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1378O ARCTIC: Durvalumab + tremelimumab and durvalumab monotherapy vs SoC in ≥ 3L advanced NSCLC treatment

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Background: PD-1/PD-L1 inhibitors (PDx) improve survival in ≥ 2L NSCLC, primarily in PD-L1 high pts. Combining PDx with CTLA-4 agents may address unmet medical needs by providing synergistic antitumor activity even in PD-L1 low/neg pts in this setting. This Phase 3 trial (NCT02352948) evaluated durvalumab (D) vs SoC and D plus anti-CTLA-4 tremelimumab (T) vs SoC in Stage IIIB/IV NSCLC.

Methods: Eligible pts had ≥2 prior systemic treatments (1 platinum-based CT), WHO PS 0/1, no prior PDx and were EGFR/ALK WT. From Q2 2015, in sub study A (SSA), PD-L1 TC ≥25% (Ventana SP263 assay) pts were randomized 1:1 to D 10 mg/kg IV

q2w for up to 12 mo or SoC (erlotinib 150 mg QD PO, gemcitabine 1000 mg/m^2 IV [day 1, 8, and 15 of a 28-day cycle] or vinorelbine 30 mg/m^2 IV [day 1, 8, 15, and 22 of a 28-day cycle]). In sub study B (SSB), PD-L1 TC <25% pts were randomized 3:2:2:1 to D+T (D 20 mg/kg IV + T 1 mg/kg IV q4w for up to 12 wks then D 10 mg/kg IV q2w for 34 wks); SoC (as SSA); D (as SSA); or T 10 mg/kg IV q4w for 24 wks then q12w for 24 wks. Co-primary endpoints were OS and PFS for D+T vs SoC in SSB and D vs SoC in SSA. Secondary endpoints included 12-mo OS and PFS, ORR, safety and QoL. All 5% alpha was given to SSB (4% OS; 1% PFS); SSA was descriptive with no statistical testing.

Results: Due to recruitment challenges 126/250 (SSA) and 469/600 (SSB) planned pts were randomized (DCO Feb 09 2018). Baseline characteristics were well balanced. In SSB, median OS was 11.5 vs 8.7 mo with D+T vs SoC (HR 0.80 [95% CI 0.61, 1.05]; p = 0.109). 12-mo OS rates were 49.5% and 38.8%. Median PFS was 3.5 vs 3.5 mo (HR 0.77 [0.59, 1.01]; p = 0.056) with 12-mo PFS rates of 20.6% and 8.0%. ORR was 14.9% D+T and 6.8% SoC. In SSA, median OS was 11.7 vs 6.8 mo with D vs SoC (HR 0.63 [0.42, 0.93]). 12-mo OS rates were 49.3% and 31.3%. Median PFS was 3.8 vs 2.2 mo (HR 0.71 [0.49, 1.04]) with 12-mo PFS rates of 19.4% and 9.9%. ORR was 35.5% D and 12.5% SoC. Grade ≥3 treatment-emergent AEs were 46.8% D+T and 54.5% SoC in SSB; 45.2% D and 66.7% SoC in SSA.

Conclusions: In the ≥3L setting, D monotherapy provided a clinically meaningful improvement in OS vs SoC in PD-L1 TC ≥25% pts. D+T did not significantly improve OS or PFS vs SoC in PD-L1 TC <25% pts. D+T, D and T exhibited manageable safety profiles. Further biomarker analyses may help identify pts who may benefit most from D+T, D or T in advanced NSCLC.

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