INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Clinical efficacy and safety of Chinese herb injections combination with Docetaxel combined with cisplatin (DP) chemotherapy for advanced non-small cell lung cancer: A protocol for Bayesian network meta-Analysis

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Review question / Objective: **The aim of this study will to be assess the clinical efficacy and safety of different Chinese herb injections(CHIS) combined with Docetaxel combined with cisplatin (DP) chemotherapy for advanced non-small cell lung cancer and to provide evidence for rational selection of CHIs by using network meta-analysis.**

Information sources: **Eight public domain electronic databases will be systematically searched with a time frame of build to May 2022. The databases are as follows: PubMed, Cochrane Library, Embase, Web of Science, Chinese National Knowledge Infrastructure, WanFang database, China Biology Medicine Database and Chongqing VIP Chinese Scientific Journals Full-text Database. Searches will be performed using the following keywords: herbal injections and (lung cancer or lung malignancy or NSCLC) and platinum-based chemotherapy. We will modify the search strategy to accommodate all databases. The language of articles is limited to Chinese and English.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 September 2022 and was last updated on 17 September 2022 (registration number INPLASY202290081).

INTRODUCTION

Review question / Objective: **The aim of this study will to be assess the clinical efficacy and safety of different Chinese herb injections(CHIS) combined with Docetaxel combined with cisplatin (DP) chemotherapy for advanced non-small cell lung cancer and to provide evidence for rational selection of CHIs by using network meta-analysis.**

Condition being studied: **Lung cancer is the most common cause of cancer death**

worldwide. Among lung cancer patients, NSCLC is diagnosed in approximately 85% of patients, with lung adenocarcinoma (LUAD) and lung squamous cell carcinoma (LUSC) being the most common subtypes. Approximately two-thirds of NSCLC cases have progressed to stage III/IV at the time of diagnosis. Platinum-based chemotherapy (PBC) is still the recommended treatment for NSCLC patients with advanced disease progression and metastasis, but platinum-based chemotherapy-related adverse reactions seriously reduce the quality of life of patients. Docetaxel combined with cisplatin (DP) chemotherapy is one of the most effective regimens for the treatment of NSCLC. Docetaxel is a semi-synthetic taxa, and its mechanism of action is basically the same as paclitaxel. In the cell proliferation cycle, it can promote the assembly of tubulin into microtubules, induce the formation of non-functional microtubules and make them unable to depolymerize, thus inhibiting the proliferation of tumor cells and playing an anti-tumor role. Docetaxel was twice as active as paclitaxel and did not change the number of protofilaments. Cisplatin is considered one of the most important drugs in the treatment of NSCLC. The effective rate of single drug is 16%-20%. The DP chemotherapy has certain advantages, but myelosuppression is the main toxic side effect of it, and some patients often cannot be treated successfully due to severe myelosuppression, immune dysfunction, liver and kidney function damage, gastrointestinal reactions, etc. Traditional Chinese medicine has certain advantages in improving the quality of life of patients. A variety of traditional Chinese medicine injections are widely used in clinical practice in combination with platinum chemotherapy drugs. A large number of clinical studies have shown that the combination of TCM injections and chemotherapy regimens plays a certain role in enhancing efficacy and attenuating toxicity, with good safety. At present, there is still a lack of evidence-based support for multiple TCM injections combined with DP chemotherapy, and the clinical promotion of TCM injections is difficult, which limits its application.

METHODS

Participant or population: Patients with stage III-IV NSCLC were diagnosed by pathological or cytological examination. Gender, race, age, economic and educational status were not restricted. Patients did not receive any concomitant radiotherapy, non-DP chemotherapy, or herbal therapy in this study.

Intervention: In the experimental group, the DP chemotherapy was combined with at least one herbal injection. There were no restrictions on the type, dose, duration of chemotherapy drugs or herbal injections. Patients in the control group received only DP chemotherapy.

Comparator: We will compare the efficacy and safety of CHIS combined with DP chemotherapy versus DP chemotherapy alone.

