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ORIGINAL ARTICLE

Astragalus-containing Traditional Chinese Medicine, with and without prescription based on syndrome differentiation, combined with chemotherapy for advanced non-small-cell lung cancer: a systemic review and meta-analysis

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ABSTRACT

Objective Traditional Chinese Medicine (TCM) is used in China as part of the treatment for non-small-cell lung cancer (NSCLC) and often includes prescription of herbal therapy based on syndrome differentiation. Studies of various *Astragalus*-based Chinese medicines combined with platinum-based chemotherapy in the treatment of lung cancer are popular in East Asia, particularly in China. The aim of the present study was to perform a systematic review and meta-analysis comparing platinum-based chemotherapy alone with platinum-based chemotherapy plus *Astragalus*-based Chinese botanicals, with and without prescription based on syndrome differentiation, as first-line treatment for advanced NSCLC.

Methods We searched the Chinese Biomedical Literature database, the China National Knowledge Internet, the VIP Chinese Science and Technology Periodicals Database, PubMed, EMBASE, the Cochrane databases, and abstracts presented at meetings of the American Society of Clinical Oncology, the World Conference on Lung Cancer, the European Society for Medical Oncology, and the Chinese Society of Clinical Oncology for all eligible studies. Endpoints were overall survival; 1-year, 2-year, and 3-year survival rates; performance status; overall response rate; and grade 3 or 4 adverse events. Subgroup analyses based on herbal formulae individualized using syndrome differentiation or on oral or injection patent medicines were performed using the Stata software application (version 11.0: StataCorp LP, College Station, TX, U.S.A.) and a fixed-effects or random-effects model in case of heterogeneity. Results are expressed as a hazard ratio (HR) or relative risk (RR), with corresponding 95% confidence intervals (CIs).

Results Seventeen randomized studies with scores on the Jadad quality scale of 2 or more, representing 1552 patients, met the inclusion criteria. Compared with platinum-based chemotherapy alone, the addition of *Astragalus*-based TCM to chemotherapy was associated with significantly increased overall survival (HR: 0.61; 95% CI: 0.42 to 0.89; $p = 0.011$); 1-year (RR: 0.73; 95% CI: 0.65 to 0.82; $p < 0.001$), 2-year (RR: 0.3344; 95% CI: 0.237 to 0.4773; $p < 0.001$), and 3-year survival rates (RR: 0.30; 95% CI: 0.17 to 0.53; $p < 0.001$); performance status (RR: 0.43; 95% CI: 0.34 to 0.55; $p < 0.001$); and tumour overall response rate (RR: 0.7982; 95% CI: 0.715 to 0.89; $p < 0.001$). Subgroup analyses indicated that *Astragalus* herbal formulae given based on syndrome differentiation were more effective than *Astragalus*-based oral and injection patent medicines. Side effects—including anemia, neutropenia, thrombocytopenia, fatigue, poor appetite, nausea, and vomiting—were significantly more frequent with platinum-based chemotherapy alone than when platinum-based chemotherapy was combined with *Astragalus*-based TCM.

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Conclusions *Astragalus*-based Chinese botanical therapy, especially when based on syndrome differentiation, is associated with increased efficacy of platinum-based chemotherapy and decreased platinum-derived toxicities for patients with advanced NSCLC.

Key Words *Astragalus,* TCM, chemotherapy, advanced non-small-cell lung cancer

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INTRODUCTION

Cancers of the lung and bronchus are the most common causes of cancer death. The overall 5-year survival rate (SR) for patients with non-small-cell lung cancer (NSCLC) is about 17.1%. Among NSCLC patients, those with advanced-stage disease are treated with standard therapies such as chemotherapy alone (20%), radiation therapy alone (17%), or a combination of the two (35%)[1–3]. All such therapies have both high toxicity and limited efficacy.

