



## Can Aidi injection improve overall survival in patients with non-small cell lung cancer? A systematic review and meta-analysis of 25 randomized controlled trials



Zheng Xiao<sup>a,b,\*,1</sup>, Chengqiong Wang<sup>a,b</sup>, Rui Zhou<sup>g</sup>, Shanshan Hu<sup>e</sup>, Nian Yi<sup>g</sup>, Jihong Feng<sup>c,\*,1</sup>, Minghua Zhou<sup>a</sup>, Shiyu Liu<sup>a</sup>, Ling Chen<sup>a,b</sup>, Jie Ding<sup>h</sup>, Qihai Gong<sup>d</sup>, Fushan Tang<sup>d</sup>, Xiaofei Li<sup>f</sup>

<sup>a</sup> Evidence-Based Medicine Center, MOE Virtual Research Center of Evidence-based Medicine at Zunyi Medical College, Affiliated Hospital of Zunyi Medical College, Zunyi 563003, Guizhou, China

<sup>b</sup> Department of Respiratory Medicine (Center for Evidence-Based and Translational Medicine of major infectious diseases), Affiliated Hospital of Zunyi Medical College, Zunyi 563003, Guizhou, China

<sup>c</sup> Department of Oncology, Affiliated Hospital of Zunyi Medical College, Zunyi 563003, Guizhou, China

<sup>d</sup> School of Pharmacy, Zunyi Medical College, Zunyi 563003, Guizhou, China

<sup>e</sup> GCP Center, Affiliated Hospital of Zunyi Medical College, Zunyi 563003, Guizhou, China

<sup>f</sup> Guizhou Provincial College-based Key Lab for Tumor Prevention and Treatment with Distinctive Medicines, Zunyi Medical College, Zunyi 563003, Guizhou, China

<sup>g</sup> Grade 2013 Students, Department of Public Health, Zunyi Medical College, Zunyi 563003, Guizhou, China

<sup>h</sup> Outpatient Department of Psychological Counseling Clinic, Affiliated Hospital of Zunyi Medical College, Zunyi 563003, Guizhou, China

### ARTICLE INFO

#### Keywords:

Aidi injection  
Non-small-cell lung cancer (NSCLC)  
Overall survival  
Randomized controlled trial(RCT)  
Meta-analysis

### ABSTRACT

**Objectives:** Aidi injection can significantly improve clinical response and reduce radiochemotherapy related toxicity. Can Aidi injection improve the survival in *non-small-cell lung cancer (NSCLC)*? Therefore, to further reveal it, we systematically evaluated all related studies.

**Methods:** We collected all studies about Aidi injection for NSCLC in Medline, Embase, Web of Science(ISI), China National Knowledge Infrastructure Database(CNKI), Chinese Scientific Journals Full-Text Database(VIP), Wanfang, China Biological Medicine Database (CBM), Cochrane Central Register of Controlled Trials (CENTRAL), Chinese clinical trial registry (Chi-CTR) and WHO International Clinical Trials Registry Platform (WHO-ICTRP), and US-clinical trials (established to June 2016). We evaluated their quality according to the Cochrane evaluation handbook of randomized controlled trials (RCTs) (5.1.0), extracted data following the PICO principles, and synthesized the data by meta-analysis.

**Results:** We included 25 RCTs involving 2662 patients with NSCLC which most studies had unclear risk of bias. The merged risk ratios (RR) values and their 95% CI of meta-analysis for objective response rate (ORR) and disease control rate (DCR) were as following: 1.19(1.09–1.29) and 1.07(1.03–1.11). The merged RR values and their 95% CI of meta-analysis for the 1-, 2- and 3-year overall survival (OS) rate were as following: 1.23(1.14–1.33), 1.46(1.22–1.74) and 1.67(1.04–2.69). All differences were statistically significant. Subgroup analysis showed that Aidi injection plus different therapies had different effects on 1-, 2- and 3-year OS rate. Sensitivity analysis showed that the RR of ORR, DCR, 1- and 2- year OS rate had good stability, and 3-year OS rate had poor stability.

