'Value' of new drug therapies for the treatment of Chronic Lymphocytic Leukemia (CLL)

Health Technology Assessment in India (HTAIn)
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Policy Brief

Executive Summary:

Chronic Lymphocytic Luekemia (CLL) though less common in India than the west, has high morbidity burden. The cost- effectiveness of treatment therapies with the following three drug regimes, i.e., chlorambucil plus prednisolone (CP), bendamustine plus rituximab (BR), and ibrutinib for the treatment of CLL in India is assessed here.

Ibrutinib is proven to be more effective than BR which has shown better effectiveness than CP. However, CP is cheapest while Ibrutinib is the costliest amongst these three regimes in India. Being a chronic disease, a patient of CLL requires around 2 lines of therapies in a lifetime. Here we evaluate which combination therapy of the above drugs provides best value for the treatment of CLL in Indian context. The incremental costs of a treatment line and its potential health gains are compared conducting a Health Technology Assessment (HTA). Literature review, primary data collection, and economics evaluation via Markov model was done for the HTA.

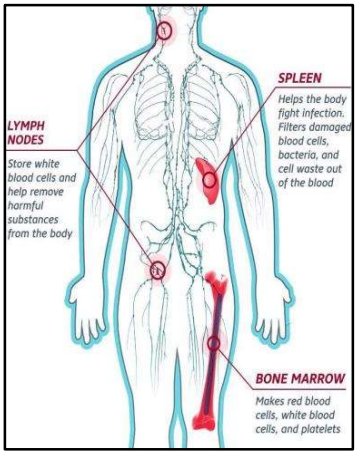


Image Source: https://www.gazyva.com/first-line-cll/about-cll/what-it-is.html

Treatment of CLL through BR as 1st line therapy and Ibrutinib as 2nd line therapy costs INR 3,44,852 to gain 1QALY when compared to treatment arm of 1st line CP and 2nd line BR.

Recommendations

- Treatment of CLL with 1st line CPand 2nd line BR is the most cost-effective option at current prices of drugs in India.
- We recommend reimbursement of this cost-effective strategy for all public funded insurance schemes.
- However, if the prices of both BR and ibrutinib are reduced by 80%, treatment with strategy of BR as 1st line and ibrutinib as 2nd line therapy becomes cost-effective for India.
- Hence, we recommend reducing the prices accordingly to consider it for reimbursement schemes.

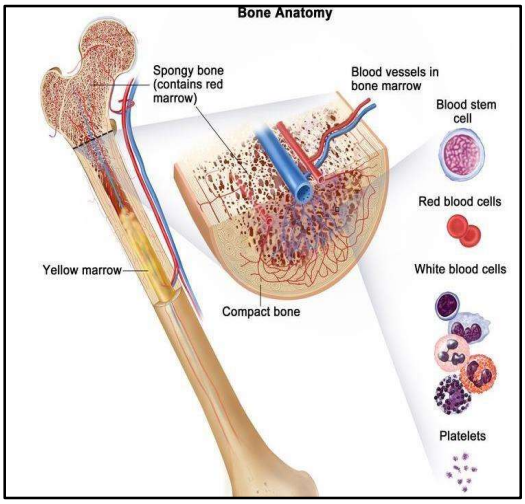
Context:

Chronic lymphocytic leukaemia (CLL) in India accounts for around 7673 new cases and approximately 6195 deaths annually. The CLL patients are generally diagnosed at younger age with poor performance status and have high morbidity burden. While patients in stage 0, I and II are mostly kept on observation and treatment is initiated when there is progression, those in stage III and IV are immediately put on radical treatment.

Chlorambucil, a drug no longer in practice in developed nations, is still commonly prescribed in India mainly for financial reasons. Newer drugs like Bendamustine and ibrutinib have shown greater effectiveness than chlorambucil based therapies.

Though these newer drug regimens lead to improved survival, they are also associated with higher cost as well as high incidence of side effects.

Regarding anti-CLL drugs, no economic evaluations are reported from India or even the South-East Asia Region (SEAR). All the existing literature on cost-effectiveness of these drugs has been reported from the context of developed countries. However, none of the economic evaluation has directly compared the three drugs in question, i.e., chlorambucil, bendamustine and ibrutinib.



https://www.cancer.gov/types/leukemia/patient/cll-treatment-pdq

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Aims and Objectives:

This policy brief addresses the policy question of whether different combination therapies of newer drugs, Bendamustine plus Rituximab (BR) and ibrutinib are cost- effective options for treatment of CLL in India. It summarizes the results of a HTA study on BR and Ibrutinib conducted by HTA Resource Hub PGIMER.

Treatment arms compared in the study:

Arm A: 1st Line Chlorambucil +Prednisolone (CP) followed by 2nd line Bendamustine +Rituximab (BR) Arm B: 1st line CP followed by 2nd line Ibrutinib Arm C: 1st line BR followed by 2nd line Ibrutinib Arm D: 1st line Ibrutinib followed by 2nd line BR
Scenario Analysis: Done to compare single line therapies of CP, BR, and Ibrutinib

Methods and Approach:

- HTA was done using Markov modelling technique (Fig. 1) to estimate the lifetime costs and health consequences for patients of chronic lymphocytic leukemia. Treatment done with different combination therapies (arm B, C, D) was compared with the treatment with 1st line CP and 2nd line BR (arm A).
- The health outcomes were evaluated in terms of life years (LY) and quality adjusted life years (QALY) lived. The cost effectiveness was assessed in terms of incremental cost effectiveness ratio (ICER) between the intervention and control arm.
- Literature review was done, and clinical effectiveness data was taken from studies by Hillmen et al and Woyach et al for-1st line drugs and Ghia et al and Xiaojun et al for-2nd line drugs. Trial data was extrapolated using standard methods and extrapolated data was used for analysis.
- Data was collected on OOPE and quality of life values (CADCQoL database) while the health system costs were derived from the previously undertaken costing studies from India.

