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Budget Impact Analysis of Chronic Myeloid Leukemia Treatment in Patients with Imatinib Failure from the Brazilian Public Health System Perspective: Supporting Health Care Decisions on Central and Local Levels

Análise do Impacto no Orçamento do Tratamento de Pacientes com Leucemia Mieloide Crônica que Falharam a Imatinibe pela Perspectiva do Sistema de Saúde Público Brasileiro: Auxiliando Decisões em Saúde nos Níveis Central e Local

Análisis del Impacto Presupuestario del Tratamiento de Pacientes con Leucemia Mielógena Crónica que Fallaran a Imatinibe por la Perspectiva del Sistema Público de Salud Brasileño: Apoyando Decisiones en Salud en los Niveles Central y Local

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Abstract

Introduction: In recent years, it has been increasingly recognized that a comprehensive health technology assessment should include not only a cost-effectiveness analysis, but also a budget impact analysis. **Objective:** A budget impact analysis was conducted to assess the costs of the treatment for patients with chronic myelogenous leukemia within a period of three years after imatinib failure from both central level (Brazilian public health system) and local level (public hospital) perspectives. **Methods:** A decision model based on clinical and epidemiological data was developed to compare current treatment options (dasatinib and imatinib) reimbursed by the Brazilian government with different scenarios that included nilotinib. **Results:** In our base case using official pharmaceutical prices, adding nilotinib to the mix of technologies is expected to increase total expenses within the next three years at the central level by up to R$11,360,282 or R$17,930 per patient per year, and at the local level by up to R$16,437 per patient per year. In the alternative case, based on prices from the latest public tenders, adding nilotinib to the mix of technologies is expected to increase total expenses within the next three years at the central level by up to R$31,692,792 or R$26,000 per patient per year, and at the local level by up to R$26,600 per patient per year. **Conclusion:** Results from this analysis can be used to estimate the affordability for the next three years of treatments for different chronic myelogenous leukemia phases in patients who are resistant to or intolerant of imatinib.

Key words: Leukemia, Myelogenous, Chronic, BCR-ABL Positive; Economics; Health Care Costs; Drug Therapy

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INTRODUCTION

Health care expenses are increasing around the world. As other countries, Brazil has experienced rapid increases in health care expenditures in recent years. According to the World Health Organization, total health expenditures increased from 6.7% of the Brazilian gross domestic product (GDP) in 1995 to 8.6% in 2007[1]. During this period, total health care expenditures per capita increased by 85%.

Health technology assessments are becoming the method of choice for promoting health care expenditure rationalization by systematically evaluating safety, efficacy, and cost-effectiveness of a given health technology, such as a medication[2]. In recent years, it has been increasingly recognized that any comprehensive health technology assessment should include not only a cost-effectiveness analysis, but also a budget impact analysis (BIA).

The BIA can provide estimates of the financial costs of using a given drug in the administrator's health care practice or institution. Specifically, BIAs yield predictions of how changing the combination of drugs or other treatments for a specific disease will affect either practice or institution spendings for that condition. BIAs can help administrators to evaluate the affordability of different options by predicting each technology impact in the short term.

BIAs are often used at a central level to make decisions for an entire health care system, such as reimbursement decisions for a health management organization. However, BIAs can also be valuable at the local level, although they are rarely used for this purpose, partly because they are perceived as too expensive for smaller settings[3].

An example of a decision to which a BIA could contribute to is on the choice of treatments to be offered for Chronic Myeloid Leukemia (CML), particularly in CML patients who become resistant to first-line treatment. CML is a blood cancer whose risk increases with age. Each of the three clinical phases of CML — chronic phase (CP), accelerated phase (AP), and blast phase (BP) — is more resistant to treatment than the previous phase. Imatinib mesylate (Gleevec®, Glivec®), a tyroskine kinase inhibitor (TKI), is the standard of care for CML[4] and is associated with high response rates, especially when used in CP CML. However, CML sometimes becomes resistant to imatinib[5]. Options for patients whose disease has become resistant to imatinib or who cannot tolerate this treatment include either increasing the imatinib dose or using second-generation TKIs dasatinib (Sprycel®) and nilotinib (Tasigna®). Both drugs may not only produce complete hematologic and cytogenic responses but also increase overall survival in patients with imatinib-resistant CML[5-6]. Current Brazilian government guidelines for CML management do not dictate whether to increase the imatinib dose or to use dasatinib or nilotinib after failure of first-line imatinib therapy[7].

A budget impact model was developed to evaluate the total budget costs and impact, on both central (Brazilian public health care system [SUS]) and local (public hospitals reimbursed by the government) levels, of TKIs in patients with diagnosed CML who have become imatinib resistant. The model was based on the BIA guidelines from the International Society for Pharmacoeconomics and Outcomes Research (ISPOR), with some modifications[8].

