GENITOURINARY TUMOURS, NON-PROSTATE

LBA6_PR JAVELIN renal 101: A randomized, phase III study of avelumab + axitinib vs sunitinib as first-line treatment of advanced renal cell carcinoma (aRCC)

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Background: In a phase 1b trial, 1L A + Ax had encouraging antitumor activity for patients (pts) with aRCC (Lancet Oncol. 2018;19:451).

Methods: Eligible pts with clear-cell aRCC, ECOG ≤ 1, and no prior systemic therapy were randomized 1:1 (stratified by ECOG and geographic region) to receive A 10 mg/kg IV Q2W + Ax 5 mg PO BID in 6-wk cycles or S 50 mg PO QD on schedule 4/2; all prognostic risk groups were included. Primary endpoints were progression-free survival (PFS; by blinded independent central review [BICR] per RECIST v1.1) and overall survival (OS) in pts with PD-L1+ tumors (≥ 1% of immune cells). Secondary endpoints included PFS by BICR and OS irrespective of PD-L1 expression, objective response (OR), and safety.

Results: As of 20 Jun 2018, 886 pts were randomized (A + Ax: N = 442; S: N = 444); of these, 21%/62%/16% had favorable/intermediate/poor IMDC risk criteria (not reported in < 1%). In 560 pts (63.2%) with PD-L1+ tumors, median PFS was 13.8 vs 7.2 mo in A + Ax vs S arms, respectively (HR = 0.61; p < .0001; Table). Median PFS in pts irrespective of PD-L1 expression was 13.8 vs 8.4 mo (HR = 0.69; p = .0001). PFS and OR results favored A + Ax in pts irrespective of PD-L1 expression and in all MSKCC/IMDC prognostic risk groups. OS data were immature at data cutoff (< 16% of pts with events). In A + Ax vs S arms, grade ≥3 treatment-emergent adverse events occurred in 71.2% vs 71.5% of pts and led to discontinuation of any study drug in 22.8% vs 13.4%; deaths due to study treatment toxicity occurred in 0.7% vs 0.2% of pts.

Conclusions: This randomized phase 3 trial met its primary objective of significantly improving PFS in pts with PD-L1+ aRCC treated with A + Ax vs S. PFS and OR benefit was also observed in pts irrespective of PD-L1 expression and across all prognostic risk groups. The safety profiles were consistent with those of prior studies of each drug. These results support A + Ax as a potential new 1L standard-of-care for pts with aRCC.

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Table: LBA6_PR

Pts with PD-L1+ tumors	A + Ax (N = 270)	S (N = 290)
PFS per BICR (primary endpoint) Median (95% CI), mo	13.8 (11.1, not estimable)	7.2 (5.7, 9.7)
Stratified hazard ratio (95% CI); 1-sided p value	0.61 (0.475, 0.790); p < .0001	
Confirmed objective response rate per BICR Objective response rate (95% CI), %	55.2 (49.0, 61.2)	25.5 (20.6, 30.9)
Stratified odds ratio (95% CI); 1-sided p value	3.732 (2.532, 5.371); p < .0001	
Pts irrespective of PD-L1 expression	A + Ax (N = 442)	S (N = 444)
PFS per BICR Median (95% CI), mo Stratified hazard ratio (95% CI); 1-sided p value	13.8 (11.1, not estimable) 0.69 (0.563, 0.840); p = .0001	8.4 (6.9, 11.1)
Confirmed objective response rate per BICR Objective response rate (95% CI), %	51.4 (46.6, 56.1)	25.7 (21.7, 30.0)
Stratified odds ratio (95% CI); 1-sided p value	3.098 (2.300, 4.148); p < .0001	