

Financial Burden of Progression of Chronic Myeloid Leukemia (CML) Patients Who Failed Two or More Tyrosine Kinase Inhibitors Treatment in the Brazilian Private Market Perspective

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Kim H¹, Silva V², de Oliveira D³, Kashiura D⁴

¹Novartis Biociências SA, São Paulo, SP, Brazil, ²Novartis Biociências SA, São Paulo, Brazil, ³Novartis Biocências SA, São Paulo, SP, Brazil, ⁴Novartis Brazil, Sao Paulo, SP, Brazil

INTRODUCTION

- Chronic myeloid leukemia (CML) is a hematological neoplasm that, if properly treated in initial stages (chronic phase; CP), progression to advanced phases can be significantly delayed or avoided.¹
- Treatment with tyrosine kinase inhibitors (TKI) have changed the disease course over time. Although treatment with 1st and 2nd generation TKIs as first- (1L) and second-line (2L) treatments are established and reimbursed in Brazil, in later lines, the availability of effective TKIs is limited and eligibility to hematopoietic stem cell transplantation (HSCT) is rare.^{2,3}
- New options are emerging for patients who progressed after two prior TKIs; hence, understanding the current cost of treatment is key to drive appropriate decision making in the Brazilian Private Healthcare System.
- The objective of this study is to analyze the financial burden of CML-CP treatment for patients who failed two or more prior TKIs from the Brazilian Private Healthcare System perspective.

METHODS

- This study estimated the financial burden of 3L and 4L of CML from the Brazilian Private Healthcare System perspective, including drug, monitoring and HSCT costs.
- Target population was obtained through an epidemiological approach considering adult patients diagnosed with CML-CP, who were previously treated with at least 2 TKIs. From the Brazilian population covered by private insurance, a prevalence of 5 per 100,000 inhabitants⁴ was considered of which 90% of patients were in the CP⁵. It was assumed that 30% of patients would progress from 1L to 2L and 50% to 3L.
- Treatment switch from 3L to 4L was estimated as the percentage of failure (75%) to 2nd generation TKI, as reported by Akard et al. (2013)⁶.
- Patients who failed 3L treatment and were ineligible to receive HSCT were assumed to be treated with ponatinib in 4L, the only TKI currently approved in Brazil after two prior TKIs at the time of this study.
- Resource usage in 3L and treatment duration was based on Atallah et al. (2022)⁷. Drug costs were extracted from *Câmara de Regulação do Mercado de Medicamentos* (CMED) list price (ex-factory price with 18% tax). Monitoring costs were extracted from *Classificação Brasileira Hierarquizada de Procedimentos Médicos* (CBHPM). The USD presented costs considered the exchange rate of 1 USD = 5.07 BRL.
- Cost of HSCT was extracted by published literature for the Brazilian perspective⁸ and adjusted by inflation (768,800 BRL [151,637 USD]).

RESULTS

- A total of 375 patients in CML-CP who previously received two TKIs were estimated from the Brazilian Private Healthcare System in 2023.
- In 3L, only 6.08% of patients were eligible for HSCT (26,908,000 BRL [5,307,298 USD]). Among the patients treated with TKIs, 93.3% received nilotinib or dasatinib (87,891,511 BRL [17,335,604 USD]) and 6.7% received ponatinib (12,244,928 BRL [2,415,173 USD]).
- In 4L, 6.80% were eligible for HSCT, with total cost of 22,487,400 BRL (4,435,385 USD), and all the remaining patients were assumed to receive ponatinib, with total cost of 114,551,663 BRL (22,594,016 USD).
- Follow-up and monitoring costs were 8,895 BRL (1,754 USD) and 6,129 BRL (1,209 USD) for 3L and 4L, respectively.
- The total cost of 3L and 4L was 127,143,335 BRL (22,077,581 USD) and 137,045,192 BRL (27,030,610 USD), respectively.

CONCLUSION

- CML patients in later lines of therapy demonstrate relevant disease management-related expenditures. Among the TKIs, ponatinib use in 4L demonstrated the highest treatment cost. Although HSCT is associated with elevated costs, its eligibility is limited to a small patient population.
- Significant costs regarding failure of second line treatment highlight the medical unmet need for new effective technologies in CML treatment landscape, especially in later lines.
- It is important to highlight that this model only analyzed the treatment costs and did not assess the cost-effectiveness of the interventions.

