NETWORK META-ANALYSIS OF THERAPEUTIC ALTERNATIVES IN UNTREATED METASTATIC SQUAMOUS NON-SMALL-CELL LUNG CANCER

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BACKGROUND AND IMPORTANCE

Multiple therapeutic alternatives are used in **untreated metastatic squamous non-small-cell lung cancer** (umSNSCLC). **Paclitaxel-carboplatin-pembrolizumab** combination (PC pembrolizumab) has been recently authorised in this indication.

AIM AND OBJECTIVES

To assess the comparative efficacy among different therapeutic alternatives used in mSNSCLC through a **network meta-analysis** (NMA).

MATERIAL AND METHODS

A search was conducted on 19/02/2020:

- **Inclusion criteria:** phase II/III randomised clinical trials (RCT), including drugs used in umSNSCLC, and overall survival (OS) as efficacy endpoint.
- **Exclusion criteria**: mSNSCLC population with EGFR- or ALK-mutations, RCT without a comparator common to the evaluated alternatives.

✓ Pooled hazard ratios (HR) → calculated by **Bayesian methods**, through the combination of direct and indirect evidence by the NMA.

✓ Fixed and random effects evaluated. **Deviance information criteria (DIC)** statistics → used to compare the models.

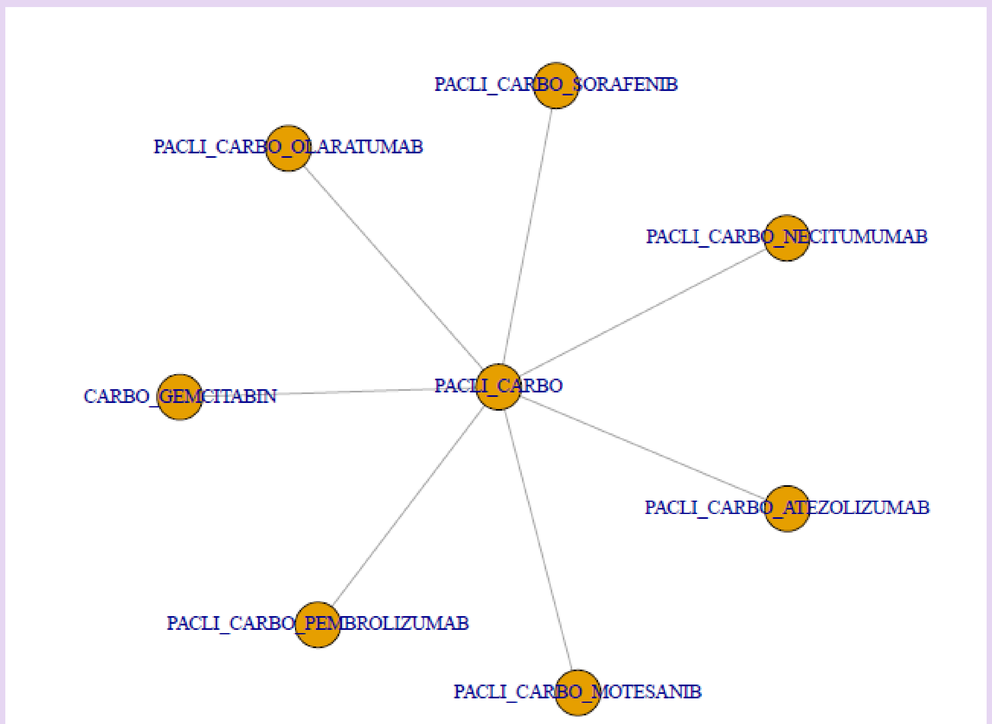
✓ Agreement of direct and indirect estimations → assessed by **node-splitting models** → to evaluate consistency of NMA.

Δ → maximum acceptable difference as clinical criterion of non-inferiority. Set at 0.70 (and its inverse, 1.43), used to calculate the sample size in PC-pembrolizumab trial.

RESULTS

- **9 RCT** were selected. **PC** was the **common comparator**. DIC value for **fixed-effects model** was more favourable.
- No statistical differences between direct and indirect evidence were found, therefore **NMA was consistent.**
- **PC-pembrolizumab** combination was considered as **reference** (treatment with the greatest magnitude of effect).
- HR for **OS** were:

TREATMENT	HR (CI95%)
carboplatin-gemcitabine	1.4 (0.89 to 2.3)
PC	1.6 (1.2 to 2.1)
nab-PC-atezolizumab	1.5 (1.1 to 2.1)
PC-figitumumab	1.8 (1.3 to 2.5)
PC-motesanib	1.4 (0.96 to 2.0)
PC-necitumumab	1.3 (0.66 to 2.5)
PC-olaratumab	2.1 (0.86 to 5.0)
PC-sorafenib	2.9 (1.7 to 4.8)
pembrolizumab monotherapy	1.2 (0.82 to 1.7)



- Carboplatin-gemcitabine, PC-motesanib, PC-necitumumab, PC-olaratumab and pembrolizumab did not present statistically significant difference with PC-pembrolizumab. Statistically significant benefit was observed for PC-pembrolizumab over PC, nab-PC-atezolizumab, PC-figitumumab and PC-sorafenib. According to delta value there could be clinically relevant differences among them.

CONCLUSION AND RELEVANCE

NMA showed no significant differences in OS between PC-pembrolizumab and carboplatin-gemcitabine, PC-motesanib, PC-necitumumab, PC-olaratumab and pembrolizumab in umSNSCLC, but there could be possible clinically relevant differences. PC, nab-PC-atezolizumab, PC-figitumumab and PC-sorafenib were inferior to PC-pembrolizumab, with probably clinically relevant differences.