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Abstract # **LBA9012**

Phase III, randomized, double-blind study of elesclomol and paclitaxel versus paclitaxel alone in stage IV metastatic melanoma (MM).

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Background: Elesclomol is an investigational first-in-class oxidative stress inducer that increases oxidative stress in cancer cells leading to mitochondria-induced apoptosis.

Methods: Patients (pts) with Stage IV MM, no prior chemotherapy, LDH μ 2x ULN were randomized (1:1) to either 213 mg/m^2 elesclomol in combination with 80 mg/m^2 paclitaxel (ELPAC) or 80 mg/m^2 paclitaxel alone (P); both were given weekly x3 followed by 1 week rest until disease progression. Pts were stratified by prior non-cytotoxic treatment, M1 grade, and LDH. The primary endpoint was PFS with >90% power to detect a 2-month improvement. The primary PFS analysis was planned once all pts had been enrolled and at least 164 PFS events had occurred.

Results: 651 pts were enrolled between September 2007 and February 2009. Prognostic factors were generally well balanced. PFS analysis was based on investigator assessment of 411 pts (219 events). Median PFS was 3.5 m (95% CI 2.7-3.7) in ELPAC and 1.9 m (95% CI 1.9-3.3) in P [HR 0.88; 95% CI 0.67-1.16, p=0.3695]. The median number of cycles was 3 in ELPAC and 2 in P. Safety analysis showed increased signals on ELPAC including increased ≥Gr 3 AEs (N=405, 32.8% vs. 23.5%), increased AEs leading to death (N=405, 3.5% vs <1%) and increased overall deaths (N=651, 80 vs 53; 80% censored). Most common AEs in ELPAC were fatigue (32.8%), alopecia (31.3%) and nausea (27.9%).

Conclusions: There was an improvement in PFS in the ELPAC arm, but it did not achieve statistical significance. In February 2009, the study was halted based on the recommendation of the DMC to unblind the study after the DMC observed increased deaths on the ELPAC arm. The DMC could not determine whether the observed increased deaths were treatment related or not. Of note, in this analysis there were no specific target organ toxicities attributable to ELPAC that could explain the imbalance of deaths. OS data continues to be collected to determine if the observed imbalance in OS persists as the data mature.