METHODS

The Brazilian government modified its guidelines for managing CML to include imatinib as the first-line treatment of choice in 2008; therefore, this study population is limited to patients who were diagnosed with CML that year and became resistant to or intolerant of first-line doses of imatinib (400 mg in CP, 600 mg in AP and BP). Patients were segmented by disease phase (CP, AP, and BP) because treatment posology and clinical outcome vary by stage.

The size of this target population fluctuates based on annual survival and prevalence growth rates. For that reason, treatment costs and the average number of patients receiving treatment with each therapy option (imatinib, dasatinib, and nilotinib) were determined by using a three-year time horizon from the central (public health system) and local (public hospital) system perspectives.

The populations receiving therapy were modeled according to different market share (per patient) scenarios. Although this approach differs from the ISPOR recommendations, it was selected as the method of choice because no patient distribution data including only patients with CML who were imatinib resistant or intolerant were available. The four different modeled scenarios were: scenario 1: escalated doses of imatinib only; scenario 2: dasatinib and escalated doses of imatinib; scenario 3: nilotinib and escalated doses of imatinib; scenario 4: dasatinib, nilotinib, and escalated doses of imatinib.

Scenario 2 (dasatinib and escalated doses of imatinib) was chosen as the baseline comparator because it reflects the currently available option for CML treatment after imatinib failure according to Brazilian government guidelines. This scenario was used as the baseline to estimate the budget impacts of Scenarios 1, 3, and 4. No discount rate was applied.

Target population

Figure 1 schematically shows how the target population was identified in Year 1 for the central perspective analysis. Data on the Brazilian incidence of leukemia were obtained from the Instituto Nacional de Câncer (the Brazilian National Cancer Institute)[9]. The proportion of cancer patients with CML was calculated using data from Quintas-Cardama *et al.*[10] and of patients with the Philadelphia (Ph) chromosome translocation (which is suitable for TKI treatment), from Hehlmann *et al.*[11] The proportion of patients in each phase was determined based on government guidelines and the proportion of patients with CML experiencing imatinib failure, on Lahaye *et al.*[12].

For the local perspective analysis, a hypothetical hospital with 50 new cases of CML per year was simulated. This hospital has the same patient segmentation and CML-resistant proportions as in the central perspective analysis.

Table 1 lists the target populations for the central and local perspective analyses.

Annual survival rates for the central and local perspectives were based on the best response to treatment and level of response from clinical studies (Table 2)[5-6, 13-17]. The annual prevalence growth rate of 12.4% was based on data from a public database (DATASUS)[18]. The average number of patients was then adjusted by using the half-cycle method.

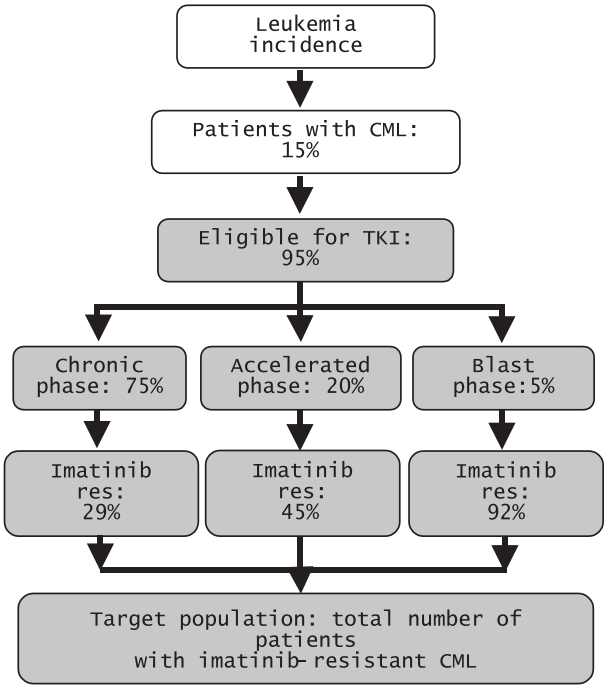


Figure 1. Strategy for identifying the target population for the central perspective analysis, year

To determine the proportion of patients on each therapy (imatinib, dasatinib, and nilotinib), the treatment options were classified into first-generation TKIs (imatinib) and second-generation TKIs (nilotinib and dasatinib). Based on expert opinion, the proportion of

