

## Prostvac's glimmers of hope evaporate



Jacob Plieth

Bristol-Myers Squibb buying into Bavarian Nordic's Prostvac in 2015 clearly gave the market false hope about this prostate cancer vaccine. It would otherwise be hard to explain Bavarian's 50% share price collapse this morning on the news – inevitable, many will say – that Prostvac had flunked its pivotal trial.

As such this should serve as a reminder to investors of the glaring warning signs, including the trial's delay owing to patients living longer and Bavarian's subtle recent de-emphasisation of Prostvac. Bristol's bet was extremely cautious, and the failure is yet another indication of the difficulty of running prostate cancer trials.

The problem for many prostate cancer treatment developers lies in the advent of highly efficacious new drugs like Xtandi and Zytiga. When progressing placebo recipients switch to these drugs this risks wiping out the benefit of active treatment, something that has already claimed the scalps of tasquinimod, orteronel and custirsen, among others.

It is not yet clear what went wrong in Prostvac's phase III trial, Prospect, but this is one possibility. A more serious concern might be whether all subjects might have been denied more efficacious treatments by enrolling into the study.

### Placebo outperformance

On an analyst call today Bavarian's chief executive, Paul Chaplin, said: "Placebo has certainly outperformed what we were anticipating." He would not speculate further since the group is only now unblinding the data.

Mr Chaplin highlighted Bavarian's recent shift from mono-immunotherapy to combinations, for instance with Yervoy and/or Opdivo, and said a planned capital markets day on September 21 would go ahead.

Whatever the reasons, it is clear that Prospect abysmally failed to replicate the relative median overall survival advantage, 25.1 months versus 16.6 for placebo, seen in a phase II study that prompted the pivotal programme's commencement.

Since then two interim analyses had recommended Prospect's continuation, but these might have set very low bars for ploughing on. Yesterday Bavarian said a third analysis [recommended immediate discontinuation for futility](#), with Jefferies analysts saying they assumed the survival curves between active and placebo arms to be "almost overlapping".

For some the writing was on the wall when in January Bavarian revealed that [readout from Prospect would be delayed](#) from early 2017 to the second half, and curiously opined that this "could ... be indicative of a therapeutic effect of Prostvac".

This ignored the more likely possibility – based on historical precedent of delays to event-driven oncology trials – that all patients, including those on placebo, were living longer. Cancer vaccines, after all, have a lamentable track record ([Therapy focus – against the odds, cancer vaccines plough on](#), February 27, 2017).

### What else is left?

Despite this Jefferies had assigned a 40% chance of Prospect succeeding, and even called this stance "cautious". The analysts now say Prostvac's failure likely also means curtains for Bavarian's phase II bladder cancer vaccine CV-301; this comprises a similar backbone and co-stimulatory molecules to Prostvac.

In hindsight Bavarian's increase in announcements about its RSV programme now looks like a subtle move to take attention away from Prostvac. Jefferies says the RSV project and smallpox and other vaccines should now provide a floor to Bavarian's valuation.

Investors following other cancer vaccine players would do well to take note of Bavarian's failure. Northwest Biotherapeutics remains schtum about its study of DCVax-L in glioblastoma – even though it said final data from this study were being analysed almost a year ago no results have yet been disclosed.

And what about Bavarian's Bristol deal? Ultimately this was only an option – obviously not exercised before the

Prospect readout – and cost Bristol just \$60m. [Back in 2015](#) that was a small price to pay for a piece of the action, just in case.

Study	Trial ID
Prospect	NCT01322490

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