Evaluate Vantage

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Clinical developments over the Christmas period

Elizabeth Cairns

The most important clinical readouts of the holiday period concerned Google Health, Axsome, Wave and Spectrum.

While for many the time between Christmas and the New Year represents a dead period the financial markets mostly remain open, and stock-moving events happen.

Thus the holiday period just ended saw Google Health and Axsome Therapeutics celebrate clinical trial wins. A much worse fate awaited Wave Life Sciences and Spectrum Pharmaceuticals, which found that – the holiday period notwithstanding – there was no way to bury negative clinical trial readouts.

January 1:

In September Deepmind, which had previously had some success using artificial intelligence to analyse ophthalmological images, was incorporated into **Google Health**. The resulting group has now published data showing that using a Google Health algorithm to analyse mammograms could be as good as human analysis.

The AI system was used to identify tumours in mammograms of women with known cancer status. When using standard US diagnostic criteria the software was significantly superior to radiologists' findings, reducing false positives by 5.7% and false negatives by 9.4%. When using the more stringent UK diagnostic pathway, in which each mammogram is assessed by two radiologists, the reductions in false positives and negatives were 1.2% and 2.7% respectively; these were significant for non-inferiority only.

Much more testing will be necessary if this is to be incorporated into clinical practice. 95% of the mammograms came from Hologic machines; in the real world the sources would be much more diverse, and performance could slip. Moreover, since AI systems are intended to learn and improve over time, it would be crucial to monitor the system's performance to ensure that it gets better – or at least that it does not deteriorate.

December 30:

As 2019 wound to a close **Axsome Therapeutics**' phase III Momentum trial of the triptan-NSAID combo AXS-07 hit its two primary endpoints, beating placebo on alleviating migraine symptoms two hours after administration. This might well be good enough for approval, but it is unclear whether the hit is emphatic enough to justify doctors using the drug.

As well as the co-primary hits, the company said AXS-07 was superior to rizatriptan and MoSEIC meloxicam, its component drugs, on the measure of total pain freedom at 2-24 hours post-dose. But this is an easier measure

than the two-hour cutoff, particularly since Momentum was intended to prove AXS-07's worth as an acute treatment.

Momentum trial data				
	AXS-07	**Placebo**	**Rizatriptan**	**MoSEIC meloxicam**
% of patients pain-free at 2hr*	19.9	6.7		
P value vs placebo	*<0.001*			
% with absence of most bothersome symptom*	36.9	24.4		
P value vs placebo	*0.002*			
% pain-free at 2-24hrs	16.1	5.3	11.2	8.8
P value vs AX-07		*<0.001*	*0.038*	*0.001*
**Co-primary endpoints. Source: company release.*				

Separate published data on Merck & Co's branded rizatriptan, Maxalt, shows rates of pain freedom at two hours of up to 42% – much higher than AXS-07's 19.9%, though this might have been in an easier-to-treat population. Axsome intends to file AXS-07 in the second half of next year

Meanwhile, **Wave Life Sciences** fell 49% as its last chance of ending the year on a positive note evaporated with the results of the Precision-HD2 trial of WVE-120102 in Huntington's disease. That was the second shoe to drop in December after the group canned development of suvodirsen for Duchenne muscular dystrophy (*Wave crashes as Duchenne data disappoint, December 16, 2019*).

The Huntington's setback is especially damning as it throws into question Wave's "stereopure antisense oligonucleotide" concept. While the study theoretically succeeded, showing a 12% reduction in mutant huntingtin (mHTT) protein, this was inferior to the 40% or greater mHTT knockdown Roche and Ionis are achieving with RG6042.

Wave's remaining hope now is to dial up the WVE-120102 dose, raising two concerns. Firstly the analysis it uses to back a dose-response relationship in Precision-HD2 looks questionable; and secondly, if it is not, then there still remains the risk of dialling up toxicity and eliminating any therapeutic window that might exist.

December 26:

Spectrum Pharmaceuticals looked to have had a good shot at a targeted approach to a hard to treat lung cancer niche with its Her2 inhibitor poziotinib (*The first test of Spectrum's shift, November 28, 2019*).

But it all unravelled on Boxing Day, as Spectrum crashed 60% on the failure of Cohort 1 of the Zenith20 study in 115 previously treated NSCLC patients with EGFR exon 20 insertion mutations. The intent-to-treat analysis showed an objective response rate of just 14.8%, missing a threshold for success; data from cohorts 2 and 3 are expected this year.

December 24:

Finally, just before Christmas **Acasti Pharma** delayed readout of the Trilogy-1 of its fish oil project CaPre, meaning that both CaPre studies should now yield data this month (*Acasti plays catch-up to Amarin's Vascepa, November 20, 2019*). This might represent a minor delay, but fearing that it could hint at greater problems shareholders sent the company down 24%.