Table 1. Target population

	%	Year 1		Year 2		Year 3	
		Perspective					
		Central	Local	Central	Local	Central	Local
Patients with leukemia		9,540[a]	-	-	-	-	-
Patients with CML	15%[b]	1,431	-	-	-	-	-
Patients with Ph+ CML	95%[c]	1,359	50	-	-	-	-
Chronic phase	75%[d]	1,020	38	1,146	42	1,288	47
Accelerated phase	20%[d]	272	10	306	11	343	13
Blast phase	5%[d]	68	3	76	3	86	3
Imatinib-resistant or intolerant patients		481	18	540	20	607	22
Chronic phase	29%[e]	296	11	332	12	374	14
Accelerated phase	45%[e]	122	5	138	5	155	6
Blast Phase	92%[e]	63	2	70	3	79	3
Growth in prevalence of TKI use for imatinib-resistant CML	12.4%[f]						

CML: chronic myelogenous leukemia; Ph+: Philadelphia (Ph) chromosome translocation; TKI: tyrosine kinase inhibitor.
(a) INCA report, 2008[9]; (b) Quintás-Cardama *et al.*, 2006[10]; (c) Hehlman *et al.*, 2007[11]; (d) Portaria SAS 649, 2008[7]; (e) Lahaye *et al.*, 200512;
(f) Ministério da Saúde - Sistema de Informações Hospitalares do SUS (SIH/SUS). Preliminary data updated on 11.Sep.2009[18].

patients in each category (first- versus second-generation TKIs) was calculated for all CML phases. When both second-generation TKIs were available (Scenario 4), a 50/50 split was assumed to avoid bias. Clinical short-term data show that second-generation TKIs have higher efficacy than first-generation TKIs, especially for the advanced phases of the disease. Therefore, an increase was projected in the market shares of second-generation TKIs for AP and BP CML for the second and third years of the analysis.

Sensitivity analyses

The official factory prices were used for the reference case. For the public health system perspective, a search was conducted in public sources for the actual sales prices from the latest tenders; this search revealed that these prices are substantially lower than the official factory prices. Therefore, to better evaluate actual prices set by the pharmaceutical industry, a "what-if" scenario analysis was conducted to compare the effects of the actual prices paid with those of the official prices. By using this strategy, we tried to cover most of the prices being used in real life; however, we acknowledge that there will be negotiations with different prices used in this study that are not public.

To evaluate the model's robustness, a probabilistic sensitivity analysis (PSA) was conducted using a second-order Monte Carlo simulation that took into consideration the uncertainties of the parameters. A triangular distribution was assumed for the annual prevalence growth rate and the proportion of patients in each CML phase because values were available for the worst case (minimum value), the best case (maximum

Table 2. Number of patients per treatment arm and average number of patients receiving treatment per year from the public health system (central) perspective

CML Phase, treatment, and dose	Annual mortality rate (a)	Year 1			Year 2			Year 3		
		% of patients	Average # of patients		% of patients	Average # of patients		% of patients	Average # of patients	
			Central	Local		Central	Local		Central	Local
Scenario 1										
CP Ima 600 mg	13.90%	90%	248	9	90%	278	10	90%	313	12
CP Ima 800 mg	13.90%	10%	28	1	10%	31	1	10%	35	1
AP Ima 800 mg	62.00%	100%	84	3	100%	95	3	100%	107	4
BP Ima 800 mg	85.10%	100%	36	1	100%	40	1	100%	45	2
Total			396	15		444	16		500	18
Scenario 2 (baseline)										
CP Ima 600 mg	13.90%	54%	149	5	54%	167	6	54%	188	7
CP Ima 800 mg	13.90%	6%	17	1	6%	19	1	6%	21	1
CP Dasa 100 mg	6.70%	40%	114	4	40%	128	5	40%	144	5
AP Ima 800 mg	62.00%	40%	34	1	30%	28	1	20%	21	1
AP Dasa 140 mg	26.70%	60%	64	2	70%	83	3	80%	107	4
BP Ima 800 mg	85.10%	20%	7	0	10%	4	0	5%	2	0
BP Dasa 140 mg	64.10%	80%	34	1	90%	43	2	95%	51	2
Total			418	15		473	17		535	20

Table 2. Cont.

