

Axitinib combination therapies versus sunitinib for renal cell carcinoma



Two phase 3 trials in patients with advanced renal cell carcinoma have shown that treatment with anti-PD-1 or PD-L1 inhibitors plus axitinib result in improved progression-free survival, compared with sunitinib alone.

In the first trial, Brian I Rini (Cleveland Clinic Taussig Cancer Institute, Cleveland, OH, USA) and colleagues randomly assigned patients to pembrolizumab (200 mg once every three weeks) plus axitinib (5 mg twice daily; n=432) or to sunitinib alone (50 mg once daily for the first four weeks of each six-week treatment cycle; n=429). The co-primary endpoints were overall survival and progression-free survival. After a median follow-up of 12.8 months (range 0.1–22.0), the estimated percentage of patients who were alive at 12 months was 89.9% (95% CI 86.4–92.4) in the pembrolizumab plus axitinib group

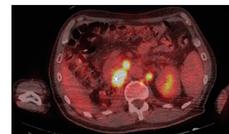
and 78.3% (73.8–82.1) in the sunitinib group. The median progression-free survival in the pembrolizumab–axitinib group was 15.1 months (95% CI 12.6–17.7) in the pembrolizumab plus axitinib group and 11.1 months in the sunitinib group (8.7–12.5).

In the second trial, Robert J Motzer (Memorial Sloan Kettering Cancer Center, New York, NY, USA) and colleagues randomly assigned patients to avelumab (10 mg/kg every two weeks) plus axitinib (5 mg twice daily; n=270) or sunitinib alone (50 mg once daily for four weeks of a six-week cycle; n=290). The co-primary endpoints were progression-free survival and overall survival in patients with PD-L1-positive tumours. Median progression-free survival was 13.8 months (95% CI, 11.1–not reached) in the avelumab plus axitinib group and 7.2 months

(5.7–9.7) in the sunitinib group (hazard ratio [HR] 0.61, 95% CI 0.47–0.79; $p < 0.001$). At median follow-up for overall survival of 11.6 months and 10.7 months, respectively, 37 (14%) of 270 patients in the avelumab plus axitinib group had died compared with 44 (15%) of 290 in the sunitinib group (HR 0.82, 95% CI 0.53–1.28; $p = 0.38$).

Bernard Escudier (Institut Gustave Roussy, Villejuif, France) said “Both studies are positive and demonstrate that overall PD-L1 or PD-L1 plus axitinib does better than sunitinib”. He added that “the big questions that remain concern the duration of biotherapy—whether we can drop one of the components after a certain period—and whether we need combination in every patient or not”.

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For the study by Motzer and colleagues see *N Engl Med J* 2019; published online Feb 16. DOI:10.1056/NEJMoa1816047