

# BUDGET IMPACT MODEL OF SUBCUTANEOUS TRASTUZUMAB COMPARED WITH INTRAVENOUS TRASTUZUMAB ON THE TREATMENT OF HER-2 POSITIVE BREAST CANCER IN THE BRAZILIAN PRIVATE HEALTHCARE SYSTEM

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## INTRODUCTION

- Breast cancer is the most common cancer among women in Brazil and worldwide, second only to non-melanoma skin cancer.
- In Brazil, the National Cancer Institute (INCA) estimated 59,700 new cases in 2018. [1]
- Approximately 20% of these women have HER-2 positive status, which is associated with faster tumor growth and higher disease aggressiveness, recurrence rate, and mortality. [2, 3]
- Trastuzumab is a recombinant humanized monoclonal antibody, which selectively binds to HER-2[4] currently used in the treatment of patients with either early (eBC) or metastatic (mBC) breast cancer [5-9] and administered intravenously (IV) or subcutaneously (SC).
- The non-inferiority of the SC administration compared with the IV formulation is well demonstrated [10].

## OBJECTIVE

- To estimate the budgetary impact of trastuzumab SC compared with trastuzumab IV, in the Brazilian Private Healthcare System (PHS), to treat early and metastatic HER-2 positive breast cancer.

## METHODS

- We estimated the mean number of female beneficiaries for each size of HMO of the Brazilian PHS for 2018-2022 based on data from the National Regulatory Agency for Private Health Insurance and Plans (ANS). [11] Also, we determine the number of female beneficiaries using the distribution of the complete PHS (53% of women). We adopted four perspectives within the Brazilian PHS: 1) All the PHS; 2) A large-sized health maintenance organization (HMO); 3) a medium-sized HMO; and 4) a small-sized HMO.
- According to INCA, the incidence of breast cancer in Brazil is 56.33 cases per 100,000 women, [1] and 20% of these are HER-2 positive. [2] 96% of the patients are diagnosed with eBC and 4% with mBC. [12]
- We considered that patients with eBC received trastuzumab combined with chemotherapy (docetaxel or paclitaxel) on the first day of a 21-day cycle for 4 cycles. We assumed that 50% of patients received docetaxel and 50% paclitaxel. Following adjuvant treatment, trastuzumab is given as monotherapy until a maximum of 12 months. [13]
- For mBC in the first line therapy, we considered that patients received trastuzumab in combination with docetaxel or paclitaxel for 6 cycles and then they started receiving trastuzumab as monotherapy until the disease progression. In the second line therapy, patients received trastuzumab monotherapy in cycles of 21 days for 11 months.
- In all regimens, doses of trastuzumab IV were 8 mg/kg in the first cycle and 6 mg/kg in subsequent cycles. Trastuzumab SC doses were of 600 mg, as recommended in the package insert. [13] For docetaxel and paclitaxel, doses were 100 mg/m<sup>2</sup> and 175 mg/m<sup>2</sup>, respectively. The mean body surface area (1.67 m<sup>2</sup>) and weight (63.8 kg) of adult women in Brazil were used to calculate the doses. [14]
- For the estimation of the BIA in each one of the perspectives, we adopted a time horizon of 5 years, with progressive incorporation of trastuzumab SC with a market share projection ranging from 20% (first year) to 100% (fifth year).
- We considered only direct medical resources and costs related to treatment. The costs of the materials were extracted from the Brasindice Table, and the costs of the drugs were obtained from the Medication Market Regulation Chamber (CMED) list published in 2017, ex-factory price with 18% VAT.
- A survey was performed with 28 HMOs from all over Brazil to map fees, pricing sources and reference tables used for reimbursement of drugs, materials, and procedures.
- We conducted a univariate deterministic sensitivity analysis to evaluate the influence of the uncertainty and variability of the parameters used in the model in the results.

