Evaluate Vantage

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Astra's brodalumab hit is perfectly timed

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As Pfizer mulls the next move in its plan to acquire AstraZeneca, the UK company's case for demanding more money has just become a little stronger courtesy of a largely overlooked psoriasis project, brodalumab.

Positive data in the first of three pivotal studies bode well for the future of this anti-IL-17 antibody, though Pfizer's chief executive, Ian Read, will probably have bigger things on his mind as he faces questioning from UK politicians tomorrow. That said, Astra's plan to show that its pipeline is underappreciated has received a boost.

Astra gained rights to brodalumab, along with three other MAbs, through a smart risk-sharing deal with Amgen. Unfortunately for Astra's chief executive, Pascal Soriot, this is not something for which he can take full credit: the collaboration had been struck by his predecessor, David Brennan, four months before Mr Soriot took over the reins.

Low key?

Perhaps one reason why brodalumab had been a relatively low-key asset was that the anti-interleukin MAb space is looking crowded; however, brodalumab seems to be the only agent to inhibit the IL-17 receptor, while others bind to IL-17 itself, or to other cytokines, though the significance of the difference is not fully established.

In the phase III Amagine-1 study brodalumab met the primary endpoint of 12-week PASI 75 score reduction – 83% for the 210mg dose and 60% for 140mg – versus the placebo group's 3%. Amgen gave no p values, but said the co-primary endpoint of patients achieving 12-weeek sPGA 0 or 1 score, and secondary analyses, had also been met.

Attention now turns to full data publication, as well as two other phase III plaque psoriasis trials pitting brodalumab head to head against Stelara, Johnson & Johnson's marketed anti-IL-12/IL-23 MAb. Stelara sold $1.3bn last year.

Two additional brodalumab phase III studies are ongoing in psoriatic arthritis, but will not read out for a couple of years. *EvaluatePharma's* consensus forecasts, compiled before the phase III success was reported on Friday, see brodalimumab generating in-market sales of $651m in 2020, translating into a 75% risk-adjusted NPV of $688m for Amgen and $507m for Astra's share of the deal.

Under the alliance Amgen is leading development of brodalumab and AMG 557, a lupus B7RP-1 antibody, while Astra focuses on the mid-stage projects MEDI-2070, MEDI-7183 and MEDI-9929 (*AstraZeneca spreads the load with Amgen development deal, April 3, 2012*).

At least as good

The psoriasis biological space might be crowded, but – with the usual caveats about cross-study comparisons – brodalumab seems to be at least as good as the competition.

Among the anti-IL-17 MAbs, Novartis's secukinumab is awaiting approval on the basis of a PASI 75 improvement of up to 87%, while Lilly's ixekizumab showed 83% at one phase II dose; phase III ixekizumab studies, including against Amgen's Enbrel, are ongoing. Kyowa Hakko Kirin is also developing an anti-IL-17 MAb, KHK4827, which could yield phase III data next year.

Secukinumab has shown superiority over Enbrel, but a 640-patient trial versus Stelara only started recruiting recently, so positive data in Amagine-2 and 3 could give brodalumab a significant advantage and compensate for it being behind Novartis in development overall.

The other factor that will be closely watched is safety. ISI Group's Mark Schoenebaum wrote that rates of cancer and infections would be important as these side effects result from the use of many of the biological therapies approved in psoriasis.

Given the size of the potential market it seems strange that just last week Astra's bid defence, which made remarkably bullish peak sales forecasts for several pipeline projects, declined to put a number on brodalumab.

As the May 26 deadline for Pfizer to come back with a sweetened bid or put its case directly to Astra investors approaches, expect brodalumab to play a growing role.

Phase III brodalumab studies			
Study	**Design**	**Completion**	**Trial ID**
Amagine-1	661 plaque psoriasis pts	Completed	NCT01708590
Amagine-2	1,800 plaque psoriasis pts	Aug 2014	NCT01708603
Amagine-3	1,881 plaque psoriasis pts	Sep 2014	NCT01708629
Amvision-1	630 psoriatic arthritis pts	Jan 2016	NCT02029495
Amvision-2	495 psoriatic arthritis pts	Feb 2016	NCT02024646

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