Analysis of non-pharmacological cost savings derived from the use of fixed-dose combination of pertuzumab and trastuzumab for subcutaneous injection in patients with HER2-positive breast cancer in Spain

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BACKGROUND AND OBJECTIVES

- Human epidermal growth factor receptor-2 (HER2) is frequently overexpressed in breast cancer (BC) and associated with worse prognosis. Pertuzumab (P) and trastuzumab (Herceptin® or H) are humanised monoclonal antibodies blocking HER2 with synergistic activity due to their complementary mode of action[1-3].
- Three different treatment combinations can be administered: intravenous P plus intravenous H (P-IV+H-IV) or plus subcutaneous H (P-IV+H-SC) and the subcutaneous fixed-dose combination of P and H (PH-FDC-SC).
- The pivotal FeDeriCa study, demonstrated non-inferiority in terms of pharmacokinetics of PH-FDC-SC versus P-IV+H-IV as well as a similar efficacy and safety profile[4]. And the PHranceSCa study concluded that most patients strongly preferred PH-FDC-SC over P-IV+H-IV[5].
- Indeed, SC formulations have different advantages. In this sense, PHaTiMa-study concluded that PH-FDC-SC significantly saves active time to healthcare professionals (HCP) & patients as well as healthcare resources compared to P-IV+H-IV and P-IV+H-SC[6]. The H-Excelencia-study concluded that SC formulations of existing IV drugs (trastuzumab and rituximab) could allow to increase the hospital capacity and improve the quality of the service due to the process optimization achieved with SC formulations in Spanish hospitals[7].
- The primary objective of this analysis **is to quantify the non-pharmacological costs associated with the use of PH-FDC-SC versus P-IV+H-IV or P-IV+H-SC in patients with HER2-positive BC in Spain**. The secondary aim is **to evaluate the potential increase in hospitals' healthcare capacity with the use of PH-FDC-SC**, based on the optimized processes identified in the H-Excelencia-study.

METHODS

- In this study, a Spanish panel of experts (n=6) composed of oncologists, pharmacists and nurses validated the model assumptions made, the parameters and the resources through a round consensus process.

1. Analysis of non-pharmacological costs

- A cost-minimization model was developed to estimate non-pharmacological costs derived from the treatment of early and metastatic HER2-positive BC patients in Spain, with each of the three therapeutic combinations.
- The experts estimated that the distribution of the population of patients with eBC who received adjuvant was 90% and 10% for patients with prior neoadjuvant and without, respectively.
- The non-pharmacological costs associated with each therapy was calculated for a full course treatment (mBC: 27 cycles[8]; eBC neoadjuvant: 5 cycles; eBC adjuvant with prior neoadjuvant: 13 cycles; eBC adjuvant-only: 18 cycles[9]). Direct and indirect costs (€2023) were mostly calculated based on the resource use observed in the PHaTiMa-study[6]. Direct costs included HCP costs associated with treatment preparation and administration, the use of healthcare consumables and the use of venous access devices (VAD).
- HCP active time was reported in PHaTiMa-study for the three combinations. HCP costs (cost/minute) were calculated considering the gross salary of the HCP involved (nurse, nurses' assistants, pharmacists and pharmacists' assistants) from published Spanish Autonomous Communities[10-20] and a percentage (23.6%) of social security costs[21]. A working week of 40 hours/week for 52 weeks/year has been considered. The cost of consumables used with each combination was calculated based on the quantity used in the PHaTiMa-study[6] and their unit costs (obtained from national databases and literature[22-29]). The use of each VAD (peripheral intravenous access [PIV], peripherally inserted central catheter [PICC] and Port-a-Cath) for each combination was obtained from the expert panel (**Table 1**). The costs of VADs included the acquisition cost[30] and the costs of complications associated with its use[23,30-32] (incidences were obtained from the literature[31,33-35]).

