# Randomized Trial of Tumor Lysate Particle Only Vaccine vs. Tumor Lysate Particle-loaded, Dendritic Cell Vaccine to Prevent Recurrence of Resected Stage III/IV Melanoma: 36-Month Analysis

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## Background

- The tumor lysate, particle-loaded, dendritic cell (TLPLDC) vaccine is created by loading dendritic cells (DCs) *ex vivo* with yeast cell wall particles (YCWP) with autologous tumor lysate (TL), producing a personalized vaccine.
  - The autologous DCs are harvested either from a direct blood draw or a blood draw following the administration of granulocyte colony stimulating factor (G-CSF).
- The TLPLDC vaccine demonstrated improved 24-month DFS (62.9% vs. 34.8%, p = 0.041) compared to placebo in a per-treatment (PT) analysis in phase 2B trials with 144 patients.[1]
- A novel iteration of this vaccine concept, the tumor lysate, particle-only (TLPO) vaccine, involves TL-loaded YCWP capped with silicate and inoculated, allowing the DC to be loaded *in vivo* and circumventing the other processes of the TLPLDC production.
- The TLPO vaccine reduces time, cost, complexity, and labor-intensity of production by eliminating need for dendritic cell (DC) collection and *ex vivo* loading when compared to a classical DC vaccine model.
  - The TLPLDC versus TLPO vaccine were compared in an embedded bridging portion of the phase 2B trial of the TLPLDC vaccine.
- We present 36-month outcomes of the ongoing randomized, double-blind phase 2B trial with resected stage III/IV melanoma, comparing patients receiving placebo (autologous DCs loaded with empty YCWP), TLPLDC created after pre-treatment with G-CSF (TLPLDC+G), TLPLDC without G-CSF (TLPLDC), and TLPO vaccines.

## Methods

- Patients were randomized 2:1 to receive TLPO or TLPLDC vaccines as a continuation of the ongoing trial comparing TLPLDC to placebo.
- Treatments were given at 0, 1, 2, 6, 12, and 18 months.
- Reporting of adverse events (AE) was per a Data Safety Monitoring Plan and categorized according to the National Cancer Institute CTCAE v4.03 toxicity scale.
- Kaplan-Meier and log-rank analysis was used to compare 36-month disease free survival (DFS) and overall survival (OS) in the intention-to-treat (ITT) main arms, as well as exploratory subgroups.

**References:**
1. Vreeland TJ, Clifton GT, Hale DF, et al. A Phase IIb Randomized Controlled Trial of the TLPLDC Vaccine as Adjuvant Therapy After Surgical Resection of Stage III/IV Melanoma: A Primary Analysis. *Ann Surg Oncol.* Feb 27 2021:1-12. doi:10.1245/s10434-021-09709-1

**Trial Registration**: This is a phase IIb clinical trial registered under NCT02301611.
**Ethics Approval**: This study was approved by Western IRB, protocol 20141932.

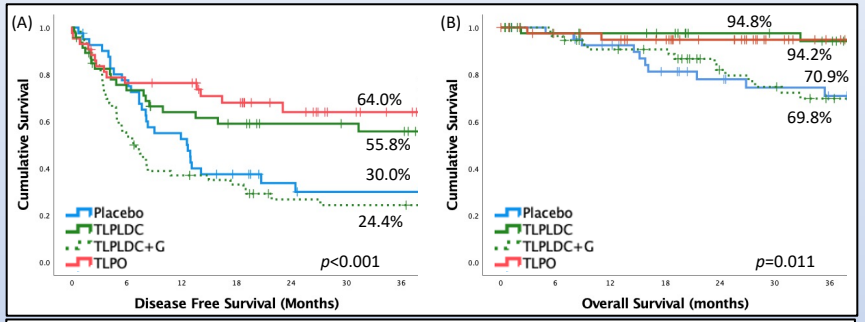


**Figure 1.** Kaplan-Meier curves demonstrating DFS (A) and OS (B) between Placebo (n=41), TLPLDC+G (n=56), TLPLDC (n=47), and TLPO (n=43).

| Arm | N | Recurrences, n (%) | Deaths, n (%) | Median Survival (months) |
|---|---|---|---|---|
| Placebo | 41 | 27 (65.9%) | 10 (24.4%) | 35.5 |
| TLPLDC+G | 56 | 41 (73.2%) | 14 (25.0%) | 33.3 |
| TLPLDC | 47 | 19 (40.4%) | 2 (4.3%) | 38.4 |
| TLPO | 43 | 14 (32.6%) | 2 (4.7%) | 25.6 |
| Total | 187 | 101 (54.0%) | 28 (15.0%) | - |

