Talimogene Laherparepvec (T-VEC) for the treatment of melanoma

Jennifer M. Gardner, MD
jen1110@uw.edu
Assistant Professor, Division of Dermatology
University of Washington

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DISCLOSURE OF RELATIONSHIPS WITH INDUSTRY

Jennifer Gardner, MD
F030 – Caring for the Cancer Patient: Updates in Cutaneous Oncology and Oncodermatology

DISCLOSURES
I do not have any relevant relationships with industry.
Outline

• What is T-VEC & How does it work?
• What have the studies shown?
• T-VEC experience at the Seattle Cancer Care Alliance (SCCA): illustrative cases
T-WHAT?

• Talimogene laherparepvec
T-WHAT?

• Talimogene laherparepVEC
T-VEC FDA-approved in October 2015

- First in class oncolytic virus therapy for the treatment of advanced melanoma
- First oncolytic immunotherapy to demonstrate therapeutic benefit against melanoma in a Phase III trial
- NCCN guidelines: recommended as a Category 1 option for Stage III melanoma with nonresectable, recurrent, or intransit disease.
- Efficacy seen in Stage IIIB, IIIC and IV M1a disease
- T-VEC has NOT been shown to affect OS or have a significant effect on visceral metastases
- Clinical trials ongoing for combination therapy
T-VEC is modified HSV-1

• Deletion of the ICP34.5 gene preferential killing of tumor cells (neurovirulence)
T-VEC is modified HSV-1

• Insertion of gene cassette encoding human GM-CSF increasing influx and activation of APC’s
T-VEC is modified HSV-1

• Deletion of ICP47 gene permits antigen presentation for virus and tumor antigens & increase replication efficiency in tumors
T-VEC is modified HSV-1

- Retention of viral thymidine kinase gene
Oncolytic Virus Therapy: How to win the Game

T-VEC: from theory to trials

Phase I Study showed biologic activity: tumor shrinkage, flattening and necrosis (Hu, 2006)

Single-Arm Phase II Study demonstrated 26% Overall Response Rate in Stage IIIIC/IV melanoma. Responses seen in injected and non-injected lesions (including visceral lesions. (Senzer, 2009)

Tumor microenvironment analysis in the phase II study showed sig increase in MART-1-specific T-cells following CR with T-VEC, found in local and distant lesions (Kaufman, 2010)
OPTiM: Phase III Study

- Randomized, open-label, phase 3 study with histologically confirmed and surgically unresectable stage IIIB, IIIC, IV melanoma
- Randomized 2:1 to get T-VEC or SQ GM-CSF

OPTiM Phase III Study

Durable response rate:
T-VEC: 16.3%
GM-CSF: 2.1%

Overall Response Rate:
T-VEC: 26.4%
GM-CSF: 5.7%

Median Overall Survival:
T-VEC: 23.3 months
GM-CSF: 18.9 months
OPTiM Phase III Study

• T-VEC is the 1st oncolytic immunotherapy to demonstrate therapeutic benefit against melanoma in a phase III clinical trial.

• T-VEC is well-tolerated

• T-VEC efficacy most pronounced in Stage IIIB, IIIC, IVM1a Disease & in treatment-naïve Dz
OPTiM Trial

- Median Time to Response: 4.1 months (95% CI 1.2-16.1 months)
- Median Time to Failure: 8.2 months (95% CI 6.5-9.9 months)
T-VEC responses uninjected non-visceral lesions

T-VEC Visceral Lesions

What about combination therapy?
T-VEC + Ipilimimumab

• Phase I Study and Phase II randomized trial comparing T-VEC + Ipi to Ipi alone:

Objective Response Rate
• T-VEC + Ipi: 39%
• Ipi alone: 18%

• No Dose-Limiting Side Effects, well tolerated

Chesney J, et al. JCO. June 2017
T-VEC + Pembrolizumab

• High Overall Response Rate: 62%

• High Complete Response Rate: 33%

• Favorable changes to the tumor microenvironment

• Response was independent of baseline CD8+ tumor infiltration

T-VEC at the SCCA

- To Date: 12 patients have been treated with T-VEC
- Ages 27-88 years
- Stage 1-Stage III Disease → recurrent melanoma
- All but 1 patient heavily pre-treated
- Some have h/o irAE’s to systemic immunotherapy
- 1 pCR, several PRs, 4 off Tx following progression
T-VEC cases
Ultrasound Guided T-VEC
T-VEC at the SCCA: Lessons Learned

• Generally well-tolerated, BUT the constitutional symptoms are impressive early in the course of treatment
• “progression prior to response”
• Treated and untreated lesions respond to therapy
• PR’s, 1 CR and progression/failures
• No infectious side effects (HSV-1 or cellulitis) to date
• Immune-related side effects are not unexpected, as with other immunotherapies (panniculitis & colitis)
• Dermatologists have a role to play in treating advanced melanoma