

Therapy focus - against the odds, cancer vaccines plough on



[Jacob Plieth](#)

In spite of a near-100% track record of failure, and in the face of overwhelming scientific rationale to the contrary, late-stage development of therapeutic cancer vaccines continues. For some biotechs these troubled assets even represent a fundamental investment case.

Yet two more flops, in the form of Argos Therapeutics' long-running Adapt study of rocapuldenceI-T and an NIH-sponsored trial of Agenus's Prophage G-200, have just joined the growing list of cancer vaccine failures. This comes on the heels of a terrible year for this type of approach, which could next be tested by Bavarian Nordic, a group that remains dependent on vanishing odds of success from its pivotal Prostvac study (see table below).

Bavarian recently said [patients in the Prospect trial of Prostvac in prostate cancer](#) were living longer than expected, which would delay results from the study from early 2017 to the second half of this year. The group optimistically opined that this "could ... be indicative of a therapeutic effect of Prostvac".

This rose-tinted view ignored the other possibility - far more likely, based on historical precedent of delays to event-driven oncology trials - that all patients, including those on placebo, were living longer.

Scepticism

A recent increase in announcements about Bavarian's RSV programme could hint at subtle moves to take attention away from Prostvac. It might be that earlier futility analyses set particularly high failure criteria, and having seen the blended, blinded survival curves from Prospect Bavarian can see that probability of success is tiny.

If chances of Prostvac giving a positive readout are slim, this is nothing compared with the possible next phase III cancer vaccine trial to yield data - Northwest Biotherapeutics' study of DCVax-L in glioblastoma.

This trial has taken an inordinate amount of time, having started over 10 years ago, and was put on US clinical hold for undisclosed reasons in late 2015. Northwest recently [said the hold had been lifted](#), and that it would analyse the dataset as it stands - with only 331 of a planned 348 patients recruited.

The group claims to have reached the intended number of disease progressions, the primary endpoint, but wants to wait for 233 deaths to be able to read out the important secondary overall survival endpoint. Thus investors have months more to wait, with the stock now languishing on the OTC bulletin board.

Selected late-stage cancer vaccine trials

Company	Project	Study	Indication	Trial ID	Data
Bavarian Nordic/BMS	Prostvac	Prospect	Prostate cancer	NCT01322490	H2 2017
Northwest Biotherapeutics	DCVax-L	-	Glioblastoma multiforme	NCT00045968	H2 2017*
Sotio	Stapuldencel-T	Viable	Prostate cancer	NCT02111577	Dec 2017
Advantagene	ProstAtak	Ulysses	Active surveillance for prostate cancer	NCT02768363	Dec 2017
Gradalis	Gemogenovatucl-T	Vital	1st-line ovarian cancer maintenance	NCT02346747	Dec 2017
Gradalis	Vigil	-	Triple-negative breast cancer	NCT02725489	May 2018
OSE Pharma	Tedopi	Atalante-1	2nd & 3rd-line NSCLC	NCT02654587	"Late 2018"
Tessa Therapeutics	TT10: EB-VST	-	Nasopharyngeal carcinoma	NCT02578641	Dec 2018
Immunocellular Therapeutics	ICT-107	-	Glioblastoma multiforme	NCT02546102	Dec 2019
Advantagene	ProstAtak	-	Adjuvant to RT in localised prostate cancer	NCT01436968	Dec 2019
Vaccinogen	OncoVAX	-	Adjuvant colorectal cancer	NCT02448173	Jul 2020
Bioven	EGF-PTI	-	Biomarker-positive, EGFR wild type NSCLC	NCT02187367	Feb 2020

*Note: *At Feb 2017 company is waiting "several months" for desired number of events under new analysis plan.*

Like Sanpower's Provenge, DCVax-L is an autologous product, whereas Prostvac is a subcutaneously injected virus vector expressing PSA, intended to lyse tumour cells and release antigens for presentation to the immune system. DCVax-L comprises autologous dendritic cells exposed to lysate taken from the tumour.

The scientific principle is similar in that both approaches aim to raise an immune response from existing T cells – a fundamental flaw of cancer vaccines. The immune system is unable ordinarily to target the desired antigens largely because it does not recognise them as foreign, so just presenting it with those same antigens might not be enough.

Cancer vaccines given as monotherapy at best stimulate existing, low-affinity T cells, a theory that likely explains their poor success rate. [Argos added to the list last week](#), prompting a 75% share price crash, while Agenus lost 16% [on the failure](#) of what is no longer even an important pipeline asset.

Yet at the same time Patrick Soon-Shiong, founder of the Nantworks network of companies, [spoke of launching a new cancer vaccine venture](#). And two cancer vaccines, Advantagene's ProstAtak and Bioven's EGF-PTI, have recently started new late-stage studies.

True, sooner or later the industry will see a cancer vaccine success, though this will likely need to involve an additional element, such as combination with a checkpoint-blocking MAb or with depletion of T regulatory cells. In the meantime there are likely to be plenty more disappointments.

To contact the writers of this story email Jacob Plieth or Robin Davison in London at news@epvantage.com or follow [@JacobPlieth](#) or [@RobinDavison2](#) on Twitter

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Evaluate HQ
[44-\(0\)20-7377-0800](tel:44-020-7377-0800)

Evaluate Americas
[+1-617-573-9450](tel:+1-617-573-9450)

Evaluate APAC
[+81-\(0\)80-1164-4754](tel:+81-080-1164-4754)

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