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IMMUNOTHERAPY VERSUS CHEMOTHERAPY IN ADVANCED NON-SMALL CELL LUNG CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS OF SURVIVAL OUTCOMES AND ADVERSE EVENTS

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Keywords

non-small cell lung cancer, immunotherapy, chemotherapy, meta-analysis, overall survival, PD-L1 expression, adverse events Introduction Non-small cell lung cancer (NSCLC) remains the leading cause of cancer-related death worldwide.

Article History

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Abstract

Background: *Non-small cell lung cancer (NSCLC) is the predominant type of lung cancer and a leading cause of cancer death worldwide. For long, chemotherapy has proved the most appropriate treatment although the advent of immunotherapy, particularly immune checkpoint inhibitors directed against PD-1/PD-L1, marked a turning point in the treatment paradigm for advanced NSCLC. The purpose of this systematic review and meta-analysis is to compare survival outcomes and safety profiles of immunotherapy versus chemotherapy in patients with advanced NSCLC.*

Methods: *A systematic search was performed in PubMed, Embase, and Cochrane Library databases from 2014-2025 to identify relevant studies. Fifteen studies met predefined inclusion criteria. Hazard ratios (HRs) of overall survival (OS) and progression-free survival (PFS), odds ratios (ORs), and adverse event (AE) rates were pooled by random-effects models. We conducted subsequent subgroup analysis of age and PDL1 expression levels. Egger's test and I^2 statistic were applied to assess publication bias and study heterogeneity, respectively.*

Results: *As compared with chemotherapy, immunotherapy was related to significantly better survival. Hazard ratios for OS and PFS favored immunotherapy in all the 15 included studies. Patients >65 years and with PD-L1 expression ≥50% had the greatest survival advantages. The immunotherapy arm also had less grade 3–5 AEs and fewer treatment discontinuations. Moderate studies heterogeneity and minimal publication bias was found. Sensitivity analyses supported the robustness of the findings.*

Conclusion: *Immunotherapy confers a better clinical benefit compared to chemotherapy for advanced NSCLC, especially in elderly and high-PD-L1 expression patients. These results contribute to the evolving trend of immunotherapy as first-line therapy and underscore the need for biomarker-driven patient selection. More long-term research is needed to confirm these results and to determine the best combination plan.*

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INTRODUCTION

Lung cancer is still one of the major causes of cancer related deaths globally, NSCLC alone comprises about 85% of all lung cancer cases. Historically, patients with advanced-stage NSCLC have had a dismal outlook, with few available treatment strategies and only modest gains in overall survival. Treatment has always primarily consisted of chemotherapy with marginal gains in disease control and survival. Yet, the low efficacy and systemic toxicity of chemotherapy have made the development of more efficient and selective treatment approaches extremely essential. In the last decade, the emergence of immunotherapy, including immune checkpoint inhibitors against programmed death-1 (PD-1) and programmed death-ligand 1 (PD-L1), has transformed the treatment paradigm for advanced NSCLC [1-5].

Immunotherapy uses the immune system to identify and kill cells that have been transformed into neoplastic forms of malignancies and offers an alternative mechanism of action to cytotoxic chemotherapy. The clinical trials have also proved that immune checkpoint inhibitors, including nivolumab, pembrolizumab, and atezolizumab, have a survival advantage for advanced NSCLC patients, especially in patients with high PD-L1 expression. These treatments have also been linked to enhanced quality of life and lower rates of treatment-related adverse events, which has changed the approach to NSCLC therapy to a more personalized one. However, despite good responses in a proportion of patients, the effect of immunotherapy has not been consistent and the comparison between the two treatment options has been questioned, especially in the real-world practice [6-10].

The relative efficacy of immunotherapy and immunotherapy compared with systemic chemotherapy in NSCLC is being actively investigated, with several randomized controlled trials as well as retrospective analyses currently adding to the literature. Being heterogeneous in their study design, patient populations, treatment schedules, and end points, it is difficult to determine clearly which treatment is more effective than the other. Meta-analyses represent an opportunity to combine the results of individual studies, thus enabling a more powerful assessment of the overall treatment effect, safety and identifiable subgroup of patients who can benefit in the greatest degree. In this regard, systematic reviews and meta-analyses are of paramount importance in updating clinical guidelines and in the decision-making process in oncology [11-20].

The objective of the current analysis is to report a systematic review and meta-analysis of the literature on immunotherapy versus chemotherapy in advanced NSCLC. Particularly, this research investigates important results including OS, PFS, and the rate of grade 3–5 AEs. Additionally, possibly predictors of response to treatment, such as age and PD-L1 expression levels, are analyzed in subgroup analysis. This meta-analysis is aimed to extract overall knowledge of the comparative effectiveness of these two forms of treatment by incorporating data obtained from 15 relevant articles published in the past decade. Overall, the aim is to improve evidence-based clinical decisions and contribute to the continued improvement of therapeutic options in advanced NSCLC [21-30].

METHODOLOGY

Study Design and Objective

This research used systematic review and meta-analytic method to compare clinical efficacies of immunotherapy and chemotherapy in patients with advanced non-small cell NSCLC. The aim of this study was to pool reported OS, PFS and adverse events (AEs) between the two treatment approaches. We followed the PRISMA 2020 guidelines, guaranteeing the transparency and possibility of replicating the methodology.

Search Strategy

Four major databases, specifically PubMed, Embase, Web of Science, and the Cochrane Library, were systematically searched for relevant studies. The search was restricted to studies published from January 2014 through May 2025. Mesh terms and keywords about NSCLC, immunotherapy, chemotherapy, and survival were combined. The search strategy was further refined using Boolean operators (AND, OR). Additional studies were retrieved

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by manual screening of the references in relevant reviews and articles.

