Evaluate Vantage

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EHA 2022 preview – some good news at last

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Positive data result in positive share price movements – something of a novelty in the current market.

As another terrible week on the Nasdaq biotechnology index draws to a close investors have celebrated some good news at last. Yesterday's unveiling of abstracts for June's European Hematology Association brought clinical data that boosted the share prices of several cell therapy-focused biotechs.

Perhaps best received were the first human data for Caribou's allogeneic Car-T therapy CB-010, sending the depressed group's stock up 22%. Updates from Gracell and Autolus also struck a chord with the markets, though for many cell therapy groups the big unanswered question remains how durable remissions – and share price uplifts – prove to be.

Crispr editing

Caribou, a company listed last year whose technology forms the basis of Intellia's Crispr work, is due to present the first efficacy data from the Antler trial of its allogeneic anti-CD19 project CB-010.

The EHA abstract, citing a relatively recent data cutoff of February 23, notes a 100% remission rate among the five evaluable lymphoma patients (six were dosed), including four complete responses. As for durability, three patients continue in remission, one at over eight months, but one relapsed at six months.

Relapses have been a big problem for allogeneic Car-T therapies from Allogene, Crispr and Precision Biosciences, so this aspect will be watched closely. CB-010 uses Crispr to knock the Car transgene into the Trac locus, to avoid graft-versus-host disease, as well as knocking out PD-1 to limit T-cell exhaustion.

Interestingly, CB-010 is edited using the usual Cas9 version of Crispr. Caribou has separately made much of an alternative technology, Crispr Cas12a, which it says is superior.

Crispr Therapeutics itself also features at EHA, courtesy of clinical data not on its lead Car asset, CTX110, but instead the anti-CD70 project CTX130, which the abstract reveals put into remission seven of 15 patients with aggressive T-cell lymphomas. Competitor Car-T assets targeting CD70 include Allogene's ALLO-316 and TCR2 Therapeutics' TC-520.

Fast manufacturing

While Novartis splashed its two-day Car-T manufacturing technology at Ash, at EHA Gracell highlights its own very similar approach in an investigator-sponsored Chinese study of GC012F, an anti-CD19/BCMA dual Car.

An oral presentation is still embargoed, but a poster reveals complete remissions in the first three B-cell lymphoma patients given a single dose, with all responses ongoing at three months. Still, with slots for apheresis still having to be booked weeks in advance, and some patients in Novartis's trials needing bridging chemo, how big a difference two-day manufacturing makes remains unclear.

Another depressed biotech, Autolus, boasts a unique approach to treating T-cell lymphoma, its Auto4 project targeting TRBC1-positive disease, but has described this programme as "technically challenging". A phase 1/2 trial was delayed by manufacturing problems, and initial data, first expected in 2020, did not materialise as the trial was upsized from 55 to 200 patients.

The EHA abstract illustrates some of the complexity of Auto4: 64 patients were assessed initially, and 24 were found to be TRBC1-positive. However, only nine of these were actually treated after eight screen failures, one death, one relapse and the non-manufacture of Auto4 product for various other undisclosed reasons.

The initial data do look promising, with five complete metabolic responses by PET scan across four dose levels, with no dose-limiting toxicities. One subject remains in partial remission six months after Auto4 infusion. With Autolus aiming to dose 200 patients it will have to hope that a simplified screening procedure speeds things along.

Selected oncology presentations at EHA 2022

Project	Mechanism	Company	Study	Data	Share movt*
CB-010	Anti-CD19 Car-T (Crispr-edited, PD-1 deleted allo)	Caribou	Antler	ORR 100% in 5 lymphoma pts (1 relapse)	+22%
GC012F	Anti-CD19/BCMA Car-T (2-day manu)	Gracell	ChiCTR2100047061	100% CR in 3 lymphoma patients	+14%
Auto4	Anti-TRBC1 Car-T	Autolus	NCT03590574	56% CR in 9 TRBC1+ve T-cell lymphoma pts	+8%
CTX130	Anti-CD70 Car-T (Crispr-edited allo)	Crispr	Cobalt-Lym	ORR 47% in 15 CD70+ve T-cell lymphoma pts	+7%
MB-106	Fh anti-CD20 Car-T	Mustang Bio	NCT03277729	ORR 94% in 16 follicular lymphoma pts	+3%
Camidanlumab tesirine	Anti-CD25 ADC	ADC Therapeutics	NCT04052997	ORR 70% in 117 classical Hodgkin pts; 8 cases of Guillain–Barré syndrome (reason for earlier clinical hold), of which 4 have not recovered	+1%
RG6234/ RO7425781	Anti-GPRC5D T-cell engager	Roche	NCT04557150	First data: ORR 68% in 34 multiple myeloma pts	-3%
Anbal-cel/ CRC01	Anti-CD19 Car-T (PD-1 & Tigit silenced)	Curocell	NCT04836507	78% CR in 9 B-cell lymphoma pts	NA
ARI0002H	Humanised anti-BCMA Car-T	(None)	NCT04309981	Presidential session, embargoed until Jun 11	NA

**May 12 close. Fh: fully human. Source: EHA.*

The EHA meeting takes place in Vienna, Austria on June 9-17.

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