Table 1. Cost inputs

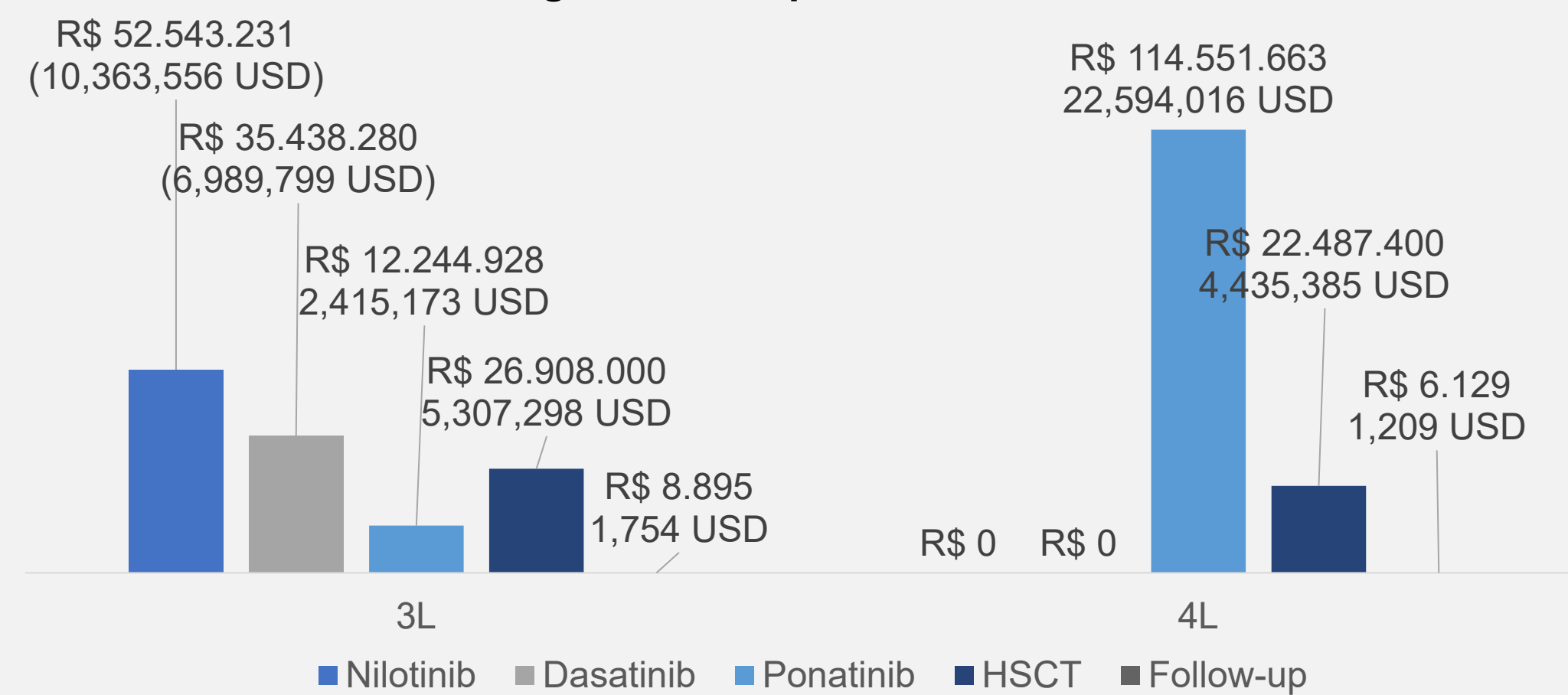
Parameter	Cost*
Drugs	
Monthly cost, BRL (USD)	
Nilotinib	16,190 (3,193)
Dasatinib	16,005 (3,157)
Ponatinib	31,075 (6,130)
HSCT	
Procedure cost, BRL (USD)**	
HSCT + follow-up + complications	768,800 (151,637)
Follow-up costs	
Trimonthly cost, BRL (USD)	
Chronic phase	1,710 (337)
Accelerated phase	10,954 (2,161)
Blastic crisis	33,448 (6,597)

HSCT: hematopoietic stem-cell transplantation.

*1 USD = 5.07 BRL

**Extracted from Vargas et al. (2021)⁸ and adjusted by inflation.

Figure 1. Cost per treatment line



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