INPLASY

Efficacy and safety of PD-1/PD-L1 and CTLA-4 immune checkpoint inhibitors in the treatment of advanced hepatocellular carcinoma :a systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - No financial support.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 October 2025 and was last updated on 14 October 2025.

INTRODUCTION

Review question / Objective The aim of this study is to investigate the efficacy and safety of PD-1/ PD-L1 inhibitors combined with ctla-4 inhibitors in the treatment of advanced hepatocellular carcinoma.

Condition being studied Hepatocellular carcinoma (HCC), the most prevalent subtype of primary liver cancer, constitutes 75% to 85% of all cases. A major clinical challenge lies in its tendency to be detected at advanced stages—a critical factor contributing to dismal survival prospects. Specifically, the 5-year survival rate for patients with advanced HCC is documented to be less than 5%.

METHODS

Participant or population People with advanced hepatocellular carcinoma.

Intervention PD-1/PD-L1 and CTLA-4 inhibitors combination therapy.

Comparator The efficacy and safety of PD-1/PD-L1 and CTLA-4 immune checkpoint inhibitors in the treatment of advanced hepatocellular carcinoma.

Study designs to be included Prospective and retrospective trials.

Eligibility criteria Trials were included if the following criteria were met (1):patients with advanced hepatocellular carcinoma aged 18 years or older were enrolled; (2):a PD-1/PD-L1 and CTLA-4 inhibitors with or without other standard treatments was given to one of the study arms; and(3):outcomes of interest in terms of efficacy (i.e.overall survival [OS],progression-free survival[PFS], objective response rate [ORR], diseasecontrol rate [DCR],and safety (i.e. treatment-related adverse events (TRAEs) and ≥ grade 3 TRAEs were reported.

Information sources Pubmed、Embase 、The Cochrane Library.

Main outcome(s) Median overall survival [mOS],median progression-free survival [mPFS], objective response rate[ORR], disease control rate [DCR],TRAEs and ≥ grade 3TRAEs.

Quality assessment / Risk of bias analysis The quality of each study was meticulously evaluated using the methodological index for non-randomized studies (MINORS).

Strategy of data synthesis We use STATA 18.0 version. A random-effect model was applied if obvious heterogeneity was present (I2 >50%), otherwise, a fixed-effect model was chosen.

Subgroup analysis We consider a subgroups analysis,by region, sample size, research scale,research methods , number of treatment lines and whether to combine other treatment therapies.

Sensitivity analysis Stata software sensitivity analysis, by deleting one after effect of changes to reflect the sensitive of the article.

Country(ies) involved China.

Keywords Advanced hepatocellular carcinoma、PD-1/PD-L1 、CTLA-4、Immune checkpoint inhibitors.

Contributions of each author

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