CML Phase, treatment, and dose	Annual mortality rate (a)	Year 1			Year 2			Year 3		
		% of patients	Average # of patients		% of patients	Average # of patients		% of patients	Average # of patients	
			Central	Local		Central	Local		Central	Local
Scenario 3										
CP Ima 600 mg	13.90%	54%	149	5	54%	167	6	54%	188	7
CP Ima 800 mg	13.90%	6%	17	1	6%	19	1	6%	21	1
CP Nilo 800 mg	7.00%	40%	114	4	40%	128	5	40%	144	5
AP Ima 800 mg	62.00%	40%	34	1	30%	28	1	20%	21	1
AP Nilo 800 mg	45.70%	60%	57	2	70%	74	3	80%	95	4
BP Ima 800 mg	85.10%	100%	36	1	100%	40	1	100%	45	2
Total			405	15		457	17		515	19
Scenario 4										
CP Ima 600 mg	13.90%	54%	149	5	54%	167	6	54%	188	7
CP Ima 800 mg	13.90%	6%	17	1	6%	19	1	6%	21	1
CP Dasa 100 mg	6.70%	20%	57	2	20%	64	2	20%	72	3
CP Nilo 800 mg	7.00%	20%	57	2	20%	64	2	20%	72	3
AP Ima 800 mg	62.00%	40%	34	1	30%	28	1	20%	21	1
AP Dasa 140 mg	26.70%	30%	32	1	35%	42	2	40%	54	2
AP Nilo 800 mg	45.70%	30%	28	1	35%	37	1	40%	48	1
BP Ima 800 mg	85.10%	20%	7	0	10%	4	0	5%	2	0
BP Dasa 140 mg	64.10%	80%	34	1	90%	43	2	95%	51	2
Total			414	15		468	17		529	19

CML: chronic myelogenous leukemia; CP: chronic phase; AP: accelerated phase; BP: blast phase; ima: imatinib; dasa: dasatinib; nilo: nilotinib. Total may not be equal to the sum due to rounding.
(a) Baseado em Kantarjian HM *et al.* (2007)[5,6]; Le Coutre PD *et al.* (2008)[13]; Shah NP *et al.* (2008)[14]; Rousselot P *et al.* (2008)[15]; Talpaz M *et al.* (2002)[16]; Sawyers CL *et al.* (2002)[17].

value), and the most likely case. The proportion of patients on CP, AP and BP always sum up 100% and vary between 67-85%, 4-31% and 2-11%, respectively. The annual mortality rates were assumed to be beta distributed because they are bound between zero and one.

Resource use and costs

The model focuses on pharmaceutical costs. For the central perspective, drug prices were used as costs (because, directly or indirectly, the Brazilian health system will pay for these costs). For the local perspective, costs were calculated by subtracting the amount that the government reimburses for the drug from the drug price.

Reimbursement amounts were obtained from the official Brazilian government reimbursement list[18]. For the reference case in the sensitivity analyses, pharmaceutical costs were based on the official factory price[19]. For the alternative case (sensitivity analyses), pharmaceutical costs were based on the average published prices of government tenders from May 2009 to August 2009[20-21].

Table 3. Pharmaceutical costs

	Government reimbursement amount	Monthly costs, base case		Monthly costs, alternative case	
		Central perspective	Local perspective	Central perspective	Local perspective
Chronic phase					
Dasatinib, 100mg/day	R$ 4,067.00	R$ 9,476.42	R$ 5,409.42	R$ 4,066.74	-R$ 0.26
Imatinib, 600 mg/day		R$ 12,639.25	R$ 8,572.25	R$ 7,777.80	R$ 3,710.80
Imatinib, 800 mg/day		R$ 16,852.34	R$ 12,785.34	R$ 10,370.40	R$ 6,303.40
Nilotinib, 800 mg/day		R$ 12,543.51	R$ 8,476.51	R$ 8,852.80	R$ 4,785.80
Accelerated phase					
Dasatinib, 140mg/day	R$ 6,092.00	R$ 14,214.63	R$ 8,122.63	R$ 6,091.74	-R$ 0.26
Imatinib, 800 mg/day		R$ 16,852.34	R$ 10,760.34	R$ 10,370.40	R$ 4,278.40
Nilotinib, 800 mg/day		R$ 12,543.51	R$ 6,451.51	R$ 8,852.80	R$ 2,760.80
Blast phase					
Dasatinib, 140mg/day	R$ 6,678.50	R$ 14,214.63	R$ 7,536.13	R$ 6,091.74	-R$ 586.76
Imatinib, 800 mg/day		R$ 16,852.34	R$ 10,173.84	R$ 10,370.40	R$ 3,691.90

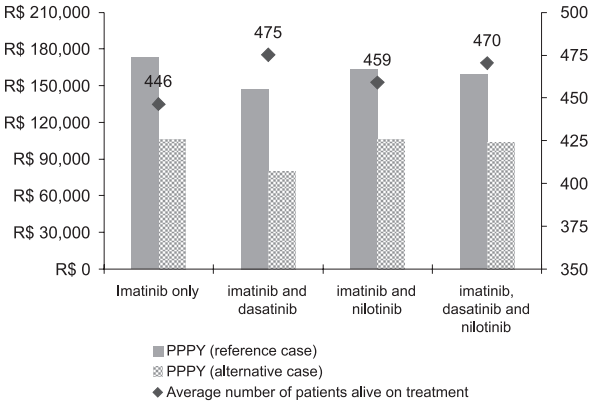
RESULTS

Total pharmaceutical costs per scenario disaggregated by treatment option, as well as average per-patient-per-year costs, are listed in table 4.

