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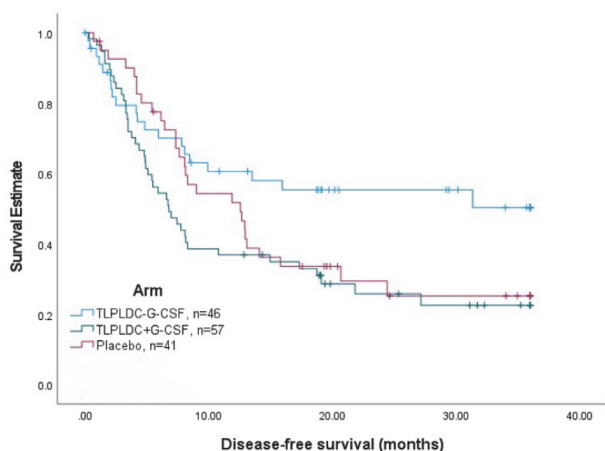
THE EFFECT OF PRETREATMENT WITH G-CSF PRIOR TO DENDRITIC CELL COLLECTION DURING THE PHASE IIB TRIAL OF AN AUTOLOGOUS DC-BASED VACCINE FOR ADVANCED, RESECTABLE MELANOMA

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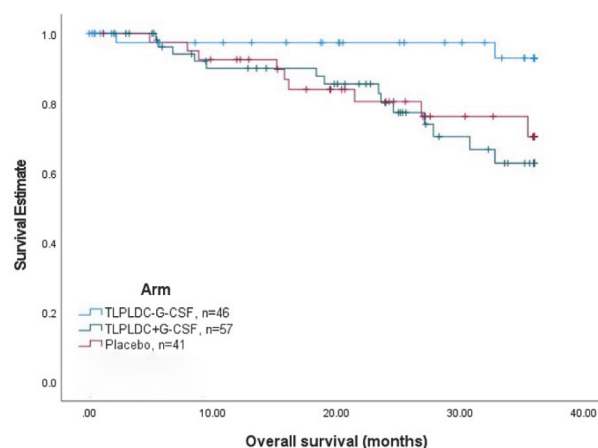
Background We have completed a prospective, randomized, multi-center, double-blind, placebo-controlled phase IIB trial of the tumor lysate, particle loaded, dendritic cell (TLPLDC) vaccine given to prevent recurrences in patients with resected stage III/IV melanoma. During the trial, granulocyte colony stimulating factor (G-CSF) was administered to some patients to mobilize dendritic cells (DCs) precursors prior to harvest, allowing for similar DC yield with reduced blood draws. This study examines the impact of DC collection methods on vaccine effectiveness.

Methods TLPLDC is produced by loading tumor lysate into pre-prepared yeast cell wall particles (YCWPs) and exposing them to autologous DCs. DC precursors were isolated either by collection of 50–70 mL of blood following pre-administration of 300µg of G-CSF 24–48 hrs prior, or collection of 120 mL of peripheral blood without G-CSF pretreatment based on patient and provider preference. Patients were randomized 2:1 to receive TLPLDC or placebo (DCs exposed to empty YCWPs). 1–1.5 × 10⁶ cells/dose were injected intradermally at 0, 1, 2, 6, 12, and 18 months. Differences in disease free survival (DFS) and overall survival (OS) were analyzed by log rank.

Results Of 144 patients randomized, 103 received TLPLDC and 41 received placebo. Within the TLPLDC group, 57 received pretreatment with G-CSF (TLPLDC+G-CSF) and 46 did not (TLPLDC–G-CSF). There were no significant clinicopathologic or treatment differences between the three treatment arms. 36-month DFS was significantly better in TLPLDC–G-CSF vs. TLPLDC+G-CSF or placebo (51.8% vs. 23.4% and 27.1% respectively, p=0.027) (figure 1).



Abstract 310 Figure 1 DFS at 36 months



Abstract 310 Figure 2 OS at 36 months

TLPLDC–G-CSF had correspondingly improved OS (92.9% vs. 62.8% and 72.3% respectively, p=0.022) (figure 2). Subgroup analysis revealed TLPLDC–G-CSF had increased DFS over TLPLDC+G-CSF or placebo in Stage IV (68.6% vs. 18.8% and 0.0% respectively, p=0.058). Similarly, the DFS survival benefit of TLPLDC–G-CSF was enhanced in patients who received prior immunotherapy (IO) (61.9% vs. 11.5% and 35.7% respectively, p=0.007) or checkpoint inhibitors (CPI) (48.5% vs. 10.6% and 37.5% respectively, p=0.039).

Conclusions TLPLDC vaccine created without G-CSF pretreatment significantly improved 36-month DFS and OS compared to TLPLDC+G-CSF or placebo in stage III/IV (resected) melanoma patients. On further subgroup analysis, the increases in OS and DFS were more profound in patients who received additional immune therapies to include CPI. Ongoing evaluation will determine if G-CSF mobilization leads to collection of phenotypically different DCs. Based on these results, we are planning a phase III trial of TLPLDC–G-CSF + CPI vs. placebo + CPI in advanced melanoma post-resection.

Trial Registration ClinicalTrials.gov Identifier: NCT02301611

Ethics Approval This study was reviewed and approved by the IRB or Independent Ethics Committee (IEC) of each participating center prior to study initiation.

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PHASE II TRIAL OF LYMPHODEPLETION PLUS ADOPTIVE CELL TRANSFER WITH OR WITHOUT DENDRITIC CELL VACCINATION IN PATIENTS WITH METASTATIC MELANOMA

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Background Adoptive cell therapy (ACT) using autologous tumor-infiltrating lymphocytes (TIL) has shown great benefit in patients with melanoma.^{1,2} It was suggested that long term tumor immunosurveillance is provided by TIL persisting