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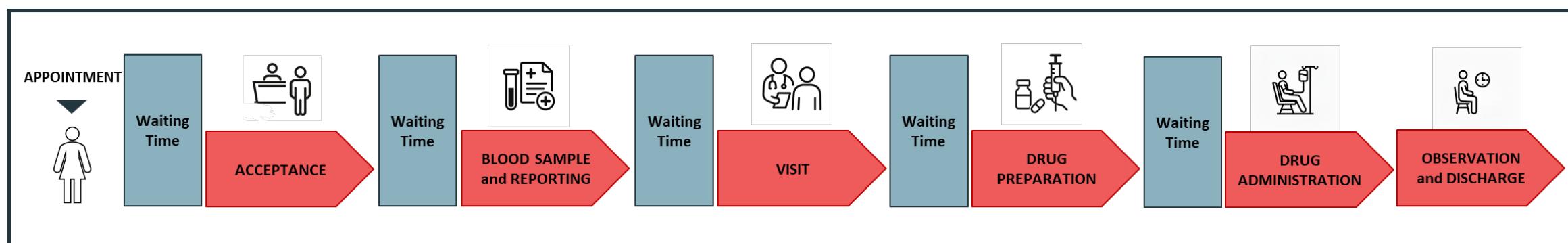
## Introduction

- Human Epidermal Growth Factor Receptor 2-positive (HER2+) breast cancer (BC) represents a significant burden in terms of female cancer prevalence and healthcare resource utilization in Italy.
- Despite notable therapeutic advancements, ensuring economic sustainability and operational efficiency remains a critical challenge for the National Healthcare Service.
- The study aimed to evaluate the managerial and economic implications of different treatment administration pathways (TAPs) for HER2+ BC patients, with the goal of optimizing hospital workflows, improving resource allocation, and enhancing patient outcomes across Italian oncology centres.

## Methods

- This project used a decision-tree model to simulate and compare five TAPs (day-hospital) in HER2+ BC patients within Italian hospital settings. The TAP involves consecutive activities spread by waiting times; all the activities are conducted over a single day.

Figure 1. The treatment administration pathway is divided into six phases.