## RESULTS

### Patient Estimate

- Table 1 presents the results of patients with eBC and mBC eligible for first and second line treatment.

Table 1. Number of eligible patients in each HMO and in the Private Healthcare System from 2018-2022

	PHS	Large HMO	Medium HMO	Small HMO
Patients with eBC	28,027	253	26	5
Patients with mBC 1L	3,376	30	4	1
Patients with mBC 2L	186	2	0	0
Total	31,589	284	30	6

HMO, health maintenance organization; PHS, private healthcare system; eBC, early breast cancer; mBC, metastatic breast cancer; 1L: first line therapy; 2L: second line therapy

### Resource Savings

- The total costs, including the cost of the drug, supporting medication, materials, and medical fees, used to calculate the BIM of IV and SC regimens, are described in Table 2.
- The budget impact analysis (BIA) shows a potential resource saving in the Brazilian PHS. Over 5 years, with the progressive incorporation of trastuzumab SC for the treatment of patients with breast cancer, it is estimated a total savings of 948,2 mBRL, 14,3 mBRL, 1,5 mBRL and 251,5 kBRL for the PHS, a large HMO, a medium HMO, and a small HMO, respectively (Figure 1).
- Table 3 shows the budgetary impact on each of the indications. Replacing the IV for the SC presentation in the treatment of eBC and mBC may lead to savings of up to 915,6 mBRL and 32,6 mBRL, respectively, for the Brazilian PHS in 5 years.

Table 2. Total cost per treatment regimen

Drug Cost	Trastuzumab monotherapy		Trastuzumab + Docetaxel		Trastuzumab+ Paclitaxel	
	EV	SC	PTC	PVA	PTC	PVA
	PTC	AVP	IV	SC	IV	SC
11,57	11,57	9,837	18,46	16,73	15,40	17,14
4,46	4,46	,22	9,58	2,34	2,97	0,21
BRL	BRL	BRL	BRL	BRL	BRL	BRL
11,57	11,57	9,837	18,46	16,73	15,40	17,14
4,46	4,46	,22	9,58	2,34	2,97	0,21
BRL	BRL	BRL	BRL	BRL	BRL	BRL
3,01	3,01	72	08,51	9,65	4,09	0,17
BRL	BRL	BRL	BRL	BRL	BRL	BRL
3,01	3,01	72	08,51	9,65	4,09	0,17
BRL	BRL	BRL	BRL	BRL	BRL	BRL
2,57	2,57	2,57	2,57	2,57	2,57	2,57
BRL	BRL	BRL	BRL	BRL	BRL	BRL

