

Januvia's surprising all clear, courtesy of Tecos



Amy Brown

Merck & Co managed to steal the thunder from its own first-quarter earnings report with a three-line press release last night, announcing a surprisingly positive result from the keenly awaited cardiovascular outcomes study of its biggest selling product, Januvia.

The huge 15,000-patient Tecos trial did not detect an increase in hospitalisations for heart failure, a signal that has prompted calls for updated safety information on other drugs in the class. The Januvia franchise is forecast to remain the company's most important revenue generator out to 2020, so with what looks like a substantial new marketing advantage in the bag the 5.8% jump in Merck shares this morning is understandable.

The brief press release left open the possibility that the full presentation of the Tecos data might still contain a numerical trend towards hospitalisation for heart failure, but Roger Perlmutter, head of R&D at Merck, ruled that out pretty emphatically on the company's first-quarter call this morning.

The two arms were "completely balanced" on this endpoint, he said. Hospitalisations for heart failure formed a specific secondary endpoint in Tecos; the other cardiovascular outcome studies conducted in this drug class only included the measure as one of a composite.

Although the lack of an explicit endpoint weakens the strength of the signal, experts at an advisory committee meeting earlier this month still felt moved to recommend an update to the safety information on both AstraZeneca's Onglyza and Takeda's Nesina. In the Savor-Timi 53 study of Onglyza a 27% increase in the rate to first event of hospitalisation for heart failure was seen; a similar but even weaker association emerged from Takeda's Examine trial.

The hope now has to be that the FDA decides to leave Januvia's label untouched, given that the design of Tecos should allow a pretty strong conclusion to be drawn on the drug's impact on this serious safety measure. The full presentation of the study is scheduled for June 8 at the American Diabetes Association's annual conference, an event that also now seems unlikely to contain any nasty surprises.

Unexpected outcome

This outcome was unexpected: the broad assumption was that the Savor-Timi and Examine studies had unearthed a class effect. And given the dramatic history of cardiac safety scares in the diabetes world – think Avandia – an even worse scenario was no doubt hovering in many an investor's mind.

The table below shows just how important the DPP-IV franchise remains to Merck, even with the rise of Keytruda, its trailblazing checkpoint inhibitor. It is also worth noting that Januvia will be a highly profitable product at this stage in its lifecycle, particularly when considering the huge R&D investment that Keytruda must be consuming.

With Merck already investing heavily to defend Januvia from newer products, it should not take too much extra input to make the most of this marketing advantage. An uplift of 10% to the Januvia franchise in 2020 would translate into a low single-digit percentage increase to earnings per share, Bernstein analysts estimated this morning.

And adding 10% to the peak sales estimate of Januvia lifts the NPV of the product by 12% to \$11.1bn, equal to a 1% rise in Merck's market cap, *EvaluatePharma's NPV Analyzer* shows. It seems that investors are hoping for an even bigger impact, although the share price reaction seen today is also likely to reflect some relief at dodging a bullet.

As *EP Vantage* pointed out earlier this month, the DPP-IVs are not growing as fast as other diabetes drug classes – mainly as a function of the later stage in their lifecycles ([Tecos tests DPP-IV heart failure hypothesis after FDA adcom, April 15, 2015](#)).

However, they are still forecast to be generating almost as much as the SGLT2 and GLP-1 classes combined in 2020. Assuming that the FDA does not come to a different conclusion on the class effect, Januvia should be able to remain head and shoulders above the rest.

Merck's top 10 sellers in 2020 - all currently marketed unless stated			
		Global sales (\$m)	
Product	Therapy area	2014	2020
Januvia + Janumet	DPP-IV diabetes therapy	6,002	6,527
Keytruda	Anti-PD-1 cancer antibody	55	4,717
Grazoprevir/Elbasvir (Phase III)	Hepatitis C combination	-	2,930
Gardasil	HPV vaccine	1,738	2,262
Simponi	Anti-TNF anti-rheumatic	689	1,379
Isentress	HIV integrase inhibitor	1,673	1,265
Zostavax	Herpes zoster vaccine	765	1,125
Remicade	Anti-TNF anti-rheumatic	2,372	852
Bridion	Anaesthetic	340	850
Varivax	Varicella vaccine	672	845

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