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Systematic Literature Review and Bayesian Network Meta-Analysis of Sugemalimab Plus Chemotherapy Versus Other First-Line Treatments for Metastatic Non-Small Cell Lung Cancer Without Sensitizing EGFR, ALK, ROS1, or RET Alterations

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Background

- The therapeutic landscape of metastatic non-small cell lung cancer (mNSCLC) has evolved with the advent of immunotherapy, providing significant clinical benefits.
- For patients without driver mutations and without contraindications to immunotherapy, therapeutic options can be determined based on performance status and Programmed-death ligand 1 (PD-L1) expression level [1, 2].
- According to European guidelines, including the European Society for Medical Oncology (ESMO) Clinical Practice Guideline, immune checkpoint inhibitors monotherapy (pembrolizumab, atezolizumab, cemiplimab) is a standard first line (1L) treatment for patients with PD-L1 expression ≥50%. Combinations of platinum-doublet chemotherapy (ChT) and anti-PD-L1 inhibitors are preferred options over platinum-based ChT in patients regardless of PD-L1 expression [1, 2].
- Sugemalimab, (SUGE) is a fully human anti-PD-L1 monoclonal antibody indicated for 1L treatment of adults with mNSCLC with no sensitising EGFR mutations, or ALK, ROS1 or RET genomic tumour aberrations. It is used in combination with platinum-based ChT for both metastatic squamous and non-squamous NSCLCs regardless of PD-L1 status [3].

Objective & Methods

- The objective was to evaluate comparative efficacy and safety of sugemalimab plus ChT versus other PD-1/PD-L1 inhibitor-based regimens authorised by European Medicine Agency (EMA) for the use in patients with 1L mNSCLC without sensitising EGFR mutations or ALK, ROS1, or RET genomic alterations. Consequently, all identified studies were evaluated in accordance with the indications approved by EMA.
- Following Liu 2023, a systematic literature review (SLR) was conducted to identify randomised controlled trials (RCTs) evaluating sugemalimab and other PD-1/PD-L1 inhibitors approved by the European Medicines Agency for the 1L mNSCLC [4].
- The SLR was performed according to the methodology outlined by the Cochrane Collaboration [5], the PRISMA guidelines [6] and in line with the standards of HTA bodies worldwide.
- A feasibility assessment confirmed the appropriateness of conducting an indirect comparison. [7, 8].

Results

- An NMA was performed to estimate the relative effectiveness of SUGE + ChT vs. relevant comparators pembrolizumab (PEMB), pembrolizumab plus ChT (PEMB + ChT), atezolizumab (ATEZ), atezolizumab plus ChT (ATEZ + ChT), atezolizumab plus bevacizumab and ChT (ATEZ + BEVA + ChT), cemiplimab (CEMI), cemiplimab plus ChT (CEMI + ChT), nivolumab plus ipilimumab and ChT (NIVO + IPI + ChT), tislelizumab plus ChT (TISL + ChT), durvalumab plus tremelimumab plus ChT (DURV + TREM + ChT).
- As an outcome of the SLR, 15 studies met the predefined eligibility criteria for NMA and reflected the EMA authorised indications [9-28]. Finally, 14 RCTs were considered in the evidence synthesis and additional 5 RCTs [29-34] supported an additional indirect comparison via BEVA + ChT.
- Given some clinical heterogeneity in baseline patient characteristics across the included studies, the use of a random-effects model was appropriate, as it accounts for potential differences that could have influenced the results of the NMA.
- The following outcomes were considered:
  - ✓ **Efficacy**: progression-free survival (PFS), overall survival (OS), objective response rate (ORR)
  - ✓ **Safety:** any adverse events (AEs), any grade 3-5 adverse events, any treatment-related adverse events (TRAEs), any serious AEs (SAEs), any immune-related AEs, any AEs leading to discontinuation from any treatment, any AEs leading to death.
- To reflect the long-term efficacy of compared interventions, the NMA used as input the data for the longest follow-up (latest data cut-off, DCO) for studies where multiple DCOs have been reported. All included studies provided sufficient information for the PFS and OS calculations, specifying the data for HR (95% CI).

NMA results of random effects model for HR on OS and PFS (mixed histology, any (all) PD-L1 expression)

Comparison	PFS HR (95% CrI)	OS HR (95% CrI)
SUGE + ChT vs. PEMB + ChT	0.74 (0.15, 3.57)	0.95 (0.37, 2.41)
SUGE + ChT vs. NIVO + IPI + ChT	0.70 (0.19, 2.52)	0.93 (0.45, 1.92)
SUGE + ChT vs. DURV + TREM + ChT	0.68 (0.19, 2.47)	0.89 (0.43, 1.85)

NMA results of random effects model for HR on OS and PFS (non-squamous histology & any (all) the PD-L1 expression)

