Evaluate Vantage

November 04, 2022

Ash 2022 preview – Affimed and Aptose score

Jacob Plieth

In oncology settings outside multiple myeloma investors have picked two early winners.

After leaving investors waiting at Asco Adicet will come into December's Ash meeting with much to prove. However, the markets will have to wait a bit longer, until Ash itself, because the abstract unveiled yesterday on ADI-001 reveals little about this gamma-delta Car-T therapy's durability.

Instead, biotech investors picked out Aptose as the early winner of yesterday's Ash abstract drop: the micro-cap ended the day up 27% on hopes for its Hanmi-derived kinase inhibitor tuspetinib. However, it was Affimed that made a claim to having one of the meeting's most convincing efficacy datasets, with its NK-cell engager AFM13.

Affimed ended yesterday up 9%. AFM13, which targets CD30, already impressed at last year's AACR meeting, when MD Anderson's trial combining it with NK cells sent 17 of 19 lymphoma patients into remission, and yesterday Affimed secured a source of off-the-shelf NK cells, striking a deal giving it access to Artiva's AB-101.

The clinical side was complemented by an Ash abstract detailing a dataset that now boasts a 97% overall response rate at AFM13's recommended phase 2 dose, with 17 of 24 patients in complete remission.

Awaiting Adicet

For Adicet the big reveal had come at Asco, when ADI-001, which targets CD20, put six of eight lymphoma subjects into remission. Things then became complicated, as two responders relapsed, though with Adicet claiming that one of these was not a bona fide relapse the company largely avoided a backlash, with investors happy to await longer-term data.

Ash should bring just that, and for the time being the abstract puts long-term remissions at two – assuming Adicet's arguments about the irrelevance of a skin relapse are believed – though another patient has now relapsed at six months. The remaining two short-term remissions continue, and have been joined by a third; this dataset has a July cutoff, and it is vital for Adicet to avoid showing significantly more relapses at next month's update.

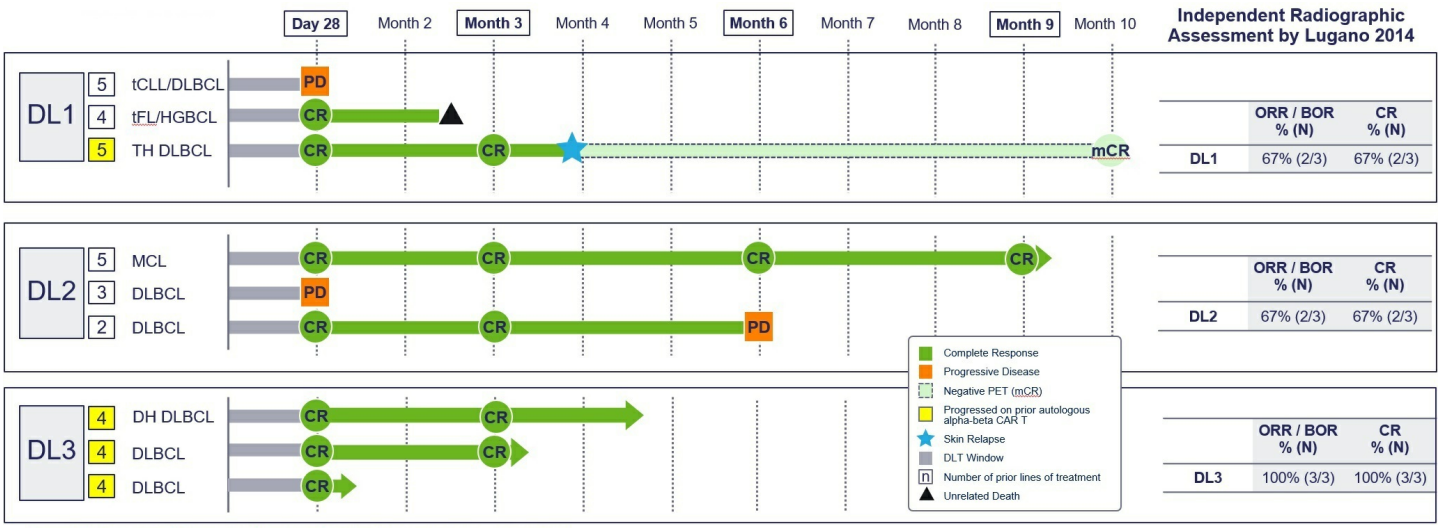

Figure 2. Preliminary Efficacy and Durability Results. Data cut-off date: 15 Jul 2022

TH=triple hit; DH=double hit; DLBCL=diffuse large B-cell lymphoma; tCLL=transformed chronic lymphocytic leukemia; HGBCL=high grade B-cell lymphoma; MCL=mantle cell lymphoma

ADI-001 in adults with B-cell malignancies. Source: Ash.

As an approach, of course, CD20-targeting has featured prominently at the previous three Ash conferences, and the 2022 instalment maintains this trend.

However, the market for T-cell engagers is becoming fiercely competitive: Roche's Lunsumio is available for follicular lymphoma in the EU and has a December 29 US Pdufa date, while its separate asset, glofitamab, is awaiting EU approval. Abbvie/Genmab's epcoritamab, having put up what could be best-in-class data, was filed in the US and EU for third-line non-Hodgkin's lymphoma a week ago.

