Tislelizumab vs Pembrolizumab for First-Line Treatment of Non-Small Cell Lung Cancer: Literature Review of Indirect Treatment Comparisons

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BACKGROUND

- Programmed cell death (PD) protein 1 (PD-1) inhibitors like tislelizumab (TIS) and pembrolizumab (PEM), with or without chemotherapy (CT) have demonstrated survival benefits among patients with advanced/metastatic non-small cell lung cancer (NSCLC), vs CT alone.[1–5]
- In particular, the structure of TIS has been modified to maximally inhibit the binding of PD-1 to PD-ligand 1 (PD-L1).[6]
- It is important to understand the comparative efficacy of PD-1 inhibitors to facilitate evidence-driven clinical decisions. However, no head-to-head trials of TIS vs PEM are available.[7]

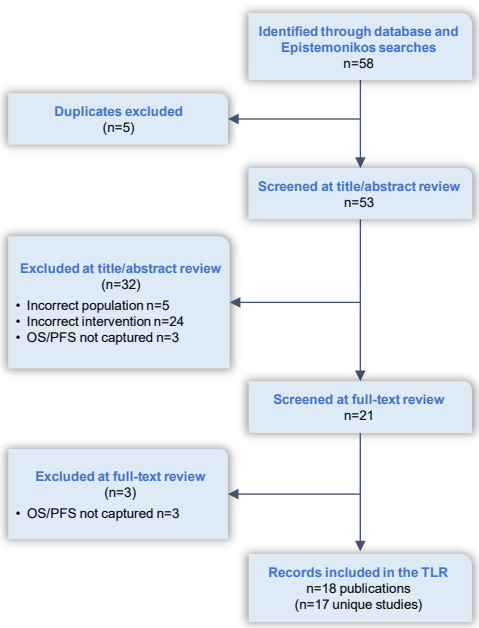
OBJECTIVE

- This targeted literature review (TLR) of published indirect treatment comparisons (ITCs) identified comparative evidence on survival outcomes for first-line (1L) NSCLC treatment with TIS or PEM regimens.

METHODS

- MEDLINE, Embase, the Cochrane Database of Systematic Reviews and Epistemonikos were searched from database inception in March and July 2025, respectively.
- ITCs reporting overall survival (OS) or progression-free survival (PFS) for TIS and PEM (as monotherapy or combination therapies) among patients with 1L NSCLC were eligible.
- Article screening was conducted by a single reviewer. Data were extracted from eligible articles by a single reviewer and all extracted information was verified by a second reviewer.

