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WFH 2018 – Roche takes haemophilia fight to factor developers

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Roche's Hemlibra has already impressed in a niche haemophilia A market: patients who have developed inhibitors. But to dominate the sector the company needed a knock-out result in the bigger population of non-inhibitor patients – and the Haven 3 trial has delivered.

The results, presented in full today at the World Federation of Hemophilia congress in Glasgow, UK, are bad news for Roche's haemophilia rivals, including factor VIII players like Sanofi and Shire (see table below). Still, with news of another patient death with Hemlibra emerging over the weekend, safety concerns could prove a stumbling block.

Gallia Levy, associate medical director at Roche, told *EP Vantage* that the death came during commercial use of Hemlibra in an elderly patient with acquired haemophilia with inhibitors, and had been deemed unrelated to the product.

She added during an interview on the sidelines of the WFH meeting that there had been no change to Hemlibra's risk/benefit profile, something supported by a lack of serious adverse events in Haven 3 and 4, also presented today.

Haven 3 evaluated Hemlibra given once weekly or once every two weeks in non-inhibitor patients, while Haven 4 tested once-monthly dosing in patients with and without inhibitors, antibodies rendering front-line factor VIII clotting factors ineffective. The data suggested similar efficacy across the three dosing regimens.

Roche hopes to market all three options, and Ms Levy said it would be up to physicians and patients to decide which worked best for them.

This could be another blow to the current incumbents, as prophylactic factor VIII therapy is less convenient, being administered intravenously several times a week.

Haven 3

But first and foremost Hemlibra had to impress on efficacy, and here Haven 3 delivered. When compared with no prophylaxis, Hemlibra once weekly and once every two weeks showed a respective 96% and 97% reduction in treated bleeds, with p values of less than 0.0001.

Perhaps more worryingly for the likes of Sanofi and Shire, Haven 3 also showed superiority to prophylactic factor VIII treatment in an intra-patient comparison in which patients were switched from the older therapies to once-weekly Hemlibra. There was a 68% reduction in treated bleeds, based on an annualised bleeding rate (ABR) of 4.8 with the factor VIII therapies versus 1.5 with Hemlibra.

Not everyone was convinced by this, however, with some pointing out that the ABR with factor VIII prophylaxis was inconsistent with previous studies, and that this might have flattered Hemlibra. Bernstein analysts noted before the WFH congress began that much lower ABRs of 1-2 had historically been seen with prophylactic factor VIII therapy.

Ms Levy said this was not an apples-to-apples comparison, telling *EP Vantage* that the Haven 3 trial used a negative binomial statistical model that was more akin to measuring the mean ABR, while the 1-2 figure is based on median values. She added that the Haven 3 ABR data fitted with previously published studies when using a like-for-like comparison.

Still, any lingering doubts about this could make physicians wary of switching well-controlled patients to Hemlibra – particularly in the notoriously conservative haemophilia market.

Switching

When asked about how she expected the market to play out if Hemlibra became available to non-inhibitor patients, Ms Levy pointed to patient preference data from Haven 3. Overall, 94% said they preferred Hemlibra,

rising to 98% in the patients who had switched from factor VIII prophylaxis.

Roche is preparing its submission for Hemlibra in non-inhibitor patients, and hopes to get the go-ahead here by the end of 2018, to add to the approval last November in inhibitor patients.

Hemlibra sales of $18m during its first full quarter on the market came in ahead of analyst expectations, but it is the non-inhibitor population that is the real money-spinner.

EvaluatePharma sellside consensus already has Roche's drug overtaking the current market leader, Shire's Advate, by 2021. If the safety of Hemlibra holds up, the latest data could hasten this process.

Top five haemophilia A products in 2024

			Global sales ($m)			
Product	**Company**	**Description**	**2018e**	**2020e**	**2022e**	**2024e**
Hemlibra	Roche	Anti-factor IXa & X bispecific MAb	291	1,635	3,179	4,442
Eloctate	Sanofi/Swedish Orphan Biovitrum	Recombinant factor VIII	1,131	1,568	1,719	1,936
Valoctocogene roxaparvovec	Biomarin Pharmaceutical	AAV-factor VIII gene therapy	-	55	481	1,318
Advate	Shire	Recombinant factor VIII	2,161	1,693	1,310	1,037
Kogenate	Bayer/CSL	Recombinant factor VIII	1,066	917	724	594

Source: EvaluatePharma.

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