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Overall Survival of Sugemalimab Plus Chemotherapy Versus First-Line PD-1/PD-L1 Inhibitor Regimens in Metastatic NSCLC: An Ethnicity-Adjusted Indirect Treatment Comparison

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Background and Objective

- In metastatic non-small cell lung cancer (mNSCLC), sugemalimab was evaluated in GEMSTONE-302 [1], conducted exclusively in an Asian population, whereas comparator trials enrolled predominantly non-Asian patients.
- Differences in ethnic composition may bias unadjusted indirect comparisons. Evidence suggests that ethnicity acts primarily as a prognostic factor rather than a treatment-effect modifier [2–4], although this has not been conclusively established.
- **Objective:** to evaluate the relative efficacy (overall survival, OS) of sugemalimab + chemotherapy (ChT) versus pembrolizumab regimens, nivolumab + ipilimumab + ChT and atezolizumab monotherapy, using an ethnicity-adjusted indirect treatment comparison (ITC).

Methods

- Targeted literature search (PubMed and Google; April 2026) to identify OS hazard ratios (HRs) by ethnicity (Asian vs non-Asian) for PD-1/PD-L1 inhibitors in advanced NSCLC.
- Ratio of hazard ratios (RHR = HR in Asian / HR in non-Asian patients) taken as reported or, where not directly reported, derived from subgroup-specific HRs assuming independence between subgroups. Prioritised source: Peng 2020 [4], as the meta-analysis in advanced NSCLC that includes 1L trials, reports OS by ethnicity and matches the sugemalimab indication. Study-level RHRs were pooled using random-effects meta-analysis.
- GEMSTONE-302 HR adjusted on the log scale, assuming a linear relationship between the proportion of Asian patients and log(HR) [5, 6]: $\log(HR_{adj}) = \log(HR) + (Pt - Ps) \times \log(RHR)$, where Ps and Pt are the proportions of Asian patients in GEMSTONE-302 and in the target trial.
- Indirect treatment comparison of sugemalimab + ChT vs the comparator regimens [7–12], by histology and PD-L1 level, using a fixed-effect model.

Results

- Targeted literature search identified three sources reporting OS by ethnicity in advanced NSCLC [2–4]; RHR estimates were consistent, ranging from 0.90 to 1.01, none statistically significant.
- Pooled RHR (Asian vs non-Asian, 1L NSCLC; Peng 2020 [4]): 0.90 (95% CI 0.68–1.19).
- Ethnicity adjustment attenuated the sugemalimab effect vs ChT (Table 1).
- All ethnicity-adjusted indirect comparisons of OS were statistically non-significant across histologies and PD-L1 levels (HR 0.83–1.33; all 95% CI include 1.0; Figure 1).

Limitations

- The adjustment relies on external RHR estimates, and ethnicity may act as a prognostic factor rather than a treatment-effect modifier; therefore, results should be considered supportive evidence only.
- A fixed-effect model was used because the small number of studies per comparison does not allow robust estimation of between-study heterogeneity.

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Figure 1. OS hazard ratios, sugemalimab + ChT vs comparators, after ethnicity adjustment (fixed-effect ITC). Squares: HR; bars: 95% CI.