In all circumstances, Scenario 1 has the highest cost per patient under treatment. In addition, fewer patients under treatment in Scenario 1 are alive at the end of each year than in any other scenario. Scenario 2 has the opposite outcomes, with the lowest average cost and the highest number of patients under treatment who are still alive. Average costs, as well as total number of patients under treatment per year from the central perspective, are provided in Figure 2.

Figure 3 provides the estimated budget impact for Scenarios 1, 3, and 4, and Scenario 2 serves as the baseline for both reference and alternative cases. Because the baseline has the lowest total expenses, all comparators positively impact the budget, meaning that more financial capital must be allocated to make these options affordable.

Figure 4 shows the acceptability curve generated from the probabilistic sensitivity analyses. Assuming that baseline scenario 2 represents the current reality, the acceptability curve shows the probability that a given value of financial resources will be enough to cover the expenses of a different scenario. A hypothetical case has been considered in which an extra R$ 3 million is available to the health care system to cover the extra expenses from incorporating nilotinib into the CML treatment guidelines. According to the probabilistic sensitivity analysis, the probability that this extra budget is enough to cover the patient distribution from Scenario 4 is 75%.



Abbreviations: PPPY, per patient per year.

Figure 2. Overall average costs and number of patients under treatment per year by scenario, central perspectiv

Table 4. Total pharmaceutical costs per scenario and average per-patient-per-year costs, by treatment option and perspective

	Reference case				Alternative scenario			
	Year 1	Year 2	Year 3	Total	Year 1	Year 2	Year 3	Total
Central perspective								
Scenario 1	$68,379,601	$76,856,399	$86,384,038	$231,620,037	$42,078,665	$47,295,021	$53,158,032	$142,531,717
Imatinib	$68,379,601	$76,856,399	$86,384,038	$231,620,037	$42,078,665	$47,295,021	$53,158,032	$142,531,717
PPPY	$172,942	$172,942	$172,942	$172,942	$106,423	$106,423	$106,423	$106,423
Scenario 2	$64,678,025	$72,809,892	$81,964,748	$219,452,665	$34,193,495	$37,963,170	$42,229,226	$114,385,892
Imatinib	$34,620,924	$36,139,896	$37,968,560	$108,729,380	$21,304,633	$22,239,362	$23,364,665	$66,908,659
Dasatinib	$30,057,101	$36,669,996	$43,996,188	$110,723,286	$12,888,862	$15,723,809	$18,864,562	$47,477,232
PPPY	$154,778	$134,798	$153,317	$147,631	$81,827	$80,286	$78,991	$80,368
Scenario 3	$66,571,816	$74,498,843	$83,368,186	$224,438,844	$43,321,982	$48,638,468	$54,607,327	$146,567,777
Imatinib	$40,511,947	$43,588,875	$46,806,099	$130,906,921	$24,929,784	$26,823,229	$28,803,008	$80,556,021
Nilotinib	$26,059,868	$30,909,968	$36,562,087	$93,531,923	$18,392,198	$21,815,239	$25,804,319	$66,011,756
PPPY	$164,182	$163,065	$161,953	$163,067	$106,842	$106,461	$106,082	$106,462
Scenario 4	$65,619,962	$73,648,098	$82,659,029	$221,927,090	$38,205,350	$42,602,345	$47,589,601	$128,397,296
Imatinib	$34,620,924	$36,139,896	$37,968,560	$108,729,380	$21,304,633	$22,239,362	$23,364,665	$66,908,659
Dasatinib	$17,969,105	$22,053,218	$26,409,426	$66,431,749	$7,704,618	$9,455,364	$11,322,776	$28,482,759
Nilotinib	$13,029,934	$15,454,984	$18,281,044	$46,765,962	$9,196,099	$10,907,619	$12,902,160	$33,005,878
PPPY	$160,680	$159,120	$157,702	$159,167	$104,563	$103,886	$103,297	$103,915
Local perspective								
Scenario 1	$1,676,939	$1,884,824	$2,118,479	$5,680,243	$709,602	$797,569	$896,441	$2,403,612
Imatinib	$1,676,939	$1,884,824	$2,118,479	$5,680,243	$709,602	$797,569	$896,441	$2,403,612
PPPY	$115,315	$115,315	$115,315	$115,315	$48,796	$48,796	$48,796	$48,796
Scenario 2	$1,481,967	$1,661,041	$1,863,012	$5,006,019	$360,759	$379,393	$401,556	$1,141,707
Imatinib	$859,476	$901,963	$952,105	$2,713,543	$369,708	$390,707	$414,979	$1,175,395
Dasatinib	$622,491	$759,077	$910,907	$2,292,476	-$8,949	-$11,315	-$13,424	-$33,687
PPPY	$96,424	$83,612	$94,748	$91,595	$23,473	$21,815	$20,422	$21,903
Scenario 3	$1,586,651	$1,768,298	$1,970,599	$5,325,548	$731,532	$817,165	$912,786	$2,461,483
Imatinib	$990,280	$1,067,360	$1,148,333	$3,205,974	$417,174	$450,727	$486,187	$1,354,089
Nilotinib	$596,371	$700,938	$822,265	$2,119,574	$314,357	$366,438	$426,599	$1,107,394
PPPY	$106,392	$105,235	$104,083	$105,237	$49,053	$48,631	$48,212	$48,632
Scenario 4	$1,526,246	$1,704,474	$1,904,709	$5,135,428	$517,948	$562,624	$614,870	$1,695,441
Imatinib	$859,476	$901,963	$952,105	$2,713,543	$369,708	$390,707	$414,979	$1,175,395
Dasatinib	$368,585	$452,042	$541,471	$1,362,098	-$8,939	-$11,302	-$13,409	-$33,650
Nilotinib	$298,186	$350,469	$411,133	$1,059,787	$157,179	$183,219	$213,300	$553,697
PPPY	$104,123	$102,689	$101,351	$102,721	$48,006	$47,455	$46,946	$47,469

