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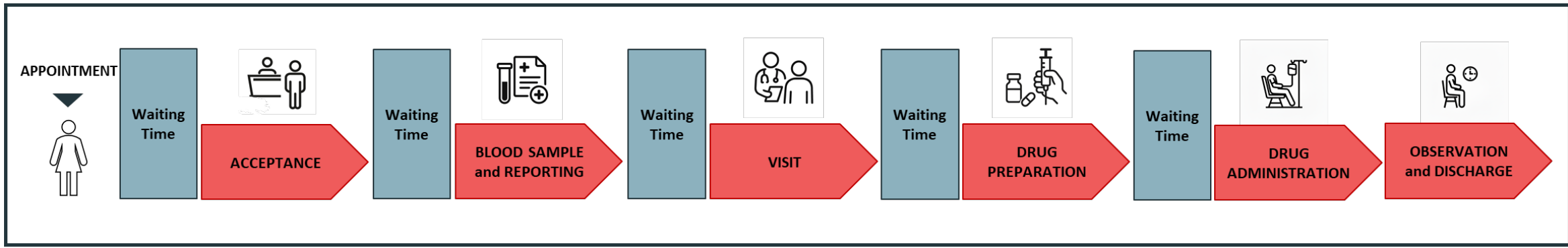
Introduction

- 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.

