Trial Watch

ONCOLYTICS IN THE CLINIC

A vaccinia virus-based oncolytic drug, JX-594 (also known as Pexa-Vec; Jennerex), has been used to treat patients with advanced hepatocellular carcinoma (HCC) in a randomized Phase II dose-finding trial.

The trial was stopped early owing to a significant survival benefit in patients in the high-dose group: 30 patients (16 in the high-dose group (10^9 plaque-forming units (PFUs) per dose) and 14 in the low-dose group (10^8 PFUs per dose)) had been treated. Of these patients, 29 received all three planned doses of virus injected directly into up to five intrahepatic tumours on days 1, 15 and 29. JX-594 was well tolerated and no treatment-related deaths occurred. The median overall survival was 9 months for the entire study population: the median overall survival for the high-dose group was 14.1 months compared with 6.7 months for the low-dose group. Importantly, evidence of tumour lysis was also seen in tumours that were not directly injected with JX-594, and 11 of 16 patients developed complement-dependent cytotoxicity to one of four HCC cell lines, indicating the induction of an immune response to HCC in some patients.

ORIGINAL RESEARCH PAPER Heo, J. *et al.* Randomized dose-finding clinical trial of oncolytic immunotherapeutic vaccinia JX-594 in liver cancer. *Nature Med.* 10 Feb 2013 (doi:10.1038/nm.3089)

AVOIDING RELAPSE

Patients with leukaemia who develop graft versus host disease (GVHD) after allogeneic (matched donor) haematopoietic cell transplants (HCTs) have reduced relapse rates owing to the graft versus leukaemia (GVL) effect of the immune response, but GVHD results in significant morbidity and mortality. A study in 11 patients at high risk of relapse or who had relapsed after HCT examined the efficacy of treatment with donor-derived HLA-restricted *ex vivo*-expanded $CD8^+$ cytotoxic T lymphocytes (CTLs) that target Wilms tumour antigen 1 (WT1), which is often overexpressed in leukaemia.

Direct evidence of anti-leukaemic activity after CTL infusion was seen in two patients: one with advanced progressive disease who showed a transient response, and one with minimal residual disease who remained in remission at the end of the study. Three additional patients at a high risk of relapse after HCT also entered complete remission and were alive at the end of the study. The persistence in the blood of $CD8^+$ CTLs that target WT1 was much longer in the four patients treated with $CD8^+$ CTLs grown in the presence of interleukin-21 (IL-21) compared with those treated with $CD8^+$ CTLs that were not exposed to IL-21. IL-21 suppresses terminal differentiation of T cells and might enable the generation of long-lived memory T cells. Thus, the use of donor-derived, IL-21-exposed, WT1-targeting $CD8^+$ CTLs in patients with high-risk WT1-positive disease requires further investigation.

ORIGINAL RESEARCH PAPER Chapuis, A. G. *et al.* Transferred WT1-reactive $CD8^+$ T cells can mediate antileukemic activity and persist in post-transplant patients. *Sci. Transl Med.* **5**, 174ra27 (2013)