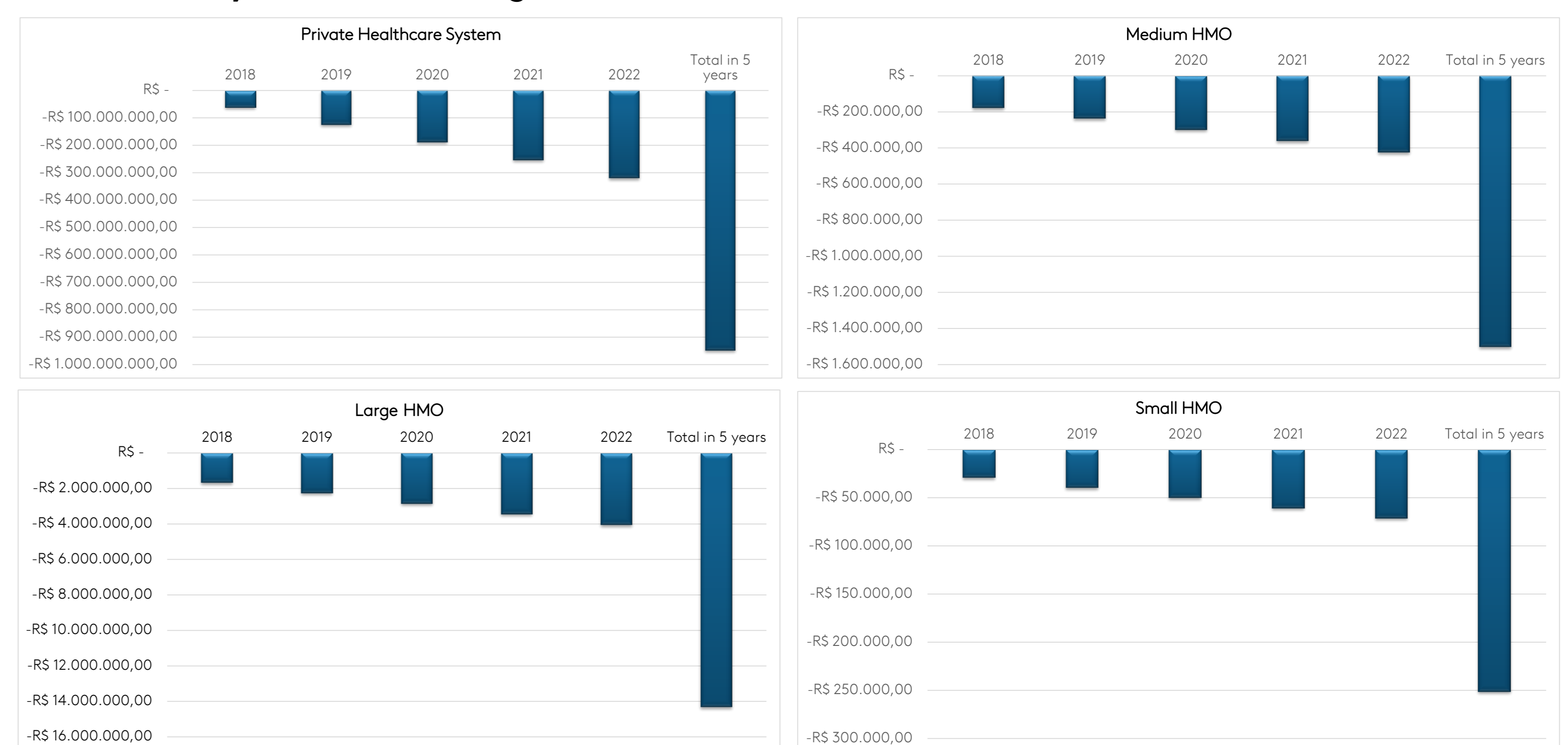
PTC, port-a-cath administration; PVA, peripheral venous access administration; IV, intravenous; SC, subcutaneous; Considering trastuzumab IV dose of 6 mg/kg and SC dose of 600 mg. Other costs: supporting medication, materials and medical fees.

Table 3. Budgetary impact of breast cancer treatment with trastuzumab SC

	Early breast cancer		Budgetary impact
	IV treatment cost	SC treatment cost	
PHS	7,263,563,099	6,347,906,365	-915,656,733
Large HMO	65,583,506	57,315,941	-8,267,564
Medium HMO	6,852,253	5,988,446	-863,806
Small HMO	1,153,032	1,007,678	-145,353
Metastatic breast cancer			
PHS	674,498,574	641,872,432	-32,626,141
Large HMO	11,701,817	5,652,175	-6,049,642
Medium HMO	1,235,607	597,007	-638,599
Small HMO	205,446	99,211	-106,234