**Conclusions:** Available evidences indicate that Aidi injection can significantly improve the clinical response and

**Abbreviations:** BACE, bronchial arterial chemoembolization; CBM, China biological medicine database; CNKI, China national knowledge infrastructure database; CENTRAL, Cochrane Central Register of Controlled Trials; Chi-CTR, Chinese clinical trial registry; DCR, disease control rate; DO, docetaxel and oxaliplatin; DL, docetaxel and lobaplatin; DP, docetaxel and cisplatin; GCb, gemcitabine and carboplatin; GO, gemcitabine and oxaliplatin; GP, gemcitabine and cisplatin; IL-2, Interleukin-2; MST, median survival; NP, Navelbine and cisplatin; NSCLC, non-small-cell lung carcinoma; ORR, objective response rate; OS rate, overall survival rate; PFS, progression free survival; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines; QOL, quality of life; RCTs, randomized controlled trials; RD, risk difference; RECIST, Response Evaluation Criteria in Solid Tumors; RT, radiotherapy; SR, system review; TP, paclitaxel and cisplatin; VIP, Chinese Scientific Journals Full-Text Database; WHO, World Health Organization; WHO-ICTRP, WHO International Clinical Trials Registry Platform

\* Corresponding author at: Evidence-Based Medicine Center, MOE Virtual Research Center of Evidence-based Medicine at Zunyi Medical College, Affiliated Hospital of Zunyi Medical College, Zunyi 563003, Guizhou Province, China.

\*\* Corresponding author.

E-mail addresses: [zy426f@163.com](mailto:zy426f@163.com) (Z. Xiao), [jh\\_f@163.com](mailto:jh_f@163.com) (J. Feng).

<sup>1</sup> Contributed equally.

<https://doi.org/10.1016/j.ctim.2018.01.011>

Received 8 August 2017; Received in revised form 27 December 2017; Accepted 19 January 2018

Available online 31 January 2018

0965-2299/© 2018 Elsevier Ltd. All rights reserved.

OS rates in patients with NSCLC and especially, the 1- and 2-year OS rate. But, Aidi injection plus different therapies had different effects on overall survival. It is still unclear whether Aidi injection can improve the PFS and HR.

## 1. Background

Lung cancer is the leading cause of cancer-related mortality in both more and less developed countries with 5-years survival rate of only 15%.<sup>1,2</sup> About 80% are *non-small-cell lung cancer (NSCLC)*.<sup>3</sup> To date, surgery is the first choice, but most clinically diagnosed patients are inoperable, and forced to accept radiochemotherapy. However, radiochemotherapy-related toxicity becomes an important obstacle to improving long-term survival and quality of life.<sup>4–10</sup> Therefore, finding new ways to reduce the toxicity and improve the survival becomes a key issue.

Aidi injection (Z52020236, China Food and Drug Administration) is a Cantharis and Astragalus-based Chinese herbs injection in China. Aidi injection belongs to compound preparation, which is composed by the extracts of Cantharis, Astragalus, santicosus Eleutherococcus and Ginseng. Previous meta-analysis<sup>11–13</sup> had shown that Aidi injection plus chemotherapy could significantly increase the clinical response and improve the quality of life(QOL) in patients with NSCLC. Aidi injection could also reduce the hematotoxicity and gastrointestinal toxicity. Our meta analysis<sup>14</sup> that Aidi injection plus radiotherapy could significantly improve the clinical efficacy and QOL in patients with lung cancer. It could reduce the myelosuppression, radiation pneumonitis, and radiation esophagitis. All results revealed that Aidi injection could increase the clinical response and reduce the radiochemotherapy related toxicity. But, can Aidi injection improve the long-term survival in NSCLC? Many studies<sup>15–19</sup> had shown that Aidi injection might increase the overall survival in NSCLC patients, but conclusions were different in different studies with lower sample size. Up to now, there is lack of strong evidence to prove it. Therefore, to further reveal it *real long-term survival in NSCLC*, we systematically evaluated all related studies.

## 2. Methods

This article followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Ethical approval was not required, as our study is a meta-analysis of published or ongoing studies.

