Evaluate Vantage

May 19, 2017

Snippet roundup: Bladder cancer nod for Keytruda and success for Syndax in melanoma

Edwin Elmhirst

Welcome to your weekly roundup of *EP Vantage*'s snippets – short takes on smaller news items.

This week, May 15 to 19, 2017, we had thoughts on the following: Another miss for Sirtex; Keytruda gets full approval in bladder cancer; Syndax surges on melanoma combination; Another chink appears in Abbvie's Humira biosimilar armour; Saving children with a Flourish; Biogen doubles down on stroke.

These snippets were previously published daily via twitter.

Another miss for Sirtex

May 19, 2017

If Sirtex was in trouble following the miss in its phase III hepatocellular carcinoma trial last month, that trouble has now intensified. Its SIR-Spheres, radioactive microbeads intended to kill tumours, have had no effect on survival in patients with colorectal cancer, according to an analysis of combined data from three trials released in the Asco abstracts on Wednesday. The beads were under investigation in the Sirflox, Foxfire and Foxfire-Global trials as first-line treatment for patients with liver metastases from colorectal cancer, and while the product showed "higher response rates and improved liver-specific progression-free survival", the primary endpoint of overall survival was missed. The SIR-Spheres are approved as salvage therapy, but all Sirtex's efforts to move them further forward in the treatment cascade have come to nothing. The group's shares fell 28% yesterday, closing at Aus$10.75.

Keytruda gets full approval in bladder cancer

May 19, 2017

Perhaps the definition of last but not least, Merck's Keytruda has finally achieved US approval in bladder cancer, becoming the only approved anti-PD-1 to have actually been shown to work in the disease. It simultaneously won accelerated approval for first-line use in urothelial carcinoma patients ineligible for cisplatin-containing chemotherapy, based on response rates and duration, and full second-line approval based on an improvement in overall survival. Now US patients have access to a drug with a proven survival benefit the prospects for rivals Opdivo or Imfinzi might dim – but not as much as those for Roche's Tecentriq, the only anti-PD-1/PD-L1 MAb to be shown to have no survival benefit in bladder cancer. Even if the FDA does not revoke Tecentriq's US approval, granted for second-line use on an accelerated basis exactly a year before Keytruda's, sales will surely suffer.

US approval status for anti-PD-1/PD-L1 MAbs in urothelial bladder cancer

Relevant date	Status	Study data	Trial ID
Tecentriq (Roche)			
18 May 2016	Accelerated approval for 2nd-line use	15% ORR in Imvigor-210 study	NCT02951767
17 Apr 2017	Accelerated approval for 1st-line (chemo ineligible) use	24% ORR in Imvigor-210 study	NCT02951767
10 May 2017	Failure to show OS benefit in 2nd-line use	Imvigor-211 study	NCT02302807
Opdivo (Bristol-Myers Squibb/Ono)			
2 Feb 2017	Accelerated approval for 2nd-line use	20% ORR in Checkmate-275 study	NCT02387996
Imfinzi (Astrazeneca)			
1 May 2017	Accelerated approval for 2nd-line use	17% ORR in Study 1108	NCT01693562
Bavencio (Pfizer/Merck KGaA)			
9 May 2017	Accelerated approval for 2nd-line use	13% ORR in Javelin Solid Tumor study	NCT01772004
27 Aug 2017	PDUFA date for maintenance treatment approval	16% ORR in Javelin Bladder 100 study	NCT02603432
Keytruda (Merck & Co)			
18 May 2017	Full 2nd-line approval	OS 10.3mth vs 7.4mth in Keynote-045 study	NCT02256436
18 May 2017	Accelerated approval for 1st-line (chemo ineligible) use	24% ORR in Keynote-052 study	NCT02335424

Syndax surges on melanoma combination

May 18, 2017

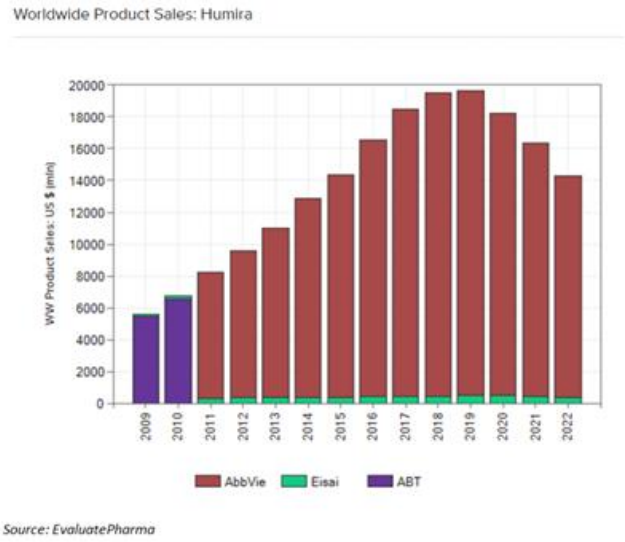
The first look at data from a phase II trial of HDAC inhibitor entinostat in melanoma prompted Syndax shares to climb above their 2016 IPO price yesterday, surging 45%. The company notably managed to lure Astrazeneca's former chief medical officer, Briggs Morrison, to lead the company two years ago, but it has struggled to make much headway on the stock market since floating in April last year. A presentation at Asco next month could change that – it is presenting a poster on a combination of entinostat with Keytruda in metastatic melanoma, specifically patients who have progressed after initial checkpoint inhibitor therapy. Yesterday it said 31% of patients (4 of 13) in the first cohort of the melanoma arm in its Encore 601 study achieved an objective response; three patients remained on therapy after the data cut off. A further 21 patients are already being recruited into an expansion phase and the company is shooting for an overall ORR of 25%, so the readout from the initial cohort is encouraging; full data should emerge early next year. Syndax believes that these results support the theory that entinostat "re-sensitises" tumours after they have stopped responding to checkpoint blockade – one patient with a confirmed partial response converted from a PD-L1 negative, non-inflamed gene signature in a pre-treatment tumour biopsy to PD-L1 positive, inflamed gene signature after treatment with the combination.

