Primary analysis of a phase 1b multicenter trial to evaluate safety and efficacy of talimogene laherparepvec (T-VEC) and ipilimumab (ipi) in previously untreated, unresected stage IIIB-IV melanoma.

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Abstract Disclosures

Abstract:
Background: T-VEC, an HSV-1 derived oncolytic immunotherapy designed to induce systemic antitumor immunity, showed a ≥ 6 mos higher durable response rate vs GM-CSF in a phase 3 melanoma trial (Andtbacka et al. ASCO 2013). This phase 1b/2 study will determine the safety and efficacy of T-VEC as a priming regimen when added to ipi. **Methods:** Phase 1b studied the safety of T-VEC+ipi. Objective response rate (ORR) was also evaluated with tumor assessments q12w. Blood was collected pre- and post-treatment (tx) for correlative studies. Key criteria: unresected Stage IIIB-IV melanoma, no prior systemic tx, measurable disease, and ≥1 injectable cutaneous, subcutaneous or nodal lesion. T-VEC was given intralesionally at ≤ 4 mL of 10^6 PFU/mL at wk 1, then 10^8 PFU/mL at wk 4 and then q2w. Ipi 3 mg/kg q3w was given as 4 infusions starting wk 6. Tx continued until DLT, intolerance, all injectable tumors disappeared, or disease progression (PD) per Immune Related Response Criteria. DLT was any grade (gr) ≥ 4 adverse event (AE) or gr ≥ 3 immune-related AE within the first 6 wks of ipi tx. **Results:** Of 19 patients (pts) enrolled: 42% men, 42% ≥ 65 yrs, 58% Stage IV M1b/c; 18 pts received T-VEC+ipi. No DLTs were reported. Gr 3/4 AEs occurred in 32%. 2 pts had possible immune-related gr 3/4 AEs: 1 pt had gr 3 hypophysitis (attributed to ipi) and gr 3 adrenal insufficiency and gr 3 diarrhea (both attributed to combination), and 1 pt had gr 4 amylase+lipase attributed to ipi. PD (CNS metastases) led to one gr 5 AE. By 15 Oct 13 (data cutoff), median tx duration of T-VEC was 13.3 wks. Of 17 pts with investigator assessed response, ORR was 41% (24% CR, 18% PR); 35% had SD. Median time to response was 2.9 mos. By flow cytometry, activated CD8 T cells significantly increased from baseline 1.8x after T-

VEC alone and 2.9x during T-VEC+ipi tx. **Conclusions:** T-VEC+ipi appears to be tolerable with no DLTs. In consideration with published reports, these data, although preliminary, suggest higher CR and OR rates than either agent alone and earlier responses after ipi initiation during T-VEC+ipi than with ipi alone. Additional immunophenotyping and phase 2 (ipi vs T-VEC+ipi) are ongoing. Clinical trial information: NCT01740297.