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

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. [2-4]

Trastuzumab (eBC) is a humanized monoclonal antibody, which selectively binds to HER-2 [5] currently used in the treatment of patients with either early (eBC) or metastatic (mBC) breast cancer [5,6] and administered intravenously (IV) or subcutaneously (SC).

The non-inferiority of the SC administration compared with the IV formulation is well demonstrated [5].

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 determined 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, [6] and 20% of these are HER-2 positive. [5] 96% of the patients are diagnosed at stage 1 or 2.

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. [7-11] We assumed that 50% of patients received docetaxel at 50% paclitaxel. Following adjuvant treatment, trastuzumab is given as monotherapy until a maximum of 12 months. [5-6]

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 600 mg, as recommended in the package insert. [5] For docetaxel and paclitaxel, doses were 100 mg/m² and 175 mg/m², respectively. The mean body surface area (1.67 m²) and weight (65.8 kg) of adult women in Brazil were used to calculate the doses. [5,13]

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 medicines were extracted from the Brasílinc Table, and the costs of the drugs were obtained from the Medication Market Regulation Chamber (CMED) list of drugs and costs from the Brazilian Institute of Geography and Statistics (IBGE) in 2017. [5,13,14]

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's 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 2018-2023

<table>
<thead>
<tr>
<th>Patients with eBC</th>
<th>Patients with mBC</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHS</td>
<td>Large HMO</td>
<td>Medium HMO</td>
</tr>
<tr>
<td>6,049,642</td>
<td>18,310,736</td>
<td>12,673,154</td>
</tr>
</tbody>
</table>

Table 2. Cost per treatment regimen

<table>
<thead>
<tr>
<th>Trastuzumab monotherapy</th>
<th>Trastuzumab + Docetaxel</th>
<th>Trastuzumab + Paclitaxel</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>SC</td>
<td>SC</td>
</tr>
<tr>
<td>PEC</td>
<td>AWV</td>
<td>IV</td>
</tr>
<tr>
<td>SC</td>
<td>SC</td>
<td>SC</td>
</tr>
<tr>
<td>PEC</td>
<td>PEC</td>
<td>PVA</td>
</tr>
</tbody>
</table>

Resource Savings

The total costs, including the cost of the drug, supporting medication, materials, and medical fees, used to calculate the BM of IV and SC regimes, 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 saving of R$ 5,491,985,717, R$ 5,093,769,178, and R$ 4,622,558,279 for the PHS, a large HMO, a medium HMO, and a small HMO, respectively (Figure 1).

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

<table>
<thead>
<tr>
<th>Treatment costs</th>
<th>Budgetary impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHS</td>
<td>Large HMO</td>
</tr>
<tr>
<td>-$5,093,769,178</td>
<td>-$5,491,985,717</td>
</tr>
</tbody>
</table>

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 highest 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 R$ 42,981,206 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 is 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 healthcare 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. [14]

CONCLUSION

Compared with the intravenous administration, subcutaneous trastuzumab can save up to R$ 42,981,206 costs for breast cancer treatment in the Brazilian PHS.

REFERENCES

Kashiura D., Souza PVS, Garrido SDD, Nardi EP, Alves MRD

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