



P1.261: First-Line Immunotherapy-Based Strategies in Driver-Negative NSCLC With Brain Metastases: A Network Meta-Analysis

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IASLC 2026 World
Conference on Lung Cancer

SEPTEMBER 12 – 15, 2026
SEOUL, REPUBLIC OF KOREA

INTRODUCTION

Brain metastases remain a common and clinically challenging complication of advanced driver-negative NSCLC. A range of first-line strategies has been explored, including immune checkpoint inhibitor (ICI) monotherapy, dual-ICI regimens, chemo-immunotherapy, and emerging agents such as ivonescimab. However, comparative evidence across these approaches in patients with brain metastases remains limited.

Objective: Compare first-line strategies across systemic efficacy, intracranial control, response, and safety.

METHODS

Fourteen prospective studies involving 931 patients with brain metastases were included; 13, 10, 4, 5, and 4 studies contributed to the PFS, OS, iPFS, ORR, and grade ≥ 3 AE networks, respectively.

Bayesian random-effects network meta-analysis (NMA) estimated comparative HRs/ORs with 95% credible intervals (CrIs) and rankings based on the surface under the cumulative ranking curve (SUCRA).

Treatment-stratified single-arm models summarized absolute survival, response, and safety outcomes. Risk of bias, evidence certainty, and network inconsistency were assessed.

EVIDENCE NETWORKS

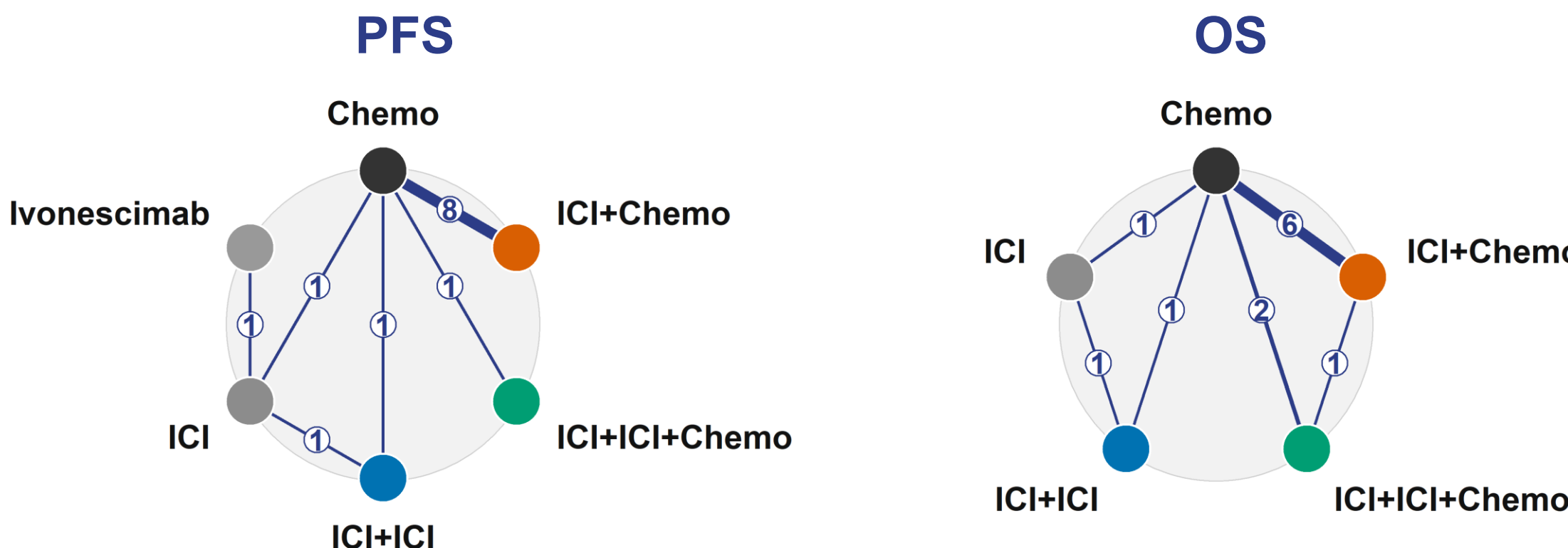


Figure 1. PFS and OS evidence networks. Nodes represent treatments; lines represent direct comparisons; edge numbers show the number of direct-comparison studies.

PFS: 13 studies and 6 treatments. OS: 10 studies and 5 treatments. Edge thickness is proportional to the number of studies informing each direct comparison.

