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Asco-GI preview – Lutathera delivers again

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When initial pivotal results of Advanced Accelerator Applications' Lutathera were chosen for presentation at the presidential symposium of last year's European Cancer Congress they generated enough interest to allow the French group to complete an $86m Nasdaq float.

Now the study has delivered again, with updated results from it highlighted by Asco as one of three abstracts to watch at its gastrointestinal cancers symposium starting on Thursday. The company reckons the data are sufficiently good to allow immediate filings in the US and EU, where it plans to commercialise Lutathera itself.

Advanced Accelerator Applications (AAA) was spun out of CERN, the European Organisation for Nuclear Research, 14 years ago, and its most advanced focus is on cancer diagnostics. Lutathera represents its first shot at a therapeutic, combining a hormone – in this case a somatostatin analogue – with a radioactive payload.

Smart concept

The pivotal Netter-1 study shows just how smart a concept this is. Its key is an amenable target – mid-gut neuroendocrine tumours – and a simple design, pitting Lutathera head to head against octreotide LAR with a single primary endpoint of progression-free survival.

At the time of analysis median PFS had not been reached, but risk of progression was cut by 79% in the Lutathera group versus octreotide ($p<0.0001$). Netter-1's authors, headed by Dr Jonathan Strosberg of the Moffitt Cancer Center, Florida, said this was the first prospective, randomised trial to show the efficacy of Lutathera.

It was also too early to determine an overall survival advantage, though at the interim analysis 13 Lutathera patients had died, versus 22 on octreotide ($p=0.0186$); there is also a key convenience advantage, with octreotide being taken daily long term versus Lutathera's four-treatment course. Netter-1 enrolled 230 patients who had progressed on a somatostatin analogue.

Neuroendocrine tumours are rare neoplasms that arise from the hormonal system, and some possess especially strong receptors for somatostatin. This explains the logic of treating patients with somatostatin analogues such as octreotide or lanreotide, and Lutathera works on the same targeting principle, with the addition of a radiotherapeutic.

An important addition to the data initially presented at September's European Cancer Congress in Vienna concerned safety: grade 3 and 4 adverse events were similar between the two treatment arms in Netter-1 except for vomiting and lyphopenia, which favoured octreotide. All-grade adverse events were generally worse with Lutathera.

Nevertheless, on a press call yesterday Dr Strosberg said the Netter-1 data showed Lutathera to provide a major therapeutic benefit for patients progressing on somatostatin analogues, who have few treatment options.

What now?

AAA told *EP Vantage* that it had been informed by the EMA and FDA that one sufficiently positive trial could be enough for filing, and therefore preparations were now under way for a submission in the first half. "In a best-case scenario we could even get approval in the US at end of the year," said a spokesperson.

As such the group is preparing for commercialisation, which given the relative rarity of the indication it is planning to do itself in the US and big five EU countries. In Japan Lutathera was licensed to Fujifilm last year, and regional deals for smaller markets will be sought.

In any case AAA already has commercial operations, given that it sells a range of nuclear medicine diagnostics such as Gluscan. These resulted in $48.1m of revenue in the first half of 2015, though operating costs mean that AAA is still loss-making.

But the diagnostic portfolio looks like something of a cash-cow, and the key reason for AAA's Nasdaq IPO was commercialisation of Lutathera. The float was well received, with AAA's stock nearly doubling by the end of 2015, though these gains have been wiped out in the ensuing market turmoil.

One still unresolved issue is whether big pharma is interested in licensing or buying radiopharmaceutical assets. The only notable purchase so far was Bayer's acquisition of Algeta, and even that took place once all the development risk of the target's Xofigo had been eliminated. Clearly the jury is still out.

Study	Design	Trial ID	Asco-GI abstract
Netter-1	Lutathera vs Sandostatin in 229 pts with NETs	NCT01578239	194

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