

**POSTER PRESENTATION**

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# Final planned overall survival (OS) from OPTiM, a randomized Phase III trial of talimogene laherparepvec (T-VEC) versus GM-CSF for the treatment of unresected stage IIIB/C/IV melanoma (NCT00769704)

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## Background

T-VEC is an oncolytic immunotherapy derived from herpes simplex virus type-1 designed to selectively replicate within tumors and to produce GM-CSF to enhance systemic antitumor immune responses. OPTiM, a randomized Phase III trial of T-VEC vs GM-CSF in patients with unresected melanoma with regional or distant metastases met the primary objective of an improvement in durable response rate (response lasting continuously for  $\geq 6$  months) with T-VEC versus GM-CSF (16% vs 2%, respectively;  $P < 0.001$ ). Most common adverse events with T-VEC were fatigue, chills, and pyrexia. No  $\geq$  grade 3 adverse events occurred in  $\geq 3\%$  of patients in either arm (Andtbacka et al., *J Clin Oncol* 2013,32[suppl]:LBA9008). At the primary analysis (PA) of secondary OS endpoint, with median follow-up of 44 (range, 32-59) months and 189 events in the T-VEC arm and 101 events in the GM-CSF arm, median (95%CI) OS was 23.3 (19.5-29.6) months for T-VEC and 18.9 (16.0-23.7) months for GM-CSF (hazard ratio [HR]=0.79; 95%CI = 0.62-1.00;  $P = 0.051$ ) (Kaufman et al., *J Clin Oncol* 2014,32[suppl]:9008a). A planned analysis of OS at 3 years from the last randomization is presented here.

## Methods

Eligible patients were  $\geq 18$  years old; had ECOG performance status (PS)  $\leq 1$ ; unresectable melanoma stage IIIB/C/IV; injectable cutaneous, subcutaneous (SC) or nodal lesions; LDH  $\leq 1.5X$  upper limit of normal;  $\leq 3$  visceral lesions (excluding lung), none  $> 3$  cm. Patients were randomized 2:1 to intralesional T-VEC (initially  $\leq 4$  mL  $\times 10^6$  pfu/mL, then after 3 wks,  $\leq 4$  mL  $\times 10^8$  pfu/mL q2w) or SC GM-CSF (125  $\mu\text{g}/\text{m}^2$  qd  $\times 14$  ds q4w).

## Results

Of 436 patients in the intent-to-treat analysis, 295 (68%) patients received T-VEC and 141 (32%) patients received GM-CSF; 57% were men; median age 63 yrs. At time of the final OS analysis with median follow-up of 49 months [range, 37-63], only 1 additional event occurred (T-VEC arm). Median (95%CI) OS was 23.3 months (95%CI = 19.5-29.6) for T-VEC and 18.9 months (16.0-23.8) for GM-CSF; HR = 0.80 (95%CI = 0.62-1.01),  $P = 0.06$  (descriptive). Five-year survival for the T-VEC arm was 33.4% (95%CI = 27.7-39.2). T-VEC effect on OS was most pronounced in patients with stage IIIB/C/IVM1a melanoma (HR = 0.57; 95%CI = 0.41-0.81,  $P = 0.001$  [descriptive]) and in patients with treatment-naive disease (HR = 0.52; 95%CI = 0.36-0.75,  $P < 0.001$  [descriptive]).

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## Conclusions

With >4 years of median follow-up for survival, a persistent relevant OS effect was demonstrated with further follow-up. Long-term follow-up continues in the registry trial (NCT02173171). T-VEC represents a novel potential therapy for patients with regionally and distantly metastatic melanoma.

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