Hospital capacity tool to assess the potential impact of using a fixed dose combination of pertuzumab/ trastuzumab for subcutaneous injection versus intravenous pertuzumab/trastuzumab in HER2+ breast cancer

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Introduction

Globally, the cancer burden continues to grow, exerting a tremendous strain on individuals and healthcare systems, and Portugal is not an exception.[1,2] Breast cancer is the most common type of cancer in Portugal corresponding to 14.8% of total new cases, of which, around 20% overexpress HER2 (1713 new patients per year). [3,4]
Intravenous pertuzumab plus trastuzumab (P IV + T IV) with chemotherapy is the standard of care treatment for patients with early and metastatic HER2+ breast cancer. [5,6] In order to achieve their clinical benefits, P IV is infused over 30–60 min and T IV over 30–90 min, usually for multiple cycles over a treatment course, with the addition of a substantial observation time.[7,8] The increased use of intravenous monoclonal antibodies has placed a strain on medical centres' capacity and time management, as well as on the resources required to prepare and administer infusions (pre and post infusions).[6,13]
In 2020, a fixed-dose combination of pertuzumab and trastuzumab for subcutaneous injection (PH FDC SC) was approved by the European Commission offering patients and healthcare providers a less invasive and faster administration versus individual intravenous infusions, with the potential to reduce time and resources in the preparation and administration procedures as well as reduce the overall time that patients spend in the treatment room. [9, 10, 11]
The aim of this study is to demonstrate the use of a capacity tool to calculate the expected impact of using PH FDC SC in the hospital capacity considering the preparation and administration of these drugs by healthcare professionals (HCPs), the infusion chair utilization rate and the time spent by patients in the hospital compared to the treatment with P IV + T IV.

Methods

We have developed a tool based on microsoft excel® to support hospitals to calculate the time needed to prepare and administer P IV + T IV versus PH FDC SC for the total number of patients with HER2+ BC treated in a hospital during one year, as well as the impact of using these treatments in the annual hospital capacity (treatment chairs utilization) and the impact on the patients, considering the time spent at the hospital to receive both drugs.
For this study, we have performed a simulation in a hypothetical hospital that treats patients with early HER2+ BC (neoadjuvant) and metastatic HER2+ BC, the indications currently reimbursed in Portugal. To customize this tool it is necessary to fill out general information about the hospital (ex.: dimension, number of patients and number of treatment cycles), the preparation, administration and monitoring active time used by the HCPs and the total amount of time spent by patients in the hospital (in the infusion chair and for monitoring) [7,8,9,12] This simulation considered 100 patients treated per indication and, for the HCPs active time and administration time, we have used data from the literature and from the SmPCs of each considered drug. The inputs considered are presented below:

Table 1: Hospital general data for one year

INPUTS		
	Number of patients treated per year (hypothetical)	**n**
	N° of patients for neoadjuvant treatment	100
	N° of patients for metastatic treatment	100
	Number of treatment cycles	
	N° of cycles for neoadjuvant treatment	4
	N° of cycles for metastatic treatment	18
	Dimension of the daycare unit	
	N° of treatment chairs	50
	N° of working days per week	5
	Average number of working hours per day	12

Table 2: HCPs active time during drugs preparation, administration and monitoring [9]

	P IV + T IV	PH FDC SC
HCP active preparation time (min)	14,1	8,0
HCP active administration time (min)	32,4	15,5

Table 3: Administration and observation time for patients [7,8,12]

	Loading dose (minutes)		Maintenance dose (minutes)	
	Administration time	**Observation time**	**Administration time**	**Observation time**
Pertuzumab	60	60	45*	45*
Trastuzumab	90	360	30**	120
PH FDC SC	8	30	5	15

*Average between 30-60 min per SmPC; ** time can be reduced to 30 min if first administration is well tolerated

Results

In this simulation, both the time spent by the HCPs to prepare the medication and the time spent by the HCPs in the treatment room to treat all patients during one year is about 2 times greater with P IV + T IV compared to PH FDC SC (**fig.1**).

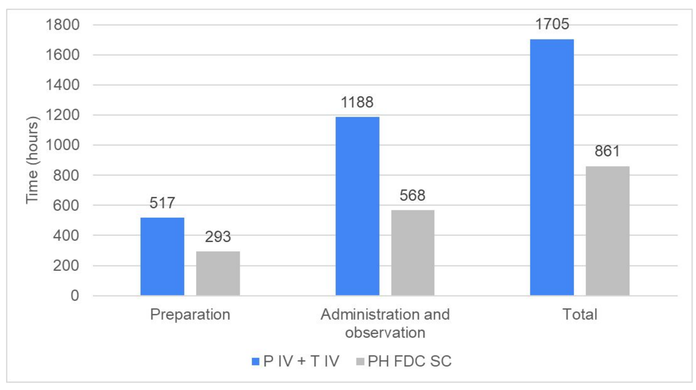
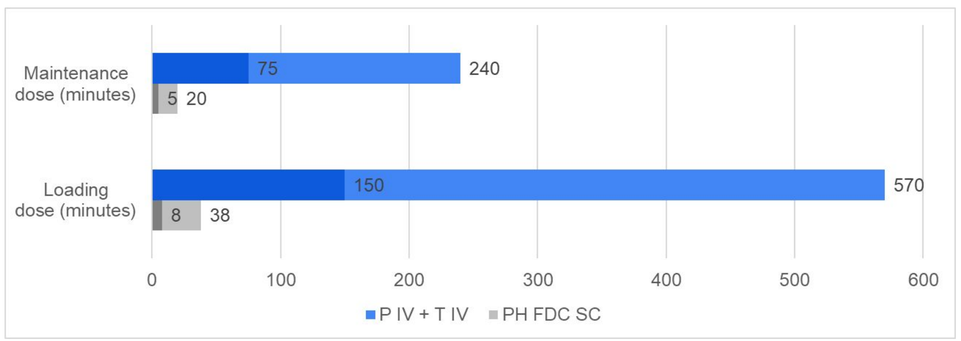


