Evaluate Vantage

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Asco 2016 – AbbVie pulls back rova-T curtain

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AbbVie's new small-cell lung cancer project has reached its first milestone since the group spent $5.8bn to acquire its originator, and the results might not be quite as spectacular as the price tag had suggested.

Rovalpituzumab tesirine achieved an 18% one-year survival rate in the phase I trial, but on average patients saw their disease worsen after less than three months. The study's chief investigator urged caution as the data were still immature, but the results led some to question whether the Illinois-based company overpaid when it bought Stemcentrx for the antibody-drug conjugate (*AbbVie caps week of cancer deals with huge Stemcentrx takeout, April 29, 2016*).

Small-cell lung cancer being an area with few treatment options, the data that rova-T has returned so far have generated excitement, earning it an oral presentation slot in two consecutive major oncology conferences. The agent delivers a cytotoxic payload by binding to delta-like ligand 3 (DLL3), a protein expressed on the tumour cells of two-thirds of small cell lung cancer patients.

Small numbers

It remains an early asset, and the trials are small and single-arm, so broad conclusions are difficult to draw. Achieving confirmed responses in 18% of patients and 39% of those with the highest levels of DLL3 is a reason to continue studying this agent, along with the 18% survival rate – 32% in the high expressers.

However, when calculated as averages, these figures look less than impressive – indeed, AbbVie and Asco both steered clear of such measurements in their press releases on the presentation. However, in discussing the results of the trial during a meeting presentation, Taofeek Owonikoko, an Emory University medical professor, said the progression-free survival was 2.8 months.

By comparison topotecan, one of the typical treatments for small cell lung cancer, has shown a time to progression in clinical trials of over three months at 13.3 weeks.

Charles Rudin, thoracic oncology chief at Memorial Sloan Kettering Cancer Center and chief investigator on the rova-T trial, urged caution about survival numbers because of the small numbers in the trial.

"The median may not be the message," Dr Rudin said. "There may be a subpopulation that has a greater [survival]. If you look at a milestone analysis, one year, or two years, it will be interesting to see how the data holds up."

Investors, however, took a more short-term view and AbbVie shares were down 4% to $62.41 in early morning trading.

AbbVie strategy

AbbVie has moved swiftly from a company with precious little oncology revenue to one that analysts believe will derive nearly a quarter of its sales from cancer treatment in 2022, moving it from 16th to eighth in market share. Two big transactions have marked this move: buying Pharmacyclics for $20bn to gain half of the economic benefit of Imbruvica, and the Stemcentrx purchase.

In both cases, investors have wondered whether AbbVie overpaid, though in the case of Pharmacyclics at least it acquired an immediate revenue stream forecast to reach $3.9bn in 2022. In the case of Stemcentrx, it hooked a very early-stage asset in a novel drug class that has yet to be proven in randomised study.

Unpartnered clinical-stage oncology products are rare enough, so $5.8bn was what it took to bring Stemcentrx in, regardless of whether it will be money well spent. Arguing in favour of the big payout is the lack of good alternative treatments and the fact that rova-T is a targeted therapy with a predictive biomarker, raising the chances of a positive result in at least the subgroup of high DLL3 expressers.

The early data gave little insight into whether this positive result will emerge. It is no surprise investors are wary.

Study	Trial ID
SCRX16-001	NCT01901653

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