Original Article

Tislelizumab plus chemotherapy *vs.* pembrolizumab plus chemotherapy for the first-line treatment of advanced non-small cell lung cancer: systematic review and indirect comparison of randomized trials

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Background: Pembrolizumab (PEM) and tislelizumab (TIS), in combination with chemotherapy, have demonstrated significant clinical benefits in first-line treatment of advanced non-small cell lung cancer (NSCLC). However, no head-to-head clinical trial has yet compared these two treatments.

Methods: We conducted a literature search of randomized trials, in which TIS plus chemotherapy or PEM plus chemotherapy were studied for the first-line treatment of NSCLC. Randomized design and the endpoint of progression-free survival (PFS) were the inclusion criteria for our analysis. Adjusted indirect comparison between TIS and PEM was performed by application of the IPDfromKM-Shiny method. This method is based on the reconstruction of individual patient data from Kaplan-Meier curves. Outcomes in terms of PFS were expressed as hazard ratio (HR) with 95% and 90% confidence interval (CI).

Results: Data were extracted from five randomized trials involving nearly 2,000 participants. In comparing PEM plus chemotherapy (n=748) or TIS plus chemotherapy (n=462) *vs.* chemotherapy alone (n=782), the Shiny method found a significant advantage in terms of PFS (HR =0.5856, 95% CI: 0.4986–0.6876 for TIS; HR =0.5573, 95% CI: 0.4969–0.6251 for PEM), thus confirming the results of the original trials. The indirect comparison of PEM plus chemotherapy *vs.* TIS plus chemotherapy showed a substantial equivalence between these two regimens (HR =0.952; 95% CI: 0.775–1.168; 90% CI: 0.801–1.130) suggesting an acceptable degree of equivalence according to regulatory criteria. Medians were 8.89 months for PEM combination, 7.97 months for TIS combination, and 5.69 for the controls.

Conclusions: The PFS of TIS combined with chemotherapy was similar to that of PEM combined with chemotherapy. Based on the HR with 90% CI, these two agents met an equivalence criterion for PEM *vs.* TIS ranging from –19.9% to +13.0%.

Keywords: Non-small cell lung cancer (NSCLC); programmed cell death 1 receptor; immunotherapy; tislelizumab (TIS); pembrolizumab (PEM)

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Introduction

Pembrolizumab (PEM) plus platinum-based chemotherapy is currently the standard of care (SOC) in previously untreated advanced non-small cell lung cancer (NSCLC); this combination is effective in both squamous and non-squamous forms of the tumor (1-3). Quite recently, tislelizumab (TIS), a humanized immunoglobulin G4 (IgG4)-variant monoclonal antibody blocking programmed cell death protein 1 (PD-1) has been approved by China's National Medical Products Administration (NMPA) for the first-line treatment of advanced NSCLC (2). In combination with chemotherapy, this drug significantly prolongs progression-free survival (PFS) compared with chemotherapy alone in patients with locally advanced or metastatic non-squamous NSCLC (4-8). No head-to-head clinical trial has directly compared these two agents in the first-line treatment of patients with advanced NSCLC. Under these circumstances, while network meta-analysis is the typical statistical tool to carry out indirect comparisons, the IPDfromKM-Shiny method (9,10) has been proposed as a new approach to compare two or more agents that have not been directly compared through a head-to-head controlled trial.

In the present analysis, we applied the IPDfromKM-Shiny method (9,10) to indirectly compare TIS plus chemotherapy *vs.* PEM plus chemotherapy in previously untreated advanced NSCLC; PFS was the endpoint. We present this article in accordance with the PRISMA reporting checklist (available at https://cco.amegroups.com/article/view/10.21037/cco-23-26/rc).

Highlight box

Key findings

- Pembrolizumab (PEM) and tislelizumab (TIS), in combination with chemotherapy, have demonstrated significant clinical benefits in first-line treatment of advanced non-small cell lung cancer; our study presents an indirect comparison between these two agents in which their efficacy is shown to be statistically equivalent.

What is known and what is new?

- Randomized studies have been performed demonstrating the superiority of PEM or TIS compared with controls.
- In the absence of a direct randomized study comparing TIS with PEM, an indirect comparison is an acceptable form of evidence; in our analysis, the strength of this demonstration is enhanced by the reconstruction of individual patient data from the graphs of Kaplan-Meier curves.

What is the implication, and what should change now?

- Since PEM and TIS have equivalent efficacy, the cost of therapy for these patients can benefit from the remarkably lower price of TIS compared to PEM.

Methods

Study design

After a standard literature search, we identified all randomized trials that compared TIS plus chemotherapy *vs.* chemotherapy alone or PEM plus chemotherapy *vs.* chemotherapy alone in previously untreated advanced NSCLC. The Shiny method (9,10) was used to reconstruct individual patient data from each trial. PFS was the endpoint of our analysis. In particular, we compared the pattern of PFS over time between these two combination regimens by reconstructing individual patient data according to the Shiny method. Their respective Kaplan-Meier curves were then analyzed through standard survival statistics. In studying these curves of PFS, the equivalence between these two agents was also investigated by application of the likelihood ratio test and by determining the hazard ratio (HR) along with 95% and 90% confidence intervals (CIs).