RESULTS

PFS

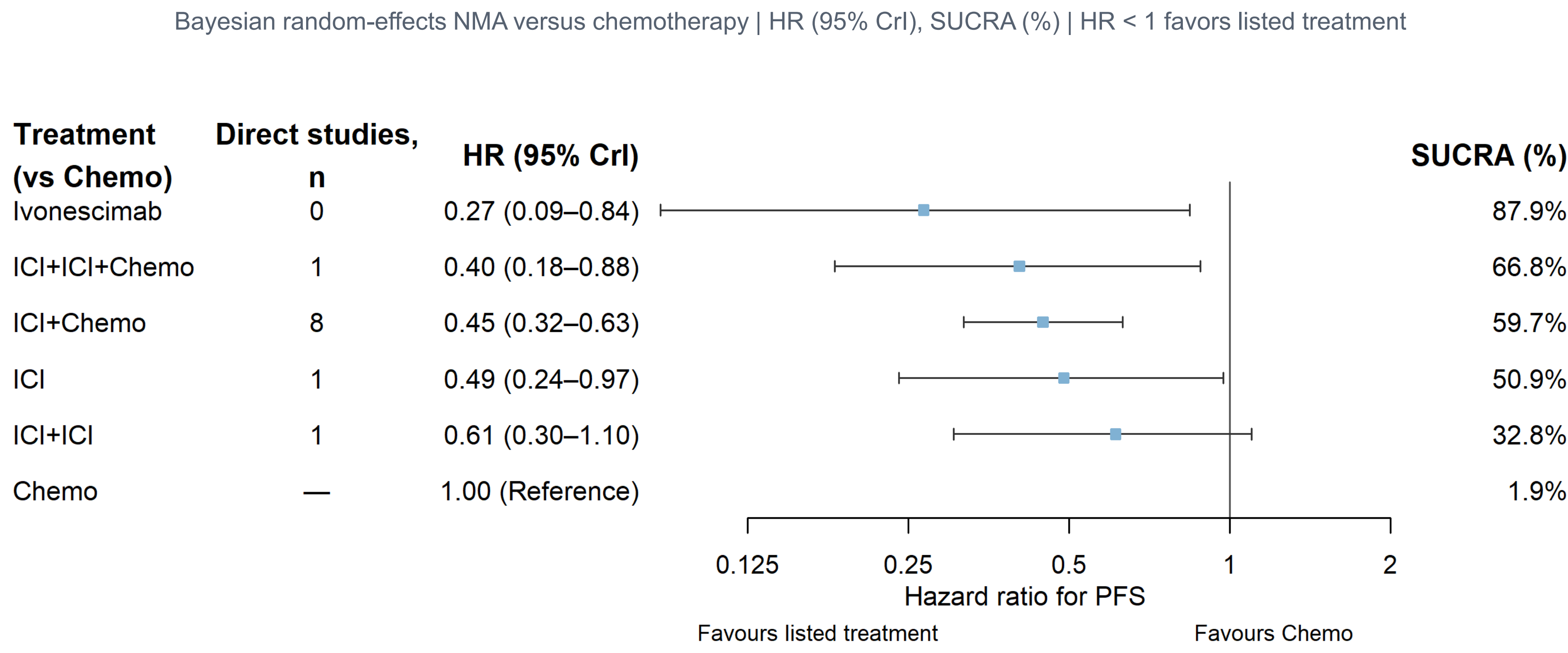


Figure 2. PFS network meta-analysis (13 studies).

OS

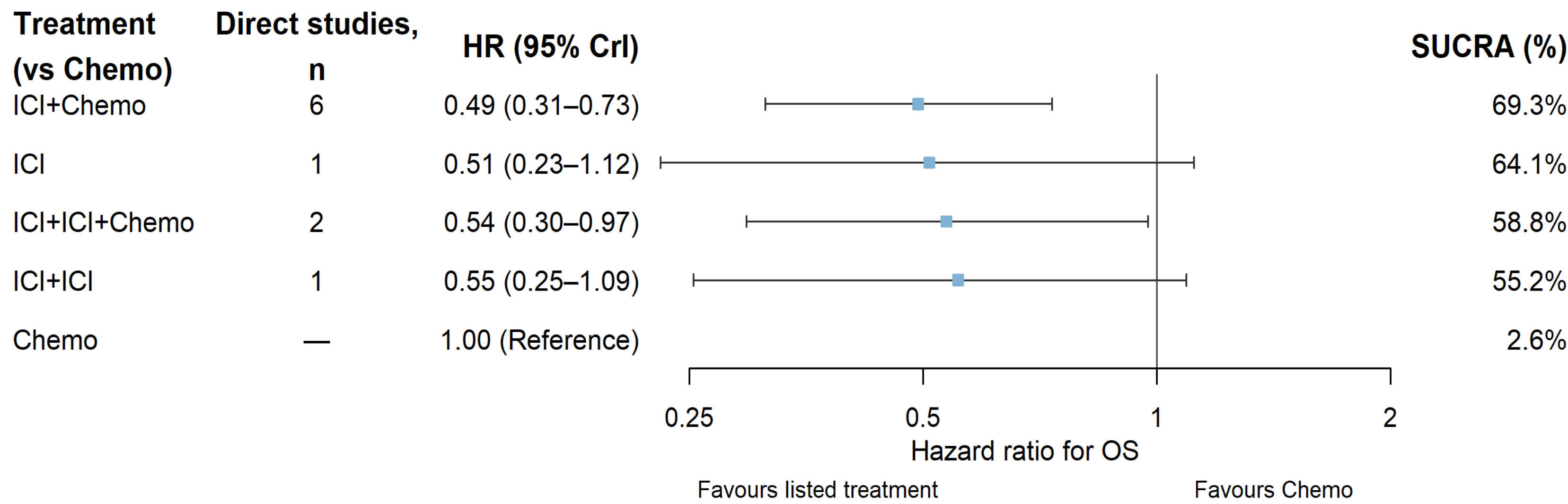


Figure 3. OS network meta-analysis (10 studies).

