PCR116

Health-Related Quality of Life in First-Line Advanced or Metastatic Non-Small Cell Lung Cancer: A Systematic Review with Focus on the PD-L1 Negative Subgroup

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BACKGROUND

- Non-small cell lung cancer (NSCLC) accounts for ~85% of lung cancers, with many diagnosed at advanced or metastatic stages and experiencing high symptom burden and poor health related quality of life (HRQoL).[1,2]
- First-line immunotherapy has improved survival compared with chemotherapy, but HRQoL outcomes, particularly in PD-L1 negative patients (PD-L1 <1%) remain underexplored.[3,4]
- This systematic literature review (SLR) evaluated HRQoL and utility outcomes of 1L therapies in advanced/ metastatic NSCLC, with a focus on PD-L1–negative patients.

METHODS

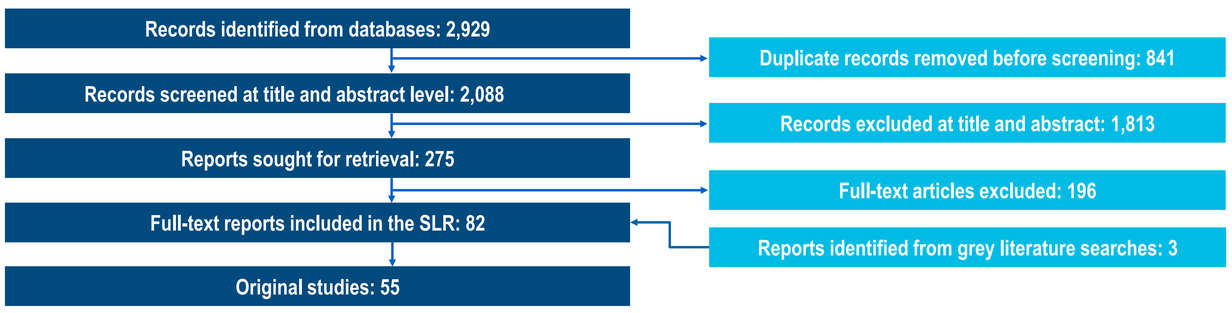
- Literature was searched (Jan 2018–Mar 2024) in Embase, MEDLINE, National Health Service Economic Evaluation Database (NHS-EED), EconLit, and International Network of Agencies for Health Technology Assessment (INAHTA), with supplementary searches of recent congress abstracts, HTA submissions, and reference lists of relevant SLRs/meta-analyses.
- Study selection followed predefined PICOS criteria (see **Table 1**).

Table 1: PICOS Criteria

PICOS	Inclusion criteria	Exclusion criteria
Population	Metastatic/advanced, non-resectable, 1L, NSCLC	Non-metastatic/advanced NSCLC or non-human
Interventions	All pharmacological interventions	Non-pharmacological interventions or surgery
Outcomes	HRQoL measures (generic, oncology/lung cancer specific PROs), symptom-scales (Lung Cancer Symptom Scale (LCSS), Brief Pain Inventory (BPI), and other pain-related measures), utility/disutility values	Any other non-relevant outcome
Study design	RCTs, single-arm trials, real-world studies (e.g. cohort, cross-sectional, and case-control studies), utility-focused studies.	Non-systematic reviews, case series, reports, commentaries and editorials
Language	English language	Non-English language article

Abbreviations: HRQoL: Health-Related Quality of Life; NSCLC: Non-Small Cell Lung Cancer; PICOS, Population, Intervention, Comparison, Outcomes, and Study characteristics; PRO: Patient-Reported Outcomes; RCT: Randomized Controlled Trial.

Figure 1: PRISMA Flow Diagram



RESULTS

- Of the 55 original studies identified, 51% (n=28) were RCT's, 33% (n=18) were real world studies, 7% (n=4) were single arm trials and the remaining were other study types.
- The majority of studies were either global or from Asia (**Figure 2**).
- Almost half of the studies reported QLQ-C30, followed by QCQ-LC13. HADS and PHQ9 were the least reported HRQoL measures (**Figure 3**).

