

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



Elizabeth L. Carpenter, MD¹, Alexandra M. Adams, MD¹, Robert C. Chick, MD¹, Guy T. Clifton, MD¹, Timothy J. Vreeland, MD¹, Franklin A. Valdera, MD¹, Ankur Tiwari, MD², Patrick M. McCarthy, MD¹, Anne E. O'Shea, MD¹, Diane F. Hale, MD¹, Phillip M. Kemp Bohan, MD¹, Annelies T. Hickerson, MD¹, John W. Myers III, MD¹, Jessica L. Cindass, MD¹, John Hynstrom, MD³, Adam C. Berger, MD⁴, James W. Jakob, MD⁵, Jeffrey J. Sussman, MD⁶, Montaser Shaheen, MD⁷, Xianzhong Yu, MD⁸, Thomas Wagner, PhD⁹, Mark B. Faries, MD¹⁰, George E. Peoples, MD¹¹

¹Brooke Army Medical Center, San Antonio, TX, ²University of Texas Health Sciences Center, San Antonio, Texas, ³Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, ⁴Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, ⁵Mayo Clinic, Rochester, MN, ⁶University of Cincinnati, Cincinnati, OH, ⁷University of Arizona, Tucson, AZ, ⁸Department of Biological Sciences, Clemson University, Clemson, SC, ⁹Orbis Health Solutions, Greenville, SC, ¹⁰The Angeles Clinic, Santa Monica, CA, ¹¹Cancer Vaccine Development Program, San Antonio, TX

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).
 - Pre-treatment with G-CSF allows for smaller blood draw aliquots, but may affect the ability of autologous DCs
- 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 IIb trials with 144 patients.¹
- The tumor lysate (TL) particle only (TLPO) vaccine utilizes a similar mechanism, but with autologous TL-loaded yeast cell wall particles (YCWP), thus reducing production time and cost by eliminating need for dendritic cell (DC) collection and *ex vivo* loading.
 - The TLPO versus TLPLDC vaccine will be compared in an embedded bridging portion of the trial.
- We present 36-month outcomes of the ongoing randomized, double-blind phase 2 trial with resected stage III/IV melanoma, comparing patients receiving placebo (autologous DCs loaded with empty YCWP), TLPLDC 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.
- Safety was measured by the Common Terminology Criteria for Adverse Events (CTCAE).
- Kaplan-Meier and log-rank analysis was used to compare 3-month disease free survival (DFS) and overall survival (OS) in the intention-to-treat (ITT) main arms, as well as exploratory subgroups.

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

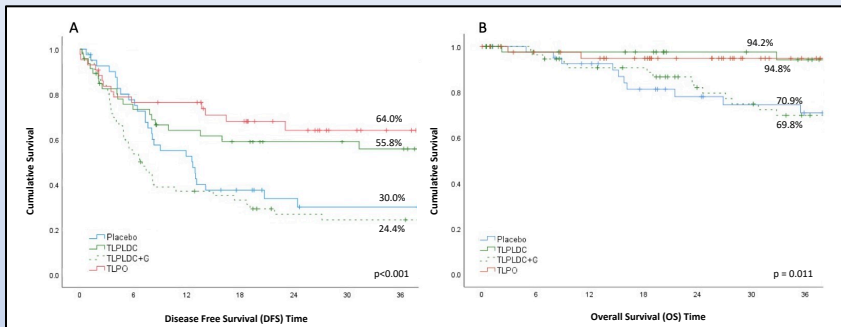


Figure 1. Kaplan-Meier curves demonstrating DFS (A) and OS (B) between Placebo (n=41), TLPLDC (n=47), TLPLDC+G (n=56), and TLPO (n=43).

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

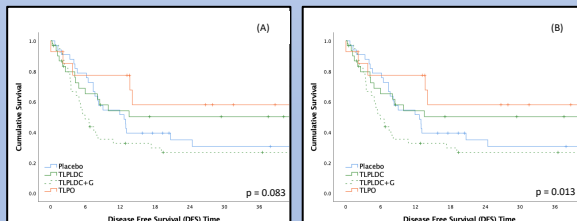


Figure 2. Kaplan-Meier curves demonstrating DFS for (A) Patients who did not receive CPI (Placebo = 33, TLPLDC n = 31, TLPLDC+G n = 39, TLPO n = 14) and (B) Patients who did receive CPI (Placebo = 8, TLPLDC n = 16, TLPLDC+G n = 17, TLPO n = 29).

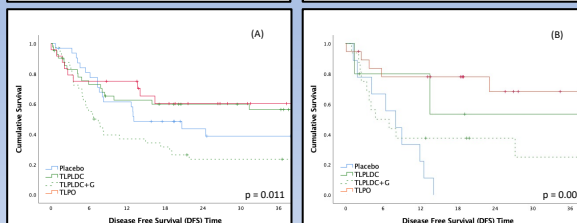


Figure 3. Kaplan-Meier curves demonstrating DFS for (A) Patients with stage III disease (Placebo = 32, TLPLDC = 42, TLPLDC+G = 40, TLPO n = 24) and (B) Patients with stage IV disease (Placebo = 9, TLPLDC n = 5, TLPLDC+G n = 16, TLPO n = 19).

Results

- A total of 187 patients were randomized with 41, 47, 56, and 43 patients enrolled in the placebo, TLPLDC, TLPLDC+G, 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; $p < 0.001$).
- Grade 3+ adverse events (AE) were not significantly different between arms ($p = 0.053$).
 - 55 AEs \geq grade 3 occurred in 31 patients (TLPLDC/TLPLDC+G =12, TLPO=11, Placebo=8)
- In the ITT analysis, 36-month DFS was 30.0% for placebo, 55.8% for TLPLDC, 24.4% for TLPLDC+G, and 64.0% for TLPO ($p < 0.001$).
- OS at 36 months was 70.9% for placebo, 94.2% for TLPLDC, 69.8% for TLPLDC+G, and 94.8% for TLPO ($p = 0.011$).
- In an exploratory subgroup analysis, 36-month DFS for those receiving CPIs prior to treatment was 28.6% for placebo, 65.3% for TLPLDC, 17.6% for TLPLDC+G, and 65.3% for TLPO ($p = 0.013$), and survival for those with stage III disease was 38.8% for placebo, 60.3% for TLPLDC, 23.4% for TLPLDC+G, and 60.3% for placebo.

Conclusions

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

References:

- 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

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, Abexa Biologics, and Pelican Therapeutics; and has received funding from the above as well as Sellas Life Sciences and Genentech. The view(s) expressed herein are those of the author(s) and do not reflect the official policy or position of Brooke Army Medical Center, the US Army Medical Department, the Department of the Army, Department of the Air Force, Department of Defense, or the US Government. The voluntary, fully informed consent of the subjects used in this research was obtained as required by 32 CFR 219 and DODI 3216.02_AF140-402.