Ash includes data on these and a fourth CD20 T-cell engager, Xencor's plamotamab, as well as a fifth, Regeneron's odronextamab. The last of those is notable for having been associated with treatment-related deaths, and spent time on clinical hold. Its Ash abstract sees Regeneron pinning hopes on step-up dosing as a means of avoiding serious cytokine release syndrome.

Notable by its absence is another CD20 bispecific, IGM's imvotamab. The lack of a competitive efficacy profile of this asset made IGM one of the biggest fallers of Ash 2021, and this year the company's presence is limited to preclinical work. IGM stock lost 8% yesterday as the group launched a $400m shelf financing.

Selected Ash oncology presentations excluding multiple myeloma					
Project	**Mech**	**Company**	**Abstract**	**Cutoff**	**Data**
AFM13	CD30 NK engager	Affimed	168	31 Jul	ORR 97%, 17/24 CR
ADI-001	CD20 gammadelta Car-T	Adicet	2018	15 Jul	7/9 CRs, 1 new relapse
Glofitamab	CD20 T-cell engager combo	Roche	4259	7 Jun	Combo with RO7227166 (CD19x4-1BBL with no monoRx actvity)
Odronextamab	CD20 T-cell engager	Regeneron	444	20 Apr	Pivotal DLBCL study: 52% ORR, 2 deaths
Plamotamab	CD20 T-cell engager	Xencor	4262	25 Jul	NHL: 9/19 ORR
INB-100	Unmodified gammadelta T cells	In8bio	3323	?	No advance on July data
AUTO4	Anti-TRBC1 Car	Autolus	4634	?	5/9 complete metabolic responses; 73 patients screened for TRBC1 to identify 10 to dose
Azercabtagene zapreleucel (PBCAR0191)	Allo CD19 Car-T (1st-gen)	Precision Bio	2005	?	Company investigating signal in transplant-relapsed patients after disappointing at Ash 2021
CTX110	Allo CD19 Car-T	Crispr	4629	22 Apr	56% ORR, 11/32 CR across 4 doses
YTB323 (rapcabtagene autoleucel)	CD19 Car-T (2-day manufacture)	Novartis	439	31 Mar	65% CR rate for dose level 2, some confounded by bridging chemo
Ziftomenib (KO-539)	MLL inhibitor	Kura	64	?	5/12 ORR in genetically driven leukaemias
SNDX-5613	MLL inhibitor	Syndax	376	?	32/60 ORR in genetically driven leukaemias
Tuspetinib (HM43239)	Kinase inhibitor (Flt3, Syk, cKit, Jak & others)	Aptose (ex Hanmi)	2758	14 Jul	AML: 16% ORR, 7/50 CRs
Imetelstat	Telomerase inhibitor	Geron	459	?	Ph3 Imerge study: focus on 11 patients (57 enrolled) who achieved >1yr transfusion independence
Emavusertib (CA-4948)	Irak-4 inhibitor	Curis	4077	Dec 2021	Clinical hold lifted in Aug
Favezelimab	Lag3 MAb	Merck & Co	2910	?	Keytruda combo, cHL 73% ORR
Source: Ash.					

Also falling yesterday on a financing deal, for $150m, including a $125m term loan, was Kura, whose MLL inhibitor ziftomenib will be held up against Syndax's similarly acting SNDX-5613. The latter disappointed last year, though it is probably too soon to call a winner.

No such problems for Aptose, a micro cap that had earlier tried to play in the non-covalent BTK arena with luxeptinib, an asset it later decided was a "cluster-selective" kinase inhibitor that also hit Flt3, PDGFR-alpha, CSF1R, Akt, Ras, Erk, Stat and Syk.

The group put on 27% yesterday on hopes of another multi-kinase molecule, tuspetinib, which inhibits Flt3, Syk, cKit and Jak and was licensed from Hanmi last year. An Ash abstract shows a 16% ORR in Flr3-mutated

and wild-type AML patients, though most responses appear to have been achieved with the lowest tuspetinib dose.

Geron's return

Finally, those investors who have been around long enough to remember the last time Ash took place in New Orleans, in 2013, will recall the controversial splash that a myelofibrosis doctor tried to make at the time with Geron's imetelstat.

Now Geron and imetelstat are back, having endured a clinical hold, and a licensing deal with Johnson & Johnson that was scrapped after data from J&J's Imbark trial failed to replicate the earlier academic success. Geron has managed to finance and undertake the phase 2/3 Imerge study, focusing on low-risk myelodysplastic syndromes, and this features at Ash.

An abstract focuses on 11 patients who achieved over one year's transfusion independence, an effect Stifel reckons differentiates imetelstat from Bristol's Reblozyl, for instance. Reblozyl this week scored in the first-line Commands trial, a finding that has put pressure on Geron stock, though Stifel notes that imetelstat targets later-line, post-Reblozyl patients.

Comprehensive topline Imerge data are due in January, with US and EU filings later in the year. Imetelstat might – or might not – be about to stage one of biotech's more amazing turnarounds.

The Ash conference is due to take on December 10-13 in New Orleans, Louisiana. Late-breaking abstracts will be revealed on November 22.