



Vaccines – the future for cancer treatment?

An innovative approach to tackling cancer is undergoing trials in the UK. But there are significant hurdles to overcome, not least cost, before it becomes readily available

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Think ‘vaccine’ and you probably envisage a small child receiving an immunisation jab against one of the deadly infectious diseases such as smallpox, diphtheria or polio. But that familiar image is only part of the

story. Over the coming years vaccines will be taking on a new role – in the treatment of cancer.

Already vaccines are making news in cancer care. Two that protect against cervical cancer have been on the market for five years. In 2010,

Provenge, for treating metastatic prostate cancer, became America’s first licensed cancer treatment vaccine when it was approved by the health protection agency, the Food and Drug Administration. Trials of the drug are due to start

in the UK in the new year. Meanwhile, clinical trials of vaccines for the treatment of at least 14 other cancer types are under way across the world. In the UK, a four-year long, late-stage trial of TeloVac for advanced pancreatic

cancer recently ended, with the results of the tests now being analysed; while an early trial of the WIN vaccine for two types of leukaemia has just begun in London and Southampton.

Cancer immunotherapy – the stimulation of the body’s own immune system to fight malignancy – is hot news. Potentially, vaccines offer two big advantages over existing treatments: they should have fewer unpleasant side effects than chemotherapy and radiotherapy, and they may not only destroy existing disease, but also prevent recurrence.

As Norman Maitland, Yorkshire Cancer Research Professor of Molecular Biology at York University puts it, ‘Over the past 50 years we have got better at poisoning people a little less while reducing side effects, but the basic mechanisms of treatment have remained the same. Immunotherapy works completely differently.’

This is no overnight success story. ‘For the past 20 years those of us who believe in cancer immunotherapy have been subjected to total frustration and ridicule,’ says Angus Dalglish, Professor of Oncology at St George’s, University of London. ‘While vaccines have worked well for individual patients treated by individual doctors, randomised trials have not brought the same benefits. Now immunotherapy is back with a vengeance.’

As ever, finance will be a major factor in the



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drugs’ development; Provenge, for example, costs around £60,000 per treatment cycle. ‘This drug has broken the glass ceiling and paved the way,’ Prof Dalglish continues. ‘It is so expensive to make that NICE (National Institute for Health and Clinical Excellence) will never approve it, but now that somebody has come up with a Rolls-Royce vaccine, a mass-produced Fiesta version will follow.’

The breakthrough to the mass market is not around the corner. It can cost £15m to put a vaccine through the necessary trials, and a few commercial investors have already got cold feet and pulled out. Experts estimate that it will be five to 10 years before cancer vaccines are in routine use. But nobody doubts that they are here to stay.

‘Everything is hanging together so well,’ says Christian Ottensmeier, Professor of Experimental

Cancer Medicine at the University of Southampton, who has had encouraging results from two small vaccine trials in prostate and bowel cancer and is leading another, partly funded by the charity Leukaemia & Lymphoma Research. ‘In our leukaemia trial we want to find out whether it is possible to induce immune responses that will eliminate the leftover leukaemia cells and push patients from measurable, controlled levels of cancer to undetectable levels where we can stop other medication and start believing they are cured.’

Patients will receive six, monthly doses of vaccine with further booster vaccinations if these are successful. The immune system has difficulty in recognising cancer cells as abnormal and harmful because – unlike a suddenly invading virus or bacterium – they emanate from cells in our own bodies that have become distorted. Cunningly, these distorted cells can actually suppress the immune system, making it even harder for it to fight back.

‘Our immune system is really good at picking up things that happen quickly,’ says Prof Ottensmeier. ‘But cancer cells have emerged from our own selves, are only subtly different and have developed slowly over a long period of time, sometimes decades.’

There are many different kinds of vaccine in development, but all aim to stimulate the patient’s immune system to recognise cancer as

a danger and to combat it. First, researchers must identify a substance – an antigen – that is over-expressed in cancer cells and which can be used as a basis for the vaccine. While some antigens are unique to particular cancers, others are common to several different types: a vaccine that is made from the second kind of antigen would obviously have a wider application.

The antigen is then combined with an adjuvant, an added ingredient such as a bacterium, which alerts the body to the presence of a foreign substance and so prompts an immune response to the vaccine antigen.