Comparison	PFS HR (95% CrI)	OS HR (95% CrI)
SUGE + ChT vs. PEMB + ChT	1.04 (0.3, 3.57)	1.16 (0.65, 2.0)
SUGE + ChT vs. ATEZ + BEVA + ChT	1.31 (0.35, 4.98)	1.00 (0.56, 1.82)
SUGE + ChT vs. ATEZ + ChT	0.9 (0.28, 2.96)	0.94 (0.55, 1.62)
SUGE + ChT vs. NIVO + IPI + ChT	0.83 (0.25, 2.86)	0.97 (0.56, 1.73)
SUGE + ChT vs. DURV + TREM + ChT	0.86 (0.23, 3.34)	1.04 (0.57, 1.91)

NMA results of random effects model for HR on OS and PFS (mixed histology & PD-L1 expression less than 1%)

Comparison	PFS HR (95% CrI)	OS HR (95% CrI)
SUGE + ChT vs. PEMB + ChT	0.85 (0.23, 3.1)	0.83 (0.25, 2.74)
SUGE + ChT vs. NIVO + IPI + ChT	0.82 (0.29, 2.28)	1.19 (0.48, 2.94)
SUGE + ChT vs. DURV + TREM + ChT	0.74 (0.26, 2.09)	0.93 (0.37, 2.3)

NMA results of random effects model for HR on OS and PFS (mixed histology & PD-L1 expression at least 50%)

Comparison	PFS HR (95% CrI)	OS HR (95% CrI)
SUGE + ChT vs. PEMB + ChT	0.48 (0.06, 3.96)	0.86 (0.17, 4.28)
SUGE + ChT vs. PEMB	0.61 (0.15, 2.63)	0.89 (0.39, 2.05)
SUGE + ChT vs. ATEZ	0.66 (0.12, 3.48)	0.77 (0.29, 2.03)
SUGE + ChT vs. CEMI + ChT	0.85 (0.16, 4.62)	1.04 (0.38, 2.82)
SUGE + ChT vs. CEMI	0.82 (0.16, 4.23)	0.99 (0.39, 2.52)
SUGE + ChT vs. NIVO + IPI + ChT	0.64 (0.12, 3.38)	0.80 (0.31, 2.09)
SUGE + ChT vs. DURV + TREM + ChT	0.73 (0.14, 3.89)	0.94 (0.36, 2.46)

NMA results of random effects model for HR on OS and PFS (squamous histology & any (all) the PD-L1 expression)

Comparison	PFS HR (95% CrI)	OS HR (95% CrI)
SUGE + ChT vs. PEMB + ChT	0.57 (0.14, 2.2)	0.87 (0.39, 2.01)
SUGE + ChT vs. NIVO + IPI + ChT	0.60 (0.16, 2.42)	0.95 (0.41, 2.19)
SUGE + ChT vs. TISL + ChT (PC)	0.82 (0.18, 3.71)	0.91 (0.38, 2.26)
SUGE + ChT vs. TISL + ChT (nPC)	0.82 (0.18, 3.72)	0.74 (0.31, 1.82)
SUGE + ChT vs. DURV + TREM + ChT	0.48 (0.11, 2.16)	0.72 (0.3, 1.74)

NMA results of random effects model for HR on OS and PFS (mixed histology & PD-L1 expression at least 1%)

Comparison	PFS HR (95% CrI)	OS HR (95% CrI)
SUGE + ChT vs. CEMI + ChT	0.96 (0.23, 3.93)	1.24 (0.35, 4.31)
SUGE + ChT vs. NIVO + IPI + ChT	0.66 (0.16, 2.69)	0.86 (0.25, 2.97)
SUGE + ChT vs. DURV + TREM + ChT	0.68 (0.16, 2.76)	0.89 (0.26, 3.05)

NMA results of random effects model for HR on OS and PFS (mixed histology & PD-L1 expression from 1 to 49%)

