Merck halt cancer vaccine trials in another knock for sentiment

Amy Brown

Dendreon’s Provenge aside, cancer vaccines could do with some clinical success stories to boost confidence in the field. Unfortunately, this was not what was delivered today, with news that Merck KGaA and the FDA have decided to halt all ongoing trials of Stimuvax, including phase III studies in lung and breast cancer, after a sudden and severe adverse event was reported.

Merck is one of the few large drug developers to champion cancer vaccines, having bought rights to Stimuvax and a now defunct breast cancer project back in 2001. Nine years later, and with a product still years from the market, it is perhaps understandable why most other big pharma groups have stayed away. In reality it seems unlikely that this adverse event, a case of encephalitis, was caused by the vaccine but it will not help disprove a widely held conviction, compounded by Transgene’s recent failure to deliver a full blown license deal for its phase III ready vaccine, that this field remains only for the brave.

Intensified schedule

Merck said that the patient who developed encephalitis was taking part in a phase II study in multiple myeloma. The patient had also received an intensified schedule of the chemotherapy cyclophosphamide, a schedule which is not being used in the ongoing pivotal programme.

This is the first ever case of encephalitis reported in patients given Stimuvax, an agent that has been in human testing for more than a decade. Some patients have been on the drug for eight years, with no serious adverse events.

Meanwhile a spokesperson for Merck told EP Vantage that in February a data safety monitoring board completed a review of the ongoing Start trial in lung cancer, agreeing that the study should continue.

Some analysts suggested other less serious side effects might have been noted, prompting the FDA to halt studies on a single serious adverse event. However, given that data from the studies will be locked this seems unlikely, and the decision perhaps merely reflects the company and regulator deciding to pursue a very conservative path.

Gathering steam

Still, the news is disappointing, coming just as the Stimuvax project appeared to be gathering some pace with three pivotal trials ongoing.

Inspire started last December, seeking to enrol 420 Asian patients with unresectable stage III non-small cell lung cancer (NSCLC) demonstrating stable disease. Start, which commenced in early 2007, is seeking to enrol 1,300 patients with unresectable stage IIIA or IIIB NSCLC who have had a response or stable disease after at least two cycles of platinum-based chemo-radiotherapy. Lastly, Stride, which started in June last year, is being conducted in breast cancer, examining whether progression free survival can be extended in 900 patients treated with hormonal therapy who have inoperable, locally advanced, recurrent or metastatic disease.

For Merck, the news follows setbacks with flagship cancer therapy Erbitux, which was rebuffed in Europe in lung cancer, and uncertainty around the approvability of its oral MS pill Movectro (cladribine). Shares in the company were trading 1% lower in afternoon trade, at €59.59.

More devastating

For partner Oncothyreon the situation is more devastating, and shares in the Canadian company plunged 25% in early trade today, hitting $3.60, a five-month low.

Merck has the size to absorb such R&D adventures, but the cancer vaccine collaboration between the two companies over the last nine years has been a major focus for Oncothyreon’s investors.
Admittedly, Oncothyreon’s stake in the venture has been diminishing, no doubt as time lines became longer and investors increasingly refused to stump up the cash. In fact, a quick look at the tortuous route that both companies have had to tread helps illustrates why Novartis decided to keep its deal with Transgene very much at arm’s length for now (Transgene deal disappoints but were expectations too high?, March 10, 2010)

Merck first signed a cancer vaccine collaboration with Biomira, which became Oncothyreon a couple of years ago, back in 2001, buying rights to two candidates. Theratope for breast cancer was already in phase III, whilst Stimuvax, then called BLP25, was in phase IIb. The deal does not appear to have been particularly expensive; total upfront, milestones and equity investments available totalled $150m but a large proportion of this was due on BLA filings, which have not happened.

At first Biomira was sharing development costs in return for joint marketing rights and was in control of manufacturing the vaccines, but sold out of both of those clauses in the wake of the failure of the Theratope study in 2005.

**History lesson**

Clearly a small company like Biomira/Oncothyreon, and its investors, have learnt the hard way about the longevity and cost of developing these cancer vaccine products. The Stimuvax studies could restart and the project still looks like one of the most promising projects currently ongoing in this field, but it has been a very long process.

Transgene is going after the same thing that Biomira did in 2001, retaining more of the risk for more of the reward over its project, TG 4010. It targets the same tumour antigen, MUC1, as Stimuvax.

A lesson in history helps to explain why investors were so underwhelmed when the French company announced its deal last week; its shares have fallen 23% since the deal was announced, trading at €17.14 today. The hope must be in this case history will not repeat itself.