Evaluate Vantage

November 24, 2017

Upcoming events – Another SGLT2 approval due and stem cell data for Mesoblast

Joanne Fagg

Welcome to your weekly digest of approaching regulatory and clinical readouts. Merck & Co and Pfizer's ertugliflozin is due before the US regulators in December, and while approval is likely the SGLT2 inhibitor is set to enter an already crowded space (see table).

And Mesoblast will report phase III data early next year with Prochymal, now referred to as MSC-100-IV, as it hopes to move towards US approval in patients with acute graft-versus-host disease. The initial developer, Osiris, struggled for years to ramp up decent sales with the stem cell treatment, running into difficulties with reimbursement in the few countries in which it had secured approval.

Another SGLT2

Merck & Co and Pfizer have filed their SGLT2 inhibitor ertugliflozin as a monotherapy and as two fixed-dose combinations, one with Januvia, Merck's DPP-4 inhibitor, and the other with metformin. A decision is due in December.

The filings were based on the nine-trial phase III Vertis programme, which enrolled 12,600 adults with type 2 diabetes and found that ertu significantly reduced glycated HbA1c *(Snippet roundup: Wins for AcelRx, Foamix and SGLT2 developers, September 16, 2016).*

However, even if ertugliflozin is approved, it could have problems gaining traction. The diabetes market is crowded, and it is difficult to differentiate ertugliflozin's efficacy versus already marketed SGLT2s – particularly as the project has not shown a cardiovascular outcomes benefit, and data here are not due until 2019.

Astrazeneca's Farxiga is expected to become the biggest-selling SGLT2 by 2022, sitting just above Jardiance. The latter has a cardiovascular benefit claim on its label, while Farxiga's CV data are not due until H2 2018.

A CV label decision for Invokana is due by the middle of next year; although Johnson & Johnson's candidate has shown a cardiovascular benefit it could be held back by an increased risk of amputation. Invokana had previously taken the number-one spot, but forecasts have tumbled since an FDA safety alert in May *(Amputation risk adds another cut to Invokana, May 30, 2017).*

Fortunately for the competition this is not currently seen as a class effect. Most of ertugliflozin's value is assigned to its combination with Januvia. Boehringer and Lilly's Glyxambi was the first SGLT2 and DPP-4 combination launched, and it takes the third spot.

Biggest diabetes products featuring SGLT2s				
			Annual sales ($m)	
Product	**Generic name**	**Company**	**2016**	**2022e**
Farxiga/Forxiga	Dapagliflozin propanediol	Astrazeneca/Ono Pharmaceutical	907	1,832
Jardiance	Empagliflozin	Boehringer Ingelheim/Lilly	256	1,753
Glyxambi*	Empagliflozin; linagliptin	Boehringer Ingelheim/Lilly	139	1,730
Invokana	Canagliflozin	Johnson & Johnson/Mitsubishi Tanabe Pharma	1,438	1,107
Ertugliflozin & Januvia*	Ertugliflozin; sitagliptin phosphate	Merck & Co/Pfizer	-	1,011
Ertugliflozin	Ertugliflozin	Merck & Co/Pfizer	-	418
**Combination of SGLT2 and DPP-4. Source: EvaluatePharma.*				

Stem cells

Four years ago the Australian company Mesoblast acquired Osiris's stem cell assets, including Prochymal, for $20m up front. At the time the paediatric graft-versus-host disease (GvHD) treatment had conditional approval in Canada and New Zealand, but was struggling to gain reimbursement, and was only available in the US under an expanded access programme that included adults.

It is sold in Japan as Temcell HS by JCR Pharmaceuticals – the only territory where it is currently available, according to Mesoblast – where it can be used in children and adults. A four-week course of treatment for an average adult is reimbursed for up to $195,000.

Prochymal is now known as MSC-100-IV. Data from its open-label US phase III trial in 60 patients aged two months to 17 years old, which Mesoblast says might be enough for accelerated approval, are due early next year.

Participants have acute GvHD after allogeneic hematopoietic stem cell transplant that has failed to respond to treatment with steroids, and the primary measure is overall response at day 28, as well as safety. Secondary endpoints include survival at day 100.

The overall response data are expected in the first quarter of next year, while survival results, likely needed for a filing, are due in the second quarter.

Last year MSC-100-IV reported data from its expanded-access programme in 241 paediatric patients. The overall response rate at day 28 was 65%. The latest phase III trial uses Bayesian analysis, according to which it passed an interim futility analysis in November 2016.

If MSC-100-IV is approved, Mesoblast will receive a paediatric review voucher, a potentially valuable commodity. The group is also planning a label extension in adults; Credit Suisse analysts note that the adult population could be four times bigger than the paediatric market.

With the FDA recently announcing its expedited programme for regenerative medicines Mesoblast might finally get a path forward in the US. How the drug is paid for will be the bigger hurdle.

Trial	ID
Phase III in 60 acute GvHD patients (paediatric trial)	NCT02336230

To contact the writer of this story email Joanne Fagg in London at joannef@epvantage.com or follow @ByJoFagg on Twitter