INPLASY PROTOCOL

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The authors have no conflicts of interest to disclose.

Immunotherapy vs platinum for advanced or metastatic thymic carcinoma: A systematic review and meta-analysis protocol

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Review question / Objective: **Thymic carcinoma is a rare malignancy, and platinum-based chemotherapy has not previously been established as a standard treatment for advanced or metastatic thymic carcinoma. With the breakthrough and progress of immunotherapy, the possibility of curing thymic carcinoma has greatly increased. Some clinical trials have reported that compared with traditional platinum-based chemotherapy, the use of programmed death 1 and programmed death ligand 1 inhibitors alone can benefit patients and effectively prolong their overall survival. We compare the efficacy of single immunotherapy with traditional platinum-based chemotherapy in a systematic review and meta-analysis to provide a reliable basis for clinicians.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 November 2020 and was last updated on 15 November 2020 (registration number INPLASY2020110060).

INTRODUCTION

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single immunotherapy with traditional platinum-based chemotherapy in a systematic review and meta-analysis to provide a reliable basis for clinicians.

Rationale: Thymic carcinoma is a rare malignancy, and platinum-based chemotherapy has not previously been established as a standard treatment for advanced or metastatic thymic carcinoma. With the breakthrough and progress of immunotherapy, the possibility of curing thymic carcinoma has greatly increased. Some clinical trials have reported that compared with traditional platinum-based chemotherapy, the use of programmed death 1 and programmed death ligand 1 inhibitors alone can benefit patients and effectively prolong their overall survival. We compare the efficacy of single immunotherapy with traditional platinum-based chemotherapy in a systematic review and meta-analysis to provide a reliable basis for clinicians.

Condition being studied: Thymic cancer is a rare malignant disease with an incidence rate of approximately 0.02 per 100,000 person-years. About 30% of patients have advanced to advanced stages at the time of diagnosis. Patients with advanced or metastatic thymic cancer have a poor prognosis. In this case, cytotoxic chemotherapy has been used to prolong patient prognosis. Some retrospective studies and phase 2 clinical trials have been completed to investigate the efficacy of cytotoxic drugs, immune checkpoint inhibitors, and molecular targeted drugs. On the basis of these research results, platinum-based chemotherapy has received attention[9,10]. However, standard second-line treatment for advanced or metastatic thymic carcinoma patients previously treated with platinum-based chemotherapy has not yet been established. Immunotherapy is a relatively new field in the treatment of thymic carcinoma. Some clinical trials reported that PD-1 and PD-L1 inhibitors alone have better application prospects than platinum-based chemotherapy. We will conducted a systematic review and meta analysis on the efficacy comparison between immunotherapy and traditional platinum-based chemotherapy, so as to provide a reliable basis for further promotion of immunotherapy and for clinicians to formulate the best chemotherapy regimen for patients with advanced or metastatic thymic carcinoma.

METHODS

Search strategy: We will use the relevant keywords or subject terms adhered to Medical Subject Heading (MeSH) terms to search for eligible studies in the electronic databases which were mentioned above without language restrictions.

Participant or population: The participants will be adults diagnosed with advanced or metastatic thymic carcinoma histologically or cytologically confirmed who were treated with platinum-based chemotherapy, or immunotherapy. No restrictions on ethnicity, sex, education, and economic status will be applied.

Intervention: According to the means of postoperative chemotherapy for patients with advanced or metastatic thymic carcinoma, the trials included will be divided into the following categories. · immunotherapy versus molecular targeted therapy · immunotherapy versus anti-angiogenic agents · postoperative platinum-base chemotherapy versus molecular targeted therapy · platinum-based chemotherapy versus anti-angiogenic agents · platinum-based chemotherapy versus immunotherapy.

Comparator: Randomised controlled trials (RCTs) and quasi-RCTs published or unpublished will be included, which have been completed and compared postoperative platinum-base chemotherapy versus immunotherapy for patients with advanced or metastatic thymic carcinoma.

Study designs to be included: Randomised controlled trials (RCTs) and quasi-RCTs published or unpublished will be included, which have been completed and compared postoperative platinum-base chemo-

therapy versus immunotherapy for patients with advanced or metastatic thymic carcinoma.