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If chemotherapy is a nuclear missile, vaccines are more of a Trojan horse – and ideally, the effect should be permanent

◁ Trojan horse. To be successful, they must stimulate specific immune responses against the right target and these must be powerful enough to overcome the barriers that cancer cells use to protect themselves from attack by the immune system's B cells and killer T cells. Ideally, their effect should be permanent.

So far, trials have shown mixed results. Provenge is a personalised treatment that involves giving patients three fortnightly infusions of their own modified immune cells. It's been found to extend survival times by four months and improve three-year survival by 38%.

In a small trial using a different vaccine on seriously ill patients with various cancers, carried out by Prof Ottensmeier's team in conjunction with Cancer Research UK, half

showed an immune response. 'Amazingly, patients where we saw effects of vaccination lived much longer than the other group,' he says. 'We need to work out why some patients' killer T cells don't respond to the vaccine. Learning from patients who don't benefit is a vital part of research.'

Prof Dalglish has some theories of his own. In his experience, patients whose immune systems are already burdened with inflammation – for example, because they are overweight, have a poor diet, drink too much alcohol or smoke – are less likely to benefit from vaccines. This may partly explain why specialist clinics that select their candidates for vaccination carefully get better results than randomised trials.

Poor-quality trials may also be to blame. When Prof Dalglish looked



For more information

Cancer Vaccine Institute

cancervaccine.org.uk

Leukaemia & Lymphoma Research

beatbloodcancers.org

Yorkshire Cancer Research

yorkshirecancerresearch.org.uk

For general information on cancer

cancerresearch.org

closely at an unsuccessful 10-centre trial for a lung cancer vaccine, he found that it had not been properly conducted.

'Some patients were not given enough vaccinations, and other patients were not given them correctly. The trial failed the vaccine rather than the other way round.'

However, something was learnt: those who were on the vaccine had fewer side effects from chemotherapy and enjoyed a better quality of life. Other trials have shown that patients tend to respond better

to radiotherapy and chemotherapy when they are also given vaccine and that some targeted drugs can enhance the vaccines.

'Until now, cancer vaccines have been used after everything else has failed,' says Prof Maitland. 'But you get much better results when you give them to people who are immune competent.'

Patients who have been through several rounds of chemotherapy are likely to have damaged immune systems. Vaccines should probably be used much earlier on in treatment.'

So far, cancer vaccines have not produced serious side effects, though that may change as they are refined to become more powerful. There is also the risk of triggering an autoimmune response where the body attacks not only cancer cells but its own tissues.

Overall, scientists are more optimistic than they have been for years. 'Many vaccines have failed probably because they were used in the wrong context or at the wrong time in the cancer journey of patients,' says Prof Ottensmeier. 'We are now learning how to pick patients better. I believe vaccines are going to make a real difference. To be seeing tangible benefits is incredibly exciting.' ♦

CASE STUDY

Edwin Poole was diagnosed with melanoma 12 years ago at the age of 73 and was referred to Prof Dalglish after two unsuccessful operations at hospitals near his home in Wiltshire.

'I had a mole on the side of my head that suddenly started looking a bit odd so I went straight to the doctor,' says Edwin, who used to work in the building industry. 'It was diagnosed as cancerous and as a result they removed it.'

'For a few months it seemed to be OK, but then it swelled up again. This time I had a more serious operation. That didn't work either and a huge lump the size of half an egg came up in the same place.'

Over the next year, Edwin saw three oncologists. He was told that although the melanoma had not spread, nothing more could be done and the cancer would kill him sooner rather than later. As a last resort, one specialist suggested that he go to see Prof Dalglish at St George's.

'The treatment involved injections and radiotherapy. At first, I came up to London once a fortnight, then once a month and then every three months. For quite a time nothing happened and then I woke up one morning and the lump seemed smaller. After that it shrunk very rapidly and in a couple of weeks it had gone.'

'Prof Dalglish told me I could come back in 12 months, which frightened the life out of me. For three years I had an injection once a year and now I just go for annual checkups.'

'I used to feel a bit woozy for a couple of hours after the injection but there were no serious problems. I've been delighted at how things have gone. I know I wouldn't be here today if I had not had this treatment. I've had 11 years more than I expected.'