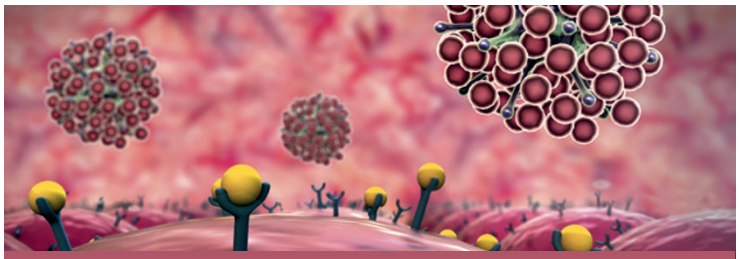
Nature Reviews Clinical Oncology **12**, 438 (2015); published online 16 June 2015; doi:10.1038/nrclinonc.2015.106



Ugreen/iStock/Thinkstoc

SKIN CANCER

T-VEC oncolytic viral therapy shows promise in melanoma

Breakthroughs in immunotherapy have led to new drug approvals, revolutionizing the management of melanoma. Now, on the basis of data from the phase III OPTiM trial, talimogene laherparepvec (T-VEC) looks set to be added to this armamentarium.

T-VEC is an oncolytic viral therapy comprising attenuated herpes simplex virus type 1 that has been modified to mediate a two-pronged attack on tumours: selective lysis of cancer cells after local injection; and promotion of global antitumour immunity. The latter effect is achieved through integration of the granulocyte-macrophage colony-stimulating factor (GM-CSF) gene into the viral genome, expression of which promotes local inflammation and antigen presentation.

In OPTiM, 436 patients with advanced-stage accessible unresectable melanoma received either intralesional T-VEC or subcutaneous GM-CSF. No approved intralesional treatments and few systemic therapies were available for melanoma at the time of trial design. "Thus, we selected GM-CSF as it is part of the viral vector and some data suggested that it might have therapeutic activity in patients with stage III–IV disease," says corresponding author Howard Kaufman.

The durable response rate—objective responses occurring within 12 months of treatment initiation and lasting ≥6 months—was improved in the T-VEC group (16.3% versus 2.1%; $P<0.001$). As Kaufman explains, "this is a particularly challenging end point, as immunotherapy can result in delayed kinetics of response and maintaining durability is not typically required nor reported in clinical studies." T-VEC also improved the overall response rate (26.4% versus 5.7%; $P<0.001$), and prolonged overall survival (median 23.3 months versus 18.9 months; $P=0.051$). "Another very significant finding was that nearly 11% of patients who received T-VEC had an objective complete response, which has not been typically seen with other melanoma treatments," Kaufman adds. Of note, although only accessible tumours were injected, responses required regression of all disease, including visceral sites.

T-VEC treatment was well tolerated (most adverse effects were low-grade), which might be important when considering drug combinations. As T-VEC promotes a systemic antitumour immune response, combinations with immune-checkpoint inhibitors might be of particular interest. "Two trials in patients with melanoma are combining T-VEC with ipilimumab or pembrolizumab, and early results of the T-VEC and ipilimumab trial are promising, demonstrating a synergistic activity," says Kaufman.

He concludes, "a joint review panel have recommended that the FDA approve T-VEC for patients with unresectable and metastatic melanoma; thus, we widely anticipate final FDA approval later this year."

David Killock

Original article Andtbacka, R. H. I. *et al.* Talimogene laherparepvec improves durable response rate in patients with advanced melanoma. *J. Clin. Oncol.* doi:10.1200/JCO.2014.58.3377