Evaluate Vantage

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Upcoming events – pivotal tests approach for Lilly and Biohaven

Amy Brown

Lilly is awaiting the first set of pivotal data with the cytokine agent it bought from Armo last year, while Biohaven heads for migraine catalysts.

Welcome to your weekly roundup of approaching clinical readouts. Lilly spent $1.6bn buying Armo Biosciences last year to access the IL-10 cytokine agent pegilodecakin, and in the coming months it will start to learn whether that was money well spent. The first crucial data to emerge will be from a phase III pancreatic cancer study called Sequoia, though hopes for success are low after Lilly talked down the trial's chances at its most recent quarterly results.

Still, few expectations are attached to most efforts in pancreatic cancer, an aggressive and fast-moving disease that has proven very hard to stop, particularly once it has spread. This is the setting of Sequoia: patients with metastatic disease, who have progressed after receiving gemcitabine-based chemotherapy.

Gemcitabine is probably the most widely used front-line treatment for metastatic pancreatic cancer, though other regimens, such as Celgene's Abraxane, are also prescribed. There are various subsequent options, which largely dependent on the nature of a patient's first-line therapy.

In fact, only one agent is approved by the FDA specifically for second-line patients who progressed on gemcitabine: Onyvide, an encapsulated formulation of irinotecan, in combination with fluorouracil/leucovorin. The Merrimack product, which was bought by Ipsen in 2017, generated 6.1 months of overall survival versus 4.2 months for 5-FU/LV alone, equating to a 32% reduction in risk of death.

This provides a yardstick of sorts for pegilodecakin, and Lilly might be hoping for a more impressive outcome. However, in July executives pointed out that Armo had moved pegilodecakin into phase III on the back of limited phase I data, and said that lung and renal cancers were more important indications, statements that appear to be guiding down expectations.

Sequoia is due to report before the end of the year, and many hope that immuno-oncology approaches will finally start to offer a way forward in the poorly served pancreatic cancer space. Keytruda, for example, in combination with Biolinerx's BL-8040, generated overall survival of 7.5 months in second-line patients in the Keynote-202 study. This was a single-arm trial, and the results came in only 17 subjects, so can hardly be treated as conclusive, but further data from a triple combination arm of that study, also due later this year, are eagerly awaited.

Prevention better than cure?

In the fourth quarter Biohaven will report results from two late-stage migraine studies.

The most important will be the prevention trial, pitting 75mg of its oral CGRP inhibitor rimegepant against placebo in 1,629 patients with 4-18 migraines per month at baseline. If positive, the data could allow Biohaven to position rimegepant as a more convenient alternative to approved injectable CGRP inhibitors.

The primary endpoint is the reduction in mean number of migraines per month, assessed over three months. Secondary measures include the proportion of patients achieving 50% reduction from baseline in mean monthly migraine days.

Hopes are high after an open-label safety trial, study 201, suggested that rimegepant could work in migraine prevention. 286 of the 1,780 study subjects took the project on a preventative as well as an as-needed basis; among these, 48% had a 50% or greater reduction in monthly migraine days.

The bar is also fairly low in terms of what the injectable CGRPs, given prophylactically, have shown in a similar episodic migraine setting.

Injectable CGRP efficacy in episodic migraine			
Product	**Company**	**Trial(s)**	**Improvement in monthly migraine days**
Aimovig	Amgen/Novartis	NCT02456740 & NCT02483585	1.0-1.9
Emgality	Lilly	NCT02614183 & NCT02614196	1.9-2.0
Ajovy	Teva	NCT02629861	1.2-1.5
All placebo adjusted. Source: product labels.			

A win for Biohaven might also revive takeover talk, which was dampened by the company's $300m fund raising in June.

Rimegepant is awaiting approval in acute migraine, where Biohaven has filed a tablet version and a fast-acting oral dissolving tablet (ODT) with the FDA; it used a priority review voucher for the latter, setting up a decision by the end of 2019.

The company is also developing an intranasal project, BHV-3500, as an acute therapy designed to have an even faster onset. Its 1,600-patient study evaluates the project dosed at 5mg, 10mg and 20mg versus placebo, with a primary endpoint of freedom from pain at two hours post dose.

The anti-CGRP landscape						
					Annual sales ($m)	
Product	**Company**	**Route of admin.**	**Migraine setting**	**Status**	**2019e**	**2024e**
Aimovig	Amgen/Novartis	Injection	Preventative	Marketed	483	1,999
Emgality	Lilly	Injection	Preventative	Marketed	169	1,153
Rimegepant	Biohaven	Oral	Acute/ preventative	Filed (acute)/phase III (preventative)	-	875
Ajovy	Teva	Injection	Preventative	Marketed	159	813
Eptinezumab	Alder	Injection	Preventative	Filed	-	773
Ubrogepant	Allergan	Oral	Acute	Filed	-	427
Atogepant	Allergan	Oral	Preventative	Phase III	-	288
Ajovy	Otsuka	Injection	Preventative	Phase III	-	34
BHV-3500	Biohaven	Intranasal	Acute	Phase II/III	-	12
Source: EvaluatePharma.						