East Asian populations, particularly those in China, commonly use herbal medicines [Traditional Chinese Medicine (TCM)] combined with chemotherapy in an effort to reduce toxicity and preserve the highest possible quality of life in lung cancer. Of particular interest in this respect is the herb *Astragalus membranaceus*. A retrospective review[4] demonstrated that patients with NSCLC who used Chinese herbal formulae alone could live for more than 2 years with their disease. That study found that *A. membranaceus* was an ingredient in 172 of the 200 analyzed Chinese herbal formulae. *In vitro* analysis has shown that *Astragalus* increases resistance to the immunosuppressive effects of chemotherapy drugs and stimulates macrophages to produce interleukin-6 and tumour necrosis factor[5,6].

Syndrome differentiation is the process of comprehensively analyzing clinical information obtained using the 4 main diagnostic TCM procedures: observation, listening, questioning, and pulse analyses. Syndromes can include yin, yang, exterior, interior, cold, heat, deficiency, and excess. Syndrome differentiation is used to guide the choice of TCM treatment with acupuncture and herbal formulae. Otherwise, because of convenience, oral and injection patent medicines containing chemicals extracted from Chinese herbs are also widely and empirically used by Chinese families and hospitals without a formal TCM clinical evaluation for specific syndrome differentiation[7].

A number of randomized controlled trials have evaluated various *Astragalus*-based Chinese medicines combined with platinum-based chemotherapy in the treatment of lung cancer. A meta-analysis by McCullough and colleagues[8] found that *Astragalus*-based Chinese herbal medicine can increase the effectiveness of platinum-based chemotherapy. However, an updated comprehensive review of TCM in the treatment of advanced NSCLC has yet to be performed. In the present study, we systematically evaluated the results of selected randomized controlled trials to elucidate whether TCM treatment based on syndrome differentiation is more effective than *Astragalus*-based therapy without such a formal evaluation.

METHODS

Search Strategy

We searched the PubMed (1966 to March 2014), EMBASE (1974 to March 2014), Chinese Biomedical Literature (1978 to March 2014), China National Knowledge Internet (1979 to March 2014), and Cochrane (1988 to March 2014) databases for relevant articles, using the key words non-small-cell lung cancer, NSCLC, *Astragalus* or Chinese herb, first line, and carboplatin- or cisplatin-based chemotherapy. We also searched papers and abstracts presented at American Society of Clinical Oncology (to 2014), World Congress of Lung Cancer (to 2014), European Society of Medical Oncology (to 2014), and Chinese Society of Clinical Oncology (to 2014) meetings.

Eligibility Criteria

Relevant clinical trials were manually selected when they met these criteria:

- Study patients had NSCLC previously untreated by chemotherapy alone
- The study was a comparison of platinum-based chemotherapy alone or with *Astragalus*-based herbal therapy (with or without TCM syndrome differentiation) in the first line
- The study had sufficient data, especially survival data, for extraction
- The study scored 2 or better on the Jadad quality scale

Systematic reviews and meta-analysis were excluded.

Date Extraction and Validity Assessment

Data extracted from eligible articles for analysis had to include the overall survival (OS) rate[9]; the 1-year, 2-year, 3-year SRs; performance status (PS); overall response rate (ORR); and percentage of patients experiencing grades 3 and 4 toxicities. We also extracted basic data in the form of the first author's name, the year of publication, lung cancer stages, and number of patients. The screening and review were performed by 2 independent reviewers searching the literature and extracting data independently. Mismatches between reviewers were resolved by consensus after a 3rd check and discussion between the reviewers[10].

Statistical Analysis

Outcomes considered were the 1-, 2-, and 3-year SRs; Karnofsky PS; ORR; and significant adverse events. Relative risk (RR) estimates were calculated using the Stata software

application (version 11.0: StataCorp LP, College Station, TX, U.S.A.)[11]. Subgroup analyses based on heterogeneity between trials used the chi-square–based Q statistic and were considered statistically significant at a p value less than 0.05 or I^2 greater than 50%[12]. In the presence of heterogeneity, data were analyzed in a random-effects model; otherwise, a fixed-effects model was used. A statistical test resulting in a p value less than 0.05 was considered to indicate a statistically significant difference. A RR less than 1 reflected a favourable response, SR (1-, 2-, or 3-year), or toxicity in the TCM plus chemotherapy arm.

