Avelumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma

RobotReviewer report

Risk of bias table

trial	design	n	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment
Motzer RJ, 2019	RCT	886	+	?	?	+

Characteristics of studies

Motzer RJ, 2019

Population	1. 15,16 Key exclusion criteria were active central nervous system metastases , autoimmune disease, and current or previous use of glucocorticoids or other immunosuppressants within 7 days before randomization. 2. Additional key inclusion criteria were the presence of at least one measurable lesion according to the Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1; age of 18 years or older; Eastern Cooperative Oncology Group (ECOG) performance-status score of 0 or 1 (on a 5-point scale in which higher numbers indicate greater disability); a fresh or archival tumor specimen; and adequate renal, cardiac, and hepatic function. 3. This phase 3 trial involving previously untreated patients with advanced renal-cell carcinoma compared avelumab plus axitinib with the standard-of-care sunitinib.
Interventio n	1. METHODS We randomly assigned patients in a 1:1 ratio to receive avelumab (10 mg per kilogram of body weight) intravenously every 2 weeks plus axitinib (5 mg) orally twice daily or sunitinib (50 mg) orally once daily for 4 weeks (6-week cycle). 2. Sunitinib was administered at a dose of 50 mg orally once daily for 4 weeks of a 6-week cycle. 3. A total of 886 patients were assigned to receive avelumab plus axitinib (442 patients) or sunitinib (444 patients).
Outcomes	1. A key secondary end point was progression-free survival in the overall population; other end points included objective response and safety. 2. Other secondary end points included progression-free survival as determined by investigator assessment, the objective response rate, adverse events, pharmacokinetic measures, tumortissue biomarkers, and patient-reported outcomes . 3. The two independent primary end points were progression-free survival and overall survival among patients with programmed death ligand 1 (PD-L1),Äìpositive tumors.

Bias	Judgement	Support for judgement
Random sequence generation	low	1. METHODS We randomly assigned patients in a 1:1 ratio to receive avelumab (10 mg per kilogram of body weight) intravenously every 2 weeks plus axitinib (5 mg) orally twice daily or sunitinib (50 mg) orally once daily for 4 weeks (6-week cycle). 2. A two-look group-sequential design with a Lan,ÄìDeMets

		(O'Brien,ÄìFleming) alpha-spending function was used to determine the efficacy boundary. 3. A total of 886 patients were assigned to receive avelumab plus axitinib (442 patients) or sunitinib (444 patients).
Allocation concealment	high/unclear	1. No assessments were performed after baseline because of early death or other reasons such as withdrawal of consent or start of new anticancer therapy (in 9 patients), stable disease less than 6 weeks after randomization (in 9 patients), or new anticancer therapy started before the first postbaseline assessment (in 2 patients), or the overall response in all assessments after baseline could not be evaluated (in 1 patient). 2. Randomization (in a 1:1 ratio) was stratified according to ECOG performancestatus score (0 vs. 1) and geographic region (United States vs. Canada and Western Europe vs. the rest of the world). 3. Tumor assessments were performed with the use of computed tomography or magnetic resonance imaging at baseline, every 6 weeks after randomization for the first 18 months, and then every 12 weeks until confirmed disease progression .
Blinding of participants and personnel	high/unclear	1. METHODS We randomly assigned patients in a 1:1 ratio to receive avelumab (10 mg per kilogram of body weight) intravenously every 2 weeks plus axitinib (5 mg) orally twice daily or sunitinib (50 mg) orally once daily for 4 weeks (6-week cycle). 2. This was a multicenter, randomized, open-label, phase 3 trial comparing avelumab plus axitinib with sunitinib. 3. The results of the interim analysis were reviewed by an external data monitoring committee on August 20, 2018.
Blinding of outcome assessment	low	1. 23 To account for the group-sequential design in this trial, the repeated confidence interval method 24 was used for the hazard ratio at the interim analysis for progression-free survival and overall survival. 2. The results of the interim analysis were reviewed by an external data monitoring committee on August 20, 2018. 3. The two independent primary end points were progression-free survival (as determined by blinded independent central review according to RECIST, version 1.1) and overall survival among patients with PD-L1,Äìpositive tumors (,â•1% of immune cells staining positive within the tumor area of the tested tissue sample).

References

1. Unable to extract citation information for file Ca renale. avelumab piu' axitinib √® meglio di solo sunitinib..pdf PMID: not found