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ASH preview – Stock-moving for some, damp squib for others

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For some time ASH 2014 had been billed as the venue at which checkpoint inhibitors would show their worth on a new battleground: haematological cancers.

Perhaps this is just a measure of unrealistic expectations, but the hotly billed entry of PD-1 inhibition into haematology now risks turning into something of a damp squib, judging by early data on Keytruda and Opdivo. Elsewhere, however, ASH could be stock moving for Roche, Seattle Genetics, Amgen and others.

In abstracts already released the message on checkpoint inhibition has been mixed. In Merck & Co's Keynote-013 study of Keytruda, 15 classical Hodgkin lymphoma patients relapsed from or unresponsive to Seattle Genetics' Adcetris showed complete remission and partial remission rates of 20% and 33% respectively.

In the Checkmate 039 trial Bristol-Myers Squibb's Opdivo gave overall response rates of 36% and 40% in diffuse large B-cell and follicular lymphomas respectively, but zero responses in 27 patients with multiple myeloma.

That said, it is important to remember that these are still very early signs, and there is still all to play for here. The Keytruda and Opdivo data will be picked apart minutely at sessions that are guaranteed to be packed to the rafters.

Moreover, it is fair to say that by far the most closely watched developments at ASH 2014 will be in chimaeric antigen receptior therapy (CART). *EP Vantage* will publish a separate overview of the CART space on Monday.

Adcetris itself has an important spot at ASH, with data from the Aethera trial being a key determinant to expanding its market to Hodgkin's lymphoma patients immediately after autologous stem cell transplant. Topline data were released in September, showing the primary endpoint of progression-free survival versus placebo hit, with a 0.57 hazard ratio and 0.001 p value.

Investors are seeking more information on the absolute PFS benefit, with Seattle saying only that placebo response was roughly in line with historical data. The ASH abstract shows median PFS running at around 24 months, and unblinded efficacy and safety data are to be presented for the first time at the conference.

Beyond oncology

Of course ASH is about more than just oncology, even if presentations on such diseases as haemophilia understandably generate less interest.

One to which investors should pay attention concerns Roche's bispecific anti-factor IXa/factor X antibody ACE 910. Comprehensive data from a first phase I study will be scrutinised closely, especially given ACE 910's potential to challenge Biogen Idec and Baxter, and the huge forecasts that some analysts have already attached to it (*Baxter scores but Roche's secret weapon waits in the wings, August 22, 2014*).

As far as justifying bullish expectations goes, Amgen and Celgene also have much to prove, the former with its BiTE antibody blinatumomab, whose developer Micromet it bought for $1.1bn, and the latter with AG-221, a joint project with Agios Pharmaceuticals.

Agios floated just over a year ago, since when its stock has more than tripled, valuing the group at $3.6bn. The focus at ASH will be a phase I trial in IDH2 mutation-positive malignancies, and particularly on nine patient deaths – one of which has been reported as "possibly related to" AG-221.

For blinatumomab Amgen is presenting a phase II ALL trial that is described as the largest prospective study in patients with minimal residual disease (MRD). Blinatumomab met the trial's primary endpoint, generating a 78% complete MRD response rate, and 98% of the complete responses were seen within the first treatment cycle.

Little to see

As in 2013 the organisers of ASH have decided to focus the meeting's plenary session, this year on December 7, at broad practice-changing issues and some early disease markers, so there is little of immediate interest here to the biopharma investor.

The same applies to this year's late-breaking abstracts, whose most interesting presentation is the failed Valor study of Sunesis's vosaroxin (Qinprezo). The company now seems to be highlighting a data dredge to tease out a benefit for its lead project, cutting the results by patients' age and allogeneic stem cell transplant status.

Sunesis lost 80% of its value when Valor flopped, but remarkably the stock is up around 30% since the late-breakers were announced. The 2014 edition of ASH might well be "more incremental than transformative", as RBC Capital Markets analysts have described it, but this does not rule out large share price swings.

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