Publication bias was evaluated using Begg funnel plots, which examine associations between effect estimates and their variances ($p > 0.05$ indicates no correlation between studies) and Egger tests, which are more specific[13,14]. All p values were 2-sided. All confidence intervals (CIS) had a 2-sided probability coverage of 95%.

RESULTS

Study Selection

The initial search, performed in March 2014, found 372 articles. Titles and abstracts were screened, and 178 articles were excluded because they did not meet the inclusion criteria; the remaining 194 full-text articles were reviewed for inclusion. Subsequently, 142 articles were excluded because of a lack of sufficient survival data for extraction, and 34 articles were excluded because of inferior quality[15]. In the end, seventeen clinical trials (1552 patients) reported in full-text publication were eligible. One clinical trial was designed to use *Astragalus* alone combined with chemotherapy; the other sixteen were designed to use TCM containing *Astragalus* as the principal drug together with chemotherapy. The quantitative 5-point Jadad scale was used to assess the quality of the included trials (Figure 1, Table I).

It is important to note that, in the included studies, *Astragalus*-based herbal formulae were developed based on syndrome differentiation and were prescribed by an authoritative and experienced chief physician, with the herbal dosages being based on the Chinese pharmacopoeia.

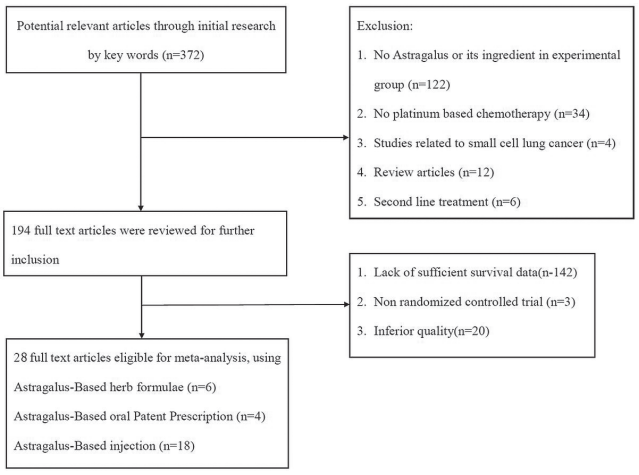

FIGURE 1 Flow chart of article selection for the meta-analysis. Seventeen studies involving 1552 patients were analyzed.

Once the diagnosis is made, the appropriate formula is prescribed and decocted (Chinese drug decoction has 3 steps: soaking, decocting, and concentrating). The formula is given twice daily. For patent oral and injection medicines, use must be based on the manufacturer's instructions; administration is not based on syndrome differentiation.

Publication Bias

Neither the Begg funnel plot ($p = 0.591$ for ORR) nor the Egger test ($p = 0.089$ for 1-year SR; $p = 0.383$ for 2-year SR; $p = 0.113$ for PS; $p = 0.075$ for ORR) revealed any obvious asymmetry in the included trials.

ORR

Five of the included trials (549 patients) reported OS. Pooled HR for OS favoured the combination of an *Astragalus*-based formula with chemotherapy over chemotherapy alone (HR: 0.61; 95% CI: 0.42 to 0.89; $p = 0.011$). Subgroup analyses showed that the OS was significantly improved in the arms using an *Astragalus*-based herbal formula (HR: 0.40; 95% CI: 0.26 to 0.61; $p < 0.001$), but not in those using an *Astragalus*-based injection (HR: 0.80; 95% CI: 0.59 to 1.10; $p = 0.169$; Figure 2).

One-Year SR

Fourteen trials (1409 patients) reported 1-year SRS. Using a fixed-effects model, the pooled RR for 1-year SR favoured the combination of an *Astragalus*-based product and chemotherapy over chemotherapy alone (RR: 0.73; 95% CI: 0.65 to 0.82; $p < 0.001$). Subgroup analysis showed that the 1-year SR was slightly improved by *Astragalus*-based oral patent medicines (RR: 0.80; 95% CI: 0.65 to 0.97; $p = 0.025$), but more so by *Astragalus*-based herbal formulae based on syndrome differentiation [RR: 0.56; 95% CI: 0.46 to 0.70; $p < 0.001$; Figure 3(A)]. However, *Astragalus*-based injection was not associated with an improved 1-year SR (RR: 0.87; 95% CI: 0.71 to 0.106; $p = 0.159$).