Figure 2: Geography of Studies

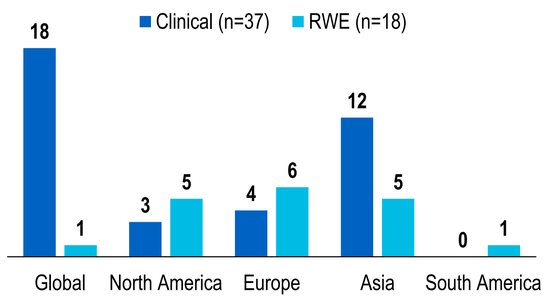
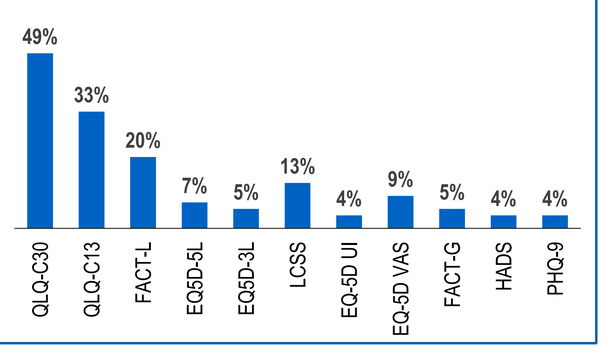


Figure 3: HRQoL Scales Reported in Studies (N=55)



Study Characteristics

The range of patient characteristics in the included studies (n=55) are shown in **Figure 4**.

Figure 4: Characteristics of Patients in the Included Studies

Population	Age	Sex	Follow-up
Overall population: 17 to 2,892	Median age: 58 to 79 years per arm	Male participants: 38% to 97% per arm	Median follow-up duration: 8.6 to 41 months
Histology	**PD-L1 status**	**Smokers**	**Metastasis**
Percent per arm NSQ: 29% to 91% SQ: 15% to 71%	Percent per arm <1%: 28.6% to 52% 1% to 49%: 28.2% to 38% ≥50%: 17% to 79.5%	Proportion of participants per arm current/former smokers: 43% to 100%	Percent per arm Brain: 0% to 100% Liver: 6% to 100% Bone: 17% to 50%

QLQ-C30 Global Health Status (GHS)

- Six studies reported difference in mean change from baseline GHS for IO combined with chemotherapy versus chemotherapy alone, with three reporting significant improvement with the combination.
  - The greatest HRQoL improvement was observed in Rationale 304 (TIS + PEM/CIS/CAR), with a 5.7-point difference at 18 weeks (**Figure 5**).
  - Both KEYNOTE-189 and KEYNOTE-407 (PEMBRO + PBC) also showed statistically significant results (**Figure 5**).

SCAN FOR:
- Digital Poster

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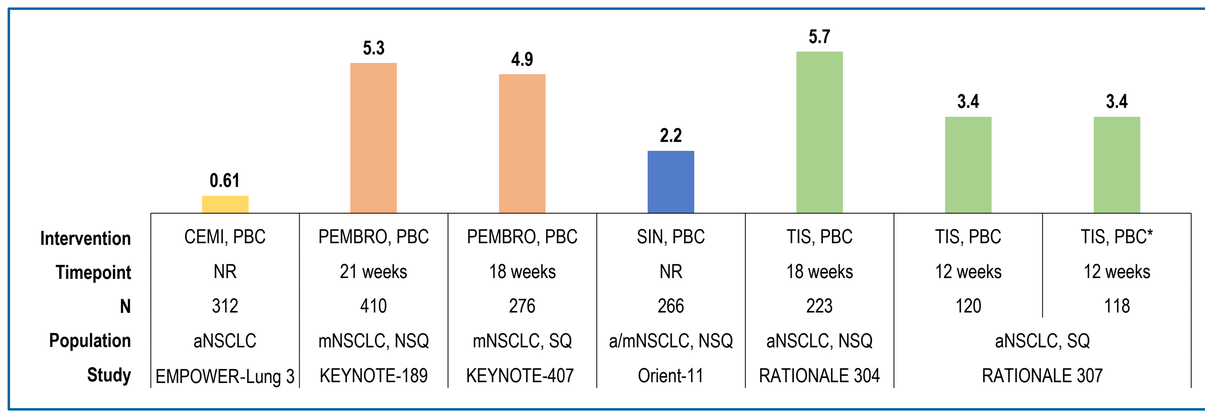
RESULTS (Continued)