iPFS

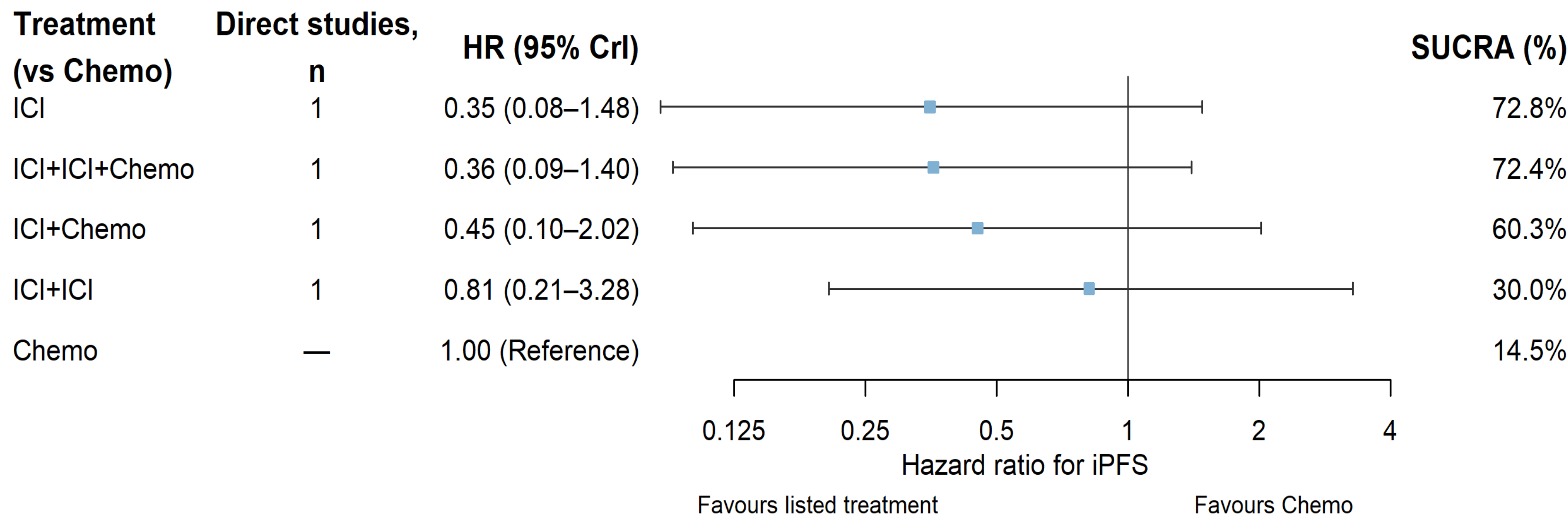


Figure 4. iPFS network meta-analysis (4 studies).

KEY RESULTS

PFS

Ivonescimab, ICI+ICI+Chemo, ICI+Chemo, and ICI improved PFS versus chemotherapy. Ivonescimab ranked highest (SUCRA 87.9%; HR 0.27, 95% CrI 0.09–0.84), supporting its potential as a PFS-leading option.

OS

ICI+Chemo and ICI+ICI+Chemo improved OS versus chemotherapy. ICI+Chemo ranked highest (SUCRA 69.3%; HR 0.49, 95% CrI 0.31–0.73) and had the most favorable OS estimate and ranking in the current network. Ivonescimab OS data were immature.

iPFS

Across four studies, point estimates generally favored active treatment, but no regimen showed a statistically clear advantage.

ADDITIONAL RESULTS

ICI+Chemo - pooled single-arm estimates

PFS 8.36 months (95% CI 6.95–10.06); OS 15.40 months (95% CI 9.58–24.76); ORR 44.2% (95% CI 33.8–55.0); grade ≥ 3 AEs 49.7% (95% CI 33.2–66.4).

These descriptive single-arm estimates were not between-treatment comparisons.

DISCUSSION AND CONCLUSION

ICI plus chemotherapy showed clinically meaningful survival benefits, while ivonescimab demonstrated promising PFS performance.

The available evidence supports ICI+Chemo as a clinically relevant first-line option for OS, while mature OS data are needed to clarify the overall survival profile of ivonescimab.

Several network comparisons were informed by few studies; treatment rankings should therefore be interpreted cautiously and confirmed as the evidence base grows.

REFERENCES & AI USE DISCLOSURE

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Li YS, et al. CTONG 2003. J Thorac Oncol. 2025;20:928–940.
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