INDIRECT COMPARISON OF PEMBROLIZUMAB PLUS CHEMOTHERAPY VERSUS PEMBROLIZUMAB IN LUNG CANCER

M.D. GIL-SIERRA1, S. FENIX-CABALLERO1, M. SANCHEZ-HIDALGO2, C. ALARCON DE LA LASTRA ROMERO2, M.D.P. BRICEÑO-CASADO1, E. RIOS-SANCHEZ1, J. DIAZ-NAVARRO1, C. MARTINEZ-DIAZ1, M. CAMEAN-CASTILLO1, J.M. BORRERO-RUBIO1, E. ALEGRE-DEL REY1.

1 HOSPITAL UNIVERSITARIO DE PUERTO REAL, PHARMACY, PUERTO REAL, SPAIN.

2 UNIVERSIDAD DE SEVILLA, PHARMACOLOGY DEPARTMENT, SEVILLA, SPAIN.

BACKGROUND

- Pembrolizumab (Pb) showed significant benefit in overall survival (OS) and progression-free survival (PFS) versus chemotherapy in patients with untreated metastatic 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: platinum 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)

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