Evaluate Vantage

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Ash 2020 – IGM averts disaster, but competition looms

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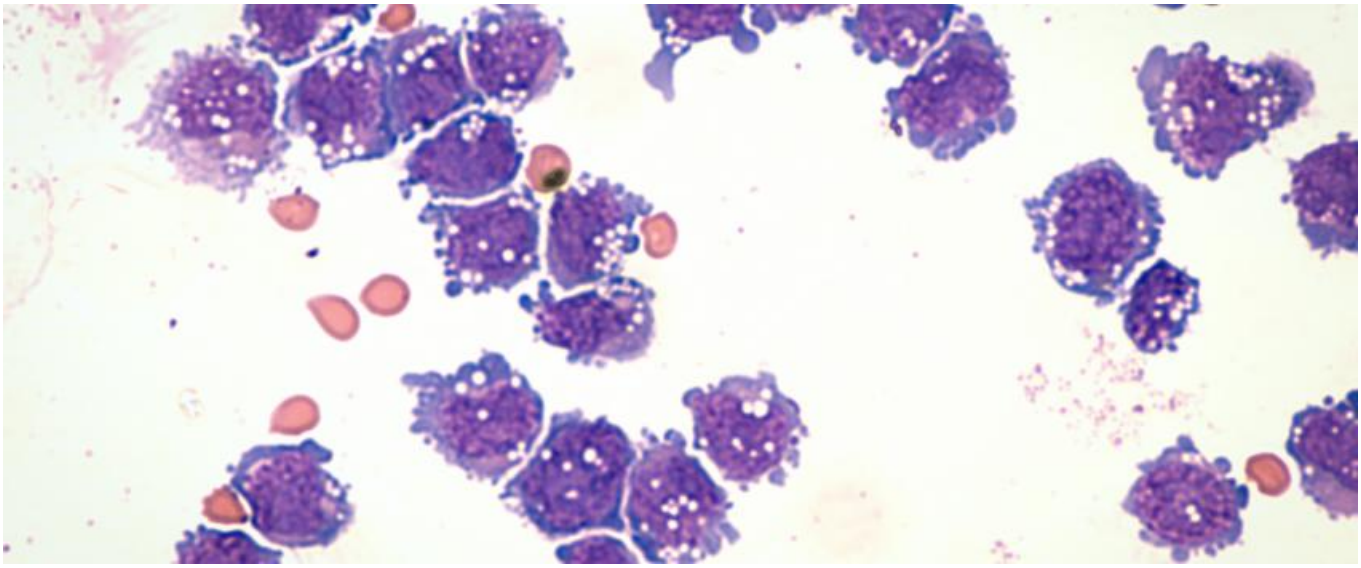

Sellside firefighting has saved the day for IGM, but Ash hears of some pretty potent anti-CD20 competition for the company.

With IGM Biosciences closing the day up 17% the company's analyst event on Saturday afternoon had clearly persuaded enough of the sellside that disappointing Ash data with its anti-CD20 bispecific, IGM-2323, was not the whole story after all.

But this is a crowded space, and more traditionally designed CD20 bispecifics are showing impressive efficacy in many more lymphoma patients. Illustrating the abundance of riches, Ash saw Roche boast two different assets, mosunetuzumab and glofitamab, while Genmab's epcoritamab is delivered subcutaneously.

Best in class?

Jefferies went as far as describing epcoritamab, which Genmab has partnered with Abbvie, as best in class, and SC administration could be a game changer.

Copenhagen University Hospital's Dr Martin Hutchings said that not only could this offer a convenience advantage, it could also help mitigate cytokine release syndrome. In addition, much of the dosing can be done at home, where side effects can also mostly be managed, he told Ash on Sunday.

In terms of efficacy epcoritamab's non-Hodgkin's lymphoma data were broken down into diffuse large B-cell lymphoma and follicular lymphoma, and the remission rates were 68% and 90%. At the high end of dosing (48-60mg) the DLBCL response rate rose to 91%, said Dr Hutchings.

A separate CD20 bispecific, Regeneron's odronextamab, also boasted a 90% response rate in follicular lymphoma, but with five treatment-related deaths there are serious question marks over its toxicity. Remarkably, Dr Rajat Bannerji from Rutgers Cancer Institute of New Jersey said this project had an "acceptable risk-benefit profile".

Those interested in basic science will note these antibodies' designs. Odronextamab and Roche's mosunetuzumab are normal-sized MAbs with differing binding domains on their two Fab arms, epcoritamab is a Duobody construct, while glofitamab uses a 2+1 design comprising two CD20-binding domains, one CD3 binder and a silent Fc region.

Of course, all are typical IgG antibodies, while IGM's uniqueness is the use of the more complex, but potentially

more potent, IgM type. It should also be stressed that competition in the CD20 arena might not bother IGM too much, as IGM-2323 might simply serve as a test case for broader applicability of its IgM technology.

Selected anti-CD20 bispecifics presented at Ash 2020				
Project	Odronextamab (REGN1979)	Mosunetuzumab (RG7828)	Epcoritamab (GEN3013)	Glofitamab (RG6026)
Company	Regeneron	Roche	Genmab/Abbvie	Roche
Format	1 + 1	1 + 1	1 + 1 Duobody, silent Fc, SC	2 + 1, silent Fc
Setting	≥2L NHL	≥3L FL	≥2L NHL	≥2L NHL
Efficacy	FL: 90% ORR, 21/30 CR DLBCL: 40% ORR, 11/35 CR	68% ORR, 32/62 CR	FL: 90% ORR, 5/10 CR DLBCL: 68% ORR, 10/22 CR	64% ORR, 28/52 CR
Treatment-related AEs	64% ≥gr3, 45% serious	36% ≥gr3, 15% serious	Highest was gr3 anaemia ~11%; ~6% had gr3 pyrexia, fatigue & hypotension	35% ≥gr3, 54% serious, mostly neutropenia
Treatment-related deaths	5* (4%)	1** (2%)	0 (0%)	0 (0%)
*FL=follicular lymphoma; DLBCL=diffuse large B-cell lymphoma; both are subsets of NHL=non-Hodgkin's lymphoma; CR=complete remission; ORR=overall response rate. Deaths due to: *gastric perforation, pneumonia, pneumocystitis, tumour lysis syndrome & toxoplasmosis; **pneumonia.*				

Dr Hutchings also profiled Roche's glofitamab on Sunday, saying step-up dosing had improved overall remission rates to 64%. Among 105 other subjects given the previous fixed-dosing regimen the ORR was 51%, with 38 complete remissions.

Glofitamab hails from Roche's pharma division, while mosunetuzumab is derived from its internally competing Genentech division. The latter's trial was presented today by Dr Sarit Assouline, of Jewish General Hospital, who cited a 68% overall remission rate in follicular lymphoma, with a 52% rate of CRs.

While this seems lower than for some other assets in this less aggressive lymphoma subtype, the trial enrolled a later-line population, comprising no second-line patients. There was also one mosunetuzumab-related death, though overall toxicity looked relatively manageable.

Interestingly, Dr Assouline told Ash that this project was also being developed for SC delivery, but said only time would tell which of the bevy of anti-CD20 bispecifics came out best.

An earlier presentation had shown a 64% ORR for mosunetuzumab in a first-line cohort of DLBCL patients who were elderly or unfit. A sixth anti-CD20 bispecific, Xencor's plamotamab, did not feature at this year's Ash, but previously yielded disappointing efficacy.

It seems that Roche, which already sells the anti-CD20 MAbs Rituxan and Gazyva, will not give up market share without a fight. Having to choose between two wholly owned assets that are now in pivotal development is a nice problem to have.