Pembrolizumab plus axitinib versus sunitinib as first-line therapy for advanced renal cell carcinoma (RCC): Updated analysis of KEYNOTE-426.

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Abstract Disclosures

Abstract

5001

Background: The randomized, open-label, phase 3 KEYNOTE-426 study (NCT02853331) demonstrated that pembrolizumab (pembro) + axitinib (axi) significantly improved OS, PFS, and ORR vs sunitinib as first-line therapy for advanced RCC (aRCC) at the first pre-planned interim analysis (minimum study follow-up of 7 mo). Updated analyses are presented here. **Methods:** Treatment-naive patients (pts) with clear cell aRCC, KPS ≥70%, and measurable disease (RECIST v1.1) were randomly assigned 1:1 to receive pembro 200 mg IV Q3W for up to 35 doses + axi 5 mg orally BID or sunitinib 50 mg orally QD on a 4-wk on/2-wk off schedule until progression, toxicity, or withdrawal. Randomization was stratified by IMDC risk (favorable vs intermediate vs poor) and geographic region (North America vs Western Europe vs rest of world). Primary end points were OS and PFS. Secondary end points were ORR, DOR, and safety. All *P* values are nominal. A post-hoc exploratory analysis was done to evaluate association of depth of response (maximum reduction from baseline in sum of diameters of target lesions) and OS using landmark analysis up to 6 mo after randomization. **Results:** 861 pts were randomly assigned (pembro + axi, n = 432; sunitinib, n = 429). Median (range) duration of follow-up for all pts was 27.0 mo (0.1-38.4). Pembro + axi improved OS (HR, 0.68 [95% CI, 0.55-0.85]; *P* < 0.001; 24-mo OS rate, 74% vs 66%) vs sunitinib. Median (95% CI) OS was not reached with pembro + axi and was 35.7 mo (33.3-NR) with sunitinib. Pembro + axi improved PFS (HR, 0.71 [95% CI, 0.60-0.84]; *P* < 0.001; 24-mo PFS rate, 38% vs 27%) vs sunitinib. For pembro +axi vs sunitinib respectively, median (95% CI) PFS was 15.4 (12.7-18.9) vs 11.1 mo (9.1-12.5); ORR was 60% vs 40% (*P* < 0.0001); CR rate was 9% vs 3%; and median DOR was 23.5 mo (range 1.4+ to 34.5+) vs 15.9 mo (range 2.3-31.8+). In general, the pembro + axi benefit was observed in all subgroups tested, including IMDC risk and PD-L1 expression subgroups. Post-hoc landmark analysis at 6-mo showed that pts on pembro + axi with ≥80% target lesion reduction had OS similar to that of pts with CR per RECIST v1.1 based on Kaplan-Meier curves and HR [95% CI] estimates (0.20 [0.05-0.84] vs. 0.10 [0.01-0.76], respectively) vs pts with 0-30% target lesion reduction. No new safety signals were observed. **Conclusions:** Pembro + axi continued to demonstrate superior and durable antitumor activity vs sunitinib in pts with first-line aRCC with a 27-mo median follow up; no new safety signals were observed. Clinical trial information: NCT02853331.

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