PHS, Private healthcare system; HMO, health maintenance organization

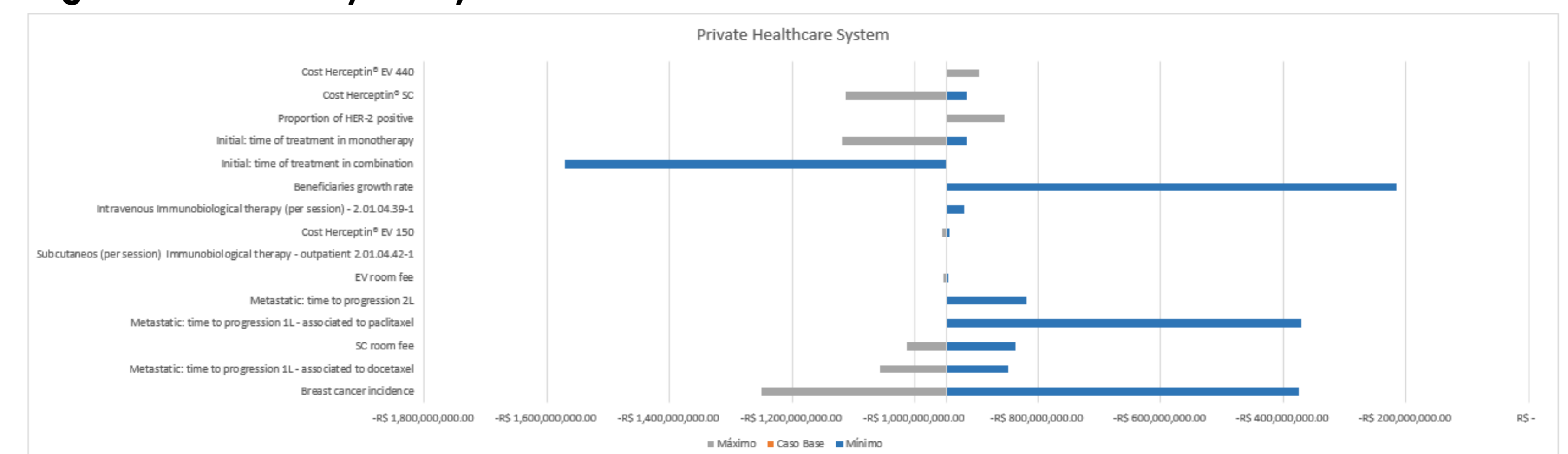
Figure 1. Budgetary impact of the progressive incorporation of trastuzumab in the private healthcare system and in large, medium and small HMOs



### Resource Savings

- In all perspectives, the incidence of breast cancer, the treatment time in monotherapy for eBC, and the hospital room fees were the parameters that influenced the most the results (Figure 2).

Figure 2. Sensitivity Analysis



## DISCUSSION

- Therapy with trastuzumab SC showed a lower cost compared with trastuzumab IV in the treatment of eBC and mBC in the Brazilian PHS in general and in all small, medium and large HMOs. Among the assessed costs, the hospital room fee and medical fees were some of the factors that contributed most to the savings.
- The results demonstrated that the incorporation of trastuzumab SC brings a saving of 12,6% in the cost of treatment of eBC and up to 51% of mBC. In total, the potential savings, for the PHS is up to 948,2 mBRL over 5 years. Given the scenario of scarce resources and the need for savings this result shows a critical strategy to be considered for reducing the cost of breast cancer treatment in Brazil.
- There are some limitations in the study, such as the uncertainty of the incidence of breast cancer in the country, mainly due to the difficulty in having epidemiological data from PHS. Also, hospital room fees and the prices of drugs and materials paid by HMOs differ greatly. The survey with the HMOs provided real industry data, but there is uncertainty associated with the accuracy of respondents and sample size. However, there are still resources savings in all scenarios, giving credibility and robustness to the presented results.
- Replacing the IV by the SC presentation of trastuzumab potentially reduces the drug preparation time, decreases the time spent by health professionals for the drug infusion, and optimizes the use of medical resources. These factors may result in reduced administration costs. [15] Also, patients tend to prefer the SC formulation because it causes less discomfort and pain, and reduces the time spent in clinics or hospitals. [6, 16]

## CONCLUSION

- Compared with the intravenous administration, subcutaneous trastuzumab can save up to 948,2 mBRL costs for breast cancer treatment in the Brazilian PHS.

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