Search strategy

A systematic search was conducted through PubMed, Embase, Web of Science and Cochrane Library databases (from inception to 31 December 2022) to select randomized controlled trials that compared TIS plus chemotherapy or PEM plus chemotherapy *vs.* chemotherapy for first-line treatment of advanced NSCLC. Keywords included "NSCLC", "non-small cell lung cancer", "tislelizumab" and "pembrolizumab". Studies were restricted to "randomized controlled trial" or "clinical trial".

Selection criteria

The inclusion criteria of these clinical studies were as follows: (I) randomized phase 2 or 3 clinical trial; (II) all patients diagnosed with advanced (stage IIIB) or metastatic (stage IV) NSCLC; (III) studies designed to compare PFS between TIS or PEM plus chemotherapy *vs.* chemotherapy alone; (IV) first-line treatment setting; (IV) PFS presented through a Kaplan-Meier curve. Exclusion criteria were: (I) not a randomized study (e.g., retrospective study, case

report, review, systematic review, meta-analysis, etc.); (II) studies employing other therapies in first-line other than chemotherapy or immunotherapy; (III) insufficient data (e.g., no publication of the PFS Kaplan-Meier curve); (IV) duplicate publication.

Data extraction

The graphic files of the Kaplan-Meier curve for the treatment arm and the control arm were extracted from each trial. Two investigators independently examined each article and extracted the total number of patients and the total number of events for the treatment group and the controls. When the total number of events for each arm was not explicitly reported, the study was excluded from the analysis; however, in cases where the total number of events was reported (i.e., the sum of the events observed in both arms without the detail of the events in each arm), the events per arm were estimated from the total number in both arms and the HR. Finally, according to the IPDfromKM procedure, firstly each curve was digitized using the Webplotdigitizer software and then the digitized curve was converted into a file of reconstructed patients using the online version of the Shiny software; this conversion required to input the total number of patients and the total number of events for each arm. As a final result, the patient reconstruction procedure generated two Excel files per trial (one for the treatment group, the other for the control group), in which the information for each patient included their status (i.e., with event/without event) and the time of the last observation (i.e., months elapsed from randomization).

Statistical analysis

Conventional survival statistical analyses were performed to estimate the HR (with 95% and 90% CI) for each of the following three comparisons: PEM plus chemotherapy *vs.* chemotherapy; TIS plus chemotherapy *vs.* chemotherapy, and TIS plus chemotherapy *vs.* PEM plus chemotherapy. These statistical analyses were carried out under the R-platform; various R-packages were run, including those that generate the Kaplan-Meier graph from individual patient data. Regarding the equivalence testing between PEM and TIS, the interval of equivalence was estimated using 90% boundaries as suggested by the literature on this topic (11). Finally, as recommended by the Shiny procedure, the Kaplan-Meier curves of the control groups were assessed in a separate analysis to determine the degree of heterogeneity in this clinical material. For this purpose, the likelihood ratio test was applied. Despite its simple design, this comparison across all control groups included in the analysis is known to provide valuable information for the heterogeneity assessment (10,12).

Results

Characteristics of included clinical trials

We identified more than 1,500 records from our initial search including the online databases mentioned above. After application of our inclusion criteria and exclusion of duplicate entries, 62 studies were initially selected. The full text of these 62 studies was read. Finally, 5 studies were included in our analysis (*Figure 1*). Regarding these 5 studies, information on study characteristics, including first author name, histology, and enrolled patients in both intervention and control arms, is summarized in *Table 1*. The assessment of the risk of bias for these 5 studies was performed by at least two authors using Cochrane risk of bias tool (13). The results are presented in *Figures 2,3*; disagreements among investigators were resolved through the involvement of a third researcher.

Analysis of PFS

In a preliminary analysis, numerous questions arose in managing these five trials according to the methodology of the Shiny method. Regarding the three patient cohorts who were treated with TIS [studies by Lu *et al.* (4) and by Wang *et al.* (5), the latter including two different treatments; namely TIS plus CT and TIS plus nab-CT; see *Table 1*], one question was focused on the degree of homogeneity across the three patient groups who were given these TIS-containing regimens. Therefore, a separate Shiny analysis was conducted on the above patients to assess whether these three patient groups treated with TIS could be pooled into a single group. The results of this separate analysis (see Appendix 1 and *Figure 4* for details) suggest that pooling these three groups into a single group is acceptable; hence, the pooled group has been denoted as TIS group. Likewise, the same question applies to the three patient groups who were treated with PEM [studies by Awad *et al.* (6), Paz-Ares *et al.* (7), and Rodríguez-Abreu *et al.* (8), see *Table 1*]. Another separate Shiny analysis was therefore carried out to establish whether these three patient groups could be