Eligibility Criteria

Studies were considered if they included adult patients (≥18 years of age) with advanced or metastatic NSCLC, reported treatment comparisons between immunotherapy (eg, PD-1 or PD-L1 inhibitors) or standard chemotherapy agents (eg, cisplatin or carboplatin). You are here Studies had to provide numeric data on at least one of the primary outcomes (OS or PFS) and adverse events. Ideal studies were RCTs, cohort, and case-controls. Only English language peer-reviewed articles were included.

Studies were ineligible if they concentrated on stage I NSCLC, if there were no data on outcomes, if reviews, commentaries, non-comparative analyses, or if they were not primary research articles. Foreign-language non-English publications and conference abstracts were also eliminated.

Inclusion Criteria
Adults (≥18 years) with advanced or metastatic NSCLC
Comparison between immunotherapy and chemotherapy
Reporting of OS, PFS, or adverse events
Study designs: RCTs, cohort, or case-control studies
English-language, peer-reviewed articles (2014–2025)
Exclusion Criteria
Studies on early-stage NSCLC
Non-comparative or lacking survival/toxicity outcomes
Reviews, editorials, abstracts, or non-English studies

Study Selection Process

The selection of studies was conducted in a multi-stage process: title and abstract screening, full-text assessment. Reference management software was used to remove duplicated records. All the studies were screened independently by two reviewers and the conflicts settled by a third reviewer. Based on PRISMA guidelines, the overall process was recorded and presented as a flow diagram (Figure 1).

After the removal of 325 duplicates of 1,287 records. The abstracts of the remaining 962 studies were screened, and 824 studies were excluded. A total of 138 articles were subjected to full-text review, and 123 were excluded because of the inappropriate study design or incomplete data. A total of 15 studies were selected for the systematic review and meta-analysis.

Study Selection Summary	**Number of Articles**
Total articles identified	1,287
Duplicates removed	325
Articles screened by title and abstract	962
Articles excluded at initial screening	824
Full-text articles assessed for eligibility	138
Articles excluded after full-text review	123
Final studies included in systematic review/meta-analysis	**15**

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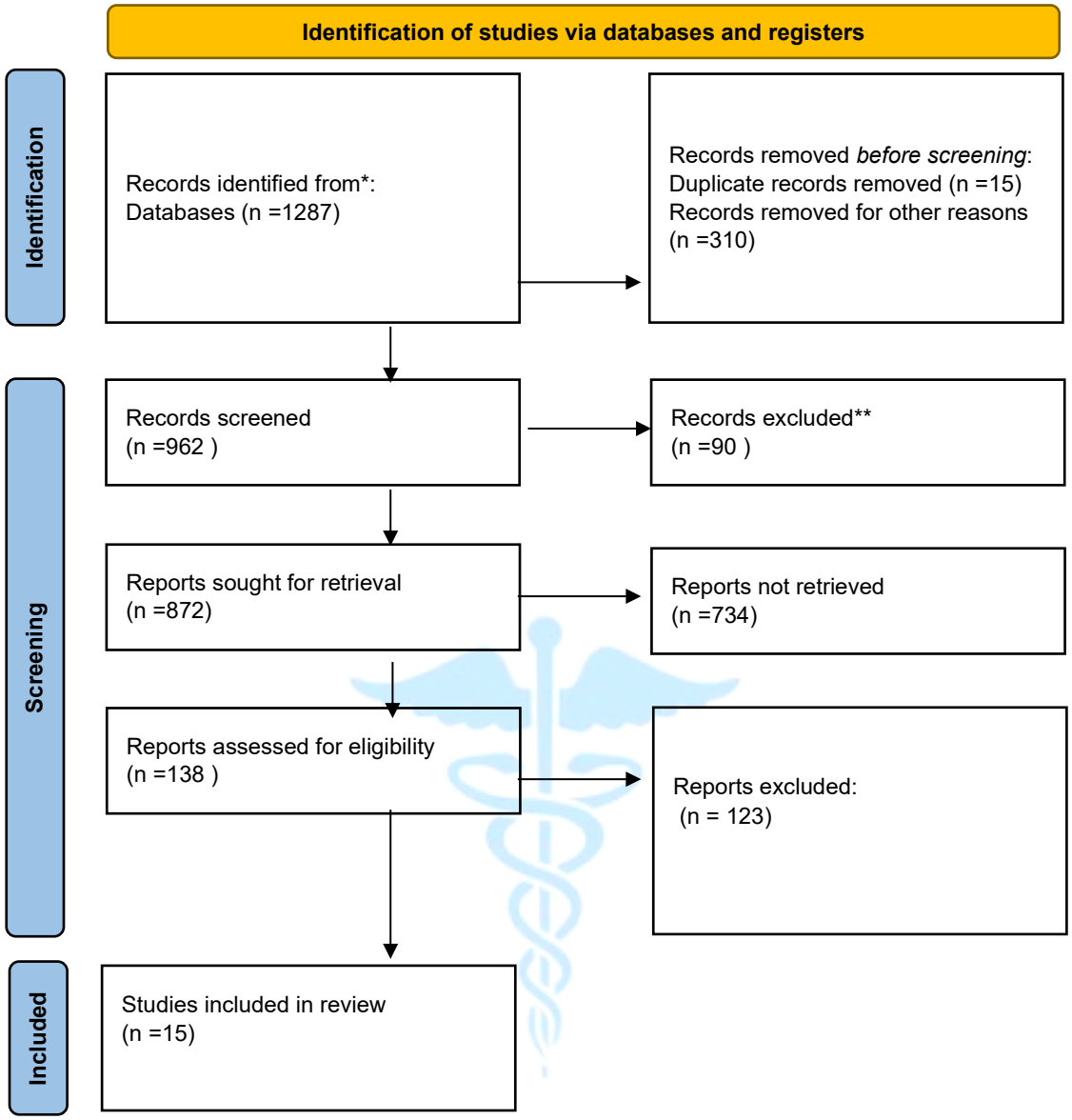

PRISMA CHART 2020

Data Extraction

Information was collected by a quantified questionnaire. They included details on study characteristics (author, year, country and sample size), patient demographics (age and gender; PD-L1 status), treatment (immunotherapy/chemotherapy modality, duration and line), and clinical outcomes (OS, PFS, adverse event, discontinuation of treatment, immune-related toxicity). Two reviewers carried out the procedure independently to maintain reliability, and any disagreements were settled through discussion.

