Evaluate Vantage

October 16, 2015

Upcoming events: Voyage ending for guselkumab and binimetinib

Elizabeth Cairns

Welcome to your weekly digest of approaching regulatory and clinical readouts. Two agents are about to report phase III results in their first indications: Johnson & Johnson's guselkumab in psoriasis and Array Biopharma's binimetinib in NRAS-mutant melanoma.

J&J will hope it can steal a march on its psoriasis rivals, several of which have run into difficulties recently. But Array looks to be facing stiffer competition: even if binimetinib does hit the market on schedule it will still be some time behind the likes of Yervoy and Opdivo, and therefore seems doomed to limited sales.

Fantastic Voyage?

The novel mechanism of action of J&J's IL-23-targeting antibody guselkumab means the drug could sidestep issues seen with the likes of brodalumab, AstraZeneca's IL-17 MAb.

Reports of suicidal ideation with brodalumab spurred Amgen to pull out of its partnership with Astra in May, and analyst forecasts tumbled accordingly. But this did not stop Valeant getting involved in the project, so there might still be some hope left (*Baffling Valeant strikes for troubled Astra psoriasis project, September 1, 2015*).

Novartis's approved IL-17-targeting agent, Cosentyx, has also been linked with suicide ideation – it will be interesting to see whether Lilly's ixekizumab, submitted to the FDA in Q1, will throw up any similar concerns.

And it is not just anti-IL-17s that have been in the spotlight recently – Pfizer just received a bombshell in the form of an FDA complete response letter for its JAK-3 inhibitor Xeljanz. There are currently no further details, but safety issues are one possibility (*Xeljanz stumbles again with US knockback, October 15, 2015*).

All of this might be good news for J&J if guselkumab comes through in the phase III Voyage 1 and 2 studies. Phase II data were encouraging, with the drug outperforming Humira on efficacy, but there was a suggestion of cardiovascular problems, which will be closely watched (*Therapeutic focus – Another strong contender added to full psoriasis pipeline, March 25, 2014*).

If these fears turn out to be unfounded, J&J may be able to press home its first-in-class advantage – the only other IL-23 MAb in late-stage development is Merck & Co's tildrakizumab. Two phase III trials of that project were due to report last year but the drug is no longer listed in Merck's pipeline.

Late-stage targeted psoriasis agents

Status	Project	Company	Pharma class	Psoriasis 2020e sales ($m)
Filed	Ixekizumab	Eli Lilly	IL-17A MAb	782
Filed	Brodalumab	AstraZeneca	IL-17A MAb	191
Filed	Xeljanz	Pfizer	JAK-3 inhibitor	309
Phase III	Guselkumab	Johnson & Johnson	IL-23 MAb	153
Phase III	Tildrakizumab	Merck & Co	IL-23 MAb	-

If guselkumab does cause heart problems it will not threaten the dominant anti-TNF drugs. It could be back to the drawing board for J&J and psoriasis in general.

Finding Nemo

The phase III Nemo trial is comparing the efficacy and safety of Array BioPharma's binimetinib as a monotherapy with that of dacarbazine, and to that purpose has enrolled nearly 400 patients with advanced

unresectable or metastatic NRAS mutation-positive cutaneous or unknown primary melanoma.

Nemo's primary endpoint is progression-free survival with overall survival as a secondary endpoint. Phase I/II results presented at the European Society of Medical Oncology Meeting in September 2014 showed that patients given binimetinib achieved PFS of 3.6 months; historical PFS data for dacarbazine in NRAS melanoma is roughly 1.8 months, Wells Fargo analysts write. According to the analysts, Array believes that a doubling in PFS versus dacarbazine would be accepted as clinically meaningful.

It is even possible that Array's drug will show superiority on overall survival, they say; the phase I/II overall survival data showed 12.2 months for binimetinib whereas the figure for dacarbazine is around 8.2 months. Nemo's protocol allows for statistical testing of overall survival superiority for binimetinib twice in the study, but only if the primary endpoint of PFS is met first. If a showing of superiority on overall survival emerges during 2016 this might enable a broader label claim for binimetinib.

If Nemo hits its primary endpoint the company could file binimetinib and gain approval next year. Having regained the rights to the drug – along with an impressive payout – from Novartis in January, Array will reap the entirety of its predicted melanoma sales, which *EvaluatePharma*'s consensus puts at $13m next year and $213m in 2020 (*Array plays its Braf/Mek hand to perfection, January 26, 2015*).

But this is small beer in melanoma. The limited patient population binimetinib can treat plus the overwhelming success of other products, most notably the immunotherapies, means this area is strewn with predicted blockbusters – Opdivo, Keytruda, Yervoy and Mekinist are all forecast to break $1bn in sales in 2020.

Drug	Trial name	Primary completion date	ID
Guselkumab	Voyage 1	October 2015	NCT02207231
Guselkumab	Voyage 2	September 2015	NCT02207244
Guselkumab	Navigate	August 2016	NCT02203032
Binimetinib	Nemo	September 2015	NCT01763164

To contact the writer of this story email Madeleine Armstrong or Elizabeth Cairns in London at news@epvantage.com or follow @medtech_ma or @LizEPVantage on Twitter