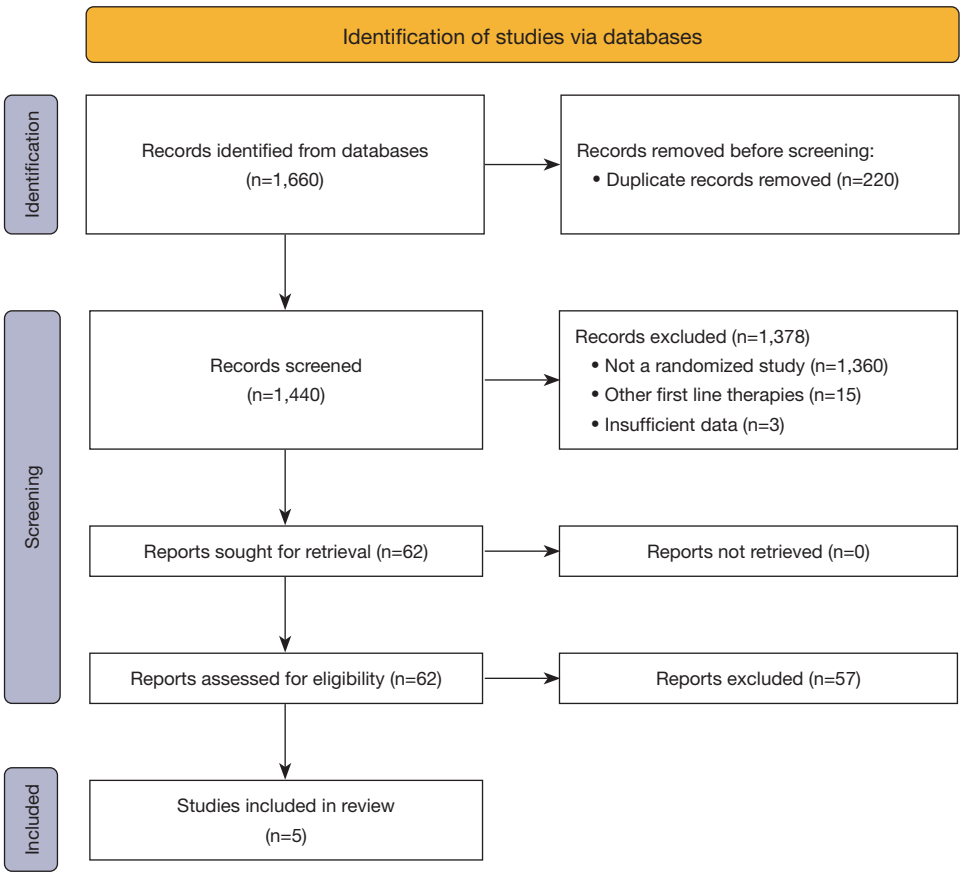

Figure 1 Flow chart of literature retrieval and selection according to PRISMA 2020 Guidelines. PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses.

Table 1 Characteristics of the 5 trials included in the Shiny analysis

First author	Histology	Treatment arm		Control arm	
		Treatment	Events	Treatment	Events
Wang (5)	Squamous	TIS + CT	52/119	CT	80/121
		TIS + nab-CT	57/120		
Lu (4)	Nonsquamous	TIS + PP	90/223	PP	68/111
Awad (6)	Nonsquamous	PEM + PC	36/60	PC	49/63
Rodríguez-Abreu (8)	Nonsquamous	PEM + PP	336/410	PP	196/206
Paz-Ares (7)	Squamous	PEM + nab-CT	206/278	nab-CT	250/281

All trials were phase-III. TIS, tislelizumab; CT, carboplatin and paclitaxel; nab-CT, carboblatin and paclitaxel nanoparticle albumin-bound; PP, pemetrexed and platinum; PEM, pembrolizumab; PC, pemetrexed and carboplatin.

pooled into a single group; also in this case, the results (see Appendix 2 and *Figure 5* for details) suggest that pooling these 3 groups into a single group ("PEM group") is acceptable, even though more caution is needed in this case. In fact, while the PFS pattern observed in the trial by Awad *et al.* (6) was significantly better than that observed in the trials by Paz-Ares *et al.* (7) and Rodriguez-Abreu *et al.* (8) (*Figure 5*), the small size of the trial by Awad

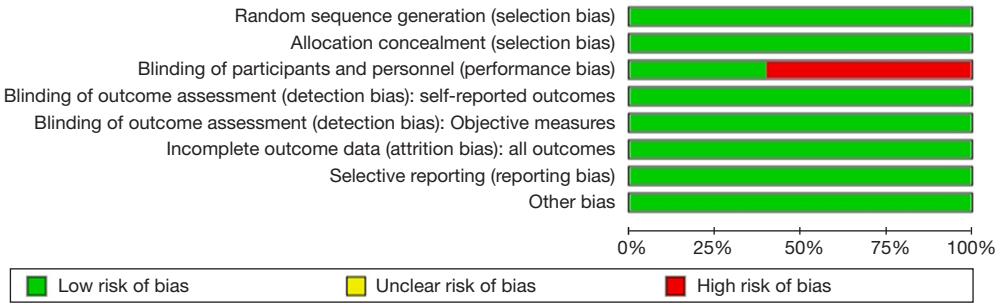

Figure 2 Risk of bias graph of the five included studies.