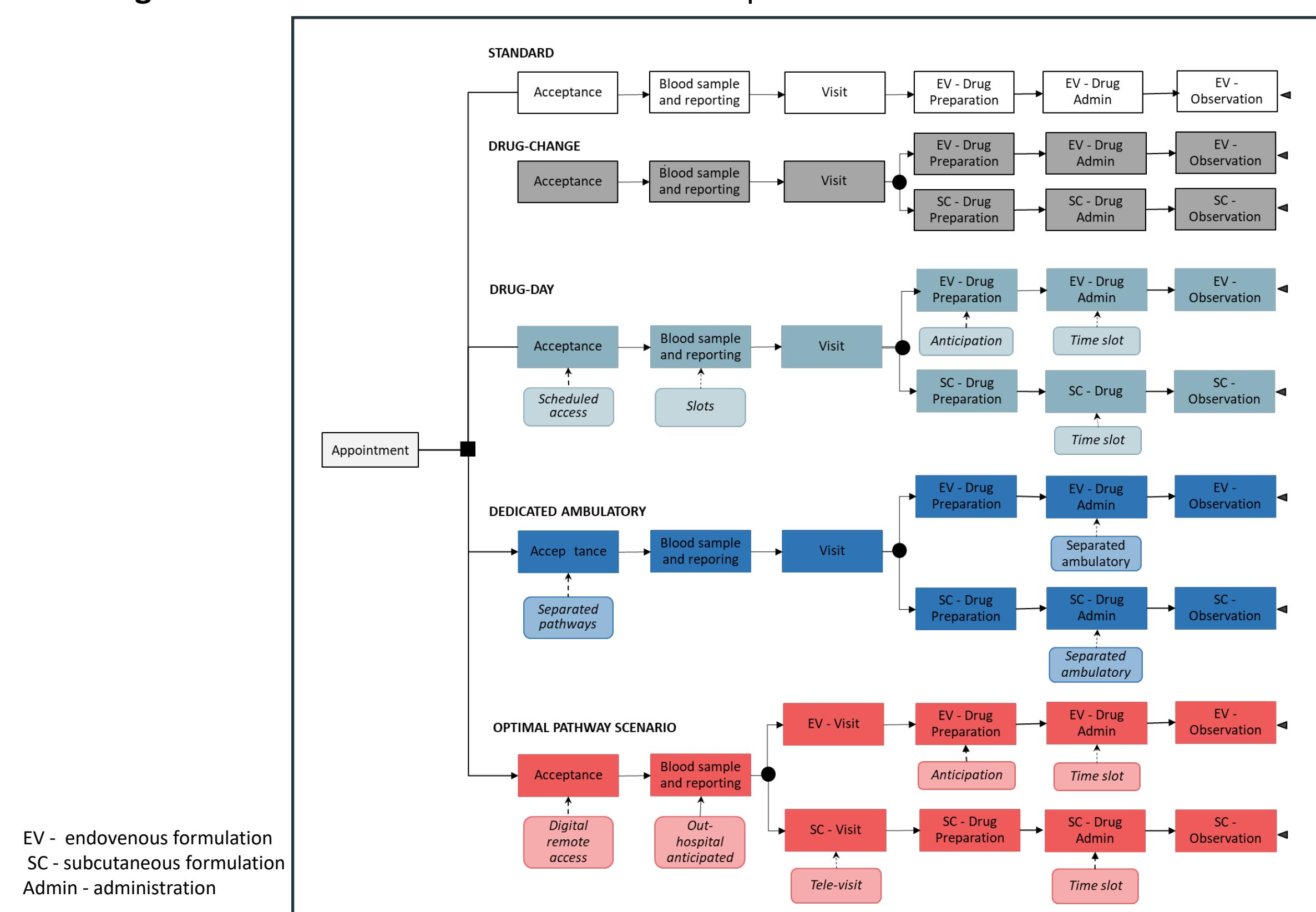


### TAP TYPES

- ✓ Standard (endovenous – EV - formulation only).
- ✓ Drug-Change (introducing subcutaneous – SC - formulation).
- ✓ Drug-Day (with time-based improvements).
- ✓ Dedicated Ambulatory (with spatial optimization).
- ✓ Optimal Pathway (integrating major achievable improvement actions).

The Standard TAP is the actual practice, the other four TAPs include improvement actions to optimize time and effort required by figures involved, as shown in Figure 2.

Figure 2. Decision-Tree model with TAPs for patients with HER2+ BC in Italian oncological centers



- The model estimates efficiency outcomes: patient crossing time, as a whole (total) and divided into activity and waiting time; healthcare professional (HCP) activity time and infusion chair occupation time; patient total times which adds the travel time to the crossing time, and caregiver time to assist the patient. Times are reported in hours.
- Costs are reported in euros (€) and divided into direct healthcare costs, including HCP work, infusion chair occupation, pharmacological treatment purchase and adverse events management, and indirect costs related to productivity losses for patients and caregivers.
- Model inputs are taken from literature or from expert opinion research or survey. All outcomes and costs are reported as monthly per 100 patients values and differences to the standard TAP (as reference).
- A One-Way Sensitivity Analysis was applied to patient total time and the HCP activity time, total direct cost and the total cost. A probabilistic sensitivity analysis was implemented to compute confidence intervals for outcome and cost estimates. (Monte Carlo simulation)

## Results

Table 1. Monthly crossing times (hours) for 100 patients in different TAPs compared with standard one

OUTCOMES	VALUE (IC 95%)				
	STANDARD	DRUG-CHANGE	DRUG-DAY	DEDICATED AMBULATORY	OPTIMAL PATHWAY
HCP Time, hours	140.3 (125.0 ; 155.7)	111.6 (100.6 ; 122.3)	102.0 (91.8 ; 112.1)	104.2 (93.8 ; 114.4)	92.5 (82.8 ; 102.2)
Difference (vs STANDARD)		-28.7 (-39.5 ; -18.9)	-38.3 (-49.3 ; -28.8)	-36.1 (-47.1 ; -26.7)	-47.8 (-59.0 ; -38.1)
Ref					
Inf Chair Occup Time, hours	243.4 (197.0 ; 292.8)	93.4 (75.5 ; 114.2)	93.4 (75.5 ; 114.2)	93.4 (75.5 ; 114.2)	93.4 (75.5 ; 114.2)
Difference (vs STANDARD)		-150.0 (-188.6 ; -114.9)	-150.0 (-188.6 ; -114.9)	-150.0 (-188.6 ; -114.9)	-150.0 (-188.6 ; -114.9)
Ref					
Patient in-hospital Time, hours	560.0 (493.0 ; 630.4)	281.8 (250.0 ; 314.5)	193.5 (175.4 ; 213.1)	192.8 (175.0 ; 212.1)	174.9 (157.3 ; 194.6)
Difference (vs STANDARD)		-278.1 (-336.6 ; -223.7)	-366.5 (-433.1 ; -306.0)	-367.2 (-433.7 ; -306.5)	-385.1 (-451.9 ; -323.7)
Ref					
Waiting Time	325.7 (288.5 ; 364.5)	304.5 (267.9 ; 342.7)	274.5 (240.6 ; 311.5)	295.3 (259.9 ; 332.1)	170.8 (146.0 ; 195.9)
Difference (vs STANDARD)		-21.2 (-27.4 ; -14.8)	-51.2 (-60.1 ; -42.2)	-30.4 (-37.1 ; -23.7)	-154.9 (-176.2 ; -134.7)
Ref					
Total Time	885.7 (810.8 ; 963.4)	586.4 (537.2 ; 641.2)	468.0 (427.7 ; 510.4)	488.0 (446.6 ; 531.3)	345.6 (314.0 ; 379.8)
Difference (vs STANDARD)		-299.3 (-357.5 ; -244.2)	-417.7 (-482.3 ; -357.3)	-397.6 (-463.2 ; -335.9)	-540.0 (-606.9 ; -473.2)
Ref					
Patient Total Time, hours	1,123.9 (1,032.6 ; 1,214.9)	824.6 (755.9 ; 894.3)	706.2 (646.2 ; 770.0)	726.3 (664.4 ; 791.9)	371.2 (338.4 ; 405.4)
Difference (vs STANDARD)		-299.3 (-357.5 ; -244.2)	-417.7 (-482.3 ; -357.3)	-397.6 (-463.2 ; -335.9)	-752.7 (-831.3 ; -676.1)
Ref					
Caregiver Total Time, hours	729.6 (576.1 ; 882.6)	535.2 (422.5 ; 645.6)	458.4 (362.2 ; 553.8)	471.4 (372.2 ; 568.9)	241.0 (190.5 ; 293.3)
Difference (vs STANDARD)		-194.3 (-250.2 ; -145.6)	-271.2 (-338.7 ; -207.1)	-258.2 (-323.4 ; -195.9)	-488.6 (-599.3 ; -379.3)
Ref					
Adverse Events, N	0.41 (0.33 ; 0.47)	0.14 (0.12 ; 0.17)	0.14 (0.12 ; 0.17)	0.14 (0.12 ; 0.17)	0.14 (0.12 ; 0.17)
Difference (vs STANDARD)		-0.26 (-0.32 ; -0.21)	-0.26 (-0.32 ; -0.21)	-0.26 (-0.32 ; -0.21)	-0.26 (-0.32 ; -0.21)
Ref					

