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Clinical and Humanistic Burden in Patients with Chronic Myeloid Leukemia in Early Lines of Treatment: A Literature Review

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CONCLUSIONS

- As a chronic disease, CML requires long-term therapy, underscoring need for effective and tolerable treatments.
- However, despite the availability of TKIs as early lines of treatment, CP-CML carries significant clinical burden and reduces QoL, notably more in female and young patients due to escalating symptoms, treatment intolerance and resistance.
- Effective and safe treatments are crucial for early CP-CML patients to reduce treatment switching, treatment-resistance, AEs and increase TFR eligibility.
- Wide variations observed in some of the clinical burden parameters can be attributed to differences in sample size, follow-up duration, and patient demographics
- No studies were identified addressing caregiver burden. To fill this evidence gap, further research is warranted.

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INTRODUCTION

- Chronic myeloid leukemia (CML) is a rare blood cancer characterized by the abnormal proliferation of myeloid cells in the bone marrow, leading to high levels of immature white blood cells in the blood.
- Despite the availability of tyrosine kinase inhibitors (TKIs) for the treatment of chronic phase-CML (CP-CML), there is still an unmet need for novel treatments due to resistance, intolerability, and side effects of the TKIs.
- Therefore, we conducted a literature review to understand the clinical and humanistic burden in CML patients receiving early lines of treatment.

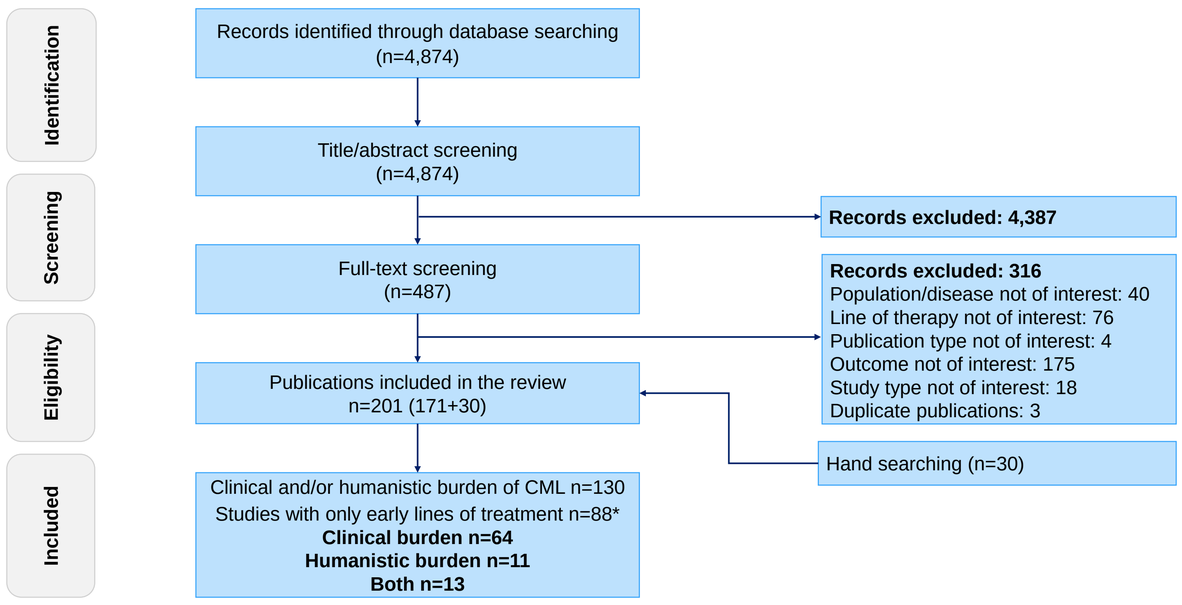
METHODS

- MEDLINE® and Embase® databases were searched for English language publications up to June 16, 2023. Additionally, hand-searching of conference proceedings and a snowball search were performed.
- Studies were selected using pre-defined inclusion/exclusion criteria, focusing on clinical and humanistic burden data for adult CML patients who were newly diagnosed or undergoing 1L treatment, as well as those previously treated or undergoing 2L treatment.
- Observational/real-world evidence studies published in English were included.
- A single reviewer screened titles and abstracts of citations and excluded those not meeting the eligibility criteria.
- Full texts of the remaining citations were retrieved and screened. Studies meeting the inclusion criteria were included and data was extracted.
- Studies evaluating early lines of treatment in CML (1L and/or 2L) were included in this poster.