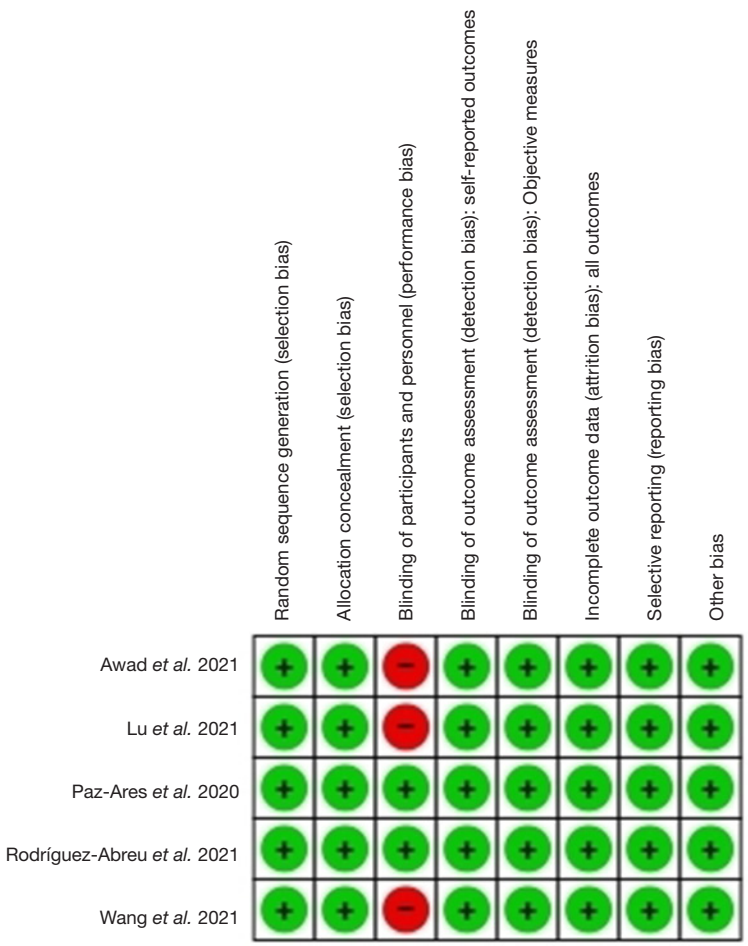

Figure 3 Risk of bias summary. Green, low risk of bias; red, high risk of bias.

et al. (6) should be kept in mind as a potential confounding factor. More importantly, this choice of pooling these three groups into a single group seems to be fully justified by our finding that the controls of the trial by Awad *et al.* (6) had a significantly better prognosis than that of the other 5 patient groups. Hence, the better outcomes found for Awad's trial compared with the trials by Paz-Ares (7) and Rodríguez-Abreu (8) likely do not depend on the

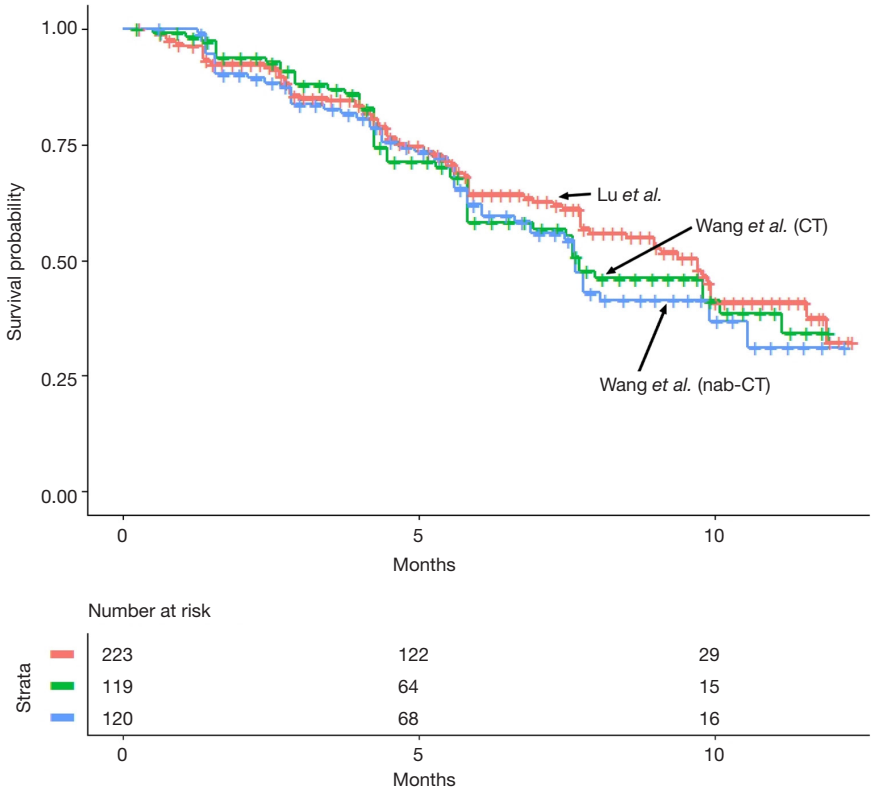

Figure 4 Kaplan-Meier curves of reconstructed patients for the three treatments based on TIS (data from three patient cohorts). The three patient groups can be identified as follows: trial by Lu *et al.*, n=223 (4); trial by Wang *et al.* (arm treated with CT), n=119 (5); trial by Wang *et al.* (arm treated with nab-CT), n=120 (5). See *Table 1* and Appendix 1 for further details. Endpoint: progression-free survival. CT, carboplatin and paclitaxel; nab-CT, carboblatin and paclitaxel nanoparticle albumin-bound; TIS, tislelizumab.

better efficacy of the PEM + pemetrexed and carboplatin (PC) treatment, but on the characteristics of the patients enrolled in Awad's trial.

