INDIRECT COMPARISON OF PEMBROLIZUMAB PLUS CHEMOTHERAPY VERSUS PEMBROLIZUMAB IN LUNG CANCER

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BACKGROUND

- ✓ **Pembrolizumab** (Pb) showed significant benefit in **overall survival** (OS) and **progression-free survival** (PFS) versus chemotherapy in patients with untreated metastasic non-small-cell lung cancer (NSCLC) and ≥50% PD-L1 expression.
- ✓ **Pembrolizumab-chemotherapy combination** (Pb-CT) also showed significant benefit in **OS** and **PFS** over chemotherapy in patients with untreated non-squamous NSCLC, regardless of PD-L1 value. It lacks clinical trials of Pb-CT vs. Pb alone.

PURPOSE

To develop an **adjusted indirect treatment comparison** (ITC) between Pb and Pb-CT in non-squamous NSCLC with PD-L1 ≥50%.

MATERIAL AND METHODS

Bibliographic search

ITC: Bucher's method with hazard ratio (HR) and 95% confidence intervals (CI).

- ✓ Phase III randomized clinical trials
- ✓ Pb and Pb-CT
- ✓ Similar non-squamous NSCLC population (without EGFR or ALK mutations and PD-L1 ≥ 50%), follow-up period and endpoints.

RESULTS

- ✓ Two trials were selected, one of each regimen

LIMITATIONS

- Differences in control treatment: platin doublets with pemetrexed vs. several drugs (pemetrexed subgroup selected for PFS comparison; subgroup data lack for OS comparison).
- Masking: double-blind versus open-label design
- Population: patients with PD-L1 ≥50% vs. all patients (subgroup data used) and inclusion of 18% patients with squamous tumour.
- Follow-up period: Pb (11.2 months) and Pb-CT (10.5 months)

Reference	PFS	OS
Pb-CT vs.CT	HR=0.36 (95%CI, 0.25-0.52, PD-L1 ≥50% subgroup)	HR=0.42 (95%CI, 0.26-0.68, PD-L1 ≥50% subgroup).
Pb vs. CT	HR 0.63 (95%CI, 0.44-0.91, subgroup platinum+pemetrexed).	HR 0.60 (95%CI, 0.41-0.89)
Pb-CT vs. Pb (ITC)	HR=0.57(95%CI, 0.40-0.96)	HR=0.70(95%CI 0.38-1.30)

Significant **differences** in PFS.

No significant **differences** in OS (broad 95%CI: uncertainty).

CONCLUSION

1. **Pb-CT** showed **benefit** in **PFS** over Pb monotherapy for **non-squamous NSCLC and ≥50% PD-L1 expression** receiving pemetrexed combinations.
2. OS benefit is doubtful (potential bias and large 95%CI).
3. **Monotherapy Pb reserves platinum doublet for later use**; additional data for OS in pemetrexed subgroup is needed.
4. **Toxicity** of **adding chemotherapy**: combined regimen should be considered **cautiously.**

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