bold claim remains to be proved, but for now the company's validation of CD7 should make others take note.

This is an updater version of a story published earlier.