A total of 11 patient cohorts were included in our Shiny analysis (i.e., two cohorts per trial plus the third cohort of Wang's trial). *Figure 6* shows the typical multi-treatment graph which was generated by our Shiny analysis. In comparing PEM plus chemotherapy (n=748) or TIS plus chemotherapy (n=462) *vs.* chemotherapy alone (n=782), the combination treatments showed—in both cases—a significant advantage in terms of PFS compared with chemotherapy alone. The HR was 0.5856 (95% CI: 0.4986–0.6876) for TIS plus chemotherapy and 0.5573 (95% CI: 0.4969–0.6251) for PEM plus chemotherapy. As expected, these findings confirmed the results of the original trials. Medians were 8.89 months for PEM combination, 7.97 months for TIS combination, and 5.69 months for the controls. The most interesting result of our analysis is represented by the indirect comparison of PEM plus chemotherapy *vs.* TIS plus chemotherapy. This comparison showed a substantial equivalence between these two agents (HR =0.952; 95% CI: 0.775–1.168). According to regulatory recommendations (11), if the CI is expressed based on the 90% boundaries of HR, the degree of equivalence is expressed by the HR of 0.952 (90% CI: 0.801–1.130). This implies that, in the comparison of PEM *vs.* TIS, the boundaries of HR range from –19.9% to +13.0%; this result reasonably supports the conclusion that, in terms of efficacy, these two treatments are equivalent.

Assessment of heterogeneity across the 5 control groups

The Kaplan-Meier curves of reconstructed patients for the 5 control groups are shown in *Figure 7*. In this analysis, the likelihood ratio test was 31.43 [4 degrees of freedom (df), P<0.001], while concordance was 0.531 [standard error (se) =0.013]. Clearly, the heterogeneity in these datasets

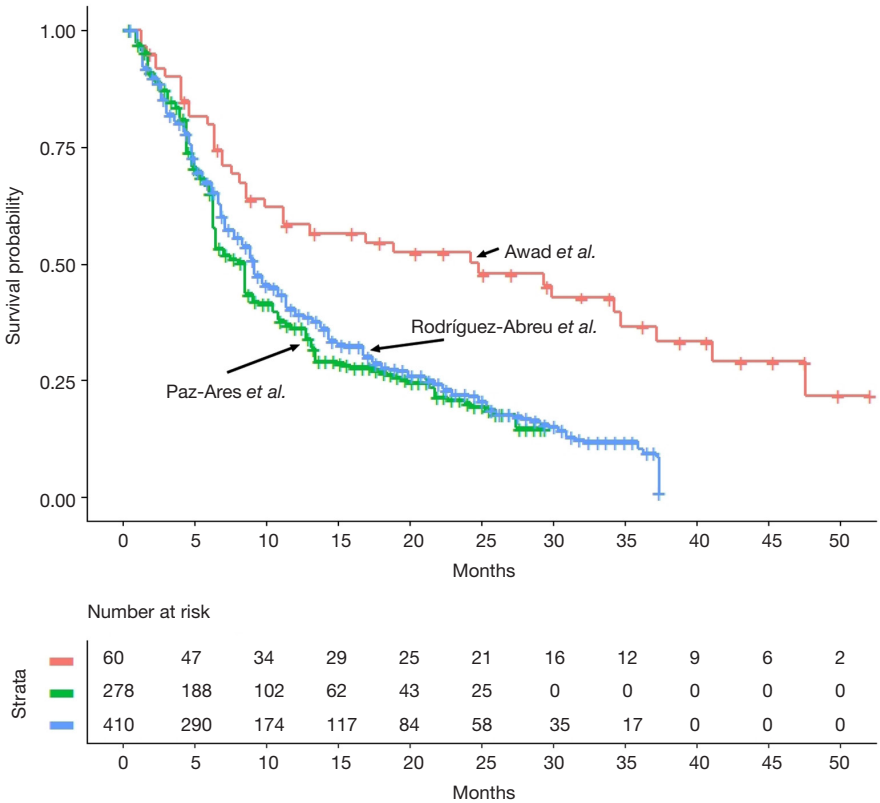

Figure 5 Kaplan-Meier curves of reconstructed patients for the three treatments based on PEM (data from three patient cohorts). The three patient groups can be identified as follows: trial by Awad *et al.*, n=60 (6); trial by Paz-Ares *et al.*, n=278 (7); trial by Rodríguez-Abreu *et al.*, n=410 (8). See *Table 1* and Appendix 2 for further details. Endpoint: progression-free survival. PEM, pembrolizumab.

depends on the more favorable outcomes observed for the control group of the trial by Awad *et al.* compared with the other 4 control groups. Medians of PFS were as follows: Lu *et al.* trial (n=111), 7.50 months (95% CI: 5.61–7.96); Wang *et al.* trial (n=121), 5.69 months (95% CI: 4.33–5.69); Awad *et al.* trial (n=63), 10.20 months (95% CI: 6.49–17.91); Paz-Ares *et al.* trial (n=281), 5.20 months (95% CI: 4.49–6.00); Rodríguez-Abreu *et al.* (n=206), 5.08 months (95% CI: 4.71–5.70).