PPPY: per patient per year.

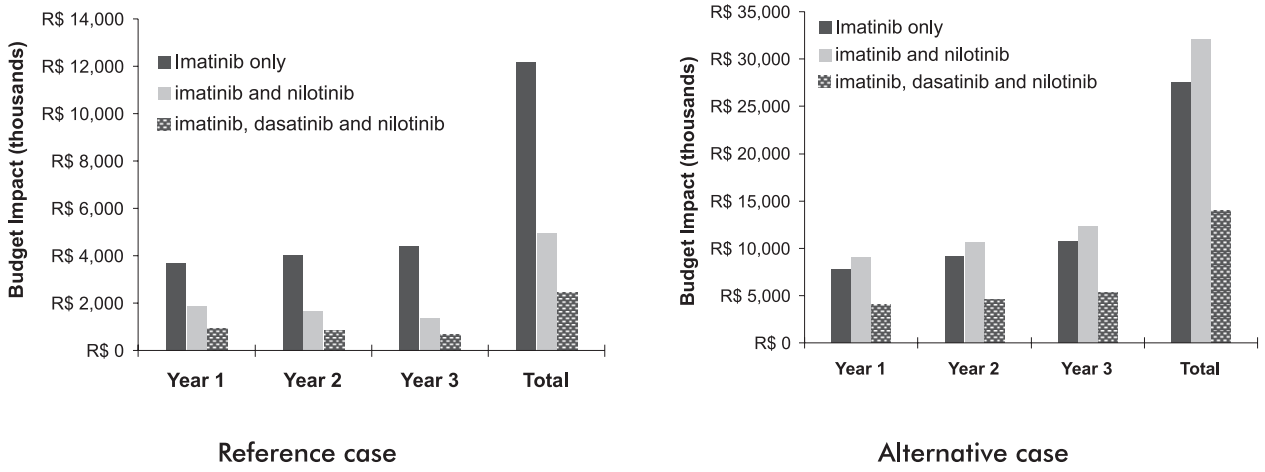
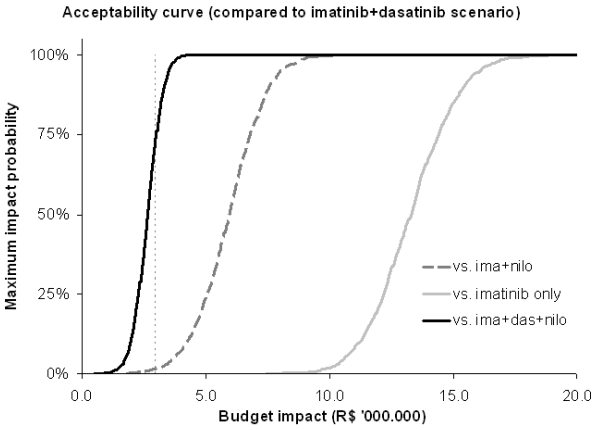


Figure 3. Estimated budget impact, central perspective



Abbreviations: ima, imatinib; das, dasatinib; nilo, nilotinib

Figure 4. Acceptability curve (compared to imatinib + dasatinib scenario)

DISCUSSION

Even though more patients are alive under treatment in Scenario 2 than in the other ones, this scenario has the lowest total expenses because the lower average cost per patient under treatment offsets the extra costs for treating more patients. This is valid for both reference and alternative case.

