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RECEIVED 01 September 2023  
ACCEPTED 07 November 2023  
PUBLISHED 01 December 2023

CITATION  
Zhang Y, Huang C and Li S (2023) Influence of treatment-related lymphopenia on the efficacy of immune checkpoint inhibitors in lung cancer: a meta-analysis. *Front. Oncol.* 13:1287555. doi: 10.3389/fonc.2023.1287555

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# Influence of treatment-related lymphopenia on the efficacy of immune checkpoint inhibitors in lung cancer: a meta-analysis

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**Background:** Treatment-related lymphopenia (TRL) is common in patients with lung cancer, particularly in those with radiotherapy. However, the influence of TRL on the efficacy of immune checkpoint inhibitors (ICIs) for patients with lung cancer remains poorly understood. We performed a systematic review and meta-analysis to investigate the influence of TRL on survival of lung cancer patients on ICIs.

**Methods:** In order to accomplish the aim of the meta-analysis, a comprehensive search was conducted on databases including PubMed, Embase, Cochrane Library, and the Web of Science to identify observational studies with longitudinal follow-up. The Cochrane Q test was employed to evaluate heterogeneity among the included studies, while the  $I^2$  statistic was estimated. Random-effects models were utilized to merge the results, considering the potential impact of heterogeneity.

**Results:** Ten cohort studies with 1130 lung cancer patients who were treated with ICIs were included. Among them, 427 (37.8%) had TRL. Pooled results showed that compared to patients without TRL, patients with TRL were associated with poor progression-free survival (hazard ratio [HR]: 2.05, 95% confidence interval [CI]: 1.62 to 2.60,  $p < 0.001$ ;  $I^2 = 22\%$ ) and overall survival (HR: 2.69, 95% CI: 2.10 to 3.43,  $p < 0.001$ ;  $I^2 = 0\%$ ). Sensitivity analysis limited to patients with non-small cell lung cancer showed similar results (HR: 2.66 and 2.62, both  $p < 0.05$ ). Moreover, subgroup analyses according to the diagnostic criteria of TRL, regression analysis model (univariate or multivariate), and indications of ICIs (for locally advanced or advanced lung cancer) showed consistent results ( $p$  for subgroup difference all  $> 0.05$ ).

**Conclusion:** TRL was associated with poor survival of lung cancer patients who were treated with ICIs.

## KEYWORDS

lung cancer, lymphopenia, immunotherapy, survival, meta-analysis

# Lymphopenia Treatment Manual Guide

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