

# Liver cancer survival time tripled by virus

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The virus used in the vaccine that helped eradicate smallpox is now working its magic on liver cancer. A genetically engineered version of the *vaccinia* virus has trebled the average survival time of people with a severe form of liver cancer, with only mild, flu-like side effects.

Thirty people with hepatocellular carcinoma received three doses of the modified virus – code-named JX-594 – directly into their liver tumour over one month. Half the volunteers received a low dose of the virus, the other half a high dose. Members of the low and high-dose groups subsequently survived for, on average, 6.7 and 14.1 months respectively. By contrast, [trials several years ago](#) showed that sorafenib, the best existing medication for this cancer, prolonged life by only three months.

Two of the patients on the highest viral dose were still alive more than two years after the treatment. "It's a very substantial survival benefit," says Laurent Fischer, president of [Jennerex](#), the company in San Francisco developing the treatment under the trade name Pexa-Vec.

Besides shrinking the primary tumour, the virus was able to spread to and shrink any secondary tumours outside the liver. "Some tumours disappeared completely, and most showed partial destruction on MRI scans," says David Kim, head of the study at Jennerex. Moreover, the destruction was equally dramatic in the primary and secondary tumours.

"This clinical trial is an exciting step forward to help find a new way of treating cancers," says Alan Melcher of the University of Leeds, UK, who was not involved in the study. "It helps demonstrate the cancer-fighting potential of viruses, which have relatively few side effects compared with traditional chemo or radiotherapy," he says. "If it proves effective in larger trials, it could be available to patients within five years."

The fact that the virus appears able to spread to secondary tumours suggests that simply injecting the virus into the bloodstream may be effective. A trial to compare this treatment with injecting the virus directly into a tumour is under way.

## Targeted at cancer

The virus has had a gene coding for an enzyme called thymidine kinase snipped out. The enzyme enables the virus to recognise and infect dividing cells. By removing the gene, the virus's developers have reduced the likelihood of healthy dividing cells being infected.

Instead, the virus exclusively attacks cancerous tissue, by targeting two genes that have increased activity in tumour cells. One gene is associated with an epidermal growth factor receptor, which stimulates the cancer to grow. The other is associated with a vascular endothelial growth factor, which enables the cancer to recruit its own blood supply. The virus reduces the activity of both genes, causing the infected cancer cell to wither and die.

What's more, the virus carries extra genes to prod the body's own immune system into action against the cancer. One produces granulocyte colony stimulating factor, a protein that encourages production of extra white blood cells at sites of infection. The other produces a

protein not naturally found in humans, called Lac-Z, that earmarks infected cells for destruction.

Fischer says that to date, more [than 200 people have received the virus](#), which has also shown promise against other types of cancer, including those of the kidney and skin. But he warns that not everyone sees a benefit. "We know why patients respond, but not why they don't," he says.

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