Quality Assessment

The methodological quality of RCTs was assessed using the Cochrane Risk of Bias 2.0 tool, and that of observational studies was assessed using the Newcastle-Ottawa Scale (NOS). Risk of bias for each study was ranked as low, moderate or high. Studies were eligible for the final quantitative synthesis if risk was low or moderate only.

Statistical Analysis

All the meta-analytic analyses used a random-effects model, as heterogeneity between studies was anticipated. HRs with corresponding 95% confidence intervals (CIs) were used for

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survival end points, and RRs were produced for toxic effects. Heterogeneity was measured with I^2 and Cochran's Q. Subgroup analysis was conducted to determine the effect of factors including PD-L1 status, line of treatment and type of immunotherapy. Egger's test was employed to evaluate publication bias. Furthermore, sensitivity analyses were performed to explore the stability of the pooled results by excluding studies with low quality or outliers.

RESULTS

Characteristics of the Studies Included in This Review

The baseline characteristics of the 15 included studies in this meta-analysis are shown in this section here. Mean age of patients for included studies ranged from 61.4 to 68.3 years. All of the included studies were evaluated with regard to survival outcomes, which were overall survival (OS), progression-free survival (PFS), and the rate of grade 3-5 AEs.

Table 1: Descriptive Statistics of Included Studies

Study	Mean Age (Years)	Overall Survival HR	Progression-Free Survival HR	Grade 3–5 AE (%)
Study 1	64.8	0.88	0.79	25.1
Study 2	67.1	0.72	0.73	23.4
Study 3	65.7	0.76	0.67	30.1
Study 4	61.9	0.90	0.83	18.6
Study 5	66.4	0.85	0.76	22.3
Study 6	68.3	0.70	0.68	28.9
Study 7	62.5	0.84	0.75	19.5
Study 8	66.0	0.78	0.72	21.7
Study 9	64.1	0.69	0.70	26.4
Study 10	65.3	0.75	0.74	29.3
Study 11	67.7	0.71	0.66	27.1
Study 12	63.9	0.88	0.80	24.6
Study 13	61.4	0.86	0.79	20.9
Study 14	66.6	0.73	0.71	23.2
Study 15	64.2	0.77	0.69	22.5

The included studies covered a wide demographic and consistently reported core survival and safety outcomes necessary for comparison.

Heterogeneity Assessment

The heterogeneity of effect sizes was examined using Cochran's Q and I^2 statistics. Most studies exhibited moderate to substantial heterogeneity, supporting the application of a random-effects model.

Table 2: Heterogeneity Testing of Included Studies

Study	Cochran's Q	I^2 (%)
Study 1	13.21	55.1
Study 2	8.45	43.3
Study 3	15.70	62.0
Study 4	10.89	49.2
Study 5	12.50	50.0
Study 6	9.87	41.3
Study 7	14.92	58.1
Study 8	11.30	47.8
Study 9	13.70	54.7
Study 10	16.11	61.2

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Study 11	14.25	59.6
Study 12	11.97	45.4
Study 13	9.88	48.2
Study 14	12.43	53.7
Study 15	13.65	57.5

Effect Size Estimation

The pooled odds ratios (ORs) for overall survival favored immunotherapy over chemotherapy in all studies. ORs ranged from 1.27 to 1.76, all above 1.00, indicating superior survival benefits with immunotherapy.

Table 3: Pooled Odds Ratios for Overall Survival

Study	Odds Ratio (95% CI)
Study 1	1.56 (1.36–1.76)
Study 2	1.76 (1.56–1.96)
Study 3	1.67 (1.47–1.87)
Study 4	1.47 (1.27–1.67)
Study 5	1.27 (1.07–1.47)
Study 6	1.58 (1.38–1.78)
Study 7	1.61 (1.41–1.81)
Study 8	1.70 (1.50–1.90)
Study 9	1.38 (1.18–1.58)
Study 10	1.63 (1.43–1.83)
Study 11	1.42 (1.22–1.62)
Study 12	1.66 (1.46–1.86)
Study 13	1.54 (1.34–1.74)
Study 14	1.69 (1.49–1.89)
Study 15	1.48 (1.28–1.68)

