World first as viral immunotherapy for skin cancer shows patient benefit in phase III trial

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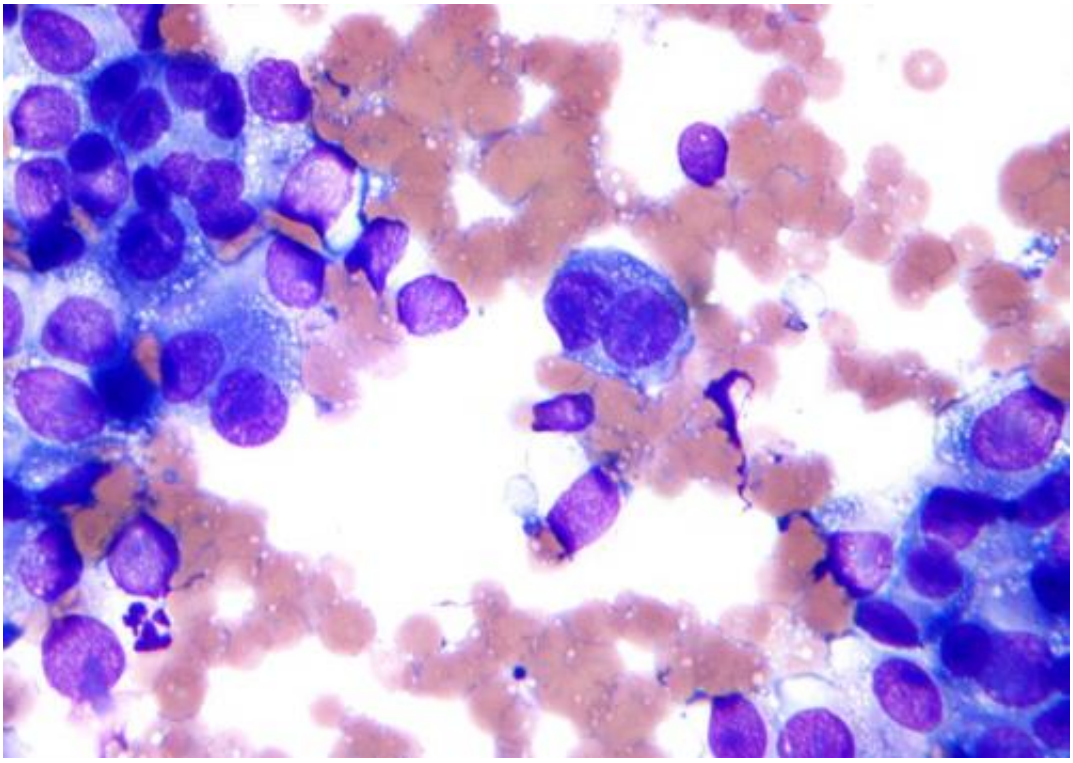

Micrograph of malignant melanoma. Cytology specimen. Field stain. Credit: Nephron/Wikipedia

A genetically engineered herpes virus can halt the progression of skin cancer by killing cancer cells and sparking the immune system into action against tumours, a landmark clinical trial has shown.

It is the first time that a phase III trial of viral immunotherapy has

definitively shown benefit for patients with cancer.

The trial was led in the UK by researchers at The Institute of Cancer Research, London, and The Royal Marsden NHS Foundation Trust, and involved 64 research centres worldwide including the University of Oxford.

Researchers randomised 436 patients with aggressive, inoperable malignant melanoma to receive either an injection of the viral therapy, called Talimogene Laherparepvec, or a control immunotherapy.

Some 16.3 per cent of the group given Talimogene Laherparepvec—known as T-VEC—showed a durable treatment response of more than six months, compared with 2.1 per cent given the control treatment.

Some patients had a response extending past three years, a mark oncologists often use as a proxy for cure in immunotherapy.

Importantly, responses to treatment were most pronounced in patients with less advanced cancers (stage IIIB, IIIC, IVM1a) and those who had yet to receive any treatment—underlining the potential benefits of T-VEC as a first-line treatment for metastatic melanoma which cannot be surgically removed.

Patients with stage III and early stage IV melanoma treated with T-VEC—a total of 163 people—lived an average of 41 months. This compared with an average survival of 21.5 months in the 66 earlier-stage patients who received the control immunotherapy.

The trial was funded by the manufacturer of T-VEC, Amgen, and is published in the *Journal of Clinical Oncology*.

T-VEC is a modified form of herpes simplex virus type-1 which multiplies inside cancer cells and bursts them from within. It has been genetically engineered to produce a molecule called GM-CSF, which stimulates the immune system to attack and destroy the tumour.

T-VEC is one of a new wave of virus-based drugs to show benefits in cancer trials, and is now the first to do so in a major randomised, controlled phase III trial.

The virus has been modified to remove two key genes, called ICP34.5 and ICP47, so that it can't replicate within healthy cells. Normal cells detect and destroy T-VEC before it can cause damage—but it replicates easily in cancer cells because their infection defences are compromised by genetic errors.

UK trial leader Professor Kevin Harrington, Professor of Biological Cancer Therapies at The Institute of Cancer Research, London, and Honorary Consultant at The Royal Marsden NHS Foundation Trust, said:

"There is increasing excitement over the use of viral treatments like T-VEC for cancer, because they can launch a two-pronged attack on tumours - both killing cancer cells directly and marshalling the immune system against them. And because viral treatment can target cancer cells specifically, it tends to have fewer side-effects than traditional chemotherapy or some of the other new immunotherapies.

"Our study showed that T-VEC can deliver a significant, durable benefit for people with melanoma. It is encouraging that the treatment had such a clear benefit for patients with less advanced cancers - ongoing studies are evaluating if it can become a first-line treatment for more aggressive melanomas and advanced disease."

Professor Paul Workman, Chief Executive of The Institute of Cancer

Research, London, said:

"We may normally think of viruses as the enemies of mankind, but it's their very ability to specifically infect and kill human cells that can make them such promising cancer treatments. In this case we are harnessing the ability of an engineered virus to kill cancer cells and stimulate an immune response. It's exciting to see the potential of viral treatment realised in a phase III trial, and there is hope that therapies like this could be even more effective when combined with targeted cancer drugs to achieve long term control and cure."

More information: *Journal of Clinical Oncology*, jco.ascopubs.org/content/early … 8.3377.full.pdf+html

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