Trial	ID	Asco presentation details
Encore 601	NCT02437136	Abstract Number: 9529; Saturday, June 3

Another chink appears in Abbvie's Humira biosimilar armour

May 17, 2017

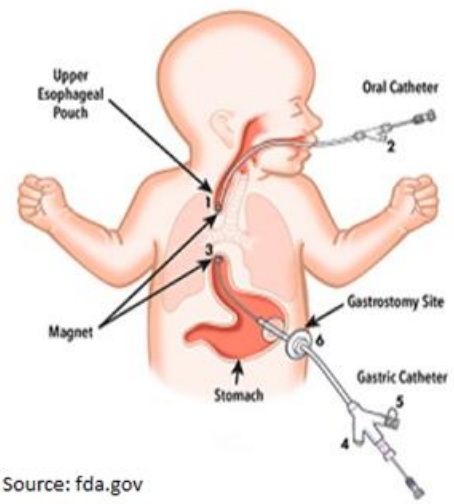
Abbvie has managed to repel many attacks against its cash cow Humira, but it looks like its defences are finally faltering. The invalidation of a key dosing patent, '135, could bring the entry of biosimilars forward to 2019, Leerink analysts believe – and Coherus and Boehringer Ingelheim are at the front of the pack of challengers. Abbvie will hope that it can still rely on three formulation patents to keep its top asset safe until 2022, but Coherus has other ideas; it has said it plans to work around these patents by using different formulations. Shares in the biosimilar specialist opened up 9% today on the inter parties review ruling, while Abbvie's stock opened down 3%. However, biosimilar developers will still need to overcome the remainder of Abbvie's large Humira patent estate unless they want to chance an at-risk launch. Another key event will be the district court battle between Abbvie and Amgen, another biosimilar developer, set to begin in autumn 2019. Abbvie's siege will have to end at some point – but the only question is when.



Saving children with a Flourish

May 15, 2017

The FDA has approved, via a humanitarian device exemption, the first device of its kind to treat a birth defect in infants up to one year old that causes a gap in their oesophagus. The Flourish paediatric oesophageal atresia anastomosis device, which will be sold by Cook Medical, uses magnets to pull the upper and lower oesophagus together. It is not implanted surgically, but the positioning process is quite involved: two catheters are inserted into the patient, one through the mouth and one through the stomach. The magnetic ends of the two catheters attract, pulling the two ends of the oesophagus together over the course of several days. When the catheters are removed, the patient can begin to feed by mouth. Oesophageal atresia affects around one in every 2,500 babies in the US, but the Flourish can only be used in a fraction of these cases: most babies born with the condition also have a tracheoesophageal fistula, which must be repaired surgically, and the device may not be used in patients with a fistula or who have had a fistula repaired in a prior surgery.



Biogen doubles down on stroke

May 15, 2017

Biogen’s appetite for high-risk neuroscience projects shows no sign of abating. Its latest move, buying Remedy Pharmaceuticals’ stroke candidate Cirara for $120m up front plus undisclosed milestones, gives it an asset that is far from a sure thing, having failed in phase II. A novel mechanism of action – Sur1-Trpm4 channel inhibition – and orphan drug designation have likely tempted the bigger company. Cirara targets large hemispheric infarction (LHI), a severe form of stroke characterised by brain swelling, which makes up around 15% of ischaemic stroke cases. Biogen is also studying its multiple sclerosis therapy Tysabri in stroke, but in the mild-to-moderate acute ischaemic form. The latest deal could therefore give it broader coverage of the market, but Biogen still has it all to do. The company plans to start a phase III trial of Cirara next year, which might differ from the Charm study that Remedy had planned, and will hope that any glimmers of efficacy translate into solid benefits.

Biogen's stroke pipeline

Project	Target population	Status	Trial
Cirara	Large hemispheric infarction	Phase III ready	Charm; NCT02864953 (not yet recruiting)
Tysabri	Mild-to-moderate acute ischaemic stroke	Phase II	Action2; NCT02730455

Source: EvaluatePharma, company website

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