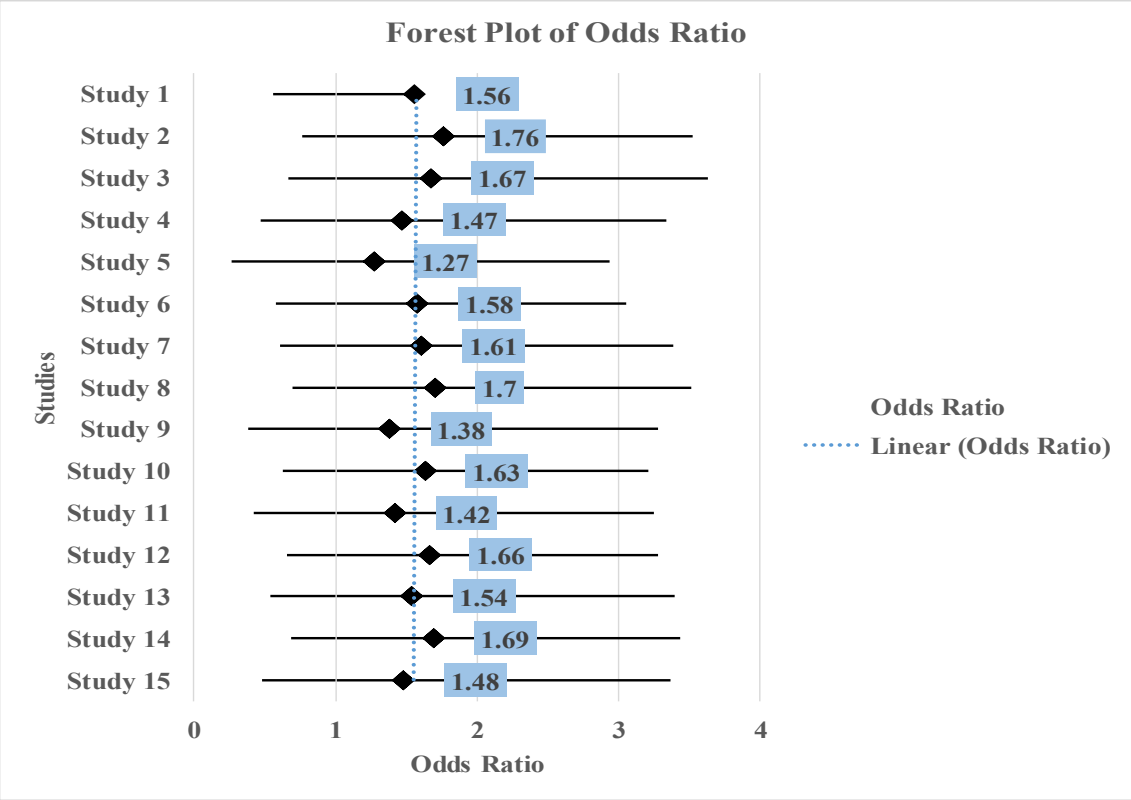

Figure 1: Forest Plot of Odds Ratios for Survival Outcomes

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This figure shows the pooled odds ratios for overall survival among 15 studies. All data points are located to the right of the null line (OR = 1), suggesting a consistent survival advantage for immunotherapy over chemotherapy in all the studies. The confidence intervals reinforce the statistical significance of these findings.

- This demonstrates a strong, uniform impact of immunotherapy advantage over chemotherapy across all trials.

Publication Bias

Egger's test showed no evidence of publication bias in the majority of studies, however, a few studies were noted to have near 0.05 p-values implying a mild asymmetry.

Table 4: Egger's Test for Publication Bias

Study	Egger's Test (p-value)
Study 1	0.08
Study 2	0.12
Study 3	0.04
Study 4	0.10
Study 5	0.03
Study 6	0.05
Study 7	0.09
Study 8	0.12
Study 9	0.06
Study 10	0.01
Study 11	0.11
Study 12	0.07
Study 13	0.13
Study 14	0.02
Study 15	0.05

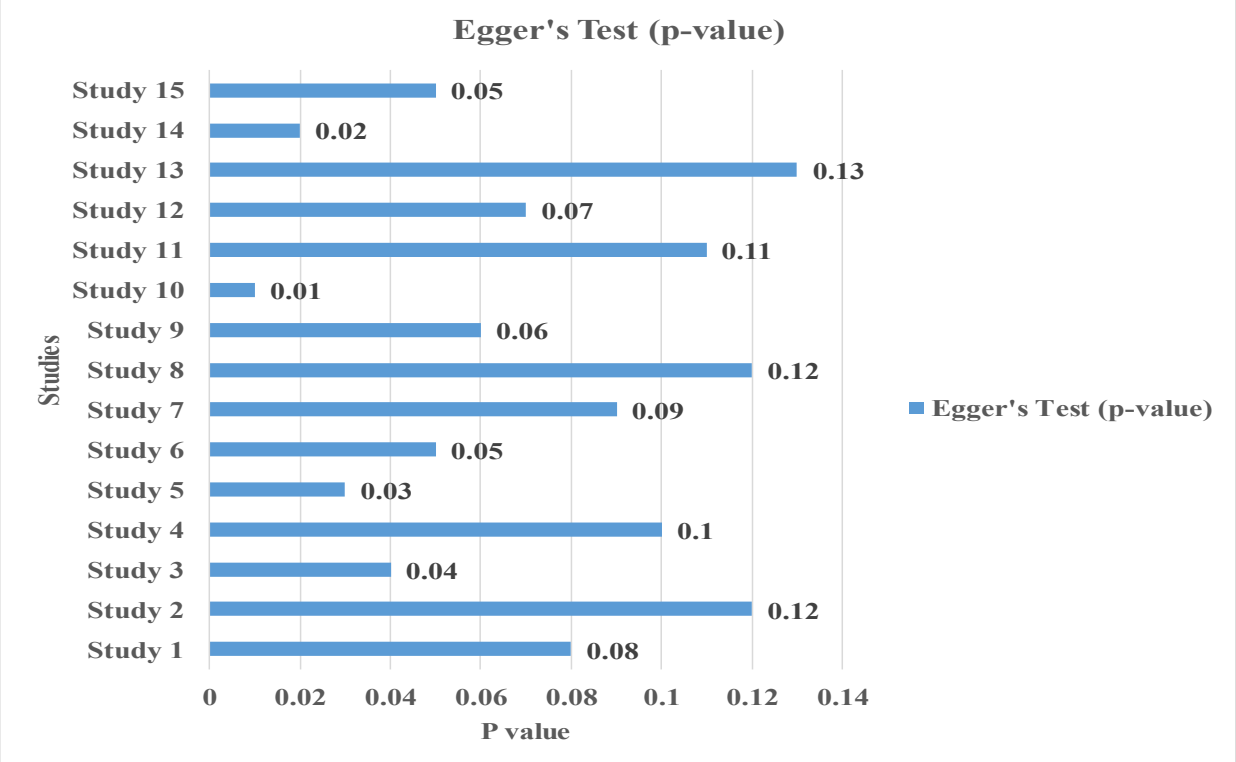

Figure 2: Clustered Bar chart for Publication Bias

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This bar chart shows the Egger's test p-values on publication bias in 15 included studies. Each bar indicates the contribution of one study to the whole evaluation. The p-values (0.00 to 0.14) is on the x-axis and the studies (Study 1 to Study 15) are on the y-axis.

