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Ash 2021 preview – as competition grows Autolus monetises

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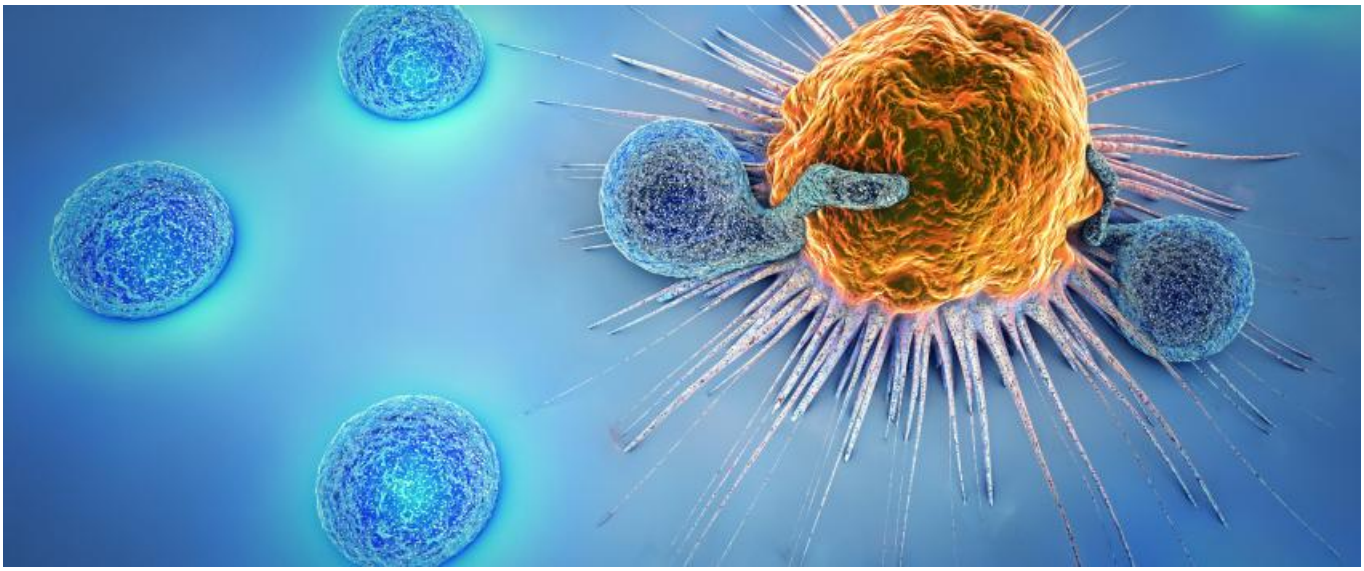

Several cell therapy presentations will vie for attention at Ash, though today the spotlight falls on Autolus.

With $150m of funding secured from Blackstone this morning the heat is off Autolus to present earth-shattering obe-cel data at Ash. Given that Autolus was down 40% year to date the bull case is that Blackstone has already seen what it likes in the data, and has effectively called the bottom.

Then again, it is hard not to be disappointed by Autolus's fall from a company working on cutting-edge cell therapy to one seeking to commercialise a run-of-the-mill CD19 Car. Other Ash presentations give a clue about the group's future competition, though for now perhaps the best thing is that obe-cel has been monetised.

For a $100m equity stake plus $50m in cash Blackstone secures an interest in obe-cel, will receive a single-digit sales royalty, and will pay a further $100m in milestone-based development financing. The private equity group has also secured a seat on Autolus's board.

Prelude?

This might be enough for some to see this as a prelude to a takeout, though a $50m equity stake implies extremely early days. Still, it cannot be disputed that PE usually strikes when equity prices hit rock bottom, and Autolus has had quite the fall from grace.

When the Ash abstracts went live last Thursday Autolus analysts focused on the Felix trial of obe-cel, an autologous anti-CD19 Car with a novel binding domain, in adult ALL. However, the placeholder abstract gave away no data, discussing the automation of an academic manufacturing process.

Thus all investors have to go on for now is Autolus's word – plus Blackstone's implied endorsement – that Felix is seeing one-month response rates in line with those in the academic Allcar19 trial, which showed 85% ORR in 20 subjects, no serious cytokine release and a 15% rate of neurotoxicity.

This might be an improvement over the likes of Yescarta, but an autologous CD19 Car hardly moves the needle today. *Evaluate Pharma* lists 49 such assets in phase 1 and 2 trials alone, for instance.

Selected CD19-directed cell therapy presentations					
Project	**Company**	**Trial**	**Abstract**	**Cutoff**	**Detail**
Yescarta	Gilead	Zuma-7	2 (plenary)	18 Mar	Median EFS 8.3mth vs 2.0mth for SoC (HR=0.398; p<0.0001)
Breyanzi	Bristol Myers Squibb	Transform	91	?	Median EFS 10.1mth vs 2.3mth for SoC (HR=0.349; P<0.0001)
Obe-cel	Autolus	Felix	477	?	Adult ALL, abstract is on manufacturing process
YTB323	Novartis	NCT03960840	740	16 Apr	<2-day manufacture: At DL1 25% 3mth ORR (n=4), at DL2 75% 3mth ORR (n=8)
PBCAR0191*	Precision	NCT03666000	650	2 Aug	CD19+ ALL: day ≥28 CR rate is 33% (2/6) in DL3/4a and sLD, 80% (4/5) in DL3/4a with eLD and 75% (3/4) in DL4b with sLD
ALLO-501A*	Allogene	Alpha-2	649	9 Jul	Discusses consolidation therapy; programme on clinical hold
FT596**	Fate	NCT04245722	823	25 Jun	53% ORR (n=17), notes retreatment

*DL=dose level, sLD=standard lymphodepletion, eLD=extensive lymphodepletion. *allogeneic; **allogeneic NK cell therapy; all others are Car-T. Source: Ash.*

As ever, Ash offers an insight into more cutting-edge cell therapy approaches, notwithstanding the fact that Yescarta and Breyanzi's respective second-line lymphoma trials, Zuma-7 and Transform, take centre stage thanks to a plenary and key oral presentations.