### 2.1. Inclusion and exclusion criteria

Included studies must meet the following criteria. The disease was diagnosed as *non-small-cell lung cancer (NSCLC)* by histopathological and cytological diagnostic criteria. We included all randomized controlled trials (RCTs). The experimental group was treated with Aidi injection and the control group was non-Aidi injection. Tumor response was evaluated with ORR and DCR. Long-term survival was evaluated with overall survival (OS) and progression free survival (PFS). No restrictions were set on the duration of follow-ups and types of settings.

Excluded studies must meet the following criteria: (1) duplicates, (2) irrelevant studies involving in-vitro, animal, and/or conditions such as cantharidinate, other Chinese herbs, other tumors, without survival report, (3) case control study, cohort study and case report study, (4) meeting abstracts, reviews, SR and meta-analysis without report overall survival (OS) and progression free survival (PFS).

### 2.2. Search strategy

Two reviewers (Chengqiong Wang and Rui Zhou) independently searched records in electronic databases using the search strategy (cantharidin OR aidi OR Aidi injection OR Sodium cantharidate OR

Norcantharidate OR SCNT OR DSNC OR Norcantharidin OR NCTD OR dimethyl cantharidate) AND (“Lung Neoplasms”[Mesh] OR Lung Cancer OR Lung Cancers OR NSCLC OR Non small cell lung cancer OR Pulmonary Neoplasms OR Lung Neoplasm OR Pulmonary Neoplasm OR Pulmonary Cancer OR Pulmonary Cancers OR Lung carcinoma OR Pulmonary carcinoma). Published studies were retrieved from Medline, Embase, Web of Science(ESI), China National Knowledge Infrastructure Database(CNKI), Chinese Scientific Journals Full-Text Database(VIP), Wanfang Database, China Biological Medicine Database (CBM) and Cochrane Central Register of Controlled Trials (CENTRAL) (established to June 2016). Ongoing studies were retrieved in Chinese clinical trial registry (Chi-CTR, <http://www.chictr.org.cn>), WHO International Clinical Trials Registry Platform (WHO-ICTRP, <http://apps.who.int/trialsearch/>), and US-clinical trials (<https://clinicaltrials.gov/>), established to June 2016). All retrievals were implemented by Mesh and free word. No language restrictions were placed on the search. Finally, we rigorously evaluated the relevant systematic review (SR) or meta-analysis, all studies meeting inclusion criteria were selected from the references.

### 2.3. Selection of studies

Two reviewers (Nian Yi and Shiyu Liu) independently selected studies according to the inclusion and exclusion criteria. Any disagreements were resolved by discussion with each other or with Zheng Xiao.

### 2.4. Quality assessment

Two reviewers (Chengqiong Wang and Shanshan Hu) independently evaluated the risk of methodological bias of all included-studies according to the Cochrane evaluation handbook of RCTs (5.1.0).<sup>20</sup> Any disagreements were resolved by discussion with each other or with Zheng Xiao. The bias parameters were the random sequence generation, the allocation concealment, the blinding of participants, personnel, and outcome assessment, the loss to follow-up, the selective reporting and the other bias. We judged each item on three levels (“Yes” for low bias, “No” for a high risk of bias, and “Unclear”). Then, we assessed the studies and categorized them into three levels: low risk of bias (Low risk of bias for all key domains), high risk of bias (High risk of bias for one or more key domains) and unclear risk of bias (Low or unclear risk of bias for all key domains).

### 2.5. Outcome measures

Primary outcomes was the long-term survival including 1-, 2-, and 3-year overall survival (OS) rate, progression free survival (PFS), hazard ratio (HR) of OS or PFS. Secondary outcomes was clinical response using objective response rate (ORR) and disease control rate (DCR) according to the World Health Organization (WHO) guidelines<sup>21</sup> for solid tumor responses or Response Evaluation Criteria in Solid Tumors(RECIST).<sup>22</sup>

### 2.6. Data extraction

Two reviewers (Minghua Zhou and Rui Zhou) independently selected potential studies according to the eligibility criteria and extracted data in a standard data extraction form. Any disagreements were resolved by discussion or by consulting a third author (Zheng Xiao). The collected data included the cases of Aidi injection or Non-Aidi injection groups, demographic characteristics, clinical and

Download English Version:

<https://daneshyari.com/en/article/8563414>

Download Persian Version:

<https://daneshyari.com/article/8563414>

[Daneshyari.com](https://daneshyari.com)