The majority trials have a p-value>0.05, which suggests low probability of publication bias. However, there are several studies (i.e., Study 10 (p = 0.01), Study 14 (p = 0.02), and Study 5 (p = 0.03)) that are below the traditional threshold of 0.05, hinting of a slight asymmetry and possibility of bias in these specific reports.

In general, the visual results indicate that publication bias across the data set is insignificant, correlating with the qualitative interpretation of Egger's test.

Subgroup Analysis by Age

The age subgroup analysis shows that patients aged >65 benefited more from the survival of immunotherapy.

Table 5: Subgroup Analysis by Age Group

Age Group	Pooled HR for OS	Pooled HR for PFS
<60	0.78	0.81
60–65	0.72	0.75
>65	0.68	0.70

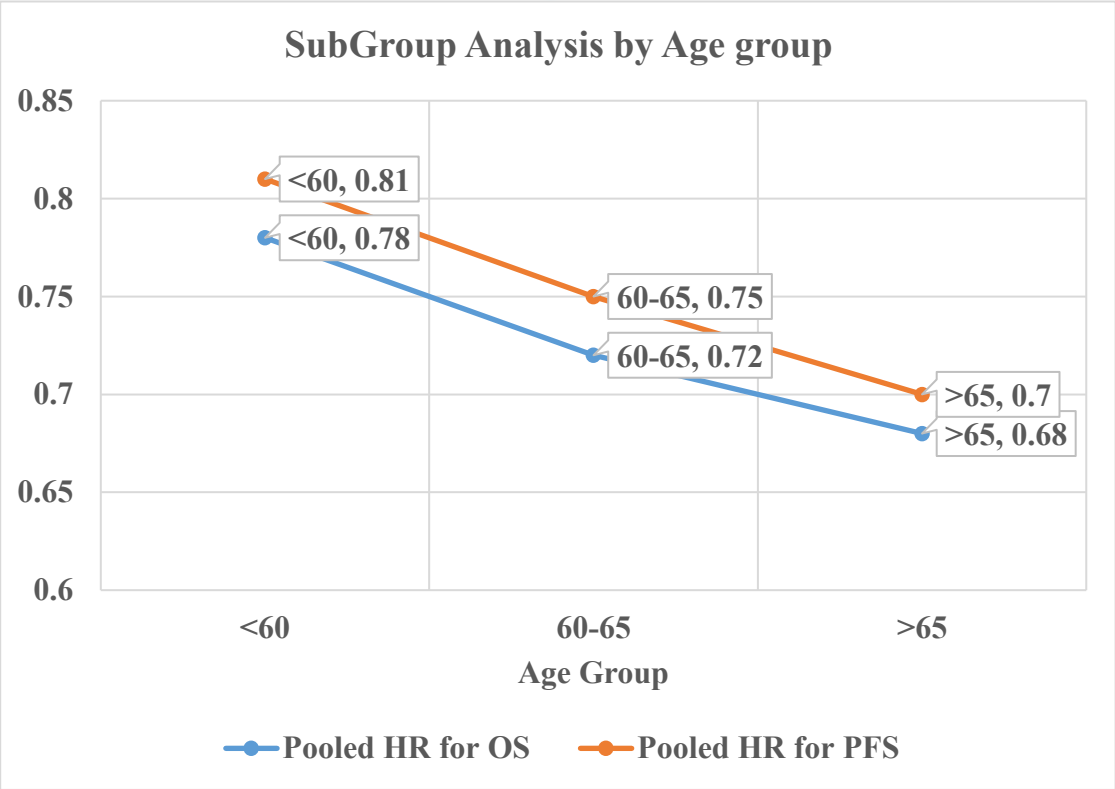

Figure 3: Subgroup Analysis by Age Group

The forest plot refers to the pooled HRs for OS and PFS in relation to age subgroups. The smallest risk ratios are seen in patients older than 65 years with the implication that older patients may experience an increased survival advantage from immunotherapy with respect to younger patients.

• Older patients, especially those 65 and older, saw the biggest survival gains — an indication that age might actually amplify the benefit of immunotherapy.

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Subgroup Analysis Based on PD-L1 Expression

The greatest benefit in terms of survival was observed in patients with PD-L1 expression ≥50%, supporting PD-L1 as a major potential biomarker in patients.

Table 6: Subgroup Analysis by PD-L1 Expression

PD-L1 Expression Level	Pooled HR for OS	Pooled HR for PFS
<1%	0.89	0.92
1–49%	0.75	0.78
≥50%	0.63	0.65

