Long et al. Journal for ImmunoTherapy of Cancer 2015, 3(Suppl 2):P181
http://www.immunotherapyofcancer.org/content/3/S2/P181

Journal for ImmunoTherapy of Cancer

POSTER PRESENTATION Open Access

A Phase I/III, multicenter, open-label trial of talimogene laherparepvec (T-VEC) in combination with pembrolizumab for the treatment of unresected, stage IIIb-IV melanoma (MASTERKEY-265)

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From 30th Annual Meeting and Associated Programs of the Society for Immunotherapy of Cancer (SITC 2015) National Harbor, MD, USA. 4-8 November 2015

Background

T-VEC is a herpes simplex virus-1-based oncolytic immunotherapy designed to selectively replicate in tumors, produce GM-CSF, and stimulate antitumor immune responses. OPTiM, a Phase III trial of T-VEC vs GM-CSF in unresectable stage IIIB-IV melanoma, improved the primary endpoint of durable response rate (DRR) in the T-VEC arm (16 vs 2%).[1] Pembrolizumab, a human programmed death receptor-1 (PD-1)-blocking antibody approved for the treatment of advanced metastatic or unresectable melanoma, has demonstrated superiority over the CTLA-4-blocking antibody ipilimumab in patients with stage III or IV melanoma that received no more than one prior line of systemic therapy (PFS HR 0.58, OS HR 0.63-0.69).[2] Combining T-VEC with pembrolizumab may enhance antitumor immune responses vs either therapy alone. Here, we describe a Phase Ib/III study assessing the safety and efficacy of T-VEC + pembrolizumab in unresected stage IIIB-IV melanoma. Twenty-one patients enrolled in Phase Ib December 2014 through March 2015 at 11 institutions in Australia, Spain, Switzerland, and the United States.

Methods

Primary objective for Phase Ib: assess dose-limiting toxicities of T-VEC + pembrolizumab. Key secondary objectives for Phase Ib: best OR, DRR, duration of response, disease control rate, PFS by investigator using modified immune-related response criteria (irRC), OS, treatment-emergent/related AEs, and potential blood/tumor biomarkers for response/resistance to combination treatment. Key eligibility criteria for Phase Ib: stage IIIB-IV melanoma naïve to systemic treatment (except adjuvant), injectable lesions, ECOG PS 0-1, no active cerebral metastases, no autoimmunity/immunosuppression, and no active herpetic infection. In Phase Ib, T-VEC is injected into cutaneous, subcutaneous, or nodal lesions at up to 4 mL of 10^6 plaque forming units (PFU)/mL day 1, then at up to 4 mL of 10^8 PFU/mL day 22 and Q2W. Pembrolizumab is given 200 mg IV Q2W. Treatment with both therapies continues until (whichever comes first): CR or PD per irRC, intolerance, for up to 2 yrs or, for T-VEC, when there are no longer injectable lesions. The randomized portion of the study comparing T-VEC + pembrolizumab to pembrolizumab alone was originally designed as a Phase II study. An updated Phase III design will be presented.

Trial registration

ClinicalTrials.gov identifier NCT02263508.

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Published: 4 November 2015

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doi:10.1186/2051-1426-3-S2-P181
Cite this article as: Long *et al.*: **A Phase I/III, multicenter, open-label trial of talimogene laherparepvec (T-VEC) in combination with pembrolizumab for the treatment of unresected, stage IIIb-IV melanoma (MASTERKEY-265).** *Journal for ImmunoTherapy of Cancer* 2015 **3**(Suppl 2):P181.