To our knowledge, this is the first article in the scientific literature describing a BIA targeting the costs of CML treatment after first-line imatinib failure. Danese *et al.*[22] studied the budget impact of adding erlotinib in combination with gemcitabine for the treatment of pancreatic cancer from a private payer perspective using country-specific epidemiological, demographic, and costing data. Within one year, the inclusion of erlotinib would result in an incremental cost of US$120,000. In a different study, Sorensen and Andersen[23] estimated the budget impact of adding tumor necrosis factors inhibitors (anti-TNFα) to the treatment of rheumatoid arthritis from a public payer perspective. Their data sources included clinical literature, country-specific national health surveys, registry data, and fee schedules. Within five years, the inclusion of anti-TNFα would result in incremental costs ranging from €17 to €188 million, depending on the scenario. Both studies provided insightful information for decision makers.

The construction of acceptability curves by PSA is widely used to quantify and graphically represent uncertainty in cost-effectiveness studies[24]. In a recent review of the literature, however, Orlewska *et al.*[25] found that only 5 out of 46 budget impact studies performed probabilistic sensitivity analysis. This method was adopted for the current study to provide further insight into the likelihood that an additional budget will be enough to afford any scenario considered in this analysis. Figure 4 can also be analyzed the other way around to determine, within a specific level of certainty, how many extra financial resources must be available to afford a given scenario. This is valuable information for decision makers during budget negotiations.

Nilotinib's incorporation into the Brazilian public health system will increase expenses at both central and local levels. To ensure that Scenario 4 is affordable, the health care system would need R$ 4.25 million more than it would spend for Scenario 2. Adopting Scenario 3 would require an even greater additional budget of R$ 10.35 million.

Government reimbursement for CML treatment is supposed to cover not only pharmaceutical expenses, but also the specialist outpatient visit. Given the pharmaceutical industry's current pricing strategies (alternative scenario), dasatinib is the only option for

which costs do not exceed the government reimbursement amount. Using dasatinib therefore allows hospitals to cover at least part of the costs with specialist outpatient visits that patients may incur, especially in AP CML.

Not every new technology will generate extra financial expenses during the first years. Scenarios that included nilotinib in the current study resulted in increased expenses when compared to the baseline scenario (imatinib and dasatinib). However, Scenario 1, which included only imatinib, also resulted in increased expenses. These results show that when dasatinib is incorporated into the public health system, it reduces financial expenses.

When considering adapting a budget impact model from a central level (the most common perspective used in the literature) to a local level, it is important to remember that some of the input values remain unchanged whereas others must be changed. Specifically, the target population should be based on hospital records and it is reasonable to assume that the distributions of CML disease phases are the same, either at local or central levels (unless strong evidence shows the contrary). Furthermore, efficacy data from large multinational clinical trials are the main source of effectiveness information on health technology assessments. If data on a pool of patients from different countries are considered a reliable source of information for national analyses, it is acceptable to use the same mortality rates for both central and local level analyses.

Finally, costs depend on the perspective and can have a substantial impact on the results. In this analysis, from a central perspective, the annual cost for treating a patient who has BP CML with dasatinib 140 mg is R$ 6,091.74 in the alternative case. In contrast, from a local perspective, the same treatment in the same scenario leads to a saving of R$ 586.50.

The present study has limitations. Due to the fact that no data were available to estimate the mortality rate associated with the use of imatinib 600mg/day to treat CP CML, an assumption was made that the mortality rate was the same as that of imatinib 800mg/day. The analysis was limited to diagnosed cases of CML after imatinib failure because imatinib was only established in Brazil as first-line of treatment for CML in 2008. Furthermore, nilotinib was treated in this analysis as if the Brazilian government reimburses for this drug, even though current Brazilian government guidelines for CML management do not include nilotinib. We determined the proportions of patients in each phase of the disease (Chronic, Accelerated and Blast) based on the information in the current Brazilian government guidelines for CML management. It may differ from actual practice in the hospitals. Finally, only pharmaceutical costs and not total costs were taken into account since they were considered to be the most significant component of total costs in CML CP patients, which represents the majority of the target population of the study. Regarding the fact that not all prices are public, our study might not be covering all price ranges used in real life, but since we have used values published in public tenders we believe it is representative of the public healthcare system. Moreover, one should be aware that all retrospective and database based studies may be impacted by bias due to incorrect data entry. This study was done from 2009 to early 2010, before the publication of the new government prices for imatinib, later on 2010.