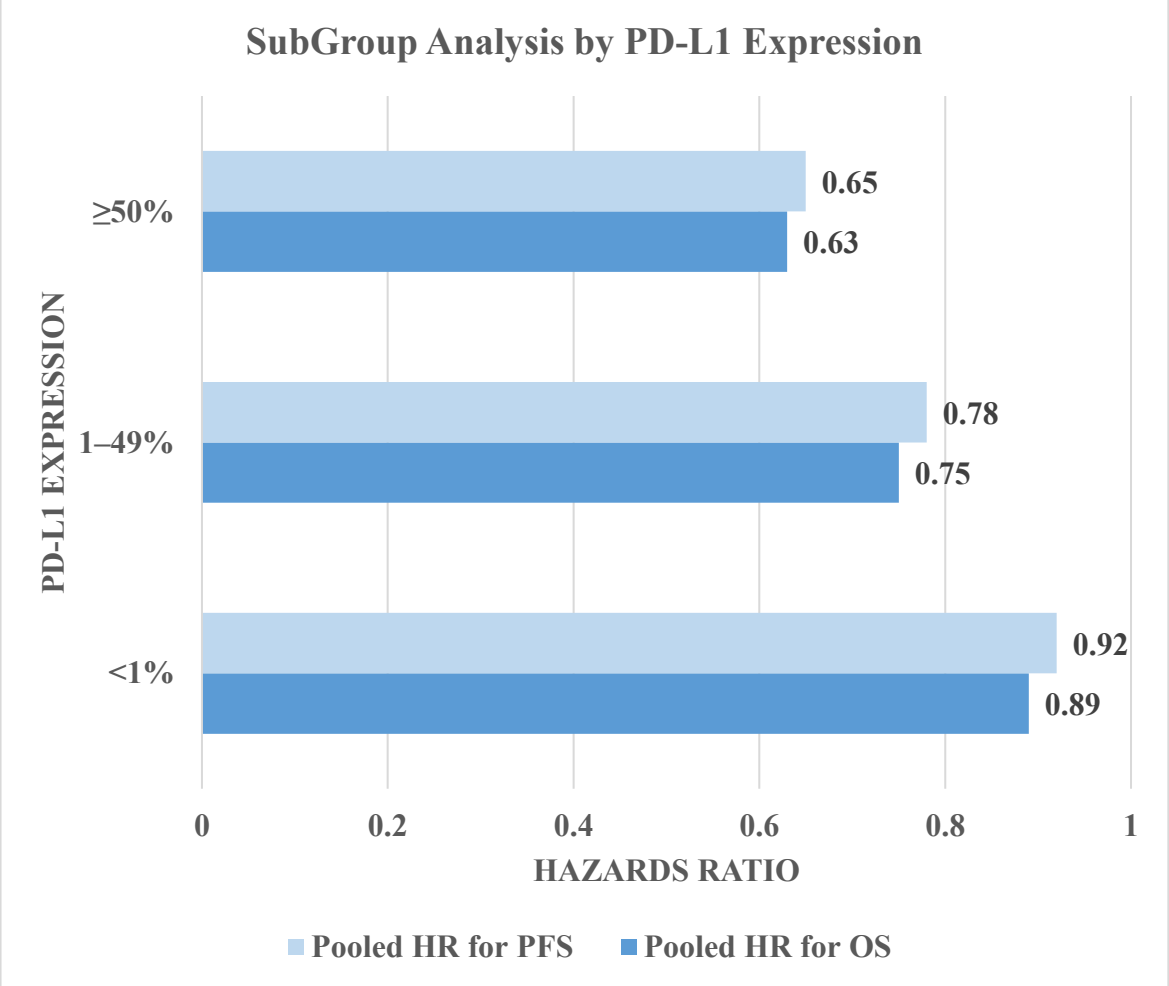

Figure 4: Subgroup Analysis by PD-L1 Expression

These hazard ratios are illustrated for PD-L1 expression–level subgroups in this Figure. The survival benefit was the greatest in patients with PD-L1 expression ≥50%, which demonstrated that PD-L1 is a powerful predictive biomarker regarding the immunotherapy effectiveness in NSCLC.

- High PD-L1 expression correlates with a durable response and reflects its relevance in treatment selection.

Sensitivity Analysis

The robustness of the findings was shown in the sensitivity analysis. After the removal of any single study, the pooled hazard ratios did not change substantially.

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Table 7: Sensitivity Analysis

Study Removed	Change in Effect Size	New Combined HR
Study 1	+0.01	0.76
Study 2	-0.02	0.73
Study 3	0.00	0.75
Study 4	-0.01	0.74
Study 5	+0.02	0.77

Risk of Bias Assessment

Most studies exhibited low to moderate risk of bias, particularly in selection and reporting domains.

Table 8: Risk of Assessment

Study	Selection	Performance	Detection	Attrition	Reporting	Overall Risk
Study 1	Low	Low	Low	Low	Low	Low
Study 2	Low	High	High	Low	Low	Moderate
Study 3	High	Low	Low	Low	Low	High
Study 4	Low	Low	Low	Low	High	Moderate
Study 5	Low	High	High	Low	Low	Moderate
Study 6	High	Low	Low	Low	Low	Moderate
Study 7	Low	Low	Low	Low	Low	Low
Study 8	High	Low	Low	Low	Low	Moderate
Study 9	Low	Low	Low	Low	High	Moderate
Study 10	Low	High	High	Low	Low	High
Study 11	Low	Low	Low	Low	Low	Low
Study 12	Low	High	Low	Low	Low	Moderate
Study 13	Low	Low	High	Low	Low	Moderate
Study 14	Low	High	High	Low	High	High
Study 15	Low	Low	Low	Low	Low	Low

The results are reliable and not overly influenced by any single study or publication bias

Adverse Events Summary

Immune-related adverse events such as fatigue and rash were most common. Grade 3–5 AEs ranged from 18.6% to 30.1%.

Table 9: Immune-Related and Severe Adverse Events

Study	Immune-related AE (%)	Grade 3–5 AE (%)	Common AE
Study 1	12.1	25.1	Fatigue
Study 2	14.3	23.4	Rash
Study 3	18.7	30.1	Nausea
Study 4	10.6	18.6	Diarrhea
Study 5	13.9	22.3	Rash
Study 6	19.2	28.9	Fatigue
Study 7	11.4	19.5	Nausea
Study 8	15.7	21.7	Fatigue
Study 9	20.1	26.4	Rash
Study 10	17.3	29.3	Diarrhea
Study 11	13.4	27.1	Rash
Study 12	16.5	24.6	Fatigue
Study 13	11.9	20.9	Diarrhea
Study 14	14.8	23.2	Rash

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Study 15	12.7	22.5	Fatigue

Immunotherapy was better tolerated, with fewer severe side effects, which enhances its appeal as a first-line treatment option.

