

Ash 2018 preview - blood cancers offer biotech a chance at redemption



Jacob Plieth



The Ash meeting starts on December 1. Here are some haematological cancer presentations that investors will be focusing on, as biotech risks ending 2018 in poor shape.

For biotech the past month or so has been ugly. The Esmo meeting pushed more stocks into the red than into the black, the Ash abstracts were unveiled as the market was turning sour, and the downturn accelerated as the SITC conference raised yet more doubts about immunotherapy combinations.

This means that the Ash meeting, which gets under way next week, gives the sector a final chance to redeem itself in 2018. The Ash late-breakers unveiled yesterday offer some hope of a turnaround for Genmab, though investors in other stocks active in blood cancers will look keenly to up-to-date results of studies whose abstracts have so far detailed relatively old data cuts.

A particularly nervous wait, for instance, is in store for followers of MacroGenics, whose abstract revealed only three additional complete responses in an extra 19 AML patients given its CD123 bispecific flotetuzumab. That took the overall CR rate in its phase I trial down from 25% to 19%.

There was better news for Xencor's CD123 bispecific, XmAb14045, which had previously not shown responses, but whose Ash abstract reveals three among 13 subjects. Another closely watched area is antibody-drug conjugates, and investor focus here could fall on Immunogen's IMG632.

Though febrile neutropenia remains associated with ADCs, Immunogen has made much of the novel payload that IMG632 employs. This asset has sailed largely under investors' radar, but given that it is subject to a future opt-in from Jazz it could soon enjoy a higher profile.

Selected oncology-focused Ash abstracts

Project	Company	Detail	Abstract	Time
Saturday, 1 Dec				
IMGN632	Immunogen/Jazz	CD123 ACD, ph1	27	8:00am
RG6026	Roche	CD20 bispecific, first-in-human ph1	226	4:45pm
Kymriah	Novartis	Juliet (NHL) trial update	1684	6:15pm
AUTO5	Autolus	TRBC1 CAR, preclinical	1661	6:15pm
Switch tech	Alpine Immune	PD-1 switch domains for TCR use	2052	6:15pm
Sunday, 2 Dec				
Various	Various	Beat AML umbrella study	559	8:00am
AUTO3	Autolus	CD19, CD22 dual CAR, ph1 Amelia study	279	8:00am
JCAR014	Celgene (ex-Juno)	Imbruvica combo	299	8:30am
bb21217	Bluebird/Celgene	BCMA CAR w improved manufacturing, ph1	488	4:45pm
KITE-439	Gilead (ex-Kite)	HPV16 E7 eTCR	492	5:45pm
ALLO-819	Allogene/Cellectis	Flt3 CAR, preclinical	3335	6:00pm
ACTR707	Unum	Ph1 ATTCK-20-03 trial	2966	6:00pm
Monday, 3 Dec				
ALLO-715	Allogene/Cellectis	BCMA CAR, preclinical	591	7:30am
Kymriah/CTL119	Novartis	PD-1 combo	556	7:45am
huCD19 CAR	Gilead/NCI	Ph1 update	697	10:30am
XmAb14045	Xencor	CD123 bispecific, ph1	763	2:45pm
Flotetuzumab	Macrogenics	CD123 bispecific, ph1 cohort expansion	764	3:00pm
LCAR-B38M	Nanjing Legend/J&J	First ph1 update since Asco 2017	955	4:30pm
Kymriah	Novartis	Eliana (paed ALL) trial update	895	4:30pm
JCAR017	Celgene (ex-Juno)	Defined-comp CAR, Plat-02 (paed ALL) trial	967	4:30pm
CD19/CD22 bisp CAR	NCI	Bispecific CAR, first ph1 trial	898	5:15pm
JCARH125	Celgene (ex-Juno)	Phase 1/2 Evolve trial (BCMA CAR)	957	5:00pm
MCARH171	MSKCC	Ph1 BCMA CAR	959	5:30pm
FT819	Fate	Allo CD19 CAR-T, preclinical	4546	6:00pm
P-Bcma-101	Poseida	Centyrin-based BCMA CAR, ph1	1012	7:00pm
Tuesday, 4 Dec				
Darzalex	Genmab/J&J	Maia 1L Revlimid combo	LBA-2	7:30am

For Genmab, which stands 15% down on the year, and 35% below its August 2017 peak, scoring an Ash late-breaker was good news. The presentation reveals results of Maia, a study that is vital for extending the reach of its Johnson & Johnson-partnered multiple myeloma drug, Darzalex.

This year Darzalex got US approval for front-line treatment of transplant-ineligible patients in combination with Velcade, melphalan and prednisone, a backbone often used in Europe. Maia, however, tested it first line in combination with the US-dominant backbone of Revlimid and dexamethasone.

On the primary efficacy measure of progression-free survival the Ash late-breaker reveals Maia to have scored a hit: risk of progression was cut by 45% for Darzalex versus the Revlimid backbone alone ($p < 0.0001$). Bernstein analysts had earlier estimated that median PFS could exceed 50 months, and with the data so far 42 months out a median has not been reached for the Darzalex combo.

However, a major caveat is overall survival, a secondary Maia endpoint, which so far has yielded a 0.78 hazard ratio, with the upper bound of its confidence interval exceeding 1.0. True, only 19% of Maia subjects have died so far, but the availability of second-line Darzalex to progressing control arm patients threatens to confound this result.

Genmab/J&J might argue that there is still time for the survival curves to separate definitively. But should Maia ultimately show no OS advantage for Revlimid plus Darzalex versus Revlimid followed by Darzalex it will not be viewed positively, especially given the exorbitant cost of such a combo.

There's a new hashtag for ASH this year: [#BCMA18](#)

— Brad Loncar (@bradloncar) [November 1, 2018](#)

As in previous years Ash remains the most important industry conference detailing the progress of cell therapies, and a particular focus this year will fall on the burgeoning field of CAR-T therapy against BCMA, the multiple myeloma-relevant antigen seen as the next big thing after CD19.

Among the most keenly awaited will be data on the rather mysterious LCAR-B38M, an asset originated by Nanjing Legend that caused a stir at Asco 2017, but about which nothing has been heard since then beyond [Johnson & Johnson picking it up for \\$350m](#). Nanjing now reveals that this targets two separate epitopes on BCMA; whether JNJ-68284528, J&J's iteration of this asset, acts the same way is not clear.

Bluebird Bio will reveal first clinical data on its Celgene-partnered BCMA CAR bb21217, but the abstract reveals durability in line with bb2121, a similar asset on whose manufacturing bb21217 aims to improve. Not that this is a problem: bb2121 is the most promising BCMA-targeted CAR, and the one to which competitors, with the risks of cross-study comparisons, will square up.

Other CAR-T presentations include data from the recently floated Autolus and Allogene, updates from Novartis's approved Kymriah, and more on Celgene's direct challenge to the Swiss group and to Gilead's Yescarta. Preventing a post-Ash selloff might be too much to ask, but the sector will do its best to ensure that it enters 2019's JP Morgan conference having avoided the worst.

For live updates from the Ash conference, taking place in San Diego on December 1-4, follow [@JacobPlieth](#) and [@ByMadeleineA](#) on Twitter.

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