If one assumes the trial by Lu *et al.* as a reference, the values of HR regarding the comparisons between each of the other five control groups *vs.* the control group of Lu *et al.* are the following:

- Wang *et al.* (5) *vs.* Lu *et al.* (4): HR =1.3463 (95% CI: 0.9735–1.8620);
- Awad *et al.* (6) *vs.* Lu *et al.* (4): HR =0.5956 (95% CI: 0.4049–0.8762);
- Paz-Ares *et al.* (7) *vs.* Lu *et al.* (4): HR =1.2570 (95% CI: 0.9593–1.6472);
- Rodríguez-Abreu *et al.* (8) *vs.* Lu *et al.* (4): HR =1.3071 (95% CI: 0.9900–1.7258).

It is difficult to explain why the patients enrolled in the trial by Awad *et al.* (6) had a more favorable prognosis. Probably, as the authors speculated, these better results in terms of PFS might be due to an increased variability associated with the smaller patient population as well as the possible inclusion of patients with better prognosis in KEYNOTE-021.

Discussion

To our knowledge, in the area of first-line treatments for advanced NSCLC this is the first indirect comparison in which the Shiny method has been used to assess the efficacy of TIS combined with chemotherapy in comparison with PEM combined with chemotherapy. The main result of our analysis is that TIS and PEM, given for this clinical indication, prove to be similar in terms

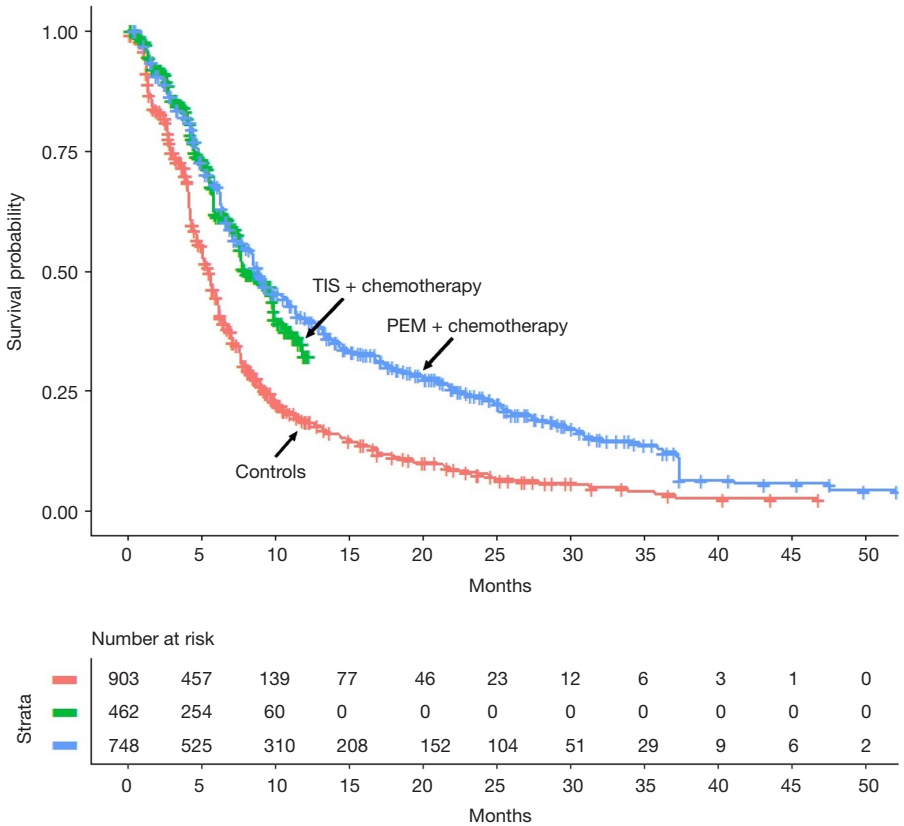

Figure 6 Main analysis: the figure shows the typical multi-treatment graph generated by the Shiny analysis. Endpoint: progression-free survival. TIS, tislelizumab; PEM, pembrolizumab.

of efficacy. This finding of a substantial equivalence has a remarkable clinical relevance, but has also important budget implications because, at least in China, the cost of TIS is much cheaper than that of PEM. According to Luo *et al.* (14) and Liang *et al.* (15), the acquisition cost for TIS in China is 88% lower than that of PEM; furthermore, one should also keep in mind that, in 2023, TIS is expected to enter the European market (16).