Two-Year SR

Five trials (533 patients) reported 2-year SRS. Using a fixed-effects model, the pooled RR for 2-year SR favoured the combination of an *Astragalus*-based product and chemotherapy over chemotherapy alone (RR: 0.33; 95% CI: 0.23 to 0.47; $p < 0.001$). Subgroup analyses showed that the 2-year SR was slightly improved with an *Astragalus*-based injection (RR: 0.56; 95% CI: 0.36 to 0.87; $p = 0.01$) and significantly improved with *Astragalus*-based herbal formulae [RR: 0.20; 95% CI: 0.11 to 0.36; $p < 0.001$; Figure 3(B)].

Three-Year SR

Three trials (360 patients) reported 3-year SRS. Using a fixed-effects model, the pooled RR for 3-year SR favoured the combination of an *Astragalus*-based product and chemotherapy over chemotherapy alone (RR: 0.30; 95% CI: 0.17 to 0.53; $p < 0.001$). Subgroup analyses were not available because of limited data [Figure 3(C)].

Karnofsky PS

Eight trials reported Karnofsky PS data. Using a fixed-effects model, the pooled RR for PS favoured the combination of an *Astragalus*-based product and chemotherapy

TABLE I Characteristics of seventeen published clinical trials included in the meta-analysis

Reference	TNM stage	Pts (*n*)	Study arm	Median OS	Survival rate (%)			ORR (%)	Karnofsky PS	Jadad score
					1-Year	2-Year	3-Year			
Liu *et al.*, 1997[16]	II,	52	Mitomycin–doxorubicin–cisplatin	NA	67.7	47.7	NA	NA	25	3
	III,		plus Jifukang Oral Solution[a]							
	IV	25	vs. mitomycin–doxorubicin–cisplatin	NA	40	0	NA	NA	8	
Liu *et al.*, 2001[17]	II,	80	Mitomycin–doxorubicin–cisplatin	12.1	71.9	46.4	29.2	87.5	32.5	2
	III,		plus *Astragalus*-based formulae							
	IV	64	vs. mitomycin–doxorubicin–cisplatin	8.3	37.6	13.7	9.8	71.8	9.4	
Liu *et al.*, 2004[18]	III,	48	Hydroxycamptothecin–etoposide–platinum	10.5	56.5	NA	NA	43.5	NA	3
	IV		plus Bo Er Ning capsules[b]							
		38	vs. hydroxycamptothecin–etoposide–platinum	7.3	11.6	NA	NA	35.3	NA	
Luo *et al.*, 2005[19]	III,	36	Vinorelbine–cisplatin plus Aidi injection[c]	NA	NA	NA	NA	52.8	NA	2
	IV	36	vs. vinorelbine–cisplatin	NA	NA	NA	NA	36.1	NA	
Lv *et al.*, 2005[20]	III,	48	Doxorubicin–cyclophosphamide–cisplatin	20	87.5	56.3	33.3	75	NA	2
	IV		plus Aidi injection[c]							
		48	vs. doxorubicin–cyclophosphamide–cisplatin	8	60.4	29.2	12.5	47	NA	
Luo *et al.*, 2006[21]	IIIB,	25	Paclitaxel–cisplatin	10.2	47	NA	NA	48	36	2
	IV		plus *shenqi fuzheng* injection[b]							
		25	vs. paclitaxel–cisplatin	9.3	41	NA	NA	40	16	
Luo *et al.*, 2007[22]	IIIB,	30	Paclitaxel–cisplatin	NA	71.5	NA	NA	60	60	2
	IV		plus *shenqi fuzheng* injection[b]							
		30	vs. paclitaxel–cisplatin	NA	52.6	NA	NA	50	16.7	
Fan *et al.*, 2008[23]	IIIB,	26	Vinorelbine–cisplatin plus Aidi injection[c]	10.7	42	NA	NA	46	NA	2
	IV	26	vs. vinorelbine–cisplatin	9.4	38	NA	NA	42	NA	
Xu *et al.*, 2008[24]	IIIB,	49	Vinorelbine–cisplatin plus Aidi injection[c]	11.6	47	22	NA	38.8	NA	3
	IV	47	vs. vinorelbine–cisplatin	10.1	42	15	NA	31.9	NA	
Zhang *et al.*, 2008[25]	IIIB,	41	Gemcitabine–cisplatin plus Aidi injection[c]	NA	64.1	NA	NA	48.8	79.5	3
	IV	37	vs. gemcitabine–cisplatin	NA	37.1	NA	NA	40.5	42.9	
Zhang *et al.*, 2009[26]	III,	30	Docetaxel–cisplatin	NA	73.3	NA	NA	60	18	2
	IV		plus Zhen Qi Fu Zheng capsules[d]							
		28	vs. docetaxel–cisplatin	NA	53.6	NA	NA	50	4	
Zhao *et al.*, 2009[27]	IIIB,	43	Vinorelbine–cisplatin plus Aidi injection[c]	10.5	NA	NA	NA	55.8	55.1	2
	IV	40	vs. vinorelbine–cisplatin	9.7	NA	NA	NA	47.5	34.2	
Xu *et al.*, 2010[28]	III,	62	Vinorelbine–cisplatin or	14.5	54.8	24.6	13.2	28.3	NA	3
	IV		gemcitabine–cisplatin or							
			mitomycin C–vinblastine–cisplatin							
			plus *Astragalus*-based formulae							
		58	vs. vinorelbine–cisplatin or	11	35.6	3.7	0	18.2	NA	
			gemcitabine–cisplatin or							
			mitomycin C–vinblastine–cisplatin							
Yang *et al.*, 2010[29]	IIIB,	30	Gemcitabine–cisplatin plus *kangai* injection[e]	NA	NA	NA	NA	33.3	63.3	2
	IV	30	vs. gemcitabine–cisplatin	NA	NA	NA	NA	30	36.7	
Chen *et al.*, 2012[30]	IIIB,	42	Gemcitabine–cisplatin	NA	33.3	NA	NA	57.1	NA	2
	IV		plus Zhen Qi Fu Zheng capsules[d]							
		42	vs. gemcitabine–cisplatin	NA	31	NA	NA	52.4	NA	

