REFERENCES AND/OR ACKNOWLEDGEMENTS

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No conflict of interest.

2SPD-009 ANALYSIS OF OLAPARIB AND TALAZOPARIB AS POSSIBLE THERAPEUTIC ALTERNATIVES IN ADVANCED BREAST CANCER AND A GERMLINE BRCA MUTATION

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Background To date, the main treatment in advanced breast cancer (ABC) with BRCA mutation is a non-specific chemotherapy of the physician's choice.

Purpose To establish whether olaparib and talazoparib can be declared equivalent therapeutic alternatives (ETA) in patients with ABC and a BRCA mutation, through an indirect treatment comparison (ITC) using a common comparator.

Material and methods A bibliographic search was conducted to identify a phase III clinical trial with olaparib or talazoparib in a similar ABC population (with BRCA mutation), duration and endpoints. An ITC was done according to Bucher's method, using the ITC calculator from the Canadian Agency for Health Technology Assessment. Physician's choice (capecitabine, eribulin or vinorelbine) was used as a comparator. Delta value (Δ), maximum acceptable difference as a clinical criterion of no-inferiority, was set at 0.650 (and its inverse, 1.538). If the 95% CI deviated from the delta margin, this probability was calculated using the Shakespeare method.

Results Clinical trials included were: open-label, randomised, HER 2-negative, capecitabine, eribulin or vinorelbine as comparator, ECOG 0–1, pretreated with taxane, anthracycline or both, and if platinum was used without progression to this one. The primary end point was radiologic progression-free survival (PFS). Two trials were included, one of each drug. Both of them were open-label trials, randomised, in patients with HER2-negative ABC, ECOG 0–1 and pretreated with taxane, anthracycline or both. Differences were found in the percentage of patients with ECOG 0–1 (olaparib 72.2% vs. talazoparib 53.3%), excepting this characteristic the population of both studies was similar. The results of each trial, as well as the ITC conducted, are summarised in the following table 1:

Abstract 2SPD-009 Table 1

Reference	PFS: HR (95% CI)
Olaparib	0.58 (0.43–0.80)
Talazoparib	0.54 (0.41–0.71)
ITC	1.074 (0.71–1.626)

The 95% CI was broad (high level of uncertainty) and exceeds the equivalence margin, and the probability of a result falling out the delta margin was <4.5%.

Conclusion ITC showed no statistically differences in PFS between olaparib and talazoparib.

There is a probable clinical equivalence between both drugs. Although a fraction crosses the confidence interval, this is not statistically significant.

Olaparib and talazoparib could be considered as ETA in most patients with advanced breast cancer.

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2SPD-010 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. The 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 A bibliographic search was conducted to select phase III randomised clinical trials with Pb and Pb-CT in a similar non-squamous NSCLC population (without EGFR or ALK mutations and PD-L1 ≥50%), follow-up period and endpoints. ITC was elaborated using Bucher's method with hazard ratio (HR) and 95% CI.

Results Two trials were selected, one of each regimen. Limitations found: differences in control treatment – platin doublets with pemetrexed vs. several drugs (pemetrexed subgroup was selected for PFS comparison; subgroup data lack for OS comparison) – masking (double-blind vs. open-label design), included population (only patients with PD-L1 ≥50% vs. all patients, then subgroup data were used; and inclusion of 18% patients with squamous tumour). The follow-up period of Pb and Pb-CT trials were 11.2 and 10.5 months, respectively. The results of pivotal trials and ITC are shown below:

Abstract 2SPD-010 Table 1

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

Significant differences in PFS between Pb-CT and Pb results were observed. No significant differences in OS results were found (broad 95% CI with a high level of uncertainty).

Conclusion Pb-CT showed benefit in PFS over Pb monotherapy for patients with non-squamous NSCLC and ≥50% PD-L1 expression receiving pemetrexed combinations. Overall survival benefit is doubtful because of potential bias and large