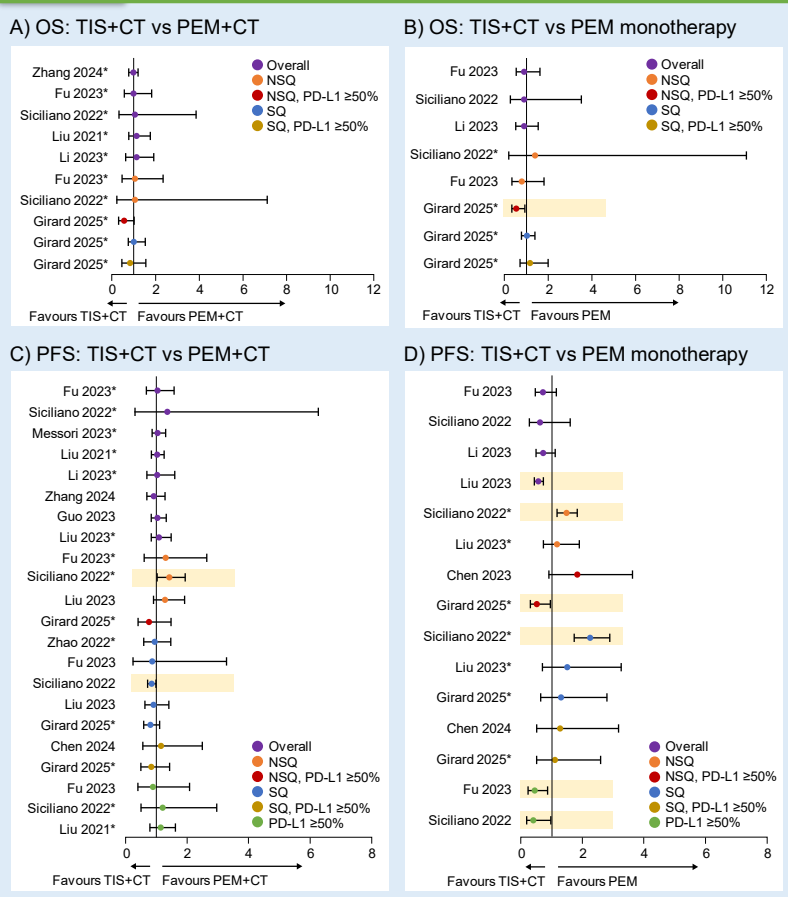
Figure 1 PRISMA flowchart



RESULTS

- Of 53 abstracts screened and 21 potentially eligible full-texts reviewed, 18 articles on 17 unique studies were ultimately eligible (Figure 1).
- Fourteen studies were network meta-analyses (NMAs), two were Bucher ITCs and one reconstructed individual patient data using IPDfromKM-Shiny. Most ITCs used CT as the connecting node, except three NMAs which also included PD-1 inhibitors as nodes.
- Eight ITCs compared TIS vs PEM regimens for OS, with none reporting significant differences for TIS+CT vs PEM+CT and only one reporting a significant difference for TIS+CT vs PEM, in non-squamous patients (NSQ) with PD-L1 ≥50% (Figure 2A, B).
- Fifteen ITCs compared PFS outcomes between TIS and PEM regimens; no significant differences were seen in overall analyses for TIS+CT vs PEM+CT and only one NMA showed a significant difference for TIS+CT vs PEM. Some significant results were observed in specific subgroups (Figure 2C, D).
- In subgroup analyses for TIS+CT vs PEM+CT (Figure 2C), results were mixed; one ITC reported significantly better PFS for PEM+CT in NSQ and better PFS for TIS+CT in squamous (SQ) patients, while four other ITCs reported no significant differences. In three ITCs reporting on PFS in the PD-L1 ≥50% subgroup, there were no significant differences (Figure 2C).
- In the analyses of TIS+CT vs PEM monotherapy (Figure 2D), one ITC reported that PEM was associated with significantly better PFS in both NSQ and SQ patients.
- In two ITCs reporting PFS for the PD-L1 ≥50% subgroup, both significantly favoured TIS+CT over PEM monotherapy. Three ITCs stratified by both PD-L1 ≥50% and histology; in NSQ, one of two ITCs significantly favoured TIS+CT, but both ITCs in SQ showed no significant differences (Figure 2D).
- One ITC (not shown in the figure) compared PFS and OS for TIS vs PEM monotherapies, reporting no significant differences in the overall or stratified populations.

Figure 2 Forest plots of HRs from ITCs comparing OS and PFS



Footnotes: Figures present data from studies reporting hazard ratios (HRs). The vertical line indicates HR=1; HR<1 indicates favourable outcomes for TIS regimens. Error bars represent 95% confidence intervals (CIs) or credible intervals (CrIs). Estimates are from different ITC studies in different populations. As no meta-analysis was conducted, estimates are not directly comparable across studies and must be interpreted with caution. Yellow highlight indicates statistically significant differences. *HRs were originally reported in the literature as PEM vs TIS, and the reciprocal of the HR and CIs were calculated to align the reference group for these forest plots.

CONCLUSIONS

- In most ITCs, TIS and PEM regimens had comparable survival outcomes. OS was similar regardless of subgroup stratifications, except for a single ITC favouring TIS+CT over PEM monotherapy, in NSQ patients with PD-L1 ≥50%.
- PFS was also broadly similar in comparisons of TIS+CT vs PEM+CT. For TIS+CT vs PEM monotherapy, a number of ITCs reported comparable or favourable PFS for TIS+CT in patients with PD-L1 ≥50%, but results varied between ITCs among histology subgroups.
- While varying methodological approaches (such as the inclusion of different studies) may have led to some divergent results between ITCs, the results indicate overall similar survival outcomes with TIS+CT and PEM+CT. The use of PEM monotherapy (vs TIS+CT) should be carefully considered for specific subgroups.

Abbreviations: **1L:** first-line; **CI:** confidence interval; **CrI:** credible interval; **CT:** chemotherapy; **HR:** hazard ratio; **ITC:** indirect treatment comparison; **NMA:** network meta-analysis; **NSCLC:** non-small cell lung cancer; **NSQ:** non-squamous; **OS:** overall survival; **PD:** programmed cell death; **PD-1:** programmed cell death protein-1; **PD-L1:** programmed death-ligand-1; **PEM:** pembrolizumab; **PFS:** progression-free survival; **PRISMA:** Preferred Reporting Items for Systematic Reviews and Meta-Analyses; **SQ:** squamous; **TIS:** tislizumab; **TLR:** targeted literature review.

References

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Disclosures

Junice Ng and Lin Zhan are employees of BeOne.

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