TABLE I Continued

Reference	TNM stage	Pts (*n*)	Study arm	Median OS (months)	Survival rate (%)			ORR (%)	Karnofsky PS (%)	Jadad score
					1-Year	2-Year	3-Year			
Guo *et al.,* 2012[31,g]	III,	68	Vinorelbine–cisplatin plus *Astragalus* injection	10.7	32.4	NA	NA	42.6	NA	3
	IV	68	vs. vinorelbine–cisplatin	10.2	35.3	NA	NA	36.8	NA	
Xie *et al.,* 2012[32]	III,	102	Gemcitabine–cisplatin	NA	54.5	NA	NA	NA	NA	4
	IV		plus *Astragalus*-based formulae							
		98	vs. gemcitabine–cisplatin	NA	34.1	NA	NA	NA	NA	

[a] Jinfukang Pharmaceutical, Jilin, P.R.C.
[b] Livzon Pharmaceutical Group, Guangdong, P.R.C.
[c] Guizhou Yibai Pharmaceutical, Guizhou, P.R.C.
[d] Fuzheng Pharmaceutical Co. Ltd, Gansu, P.R.C.
[e] Changbaishan Pharmaceutical, Jilin, P.R.C.
[g] Traditional Chinese Medicine containing *Astragalus* only.
Pts = patients; OS = overall survival; ORR = overall response rate; PS = performance status; NA = not applicable.

over chemotherapy alone (RR: 0.43; 95% CI: 0.34 to 0.55; $p < 0.001$). Subgroup analyses showed that PS was significantly improved with the use of an *Astragalus*-based patent medicine (RR: 0.24; 95% CI: 0.09 to 0.62; $p = 0.003$), an *Astragalus*-based herbal formula based on syndrome differentiation (RR: 0.30; 95% CI: 0.15 to 0.61; $p = 0.001$), and the *Astragalus*-based injection (RR: 0.51; 95% CI: 0.40 to 0.66; $p < 0.001$; Figure 4).

