Evaluate Vantage

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Sesen learns a lesson in investor relations

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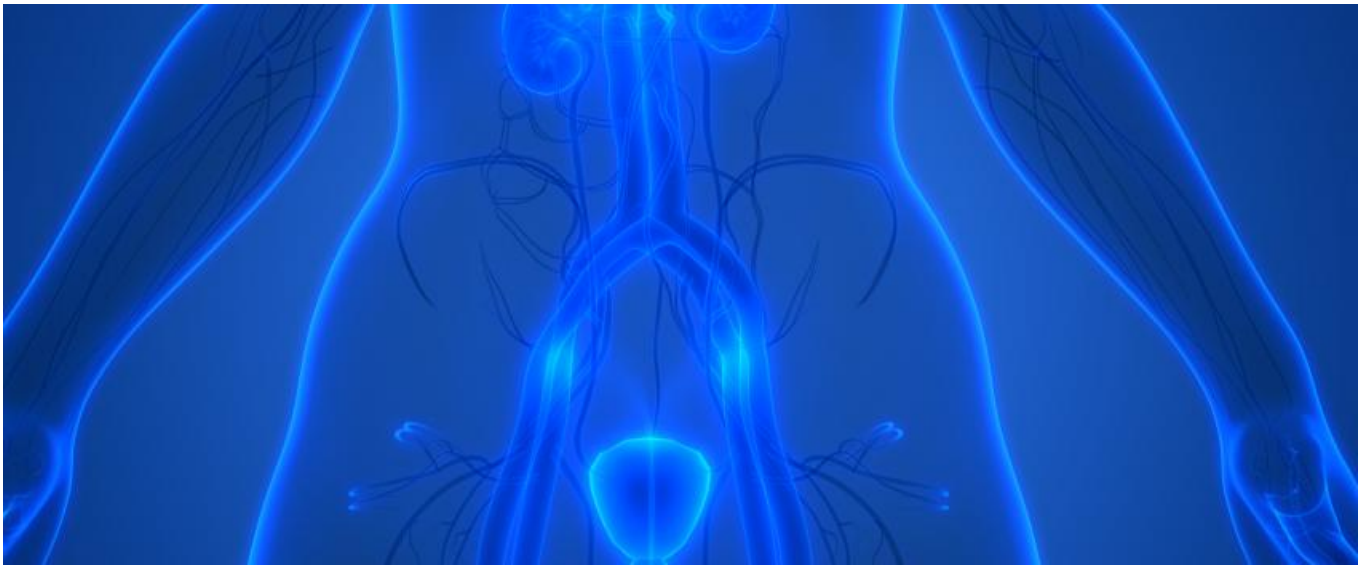

Bladder cancer data disappoint shareholders looking for signs of dose response and differentiation from Valstar.

Giving advance notice of an upcoming data readout might be polite, but in Sesen Bio's case it did not work out so well. After a run-up prompted by the group pre-announcing a call to discuss new data from its phase III trial of Vicinium, the event underwhelmed investors, who drove shares down 37%.

The fusion protein-drug conjugate did not look markedly different from valrubicin in patients with previously treated non-muscle invasive bladder cancer, and neither did the higher phase III dose appear to generate better response rates than that used in phase II. Moreover, news of a patient death due to kidney failure two years ago might have shaken investors, even if the trial's safety board has cleared Vicinium of any blame.

Sesen's disastrous session

Vicinium is a fusion protein that delivers a cytotoxic *Pseudomonas* exotoxin protein to cancer cells by binding with the epithelial cell adhesion molecule. The target population for the phase III Vista trial is patients with non-muscle invasive bladder cancer who have been treated with BCG (bacillus Calmette-Guérin) and deemed unresponsive.

Two cohorts were enrolled, one made up of subjects who had recurrence with less than six months of BCG treatment, comprising 86 patients, and a second group whose disease had recurred at between six and 11 months of BCG treatment, comprising seven.

At 12 months the first cohort had 81 evaluable patients and had a 14% complete response rate, and the second had seven evaluable and also a 14% rate. The pooled 14% complete remission rate of the two cohorts was below the 16% in phase II, which had a lighter dosing schedule, and not much above the 10% rate of valrubicin, which is marketed as Valstar by Endo International.

The lower bound of the 95% confidence interval of that pooled Vicinium population was a 7% complete response rate at 12 months; while this was hardly persuasive, Sesen executives were quick to note that it ruled out a clinically insignificant benefit, a standard specified by the FDA's guidance on bladder cancer.

Longer term

Sesen might be right that US FDA will be open to these data, given the agency's friendly stance towards all things oncology. The group plans to submit full 12-month data to a medical meeting in 2019, and these should contain information on an another important endpoint, avoidance of cystectomy, as the group prepares for a

regulatory submission.

On the other hand, as Valsar is a commercial project it is hard to ignore comparisons. Given that bladder cancer is a disease of older patients, Medicare is the chief payer, and in 2016 the programme spent on average $22,413 per beneficiary treated with Valstar. Sesen will need to be mindful of this benchmark should Vicinium gain approval.

Furthermore, Vicinium is being chased by checkpoint inhibitors – most importantly, Merck & Co had data from the Keynote-057 trial of Keytruda at Esmo, showing a 36.5% complete response rate at three months in this population, similar to the 39% of Vicinium.

If Keytruda were to show better durability it could increase Sesen's commercial challenge. And Keytruda is not alone, with Opdivo, Tecentriq and Imfinzi all being tested in this population. Moreover, Imfinzi is in a large clinical trial in combination with BCG, called Potomac, which could alter how patients progress through treatment lines.

Vicinium and its non-muscle invasive bladder cancer rivals		
Drug	**Status and setting**	**Trial ID**
Vicinium	Phase III trial in subjects previously treated with BCG	NCT02449239
Keytruda	Phase II trial in subjects unresponsive to BCG	NCT02625961
Tecentriq	Phase II trial in subjects unresponsive to BCG	NCT02844816
Imfinzi	Phase II trial in subjects refractory to BCG	NCT02901548

With that in mind, the endgame for Sesen is combination therapy, and an NCI trial with Imfinzi is already under way. News of further combination research could enliven shares, although this strategy does not always pay off in the long term, as Incyte and other companies working on PD-(L)1 combinations have found.

Complete 12-month data, along with news of a successful US submission, could give shares a lift later this year. But for now Sesen has fallen short. It might have been better to have simply delivered this news to investors without any build-up.

This story has been updated to correct the Valstar complete response rate.