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431 PROSPECTIVE, RANDOMIZED TRIAL OF THE TUMOR LYSATE, PARTICLE ONLY VACCINE COMPARED TO THE TUMOR LYSATE, PARTICLE-LOADED, DENDRITIC CELL VACCINE TO PREVENT RECURRENCE FOR RESECTED STAGE III/IV MELANOMA

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Background The autologous tumor lysate, particle-loaded, dendritic cell (TLPLDC) vaccine is safe and effective in improving 24 and 36-month disease-free survival (DFS) in patients (pts) with resected stage III/IV melanoma who completed the primary vaccine series. The tumor lysate, particle only (TLPO) vaccine has been developed to accelerate production by omitting DC isolation and ex vivo loading in favor of in vivo phagocytosis of the TL-loaded particles. We are currently conducting a randomized and double-blind trial of the TLPO vs TLPLDC to improve DFS and overall survival (OS) in patients with resected late stage melanoma.

Methods Patients with stage III/IV melanoma who were clinically disease-free after standard of care therapies were randomized to receive TLPO vs TLPLDC (2:1) as a continuation of the phase IIb trial comparing TLPLDC vs placebo (2:1). For the TLPLDC vaccine, autologous TL was loaded into yeast cell wall particles (YCWP) which were then phagocytized by isolated autologous DC ex vivo. For the placebo DC were loaded with empty YCWP. For TLPO, the autologous TL-loaded YCWP were coated with a chemoattractant and injected intradermally for in vivo phagocytosis. Some patients in the TLPLDC arm received G-CSF prior to DC harvest to minimize blood draw (60 mL instead of 120 mL without G-CSF). For all arms, six vaccine/placebo doses were administered intradermally at 0, 1, 2, 6, 12, and 18 mos. Data was analyzed by an intention-to-treat (ITT) analysis for DFS and OS by the Kaplan-Meier method and compared by log-rank test.

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Abstract 431 Figure 1 TLPO vs TLPLDC (n=20) DFS. Disease-free survival of TLPO patients compared to similar TLPLDC patients (n=20)

Abstract 431 Figure 2 TLPO vs TLPLDC (n=20) OS. Overall survival of TLPO patients compared to similar TLPLDC patients (n=20)

Abstract 431 Figure 3 TLPO vs TLPLDC subsets vs Placebo DFS. Disease-free survival of TLPO patients compared to placebo and all TLPLDC patients (n=103) stratified by use of G-CSF

Abstract 431 Figure 4 TLPO vs TLPLDC subsets vs Placebo OS. Disease-free survival of TLPO patients compared to placebo and all TLPLDC patients (n=103) stratified by use of G-CSF
Results 63 pts were randomized to TLPO (n=43) vs TLPLDC (n=20). The TLPO cohort contained more females and received less chemotherapy (0% vs 10%), but otherwise were comparable. There were no differences in DFS (p=0.948) or OS (p=0.779) between the two vaccines (figures 1&2). Comparing the TLPO pts to all other pts in the phase IIb trial [TLPLDC+G-CSF (n=57), TLPLDC-G-CSF (n=46), and placebo (n=41)] the TLPO arm had improved DFS compared to placebo (p=0.019) and TLPLDC-G-CSF (p=0.001), but roughly equivalent to the TLPLDC-G-CSF arm (p=0.276) (figure 3). A similar trend was seen in OS analysis, though differences were not statistically significant (figure 4).

Conclusions TLPO and TLPLDC vaccines (without the use of G-CSF) improve DFS in patients with resected stage III/IV melanoma compared to placebo. The TLPO vaccine may offer advantages via reduced cost and vaccine production time. TLPO should be closely considered for further clinical trials.

Trial Registration NCT02301611: Phase IIB TL + YWCP + TLPO

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REFERENCE