EFFECTIVENESS OF IMMUNOTHERAPY AS A FUNCTION OF AGE: META-ANALYSIS OF THE APPROVED COMBINATIONS IN FIRST LINE METASTATIC NON-SMALL-CELL LUNG CANCER IN PATIENTS WITHOUT EGFR, ALK or ROS1 MUTATIONS.

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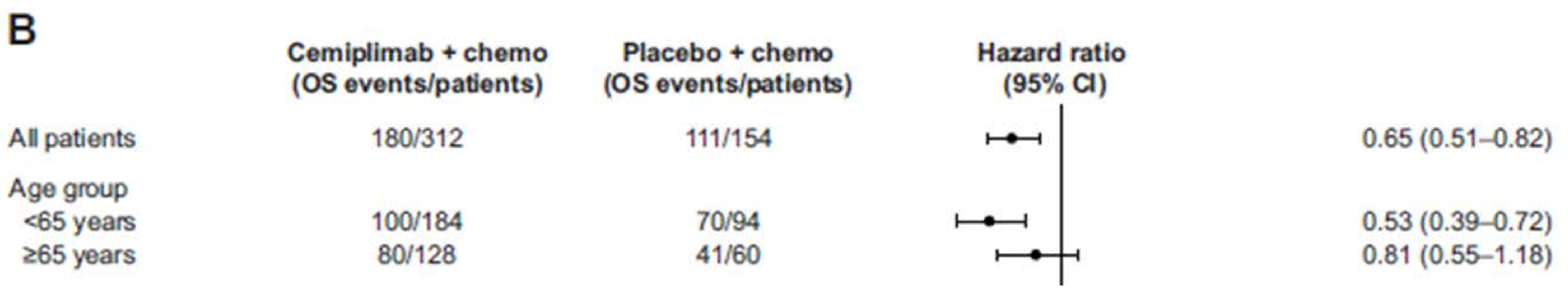
4CPS-175

BACKGROUND AND IMPORTANCE

It could be hypothesized that patients **older than 65 years old** may experience **decreased immune function** due to the natural aging process, which could lead to a **more limited response to immunotherapy** compared to those younger than 65 years old.



The *forest-plot analysis for age-dependent overall survival* from the clinical trial of cemiplimab in combination with chemotherapy in locally advanced or metastatic non-small-cell lung cancer (NSCLC), EMPOWER-Lung 3, showed a **borderline interaction** between the **subgroups younger and older than 65 years old**, with a **p-interaction=0.0895** (own calculation) and HR 0.53 (0.39-0.72), HR 0.81 (0.55-1.18), respectively.

AIM AND OBJECTIVES

To verify the consistency of the hypothesis of an age-related effectiveness by a meta-analysis considering all approved immunotherapy combinations in first-line NSCLC.

MATERIALS AND METHODS

- ✓ Phase III randomized clinical trials (CT) of pembrolizumab, atezolizumab ± bevacizumab, nivolumab + ipilimumab, durvalumab + tremelimumab and cemiplimab, in combination with chemotherapy and nivolumab + ipilimumab with similar characteristics were searched in **MEDLINE-Pubmed**.
- ✓ **Meta-analysis** (IC) was performed using Metasurv calculator.
- ✓ Primary endpoint: **overall survival** outcomes in patients **< and ≥ 65 years of age.**
- ✓ Interaction was considered significative if $p<0.05$ and doubtful if $0.05\leq p<0.1$.

RESULTS

A **pooled HR of 0.67 (95% CI 0.58-0.76), p<0.000001** was obtained in **patients younger than 65 years of age**. Heterogeneity among trials estimate values were as follows: Q 14.84, p=0.03812. I2 53% (CI 95% 0-79%).

In those **older than 65 years old**, the **combined HR obtained was 0.77 (95% CI 0.70-0.84), p<0.000001**. Heterogeneity estimate values were as follows: Q for heterogeneity 0.81 p=0.99733. I2 0% (CI 95% 0-0%).

The **calculated p-interaction between the combined HRs of the under-65 and over-65 groups was 0.0551**, which is considered a **doubtful interaction** in a subgroup analysis.

CONCLUSION AND RELEVANCE

A **significant benefit for immunotherapy-chemotherapy over chemotherapy alone** was shown in **both age groups**. There is some consistency regarding **a greater effectiveness of immunotherapy in patients under 65 years of age**, but more data would be needed to confirm this possible difference.