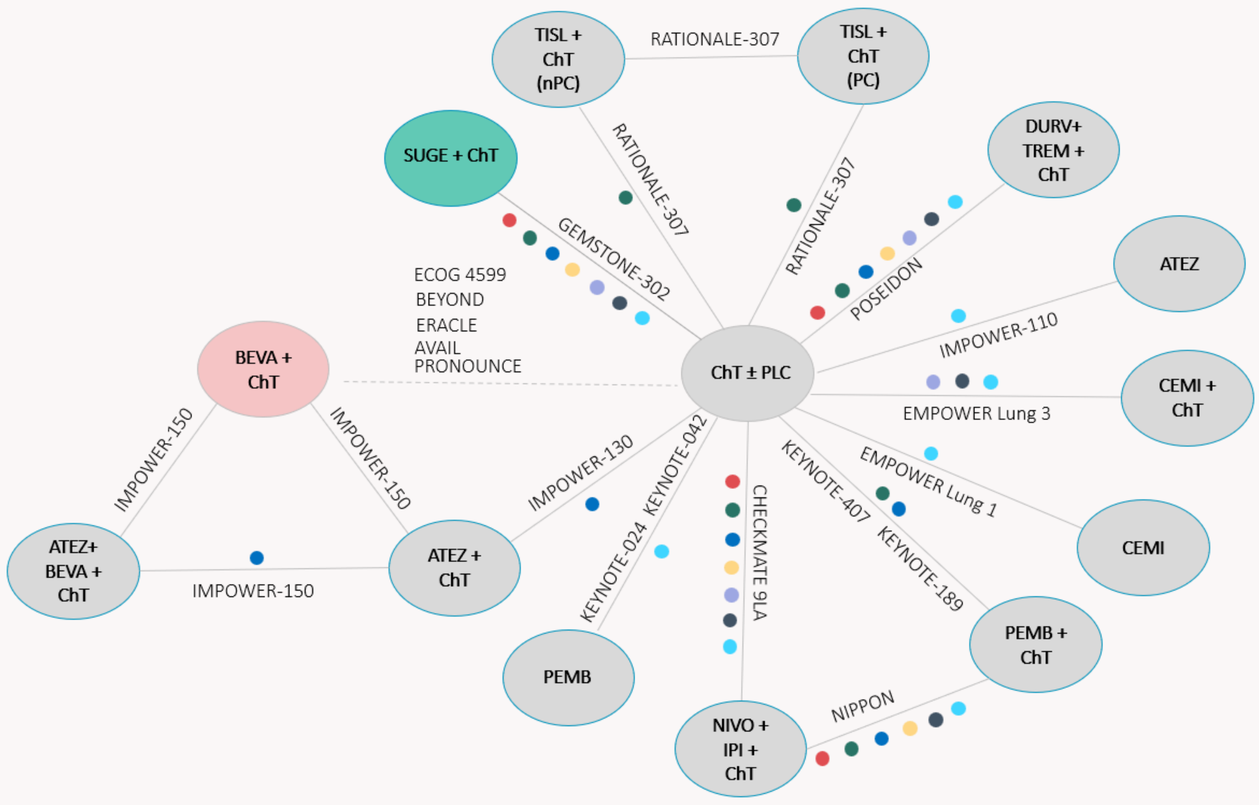
Comparison	PFS HR (95% CrI)	OS HR (95% CrI)
SUGE + ChT vs. PEMB + ChT	0.94 (0.17, 5.13)	1.68 (0.31, 8.9)
SUGE + ChT vs. CEMI + ChT	1.09 (0.27, 4.24)	1.36 (0.36, 5.08)
SUGE + ChT vs. NIVO + IPI + ChT	0.70 (0.18, 2.73)	0.97 (0.26, 3.58)
SUGE + ChT vs. DURV + TREM + ChT	NA	0.84 (0.23, 3.1)

- In terms of safety, no significant differences were observed between sugemalimab and other regimens in the overall incidence of adverse events, any grade 3 to 5 events, serious adverse events, any AEs leading to discontinuation, any AEs leading to death and any immune-related AEs).

- Results from the studies included in the NMA were stratified according to different patient populations based on histology and PD-L1 expression levels. The predefined subgroups were determined based on the available evidence for sugemalimab and on the approved indications of the comparators. Seven NMAs were conducted with the following subgroup analyses:

Meta-analysed subgroup	Definition
Mixed histology & any (all) PD-L1 expression	Studies enrolling both SCC and NSCC subgroups and any (all) PD-L1 expression
SCC histology & any (all) the PD-L1 expression	Studies enrolling only squamous NSCLC patients or if available subgroups with SCC histology from studies that included mixed histology and any (all) PD-L1 expression
NSCC histology & any (all) the PD-L1 expression	Studies enrolling only non-squamous NSCLC patients or if available subgroup with NSCC histology from studies including mixed histology and any (all) PD-L1 expression
Mixed histology & PD-L1 expression <1%	Studies enrolling both SCC and NSCC subgroups of patients with PD-L1 expression <1%
Mixed histology & PD-L1 expression ≥1%	Studies enrolling both SCC and NSCC subgroups of patients with PD-L1 expression ≥1%
Mixed histology & PD-L1 expression from 1 to 49%	Studies enrolling both SCC and NSCC subgroups of patients with PD-L1 1%–49%
Mixed histology & PD-L1 expression 50%	Studies enrolling both SCC and NSCC subgroups of patients with PD-L1 ≥50%

Networks for prespecified subgroups (coloured dots indicate particular networks for subgroups)



The RATIONALE-304 trial was not included in the network due to the absence of data for predefined subgroups

Conclusions

- The network meta-analysis showed that sugemalimab is as effective as other first-line treatment regimens for patients with metastatic non-small cell lung cancer (NSCLC) without oncogenic mutations.
- This effectiveness was consistent across all prespecified subgroups, regardless of PD-L1 expression levels or histology type, supporting sugemalimab as a viable treatment option for a broad NSCLC population.

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