COMPARATIVE EFFICACY OF IMMUNE CHECKPOINT INHIBITOR–ANTI-VEGF COMBINATIONS IN NON-SMALL CELL LUNG CARCINOMA

A network meta-analysis of randomized controlled trials

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BACKGROUND & OBJECTIVE

- VEGF-pathway inhibition may complement PD-1/PD-L1 blockade by modifying the tumour microenvironment.
- Individual ICI–anti-VEGF combinations have not been adequately compared in a unified evidence framework.
- Objective: compare efficacy across available ICI plus anti-VEGF strategies in NSCLC.

METHODS

Search Strategy
Systematic search of 3 electronic databases (PubMed, Embase, Cochrane Library) and 2 clinical trial registries (ClinicalTrials.gov, WHO ICTRP) up to March 2024.

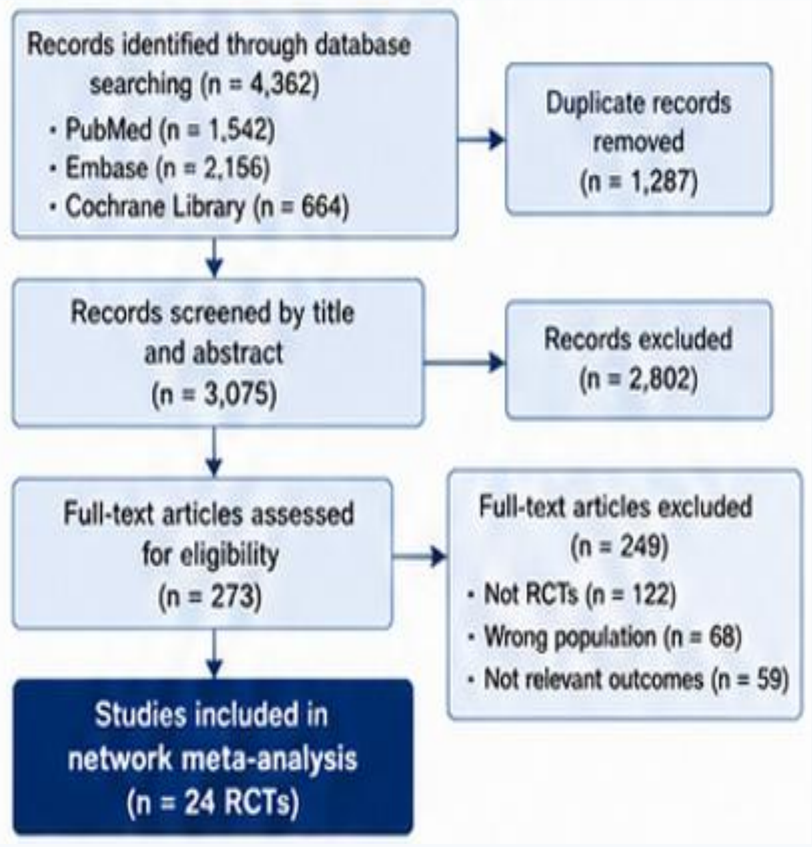
Study Selection
Randomized controlled trials (RCTs) evaluating ICI combined with anti-VEGF agents in advanced or metastatic NSCLC.

Data Extraction
Two reviewers independently extracted data on study characteristics, patient populations, and outcomes.

