PCN 175

BUDGET IMPACT ANALYSIS OF THE INCORPORATION OF MIDOSTAURIN FOR FLT3-POSITIVE ACUTE MYELOID LEUKEMIA (AML) IN THE BRAZILIAN PRIVATE HEALTHCARE SYSTEM (BPHS).

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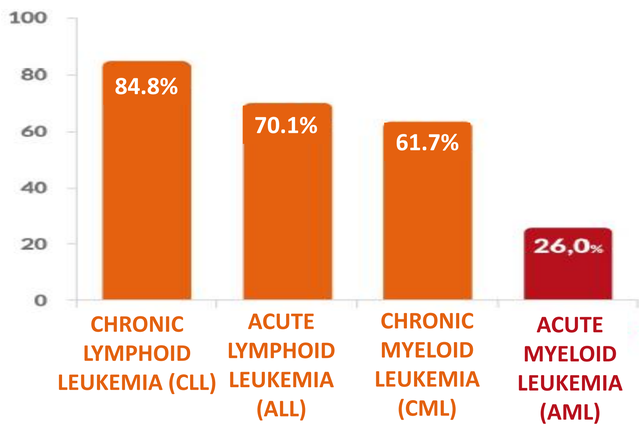
INTRODUCTION Acute myeloid leukemia (AML) is characterized by a clone transformation of hematopoietic cell progenitors through the capture and increase of chromosomal rearrangements or different genetic mutations[1].



In AML patients, the bone marrow and peripheral blood present leukocytosis and predominance of mature cells (blasts), which can be associated with functional insufficiency of bone marrow and consequent bleedings, anemia and infections[1].

AML shows the lowest five-year survival rate among other types of leukemia[2] (Figure 1).

Figure 1. 5-survival rate at age of diagnosis by leukemia[2]

AML is classified according to cytogenetic and molecular changes. Compared to them, the FLT3 (FMS-like tyrosine kinase 3) gene mutation represents one third of the patients affected by the disease[3,4] and present very unfavorable prognosis, with high rate of relapse and lower rate of survival among other types of AML[5].

The current AML treatment aims to achieve remission and prevent disease recurrence. According to national guidelines[1], the actual foreseen treatment is separated in phases as described in Figure 2.

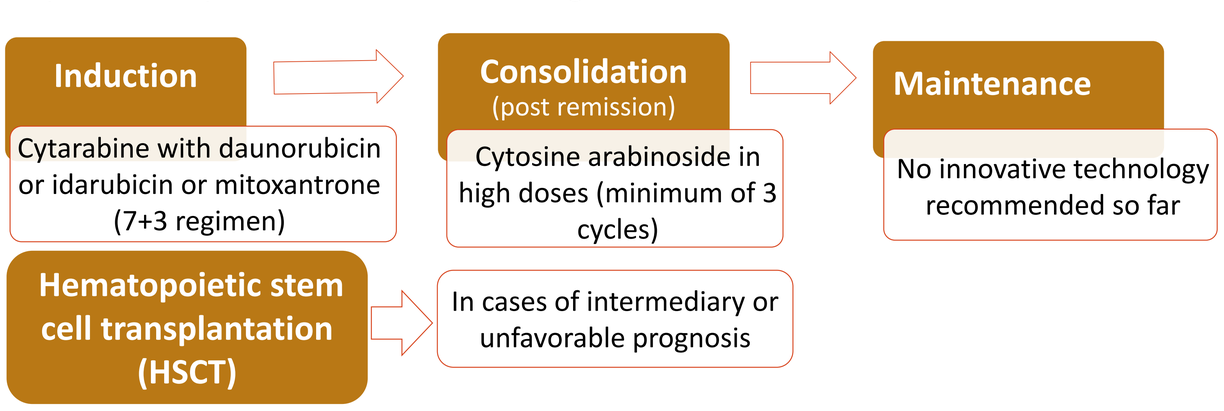


Figure 2. Phases of AML treatment[1].

Midostaurin was the first FLT3 inhibitor approved and available in Brazil for the treatment of AML patients with FLT3 mutation that could be combined with standard chemotherapy during induction and consolidation phases. Besides that, the treatment can be followed by a maintenance phase with midostaurin in monotherapy[6].

