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Immune checkpoint inhibitors combined with targeted agents for the first-line treatment of advanced unresectable hepatocellular carcinoma: a systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - None.

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 02 April 2024 and was last updated on 02 April 2024.

INTRODUCTION

Review question / Objective A meta-analysis of studies evaluating the selection of superior treatment options and effectiveness of immune checkpoint inhibitors (ICIS) combined with targeted agents for the first-line treatment of advanced hepatocellular carcinoma (HCC) in populations with different characteristics.

Condition being studied Liver cancer is the fifth most common cancer worldwide and the fourth leading cause of cancer-related deaths.Most of the patients have already been diagnosed with advanced hepatocellular carcinoma at the time of the initial diagnosis, and the optimal therapies, such as surgical resection and radiofrequency ablation, are lost, so that the prognosis of HCC patients is not good. The combination of ICIs with targeted drug therapy is a breakthrough combination.

METHODS

Participant or population Patients diagnosed with unresectable HCC who have not received systemic therapy, with no restrictions onrace, age, gender and so on.

Intervention Patients in the combination therapy group were treated with targeted drugs and ICIs (for the combinationtherapy group).

Comparator Patients in the monotherapy group were treated with targeted drugs alone (for the monotherapy group).

Study designs to be included Randomized controlled clinical research trials.

Eligibility criteria Exclusion criteria: (1) Repeated publications or duplication of data in multiple publications; those with incomplete, unavailable, or inaccessible data in full text; (2) Dissertations, conference papers, systematic evaluations,

reviews, and case reports involving non-clinical trial outcome literature; (3) Clinical trials with unclear interventions in the combined treatment group, non-randomized controlled trials, and retrospective studies; and (4) Previous systemic treatment with other regimens and not first-line treatment patients.

Information sources China National Knowledge Infrastructure (CNKI), WanFang Data, China Science and Technology Journal Database (VIP database), China Clinical Trials Registry, PubMed, ClinicalTrails.gov and the Cochrane Library were searched up to April 24, 2023.

Main outcome(s) Overall survival (OS), progression-free survival (PFS), objective response rate (ORR), disease control rate(DCR).

Additional outcome(s) Any grades treatment-related adverse events (TRAEs) and grade≥3 TAREs.

Quality assessment / Risk of bias analysis The risk of bias assessment tool recommended by the Cochrane Handbook for Systematic Evaluators 5.1.0 was used to evaluate the included RCTs.

Strategy of data synthesis Data were extracted and organized using EXCEL, and meta-analysis was performed using RevMan5.4.1 software, and for the counted data were analyzed using risk ratio (RR), hazard ratio (HR) and their 95% Ci confidence intervals for statistical analysis.

Subgroup analysis Sources of heterogeneity among studies were explored by subgroup analysis and sensitivity analysis. Combined with the results of previous published articles, this paper conducted subgroup analyses in terms of previously unexplored or partially explored aspects, the choice of different treatment regimens, adverse events of hypertension, whether or not they had received previous topical treatment and serum alpha-fetoprotein (AFP) levels, and ranked them for comparison by RR values.

Sensitivity analysis The heterogeneity of the study in each group was analyzed using the X2 test and the I2 test. If there was no statistical heterogeneity between groups (P≥0.1,I2≤50%), the fixed-effect model was used for meta-analysis; if there was statistical heterogeneity between groups (P50%), the random-effect model was selected for meta-analysis. If the heterogeneity was significant, the literature with heterogeneity and the reasons for it were analyzed by excluding the literature one by one, and comparing whether there was any difference in the analysis results before and after the exclusion. Sensitivity analysis was performed using RevMan5.4.1, and forest plots were drawn for the outcome indicators for meta-analysis.

Country(ies) involved CHINA.

Keywords Hepatocellular carcinoma, Immune checkpoint inhibitors, targeted agents.

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