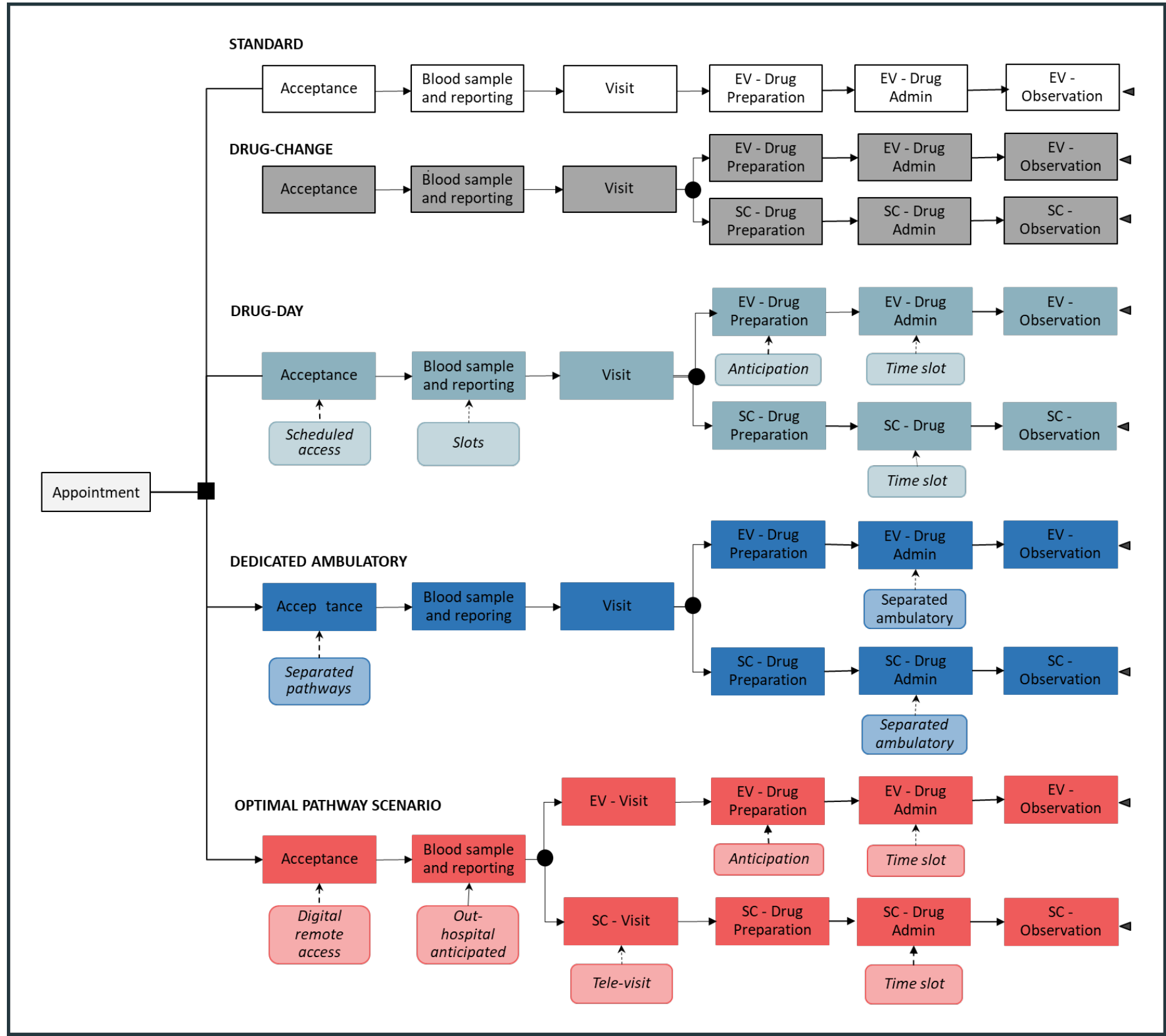


TAP TYPES

- 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)	Ref	-28.7 (-39.5 ; -18.9)	-38.3 (-49.3 ; -28.8)	-36.1 (-47.1 ; -26.7)	-47.8 (-59.0 ; -38.1)
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)	Ref	-150.0 (-188.6 ; -114.9)	-150.0 (-188.6 ; -114.9)	-150.0 (-188.6 ; -114.9)	-150.0 (-188.6 ; -114.9)
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)
Activity Time	Ref	-278.1 (-336.6 ; -223.7)	-366.5 (-433.1 ; -306.0)	-366.5 (-433.7 ; -306.5)	-385.1 (-451.9 ; -323.7)
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)	Ref	-21.2 (-27.4 ; -14.8)	-51.2 (-60.1 ; -42.2)	-30.4 (-37.1 ; -23.7)	-154.9 (-176.2 ; -134.7)
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)	Ref	-299.3 (-357.5 ; -244.2)	-417.7 (-482.3 ; -357.3)	-397.6 (-463.2 ; -335.9)	-540.0 (-606.9 ; -473.2)
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)	Ref	-299.3 (-357.5 ; -244.2)	-417.7 (-482.3 ; -357.3)	-397.6 (-463.2 ; -335.9)	-752.7 (-831.3 ; -676.1)
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)	Ref	-194.3 (-250.2 ; -145.6)	-271.2 (-338.7 ; -207.1)	-258.2 (-323.4 ; -195.9)	-488.6 (-599.3 ; -379.3)
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)	Ref	-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 - reference

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)	Ref	-€ 846 (-1,136 ; -579)	-€ 1,081 (-1,391 ; -804)	-€ 1,028 (-1,330 ; -757)	-€ 1,371 (-1,702 ; -1,087)
Infusion Chair Occupation	€ 980 (731 ; 1,277)	€ 376 (279 ; 494)	€ 376 (279 ; 494)	€ 376 (279 ; 494)	€ 376 (279 ; 494)
Difference (vs STANDARD)	Ref	-€ 604 (-815 ; -432)	-€ 604 (-815 ; -432)	-€ 604 (-815 ; -432)	-€ 604 (-815 ; -432)
Treatment	€ 281,311 (233,253 ; 334,684)	€ 274,657 (238,291 ; 316,743)	€ 274,657 (238,291 ; 316,743)	€ 274,657 (238,291 ; 316,743)	€ 274,657 (238,291 ; 316,743)
Difference (vs STANDARD)	Ref	-€ 6,655 (-56,627 ; 43,635)	-€ 6,655 (-56,627 ; 43,635)	-€ 6,655 (-56,627 ; 43,635)	-€ 6,655 (-56,627 ; 43,635)
Adverse Events	€ 2,259 (1,784 ; 2,759)	€ 797 (611 ; 1,006)	€ 797 (611 ; 1,006)	€ 797 (611 ; 1,006)	€ 797 (611 ; 1,006)
Difference (vs STANDARD)	Ref	-€ 1,462 (-1,838 ; -1,117)	-€ 1,462 (-1,838 ; -1,117)	-€ 1,462 (-1,838 ; -1,117)	-€ 1,462 (-1,838 ; -1,117)
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)	Ref	-€ 9,567 (-59,807 ; 40,507)	-€ 9,801 (-60,083 ; 40,287)	-€ 9,748 (-60,029 ; 40,338)	-€ 10,091 (-60,348 ; 39,999)
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)	€ 4,428 (3,147 ; 5,712)
Difference (vs STANDARD)	Ref	-€ 1,956 (-2,706 ; -1,338)	-€ 2,731 (-3,692 ; -1,935)	-€ 2,600 (-3,529 ; -1,843)	-€ 4,922 (-6,588 ; -3,552)
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)	€ 3,322 (1,599 ; 5,175)
Difference (vs STANDARD)	Ref	-€ 1,873 (-2,643 ; -1,255)	-€ 2,613 (-3,677 ; -1,771)	-€ 2,488 (-3,512 ; -1,681)	-€ 4,709 (-6,508 ; -3,250)
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)	Ref	-€ 3,829 (-5,155 ; -2,718)	-€ 5,344 (-7,106 ; -3,909)	-€ 5,088 (-6,781 ; -3,700)	-€ 9,631 (-12,632 ; -7,196)
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)
Difference (vs STANDARD)	Ref	-€ 13,396 (-63,581 ; 36,752)	-€ 15,145 (-65,223 ; 35,258)	-€ 14,836 (-64,912 ; 35,531)	-€ 19,722 (-69,791 ; 31,096)

Ref - reference

- One way sensitivity analysis.** Monthly total patient time was most affected by patient activity time in observation and administration phases of EV formulation. In the drug-change TAP, the percentage of patients using EV formulation is one of the parameters with major impact. In the other alternative TAPs the impact is mitigated and improvement actions applied have a major impact. Monthly total cost was most affected by patients' mean weight and percentage of patients in EV therapy in all TAPs.

Conclusions

- The adoption of SC formulation, combined with innovative pathway optimizations, enhances treatment efficiency with reduction of associated direct and indirect costs. The cost of drug purchase shows a non-significant decrease.
- These findings highlight the importance of tailoring administration strategies to the structural and organizational characteristics of individual oncology centres, in alignment with ongoing reforms within the Italian healthcare system.

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