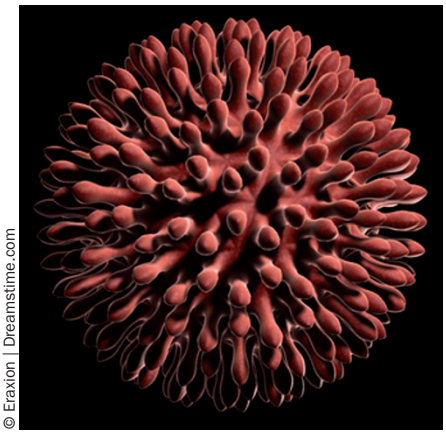
Nature Reviews Clinical Oncology **8**, 630 (2011); published online 20 September 2011; doi:10.1038/nrclinonc.2011.143

IMMUNOTHERAPY

Seek and destroy: oncolytic virus shows promise in phase I trial



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Systemic cancer viriotherapy might have come one step closer. A team of scientists from USA and Canada proved the efficacy and safety of an intravenously infused virus that selectively infected metastatic lesions in a phase I trial. "We demonstrated for the first time in medical history that a viral or genetic therapy agent could be delivered intravenously to metastatic tumors reproducibly and with expression of multiple transgenes," says David Kirn, CEO of Jennerex Biotherapeutics and one of the senior authors of the study.

The poxvirus JX–594 infects cells in which the EGFR/RAS pathway is activated and relies on this pathway to replicate, which eventually kills infected cells. Its stability in the blood, rapid spread within tissues, and the capacity to carry fairly large therapeutic transgenes rendered JX-594 a good candidate for intravenous infusion and use as therapeutic agent.

In a phase I trial in patients with various advanced-stage, treatment-refractory, metastatic solid tumors, 23 participants received six different doses of the virus (1.5×10^5 to 3×10^7 plaque-forming units kg^{-1}), which were all tolerated well. The most-common adverse effects were grade 1 or 2 flu-like symptoms lasting up to 24 h. Delivery and replication of the virus were confirmed in tissue biopsies 8–10 days after treatment. Out of eight patients who received the two highest doses, six tested positive for JX–594 by immunohistochemistry, and in five patients was the virus detected by quantitative PCR. By contrast, adjacent normal tissue was JX-594 negative. Similarly, the expression of the two transgenes encoded by the virus, a marker gene and one encoding GM–CSF to boost antitumor immunity, seemed to correlate with the administered viral dose.

The clinical response was more pronounced at higher doses, with 13 out of 23 patients achieving stable disease for ≥4 weeks. Tumor outgrowth in the time after treatment was less frequent in patients treated with high doses than in those receiving low doses. According to Kirn, this platform technology "opens up the possibility of arming JX–594 with multiple additional therapeutic transgenes that can attack cancers simultaneously via multiple mechanisms."

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Original article Breitbach, C. J. *et al.* Intravenous delivery of a multi-mechanistic cancer-targeted oncolytic poxvirus in humans. *Nature* **477**, 99–102 (2011)

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