CONCLUSIONS

According to the model developed, the options (escalate imatinib or dasatinib) currently covered by the Brazilian government health plan for the management of CML in patients who become resistant to or intolerant of imatinib minimize budget expenses for the next three years. The addition of nilotinib, a new second-generation TKI, to the mix of technologies available for CML management will increase total expenses for the public health system by up to R$ 32,080,122 per patient in the next three years. At the hospital level, this increase could reach R$ 26,008 per patient.

Budget impact models are important tools to estimate the impact of the introduction of a new technology or treatment option on total expenses. The results of this analysis can be used to address issues of the affordability in the next three years of different treatments for different phases of CML in patients who are resistant to or intolerant of imatinib.

Conflict of interest: The following authors work at Bristol-Myers Squibb Farmacêutica S/A: Elio Asano, Marcelo Nita, Wilson Braga, Elaine Rahal and Bonnie Donato; and Arthur Moellmann-Coelho received grants to participate as a clinical researcher.

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Resumo

Introdução: Tem crescido nos últimos anos o reconhecimento de que uma avaliação de tecnologias em saúde completa deve incluir não apenas uma análise de custo-efetividade, como também uma análise de impacto no orçamento. **Objetivo:** Conduziu-se uma análise de impacto no orçamento para avaliar os custos num período de três anos do tratamento de pacientes diagnosticados com leucemia mieloide crônica, após falha ao imatinibe a partir das perspectivas em nível central (Sistema Público de Saúde Brasileiro) e local (Hospital público). **Métodos:** Desenvolveu-se um modelo de decisão baseado em dados clínicos e epidemiológicos para comparar as opções de tratamento atuais (dasatinibe e imatinibe) reembolsadas pelo governo brasileiro com diferentes cenários que incluem nilotinibe. **Resultados:** No caso-base, utilizando os preços fábrica oficiais, estima-se que a adição de nilotinibe ao mix tecnológico aumente os gastos totais nos próximos três anos no nível central em até R$ 11.360.282 ou R$ 17.930 por paciente por ano, e no nível central por até R$ 16.437 por paciente por ano. No caso alternativo, baseado nos preços das últimas licitações públicas, espera-se que a adição de nilotinibe ao mix tecnológico aumente os gastos totais nos próximos três anos em até R$ 31.692.792 ou R$ 26.000 por paciente por ano, e no nível local por até R$ 26.600 por paciente por ano. **Conclusão:** Os resultados dessa análise podem ser utilizados para avaliação da viabilidade financeira nos próximos três anos de tratamentos para diferentes fases de leucemia mieloide crônica em pacientes que são resistentes e/ou intolerantes a imatinibe.

Palavras-chave: Leucemia Mielogênica Crônica BCR-ABL Positiva; Economia; Custos de Cuidados de Saúde; Quimioterapia

Resumen

Introducción: Ha aumentado el reconocimiento en los últimos años que una evaluación de tecnologías en salud completa debe incluir no solamente un análisis de coste-efectividad, como también un análisis de impacto presupuestario. **Objetivo:** Se hizo un análisis de impacto presupuestario para evaluar los costos por un período de tres años del tratamiento de pacientes diagnosticados con leucemia mieloide crónica en estos años posterior a falla a imatinibe desde las perspectivas a nivel central (Sistema Público de Salud Brasileño) y local (hospital público). **Método:** Fue desarrollado un modelo de decisión embasado en datos clínicos y epidemiológicos comparando las opciones de tratamiento actualmente (dasatinibe e imatinibe) reembolsadas por el gobierno Brasileño a diferentes escenarios que incluyen nilotinib. **Resultados:** En nuestro caso base utilizando los precios farmacéuticos oficiales, se valoró que la adición de nilotinib al mix de tecnologías aumente los gastos totales en los siguientes tres años al nivel central hasta R$11.360.282 o R$17.930 por paciente al año, y al nivel local hasta R$16.437 por paciente al año. En el caso alternativo, embasado en los precios de las últimas licitaciones públicas, se estima que la adición de nilotinib al mix de tecnologías aumente los gastos en los siguientes tres años desde el nivel central hasta R$31.692.792 o R$26.000 por paciente al año, y al nivel local hasta R$26.637 por paciente al año. **Conclusión:** Los resultados de este análisis pueden ser utilizados para evaluar la viabilidad financiero-económica en los tres años siguientes del tratamiento de pacientes en diferentes fases de leucemia mieloide crónica que están resistentes y/o intolerantes a imatinib.

Palabras clave: Leucemia Mielogenosa Crónica BCR-ABL Positiva; Economía; Costos de la Atención en Salud; Quimioterapia