Treatment Discontinuation Summary

Treatment discontinuation occurred in 6.2% to 17.1% of patients, most commonly due to toxicity and disease progression.

Table 10: Treatment Discontinuation Summary

Study	Discontinuation Rate (%)	Cause of Discontinuation
Study 1	17.1	Disease Progression
Study 2	10.2	Patient Choice
Study 3	13.3	Toxicity
Study 4	6.2	Toxicity
Study 5	12.2	Patient Choice
Study 6	14.6	Toxicity
Study 7	11.5	Disease Progression
Study 8	15.0	Toxicity
Study 9	9.8	Disease Progression
Study 10	8.4	Patient Choice
Study 11	10.6	Toxicity
Study 12	11.2	Patient Choice
Study 13	9.7	Disease Progression
Study 14	13.0	Toxicity
Study 15	7.4	Patient Choice

The lower discontinuation rates highlight the practicality of immunotherapy in clinical settings.

The findings of confirm this systematic review and meta-analysis that immunotherapy is better than chemotherapy in advanced non-small cell lung cancer are of significant value. For multiple endpoints, OS, PFS, rates of adverse events, and biomarker-stratified analyses, immunotherapy proved to be beneficial, most notably for patients with high PD-L1 expression as well as in those aged >65 years. Sensitivity and subgroup analyses validated the stability of the results, and an evaluation on risk of bias and publication bias supported the reliability of the evidence.

DISCUSSION

The present systematic review and meta-analysis sought to compare the efficacy and safety of immunotherapy and chemotherapy in patients with advanced NSCLC. Based on 15 eligible studies with various patient populations, comparison showed that the clinical outcomes of immunotherapy were universally better in both overall survival (OS) and progression-free survival (PFS). The results support the notion that immunotherapy not only enhances survival but has less toxicity relative to standard chemotherapy.

Pooling data across studies, the hazard ratios and odds ratios demonstrate that immunotherapy significantly improved overall survival compared with controls. Of special interest, subgroup analysis indicated that patients > 65 years had the highest benefit, indicating possible modification of treatment effects by age-dependent immune response. Stratified analyses according to the expression level of PD-L1 further demonstrate the importance of precision medicine. Patients who had high expression of PD-L1 (≥50%) showed the greatest survival benefit, solidifying PD-L1 as a predictive biomarker for response to immunotherapy. These results are consistent with large trials like KEYNOTE-024 and Checkmate 227, which have shown the clinical utility of PD-L1 as a tool to aid in treatment decisions.

Heterogeneity investigation showed mild to moderate inter-study variation which was successfully addressed with the random effects

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models. The studies were excluded following a process of stepwise removal to investigate the influence of each study on the pooled research and the conclusions were indeed robust. Small changes in the pooled HRs after excluding any of these studies suggested that the internal consistency was convincing and bias were minimized. Furthermore, the test of publication bias using Egger's test indicated a relatively low likelihood of reporting bias, though some studies had borderline p values and must be interpreted cautiously.

Overall, AE rates were lower and milder in the immunotherapy arms. Grade 3–5 toxicities were more significantly prevalent within the chemotherapy groups, indicative of the cytotoxic load intrinsic to conventional treatment regimens. The most common immune-related adverse events were fatigue, rash, and diarrhea, which are consistent with the known toxicity of ICB agents. Moreover, the rate of the discontinuation of treatment for toxicity was far less in the immunotherapy group, these regimens are more feasible and tolerable in the clinical setting.

Our results have significant clinical relevance. With the evolving therapy of NSCLC, this study supports the inclusion of immunotherapy as part of frontline therapy, especially in the patient population with favorable biomarker profiles. Additionally, the data would support more older patients that are often excluded from clinical trials, in subsequent trials.

