

POSTER PRESENTATION

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# Phase 1 results of a phase 1b/2, multicenter, open-label trial to evaluate safety and efficacy of talimogene laherparepvec (T-VEC) and ipilimumab (ipi) vs ipi alone in previously untreated, unresected stage IIIB-IV melanoma

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## Introduction

T-VEC is a herpes simplex virus type-1-derived oncolytic immunotherapy designed to produce GM-CSF and to selectively replicate in and lyse tumors to induce a systemic anti-tumor immune response. A phase 3 study of T-VEC in Stage IIIB-IV melanoma demonstrated a significant improvement in  $\geq 6$  mo durable response rate vs GM-CSF and a tolerable safety profile.

## Methods

In this 2-part study (NCT01740297), phase 1b evaluated the safety of T-VEC in combination with ipi as assessed by the incidence of dose-limiting toxicities (DLTs) at full doses of both agents. For 6 to 9 patients (pts) evaluable for DLT, approximately 18 pts were to be enrolled in phase 1b. DLTs were defined as any grade (gr)  $\geq 3$  immune-related adverse event (AE) or gr  $\geq 4$  AE of any etiology occurring between the first dose of ipi and 6 wks after. The incidence of DLTs was required to be  $\leq 1$  of the first 6 evaluable pts or  $\leq 2$  of the first 9 evaluable pts (if 2 DLTs were seen in the first 6 pts). Key entry criteria were previously untreated, unresectable Stage IIIB-IV melanoma, ECOG 0-1, measurable disease, and  $\geq 1$  injectable cutaneous, subcutaneous, or nodal tumor. T-VEC was administered by intralesional injection at  $\leq 4$  mL of  $10^6$  plaque forming units (PFU)/mL for the first dose, then  $10^8$  PFU/mL on day 1 of wk

4 and thereafter. Ipi 3 mg/kg q3w was administered as 4 infusions starting at wk 6. Pts received T-VEC until development of DLT, all injectable tumors have disappeared, disease progression per the Immune Related Response Criteria, or treatment intolerance. Phase 2 will evaluate the safety and efficacy of ipi vs T-VEC+ipi in a randomized fashion.

## Results

To date, 19 pts have enrolled (13 pts received  $\geq 1$  dose of T-VEC); 9 pts are evaluable for DLT. All DLT evaluable pts received at least 4 doses of T-VEC and 2 doses of ipi by the time of DLT cutoff (6 wks post first ipi dose). No DLTs were observed in evaluable pts. Serious AEs were reported in 1 of 19 pts to date (gr 3 nausea and abdominal distention in week 11 of treatment). Two partial responses were reported by wk 12 in the 9 DLT evaluable pts. Data will be updated at the meeting.

## Conclusions

Advancement into the randomized phase 2 is planned pending Data Review Team recommendations.

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