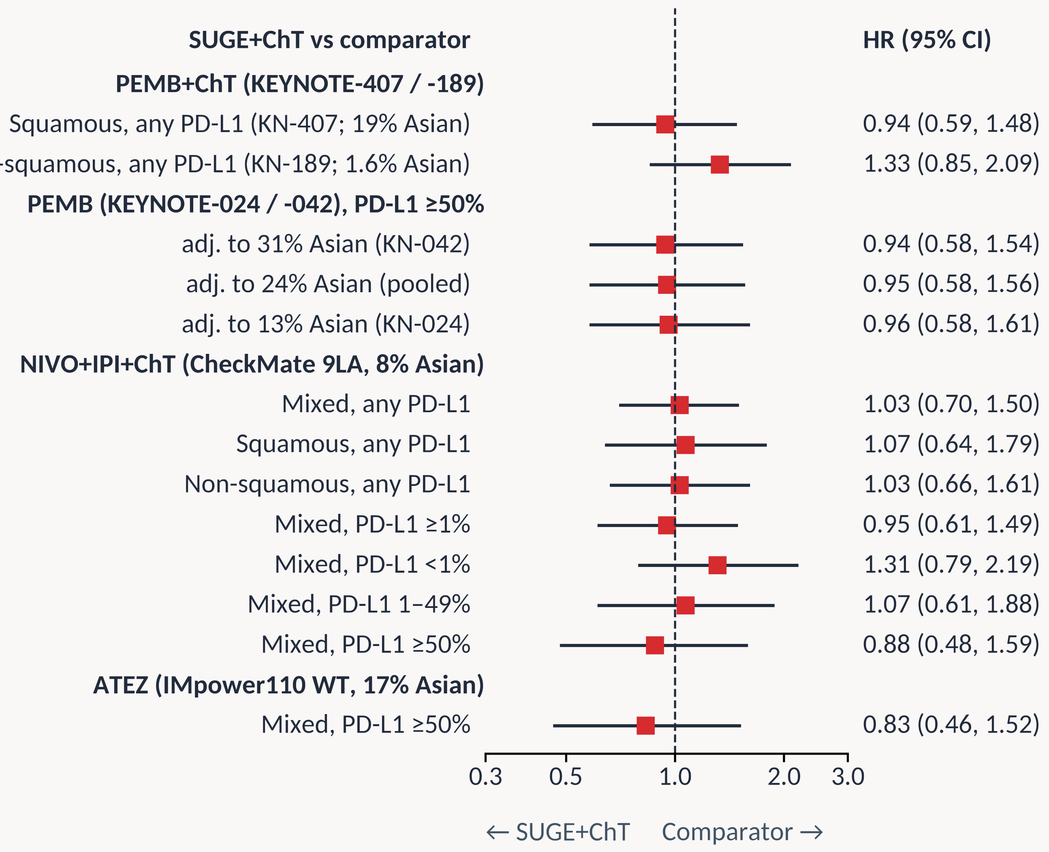

Table 1. HR for SUGE+ChT vs ChT, adjusted to the % of Asian patients in each comparator trial

Comparator trial / subgroup	% Asian in comparator trial	HR (95% CI) unadjusted (GEMSTONE-302)	HR (95% CI) adjusted to comparator trial
KEYNOTE-407 [7] Squamous, any PD-L1	19%	0.61 (0.43, 0.87)	0.66 (0.44, 1.01)
KEYNOTE-189 [8] Non-squamous, any PD-L1	1.6%	0.72 (0.53, 0.98)	0.80 (0.53, 1.21)
KEYNOTE-024 / -042 [9, 10] Mixed, PD-L1 ≥50%	31% (KN-042) 24% (pooled) 13% (KN-024)	0.58 (0.38, 0.89)	0.62 (0.39, 1.00) 0.63 (0.39, 1.01) 0.64 (0.39, 1.04)
CheckMate 9LA [11] Mixed, any PD-L1	8%	0.68 (0.54, 0.85)	0.75 (0.53, 1.06)
CheckMate 9LA Squamous, any PD-L1	8%	0.61 (0.43, 0.87)	0.67 (0.44, 1.04)
CheckMate 9LA Non-squamous, any PD-L1	8%	0.72 (0.53, 0.98)	0.79 (0.53, 1.18)
CheckMate 9LA Mixed, PD-L1 ≥1%	8%	0.63 (0.47, 0.85)	0.69 (0.47, 1.03)
CheckMate 9LA Mixed, PD-L1 <1%	8%	0.75 (0.53, 1.08)	0.83 (0.53, 1.28)
CheckMate 9LA Mixed, PD-L1 1–49%	8%	0.68 (0.45, 1.04)	0.75 (0.46, 1.23)
CheckMate 9LA Mixed, PD-L1 ≥50%	8%	0.58 (0.38, 0.89)	0.64 (0.39, 1.05)
IMpower110 (WT) [12] Mixed, PD-L1 ≥50%	17%	0.58 (0.38, 0.89)	0.63 (0.39, 1.03)

Conclusions

- Sugemalimab + ChT showed no statistically significant OS differences vs other 1L PD-1/PD-L1-based regimens in mNSCLC without oncogenic drivers, supporting its comparability within this therapeutic class.
- Findings suggest that results are robust to differences in the proportion of Asian patients across the comparator trials (1.6–31%).

Abbreviations

- 1L, first-line; ATEZ, atezolizumab; ChT, chemotherapy; CI, confidence interval; HR, hazard ratio; IPI, ipilimumab; ITC, indirect treatment comparison; KN, KEYNOTE; (m)NSCLC, (metastatic) non-small cell lung cancer; NIVO, nivolumab; OS, overall survival; PD-L1, programmed death-ligand 1; PEMB, pembrolizumab; RHR, ratio of hazard ratios (Asian vs non-Asian); SUGE, sugemalimab; WT, wild type.
- Mixed = squamous and non-squamous histology. Adjusted HR = GEMSTONE-302 HR adjusted to the % of Asian patients in the target (comparator) trial. Pooled = weighted average of the Asian proportions in KN-024 and KN-042.

References

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