

**TNT: TALIMOGENE LAHERPAREPVEC
(AN ONCOLYTIC VIRUS EXPRESSING
GM-CSF), NIVOLUMAB AND
TRABECTEDIN FOR ADVANCED
LEIOMYOSARCOMA**

A PHASE 2 STUDY [NCT# 03886311]

Neal S. Chawla, MD, Nadezhda Omelchenko, MD
Sant P. Chawla, MD, Erlinda M. Gordon, MD
Sarcoma Oncology Research Center
Santa Monica CA 90403, USA

**I and my co-authors declare
no conflict of interest.**

Background

- Intratumoral injection of Talimogene Laherparepvec (TVEC) has a local oncolytic effect and evokes a cytotoxic immuneresponse.
- The combination of Trabectedin (T) and Nivolumab (N) is a safe and effective therapy in soft tissue sarcoma (STS).
- This study aims to determine the safety and efficacy of adding TVEC to the combination of T and N in advanced leiomyosarcoma (LMS).

Objectives

Primary:

- To assess progression-free survival at 12 months

Secondary:

- To evaluate the best overall response
- Progression free survival (PFS) rate at 6 and 9 month
- Overall survival (OS) rate at 6, 9, and 12 months
- Incidence of treatment-related adverse events (TRAEs).

Eligibility Criteria

- ≥ 18 years of age
- Locally advanced or metastatic leiomyosarcoma
- Previously treated
- Measurable disease by RECIST v1.1
- At least one accessible tumor for intratumoral injection of TVEC

Treatment Schedule

- N (3 mg/kg q 2 weeks)
- T (1.2 mg/m² q 3 weeks)
- TVEC (1x10⁸ PFU/ml q 2 weeks depending on tumor size)
- A starting dose of TVEC (1x10⁶ PFU/ml) was initially given, followed by a total dose of 1x10⁸ PFU/ml q 2 weeks depending on tumor size) three weeks later

Efficacy Analysis (n=11)

- Median number of prior lines of therapy: 4 (range 1-8)
- Best Overall Response = 2 PR, 9 SD (BOR Rate 18.2%).
- Confirmed Disease Control Rate (PR+SD) = 100%.
- Median PFS = 7 months (range: 3- 18)
- 6-month PFS rate= 55%

Note: Per protocol, evaluable subjects were those who had completed at least one treatment cycle and had a follow-up CT scan

Efficacy Analysis

Modified Intention to Treat (n=11)

- Median OS = 18.2 months (range: 4- 32)
- 6-month OS rate = 91%.

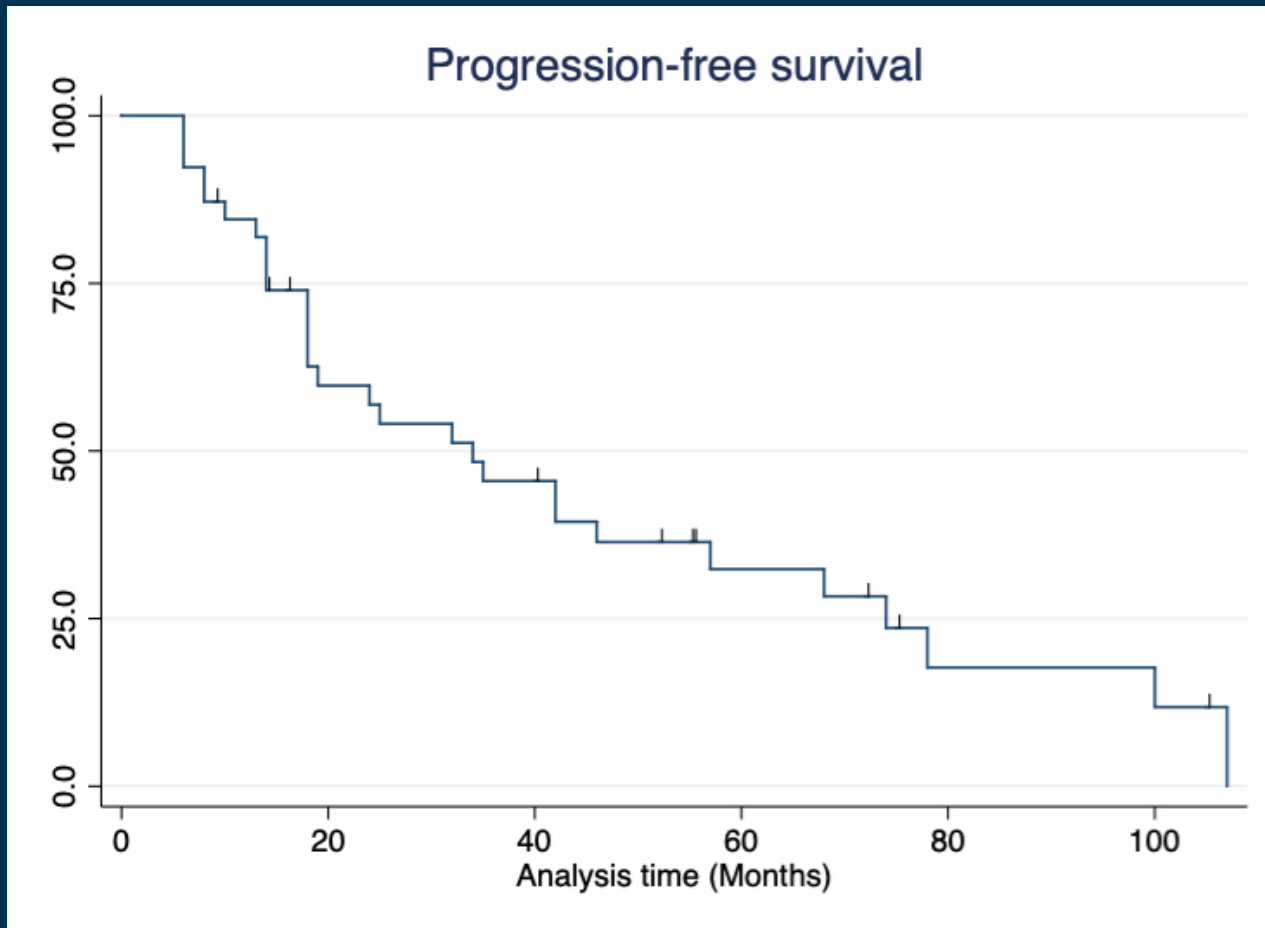
Intention to Treat = 15

- Median OS = 12 (range 0-32) months
- 6-month OS rate, 60%.

