Evaluate Vantage

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Biohaven hopes to give Allergan a headache

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Biohaven might soon be going up against Allergan in the acute migraine space, but the company believes size will not be a barrier to its success.

When two similar drugs reach the market at around the same time the money is usually on the one with the biggest developer. Biohaven hopes to buck that trend with its oral CGRP inhibitor, rimegepant, which is in a race against Allergan's ubrogepant for approval in acute migraine.

Biohaven believes that its candidate has several advantages – but phase III data have not been clear-cut and if anything have suggested better efficacy with ubrogepant. And with another, differently acting, rival, Lilly's lasmiditan, also in late-stage development, Biohaven could have a tough fight ahead.

Follow the MAbs

At least the company does not have to worry – for now – about the injectable anti-CGRP antibodies, such as Amgen/Novartis's recently approved Aimovig, as these are only suitable for preventative rather than acute migraine therapy.

But Biohaven plans to test rimegepant in prevention too, with a phase III trial slated to start by the fourth quarter.

Its chief executive, Vlad Coric, says the company could benefit from work done here by its antibody rivals: "The market's going to be nicely primed and then … if you're a patient do you want a pill or an injection?"

The group's top priority for now, though, is the acute migraine space. Here the oral CGRPs will be targeted at the four million or so US patients who either do not respond to or cannot take triptans, an old drug class that is contraindicated in patients with cardiovascular disease.

In this population the question will be how rimegepant stacks up against ubrogepant and, with the usual caveats about cross-trial comparisons, Allergan's project looks to have the efficacy edge (*Allergan could struggle to fend off calls for a carve-up, May 1, 2018*).

Still, liver enzyme elevations with higher doses of ubrogepant could be a cause for concern; this does not appear to be a problem with rimegepant.

And the lowest 25mg dose of Allergan's drug did not meet one of the co-primary endpoints, absence of most bothersome symptoms at two hours, in the Achieve 2 pivotal trial – suggesting that finding a therapeutic window for ubrogepant might still be difficult.

The simplicity of dosing with rimegepant could be a plus point, Mr Coric says: “What’s the right dose of ubrogepant – 25mg, 50mg or 100mg? They’ve talked about submitting all three doses. For us it’s very straightforward: one dose, 75mg. I wouldn’t underestimate [the importance of] that to physicians.”

This luxury stems from the fact that Biohaven first did a dose-ranging trial, after which it tested only 75mg in two pivotal studies.

Longer lasting?

But there are other advantages with Biohaven’s project, according to the chief exec, including its long-lasting effect. “Allergan is not talking about sustained pain relief up to 48 hours – the most I’ve seen it talk about is 2-24 hours.”

This sustained effect is a function of rimegepant’s longer half-life, he believes: “Ubrogepant has a 4.5-hour half-life – it’s out of your system in about a day.” Rimegepant’s half-life of 8-12 hours means that it is eliminated in around 60 hours.

This could be a reason why rimegepant has seen lower concomitant use of rescue medication. “50% of ubrogepant patients are reaching for a second dose or rescue meds, compared with only 20% of rimegepant-treated patients,” Mr Coric says.

Whether all this will help when Biohaven goes up against Allergan, which Mr Coric admits is a “formidable competitor”, is another matter.

The acute migraine landscape will likely be complicated further by the entrance of lasmiditan, which Lilly plans to file this year. Stifel analysts believe that the choice of agent could come down to patient preference, with lasmiditan apparently slightly more effective and the oral CGRPs better tolerated.

Race towards approval

Biohaven plans to file rimegepant for acute migraine in the first half of 2019 – putting it on a similar timeline to Allergan.

The company initially hopes to launch an orally disintegrating tablet (ODT) formulation of rimegepant, which starts working in 45-90 minutes. Although pivotal trials have used a traditional pill formulation, Biohaven has already carried out bioequivalence studies with the ODT version.

The company is also developing an intranasal project with an even faster onset of action of 10-15 minutes, and this is around a year and a half behind the pill and ODT versions.

Mr Coric envisages Biohaven having multiple needleless formulations of rimegepant that patients could choose from depending on how fast they needed the drug to work. “Say you’re about to give a presentation – then you might want an intranasal.”

Rimegepant could also move into first-line use versus triptans, but this would depend on factors including “single-dose efficacy, durability of effect, lack of rebound headaches and tolerability profile”, Mr Coric said – although, presumably, cost could also come into it.

As for the potential price tag, the chief exec will only say that as a small molecule rimegepant should be priced competitively to the MAbs – Aimovig, for example, is priced at $6,900 per year. "I think Amgen did a very nice job with the pricing of Aimovig. If one can think of pricing around that range, or a discount to that, I think that’s a reasonable place as to where you’ll see us land.”

Mr Coric will not be drawn on whether Biohaven will need a partner, only that the company is exploring its options. Still, with competitors like Allergan and Lilly on the horizon, it might need one.

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