Evaluate Vantage

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Nkarta: at least as good as Fate, at a tenth of the price

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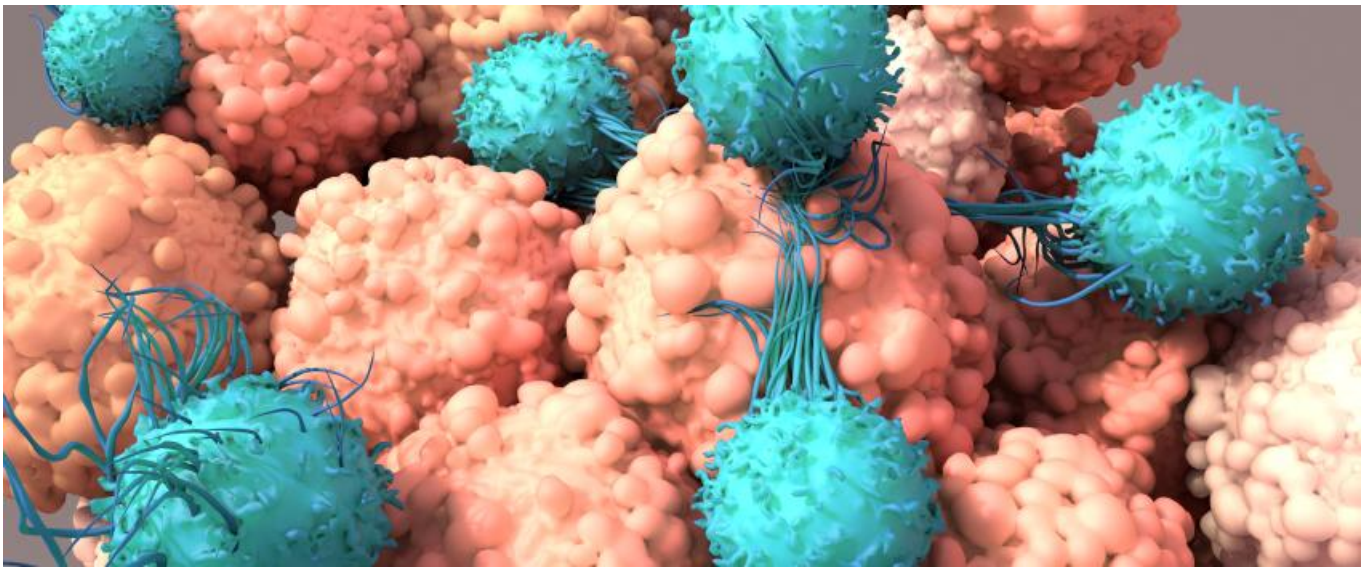


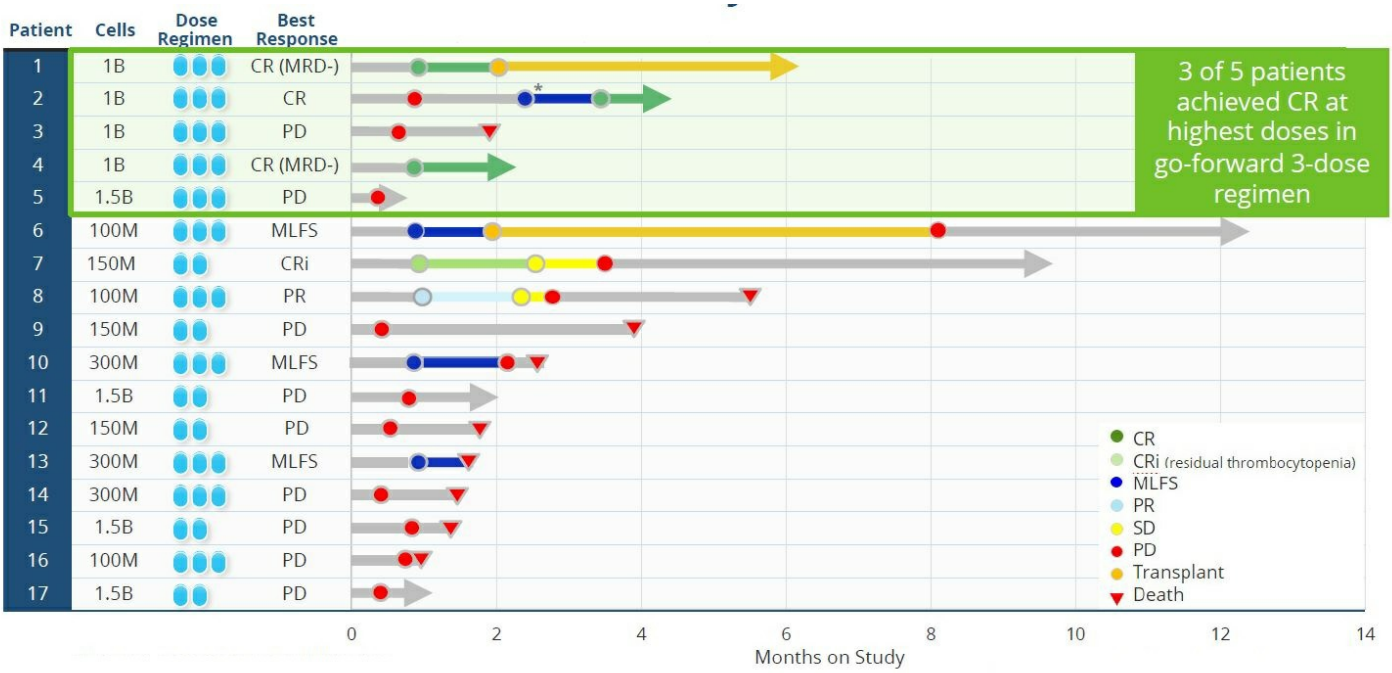
After a long wait, investors at last have early evidence that Nkarta's Car-NK cells work – with a relatively clean safety profile to boot.