Table 1: Use of VAD depending on indication and treatment

*Venous access devices**	P-IV+H-IV	P-IV+H-SC	PH-FDC-SC
mBC			
PIV	51%	51%	53%
Port-a-Cath	43%	43%	14%
PICC	6%	6%	9%
eBC (neoadjuvant treatment)			
PIV	48%	48%	63%
Port-a-Cath	22%	22%	17%
PICC	31%	31%	20%
eBC (Adjuvant after previous neoadjuvant treatment)			
PIV	48%	48%	0%
Port-a-Cath	22%	22%	0%
PICC	31%	31%	0%
eBC (Adjuvant only)			
PIV	56%	56%	83%
Port-a-Cath	7%	7%	3%
PICC	37%	37%	13%

eBC: early breast cancer; FCD: fixed-dose combination; IV intravenous; mBC: metastatic breast cancer; PIV: peripheral intravenous; P: pertuzumab; PICC: peripherally inserted central catheter; SC: subcutaneous; H: trastuzumab. *Source: panel of experts

- Indirect costs included the cost of lost productivity using the human capital method. It was calculated from patient treatment room time obtained from PHaTiMa-study[6] and the one of the companion (85% and 50% of mBC and eBC patients, respectively) was added. The average salary of women[36], considering the distribution of BC patients according to age[37] and the corresponding recorded unemployment rate in 2020[38], was used.

2. Impact of PH-FDC-SC on hospital capacity

- To quantify the impact on healthcare capacity, the processes optimized by Spanish hospitals identified in the H-Excelencia-study were used[7]. The increase in treatments administered and prepared due to the conversion from IV to SC administration were recalculated from the reduction in administration and preparation times observed with PH-FDC-SC in the PhaTiMa-study[6] (patient treatment room time and preparation time of the treatment [minutes; P-IV+H-IV: 2.99, P-IV+H-SC: 2.42, PH-FDC-SC; 1.28]) (**Table 2).**

Sensitivity analyses

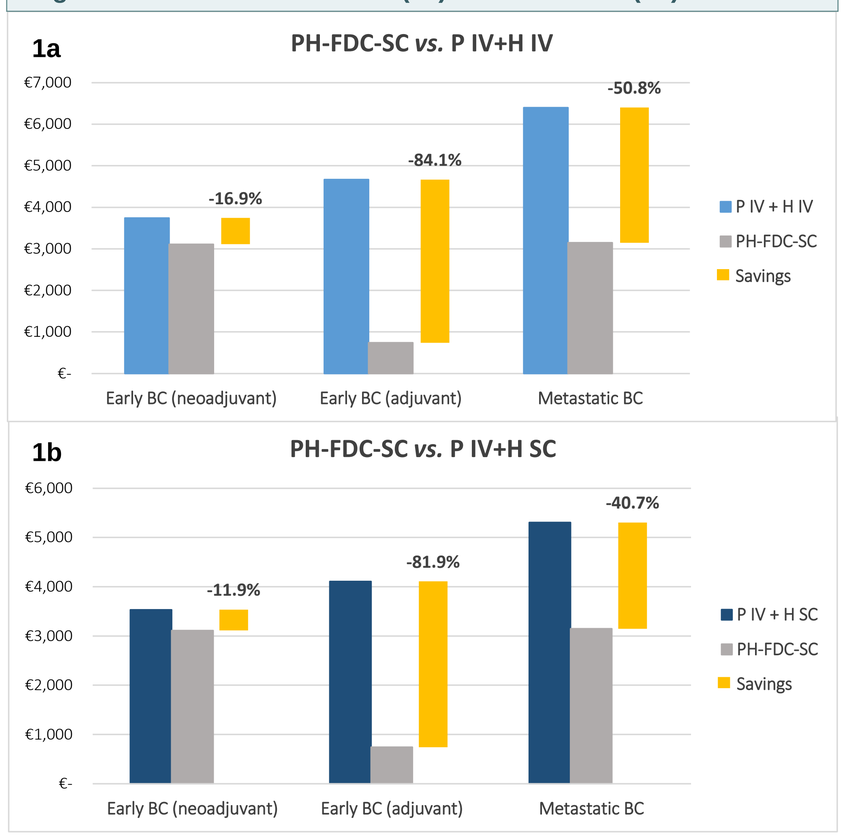
- Deterministic sensitivity analysis was carried out to evaluate the uncertainty associated with the model: 1) three alternative scenarios in parameters whose impact on results may be significant; 2) univariate analysis.