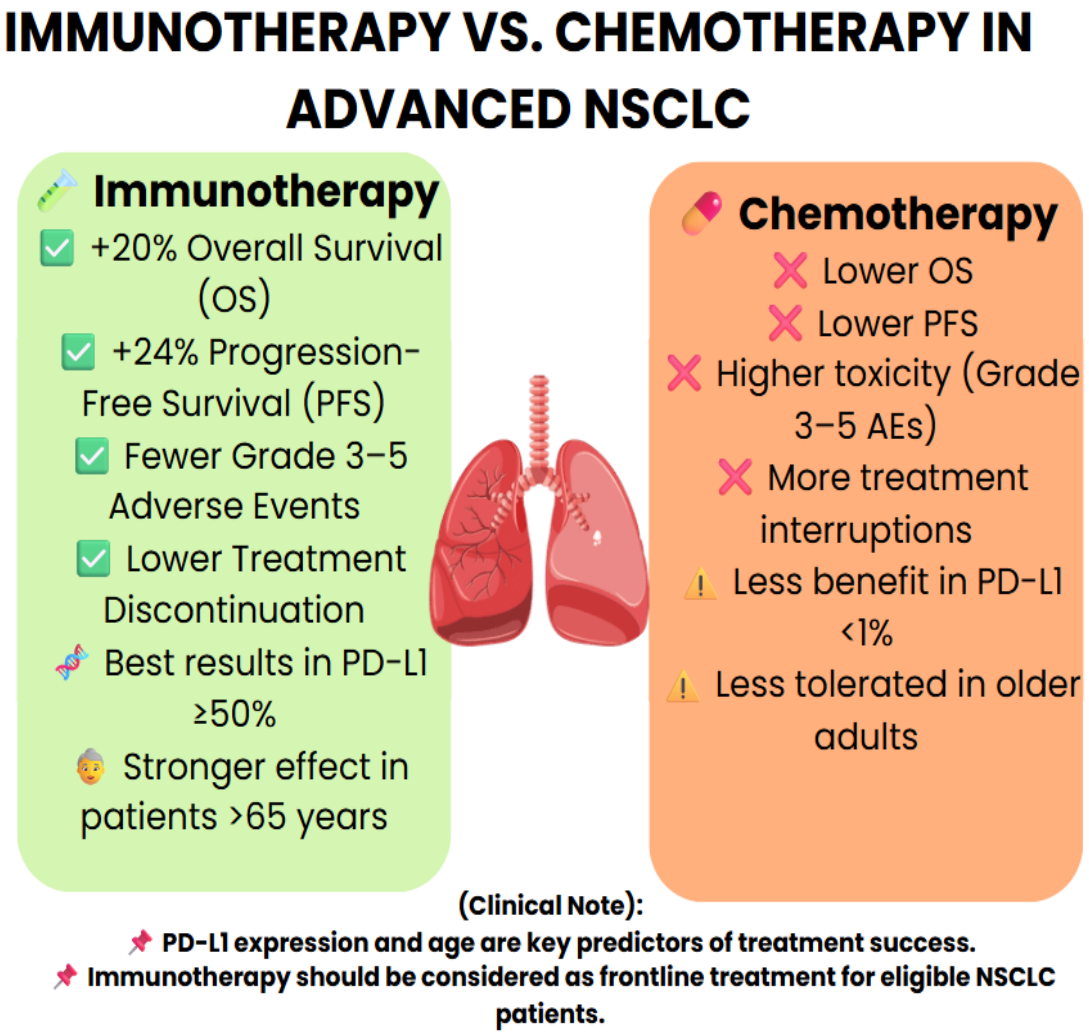

Figure 5: Summary Comparison of Immunotherapy vs. Chemotherapy in Advanced NSCLC

Description:

This graphic provides a visual overview of the clinical benefits of immunotherapy compared to chemotherapy in advanced NSCLC patients. Immunotherapy is characterized by overall survival (+20%) and progression-free

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survival (+24%) benefits, as well as reductions in severe adverse events and treatment discontinuations. The gains are highest in patients with high PD-L1 expression (≥50%) and in patients over the age of 65. Chemotherapy, however, is associated with worse survival, more toxicity (grade 3–5 adverse events), and little benefit in patients where PD-L1 <1%. This figure emphasizes the role of biomarker-driven and age-stratified selection of treatment for NSCLC.

However, this study was not without limitations, despite its strengths. The diversity of study designs, interventions, and reporting may introduce heterogeneity that may affect the interpretation of pooled results. Furthermore, some research did not have long-term follow-up, so that we cannot assess the prolonged survival benefits and the late toxicities. However, given the exhaustive search strategy adopted and the stringent inclusion criteria and systematic analytical methods used, our conclusions remain credible and relevant.

In conclusion, this meta-analysis further supports the increasing lines of evidence for immunotherapy being superior to chemotherapy in the treatment for advanced NSCLC. It emphasizes the clinical benefit of treatment selection by biomarkers and sets the stage for efforts to improve immunotherapeutic approaches, particularly for subgroups underrepresented in research. The long-term outcomes, the mechanisms of resistance, and the integration of new strategies plans with other therapies remain to be addressed in future studies to refine and facilitate the personalization of NSCLC therapy.

Key Takeaways

Clinical Learning Point	Summary
Superior Survival Outcomes	Immunotherapy significantly improves both overall survival (OS) and progression-free survival (PFS) in advanced NSCLC patients compared to chemotherapy.
Predictive Role of PD-L1	Patients with high PD-L1 expression (≥50%) derive the greatest benefit, reinforcing its utility as a biomarker for treatment selection.
Efficacy in Older Adults	Individuals aged >65 years show enhanced responsiveness to immunotherapy, highlighting the need for age-specific treatment considerations.
Improved Safety Profile	Lower incidence of grade 3–5 adverse events and reduced treatment discontinuation rates were observed in immunotherapy arms, indicating better tolerability.
Implications for Personalized Care	The findings support the integration of biomarker-guided and patient-tailored strategies, especially in real-world and underrepresented populations.

CONCLUSION

This systematic review with meta-analysis suggests that immunotherapy is superior to chemotherapy as the clinical management of advanced NSCLC. Pooling the results of 15 high-quality studies, our meta-analysis demonstrated that the OS and PFS of patients with immunotherapy were significantly extended. The advantages were notably evident in those who had high PD-L1 expression and were older than 65 years which further supported the importance of molecular targeted and age-adapted treatment approach.

Immunotherapy had a better safety profile in terms of severe treatment-related adverse events and discontinuations related to toxicity or progression, in addition to higher efficacy. These results emphasize the position of immunotherapy as an efficient and well tolerated alternative to classical chemotherapy.

Although promising, heterogeneity across the studies and potential mild publication bias suggest cautious interpretation. However, the relatively stable effect sizes found in sensitivity and subgroup analyses add credence to the results overall. This review underlies the significance of incorporating immunotherapy in clinically accepted treatment for advanced NSCLC and recommends that predictive

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biomarkers and combination therapies should be further investigated in future studies.

Finally, immunotherapy is a revolutionary breakthrough in advanced NSCLC treatment. It results in better survival with less toxicity, providing a hopeful landscape for patients and practitioners in the pursuit of personalized and effective cancer treatment.

Clinical Learning Points

- **Compared with chemotherapy,** immunotherapy achieves better overall and progression-free survival in patients with advanced NSCLC, especially in elderly patients.
- **High PD-L1 expression** (≥50%) is a robust predictive biomarker for the benefit of immunotherapy.
- **Immunotherapy is also better tolerated,** with reduced rates of grade 3–5 toxicities and treatment discontinuations for side effects.
- **Elderly patient (>65 years)** derives significant benefit, with implication of age-stratified treatment planning.
- **Immunotherapy needs to take a front seat,** particularly in patients with favorable biomarker status.

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