These will be key to determining whether Car-T can move towards front-line lymphoma therapy, and the absence at Ash of the corresponding Belinda study of Novartis's Kymriah, which failed, will disappoint those who wished to delve into the differences between the trials.

Novartis, however, is presenting two early-stage clinical abstracts, concerning the anti-CD19 Car YTB323 and the BCMA-directed PHE885, that should generate lots of interest. This is because they concern projects that Novartis claims to be able to manufacture in two days, a potential game-changer for autologous cell therapy.

Like most Ash abstracts the data described are from an early cutoff, but they could validate the company's T-Charge technology, which reduces ex vivo culture time to 24 hours and preserves naive and stem cell memory T cells in the final product.

Among other CD19-directed cell therapy approaches investors will also focus on Fate's Car-NK project FT596. At Ash 2019 this had only preclinical data and a year ago there was a sole case report, but this year's abstract details 17 patients, and response durability should be a major focus at Ash.

The FT596 abstracts cites the potential for retreating relapsed patients. Also ploughing the retreatment furrow will be the allogeneic player Allogene, though investors will focus primarily on the hold the FDA has placed on all its clinical work.

Selected multiple myeloma presentations						
Project	**Mechanism**	**Company**	**Trial**	**Abstract**	**Cutoff**	**Detail**
Cilta-cel	BCMA Car-T	J&J/Legend	Cartitude-1	549	11 Feb	98% ORR (n=97), 6 treatment-related deaths, 5 treatment-unrelated deaths
PHE885	BCMA Car-T	Novartis	NCT04318327	3864	1 Apr	<2-day manu: 100% 1mth ORR (n=6)
P-BCMA-101	BCMA Car-T	Poseida	NCT03288493	3858	30 Jun	ORR 72% in Rituxan/Revlimid combo (n=90?)
CYAD-211	BCMA Car-T (shRNA allo)	Celyad	Immunicy-1	2817	29 Jul	ORR 25% (all PRs, n=8)
REGN5458	BCMA bispecific	Regeneron	NCT03761108	160	10 Jun	73% ORR at 90mg & 200mg (n=17), high end of dosing
TNB-383B (ABBV-383)	BCMA bispecific	Abbvie	NCT03933735	900	10 May	Ex Teneobio (acq by Amgen), ≥40mg Q3W ORR 79% (n=24)
RO7297089	BCMA bispecific (via CD16)	Roche	NCT04434469	2755	30 Apr	1/18 PR suggests just hints of efficacy
MCARH109	GPRC5D Car-T	MSKCC	NCT04555551	827	28 Jul	83% ORR (n=12), 2 responses unconfirmed
Talquetamab	GPRC5D bispecific	J&J/Genmab	NCT03399799	158	19 Jul	ORR 70% (n=30) at 405µg/kg weekly; 69% in 13 subjects last year
Cevostamab	FcRH5 bispecific	Roche	NCT03275103	157	18 May	158 pts now efficacy evaluable, vs 51 a year ago
Source: Ash.						

Meanwhile, in multiple myeloma, BCMA-targeting competitors will be squaring up to Johnson & Johnson/Legend's Cartitude-1 study of cilta-cel, whose Pdufa date was recently delayed by three months to February 28, 2022.

But perhaps, following a recent trend, there will again be more interest in bispecifics than Car-T, and in follow-ons to targeting BCMA, a crowded space. Here the first ever clinical data on Memorial Sloan Kettering's Car-T asset MCARH109, which targets GPRC5D, are keenly awaited, and the early abstract data look impressive.

An update on Johnson & Johnson/Genmab's talquetamab, an anti-GPRC5D bispecific that impressed last year, should also be on investors' radar. Autolus was right to monetise obe-cel when it had the chance, but it has little time to lose when it comes to putting the cash to use.

Selected CD20-directed T-cell engagers					
Project	**Company**	**Trial**	**Abstract**	**Cutoff**	**Detail**
Mosunetuzumab	Roche	NCT02500407	127 (press)	15 Mar	≥3L FL: 79% ORR (n=90) [68% ORR at Ash 2020]
Glofitamab	Roche	NCT03075696	128	18 May	r/r FL: ORR 81% (n=43) for monoRx [ORR 64% in NHL at Ash 2020]
Plamotamab	Xencor/J&J	NCT02924402	2494	1 Jul	r/r NHL: ORR 43% (n=53) [39% ORR at Ash 2019]
Epcoritamab	Abbvie/Genmab	Epcore NHL-1	1413	15 Jul	SC dosing, but poster is on CHOP combo in 1L NHL
Igm-2323	IGM Biosciences	NCT04082936	132	30 Apr	35% ORR (n=23)
Source: Ash.					

The Ash conference is due to take place virtually, and in person, on December 11-14 in Atlanta, Georgia.

Evaluate Vantage's Jacob Plieth spoke to the biotech investor Brad Loncar in advance of ASH about the meeting's themes: