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Unlocking the potential of immune checkpoint inhibitors in advanced cervical cancer: a meta-analysis and systematic review

Zheng-rui Li[1†], Yu-Feng Wang[2†], Chen- Rong Zuo[4], Jing-Sheng Men[2], Xin-Yuan Li[5], Peng Luo[6*], Xiao-San Su[3*] and Rui-Fen Sun[4*]

Abstract

Objective This meta-analysis systematically evaluated the effectiveness and safety of immune checkpoint inhibitors (ICIs) in treating advanced cervical cancer, emphasizing their potential as transformative therapeutic options in this complex clinical landscape.

Methods EMBASE, Web of Science, PubMed, and the Cochrane Library were thoroughly searched for articles on the outcomes of ICIs in advanced cervical cancer patients. A pooled analysis was performed to evaluate the objective response rate (ORR: reported as an odds ratio (OR), progression-free survival (PFS; hazard ratio (HR), overall survival (OS; HR), and safety outcomes risk ratio (RR). Subgroup and sensitivity analyses were also conducted to identify potential sources of bias and heterogeneity.

Results Our meta-analysis included 5 studies involving 3,112 patients. Compared with standard therapies, treatment with immune checkpoint inhibitors (ICIs) significantly improved the objective response rate (ORR; OR = 1.68, 95% CI = 1.27–2.23), prolonged progression-free survival (PFS; HR = 0.72, 95% CI = 0.65–0.80), and extended overall survival (OS; HR = 0.69, 95% CI = 0.61–0.79). Subgroup analyses revealed potential predictors of treatment response. Moreover, ICIs exhibit a manageable safety profile, with adverse events consistent with known immune-related toxicities.

Conclusion This meta-analysis highlights the promising efficacy and favourable safety profile of immune checkpoint inhibitors in advanced cervical cancer. These findings suggest a paradigm shift in treatment strategies, with ICIs emerging as a potential cornerstone therapy. Further research is warranted to elucidate optimal patient selection, combination therapies, and long-term outcomes. This study provides valuable insights for clinicians and researchers, paving the way for personalized and effective treatment approaches for advanced cervical cancer.

Keywords Immunotherapy, Immune checkpoint inhibitors, Cervical cancer, Meta-analysis, Efficacy, Safety

†Zheng-rui Li and Yu-Feng Wang contributed equally to this work.

*Correspondence:
Peng Luo
luopeng@smu.edu.cn
Xiao-San Su
suxs163@163.com
Rui-Fen Sun
sunruifen@ynucm.edu.cn
Full list of author information is available at the end of the article

Introduction

Cervical cancer remains a major global health challenge, with an estimated 604,000 new cases and 342,000 deaths worldwide in 2020, reflecting persistently high incidence and mortality rates despite preventive advances [1]. Notably, developing nations bear the brunt of this burden, accounting for 85% of all global cases. Despite the availability of preventive measures such as widespread HPV vaccination and regular screening, which have significantly reduced the incidence of cervical cancer, the prognosis for cervical cancer patients coinfected with HIV remains poor [2]. Emerging evidence suggests that age is an independent prognostic factor for recurrence and post recurrence survival in patients with cervical cancer, with older patients exhibiting distinct clinical outcomes [1, 3]. Consequently, novel therapeutic strategies to improve outcomes in this patient population are urgently needed.

Immunotherapy in cancer encompasses not only adoptive cell therapy but also checkpoint inhibitors, which modulate the immune system to recognize and attack cancer cells [4]. Checkpoint inhibitors are now established as effective options for advanced cancers. Their utility spans single agent uses and rational combination strategies,as supported by prospective clinical trial data [5]. Furthermore, in the tumor microenvironment, dysfunctional T cells are a challenge. The use of PD-1 and PD-L1 antibody inhibitors as checkpoint inhibitors has become widespread [6]. T-cell exhaustion is a novel pathway for resistance to cellular immunotherapies [7]. Immune checkpoint inhibitors, particularly PD-1 and PD-L1 blockers, have significantly improved response rates in several tumor types. However, their use in patients with cervical cancer, however, remains under investigation due to variability in outcomes [8]. The addition of atezolizumab to the standard bevacizumab and platinum-based regimens can significantly increase progression-free and overall survival. However, existing studies have demonstrated inconsistencies and limitations in the application of immune checkpoint inhibitors in advanced cervical cancer [4]. Although some patients benefit from ICI therapy, others exhibit lower response rates or experience severe adverse reactions. Therefore, in this study, we focused on analysing and evaluating the overall efficacy and safety of immune checkpoint inhibitors.

This study employed an extensive database search and a stringent selection process to identify eligible studies from an initial pool of 1,602 articles. With a focus on clinical trials utilizing PD-1 and PD-L1 inhibitors for the treatment of advanced cervical cancer, this study aims to provide a comprehensive evaluation of the objective response rates, progression-free survival, and overall survival associated with these immune checkpoint inhibitors within a clinical setting. Moreover, this study conducted a thorough analysis of safety-related issues, including the incidence rates of adverse events, serious adverse events, and immune-related adverse events. Consequently, this study aims to identify more effective and safer treatment options for advanced cervical cancer, with the goals of enhancing patient prognosis and quality of life and informing future clinical practice and research directions.

Methods

Registration

This study was meticulously conducted under the guidelines described in the PRISMA (Supplementary Material 1) and registered in PROSPERO (CRD42024477726).

Literature source

We conducted a systematic literature search on May 12, 2023, via PubMed, Web of Science, and the Cochrane Library. The search strategy combined MeSH terms and free-text keywords (e.g.,'immune checkpoint inhibitors','advanced cervical cancer','clinical trial'), with no date restrictions applied.

Our search strategy, which integrated both MeSH terms and free-text terms, was segmented into nine distinct parts. The first part focused on"immune checkpoint inhibitors,"followed by"pembrolizumab,""nivolumab,""durvalumab,"and culminated in the ninth part, which addressed"cervical cancer."The first five parts were combined via the"OR"operator, whereas the ninth part was integrated with the others using"AND."The detailed search strategies are described in the supplementary materials. To avoid duplication, only the most recent publication was included in our meta-analysis. Additionally, we reviewed relevant articles and searched clinical trial registries, including ClinicalTrials.gov, to identify registered trials. This approach ensured the comprehensiveness of our clinical trial inclusion. Furthermore, we searched relevant conferences, including the European Society for Medical Oncology (ESMO) Congress, the American Society of Clinical Oncology (ASCO) Annual Meeting, and other major cervical cancer conferences. The literature retrieval followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Eligibility criteria

Inclusion criteria

The studies included were clinical trials that concentrated on patients with advanced cervical cancer who were receiving treatment with either single immune checkpoint inhibitors, either as monotherapy or in

combination with radiochemotherapy. These trials evaluated the efficacy and safety of the treatments, including adverse reactions.

Exclusion criteria

1. Reviews, meta-analyses, and case reports. 2. Studies unrelated to advanced cervical cancer. 3. Studies involving only single immune checkpoint inhibitor treatment (were excluded if they focused solely on monotherapy without combination therapy). 4. Studies that did not report on treatment safety. 5. Duplicated publications. Language restrictions were not imposed.

Data extraction

Initially, two researchers independently screened titles and abstracts, excluding studies that did not meet the inclusion criteria. Next, potentially eligible full texts were carefully reviewed to determine final inclusion. Disagreements were resolved through discussion and, if necessary, by consulting a third expert. Data extraction was conducted by two independent researchers via a predesigned form, that captured basic information (authors, year, location), study design, detailed intervention measures, and both primary and secondary outcome results. The extracted data were cross validated for accuracy.

Research objectives

This study conducted a meta-analysis on the effectiveness and safety of ICIs in treating advanced cervical cancer. The specific objectives are as follows:

A. Efficacy assessment: Assessment of the effectiveness of ICIs in advanced cervical cancer patients. We will focus on key performance indicators: the objective response rate (ORR), median progression-free survival (PFS), and median overall survival (OS). These metrics will help us assess the impact of ICIs on patient survival and disease progression.
B. Prognostic Factors Exploration: To identify and analyse factors that influence the outcomes of ICI treatments in advanced cervical cancer, such as patient age, cancer stage, and histological type. The insights gained will be pivotal in tailoring personalized treatment strategies.
C. Safety analysis: To investigate the safety profile of ICIs in this patient population by examining the incidence and severity of adverse events were examed. These events included any adverse events, adverse events of Grade 3 or higher, serious adverse events (SAEs), any immune-related adverse events, and immune-related adverse events of Grade 3 or higher. Our goal was to assess the tolerability and overall safety of these treatment protocols.
D. Recommendations and Implications: To address limitations and gaps in the use of ICIs for treating advanced cervical cancer, we aim to suggest practical improvements for future clinical research and practice. This study aims to equip clinicians with more precise treatment options and provide patients with more effective and safer therapeutic alternatives, ultimately enhancing patient outcomes and quality of life.

Study quality

Randomized controlled trials (RCTs) were assessed for potential bias via the Cochrane risk of bias tool (RoB 2.0), which evaluates various types of bias, including performance bias, detection bias, attrition bias, reporting bias, and other potential biases. The quality of non-randomized studies was evaluated according to the MINORS criteria, which consists of nine components: specificity of study objectives, uniformity of recruitment, data collection methods, appropriateness of outcome measures, objectivity of outcome assessment, adequacy of follow-up, attrition rate below 5%, and sample size estimation. Bias risk assessments were carried out independently by two researchers. Disagreements were resolved by a third author. Quality assessments for RCTs were conducted via RevMan software.

Data analysis

Statistical analysis of the data was performed via Stata version 17.0, and the results were visualized with forest plots. Effect sizes and 95% confidence intervals (CIs) were estimated via the random effects DerSimonian-Laird method. The incidence of adverse events was calculated as the ratio of the total number of patients experiencing events to the total number of participants. The influence of each study was based on its sample size and the proportion of enrolled patients. Heterogeneity among studies was assessed using the I^2 statistic and p values; $I^2 > 50\%$ or $p < 0.1$ was considered significant. Publication bias was assessed using funnel plots (not performed if fewer than 10 studies were included) and Egger's test was used.

Results

Study characteristics

In this meta-analysis, our initial search identified 1,602 relevant articles, from which we ultimately included five [9–13]. A total of 3,112 patients were enrolled across the included studies (Fig. 1). All studies were published in English. The patient characteristics are shown in Table 1. These studies were conducted from 2022–2024.

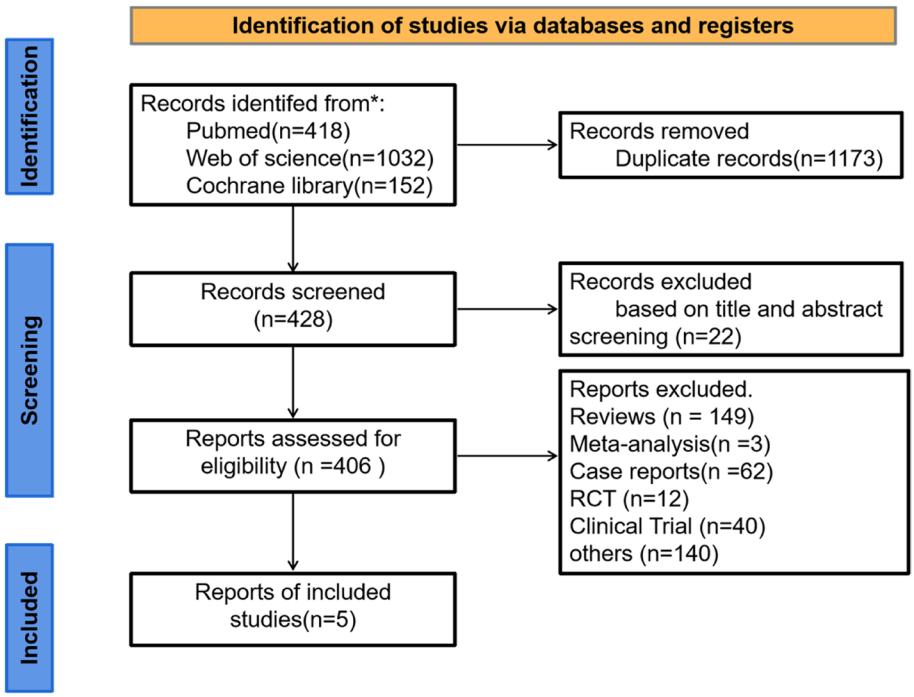


Fig. 1 PRISMA flowchart for the selected studies included in the meta-analysis

Table 1 The basic characters of included studies

Author/Year	Age	Sample Size	Intervention		Median Follow-Up Time	Median PFS	Median OS
			Experimental group	Control group			
Tewari 2022	51/50	304/304	Cemiplimab	Chemotherapy	18.2 months	2.8/2.9 months	Tewari 2022
Lorusso 2024	49/50	529/531	Pembrolizumab + Chemoradiotherapy	Placebo + Chemoradiotherapy	17.9 months	NR/NR	Lorusso 2024
Nishio 2022	54/50	35/22	Pembrolizumab + Chemotherapy	Placebo + Chemotherapy	23.2 months	NR/11.5 months	Nishio 2022
Colombo 2021	51/50	308/309	Pembrolizumab	Placebo	22 months	10.4/8.2 months	Colombo 2021
Monk 2023	50/48	385/385	Durvalumab + Chemotherapy	Placebo + Chemotherapy	18.5/18.4 months	NR/NR	Monk 2023

Study quality

The quality evaluation revealed that 5 articles were of high quality. (Supplementary Material 2).

Objective response rate in advanced cervical cancer treatment

We assessed the objective response rate (ORR) of ICIs in advanced cervical cancer patients by integrating data from five randomized controlled trials. The pooled odds ratio (OR) and 95% confidence interval (CI) from these studies, as shown in (Fig. 2), (OR = 1.68, 95% CI: 1.27–2.23), indicate significant treatment efficacy.

Sensitivity analysis was performed to evaluate the influence of individual studies on the pooled meta-analysis results. We illustrate how pooled estimates vary with the exclusion of each study, confirming the robustness of the analysis. (Figure S1). Even though there were small differences in how much each study affected the results, the overall trustworthiness of the findings remained high. These findings indicate that immune checkpoint inhibitors work well in treating advanced cervical cancer.

Median progression-free survival of advanced cervical cancer patients treated with immune checkpoint inhibitors

This meta-analysis assessed the efficacy of ICIs for the treatment of advanced cervical cancer by synthesizing

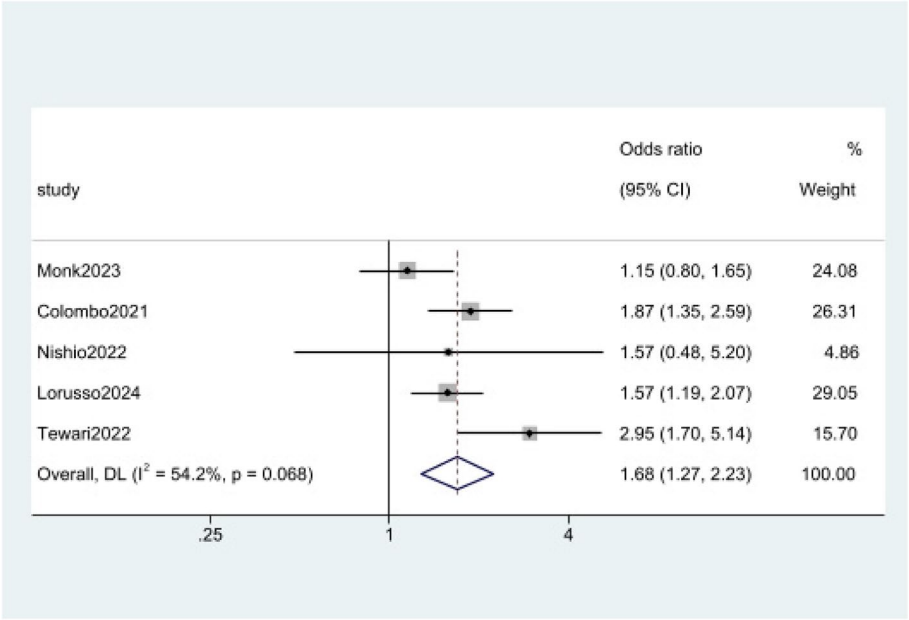


Fig. 2 Forest plot of the ORR for the treatment of advanced cervical cancer with immune checkpoint inhibitors

data from five studies to assess the median progression-free survival (PFS). Specifically, the pooled analysis revealed that the use of ICIs resulted in a hazard ratio (HR = 0.72, 95%CI: 0.65–0.80), indicating a statistically significant reduction in the risk of disease progression (Fig. 3A).

We conducted a sensitivity analysis to evaluate the stability of the results. Despite the impact of individual study exclusions, the pooled results remained robust (Figure S2). Subgroup analysis revealed variations in treatment effects among patient subsets, suggesting potential differential treatment responses. The hazard ratio (HR = 0.7, 95% CI: 0.61–0.79) (Fig. 3B).

Median overall survival and subgroup analysis of immune checkpoint inhibitors for advanced cervical cancer

We assessed the median overall survival (OS) of advanced cervical cancer patients treated with ICIs. The pooled analysis demonstrated that patients treated with ICIs have a significantly longer median OS (HR = 0.69, 95% CI: 0.61–0.79), suggesting a substantial association with prolonged survival (Fig. 4A). We conducted a sensitivity analysis to assess the influence of individual studies on the pooled results (Figure S4). The sensitivity analysis revealed that while excluding individual studies influenced the estimates, the pooled results remained robust, indicating a consistent effect of ICIs on improving OS. Additionally, to understand treatment efficacy in different patient subgroups, we performed a subgroup analysis focusing on patients with an OS of more than 1 year. (Fig. 4B).

Safety analysis of immune checkpoint inhibitors for the treatment of advanced cervical cancer

This section provides a comprehensive evaluation of the safety profile of ICIs in the treatment of advanced cervical cancer, including adverse events (AEs), grade 3 or higher AEs, serious adverse events (SAEs), and immune-related adverse events (irAEs). The analysis included a pooled assessment of various adverse events and a sensitivity analysis to determine how individual studies affected the overall results.

Any adverse events

The meta-analysis revealed no statistically significant increase in the risk of adverse events associated with immune checkpoint inhibitor therapy (OR = 0.83, 95% CI: 0.53–1.30) (Fig. 5A). Sensitivity analysis indicated the robustness of these results, as the 95% confidence interval consistently included 1 upon the exclusion of any single study (Figure S5).

Grade 3 or above adverse events

For more severe adverse events, the pooled odds ratio (OR = 1.08, 95% CI: 0.80–1.46), indicating no significant increase in risk (Fig. 5B). Sensitivity analysis also confirmed that these results were robust. This is because removing any study did not significantly change the overall estimation (Figure S6). These findings suggest that the safety profile of immune checkpoint inhibitors is favourable in this patient group.

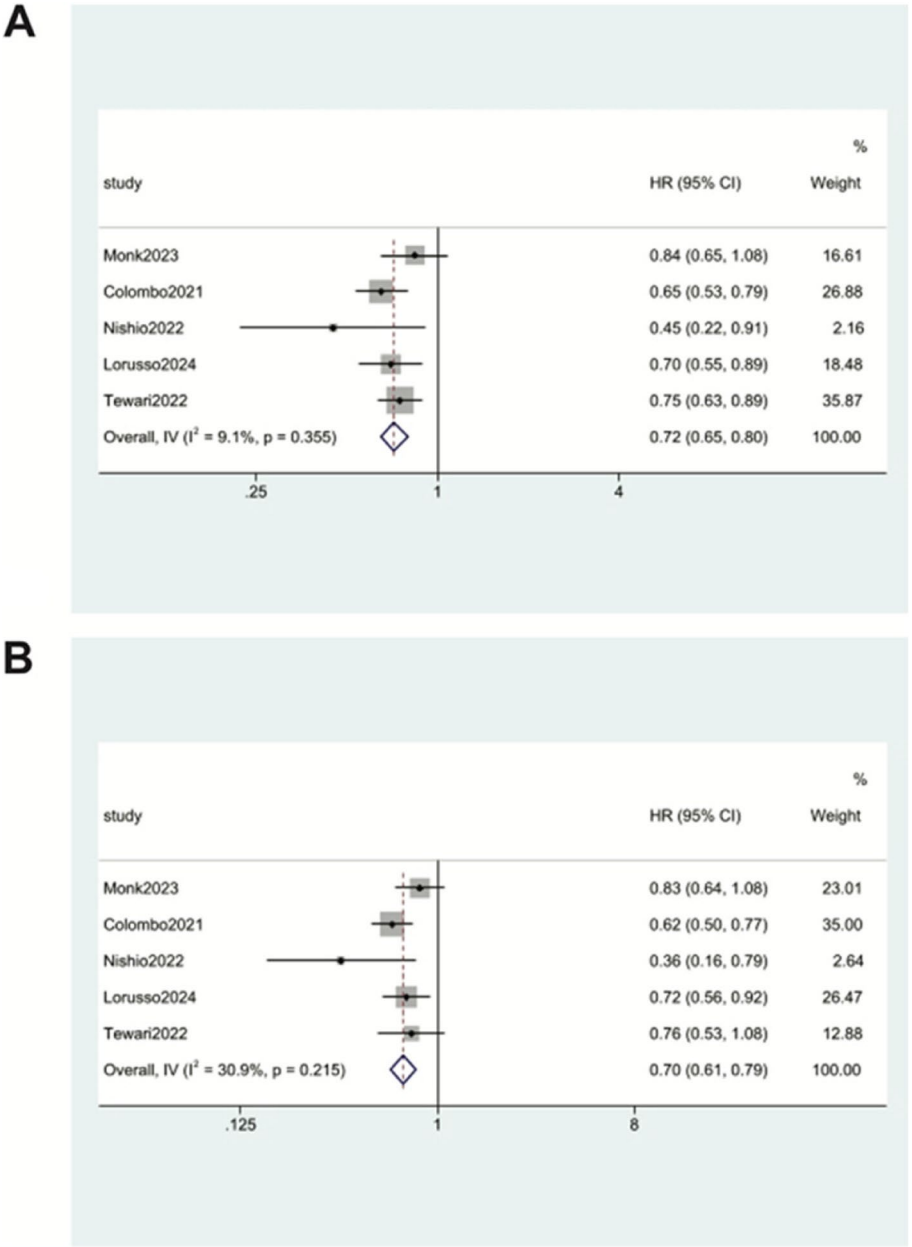


Fig. 3 The median PFS of patients with advanced cervical cancer treated with ICIs. B. Diagram for subgroup analysis with PFS greater than 1. This chart focuses on a specific subgroup of patients with PFS greater than 1 and analyses the efficacy of immune checkpoint inhibitor therapy in this subgroup

Serious adverse events (SAEs)

In the pooled analysis, the odds ratio for serious adverse events significantly increased to 3.34 (95% CI: 2.02–5.54), indicating a significant increase in the risk of serious adverse events during treatment (Fig. 5C). The sensitivity analysis revealed some variability in the results; however, the pooled results still demonstrated statistical significance (Figure S7).

Any immune-related adverse events (irAEs)

The odds ratio for immune-related adverse events was 1.34 (95% CI: 1.06–1.69), suggesting a slight to moderate increase in the risk during treatment (Fig. 5D). Sensitivity analysis confirmed the consistency of these findings, demonstrating the stability of the results upon the exclusion of any study (Figure S8). Additionally, no grade 3 or above immune-related adverse events were observed.

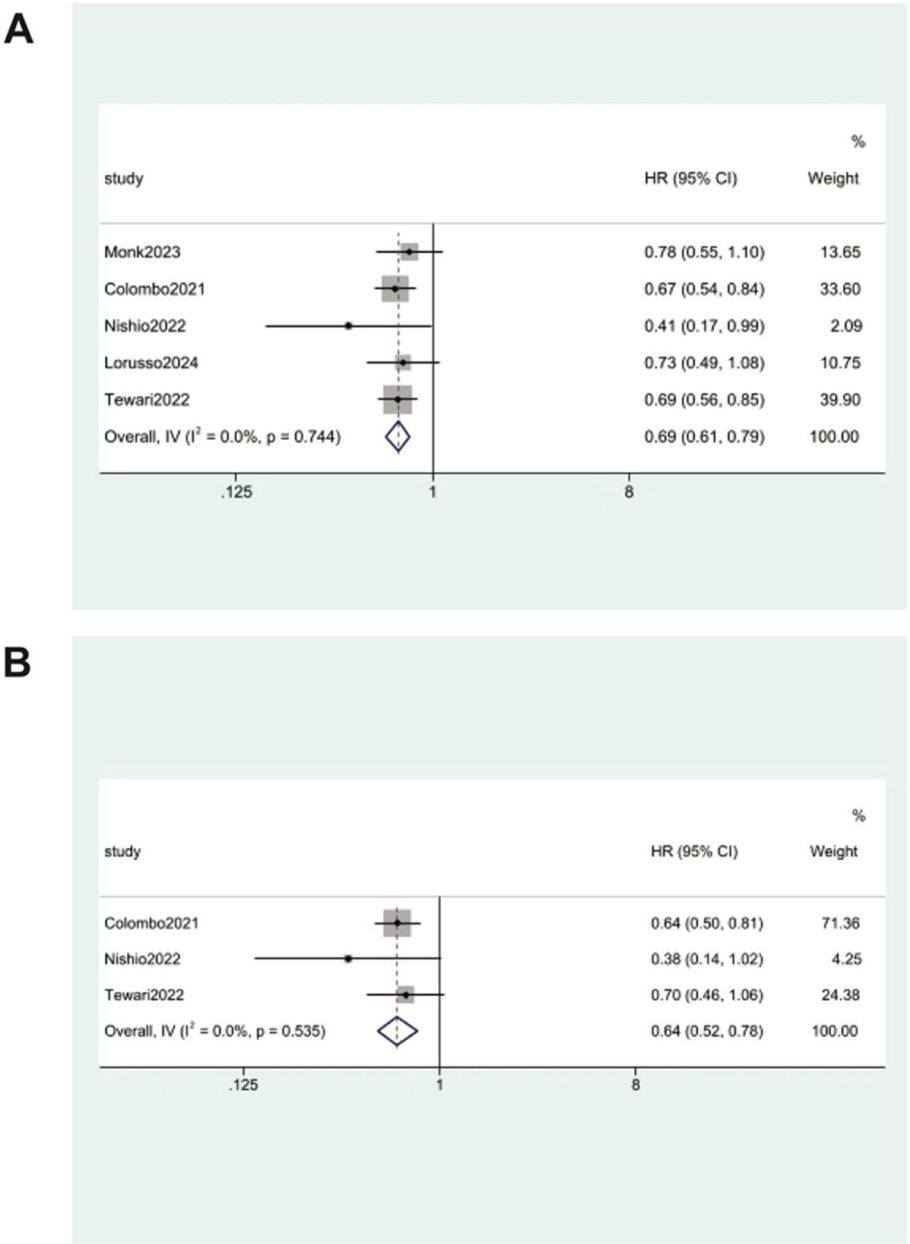
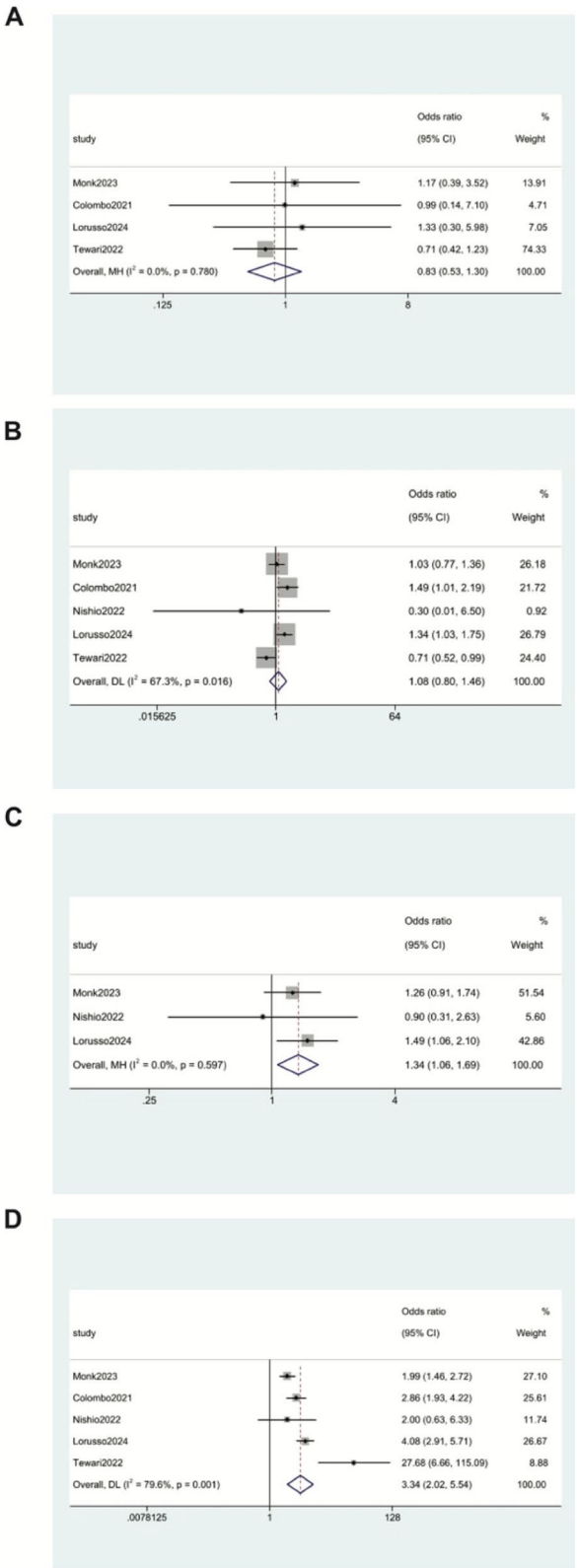


Fig. 4 A. Forest plot of median OS in patients with advanced cervical cancer treated with ICIs. B. Subgroup analysis plot for patients with an OS greater than 1

Bias and Heterogeneity Risk

In this meta-analysis, we performed a risk-of-bias assessment for the included studies via a standardized tool, which demonstrated that most studies presented a low risk of bias across most domains. Studies including Colombo (2021), Lorusso (2024), Monk (2023), Nishio (2022), and Tewari (2022) demonstrated a low risk of bias with green indicators across domains such as random sequence generation, allocation concealment, participant and personnel blinding, outcome assessment blinding, completeness of outcome data, selective reporting, and other potential biases (Fig. 6).

To assess heterogeneity risk, we evaluated the statistical consistency of the results. The risk across most bias domains was found to be within acceptable limits, suggesting that the included studies were not significantly biased in any major domain (random sequence



◀ **Fig. 5** **A** Forest plot of the pooled analysis of any adverse events. **B** Forest plot of the pooled analysis of Grade 3 or above adverse events. **C** Forest plot of pooled analysis of serious adverse events (SAEs). **D**. Forest plot of the pooled analysis of any immune-related adverse events (irAEs)

generation, allocation concealment, blinding, outcome assessment blinding, and other biases) (Fig. 7).

Discussion

In managing advanced cervical cancer, a multidisciplinary approach is standard. It includes radiation therapy, chemotherapy, and targeted therapy [14]. Radiation therapy, a cornerstone of treatment, includes external beam radiation and brachytherapy (endoluminal radiotherapy). It effectively controls local tumor growth and alleviates symptoms [15]. Concurrent chemoradiotherapy, which often incorporates platinum-based drugs such as cisplatin, enhances treatment efficacy by leveraging the radio sensitizing properties of these agents. This approach has been shown to improve patient prognosis by effectively targeting cancer cells and enhancing the overall response to treatment [16]. Targeted therapy, which is specifically indicated for patients who test positive for certain molecular markers, has the potential to provide substantial therapeutic benefits through agents such as bevacizumab, which inhibits angiogenesis and thereby suppresses tumor growth [17, 18].

On the basis of recent clinical trial data, the median survival of patients with stage III cervical cancer receiving standard treatment regimens, such as concurrent chemoradiotherapy, varies between 15 and 30 months [19]. In stage III A cervical cancer, which extends to the lower third of the vagina without pelvic wall invasion, the 5-year survival rate is approximately 35% to 50%. In contrast, for stage III B patients, with pelvic wall invasion or hydronephrosis, the 5-year survival rate is approximately 30% to 40%. Patients with stage IV a cervical cancer, involving adjacent organ invasion, have a median survival of approximately 10–15 months. For stage IV B patients, with distant metastases to organs such as the lungs, liver, and bones, the median survival is typically less than 10 months [20]. The 5-year survival rate for stage IV A cervical cancer is approximately 15% to 20%, whereas for patients with stage IV B cervical cancer, it is less than 10%. Drug resistance significantly impacts the efficacy and prognosis of systemic treatment for advanced cervical cancer, including both chemotherapy and targeted therapy [21]. The prevalence of drug resistance in the treatment of advanced cervical cancer treatment is high, with chemotherapy resistance rates exceeding 70%, including both initial and acquired resistance, as reported

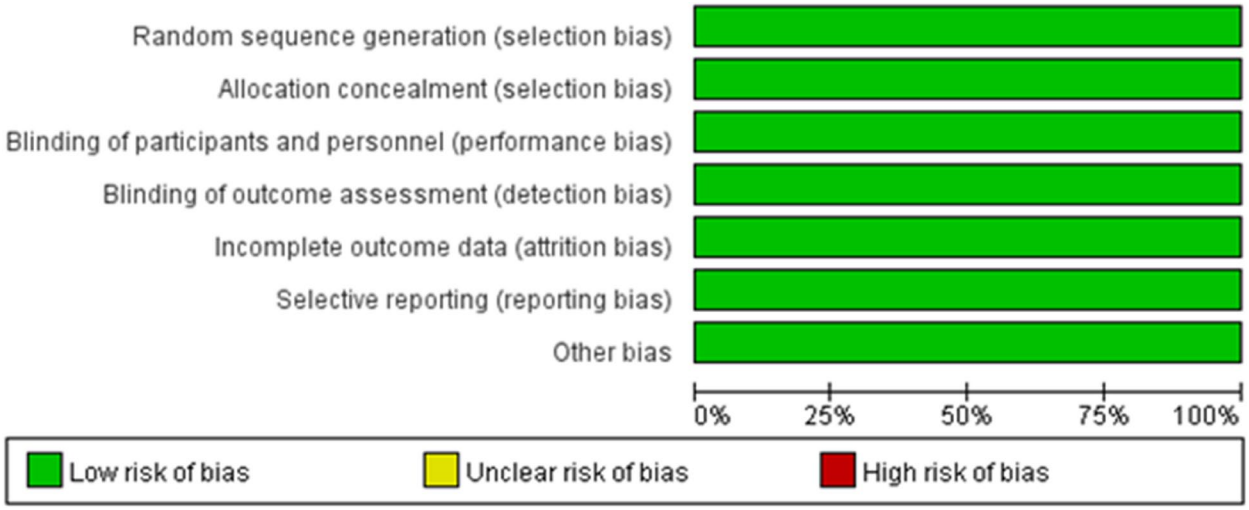


Fig. 6 Bar chart depicting bias risk, displaying the percentage of low bias risk in each bias domain. The green bars represent the percentage of low bias risk across all included studies in domains such as random sequence generation, allocation concealment, blinding (participants and personnel), blinding of outcome assessment, completeness of outcome data, selective reporting, and other biases

in recent clinical trials. Furthermore, high resistance rates are also observed with targeted therapies. Overcoming drug resistance remains a significant challenge in improving the prognosis of patients with advanced cervical cancer [22, 23]. However, the exploration and implementation of novel therapeutic approaches offer renewed hope for patients with drug-resistant disease.

The results of this study demonstrate that immune checkpoint inhibitors exhibit promising efficacy and a favorable safety profile in the treatment of advanced cervical cancer, potentially enhancing patient outcomes through immune-mediated tumor control. The therapeutic efficacy of ICIs is mediated primarily by modulating two key immunomodulatory pathways: the PD-1/PD-L1 axis and the CTLA-4 pathway [24, 25]. The PD-1 receptor, which is expressed on the surface of activated T cells, interacts with its ligands, PD-L1 and PD-L2, which are predominantly expressed by dendritic cells and macrophages [26, 27]. The interaction between PD-1 and its ligands provides a coinhibitory signal that regulates the magnitude and duration of the T-cell response, thereby preventing unwarranted immune activation and minimizing damage to healthy tissues. Within the tumor microenvironment, tumor cells may upregulate PD-L1, which engages with PD-1 on T-cells, thereby inhibiting T-cell activity and promoting immune evasion [28–32]. PD-1/PD-L1 inhibitors disrupt this interaction, thereby reinvigorating the antitumor T-cell response. The dominance of CTLA-4 over CD28 in binding to CD80/86 (Kd = 0.4 μM vs. 4 μM) creates a key immune checkpoint. In the CheckMate 358 trial, dual CTLA-4/PD-1 blockade improved 2-year survival to 38% versus 17% with chemotherapy in patients with recurrent cervical cancer, validating this mechanism as a therapeutic target. Ongoing trials (NCT04516616) are exploring biomarkers to predict response [26, 33]. Upon binding to CD80/CD86, CTLA-4 recruits phosphatases such as SHIP2 and PP2 A to the cell membrane, which attenuate the TCR and PI3 K/AKT signalling pathways, thereby inhibiting T-cell activation and proliferation. Anti-CTLA-4 antibodies prevent CTLA-4 binding to CD80/CD86, thereby preventing T-cell inhibition and enhancing T-cell activation and proliferation. Furthermore, CTLA-4 captures CD80 and CD86 through trans-endocytosis, sequestering them from antigen-presenting cells (APCs) and reducing T-cell stimulation [24, 34, 35]. In conclusion, immune checkpoint inhibitors strengthen the body's antitumor immune response by targeting the PD-1/PD-L1 and CTLA-4 pathways, thereby reactivating T cell recognition and attack on tumor cells [36].

In treating advanced cervical cancer, pembrolizumab, an anti-PD-1 monoclonal antibody, is among the most frequently utilized immune checkpoint inhibitors [37]. Based on the findings of the KEYNOTE-158 clinical trial, pembrolizumab has received approval for monotherapy in patients with recurrent or metastatic cervical cancer that progresses following chemotherapy, specifically in those with PD-L1-expressing tumors (CPS $\geq$1). Furthermore, the KEYNOTE-826 study endorses the combination of pembrolizumab with platinum-based chemotherapy, with the potential inclusion of bevacizumab, for patients with persistent, recurrent, or metastatic cervical cancer after initial therapy, leading to significant improvements in overall response rates, as well as in survival and progression-free survival [38, 39].

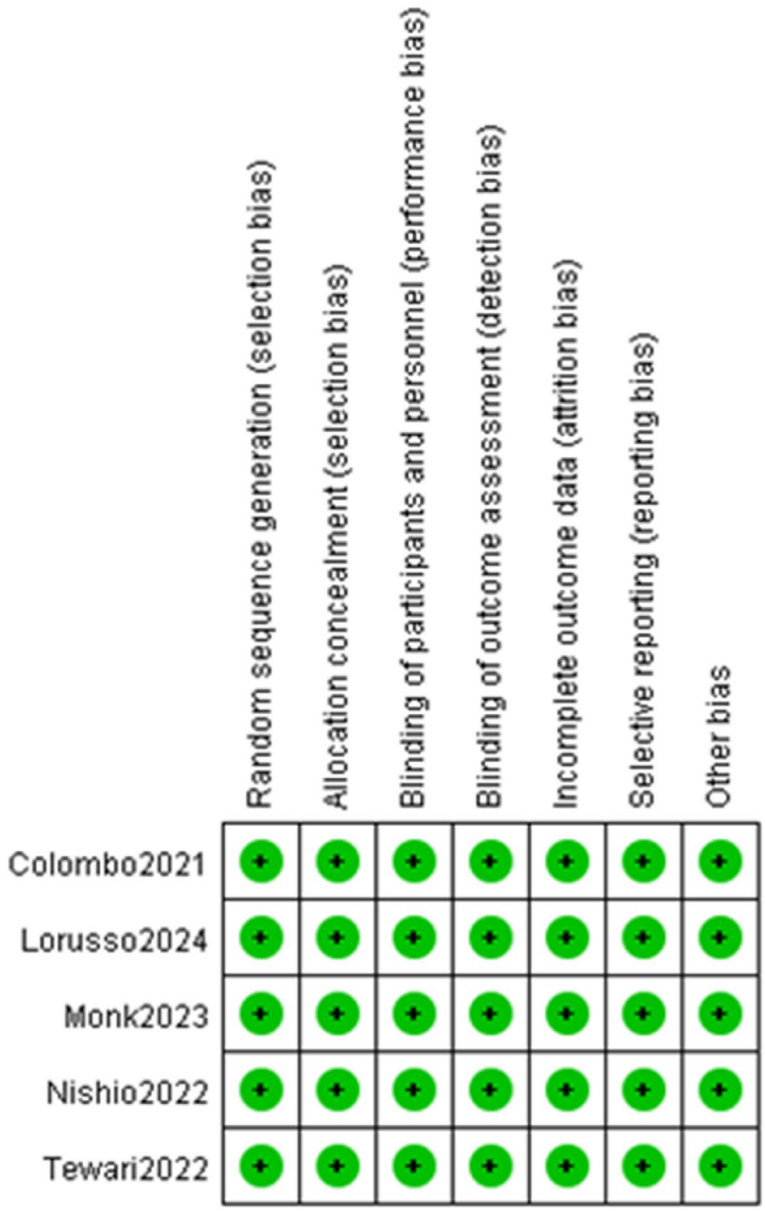


Fig. 7 Bias risk assessment plot for each study. The green squares represent low bias risk, with each square corresponding to a bias domain, including random sequence generation, allocation concealment, blinding (participants and personnel), blinding of outcome assessment, completeness of outcome data, selective reporting, and other biases. The figure illustrates the performance of five studies (Colombo, 2021; Lorusso, 2024; Monk, 2023; Nishio, 2022; and Tewari, 2022) across different bias risk domains

