Pembrolizumab 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
Ca renale pembrolizumab piu' axitinib √® meglio di sunitinib.pdf	RCT	861	+	+	?	+

Characteristics of studies

Ca renale pembrolizumab piu' axitinib √® meglio di sunitinib.pdf

Population	1. Me thods Patients Eligible patients were 18 years of age or older; had newly diagnosed or recurrent stage IV (according to the American Joint Commission on Cancer, seventh edition, classification) clear-cell renal-cell carcinoma; had received no previous systemic therapy for advanced disease; had a Karnofsky performance-status score of 70 or more (on a scale from 0 to 100, with lower scores indicating greater disability) 2. Patients were excluded if they had symptomatic central nervous system metastases, active autoimmune disease, or poorly controlled hypertension (systolic blood pressure ,â•150 mm Hg or diastolic blood pressure ,â•90 mm Hg), if they had had an ischemic cardiovascular event or New York Heart Association class III or IV congestive heart failure within 1 year before screening , or if they were receiving systemic immunosuppressive treatment. 3. 11 We conducted the KEYNOTE-426 trial to determine whether pembrolizumab plus axitinib would result in better outcomes than sunitinib in patients with previously untreated advanced renal-cell carcinoma.
Intervention	1. In an open-label, phase 3 trial, we randomly assigned 861 patients with previously untreated advanced clear-cell renal-cell carcinoma to receive pembrolizumab (200 mg) intravenously once every 3 weeks plus axitinib (5 mg) orally twice daily (432 patients) or sunitinib (50 mg) orally once daily for the first 4 weeks of each 6-week cycle (429 patients). 2. Axitinib was administered orally at a dose of 5 mg twice daily; the dose could be increased to 7 mg, then 10 mg, twice daily if safety criteria were met and reduced to 3 mg, then 2 mg, twice daily to manage toxic effects. 3. Sunitinib was administered orally at a dose of 50 mg daily for the first 4 weeks of each 6-week cycle; the dose could be reduced to 37.5 mg, then 25 mg, for the first 4 weeks of each 6-week cycle to manage toxic effects.
Outcomes	1. The primary end points were overall survival and progression-free survival in the intention-to-treat population. 2. The dual primary end points were overall survival and progression-free survival according to RECIST, version 1.1, as determined by blinded, independent central review.

3. expression in archival or newly obtained, formalin-fixed tumor samples was assessed at a central laboratory with the use of the PD-L1 IHC 22C3 pharmDx assay (Agilent Technologies) and was characterized according to the combined positive score, which was calculated as the number of PD-L1,Äì positive cells (tumor cells, lymphocytes, and macrophages) divided by the total number of tumor cells, multiplied by 100.

Bias	Judgement	Support for judgement
Random sequence generation	low	1. In an open-label, phase 3 trial, we randomly assigned 861 patients with previously untreated advanced clear-cell renal-cell carcinoma to receive pembrolizumab (200 mg) intravenously once every 3 weeks plus axitinib (5 mg) orally twice daily (432 patients) or sunitinib (50 mg) orally once daily for the first 4 weeks of each 6-week cycle (429 patients). 2. The stratification factors used at randomization were applied to all stratified analyses. 3. Axitinib was administered orally at a dose of 5 mg twice daily; the dose could be increased to 7 mg, then 10 mg, twice daily if safety criteria were met and reduced to 3 mg, then 2 mg, twice daily to manage toxic effects.
Allocation concealment	low	1. Randomization was stratified according to International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) risk group (favorable , intermediate, or poor risk) and geographic region (North America, Western Europe, or the rest of the world). 2. The stratification factors used at randomization were applied to all stratified analyses. 3. * Response was assessed according to Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1, by means of blinded, independent central review of radiologic imaging.
Blinding of participants and personnel	high/unclear	1. In an open-label, phase 3 trial, we randomly assigned 861 patients with previously untreated advanced clear-cell renal-cell carcinoma to receive pembrolizumab (200 mg) intravenously once every 3 weeks plus axitinib (5 mg) orally twice daily (432 patients) or sunitinib (50 mg) orally once daily for the first 4 weeks of each 6-week cycle (429 patients). 2. In this open-label, phase 3 trial, patients were randomly assigned in a 1:1 ratio to receive pembrolizumab (Keytruda, Merck Sharp & Dohme) 3. * Response was assessed according to Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1, by means of blinded, independent central review of radiologic imaging.
Blinding of outcome assessment	low	1. In an open-label, phase 3 trial, we randomly assigned 861 patients with previously untreated advanced clear-cell renal-cell carcinoma to receive pembrolizumab (200 mg) intravenously once every 3 weeks plus axitinib (5 mg) orally twice daily (432 patients) or sunitinib (50 mg) orally once daily for the first 4 weeks of each 6-week cycle (429 patients). 2. An independent data and safety monitoring committee oversaw the trial, periodically assessed safety, and assessed efficacy at the prespecified interim analysis. 3. The patients who were not assessed included those who did not have any postbaseline imaging assessments.

References

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