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.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

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

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95% CI. Monotherapy Pb reserves platinum doublet for later use, and additional data for OS in the pemetrexed subgroup is needed for addressing the benefit of the combination. Taking into account the toxicity of adding chemotherapy, the combined regimen should be considered cautiously.

REFERENCES AND/OR ACKNOWLEDGEMENTS

None.

No conflict of interest.

2SPD-011 NETWORK META-ANALYSIS OF FIRST-LINE ANTIANGIOGENIC DRUGS IN ADVANCED RENAL CELL CARCINOMA

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Background Advanced renal cell carcinoma (RCC) presents multiple therapeutic alternatives. Recently, tivozanib has been authorised in this indication.

Purpose To perform a network meta-analysis (NMA) to provide a comprehensive treatment comparison of the efficacy of first-line antiangiogenic treatment in RCC.

Material and methods A review in the Pubmed database and the European Medicines Agency was done. Inclusion criteria: pivotal randomised clinical trials (CT), including antiangiogenic drugs (sunitinib, pazopanib, sorafenib, tivozanib, interferon and bevacizumab) in treatment-naive patients with RCC, with the most mature data of progression-free survival (PFS). Subgroups of CT with pre-treated and treatment-naive patients were assessed. Exclusion criteria: pivotal CT without a comparator common to the alternatives evaluated. The evaluated outcome was PFS. NMA combined direct and indirect evidence to calculate pooled hazard ratios (HR) by Bayesian methods. Fixed and random effects were evaluated. Models were compared using deviance information criteria (DIC) statistics. The consistency of NMA was assessed by node-splitting models to assess agreement of direct and indirect estimations.

Results Seven eligible CT were selected. Three CT included pre-treated patients and treatment-naive patients. No statistical interaction was found between pretreated and treatment-naive patients, so global results were used for the analysis. Inclusion criteria involved 0–1 (ECOG) performance status in all CT. Sorafenib studies included patients with life expectancy $\geq$3 months. The value of DIC was found more favourable for the fixed-effects model. NMA was consistent because node-splitting models detect no statistical differences between direct and indirect evidence. Regarding sunitinib (treatment with the greatest magnitude of effect), HR for PFS were: 0.39 (CI 95% 0.30 to 0.51) vs. placebo, 0.56 (0.47 to 0.66) vs. interferon, 0.74 (0.56 to 0.97) vs. sorafenib, 0.89 (0.70 to 1.1) vs. bevacizumab plus interferon, 0.92 (0.65 to 1.30) vs. tivozanib, and 0.93 (0.80 to 1.10) vs. pazopanib. CI 95% for HRs among bevacizumab plus interferon, pazopanib, sunitinib and tivozanib included a neutral value. Tivozanib (HR 0.74; 0.56 to 0.97) and sunitinib (0.80; 0.64 to 0.99) – but no other antiagiogenics – showed benefit over sorafenib. Statistically significant benefit was found between all drugs over interferon and placebo.

Conclusion The NMA provided a review of the relative efficacy of current antiangiogenic alternatives for RCC in terms of PFS. Bevacizumab plus interferon, pazopanib, sunitinib and tivozanib showed no differences. Sorafenib was inferior to sunitinib and tivozanib.

REFERENCES AND/OR ACKNOWLEDGEMENTS

None.

No conflict of interest.

2SPD-012 RELATIVE VALUE UNITS AS A PRODUCTIVITY SCORE OF MANAGEMENT OF ONCOLOGY MEDICATION IN SPECIAL SITUATIONS

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Background Relative value units (RVU) as a clinical management tool prove to be useful in measuring different pharmaceutical activities. However, little is known about RVU for the management of medication in special situations.

Purpose To measure productivity in the management, dispensation, elaboration and pharmaceutical care activity of oncology medication in special situations: expanded or early access (EA) and 'off-label' use in a pharmaceutical department by estimating RVU.

Material and methods Retrospective and observational study performed in a tertiary hospital. Data from all EA and off-label use oncology drugs requests were collected from January 2015 to February 2018 (38 months).

Variables collected active drug, kind of drug in special condition (EA/'off-label') and length of treatment. Pharmaceutical processes included: management, dispensation, elaboration and pharmaceutical care.

RVU assigned to each activity have been obtained from a standardised document drawn up by the Spanish Society of Hospital Pharmacists.[1]

Results Seventy-five oncology drug requests were analysed, of which 58 (77.3%) were EA. Nivolumab nine (13%), pertuzumab/cabonzatinib seven (10%), bevazicumab/liposomal irinotecan six (9%) and trametinib/durvalumab five (7%) were the most requested. The average length of treatment was 5.9 months.

Abstract 2SPD-012 Table 1

Activity area	RVU value	Total produced RVUs
1. Management area	19.82	4677.52*
1.1. Processing of drugs (initial and consecutive application)		
2. Dispensation area		
2.1. Successive dispensations in outpatient	5.08	960.12
3. Elaboration area	16.02	128.16
3.1. GMP of new cytotoxic preparation	79.15	23190.95
3.2. Elaboration of cytotoxic drug		
4. Pharmaceutical care area	39.58	1385.3
4.1. To inpatient about specific drug therapy	13.19	3403.02
4.1.1. Initial	21.11	675.52
4.1.2. Successive		
4.2. To outpatient.		
4.2.1. Initial		

*In total, 4,320.76 (92.4%) were processing of EA drugs.

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