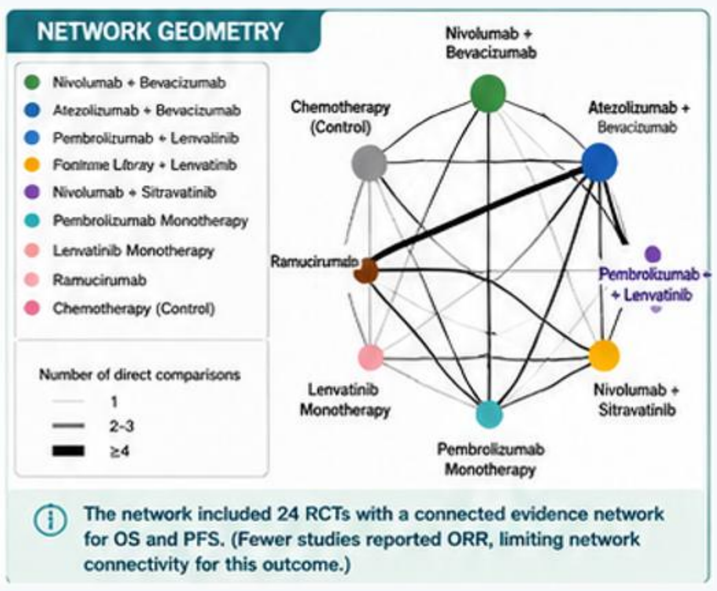
Outcomes
Overall survival (OS) and progression-free survival (PFS) analyzed using hazard ratios (HR); objective response rate (ORR) analyzed using odds ratios (OR) per RECIST 1.1.

Statistical Analysis
Frequentist NMA using the netmeta package in R. Ranking of treatments performed using P scores.

STUDY SELECTION & ANALYSIS



NETWORK GEOMETRY



The network included 24 RCTs with a connected evidence network for OS and PFS. (Fewer studies reported ORR, limiting network connectivity for this outcome.)

1. OVERALL SURVIVAL (OS) – VS CHEMOTHERAPY

Treatment	HR (95% CI)	P value	P score (Ranking)
Nivolumab + Bevacizumab	0.66 (0.50 – 0.88)	0.004	0.92 (1)
Atezolizumab + Bevacizumab	0.79 (0.65 – 0.95)	0.015	0.72 (2)
Nivolumab + Sitravatinib	0.77 (0.59 – 1.00)	0.049	0.64 (3)
Pembrolizumab + Lenvatinib	0.86 (0.67 – 1.11)	0.24	0.46 (4)
Pembrolizumab Monotherapy	0.89 (0.73 – 1.09)	0.26	0.36 (5)
Ramucirumab	0.94 (0.74 – 1.18)	0.58	0.28 (6)
Lenvatinib Monotherapy	1.03 (0.77 – 1.37)	0.84	0.18 (7)

HR < 1 favors treatment over chemotherapy.

2. PROGRESSION-FREE SURVIVAL (PFS) – VS CHEMOTHERAPY

Treatment	HR (95% CI)	P value	P score (Ranking)
Nivolumab + Bevacizumab	0.46 (0.27 – 0.81)	0.007	0.90 (1)
Nivolumab + Sitravatinib	0.58 (0.38 – 0.88)	0.010	0.74 (2)
Atezolizumab + Bevacizumab	0.64 (0.47 – 0.88)	0.006	0.63 (3)
Pembrolizumab + Lenvatinib	0.72 (0.50 – 1.03)	0.074	0.44 (4)
Pembrolizumab Monotherapy	0.85 (0.64 – 1.12)	0.24	0.31 (5)
Ramucirumab	0.93 (0.68 – 1.27)	0.63	0.22 (6)
Lenvatinib Monotherapy	1.07 (0.78 – 1.48)	0.67	0.16 (7)

HR < 1 favors treatment over chemotherapy.

