

Treatment-related Death in Cancer Patients Treated with Immune Checkpoint Inhibitors: A Systematic Review and Meta-analysis.

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Abstract

AIMS: We carried out a meta-analysis to determine the risk of treatment-related death associated with immune checkpoint inhibitor use in cancer patients.

MATERIALS AND METHODS: We examined data from the Medline and Google Scholar databases. We also examined original studies and review articles for cross-references. Eligible studies included randomised phase II and phase III trials of patients with cancer treated with ipilimumab, pembrolizumab, nivolumab, tremelimumab and atezolizumab. The authors extracted relevant information on participants, characteristics, treatment-related death and information on the methodology of the studies.

RESULTS: After exclusion of ineligible records, 18 clinical trials were included in the analysis. The odds ratio for treatment-related death for CTLA-4 inhibitors (ipilimumab and tremelimumab) was 1.80 (95% confidence interval 1.25, 2.59; P=0.002) and for PD-1/PD-L1 inhibitors (nivolumab, pembrolizumab and atezolizumab) was 0.63 (95% confidence interval 0.31, 1.30; P=0.22). Treated cancer seems to have no effect on the risk of treatment-related death.

CONCLUSIONS: Analysis of our data showed that CTLA-4 inhibitors (ipilimumab and tremelimumab) in a higher dose (10 mg/kg) seem to be associated with a higher risk of treatment-related death compared with control regimens, whereas PD-1/PD-L1 inhibitors (nivolumab, pembrolizumab and atezolizumab) do not cause the same risk. Clinicians have to be fully aware of these differential risks and counsel their patients appropriately.

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KEYWORDS: Atezolizumab; ipilimumab; nivolumab; pembrolizumab; treatment-related death; tremelimumab

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