Immune checkpoint inhibitors for advanced cervical cancer stimulate the immune system and increase the capacity of the patients' T cells to identify and combat tumor cells. Clinical studies have demonstrated that immune checkpoint inhibitors markedly prolong the overall survival of patients with advanced or recurrent cervical cancer. The KEYNOTE-826 trial has shown that pembrolizumab combined with chemotherapy can significantly improve OS in advanced cervical cancer patients compared to chemotherapy alone. This combination not only increases OS but also helps some patients achieve long-lasting tumor remission and maintain stable disease after treatment. These results emphasize the importance of immune checkpoint inhibitors in cervical cancer treatment and provide valuable guidance for future therapies [38, 40]. When considering the use of chemotherapy plus bevacizumab (CT + Bev) in advanced cervical cancer, it is important to look at how different patient subgroups

benefit, especially when treatment is guided by biomarkers. Studies have found that patients with high HIF-1α expression in their tumors may respond better to CT + Bev [41]. Yıldırım observed significantly better survival in HIF-1α-positive patients treated with CT + Bev. This shows that treatments based on tumor biology are very important. Future research should continue to explore these biomarkers to improve treatment strategies for advanced cervical cancer. Also, combining immunotherapy with biomarker-guided CT + Bev could offer more targeted treatment options and potentially enhance patient outcomes.

Reports indicate that a subset of patients receiving durable therapy may achieve complete remission, characterized by tumor disappearance, a rare outcome with traditional chemotherapy. In contrast to chemotherapy, immune checkpoint inhibitors typically induce mild to moderate adverse effects, predominantly involving the skin, gastrointestinal tract, and endocrine system. Most immune-related adverse effects are reversible with timely intervention. Owing to the infrequent and manageable nature of adverse reactions, patients may experience improved quality of life. For patients exhibiting resistance or intolerance to chemotherapy, immune checkpoint inhibitors present novel therapeutic options, bridging a treatment gap. Detecting PD-L1 expression levels in tumor tissues allows for the prediction of patient responses to immunotherapy, enabling the selection of patients most likely to benefit and enhancing treatment efficiency [30, 42].

The therapeutic efficacy of immune checkpoint inhibitors in advanced cervical cancer is potentially correlated with biomarkers, including PD-L1 expression, MSI status, and TMB. Before initiating treatment, the assessment of relevant biomarkers—PD-L1 expression, MSI, and TMB—and careful monitoring for potential immune-related adverse events, including rash, enteritis, pneumonia, endocrine disorders (e.g., thyroid dysfunction, diabetes), and hepatitis [43, 44]. Close surveillance of the patient's condition throughout treatment is essential, with prompt intervention for any adverse events. Immune checkpoint inhibitors (ICIs) represent a novel therapeutic approach for advanced cervical cancer, particularly advantageous for patients who are unable to endure conventional chemotherapy regimens. Agents such as pembrolizumab have demonstrated efficacy as first-line treatments for advanced cervical cancer characterized by PD-L1 positivity, as evidenced by the findings of the KEYNOTE-826 trial. Furthermore, ICIs have the potential to provide benefits across various treatment contexts. A comprehensive understanding of these diverse applications will enable the optimization of treatment strategies, ultimately enhancing patient outcomes [45, 46]. Importantly, immunotherapy is not indicated for all patients; thus, its efficacy and safety must be assessed and managed with professional medical oversight. Clinicians should tailor treatment plans according to the patient's unique clinical profile and biomarker status. Our study used narrow criteria to focus on advanced cervical cancer combination therapies. But this has downsides. We didn't look at subgroups based on treatment (single vs. combined), cancer type (SCC vs. adenocarcinoma), or PD-L1 levels. This limits the depth of our results. Future research should include these factors in subgroup analyses. This would give a better picture of treatment effects and help create more personalized treatment plans. Immunotherapy is changing quickly. New methods like mixing treatments and tailoring them to patients are showing potential to boost effectiveness. Future meta-analyses should include these new therapies to fully evaluate their pros and cons.

Conclusion

This meta-analysis revealed that immune checkpoint inhibitors work well and are safe for treating advanced cervical cancer. These findings suggest a paradigm change in treatment strategies, with ICIs having potential as a main therapy. Further research is warranted to elucidate optimal patient selection, combination therapies, and long-term outcomes. This meta-analysis supports the integration of ICIs into treatment strategies for selected patients with advanced cervical cancer.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12885-025-14264-z.

Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

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Authors' contributions

All the authors contributed to the study conception and design. Writing—original draft preparation: Zheng-rui Li, Yu-Feng Wang, Xiao-San Su, Rui-Fen Sun, Peng Luo; Writing—review and editing: Zheng-rui Li, Yu-Feng Wang; Conceptualization: Zheng-rui Li, Yu-Feng Wang; Methodology: Zheng-rui Li, Yu-Feng Wang; Formal analysis and investigation: Zheng-rui Li, Yu-Feng Wang, Chen-Rong Zuo, Jing-Sheng Men, Xin-Yuan Li; Funding acquisition: Yu-Feng Wang; Resources: Xiao-San Su, Rui-Fen Sun; Supervision: Xiao-San Su, Rui-Fen Sun and all the authors commented on previous versions of the manuscript. All the authors read and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]College of Basic Medical Science , Yunnan University of Chinese Medicine, kunming 650500, China. [2]School of Medicine, Shanghai Jiao Tong University, Shanghai 200000, China. [3]Scientific Research and Experimental Center, Yunnan University of Chinese Medicine, Kunming 650500, China. [4]College of Nursing, Yunnan University of Chinese Medicine, No. 1076, Yuhua Street, Chenggong District, Kunming 650500, China. [5]Fujian University of Traditional Chinese Medicine, Fuzhou 350122, China. [6]Department of Oncology, Zhujiang Hospital, Southern Medical University, Guangzhou 510280, Guangdong, China.

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