Evaluate Vantage

March 12, 2014

Oxigene soars on surprisingly positive news from disappointing drug class

Amy Brown

Oxigene is used to setback and disappointment. This is perhaps why the first version of a press release unveiling positive results from a phase II study of its long-tested agent Zybrestat declared the trial a failure, before a corrected version was hastily released.

The PR slip-up aside, the results are a notable signal of efficacy from a drug class, the vascular disrupting agents, that has all but been consigned to R&D history. Investors' reaction to the news is not surprising in the current market, but this is a field that has yielded little despite much research over the last decade. With minimal industry-backed work ongoing, any resurrection of the class or Zybrestat remains some way away.

Twilight Zone

A biotech does not have to boast much to achieve a sizeable valuation these days, so the diminutive $23m market value with which Oxigene started the week was a sure sign of years of abject failure. And although the stock has doubled on the news, the company's valuation remains tiny, no doubt reflecting the financial dire straits in which Oxigene has been wallowing over the past few years.

The failure of Zybrestat to demonstrate convincing efficacy – it was tested in phase II in lung or thyroid cancers and in eye disorders – and the company's ongoing financial struggles have deterred investors, even in these times of plenty. The study that provided today's lift was not even being funded by Oxigene, being run by the NCI's Gynecologic Oncology Group (GOG).

Vascular disrupting agents were once a hot cancer research area, but most candidates have fallen by the wayside. Sanofi's ombrabulin and Antisoma's vadimezan, at the time licensed to Novartis, made it into phase III, but got no further (*Twilight of the vascular disrupting agents, January 16, 2013)*.

Other than Zybrestat, only one other agent is being seriously pursued in clinical studies: Bionomics' BNC105.

The Australian drug researcher reported encouraging early response data from a phase I/II ovarian cancer study earlier this year, testing the agent in combination with carboplatin or gemcitabine in women with partially platinum-sensitive recurrent disease. A larger renal cancer study called Disruptor-1 is testing BNC105 in combination or following Novartis's tyrosine kinase inhibitor Afinitor, and is due to read out in the next few weeks.

Unlocking utility

The vascular disrupting agents have a plausible mechanism of action – they work by attacking the vasculature of solid tumours, restricting their blood supply – echoing the strategy of angiogenesis inhibitors like Avastin, which prevent the growth of new blood vessels.

The GOG study with Zybrostat seems to suggest that, as is increasingly recognised to be the case with other targeted anticancer agents, a combination approach is needed to unlock their utility.

The study recruited 107 patients with platinum-sensitive and resistant recurrent ovarian cancer, who received either Avastin or Avastin plus Zybrestat. Women in the combination arm lived for significantly longer before their cancer progressed ($p<0.05$). The difference between objective response rates, a secondary measure, was not significantly different, while overall survival data are not yet available.

Avastin is approved in Europe to treat newly diagnosed ovarian cancer, but the failure of the antibody to generate convincing overall survival data across several phase III studies has prevented Roche from seeking a US licence. So should the GOG study eventually find that women live longer with the combination it will be a notable finding for both agents.

In the meantime, further data are needed to assess the significance of this study.

"We still don't know a lot of important information, like the actual PFS rates in both arms and the timeframe

over which this analysis was carried out," says Christian Glennie, an analyst with Edison Investment Research. "But this is encouraging data for vascular disrupting agents, and timely with the Bionomics data due in the next few weeks."

Should another positive trial for a vascular disrupting agent emerge, the class could well warrant another look.

Trial ID	Product	Indication
NCT01034631	BNC105	Renal cancer
NCT01624493	BNC105	Ovarian cancer
NCT01305213	Zybrestat	Ovarian cancer

To contact the writer of this story email Amy Brown in London at AmyB@epvantage.com or follow@AmyEPVantage on Twitter