Cost-effectiveness of Tyrosine-kinase Inhibitors for the treatment newly diagnosed Chronic Myeloid Leukemia: Is Imatinib old news?

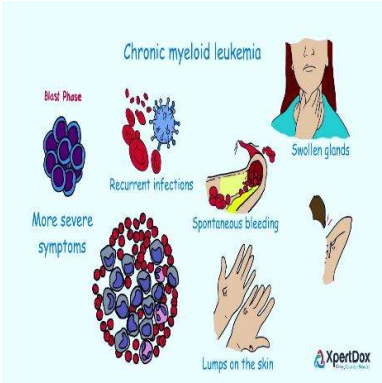
Health Technology Assessment in India (HTAIn)

Policy Brief

Executive Summary:

Chronic Myeloid Leukaemia (CML) is the commonest adult leukaemia in India and the annual incidence ranges from 0.8-2.2/100,000 population and 0.6-1.6/100,000 population in females in India (1). The introduction of tyrosine-kinase inhibitors (TKIs) such as Imatinib, has drastically changed the treatment and natural history of the disease with an improvement in the 5-year survival rate from approximately 20% to over 90% (1,2). Also, second-generation TKIs such as Dasatinib and Nilotinib have also demonstrated efficacy for treating incident CML patients in chronic phase (CP).

In this analysis, we aimed to determine the most cost-effective treatment option for newly diagnosed CML-CP patients in India. Using a Markov model, the clinical effectiveness and costs of Imatinib, Nilotinib and Dasatinib were estimated. Incremental cost per QALY gained with a given treatment option was compared against the next best alternative, and assessed for cost-effectiveness.



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We found that imatinib is a non-dominated treatment option with an average cost of ₹ 64,323 per QALY lived which is cost-effective in the Indian scenario.. Moreover, Dasatinib patients incurred an incremental cost of ₹ 237,583 per QALY gained as compared to Imatinib treatment.

Policy Recommendations:

- As per the current reimbursement rates, Imatinib is the most cost-effective treatment option for CML-CP patients.
- Dasatinib offers better health outcomes than imatinib and a 21% reduction in the reimbursement rate is required to make it a cost-effective treatment option for India.
- The use of Nilotinib is currently not value for money in the Indian context.
- There is a need to produce significant clinical literature with respect to Nilotinib and Dasatinib in the Indian context.

Background and Gap in Literature:

National Cancer Grid (NCG) guidelines recommend the use of first-generation Tyrosine-kinase Inhibitor (TKIs): Imatinib as the first-line therapy for newly diagnosed CML-CP patients. In the past decade, second-generation TKIs such as Dasatinib and Nilotinib have demonstrated efficacy for treating incident CML-CP cases and were therefore granted approval for the first-line treatment globally (3,4). The second-generation TKIs produce more rapid molecular responses than imatinib at standard doses of 400 mg daily, but five-year OS does not differ between the three TKIs (3,4).

Most incident CML-CP patients require life-long, daily TKI-based care. This causes an immense financial burden on the cancer patients and their families. The launch of generic imatinib in the market, reimbursement of imatinib in the health benefit package (HBP) and introduction of Glivec International Patient Assistance Program (GIPAP) have provided some relief to the patients in terms of better health outcomes at lower costs. Dasatinib is also a part HBP under India's publicly financed national health insurance scheme – Ayushman Bharat Pradhan Mantri Jan Aarogya Yojana (ABPM-JAY) (5). Therefore, the health system spending on incident CML-CP after generic versions of TKIs (Imatinib and Dasatinib) becomes available is the subject of great interest among patients, physicians, and payers.

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Aims and Objective

This policy brief addressed the policy question of the most cost-effective treatment option for newly diagnosed CML-CP patients from the point of view of reimbursement rates set under AB PM-JAY scheme. It summarizes the results of a Economic evaluation study on various CML treatment regimens, conducted by the HTA Resource Hub, PGIMER, Chandigarh.

Treatment arms:

1. Imatinib 400mg once daily;
2. Nilotinib 300mg twice daily;
3. Dasatinib 100mg once daily.

Methods and Approach

We undertook this cost-effectiveness analysis (CEA) using a societal perspective, which accounted for both health system and patients' costs. We compared the costs and consequences associated with Imatinib, Nilotinib and Dasatinib from the societal perspective. Our methodological principles are consistent with the Indian reference case for conducting economic evaluations used by the agency for Health Technology Assessment in India (HTAIn).

