

EFFICACY AND SAFETY OF NIVOLUMAB AND IPILIMUMAB COMBINED WITH CHEMOTHERAPY OR ALONE VERSUS CHEMOTHERAPY AS FIRST-LINE TREATMENT IN ADVANCED NON-SMALL CELL LUNG CANCER: A GRADE-ASSESSED META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

Minahil Ali¹ **PRESENTER**, Daniyal Naqvi², Zoha Khan³, Muhammad Suleman Khan⁴

¹Allama Iqbal Medical College, Lahore, Pakistan · ²National University of Computer and Emerging Sciences, Islamabad, Pakistan · ³Rawalpindi Medical University, Rawalpindi, Pakistan · ⁴Bahria University Health Sciences, Karachi, Pakistan

HR 0.72

Overall Survival
95% CI 0.67–0.77, p<0.00001

HR 0.69

Progression-Free Survival
95% CI 0.58–0.83, p<0.0001

RR 1.47

Objective Response Rate
95% CI 1.33–1.61, p<0.00001

BACKGROUND & OBJECTIVE

ICIs benefit advanced NSCLC, but added value/toxicity vs. chemo alone was unclear.
Objective: evaluate nivolumab + ipilimumab (± chemo) vs. chemo alone, first-line, by PD-L1/histology subgroup.

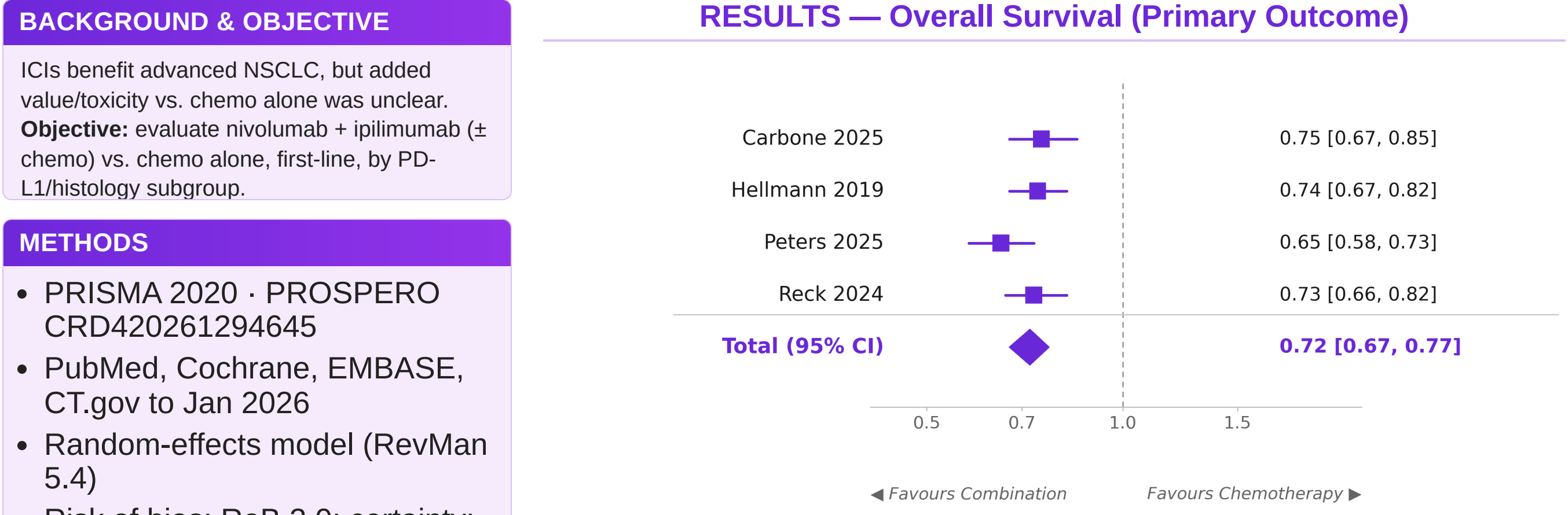
- METHODS**
- PRISMA 2020 · PROSPERO CRD420261294645
 - PubMed, Cochrane, EMBASE, CT.gov to Jan 2026
 - Random-effects model (RevMan 5.4)
 - Risk of bias: RoB 2.0; certainty: GRADE