Eligibility criteria: 1. Types of studies Randomised controlled trials (RCTs) and quasi-RCTs published or unpublished will be included, which have been completed and compared postoperative platinum-base chemotherapy versus immunotherapy for patients with advanced or metastatic thymic carcinoma. 3.1.2. Types of participants The participants will be adults diagnosed with advanced or metastatic thymic carcinoma histologically or cytologically confirmed who were treated with platinum-based chemotherapy, or immunotherapy. No restrictions on ethnicity, sex, education, and economic status will be applied. 3.1.3. Types of interventions According to the means of postoperative chemotherapy for patients with advanced or metastatic thymic carcinoma, the trials included will be divided into the following categories. · immunotherapy versus molecular targeted therapy · immunotherapy versus anti-angiogenic agents · postoperative platinum-base chemotherapy versus molecular targeted therapy · platinum-based chemotherapy versus anti-angiogenic agents · platinum-based chemotherapy versus immunotherapy.

Information sources: We will search Pubmed (Medline), Embase, Google Scholar, Cancerlit, and the Cochrane Central Register of Controlled Trials for related studies published before March 1, 2021 without language restrictions.

Main outcome(s): The primary outcomes will be postoperative overall survival of patients with advanced or metastatic thymic carcinoma who were treated with chemotherapy.

Additional outcome(s): We will assess the 5-year survival, median survival, recurrence-free survival, quality of life, and adverse events or complications of patients with advanced or metastatic thymic carcinoma who were treated with chemotherapy.

Data management: We will utilize the measures described in the Cochrane Handbook for Systematic Reviews of Interventions to pool the evidence.

Quality assessment / Risk of bias analysis: Two authors (JKQ, ZWT) will use the Cochrane Handbook for Systematic Reviews of Interventions to assess the risk of bias of each study included independently based on the following ranges: random sequence generation (selection bias); allocation concealment (selection bias); blinding of participants and personnel (performance bias); blinding of outcome assessment (detection bias); incomplete outcome data (attrition bias); selective outcome reporting(reporting bias); other bias[19]. Each domain will be assessed as high, low or uncertain risk of bias. The results and details of assessment will be reported on the risk of bias graph.

Strategy of data synthesis: The data will be synthesised by Review Manager 5.3 software. We will conduct a systematic review and meta-analysis only if the data gathered from included trials are judged to be similar enough to ensure a result that is meaningful. The Chi2 test and I2 statistic will be used to assess statistical heterogeneity among the trials included in matched pairs comparison for standard meta-analysis. The random effect model will be applied to analyse the data, if there is substantial heterogeneity (p50%) and the trials will be regarded to be obvious heterogeneous. Otherwise, we will utilize fixed effect model to analyse the data. Mantel-Haenszel method will be adopted to pool of the binary data. The results will be reported in the form of relative risk (RR) between 95% confidence interval (CI) of the date. The continuous data will be pooled by inverse variance analysis method and the results will be shown in the form of standardized mean difference (SMD) with 95% confidence interval (CI) of the date. 3.6.1 Subgroup analysis If there is high heterogeneity (I2 statistic>50%) and the data are sufficient, subgroup analysis will be conducted to search potential causes of heterogeneity. Subgroup analysis will be performed in different methods of

postoperative adjuvant therapy, ethnicity, history of smoking, tumor stage, and type of operation.

Subgroup analysis: If there is high heterogeneity (I2 statistic>50%) and the data are sufficient, subgroup analysis will be conducted to search potential causes of heterogeneity. Subgroup analysis will be performed in different methods of postoperative adjuvant therapy, ethnicity, history of smoking, tumor stage, and type of operation.

Sensibility analysis: Sensitivity analysis will be conducted to assess the reliability and robustness of the aggregation results via eliminating trials with high bias risk.

Language: None restriction.

Country(ies) involved: China.

Keywords: Thymic carcinoma; immunotherapy; platinum-based chemotherapy.

Contributions of each author:

Author 1 - Jiekun Qian - drafted the manuscript.
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