The analysis was performed under the following components:

1. **Markov model** was developed in Microsoft Excel to estimate the lifetime costs and consequences (in terms of Quality Adjusted Life-years (QALYs)* and Life-years). The model consisted of three mutually exclusive health states: Progression-free survival (PFS), Progressive disease (PD) and death. A monthly cycle length and lifetime horizon was considered (Figure 1).
2. Reimbursement rates (for Imatinib and dasatinib) and market prices (for Nilotinib) were used to estimate the treatment cost in each health state (5).
3. In order to obtain the Out-of-Pocket Expenditure (OOPE) incurred on out-patient consultations, the primary data for 602 CML patients was analysed as the part of **CADCQoL database** (6).
4. Transition probabilities and effectiveness parameters were obtained from the published Indian literature and pivotal clinical trials for each of the drugs – DASISION and ENESTnd trials (3,4,7).
5. The Quality of Life (QoL) scores were also estimated for all the health states from the primary data from **CADCQoL database** (7).

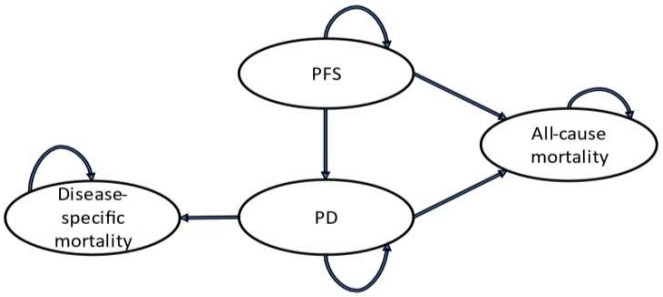
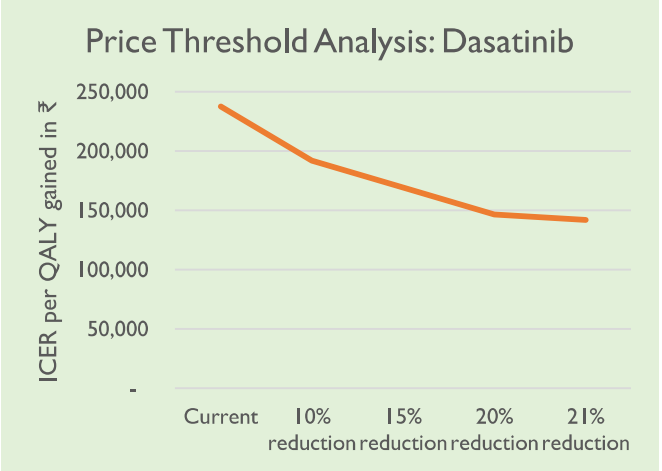


Figure 1: Schematic diagram for the Markov state transition model. PFS: Progression-Free State; PD: Progressive Disease

***Quality Adjusted Life-years:**

- QALY is a generic measure of health and is used to compare the health gains across different diseases and hence provide a uniform platform to compare effectiveness across all the different areas of healthcare.
- EQ-5D is the most utilised tool worldwide to measure QoL.

Treatment strategy (in ₹)	Cost (in ₹)	QALYs	Incremental cost per QALY gained (in ₹)
Imatinib	746,939	11.61	-
Dasatinib	1,147,877	13.30	237,583
Nilotinib	3,590,493	13.68	6,499,642



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Price Threshold Analysis

- At the current WTP threshold of one-time per capita GDP (₹ 141,225) of India, Dasatinib has a 27.7% probability of being cost-effective as compared to Imatinib in the Indian context.
- Dasatinib offers slightly better health outcomes than imatinib.
- A 21% reduction in the reimbursement rate of dasatinib will make it a cost-effective treatment option.

Results:

- Imatinib is the is the most cost-effective treatment option and incurs an average cost of ₹ 64,323 per QALY lived in the Indian context.
- Dasatinib offers better health outcomes at an incremental cost of ₹ 237,583 per QALY gained as compared to imatinib which is not cost-effective at the current WTP threshold of 1-time per capita GDP.
- Nilotinib is also not cost-effective and incurs an incremental cost of ₹ 6.5 million per QALY gained as compared to Dasatinib.

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