Study designs to be included: We will plan to include only randomized controlled trials (RCTs) comparing the efficacy and safety of CHIS in combination with DP chemotherapy and DP chemotherapy alone for the treatment of advanced NSCLC. Studies will be excluded if data are not available by contacting the authors.

Eligibility criteria: Only RCTS were included in this study to compare the efficacy and safety of TCM injection combined with DP chemotherapy and DP chemotherapy alone in the treatment of advanced NSCLC. Patients must be cytologically or pathologically proven to have NSCLC. In the experimental group, the DP chemotherapy should be combined with at least one CHIS.

Information sources: Eight public domain electronic databases will be systematically searched with a time frame of build to May 2022. The databases are as follows: PubMed, Cochrane Library, Embase, Web of Science, Chinese National Knowledge Infrastructure, WanFang database, China

Biology Medicine Database and Chongqing VIP Chinese Scientific Journals Full-text Database. Searches will be performed using the following keywords: herbal injections and (lung cancer or lung malignancy or NSCLC) and platinum-based chemotherapy. We will modify the search strategy to accommodate all databases. The language of articles is limited to Chinese and English.

Main outcome(s): The primary outcome include the effect of antitumor therapy. These include objective response rate (ORR), disease control rate (DCR).

Additional outcome(s): Additional outcomes will include safety and quality of life outcomes. These include indicators of bone marrow suppression, gastrointestinal symptoms, indicators of abnormal liver and kidney function, and Karnofsky scores.

Quality assessment / Risk of bias analysis: The risk of bias for each included study will be assessed by using the Cochrane Risk of Bias (RoB) tool for randomised controlled trials. Seven domains will be assessed in terms of selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias. The methodological quality of the included RCTs will be assessed independently by 2 researchers, and if there will be disagreement between the two researchers, we will resolve the inconsistency through discussion or with the help of senior researchers.

Strategy of data synthesis: The direct Meta-analysis and Bayesian Network Meta-analysis will be performed using ADDIS 1.16. 8 software, in which the odds ratio (OR) and 95% confi-dence interval (CI) will be used for the direct Meta-analysis, and the $\chi 2$ test combined with I2 will be used to determine the size of heterogeneity. I2 ≤ 50% indicates less heterogeneity between studies and comparative studies can be performed, while I2 > 50% indicates greater heterogeneity between studies and further sensitivity analysis will be performed. The OR and 95% CI will be used to express the outcome effect size in Bayesian Network Meta-analysis. For studies that could generate node split nodes, the node split model will be used to compare the consistency between direct and indirect comparisons, and P>0.05 indicated good consistency, and the consistency model will be used for analysis, otherwise he inconsistency model will be used for the opposite. The study of ungenerated node split nodes will be analyzed using the consistency model. For all studies using the consistency model, the stability and reliability of the results should be tested by the incon- sistency model. If inconsistency factors can be generated and the 95% CI includes 0, and in-consistency standard deviation 95% CI includes 1, the consistency model results can be considered stable and reliable, otherwise the inconsis- tency model will be used for analysis. The poten-tial scale reduction factor (PSRF) will be applied to all models to determine the convergence of the results. If the PSRF is between 1. 00 and 1. 05, the convergence of the iterative effect is good and the model is stable and reliable. Otherwise, we will use Extend button to iterate more parameters until the PSRF is between 1. 00 and 1. 05. Additionally, network evidence maps will be drawn using Stata 14.0 software.

Subgroup analysis: If heterogeneity is high, we will perform a subgroup analysis.

Sensitivity analysis: Sensitivity analyses for the primary outcome measures will be performed based on the number of included samples, year of study publication, dose of drug intervention, or duration of intervention to verify the robustness of the direct meta-analysis results. For outcome measures with more than 10 included studies, funnel plots were drawn to assess small sample effects or publication bias.

Country(ies) involved: China.

Keywords: Chinese herb injection, Docetaxel combined with cisplatin chemotherapy, non-small cell lung cancer, Protocol, Network meta-analysis.

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