Dosages:

- Chlorambucil and prednisolone was taken as 10 mg/m^{2}and of 60 mg/m^{2}respectively for five days in a 28-day cycle, for 6 cycles.
- Bendamustine was estimated as 90 mg/m^2 on day 1 and 2, along with rituximab (375 mg/m^{2}on day 1) in a 28-day cycle, for 6 cycles.
- Ibrutinib was administered at a dose of 420 mg daily.

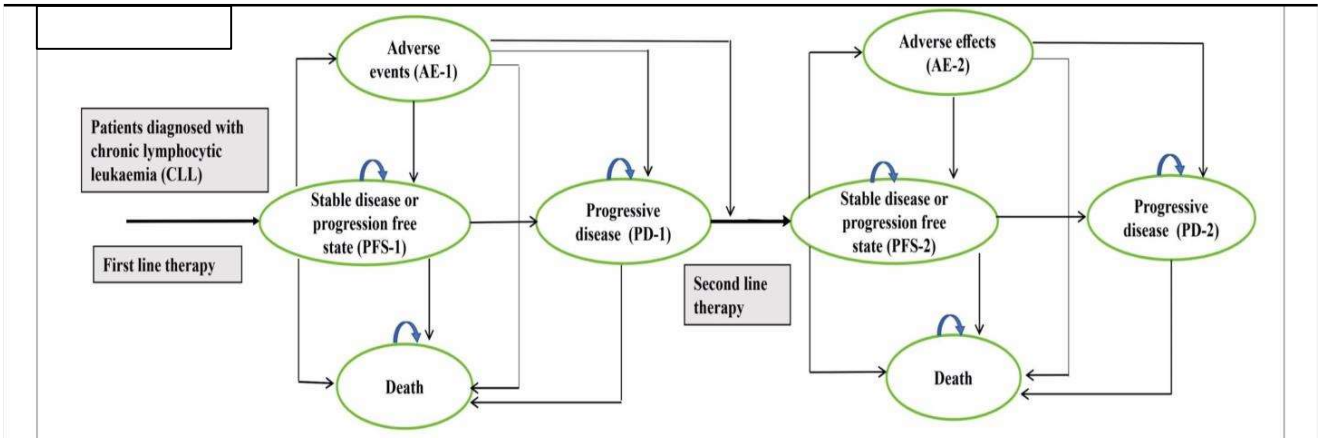

Fig. 1 : Markov Model

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Results and Discussion:

- Life Years and QALYs gained by a patient following treatment for CLL varied from 5·63 (Arm A) to 12·57 (Arm D) and 3·8 (Arm A) to 9·71 (Arm D), respectively, among the treatment arms. Similarly, lifetime costs ranged from INR 3,22,910 (Arm A) to INR 36,25,031 (Arm D) incurred on the treatment of CLL.
- This resulted in incremental cost effectiveness ratio of: INR 1,043,083 per QALY gained for Arm B; INR 3,44,852 per QALY gained for Arm C; INR 5,68,502 per QALY gained for Arm D, when compared to arm A.
- The analysis suggests that treatment of CLL with 1st line CP and 2nd line BR (Arm A) is the most cost-effective option at current prices of drugs in India.
- However, if the prices of both BR and ibrutinib are reduced by 80%, treatment with strategy of BR as 1st line and ibrutinib as 2nd line therapy (Arm C) becomes cost-effective. The threshold analysis (Fig.2) showed that the results could vary highly on varying the costs of BR and Ibrutinib.

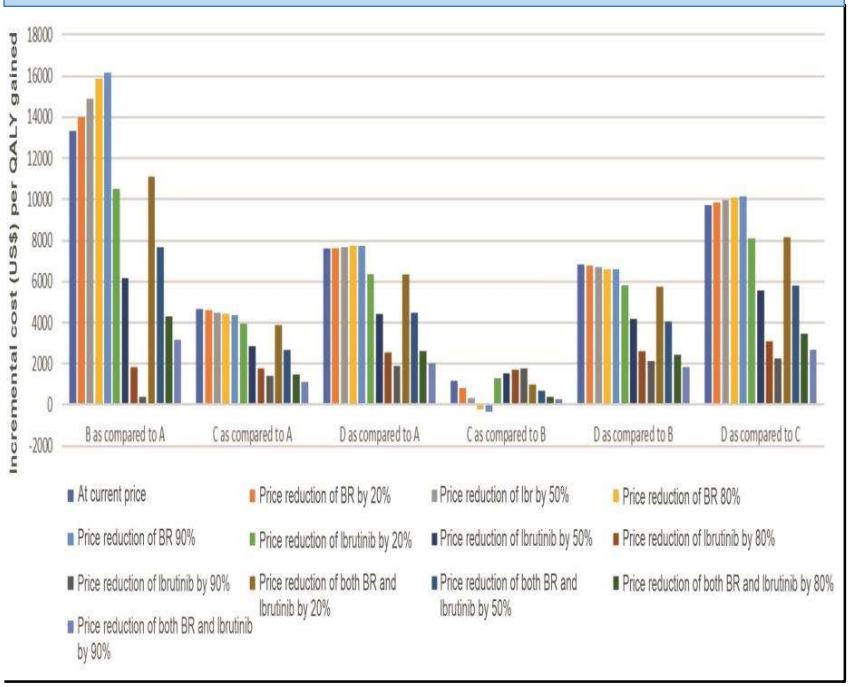

Fig. 2 Threshold Analysis

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