Figure 5: QLQ-C30 GHS Change from Baseline in Studies Reporting IO Plus Chemotherapy (n=6)

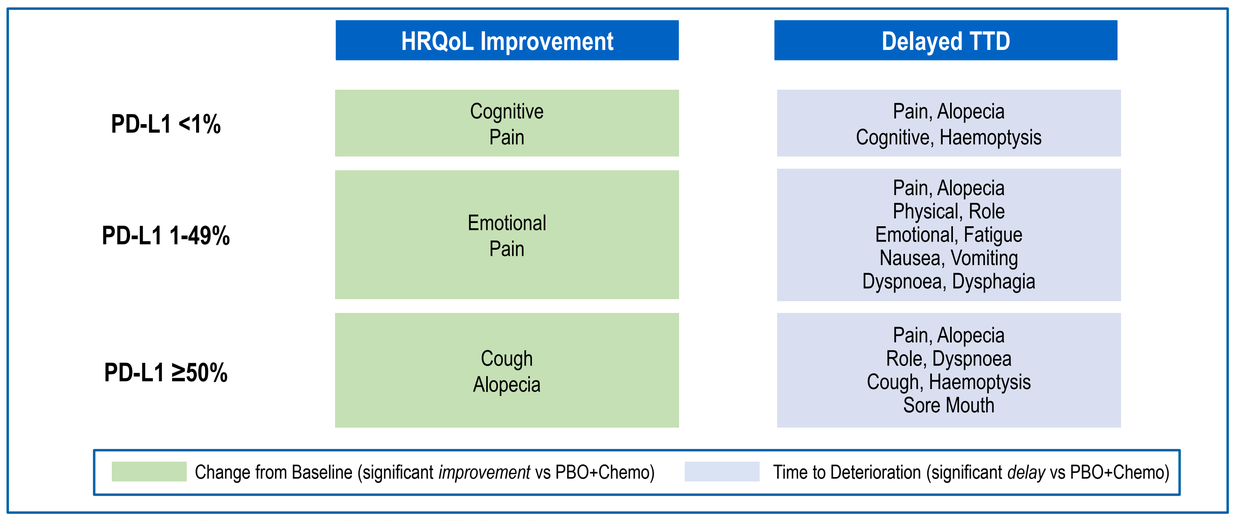


Note: *RATIONALE 307 compared Tislelizumab + Paclitaxel + Carboplatin and Tislelizumab + nab-Paclitaxel + Carboplatin to PBC. Abbreviations: a/mNSCLC: Advanced/Metastatic Non-Small Cell Lung Cancer; CAR: Carboplatin; CEMI: Cemiplimab; CIS: Cisplatin; GHS: Global Health Status; mNSCLC: Metastatic Non-Small Cell Lung Cancer; N-PAC: Nab-paclitaxel; NSQ: Non-Squamous; PAC: Paclitaxel; PBC: Platinum-Based Chemotherapy; PEM: Pemetrexed; PEMBRO: Pembrolizumab; QLQ-C30: European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire-30; SIN: Sintilimab; SQ: Squamous; TIS: Tislelizumab.

HRQoL for PD-L1 Negative Subgroups

- Ten studies reported HRQoL outcomes in subgroups based on PD-L1 expression (PD-L1 ≥1%, n=10; PD-L1 <1%, n=1); however reporting was inconsistent.
- Among these, EMPOWER-Lung 3 was the only trial to assess both PD-L1 positive and negative subgroups[5], evaluating change from baseline and time to deterioration (TTD) using the QLQ-C30 and QLQ-LC13 instruments **(Figure 6)**.
  - More consistent HRQoL benefits were observed in PD-L1 positive patients, whereas in the PD-L1 negative subgroup (<1%) benefits were more limited (**Figure 6**).
- MYSTIC and EMPOWER-Lung 1 also provided data in PD-L1 selected populations.[6-9]
  - In MYSTIC (PD-L1 ≥25%), durvalumab ± tremelimumab maintained or improved HRQoL, reduced appetite loss and fatigue, and significantly prolonged TTD in global health, functioning, and symptoms such as dyspnoea and fatigue.
  - In EMPOWER-Lung 1 (PD-L1 ≥50%), cemiplimab improved global health, functioning, and key symptoms, while consistently delaying deterioration across all functioning scales and most symptoms.