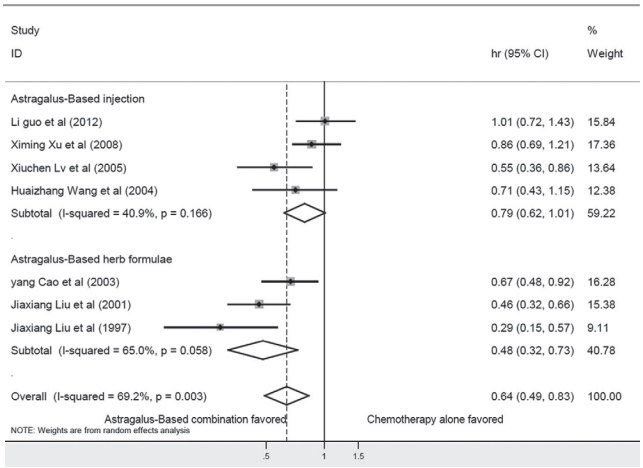

FIGURE 2 Forest plot of overall survival after treatment with *Astragalus* and platinum-based chemotherapy compared with platinum-based chemotherapy alone. Subgroups consider oral and injection herbal formulas containing *Astragalus.* hr = hazard ratio; CI = confidence interval.

Tumour ORR

The Response Evaluation Criteria in Solid Tumors defines tumour ORR as the sum of the partial and complete response rates. Twenty-six trials included ORR data. Using a fixed-effects model, the pooled ORR data significant in favoured the combination of an *Astragalus*-based product and chemotherapy over chemotherapy alone (RR: 0.79; 95% CI: 0.71 to 0.89; $p < 0.001$). In addition, the subgroup analyses showed that the tumour ORR was significantly improved with the *Astragalus*-based herbal formulae based on syndrome differentiation (RR: 0.75; 95% CI: 0.62 to 0.90; $p = 0.002$) and with the *Astragalus*-based injection (RR: 0.80; 95% CI: 0.68 to 0.93; $p = 0.004$), but not with the *Astragalus*-based oral patent medicines (RR: 0.85; 95% CI: 0.65 to 1.11; $p = 0.234$).

Safety

Adverse events were evaluated using the U.S. National Cancer Institute's *Common Toxicity Criteria,* version 2, or its *Common Terminology Criteria for Adverse Events* (version 3). Fourteen trials reported grades 3 and 4 toxicities. Compared with the combination of an *Astragalus*-based product and platinum-based chemotherapy, platinum-based chemotherapy alone was associated with more toxicities (anemia, neutropenia, thrombocytopenia, fatigue, poor appetite, nausea, vomiting; Table II).

DISCUSSION

The present study reviewed seventeen clinical trials reported in full-text publication and comprising 1552 patients. The combination of an *Astragalus*-based product and chemotherapy was associated with significant increases in OS, 1-year SR, 2-year SR, 3-year SR, PS, and tumour ORR. Notably, side effects including anemia, neutropenia, thrombocytopenia, fatigue, poor appetite, nausea, and vomiting were significantly more frequent with platinum-based chemotherapy alone than with the combination of an *Astragalus*-based product and chemotherapy.

Astragalus occupies an important place in the TCM system. It has been used for almost all diseases caused by *chi* deficiency, which is associated with cellular immune dysfunction. *Chi* is understood to be the vital energy that maintains blood circulation, warms the body, and fights diseases. In cancer patients, *chi* deficiency is the most common symptom according to the concept of TCM. Symptoms of *chi* deficiency include fatigue, lack of appetite, and depression[33].

