An engineered herpesvirus that provokes an immune response against cancer has become the first treatment of its kind to be approved for use in the United States, paving the way for a long-awaited class of therapies. On 27 October, the US Food and Drug Administration (FDA) approved a genetically engineered virus called talimogene laherparepvec (T-VEC) to treat advanced melanoma. Four days earlier, advisers to the European Medicines Agency had endorsed the drug.

With dozens of ongoing clinical trials of similar 'oncolytic' viruses, researchers hope that the approval will generate the enthusiasm and cash needed to spur further development of the approach. “The era of the oncolytic virus is probably here,” says Stephen Russell, a cancer researcher and haematologist at the Mayo Clinic in Rochester, Minnesota. “I expect to see a great deal happening over the next few years.”

Many viruses preferentially infect cancer cells. Malignancy can suppress normal antiviral responses, and sometimes the mutations that drive tumour growth also make cells more susceptible to infection. Viral infection can thus ravage a
tumour while leaving abutting healthy cells untouched, says Brad Thompson, president of the pharmaceutical-development firm Oncolytics Biotech in Calgary, Canada.

**Early attempts**
The strategy builds on a phenomenon that has been appreciated for more than a century. Physicians in the 1800s noted that their cancer patients sometimes unexpectedly went into remission after experiencing a viral infection. These case reports later inspired doctors, particularly in the 1950s and 1960s, to raid nature’s viral cupboard. Clinicians injected cancer patients with a menagerie of viruses. Sometimes the therapy destroyed the tumour, and sometimes it killed the person instead.

Unlike the wild viruses used in those mid-twentieth-century experiments, some of today’s anti-cancer viruses are painstakingly engineered. T-VEC, for example, has been altered to drastically reduce its ability to cause herpes. Researchers also inserted a gene encoding a protein that stimulates the immune system, which makes the virus even more potent against cancer (see ‘Going viral against cancer’).

**GOING VIRAL AGAINST CANCER**
The virus-based cancer therapy T-VEC infects tumour cells and destroys them by stimulating the immune system to direct an attack against malignant cells in the body.

![Diagram of T-VEC therapy](image)

As more researchers entered the field and initiated small clinical tests, they began to produce enticing anecdotes. Russell recalls the case of an individual with myeloma who remained sick after undergoing two stem-cell transplants.
A tumour on the left side of her forehead had degraded the bone underneath and was putting pressure on her brain. Yet treatment with an experimental virus sent her into complete remission (S. Russell et al. Mayo Clin. Proc. 89, 926–933; 2014). “She’s a star patient who convinced us that this oncolytic paradigm can really work,” he says.

But statistics — not anecdotes — rule over drug approvals. In 2005, regulators in China approved an oncolytic adenovirus called H101 to treat head-and-neck cancer, after evidence showed that the treatment could shrink tumours. Those trials stopped short of assessing improvements in patient survival — a measure often required for FDA approval. Since then, a medical-tourism industry has built up in China for people who cannot get the therapy in their home countries.

Then, in May this year, a team supported by biotechnology giant Amgen of Thousand Oaks, California, published promising results from a large clinical trial of T-VEC (R. H. Andtbacka et al. J. Clin. Oncol. 33, 2780–2788; 2015). The virus both shrank tumours in people with advanced melanoma and extended patient survival by a median of 4.4 months. Yet statistically, survival benefits fell just a hair’s breadth of significance. “That raised the question, ‘Well, what is statistical significance? Is this an active agent or not?’” Russell says.

He and others note that the therapy — which must be injected directly into tumours — seemed to rein in cancer elsewhere in the body as well. This is a sign that results are real and that the virus sparked an immune response as intended, Thompson says.

Room for improvement
Administering T-VEC in combination with cancer immunotherapy could prove particularly effective, notes Stephen Hodi, an oncologist at the Dana-Farber Cancer Institute in Boston, Massachusetts. In June 2014, a small clinical trial by Amgen suggested that this combination may boost effectiveness over that of the immunotherapies alone.

And researchers continue to look for ways to improve T-VEC. In particular, they would like to be able to deliver the therapy systemically, so that the virus could target tumours in organs that are difficult to reach with an injection. This would require a technique to prevent the body from mounting an immune response to the virus prematurely, which would disable it before it could reach and kill tumour cells, says Howard Kaufman, a cancer researcher at Rutgers Cancer Institute of New Jersey.

To that end, those in the field are experimenting with a smorgasbord of viruses — from poxviruses to vesicular stomatitis virus, which does not normally infect humans but causes a blistering disease in cattle. Oncolytics Biotech is studying a virus that hitch-hikes through the body on certain blood cells, camouflaged from the immune system.

If cancer-killing viruses could be delivered to their targets through the bloodstream, rather than via injection directly into the tumour, they could be used to treat a greater range of cancers. Thompson envisions a day when physicians will be able to peruse a menu of oncolytic viruses and select the best fit. “Each virus interacts with the immune system differently,” he says. “They could have a role in pretty much all cancer therapy.”
Related stories and links

From nature.com
- World’s largest cancer charity lays out field’s grand challenges  
  12 October 2015
- Cancer treatment: The killer within  
  02 April 2014
- HPV: Sex, cancer and a virus  
  20 November 2013
- Immunotherapy’s cancer remit widens  
  28 May 2013
- Nature Outlook: Cancer immunotherapy

From elsewhere
- US National Cancer Institute: Biotherapies for Cancer

For the best commenting experience, please login or register as a user and agree to our Community Guidelines. You will be re-directed back to this page where you will see comments updating in real-time and have the ability to recommend comments to other users.

2 comments

Michael Lerman  • 2015-10-29 02:51 PM
One out of 2-3 adults and one out of 7 children die of cancer. However curing cancer is not in the interest of civilized societies, it would result in a demographic catastrophe. Michael Lerman, Ph.D., M.D.

Dave Baker  • 2015-10-28 09:44 PM

See other News & Comment articles from Nature

Nature  ISSN 0028-0836   EISSN 1476-4687

partner of AGORA, HINARI, OARE, INASP, CrossRef and COUNTER