Exploratory Analysis

- Response was not related to PD-L1 positivity
- Patients with PR were ER+/PR+ and had uterine LMS.

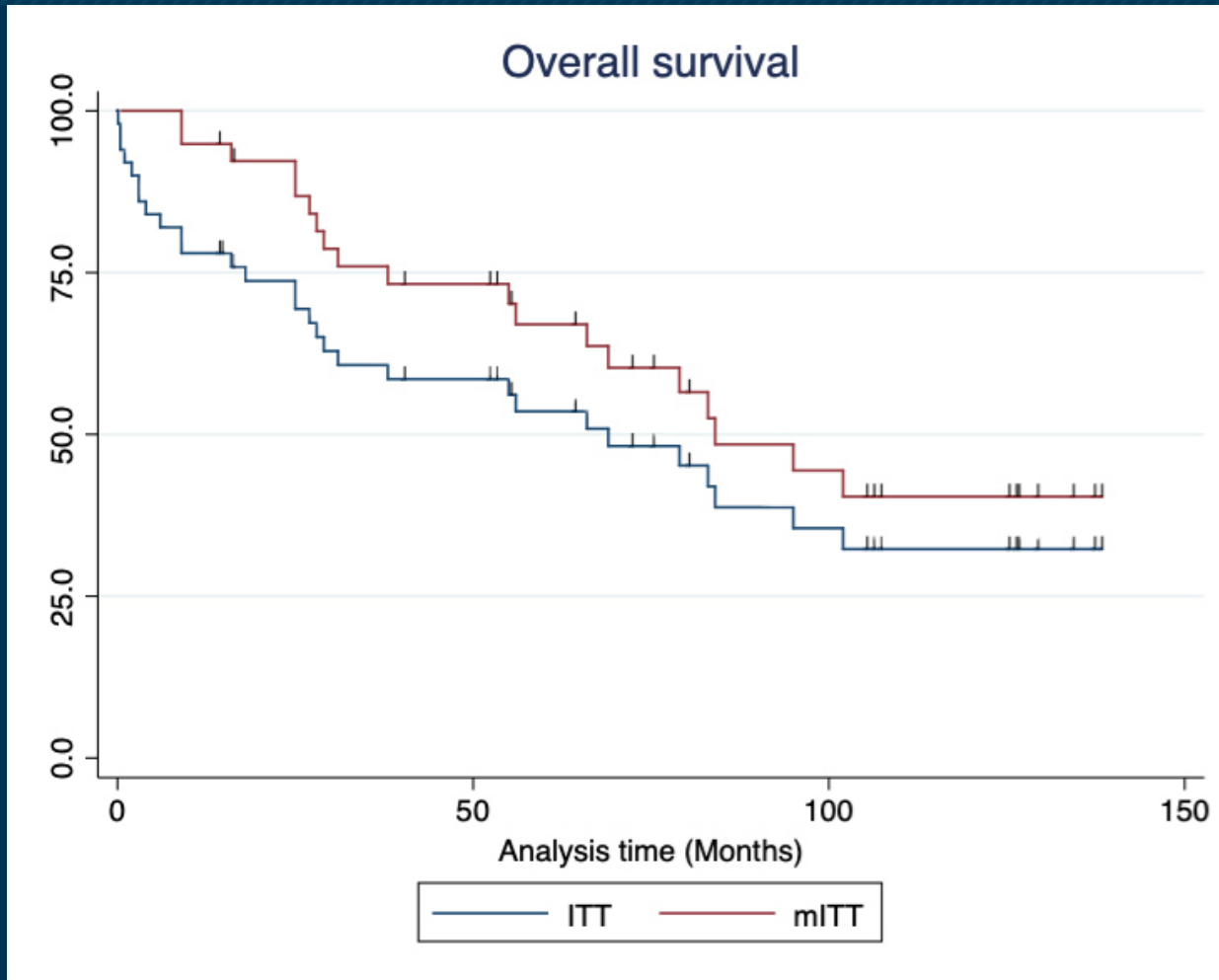
Progression free Survival



Legend: Kaplan Meier Plot of overall survival in the ITT and mITT populations of advanced leiomyosarcoma.

Percent surviving is plotted on the vertical axis as a function of treatment period in months, plotted on the horizontal axis.

Overall Survival



Legend: Kaplan Meier Plot of overall survival in the ITT and mITT populations of advanced leiomyosarcoma.

Percent surviving is plotted on the vertical axis as a function of treatment period in months, plotted on the horizontal axis.

Conclusions

These results suggest the following:

- By indirect comparison, the TNT regimen: Talimogene laherparepvec, Nivolumab & Trabectedin may be more effective than Trabectedin alone as 2nd/3rd/4th therapy for advanced leiomyosarcoma with manageable toxicity.
- Response is not related to PD-L1 positivity.
- The best responders are patients with HR+ uterine LMS.

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Thank You

nchawla@sarcomaoncology.com