Evaluate Vantage

December 15, 2016

Interview – Nordic Nanovector exits a glowing year

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Considerable success in 2016 will have Nordic Nanovector in the mood for several glasses of celebratory gløgg over the festive period. The company's stock surged almost 600% over the year as encouraging mid-stage data on its lead asset emerged, leaving it poised to start a pivotal study and able to raise $60m from investors.

Not that the Oslo-based drug developer needs the cash for the registration trial of Betalutin, an antibody-radionuclide conjugate, in follicular lymphoma. Funds are already in place for this; the new money will be used to push two further projects into the clinic and beef up manufacturing. "The company is growing – we have a strong base with Betalutin and now we are ready to go beyond," its chief executive, Luigi Costa, tells *EP Vantage*.

The first of the new projects will be a phase II combination study of rituximab and Betalutin in second-line follicular lymphoma – the agents target CD20 and CD37 respectively, antigens that are widely presented across the family of B-cell lymphomas. Nanovector published data from preclinical non-Hodgkin lymphoma models at Ash this year that pointed to synergistic effects, and says Betalutin increases the binding and uptake of rituximab in NHL tumour cells.

"If we can reactivate the CD20 antigen patients become sensitive to rituximab again, once they have already been treated multiple times but are no longer responding," Mr Costa says. "This is a very interesting opportunity from a commercial standpoint – rituximab is everywhere, it is a $7bn drug and is now off patent."

Data are unlikely to emerge until later in 2018, Mr Costa says, while news on the second new project could take even longer to arrive. This is essentially Betalutin but conjoined to a chimeric rather than a murine antibody that will hopefully allow for repeat dosing and allow Nanovector to move towards a first-line treatment. This should enter the clinic towards the end of 2017.

Bigger boost

Next year, the data will be all about Betalutin, the optimal dosage of which is still being explored. This is in Lymrit 37-01, a phase I/II study of four arms testing various pre-dose and active drug dosages.

Betalutin comprises the CD37-targeting antibody lilotomab fused to the radionuclide lutetium-177; the isotope has a half-life of 6.7 days, matching the circulation time of the antibody. Nanovector has shown that B-cell lymphomas internalise the structure, resulting in prolonged irradiation of the nucleus.

The company has also discovered that a pre-dose of cold lilotomab protects patients from dose-limiting toxicities. By blocking CD37 receptors on healthy tissues, when Betalutin is injected four hours later the active drug targets the tumour expressing CD37 antigens much more specifically.

The final stage of Lymrit 37-01 is testing whether a big pre-dose of lilotomab (100mg/m2) will allow a much higher dose of Betalutin (20MBq/kg) to be used, one that was previously ruled out owing to the side effects.

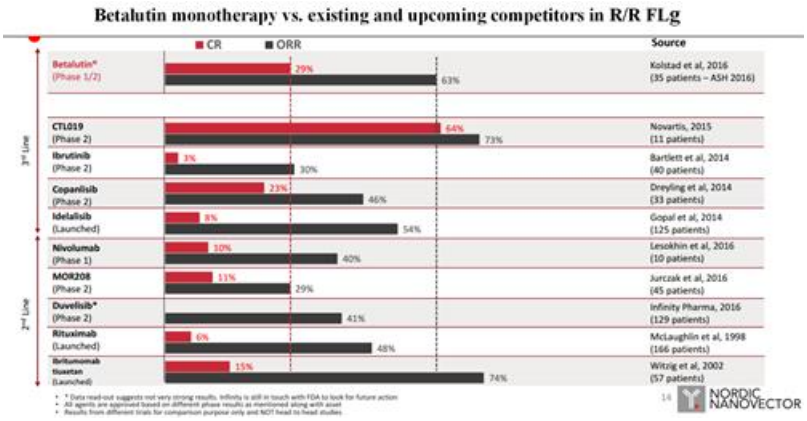
"In phase I we saw 100% responses with 20MBq so we always hoped we could go back up to 20 as it had been so effective," Mr Costa says. "Now we know that by increasing the pre-dosing with the cold antibody we can protect the patient. So all the data together make us think by increasing the dosage of Betalutin even better efficacy will emerge."

He concedes that this is not yet proven, and says data should emerge early next year from patients being tested with this new, stronger regimen.

The numbers to beat were presented at Ash this month, in the latest cut of the entire Lymrit 37-01 dataset: an overall response rate of 63% in 35 patients, with 29% in complete remission. Results were even better in the 16 patients from the phase II cohort who received 15MBq/kg of Betalutin and 40mg/m2 lilotomab pre-dose – here ORR reached 69% with CR of 38%.

Nanovector contends that these results compare very competitively with other drugs tested in this setting, as

the analysis conducted by the company below shows. Mr Costa also points out that Betalutin has the added advantage of simplicity – one single injection – and the ability to control dose-limiting toxicity.



Assuming that an even higher dose generates stronger efficacy without additional toxicity, this regimen will likely be used in a pivotal trial called Paradigme. Nanovector hopes to start this in the second half of next year and a preliminary read out could happen in the second half of 2018.

Should the development of Betalutin go to plan it will cap a strong run for Nordic Nanovector, which has benefited from a big retail following in Norway. Its links to a former local hero, Algeta, no doubt help: as well as working with radionuclides, the companies share an inventor and many of the same investors.

Given that Algeta was eventually bought by Bayer for $2.9bn the association cannot hurt. However, Mr Costa says he tries to avoid the comparison: “There are some genes of Algeta here but we are talking about very different products, different indications, a different type of radionuclide. We have the potential to be equally successful, if not more.”

However, as Mr Costa admits, in the end it will all come down to the data.

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