Our analysis has several limitations. Firstly, since the Shiny method typically deals with efficacy, the comparison between TIS and PEM will need to be integrated by further analyses comparing the safety of TIS *vs.* PEM; quite interestingly, no relevant differences have however been reported in the literature published thus far.

Among the strengths of the present study, it should be stressed that this analysis represents a new, and original application of the Shiny method that has, at the same time, both clinical and economic implications. It is well known that the most typical applications of the Shiny method include the indirect comparisons across treatments aimed at the same disease condition (10). Moreover, the one-to-many analysis (17) is another and more specific application in which, after a new treatment has become available, its place in therapy is evaluated through the typical multi-treatment Shiny graph by contrasting the new treatment against those developed previously. In the present study, since a single, well-recognized SOC could be identified (i.e., PEM combined with chemotherapy), our analysis had a quite new design ("one-to-SOC" design), that compared TIS combined with chemotherapy with a single SOC represented by PEM combined with chemotherapy. In this framework, the equivalence that we found between TIS and PEM is an original piece of information that facilitates the interpretation of the current state of the art in this field. Finally, regarding the Shiny method, while most of its initial applications were in the area of oncology (10), more recently numerous applications have been focused also on cardiology (18-21).

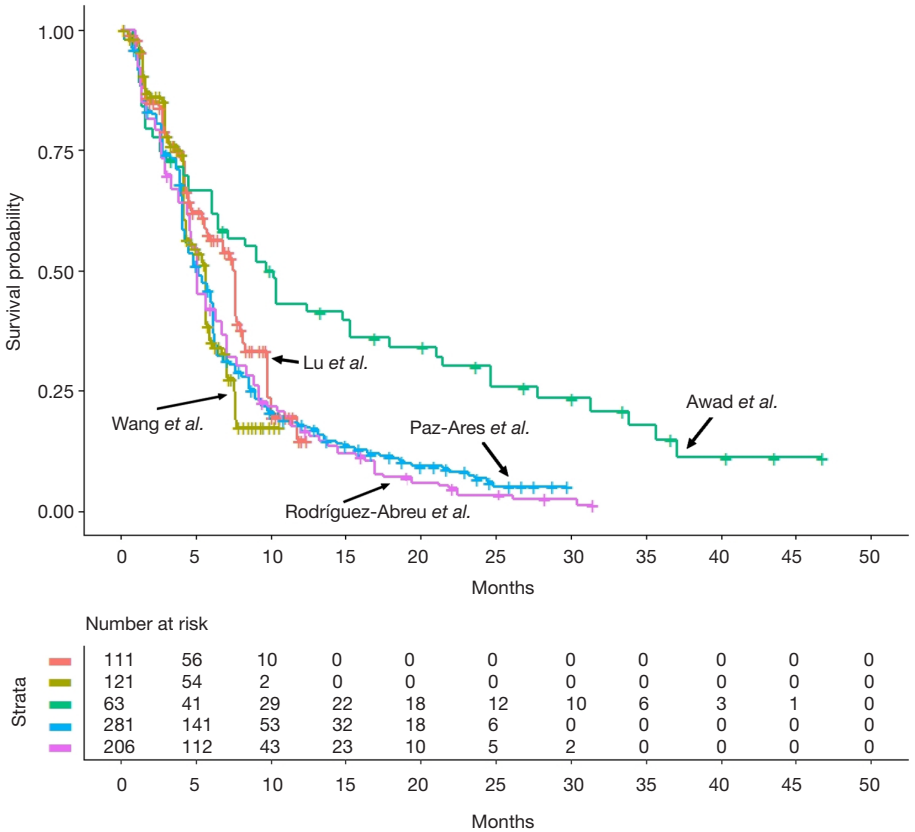

Figure 7 Kaplan-Meier curves of reconstructed patients for the five control groups. The five control groups can be identified as follows: trial by Lu *et al.*, n=111 (4); trial by Wang *et al.*, n=121 (5); trial by Awad *et al.*, n=63 (6); trial by Paz-Ares *et al.*, n=281 (7); trial by Rodríguez-Abreu *et al.*, n=206 (8). Endpoint: progression-free survival.

Conclusions

The main message from this article is that TIS and PEM have an equivalent efficacy in the first-line treatment of advanced NSCLC. This finding is another piece of knowledge generated by the Shiny method in the field of indirect comparisons based on hypothetical patients reconstructed from Kaplan-Meier curves. This thread of research has a growing impact in oncology, but covers all areas of medicine where the endpoints have the form of a time-to-event analysis.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://cco.amegroups.com/article/view/10.21037/cco-23-26/rc

