

Clin Oncol (R Coll Radiol). 2016 Oct;28(10):e127-38. doi: 10.1016/j.clon.2016.06.008. Epub 2016 Jun 20.

Treatment-associated Fatigue in Cancer Patients Treated with Immune Checkpoint Inhibitors; a Systematic Review and Meta-analysis.

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Abstract

AIMS: Fatigue is one of the most prominent side-effects of immune checkpoint inhibition. Therefore, we assessed the risk of fatigue associated with inhibitors of the immune checkpoints.

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, nivolumab, pembrolizumab and tremelimumab. The authors extracted relevant information on participants' characteristics, all-grade and high-grade fatigue and information on the methodology of the studies.

RESULTS: In total, 17 trials were considered eligible for the meta-analysis. The odds ratio for all-grade fatigue for CTLA-4 inhibitors was 1.23 (95% confidence interval 1.07, 1.41; $P = 0.003$) and for high-grade fatigue was 1.72 (95% confidence interval 1.26, 2.33; $P = 0.0005$). Moreover, the odds ratio for all-grade fatigue for PD-1 inhibitors was 0.72 (95% confidence interval 0.62, 0.84; $P < 0.0001$) and for high-grade fatigue was 0.36 (95% confidence interval 0.23, 0.56; $P < 0.00001$).

CONCLUSIONS: The analysis of data showed that CTLA-4 inhibitors seem to be associated with a higher risk of all- and high-grade fatigue compared with control regimens, whereas PD-1 inhibitors seem to be associated with a lower risk of all- and high-grade fatigue compared with control regimens.

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KEYWORDS: Fatigue; ipilimumab; nivolumab; pembrolizumab; tremelimumab

PMID: 27339403 DOI: 10.1016/j.clon.2016.06.008

[Indexed for MEDLINE]