Our meta-analysis demonstrates the potential clinical efficacy of *Astragalus*-based TCM combined with platinum-based chemotherapy in the treatment of advanced NSCLC. Treatment based on syndrome differentiation is a characteristic of TCM diagnosis and treatment. Herbal formulae prescribed by syndrome differentiation can be different

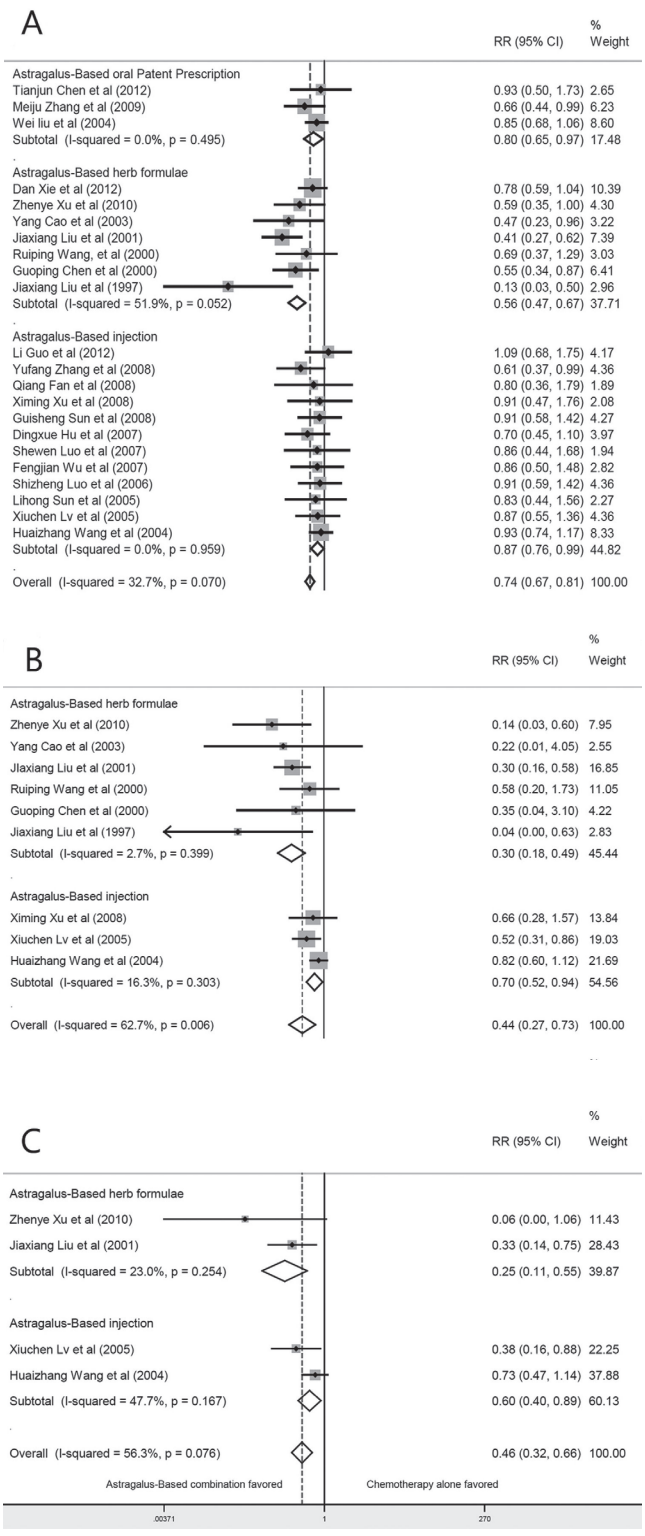

FIGURE 3 Meta-analyses (forest plots) of the seventeen studies assessing survival rates after treatment with *Astragalus* and platinum-based chemotherapy compared with platinum-based chemotherapy alone in non-small-cell lung cancer. (A) 1-Year survival. (B) 2-Year survival. (C) 3-Year survival. Subgroups consider oral use of the herb, of a prescribed *Astragalus*-based patent medicine, or of *Astragalus*-based injections. RR = relative risk; CI = confidence interval.

