

Safety and Efficacy of Combined Treatment with Tumor Infiltrating Lymphocytes (TILs) and Oncolytic Adenovirus TILT-123 for Patients with Metastatic Melanoma – Results from a Phase I Trial

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Background

Tumor Infiltrating Lymphocyte (TIL) therapy has recently proved effective in patients with metastatic melanoma. Oncolytic adenovirus TILT-123 (igrelimogene litadenorepvec) is armed with tumor necrosis factor-alpha and interleukin-2 which were selected specifically for their ability to enhance TIL cytotoxicity without the need for preconditioning chemotherapy or postconditioning IL2.

Method

In a phase I, open-label, 3+3 dose-escalating multicenter trial, patients with stage IV melanoma were treated with multiple intravenous and intratumoral injections of TILT-123 and a one- or two-time treatment with TILs. TILs were grown from resected tumor tissue and administered without pre- or post-conditioning treatment regimens. The primary endpoint of the study was safety of TILT-123. Secondary endpoints included safety and efficacy of TILT-123 in combination with TILs.

Results

Sixteen patients with CPI resistant progressive cutaneous (7), mucosal (5) and uveal (4) metastatic melanoma were treated. Median age was 65.5 years (25-75). The most frequently reported adverse events (AEs) related to TILT-123 were fever (63%) and pain at the injection site (44%) while most frequent AEs related to TIL therapy were fever (50%) and chills (24%). No dose-limiting toxicity was observed and the combination of TILT-123 and TIL therapy did not increase the severity of AEs. 31% of patients experienced treatment related serious adverse events. In d78 imaging, RECIST1.1 responses were seen in two patients while disease control rate was 38 %. Responders included one patient (cutaneous) with an ongoing partial response and one patient (mucosal) with a durable complete response. Further, two patients (uveal and cutaneous) had long lasting stable disease (> 10 months).

PET evaluation on d78 revealed disease control in 6/13 evaluable patients, including 4 partial or minor responses. On d36, after 4 injections of TILT-123 and before TILs, 4 partial or minor responses were seen in PET.

Conclusion

The combination of TILT-123 and TIL therapy is safe and feasible in patients with metastatic melanoma. Clinical activity in hard-to-treat melanoma subtypes was observed.

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