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Lack of Evidence Guiding the Selection of Immune Checkpoint Inhibitors for Non-Small-Cell Lung Cancer on Progression-Free and Overall Survival: A Systematic Review and Meta-Analysis to Fill the Gap

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BACKGROUND

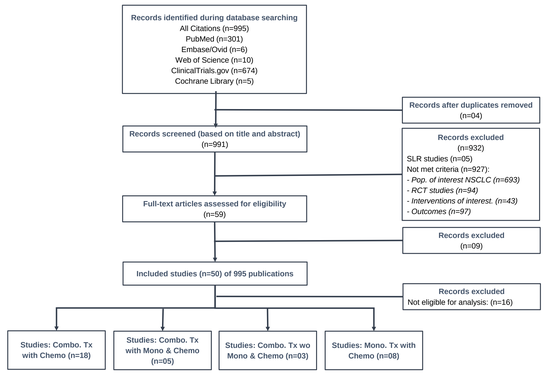
- The American Cancer Society's estimates for lung cancer in the US for 2025 are about 226,650 new cases of lung cancer (110,680 in men and 115,970 in women); nearly 124,730 deaths from lung cancer (64,190 in men and 60,540 in women).[1]
- In general, an estimate of 13% all lung cancers are small-cell lung cancer (SCLCs), and around 87% are Non-SCLC.[1]
- The overall economic burden of lung cancer, including NSCLC in the US was estimated at $ $208.9 billion in 2020.[2] Thus, a timely and effective treatment of NSCLC is important both clinically and economically.[2]
- Immune checkpoint inhibitors (ICIs) represent a form of cancer therapy that leverages components of the immune system to target and eliminate tumor cells.[3]
- Progression-free survival (PFS) and overall survival (OS) are commonly used to evaluate new cancer treatments efficacy.
- Clinical practice guidelines endorse ICIs for managing NSCLC. However, optimal treatment strategies remain unclear.

OBJECTIVE

To compare the reported ICI therapies for NSCLC patients on PFS and OS.

METHODS

- SLR, MA, and subgroup analyses of the literature were conducted using PubMed, Embase/Ovid, Web of Science, ClinicalTrial.gov, and Cochrane Library databases through August 2024 in accordance with PRISMA guidelines.
- Clinical trials assessing monotherapy and combination ICI therapies efficacy in advanced NSCLC patients were included according to pre-specified criteria.
- Survival data, reported as Hazard Ratios (HRs) with 95% CIs, were analyzed using the random-effects DerSimonian–Laird method (using R 3.6.0 software).
- Results were presented as Forest plots and Sensitivity analysis included only studies reporting adjusted survival outcomes.
- Heterogeneity was assessed using I² and associated p-values. Bias was evaluated using funnel plot symmetry.



RCT=Randomized Controlled Trials; w.=With; w.o.=Without; RWE=Real-World Evidence; Combo=Combination; Chemo=Chemotherapy; & Mono=Monotherapy

Figure 1: Flow chart shows the literature search yield and selection studies

RESULTS

- This analysis encompassed 22 studies, of which 21 were utilized for PFS, with 9,874 advanced NSCLC patients.
- The MA on outcomes revealed significant directional differences between interventions and controls, with lower HRs: *PFS (HR = 0.83 [95% CI: 0.75-0.92])* and not significant for *OS (HR = 0.99 [95% CI: 0.71-1.38])*.
- The MA subgroup analyses of individual ICI drugs and therapeutic strategies showed significant lower HRs:
  - **Cemiplimab,** with *PFS (HR = 0.78 [95% CI: 0.76-0.7])* and *OS (HR = 0.57 [95% CI: 0.32-1.01])*.
  - **Pembrolizumab-based therapy**, with *PFS (HR = 0.83 [95% CI: 0.75-0.92])* and *OS (HR = 0.84 [95% CI: 0.43-1.63])*.
  - **Combination ICI therapy versus chemotherapy**, with *PFS (HR = 0.53 [95% CI: 0.33-0.83])* and *OS (HR = 0.57 [95% CI: 0.32-1.01])*.

LIMITATIONS

- Heterogeneity is seen across included studies.
- Sources of heterogeneity include but are not limited to trial phases and conditions, number of previous treatments, criteria or threshold for reporting adverse events, and therapeutic dosages.
- Some degree of heterogeneity was tolerated for the sake of inclusivity in this study.
- Extensive subgroup analyses were conducted to enhance the sensitivity of this analysis.