Table 2. Monthly cost (€) for 100 patients in different TAPs compared with standard one

COSTS (€)	VALUE (IC 95%)				
	STANDARD	DRUG-CHANGE	DRUG-DAY	DEDICATED AMBULATORY	OPTIMAL PATHWAY
HCP Active Time	€ 4,645 (3,973 ; 5,405)	€ 3,798 (3,216 ; 4,501)	€ 3,564 (3,006 ; 4,241)	€ 3,617 (3,054 ; 4,291)	€ 3,274 (2,747 ; 3,885)
Difference (vs STANDARD)		€ -846 (-1,136 ; -579)	€ -1,081 (-1,391 ; -804)	€ -1,028 (-1,330 ; -757)	€ -1,371 (-1,702 ; -1,087)
Ref					
Infusion Chair Occupation	€ 980 (731 ; 1,277)	€ 376 (279 ; 494)			
Difference (vs STANDARD)		€ -604 (-815 ; -432)			
Ref					
Treatment	€ 281,311 (233,253 ; 334,684)	€ 274,657 (238,291 ; 316,743)			
Difference (vs STANDARD)		€ -6,655 (-56,627 ; 43,635)			
Ref					
Adverse Events	€ 2,259 (1,784 ; 2,759)	€ 797 (611 ; 1,006)			
Difference (vs STANDARD)		€ -1,462 (-1,838 ; -1,117)			
Ref					
Total Direct Cost	€ 289,195 (241,012 ; 342,815)	€ 279,628 (242,926 ; 321,910)	€ 279,394 (242,695 ; 321,691)	€ 279,447 (242,748 ; 321,742)	€ 279,104 (242,448 ; 321,403)
Difference (vs STANDARD)		€ -9,567 (-59,807 ; 40,507)	€ -9,801 (-60,083 ; 40,287)	€ -9,748 (-60,029 ; 40,338)	€ -10,091 (-60,348 ; 39,999)
Ref					
Patient Productivity Loss	€ 7,349 (5,355 ; 9,789)	€ 5,393 (3,933 ; 7,193)	€ 4,619 (3,352 ; 6,157)	€ 4,750 (3,450 ; 6,338)	€ 2,428 (1,747 ; 3,272)
Difference (vs STANDARD)		€ -1,956 (-2,706 ; -1,338)	€ -2,731 (-3,692 ; -1,935)	€ -2,600 (-3,529 ; -1,843)	€ -4,922 (-6,588 ; -3,552)
Ref					
Caregiver Productivity Loss	€ 7,031 (4,875 ; 9,688)	€ 5,158 (3,566 ; 7,084)	€ 4,418 (3,081 ; 6,090)	€ 4,543 (3,163 ; 6,242)	€ 2,322 (1,599 ; 3,175)
Difference (vs STANDARD)		€ -1,873 (-2,643 ; -1,255)	€ -2,613 (-3,677 ; -1,771)	€ -2,488 (-3,512 ; -1,681)	€ -4,709 (-6,508 ; -3,250)
Ref					
Total Indirect Cost	€ 14,380 (10,942 ; 18,777)	€ 10,551 (8,049 ; 13,783)	€ 9,037 (6,842 ; 11,809)	€ 9,293 (7,038 ; 12,098)	€ 4,750 (3,605 ; 6,198)
Difference (vs STANDARD)		€ -3,829 (-5,155 ; -2,718)	€ -5,344 (-7,106 ; -3,909)	€ -5,088 (-6,781 ; -3,700)	€ -9,631 (-12,632 ; -7,196)
Ref					
Total Cost	€ 303,575 (255,414 ; 358,235)	€ 290,180 (254,369 ; 331,697)	€ 288,430 (252,545 ; 329,946)	€ 288,740 (252,890 ; 330,251)	€ 283,854 (247,766 ; 325,914)