In the battle of Car-NK therapy companies Nkarta today looks to have at least matched Fate Therapeutics. The big difference for investors will be where expectations had settled: before today's market open Nkarta was worth just $250m, less than a tenth of Fate's valuation.

Nkarta's data comprise 34 patients, from two studies, and investors will zero in on five subjects with median fourth-line acute myeloid leukaemia – an extremely aggressive cancer – given the highest dose of NKX101. Though a question mark hangs over response durability, three of these patients have achieved complete remissions, two with MRD negativity, with no cytokine release, neurotoxicity or graft-versus-host disease.

NKX101 is Nkarta's lead, and comprises allogeneic NK cells modified to express a Car construct targeting NKG2D ligands. With the caveat of small patient numbers a 60% ORR in this cancer seems highly promising.

Two of the remissions are only a month out, however, with one coming after a second three-dose cycle; the third patient was transplanted within a month, and remains in remission at six months.



Swimmers plot for NKX101 in AML at a 21 Apr 2022 data cut-off. Source: company presentation.

The second trial reported today concerned a separate Nkarta NK cell asset, NKX019, which targets CD19, in B-cell malignancies.

Though the efficacy here is also decent, 70% ORR in lymphoma, or 83% in patients given a high dose, these data might be of less immediate interest given that such patients can already be given autologous Car-T therapy.

However, they will be noted by those investors trying to pick winners in the NK cell therapy game, given last August's report of the first human data for Fate's rival anti-CD19 Car-NK project FT596, also in lymphoma. While these results were impressive there were doubts about the setting – only some of the lymphomas were termed aggressive – and the contribution of Rituxan, which in one cohort was combined with FT596.

NKX019 efficacy in study NCT05020678		
NKX019 dose	**3 doses (300m cells)**	**3 doses (1.0bn cells)**
ORR in NHL	2/4 (50%)*	5/6 (83%)^
ORR in ALL	0/1 (0%)	0/2 (0%)
*NHL=non-Hodgkin's lymphoma; ALL=acute lymphoblastic leukaemia. Note: *one CR; ^three CRs. Source: Nkarta presentation.*		

It must also be noted that Nkarta's NK cell approach is slightly different, and there are important distinctions between NKX019 and FT596. Nkarta sources NK cells from healthy donors, and is not at present looking at cells expressing high-affinity CD16; meanwhile, Fate uses induced pluripotent stem cells, most of which it modifies to express CD16.

Another important difference, in terms of the possible cost in lymphoma at least, is the dosing. Fate's best efficacy was achieved at just 300 million FT596 cells, while Nkarta had to take NKX019 up to a billion cells across three doses.

Either way, it is Nkarta's AML data with NKX101 that will now carry the weight of investor expectations. When *Evaluate Vantage* spoke to the company a year ago the plan was to unveil the first data at a medical conference in late 2021; with the slippage into 2022, and the all-important Ash meeting being missed, press releasing the results evidently became the best option.

NKX101 efficacy in study NCT04623944				
NKX101 dose	**2 doses (150m or 450m cells)**	**2 doses (1.5bn cells)**	**3 doses (100m or 300m cells)**	**3 doses (1.0bn or 1.5bn cells)**
ORR in AML	1/3 (33%)	0/3 (0%)	4/6 (67%)	3/5 (60%)**
ORR in MDS	0/2 (0%)	NA	NA	0/2 (0%)

*AML=acute myelogenous leukaemia; MDS=myelodysplastic syndromes. Note: **all three remissions complete, two MRD-negative. Source: Nkarta presentation.*

Not only is Nkarta today able to show what looks like a clear dose response with NKX101 in AML, it appears to have scope to dose even higher should it want to. The most common severe adverse event was thrombocytopenia at 48%, while grade ≥3 pneumonia and sepsis were seen in 24% and 10% of patients respectively.

There was no cytokine release syndrome or neurotoxicity, Nkarta said, calling this a positive differentiation versus many cell therapies, and mirroring what Fate had seen in the FT596 trial. Fate's FT538, an NK product not modified to express a Car construct, is in an early study in AML, and both this and the NKX101 trial escalate up to 1.5 billion cells.

Clearly the market will keenly await longer-term follow-up from Nkarta's trials, which is to be provided at a future medical meeting. Investors might also query why the company has so far seen zero efficacy the apparently less-intractable malignancies of ALL and myelodysplastic syndromes.

The caveats aside, the question of expectations remains live. Before surging 85% at the open this morning Nkarta was worth just $250m, 90% below its peak in December 2020. Fate's market cap stands at $3.3bn, off about 70% over the same timeframe.

This is an updated version of a story published earlier today.