Efficacy and Safety of Chemo-Immunotherapy Regimes for Recurrent or Metastatic Nasopharyngeal Carcinoma: A Network Meta-Analysis and Cost-Effectiveness Analysis

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Review question / Objective: Our study were designed by PICOS principles, listing as follows: (1) P: patients diagnosed with recurrent or metastatic nasopharyngeal carcinoma; (2)I: chemo-immunotherapy; (3) C: placebo plus chemotherapy, comparing the efficacy, safety and cost-effectiveness between the experimental and the control group; (4) O: studies reported one of the following outcomes: progression-free survival (PFS), objective response rate (ORR), overall survival (OS), probability of grade 3 adverse events, quality-adjusted life-years (QALYs), and incremental cost-effectiveness ratios (ICERs); (5) S: RCTs (Randomized controlled trials).

Information sources: PubMed, Embase, the Cochrane Library and Web of Science will be searched, with no limits for language. Search date will range from inception to May 30, 2023. Relevant articles were also extracted manually from the references of retrieved publications.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 01 May 2023 and was last updated on 01 May 2023 (registration number INPLASY202350006).
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**Condition being studied:** Recurrent or metastatic nasopharyngeal carcinoma.

**METHODS**

**Participant or population:** Patients diagnosed with recurrent or metastatic nasopharyngeal carcinoma.

**Intervention:** Toripalimab plus gemcitabine plus platinum, camrelizumab plus gemcitabine plus platinum, tislelizumab plus gemcitabine plus platinum, etc.

**Comparator:** Placebo plus gemcitabine plus platinum.

**Study designs to be included:** Randomized controlled trials will be included.

**Eligibility criteria:** The exclusion criteria as follows: (1) patients with locally advanced nasopharyngeal carcinoma; (2) efficacy was not evaluated in the experimental and control groups; (3) single arms, reviews, case reports, letters, comments etc; (4) studies lacking relevant statistics.

**Information sources:** PubMed, Embase, the Cochrane Library and Web of Science will be searched, with no limits for language. Search date will range from inception to May 30, 2023. Relevant articles were also extracted manually from the references of retrieved publications.

**Main outcome(s):** Progression-free survival (PFS).

**Additional outcome(s):** Objective response rate (ORR), overall survival (OS), probability of grade ≥3 adverse events, quality-adjusted life-years (QALYs) and incremental cost-effectiveness ratios (ICERs).

**Quality assessment / Risk of bias analysis:** The risk of bias assessment for the included articles will be done by two reviewers independently by using the Cochrane risk-of-bias tool for randomized trials and using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) for cost-effectiveness studies.

**Strategy of data synthesis:** RevMan version 5.4 software and R version 4.2.3 will be used for a meta-analysis of the data. The I² test will be used to test the heterogeneity between the results. I² >50% and p<0.1 were considered to be heterogeneous, and a random-effects model was selected in the presence of heterogeneity; otherwise, a fixed-effects model was selected. Hazard ratio (HR) was selected as the effect indicator to pool survival statistics, based on the method published by Tierney et al (2007). If HR can not extracted directly from eligible articles, Engauge Digitizer software will be used to extract relevant information. Odd ratio (OR) was selected as the effect indicator to probability of grade ≥3 adverse events and objective response rate (ORR). Drug prices were obtained through Menet and calculated as a weighted average of each drug's market share. The prices of laboratory tests and imaging examinations were obtained through the hospital's system. Treatment strategies were obtained by searching the literature, and we consulted additional clinical experts for problems that could not be solved.

**Subgroup analysis:** None.

**Sensitivity analysis:** For pooled outcomes with significant heterogeneity, sensitivity analyses were performed to explore the potential effect of heterogeneity by eliminating studies that did not use propensity scoring matching.

**Country(ies) involved:** China.

**Keywords:** recurrent or metastatic nasopharyngeal carcinoma; toripalimab; camrelizumab; tislelizumab; gemcitabine and cisplatin; chemo-immunotherapy; cost-effectiveness.
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