**Table 1**. Recurrence, Death, and Median Survival for placebo, TLPLDC+G, TLPLDC, and TLPO.

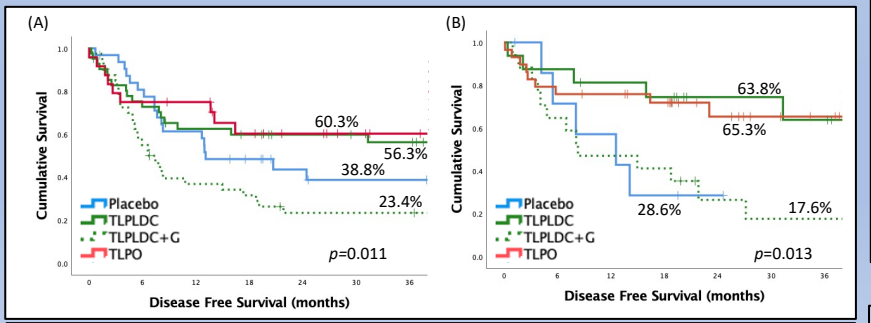


**Figure 2**. Kaplan-Meier curves demonstrating 36-month DFS for (A) Patients with Stage III disease (Placebo = 32, TLPLDC+G n = 40, TLPLDC n = 42, TLPO n = 24), and (B) Patients who received CPI therapy (Placebo = 8, TLPLDC+G n = 17, TLPLDC n = 16, TLPO n = 29).

## Results

- A total of 187 patients were randomized with 41, 56, 47, and 43 patients enrolled in the placebo, TLPLDC+G, TLPLDC, and TLPO arm, respectively.
- Pts randomized to the TLPO arm were more likely to have stage IV melanoma (22.0% for placebo, 20.4% for TLPLDC and TLPLDC+G, and 44.2% for TLPO; $p = 0.002$) and to receive prior immunotherapy (36.6% for placebo, 39.8% for both TLPLDC and TLPLDC+G, and 83.7% for TLPO; $p < 0.001$).
- Total grade 3+ adverse events (AE) were not significantly different between arms (p = 0.053).
  - AEs were deemed treatment-related if classified as "definitely," probably," or "possibly" related to vaccination by the site.
  - 2 Related AEs ≥ grade 3 were experienced by 2 patients, one each in placebo (infection, hospitalization) and TLPLDC+G arms (symptomatic anemia, hospitalization).
- In an ITT analysis, 36-month DFS was 30.0% for placebo, 24.4% for TLPLDC+G, 55.8% for TLPDC, and 64.0% for TLPO ($p<0.001$).
- OS at 36 months was 70.9% for placebo, 69.8% for TLPLDC+G, 94.2% for TLPLDC, and 94.8% for TLPO ($p = 0.011$) (Fig 1, Table 1).
- In an exploratory subgroup analysis:
  - 36-month DFS for those receiving CPIs prior to treatment was 28.6% for placebo, 17.6% for TLPLDC+G, 63.8% for TLPLDC, and 65.3% for TLPO ($p = 0.013$) (Fig 2).
  - 36-month DFS for those with Stage III disease was 38.8% for placebo, 23.4% for TLPLDC+G, 56.3% for TLPLDC, and 60.3% for TLPO ($p = 0.011$)
  - 36-month DFS for those with Stage IV disease was 0% for placebo, 25.0% for TLPLDC+G, 53.3% for TLPLDC, and 68.3% for TLPO ($p = 0.005$).

## Conclusions

- The TLPO and TLPLDC vaccines were safe and well tolerated.
- The TLPO and TLPLDC (without G-CSF) vaccines improved 36-month DFS and OS in this randomized, double-blind, phase 2B trial.
- The efficacy of the TLPO and TLPLDC vaccines will be confirmed in a phase III trial in resected Stage III/IV melanoma pts.

**Disclosures**: Dr. Wagner is an employee of Orbis Health Solutions. Dr. Peoples is employed by Orbis Health Solutions and Cancer Insight; is a consultant for Rapamycin Holdings, Heat Biologics, Abexxa Biologics, and Pelican Therapeutics; and has received funding from the above as well as Sellas Life Sciences and Genentech.
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The voluntary, fully informed consent of the subjects used in this research was obtained as required by 32 CFR 219 and DODI 3216.02_AFI40-402.