Peer Review File: Available at https://cco.amegroups.com/article/view/10.21037/cco-23-26/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://cco.amegroups.com/article/view/10.21037/cco-23-26/coif). MC declares that he is a full-time researcher of Sifact (Società Italiana di Farmacia Clinica e Terapia, Torino) and he took this role in this project. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Han Y, Liu D, Li L. PD-1/PD-L1 pathway: current researches in cancer. Am J Cancer Res 2020;10:727-42.
2. Lee A, Keam SJ. Tislelizumab: First Approval. Drugs 2020;80:617-24.
3. Zhang L, Geng Z, Hao B, et al. Tislelizumab: A Modified Anti-tumor Programmed Death Receptor 1 Antibody. Cancer Control 2022;29:10732748221111296.
4. Lu S, Wang J, Yu Y, et al. Tislelizumab Plus Chemotherapy as First-Line Treatment for Locally Advanced or Metastatic Nonsquamous NSCLC (RATIONALE 304): A Randomized Phase 3 Trial. J Thorac Oncol 2021;16:1512-22.
5. Wang J, Lu S, Yu X, et al. Tislelizumab Plus Chemotherapy vs Chemotherapy Alone as First-line Treatment for Advanced Squamous Non-Small-Cell Lung Cancer: A Phase 3 Randomized Clinical Trial. JAMA Oncol 2021;7:709-17.
6. Awad MM, Gadgeel SM, Borghaei H, et al. Long-Term Overall Survival From KEYNOTE-021 Cohort G: Pemetrexed and Carboplatin With or Without Pembrolizumab as First-Line Therapy for Advanced Nonsquamous NSCLC. J Thorac Oncol 2021;16:162-8.
7. Paz-Ares L, Vicente D, Tafreshi A, et al. A Randomized, Placebo-Controlled Trial of Pembrolizumab Plus Chemotherapy in Patients With Metastatic Squamous NSCLC: Protocol-Specified Final Analysis of KEYNOTE-407. J Thorac Oncol 2020;15:1657-69.
8. Rodríguez-Abreu D, Powell SF, Hochmair MJ, et al. Pemetrexed plus platinum with or without pembrolizumab in patients with previously untreated metastatic nonsquamous NSCLC: protocol-specified final analysis from KEYNOTE-189. Ann Oncol 2021;32:881-95.
9. Liu N, Zhou Y, Lee JJ. IPDfromKM: reconstruct individual patient data from published Kaplan-Meier survival curves. BMC Med Res Methodol 2021;21:111.
10. Messori A, Damuzzo V, Rivano M, et al. Application of the IPDfromKM-Shiny Method to Compare the Efficacy of Novel Treatments Aimed at the Same Disease Condition: A Report of 14 Analyses. Cancers (Basel) 2023;15:1633.
11. Walker E, Nowacki AS. Understanding equivalence and noninferiority testing. J Gen Intern Med 2011;26:192-6.
12. Messori A. Indirect comparison of survival data based on the Shiny method: the role of control groups in the assessment of heterogeneity. Research Square 2022. doi: https://doi.org/10.21203/rs.3.rs-2006322/v1.
13. Cochrane Collaboration. Summary assessments of the risk of bias. Available online: https://epoc.cochrane.org/sites/epoc.cochrane.org/files/public/uploads/Resources-for-authors2017/summary_assessments_of_the_risk_of_bias.pdf
14. Luo X, Zhou Z, Zeng X, et al. The Cost-Effectiveness of Tislelizumab Plus Chemotherapy for Locally Advanced or Metastatic Nonsquamous Non-Small Cell Lung Cancer. Front Pharmacol 2022;13:935581.
15. Liang X, Chen X, Li H, et al. Tislelizumab plus chemotherapy is more cost-effective than chemotherapy alone as first-line therapy for advanced non-squamous non-small cell lung cancer. Front Public Health 2023;11:1009920.
16. Pharmabiz.com. EMA accepts BeiGene's MAA for tislelizumab to treat patients with ESCC & NSCLC. Available online: http://www.pharmabiz.com/NewsDetails.aspx?aid=147951&sid=2
17. Messori A, Rivano M, Cancanelli L, et al. The "One-to-Many" Survival Analysis to Evaluate a New Treatment in Comparison With Therapeutic Alternatives Based on Reconstructed Patient Data: Enfortumab Vedotin Versus Standard of Care in Advanced or Metastatic Urothelial Carcinoma. Cureus 2022;14:e28369.
18. Sá MP, Jacquemyn X, Van den Eynde J, et al. Impact of Prosthesis-Patient Mismatch After Transcatheter Aortic Valve Replacement: Meta-Analysis of Kaplan-Meier-Derived Individual Patient Data. JACC Cardiovasc Imaging 2023;16:298-310.
19. Sá MP, Jacquemyn X, Van den Eynde J, et al. Impact of Paravalvular Leak on Outcomes After Transcatheter Aortic Valve Implantation: Meta-Analysis of Kaplan-Meier-derived Individual Patient Data. Struct Heart 2022;7:100118.
20. Jacquemyn X, Van den Eynde J, Iwens Q, et al. Transcatheter aortic valve implantation versus surgical

aortic valve replacement in chronic kidney disease: Meta-analysis of reconstructed time-to-event data. Trends Cardiovasc Med 2023;S1050-1738(23)00053-1.
21. Fong KY, Yap JJL, Chan YH, et al. Network Meta-Analysis Comparing Transcatheter, Minimally Invasive, and Conventional Surgical Aortic Valve Replacement. Am J Cardiol 2023;195:45-56.

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