RESULTS

1. Analysis of non-pharmacological costs

- The overall non-pharmacological cost per patient during the whole treatment in the different indications of the pathology is shown in **Figure 1**. The use of PH-FDC-SC versus P-IV+H-IV and P-IV+H-SC reduces non-pharmacological costs by up to:
  - Neoadjuvant treatment of eBC: -16.9% (€-631.0) and -11.9% (€-421.2), respectively.
  - Adjuvant treatment of eBC: -84.1% (€-3,924.9) and -81.9% (€-3,366.5), respectively.
  - Treatment of mBC : -50.8% (€-3,252.3) and -40.7% (€-2,157.5) respectively.
- Reduction in the use of VAD has the major impact. The savings associated with the use of VAD with PH-FDC-SC relative to both comparators vary substantially depending on the indication (-7.7%, -92.0% and -36.9% for neoadjuvant eBC, adjuvant eBC, and mBC, respectively).

Figure 1: . PH-FDC-SC versus (1a) P-IV+H-IV and (1b) P-IV+H-SC



BC: breast cancer; FCD: fixed-dose combination; IV: intravenous; P: pertuzumab; SC: subcutaneous; H: trastuzumab

2. Impact of PH-FDC-SC on hospital capacity

- The increase in treatment administration at the cancer treatment unit (considering 3.a and 3.b) and in treatments that can be prepared in the vertical laminar flow hood at the hospital pharmacy due to conversion P-IV+H-IV or P-IV+H-SC to PH-FDC-SC are shown in **Table 2.**
- In a hypothetical Spanish hospital that optimized all the processes identified in previous studies[7] with PH-FDC-SC, the capacity of treating patients with HER2-positive BC would increase by 27.87% and 20.3%, respectively.

Table 2: Impact of PH-FDC-SC on hospital capacity

	Parameters of capacity of the cancer treatment unit	Impact (%)	Resource
1	Increase in the number of treatments administered due to premedication being administered in the waiting room	0.40%	H-Excelencia[7]
2	Increase in the number of treatments that can be prepared and administered at the reference hospital because patients receiving PH-FDC-SC can be treated at hospitals closer to their homes	2.80%	H-Excelencia[7]
3.a	Increase in treatment administration at the cancer treatment unit (**considering all patients treated in the unit)** due to conversion:		
	P-IV+H-IV to PH-FDC-SC	1.7%	Recalculated
	P-IV+H-SC to PH-FDC-SC	1.3%	Recalculated
3.b	Increase in treatment administration at the cancer treatment unit (**considering only those patients treated with P and H in the unit**), due to conversion:		
	P-IV+H-IV to PH-FDC-SC	21%	Recalculated
	P-IV+H-SC to PH-FDC-SC	15.9%	Recalculated
4	Increase in treatments that can be prepared in the vertical laminar flow hood at the hospital pharmacy:		
	P-IV+H-IV to PH-FDC-SC	3.7%	Recalculated
	P-IV+H-SC to PH-FDC-SC	1.2%	Recalculated

FCD: fixed-dose combination; IV: intravenous; P: pertuzumab; SC: subcutaneous; H: trastuzumab

Sensitivity analyses

- The scenario analysis demonstrated robustness of the analysis. In addition, the greatest impact on the base case for all stage of the of cancer in one-way sensitivity analysis were the duration of treatment, consumables consumptions and VAD complication costs.

CONCLUSIONS

The use of PH-FDC-SC for the treatment of patients with HER2-positive BC improves the efficiency of the Spanish hospitals by saving non-pharmacological costs and allowing an increase in hospital capacity.

The reduction in active HCP time, healthcare consumables and time spent by the patient derived from the use of PH-FDC-SC means an economic saving in the Spanish healthcare context.

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