CONCLUSIONS

Pembrolizumab-based ICI combinations result in the most favorable PFS and OS to treat NSCLC.

ICI-based combination result in a favorable strategy than chemotherapy. .

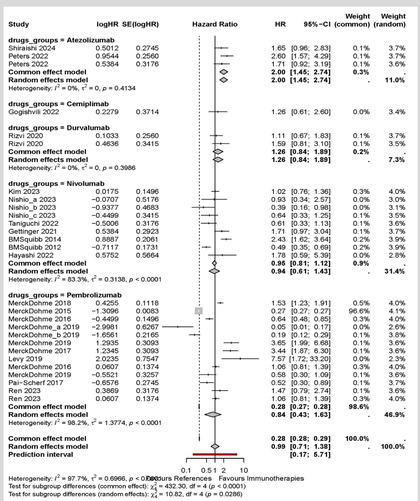


Figure 2: Analysis 1.1. comparison ICIs vs Chemo., OS.

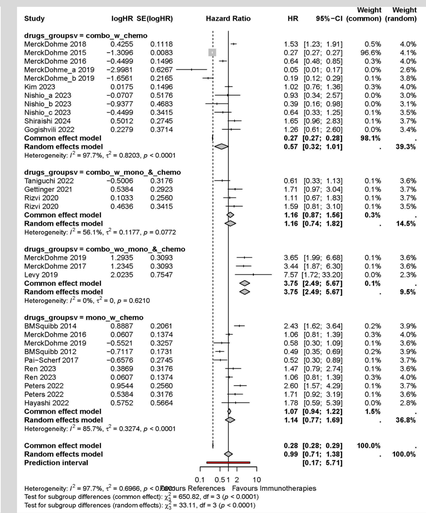


Figure 3: Analysis 1.2. comparison ICIs-combo. vs Chemo., OS.

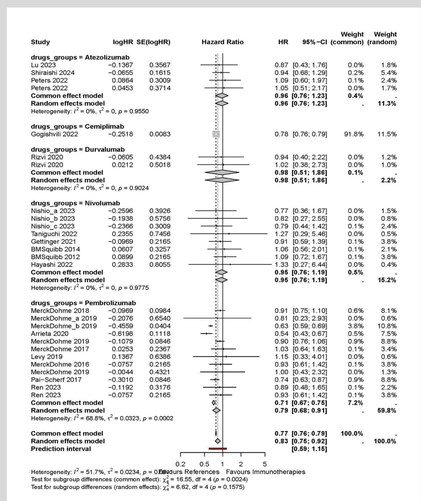


Figure 4: Analysis 2.1. comparison ICIs vs Chemo., PFS.

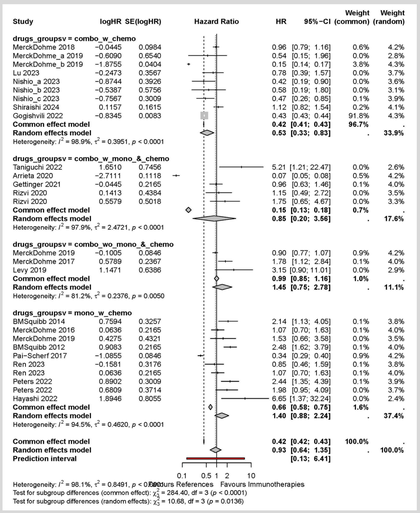


Figure 5: Analysis 2.2. comparison ICIs-combo. vs Chemo., PFS.

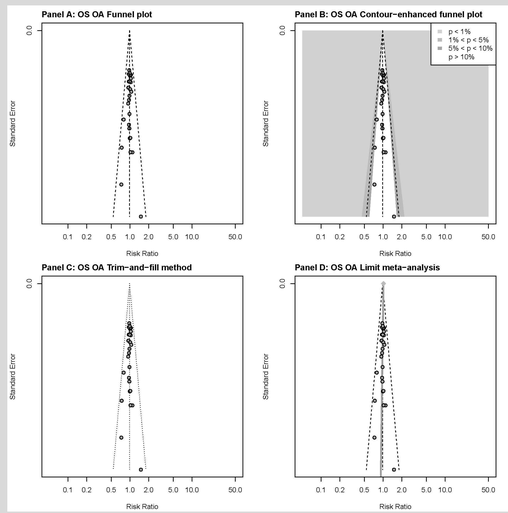


Figure 6: Assessment of bias across studies.

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