INPLASY PROTOCOL

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None declared.

Clinical efficacy and safety of NSCLC ancillary treatment with compound Kushen injection through immunocompetence regulation: A systematic review and meta-analysis

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Review question / Objective: **The purpose of study is to systematically evaluate the clinical efficacy and safety of non-small cell lung cancer (NSCLC) treatment using a combination of compound Kushen Injection (CKI) and platinum-based chemotherapy (PBC) by modulating the immune function.**
Condition being studied: **Lung cancer is a disease with exceedingly high mortalityand is the leading cause of cancer-related deaths worldwide. Approximately 85% of lung cancer patients are diagnosed with non-small cell lung cancer. The five-year survival rate of early lung cancer patients is 80%–90%, while that of terminal cancer patients is less than 5%. For patients with early lung cancer, postoperative ancillary treatment following radical surgery is necessary to prolong disease-free survival and total survival time. However, this is not applicable for terminal lung cancer patients who have missed the optimal operation time, targeted treatment, and immune treatment, where only chemotherapy and local radiotherapy can be performed. In recent years, the role of traditional Chinese medicine (TCM) in lung cancer treatment has been steadily acknowledged. Compound Kushen injection (CKI) is a Chinese patented medicine that improves the immunity level of cancer patients and inhibits the proliferation and metastasis of tumor cells. Clinically, Compound Kushen injection (CKI) is frequently used in combination with platinum-based chemotherapy (PBC) to treat non-small cell lung cancer (NSCLC).**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 08 June 2022 and was last updated on 08 June 2022 (registration number INPLASY202260032).

INTRODUCTION

Review question / Objective: **The purpose of study is to systematically evaluate the clinical efficacy and safety of non-small cell lung cancer (NSCLC) treatment using a combination of compound Kushen Injection (CKI) and platinum-based chemotherapy (PBC) by modulating the immune function.**

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METHODS

Search strategy: English databases such as PubMed, Cochrane Library, and EMbase and Chinese databases such as SinoMed, CNKI, Wanfang Data, and VIP were searched. The cutoff date was November 2021. The search mode was theme words and free words. Index words included lung cancer, pulmonary carcinoma, non-small cell lung cancer, NSCLC, RTC, randomized clinical trial, Compound Kushen Injection, CKI, and corresponding Chinese words were used for the online search. For example, in PubMed, "Compound Kushen Injection OR CKI") AND {(Lung cancer[MeSH]) OR ("pulmonary cancer" OR "carcinoma"[Text Word])} were used.

Participant or population: Paitients who were pathologically or cytologically diagnosed as non-small cell lung cancer,age ≥18 years old, sex and race were not limited. No major diseases such as heart, liver, kidney, etc.

Intervention: The group of interventions was treated with a combination of compound Kushen Injection and platinum-based chemotherapy.

Comparator: The comparative intervention was treated with platinum-based chemotherapy alone.

Study designs to be included: Randomized controlled trials (RCT).

Eligibility criteria: Inclusion criteria: (1) This type of research is an RCT; (2) RCT using compound Kushen Injection combined with platinum-based chemotherapy to treat non-small cell lung cancer. Exclusion criteria: (1) Non-RCTs including conference reports, review literature, animal tests, and theoretical experience; (2) studies with inconsistent baseline data; (3) incomplete data; (4) duplicated data or in-extractable studies; (5) experimental group treated with other medicines and Chinese medicines other than the combination of CKI and PBC; (6) and studies with fatal error were excluded from the systemic analysis.

Information sources: We searched the English and Chinese databases, for example, PubMed, Cochrane Library, SinoMed, China National Knowledeg Infrastructure (CNKI), Wanfang Data, and Technology Periodical Database (VIP). RCTs were searched from their inception to November 2021.

Main outcome(s): The key outcome indicators include the objective response rate (ORR), composed of the complete response (CR) and partial response (PR); disease control rate (DCR), which comprises CR, PR, and stable disease(DR), CD3+T cells, CD4+ T cells, CD8+ T cells, and CD4+ /CD8+ T cell ratio.

Additional outcome(s): The additional outcome indicators include natural killer cells, immunoglobulins (IgA, IgM, and IgM), adverse reactions that include a reduction

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in blood platelet and white blood cells, neutropenia, gastrointestinal response, marrow inhibition, impaired liver and kidney function, and QOL.

Quality assessment / Risk of bias analysis: Two researchers first archived the preliminarily filtered literature, extracted data independently, and then cross-checked them. In case of disagreement, a third researcher will be consulted. The included studies were evaluated using the Cochrane bias risk assessment tool. The contents under assessment include the method of random allocation, allocation concealment, blind assessment of research outcome, integrity of outcome, report bias, and other biases. The low, medial, and uncertain bias risks of the forgoing entries were determined. A diagram of the results was prepared using Review Manager 5.4 software.

Strategy of data synthesis: Research data were analyzed using the RevMan software. Binary variables and continuous variables were demonstrated by relative risk (RR), mean difference, or standardized mean difference (SMD), respectively. RR and 95% confidence intervals (95%CI) were used to indicate the effect indicators of each research result. I2 was used for the heterogeneity tests. A fixed effects model was used when I2 was very low ($P \geq 0.1$, $I2 \leq 50\%$). A random effects model was used when heterogeneity was significant ($P \leq 0.1$, $I2 > 50\%$). When more than 10 studies were included, the forest plot and funnel plot were used to test publication bias. Test sequential assay was used to evaluate the stability of results so as to exclude the effects of poor quality and underestimate or overestimate experiments on results; and a meta-regression analysis was used to examine the effects of heterogeneity and other confounding factors on the results.

Subgroup analysis: Subgroup analysis model was used to test the heterogeneity and to explain the effects of different variables on the research results. We conducted a subgroup analysis of different chemotherapeutic cycles and chemotherapeutic strategies.

Sensitivity analysis: The sensitivity assay was used to evaluate the stability of results so as to exclude the effects of poor quality and underestimate or overestimate experiments on results. To ensure the reliability and stability if the results, we conducted a sensitivity analysis to assess the impact of studies with a high risk of bias.

Language: No language restrictions.

Country(ies) involved: China.

Keywords: compound kushen injection, NSCLC, immunocompetence, chemotherapy, traditional Chinese medicine, Meta-analysis.

Contributions of each author:

Author 1 - Dan Wang - Author 1 searched the database, evaluated studies for inclusion, extracted data, and then cross-checked with Author 4. Author 3 and Author 1 assisted in literature retrieval and data analysis.
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