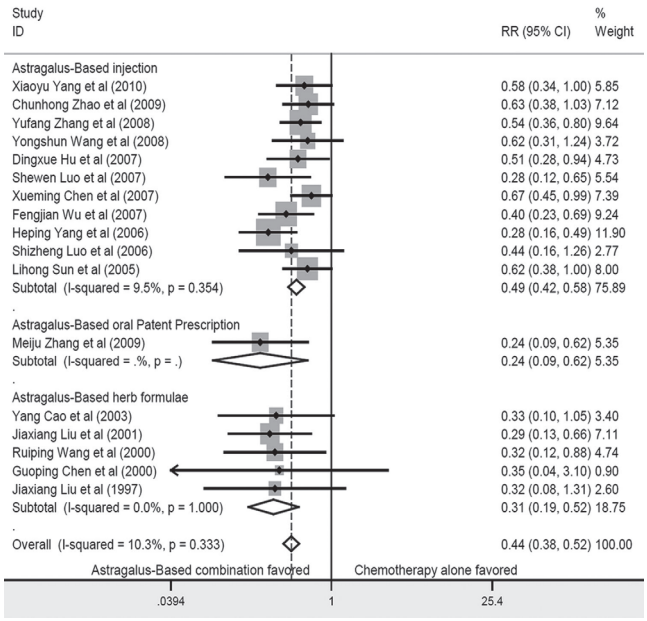

FIGURE 4 Forest plot of improvement in performance status after treatment with *Astragalus* and platinum-based chemotherapy compared with platinum-based chemotherapy alone. Subgroups consider oral use of the herb, of a prescribed *Astragalus*-based patent medicine, or of *Astragalus*-based injections. RR = relative risk; CI = confidence interval.

for each patient, as is typical of TCM. In the TCM system, patients are prescribed botanicals based on specific individual variations. Chinese patent medicines and injections generally consist of extracted and condensed elements of herbs in the form of pills, capsules, electuaries, or injectable liquids[34]; they are not based on individual syndrome differentiation. Our study is hypothesis-generating, in that, compared with *Astragalus*-based oral and injection patent medicines, *Astragalus*-containing herbal formulae based on syndrome differentiation were associated with enhanced efficacy and tolerability of platinum-based chemotherapy in patients with NSCLC.

Several limitations have to be considered when interpreting our results. First, the data extracted from the included publications were not individual patient data; they did not include tumour molecular analysis; and no single TCM provider evaluated all patients. A meta-analysis based on individual patient data, with their associated molecular, clinical, and pathologic findings, would allow for a more firm conclusion. Second, none of the herbal formulae or TCM practices used in the included studies are specific or reproducible. The study populations were limited to East Asian patients, and the results require replication in other patients from varied backgrounds. Additional high-quality, controlled, and reproducible randomized controlled trials are warranted; the results reported here should be seen as hypothesis-generating only.

CONCLUSIONS

The relatively low success rates in the treatment of advanced and metastatic NSCLC have prompted the scientific

TABLE II Adverse events[a] (grades 3 and 4) reported in seventeen published clinical trials included in the meta-analysis

Adverse event	Trials (*n*)	Patients (*n* events/total population) by trial arm		Heterogeneity		RR	95% CI	*p* Value[b]
		Chemotherapy with *Astragalus*-based therapy	Chemotherapy alone	*p* Value[b]	I^2 (%)			
Anemia	6	12/283	24/277	0.395	3.4	0.52	0.28 to 0.99	0.045
Neutropenia	14	100/632	203/613	0.524	0	0.48	0.39 to 0.59	<0.0001
Thrombocytopenia	7	16/298	43/296	0.756	0	0.38	0.22 to 0.65	<0.0001
Fatigue	3	30/219	56/213	0.405	0	0.52	0.36 to 0.77	0.001
Appetite	3	36/177	799/177	0.579	0	0.46	0.33 to 0.64	<0.0001
Nausea and vomiting	12	33/500	90/485	0.339	10.8	0.37	0.26 to 0.53	<0.0001

[a] According to the U.S. National Cancer Institute's *Common Toxicity Criteria,* version 2 or 3.
[b] By chi-square test.
RR = relative risk; CI = confidence interval.

community to adopt novel and innovative approaches in seeking more effective and less toxic treatment regimens. *Astragalus*-based Chinese herbal formulations, especially when based on individualized TCM evaluation with its resultant syndrome differentiation, could potentially offer an avenue for future study.

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CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and we declare that we have none.

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