Evaluate Vantage

March 07, 2018

No reason for partners to jump into Esperion just yet

Jonathan Gardner

The first look at heart disease results with Esperion's bempedoic acid shows that it still has much to prove. A statistically significant 23% reduction in low-density lipoprotein (LDL) has to be weighed against two cases of liver enzyme elevation and a sense that the pill might not be potent enough to help many patients reach healthy cholesterol levels.

Though the stock recovered to close down 2%, an initial 9% plunge suggested that investors did not view the data as persuasive, and could help explain why big pharma has yet to pull the trigger on a deal. With its market cap hovering around $2bn Esperion looks pricey, but the equivocal data justify the caution shown by potential partners, which did not snap up the Michigan-based group a year ago when it was worth a comparatively small $300m.

Less than 30% solution

Esperion knows, of course, that it is in no position to launch a drug into a market it estimates at 9.5 million people, and delivering persuasive data will be necessary to hook a partner or buyer that can maximise bempedoic acid's sales (*Event – Esperion faces acid test, February 26, 2018*). Thus topline data from the first of five phase III studies to read out this year might need to be followed up with stronger results.

The trial in 269 statin-intolerant subjects found a 23% reduction in LDL over baseline for those taking bempedoic acid, and a 28-point reduction over patients in the control arm, at 12 weeks. All patients were on background therapy of Zetia, and one third of the those on bempedoic acid and 28% of those given placebo were on low-intensity statins.

The mean baseline LDL level for patients in the bempedoic acid arm was 130mg/dl. The 23% reduction got bempedoic acid patients to a mean LDL level of 100mg/dl, the treatment goal of patients classified as high or moderate risk. This is, however, is still above the goals of patients classified as very high or extreme risk, who have 70mg/dl and 55mg/dl goals respectively.

This alone does not mean that bempedoic acid does not have commercial potential. Esperion's chief executive, Tim Mayleben, pointed to the 9.5 million heart disease patients who need to achieve less than a 30% reduction in LDL to meet treatment goals.

Watch this space

The emergence of liver enzyme elevations is rarely a confidence booster, and two cases here mean that safety will need to be closely watched in coming trials. One led to a discontinuation at eight weeks; the other case did not cause discontinuation, but only because the trial was ending anyway. Neither patient had enzyme levels higher than five times the upper limit of normal, meaning the elevations were considered mild.

Stifel analyst Alex Schwartz called the elevations "well within the range of an approvable drug". He wrote that the the 2,200-patient, 12-month "study 1" in patients on maximally tolerated statins should give a clearer picture of liver safety when it reads out in May.

Nevertheless, the risk that safety could be a snag for bempedoic acid has now materialised. Fortunately for Esperion, the group will have several more chances this year to provide data to support a positive risk-benefit profile.

Upcoming bempedoic acid pivotal trial readouts					
Study	**Details**	**N**	**Primary endpoint**	**Trial ID**	**Data due**
Study 4 (1002-048)	Efficacy in statin-intolerant patients, bempedoic acid + ezetimibe	269	Change in LDL-C at 12 weeks	NCT03001076	Reported
Study 1 (1002-040)	Long-term safety in patients on maximally tolerated statins, single-agent bempedoic acid	2,230	Adverse events at one year	NCT02666664	May 2018
Study 3 (1002-046)	Efficacy in statin-intolerant patients, single-agent bempedoic acid	345	Change in LDL-C at 12 weeks	NCT02988115	May 2018
1002FDC-053	Bridging study of bempedoic acid/ezetimibe combo pill	350	Change in LDL-C at 12 weeks	NCT03337308	Aug 2018
Study 2 (1002-047)	Efficacy in patients on maximally tolerated statins, single-agent bempedoic acid	779	Change in LDL-C at 12 weeks	NCT02991118	Sep 2018
Clear Outcomes	Cardiovascular outcomes study, single-agent bempedoic acid	12,600	Composite of CV adverse events	NCT02993406	2022
Source: Company presentation JP Morgan Healthcare Conference, January 2018; Clinicaltrials.gov.					

To contact the writer of this story email Jonathan Gardner in Virginia at jonathang-us@epvantage.com or follow @ByJonGardner on Twitter

More from Evaluate Vantage

Evaluate HQ
44-(0)20-7377-0800

Evaluate Americas
+1-617-573-9450

Evaluate APAC
+81-(0)80-1164-4754

© Copyright 2023 Evaluate Ltd.