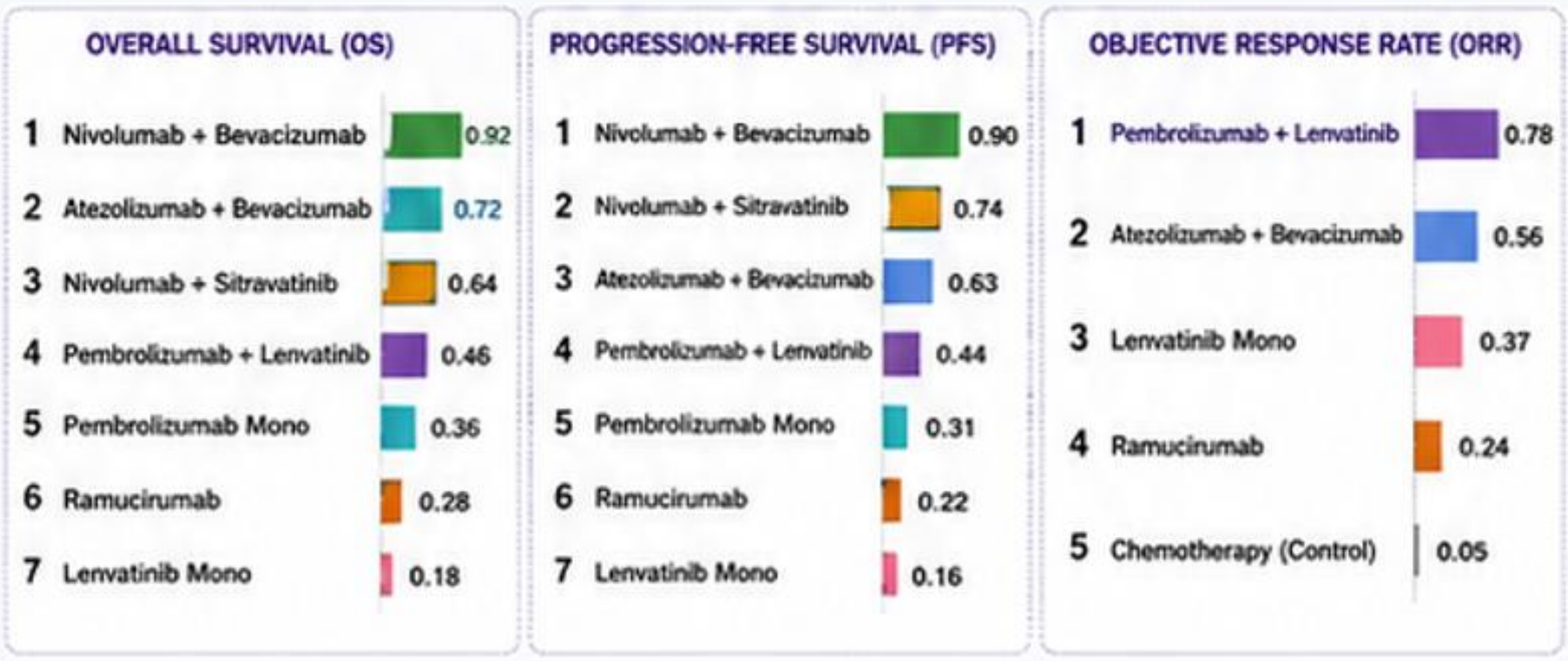
ORR Analysis

No significant advantage over chemotherapy (except indirect comparison)

Comparison	OR (95% CI)	P-value
Pembrolizumab + Lenvatinib vs Lenvatinib	4.76 (1.04–25.0)	0.044

Nivolumab-based combinations could not be included in the ORR network due to insufficient data.

TREATMENT RANKING BY P-SCORE



Nivolumab + bevacizumab ranked highest for survival; pembrolizumab + lenvatinib ranked highest for ORR.

CLINICAL INTERPRETATION

- Nivolumab + bevacizumab is the leading regimen for OS and PFS in the reported network.
- Nivolumab + sitravatinib showed favourable indirect survival comparisons versus ramucirumab + chemotherapy.
- ORR evidence is less complete and should not be used alone to infer survival benefit.

EVIDENCE LIMITATIONS

- Study-level characteristics, event counts, and risk-of-bias assessments are not provided.
- Full treatment-node list and trial-by-trial network connections are unavailable.
- Numerical P-scores and complete ORR estimates are not reported.
- Indirect comparisons rely on transitivity and consistency assumptions.

CONCLUSION

Nivolumab-based ICI–anti-VEGF combinations, particularly nivolumab + bevacizumab and nivolumab + sitravatinib, demonstrate the most favourable reported survival outcomes in NSCLC. ORR evidence remains limited; further randomized comparisons are required.

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