DSEN ABSTRACT

Assessing the potential for additive toxicity arising from the combined use of immune checkpoint inhibitors and of tyrosine kinase inhibitors

Summary

- This rapid systematic review examined the potential additive toxicity associated with combined use of immune check point inhibitors and tyrosine kinase inhibitors compared to monotherapy or standard care for individuals with renal cell or endometrial carcinoma.
- Findings are based on 8 trials and 2 cohort studies for patients with renal cell carcinoma and 2 trials for patients with endometrial carcinoma.
- We did not investigate the known benefit-risk balance of ICI/TKI combination therapies.

Key messages

- In patients with renal cell carcinoma, ICI/TKI combinations probably increase treatment-related or treatment-emergent adverse events ≥ 3 compared to TKI alone.
- In patients with endometrial carcinoma, the evidence is very uncertain about whether ICI/TKI combinations increase treatment-related or treatment-emergent adverse events ≥ 3 in endometrial carcinoma patients.

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What is the issue?

- The potential for additive toxicity arising from the combination of immune check point inhibitors (ICIs) and tyrosine kinase inhibitors (TKIs) represents a serious risk for cancer patients, who are medically vulnerable and often without access to alternate treatments. Given the availability of published evidence, there is now data to comprehensively consider this potential safety concern using a systematic review approach.

What was the aim of the study?

- The purpose of this project was to assess the additive toxicity associated with combined ICI/TKIs compared to ICI or TKI monotherapy or standard care for individuals with renal cell carcinoma or endometrial carcinoma.

How was the study conducted?

- A rapid systematic review was conducted.
- MEDLINE, EMBASE and the Cochrane Library were searched for relevant SRs, which were used to identify related primary studies. We also searched for primary studies published after the date of the last systematic review literature search.
- Titles and abstracts and potentially relevant full texts were screened by one reviewer and a second reviewer confirmed all excluded records.
- Data extraction and risk of bias (RoB) assessment were completed for primary studies by one reviewer and verified by a second reviewer. We applied the Cochrane RoB tool (v 1.0) or the Newcastle-Ottawa Scale and evaluated the certainty of evidence using GRADE.

What did the study find?

- We included 8 trials and 2 cohort studies for patients with renal cell carcinoma and 2 trials for patients with endometrial carcinoma in this review.
- In patients with renal cell carcinoma , we found an increase in both treatment-related and treatment-emergent adverse events ≥3 when ICI/TKI was compared to TKI monotherapy (moderate certainty of evidence). We found no difference in treatment-related adverse events ≥3 when ICI/TKI combinations were compared with ICI monotherapy (very low certainty of evidence).
- In patients with endometrial carcinoma, we found an increase in in both treatment-related and treatment-emergent adverse events ≥3 when ICI/TKI combinations were compared to chemotherapy (moderate certainty of evidence). We also found an increase in treatment-related adverse events ≥3 when ICI/TKI was compared to ICI monotherapy (very low certainty of evidence).

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