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

Methods: Eligible pts with clear-cell aRCC, EZOOG ≤ 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.