Fig. 1: Active HCPs time spent on preparation, administration and observation for the total n° of patients during one year of treatment (hours)

The analysis of the maximum time a patient can stay in a treatment chair or in the treatment room to be treated with these two drugs demonstrates that during the first cycle (loading dose), a patient treated with P IV + T IV can occupy a chair more than 9 hours (570 min) while a patient treated with PH FDC SC only needs a little more than half an hour (around 15 times less). Analysing the following cycles (maintenance dose), patients treated with PH FDC SC only need to sit around 20 minutes, 12 times less than patients treated with P IV + T IV (**fig.2**).



*Dark colors correspond to administration time and light colors to observation time;
**These results are considering that patients are in the infusion chair for administration and observation.

Fig 2: Time of chair occupancy per patient and per cycle

When we look at the annual occupancy rate of the infusion chairs in the treatment room considering the maximum time of chair occupancy (including administration and observation), in this hypothetical hospital, PH FDC SC can saves 5,8% of the total capacity to the hospital permitting treating more patients (**fig. 3**) considering that one infusion chair can treat more patients per day if PH FDC SC is used (**fig. 4**).

Patients with HER2+ breast cancer treated with pertuzumab and trastuzumab receive in general 4 cycles in the neoadjuvant setting and maximum 18 cycles per year in the metastatic setting [7]. When we sum up the administration and observation times corresponding to all cycles that a patient receives during one year, in the neoadjuvant and metastatic setting, patients treated with PH FDC SC can stay about 90% less time in the hospital comparing to patients receiving pertuzumab and trastuzumab individually (**fig. 5**).

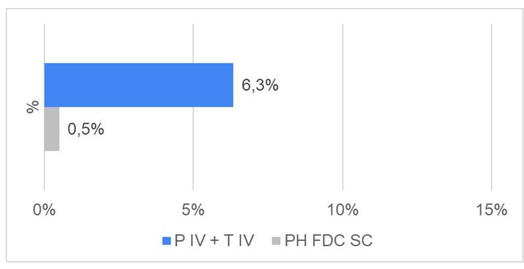
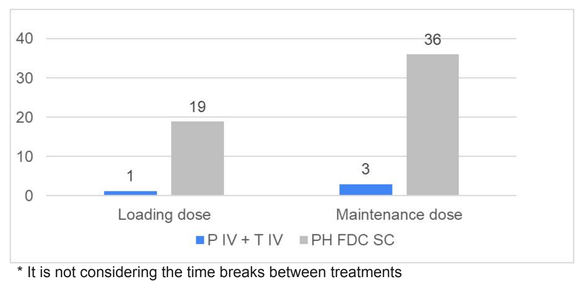
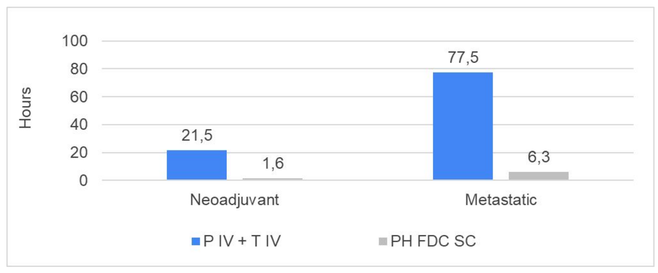


Fig. 3: Annual chair occupancy rate for the treatment of all patients (%)



* It is not considering the time breaks between treatments

Fig. 4: Maximum number of patients that can be treated in one chair per day*



* It considers only pertuzumab and trastuzumab administration and observation

Fig. 5: Duration of stay of a patient in the daycare unit to complete all cycles during one year

Discussion and conclusion

This capacity tool allows the hospital to understand what is the impact of using different treatment options for HER2+ breast cancer in the hospital capacity and resource consumption considering their own reality. The simulation showed that PH FDC SC has the potential to provide substantial time savings for the pharmacy, for the nurses and for the patients due to its easy preparation and shorter duration of administration and observation.
The results observed in this study can be justified by the time savings in the preparation of PH FDC SC considering it is a ready-to use formulation without the need for calculations, reconstitution or transfer to an IV bag [10]. From an administration and monitoring perspective it is also expected to decrease the active nurse time as they, for example, do not have to perform IV flushes or change infusion bags during the treatment [11].
Considering the infusion chairs, the administration of PH FDC SC can have a great impact on the treatment rooms facilitating the management of the infusion chairs and releasing capacity to reduce waiting lists or to perform other treatments, even in hospitals where observation occurs outside the infusion chairs.
In conclusion, this capacity tool can inform hospitals about the value of different treatments besides efficacy and safety, demonstrating the impact on the hospital day-to-day management and on patients.

Limitations

The simulation presented in this study is based in a hypothetical hospital and values can vary between hospitals with a different n° of infusion chairs, working hours and n° of patients. Furthermore, each hospital have different practices related to preparation, administration and observation tasks that may affect the results for the hospital and the patients. Time of infusion chair occupancy can also vary between hospitals depending on hospital routines. Results in fig 1. can be underestimated as the available data (table 2) is from maintenance cycles. Despite that, we believe the trend favouring time and resources savings with PH FDC SC would be maintained particularly when considering other studies about subcutaneous injections regarding the preparation and administration burden, the time patients spend in the infusion chairs and the optimization of medical

Conflicts of interest: Alexandre Cunha is employee of Roche Farmacêutica Lda.

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