Figure 6: HRQoL Improvements & Delayed Symptom Worsening by PD-L1 Status in EMPOWER-Lung 3

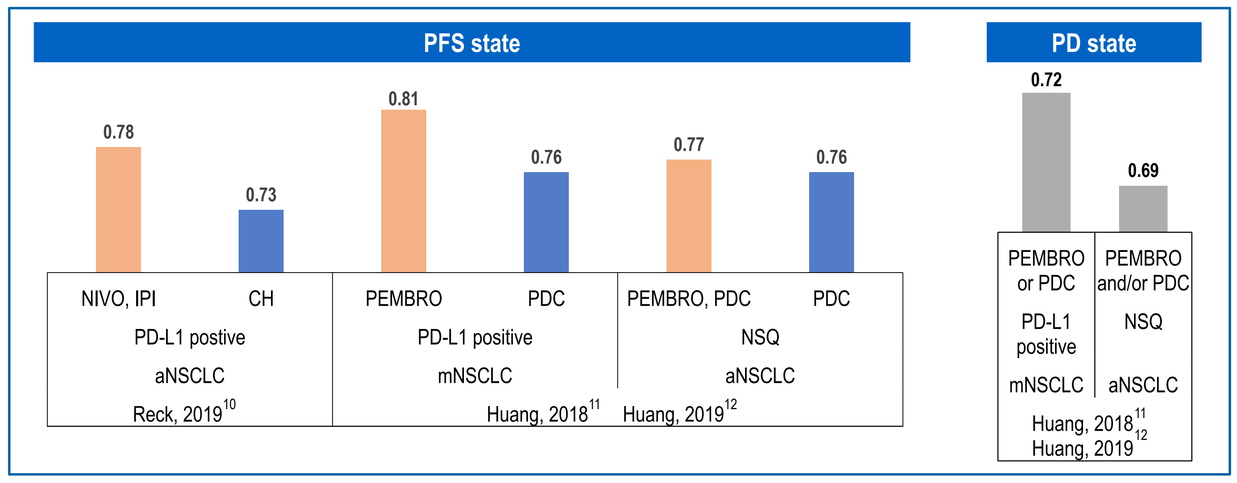


Abbreviations: HRQoL, Health Related Quality of Life; PBO, Placebo; TTD, Time to Deterioration.

Health State Utility Values

- IO combinations and monotherapy showed higher utility in the PFS state (0.77–0.81) versus chemotherapy (0.73–0.76), while utility values in PD were similar across interventions (0.69–0.72) (**Figure 7**).
- Notably, data are limited to PD-L1 positive patients, with no evidence for PD-L1 negative patients, creating uncertainty.

Figure 7: Utility values in Progression free state and progressed state



Abbreviations: aNSCLC, advanced non-small cell lung cancer; mNSCLC, metastatic non-small cell lung cancer; CH, Chemotherapy; NSQ, Non-squamous; PD, Progressed Disease; PDC, Platinum Doublet Chemotherapy; PFS, Progression Free Survival.

CONCLUSIONS

- Immunotherapy plus chemotherapy improves or maintains HRQoL in advanced NSCLC, predominantly in PD-L1 positive subgroups, though the extent of benefit may vary by treatment regimen.
- In PD-L1 negative (PD-L1 <1%) populations, current evidence shows minimal HRQoL benefit, with isolated improvements identified via a single study.
- These findings highlight a persistent unmet need for effective treatment options that meaningfully preserve or improve HRQoL in PD-L1 negative NSCLC.
- These results support biomarker-driven treatment decisions and underscore the need for further research on HRQoL outcomes in NSCLC.

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