OBJECTIVE The objective of this study was to estimate the budget impact of the incorporation of midostaurin for patients newly diagnosed with FLT3-positive AML who are fit to receive stem cell therapy under the Brazilian private healthcare system (BPHS).

METHODS A budget impact model was developed to analyze the incremental cost of midostaurin incorporation in the BPHS.

Eligible population was based on the number of patients calculated from 2019, defined according to the patient flow demonstrated in the Figure 3.

For the next five years, the calculation was performed applying a population growth rate of 0.67% each year.

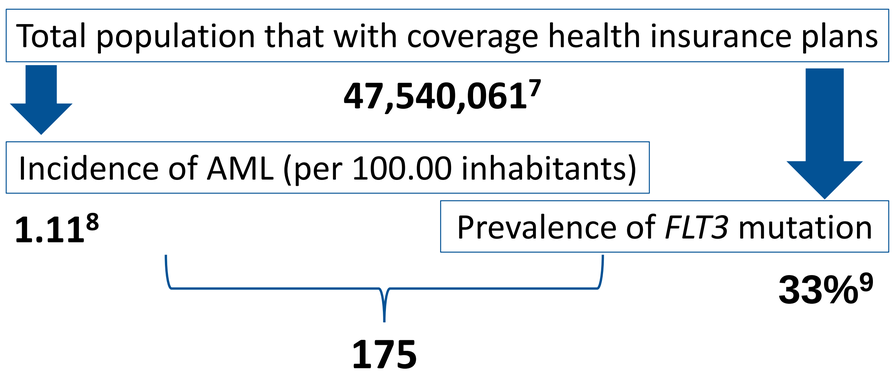


Figure 3. Eligible population to treatment in 2019.

In the scenario with midostaurin incorporation, the drug was administrated during the 3 phases of treatment (Figure 2), according to the proportion of patients in the RATIFY study[10]. Considering the scenario with no midostaurin incorporation, only the standard chemotherapy was included during the induction and consolidation. The market participation of midostaurin was estimated as 5% in the first year and 30% at the end of the fifth year.

Treatment duration was based on the RATIFY study data[10], and for this reason, the proportion of treated patients per cycle represented directly the number of treated patients in the study. This premise was adopted due to treatment free period in some patient cases.

The model considered the cost of treatment related to the first and second line treatment, according national guidelines[1]. The calculations were based on the official published prices (CMED list/March 2019), considering the factory prices, including 18% of VAT[11] and label dosage[12] of each drug (Table 1 and Table 2). The cycle consisted in 28 days.

Table 1. First line treatment costs*.

	Treatment	Group	Regimen	Vial or tablet costs (USD)	Total cost per cycle
1L	Induction	Midostaurin	Cytarabine	17.85	9,080.34
			Daunorubicin	23.90	
			Midostaurin	153.85	
		Standard Therapy	Cytarabine	17.85	417,219
			Daunorubicin	23.90	
	Consolidation	Midostaurin	Cytarabine in high dose	17.85	9,759.89
			Midostaurin	153.85	
		Standard Therapy	Cytarabine in high dose	17,85	1,156.77
	Maintenance	Midostaurin	Midostaurin	153.85	17,206.24

Table 2. Second line treatment costs*.

	Regimen	Vial or tablet costs (USD)
2L	Fludarabin	210.46
	Cytarabine	17.85
	Idarubicin	318.57
	Filgrastim	120.57
	Total cost per cycle	4,161.42

RESULTS Midostaurin incorporation demonstrated an incremental cost of approximately USD 501 thousand in the first year and USD 4 million in the fifth year. In 5 years, the treatment of patients with AML FLT3 positive showed a total accumulated incremental cost of USD 11 million (Figure 4) after midostaurin inclusion.

Figure 4. Incremental costs with midostaurin incorporation in the BPHS.

CONCLUSION Incorporation of midostaurin to BPHS leads to predictable budget impact due to a small target patient population, medical cost-offsets justified by fewer patients requiring 2nd induction, and reduction the proportion of patients in relapse, accompanied by a positive survival outcomes from RATIFY study.

*1 USD = 3.97 BRL

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