COMPARISON OF PEMBROLIZUMAB + CHEMOTHERAPY AND NIVOLUMAB + IPILIMUMAB + CHEMOTHERAPY IN METASTATIC SQUAMOUS NON-SMALL CELL LUNG CANCER WITH PD-L1< 1%

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BACKGROUND AND IMPORTANCE

First-line treatment for metastatic non-small cell lung cancer (NSCLC) includes combinations based on immunotherapy and chemotherapy. Strategies involving nivolumab + ipilimumab (NIVO + IPI) and pembrolizumab (PEMBRO) have been considered alternatives with similar clinical benefit.

However, they differ in management and toxicity, and a different effectiveness in patients with squamous and PD-L1 <1% has been hypothesised.

AIM AND OBJECTIVES

To evaluate the efficacy of PEMBRO and NIVO + IPI in patients with metastatic squamous NSCLC and PD-L1 < 1%, based on subgroup analyses of pivotal clinical trials (CTs), and to assess the economic impact.

MATERIAL AND METHODS

Data from the KEYNOTE-407 (PEMBRO) and CHECKMATE-9LA (NIVO + IPI) clinical trials were analysed to identify differences in overall survival (OS) among subgroups of patients with squamous NSCLC and PD-L1 < 1%. Interaction and indirect treatment comparison (ITC) adjusted analyses using Bucher's method, were performed to determine whether the differences between treatments were statistically significant and clinically relevant. Additionally, the budgetary impact of both therapies was evaluated in our centre.

RESULTS

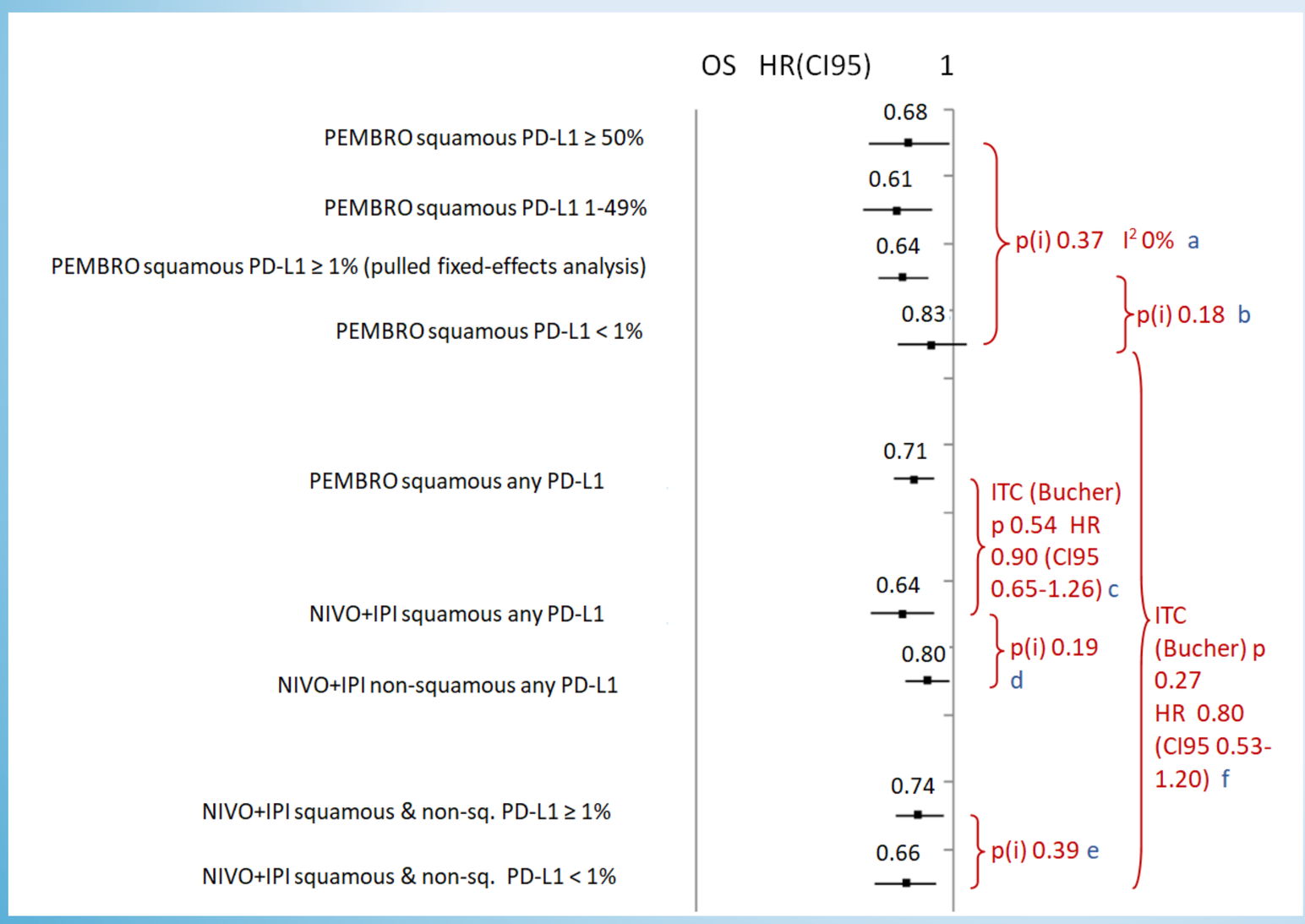

Figure 1. OS results by histology and PD-L1 expression subgroups of KEYNOTE-470 (PEMBRO+QT in squamous NSCLC; Novello et al., J Clin Oncol 2023) and CHECKMATE-7LA (NIVO+IPI+QT squamous and non-squamous; Carbone et al. J Immunother Cancer 2024), both vs QT.
a-f: Own calculations of interaction, heterogeneity and adjusted indirect comparison (Bucher method).

No statistically significant interaction was observed among the three patient subgroups based on PD-L1 for PEMBRO (p = 0.37)[a], nor for NIVO + IPI between squamous and non-squamous histologies (p = 0.19)[d].

Therefore, an ITC exclusively between PD-L1 <1% subgroups, which might lack precision by reducing the sample, may not be sufficiently justified and may be heavily influenced by chance.

An ITC between NIVO + IPI and PEMBRO in squamous NSCLC, regardless of PD-L1 expression, showed no significant differences in OS (HR 0.90; 95%CI 0.65–1.26; p = 0.54)[c].

An ITC for the PD-L1<1% subgroup showed no significant differences (HR 0.80; 95%CI 0.53–1.20; p = 0.27)[f].

PEMBRO was more cost-effective, offering a 67% savings per patient compared to NIVO + IPI, according to current hospital pricing, translating to an annual savings of €62,407 in hospital expenses.

CONCLUSION AND RELEVANCE

Subgroup analyses do not demonstrate a superior clinical benefit of NIVO + IPI over PEMBRO in patients with squamous NSCLC and PD-L1 < 1%. The apparent differences lack methodological validity and are attributable to chance. PEMBRO is the more cost-efficient option in our centre.

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