STUDY SELECTION

2 Phase 3 RCTs, 7 publications, **2,458** patients
84 records → 19 full-text → **7 included**

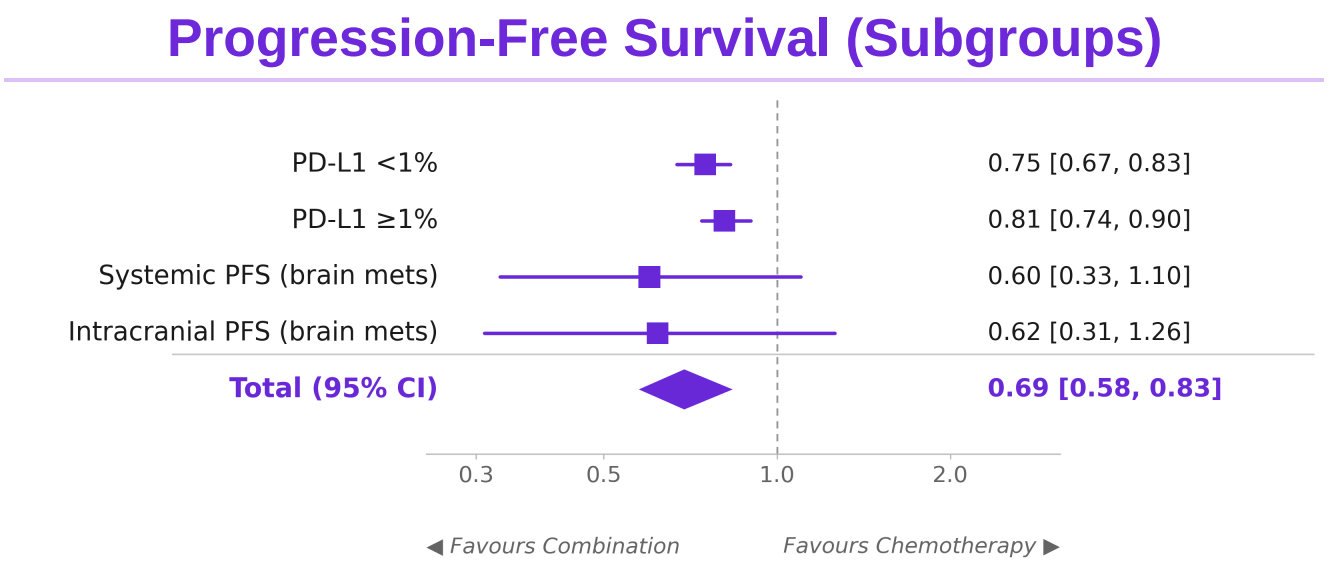
High certainty: OS & ORR (all PD-L1/histology subgroups), PFS (PD-L1 subgroups), diarrhea, rash — no serious risk of bias, inconsistency, indirectness, or imprecision.

Moderate certainty: PFS in brain metastases (systemic & intracranial), grade 3–4 TRAEs, nausea, anemia — downgraded for serious inconsistency between studies.

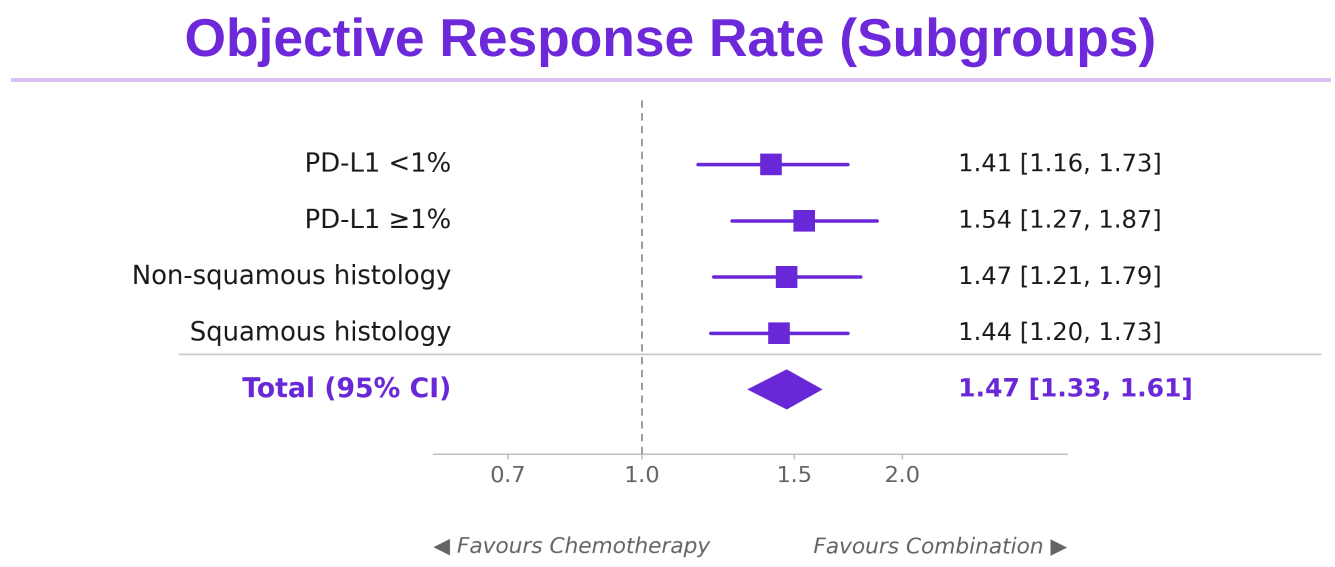


4 pooled studies: 28% lower risk of death with combination therapy ($I^2=28\%$); benefit consistent across PD-L1 <1% (HR 0.67) and $\geq 1\%$ (HR 0.76), largest in squamous histology (HR 0.63).

Heterogeneity: $I^2 = 28\%$ ($\text{Chi}^2 = 4.16$, $\text{df} = 3$, $P = 0.24$) — direction of effect was consistent across all four contributing studies, supporting the robustness of the pooled estimate.



Pooled HR 0.69 (95% CI 0.58–0.83). Significant across PD-L1 subgroups; brain-metastasis PFS favored combination directionally (not significant, small n).



Pooled RR 1.47 (95% CI 1.33–1.61, $I^2=0\%$) — a consistent 47% relative increase in ORR across PD-L1 and histology subgroups.

SAFETY — Grade ≥ 3 TRAEs		
Event	Pooled RR (95% CI)	Direction
Grade 3–4 TRAE (any)	1.06 (0.79–1.44)	NS
Diarrhea	3.69 (1.40–9.74)	↑ Combo
Rash	15.47 (2.05–116.64)	↑ Combo
Anemia	0.23 (0.07–0.76)	↓ Combo
Toxicity shifted from cytotoxic (hematologic) to immune-mediated (GI/skin) events — expert monitoring needed, not uniformly reduced risk.		

CONCLUSION

Nivolumab + ipilimumab (± chemo) **significantly reduced death and progression risk** vs. chemotherapy alone in first-line advanced NSCLC, with a higher response rate — consistent across PD-L1 subgroups and histologies, at the cost of increased immune-related toxicity requiring vigilant monitoring and biomarker-informed patient selection.