RESULTS

- Out of 4,874 records retrieved, 130 unique studies were included. Of these, 88 reported data for early lines of treatment in CML: 64 clinical, 11 humanistic, and 13 both (**figure 1**).
- Of the 88 studies (45 journal articles, 43 conference abstracts), most were conducted in the USA (n=28), followed by Italy (n=12) and Japan (n=9).
- Mean age ranged from 48.3 to 77.5 years, with 74% of the studies predominantly male.

Figure 1. Study selection flowchart

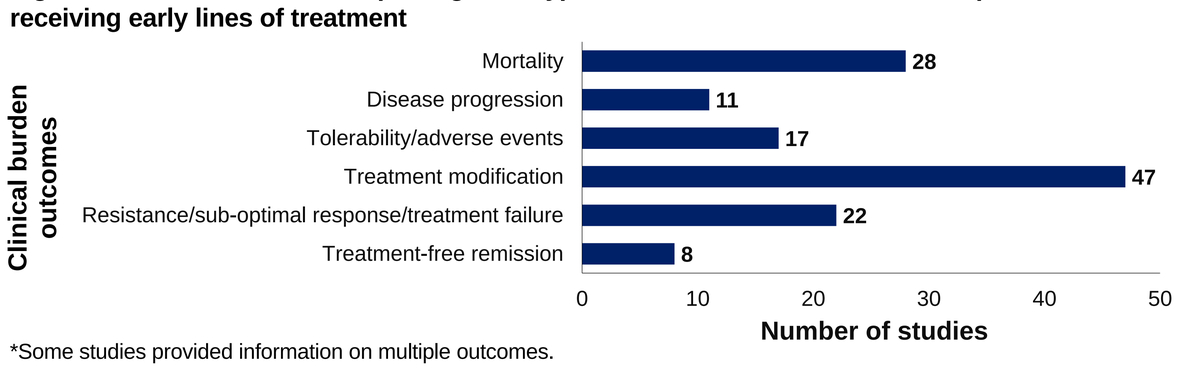


*This literature review included studies irrespective of therapy lines. Data only for early lines of treatment is included in this poster

Clinical burden (n=77*)

- Clinical burden was assessed in 77 studies (**figure 2**).

Figure 2. Number of studies reporting each type of clinical burden data for CML patients receiving early lines of treatment

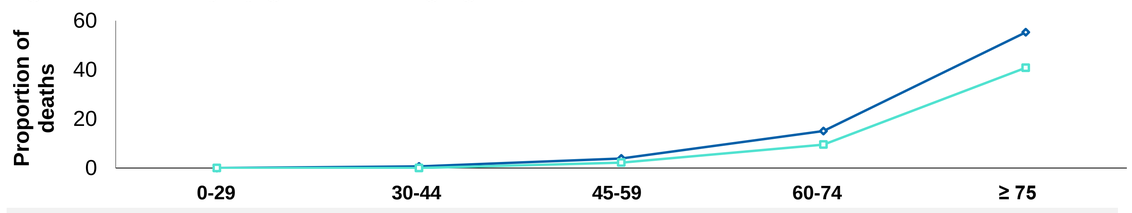


*Some studies provided information on multiple outcomes.

Mortality (n=28)

- Mortality varied widely, from 0.5% to 80%. Nineteen studies reported mortality below 50% for patients on early lines of treatment.
- CML-related deaths ranged from 1.1% to 13.8% across the included studies during early lines of treatment.
- A higher proportion of mortality was observed in male patients compared to female patients during 1L therapy in Canada (15.7% vs 10.7%) and Italy (8.74% vs 7.43%) (1, 2).
- A retrospective analysis of 2,315 CP-CML patients showed that mortality increased with age among those treated with 1L second-generation TKIs (**figure 3**) (2).

Figure 3. Mortality by gender and age groups



	0-29	30-44	45-59	60-74	≥ 75
Male	0.0	0.6	3.9	15.1	55.3
Female	0.0	0.0	2.2	9.5	40.8

Age groups (years)

Progression (n=11)

- The progression rate from chronic-phase to later disease stages varied widely (2%-77%) with early lines of treatment.

Tolerability/ adverse events (n=17)

- Most studies (n=8) reported over 50% of patients experiencing adverse events (AEs) on early lines of treatment.
- Nausea/vomiting (22.4%-77.6%), myalgia (4.9%-9.8%), and skin-rash (1.2%-6.0%) were the commonly reported AEs among CML patients undergoing early lines of treatment.

Treatment modification (n=47)

- Treatment discontinuation ranged from 0% to 54%.
- AEs, intolerance, and treatment resistance led to treatment discontinuation and switching in up to 83% and 100% of patients, respectively.

Resistance, sub-optimal response, or treatment failure (n=22)

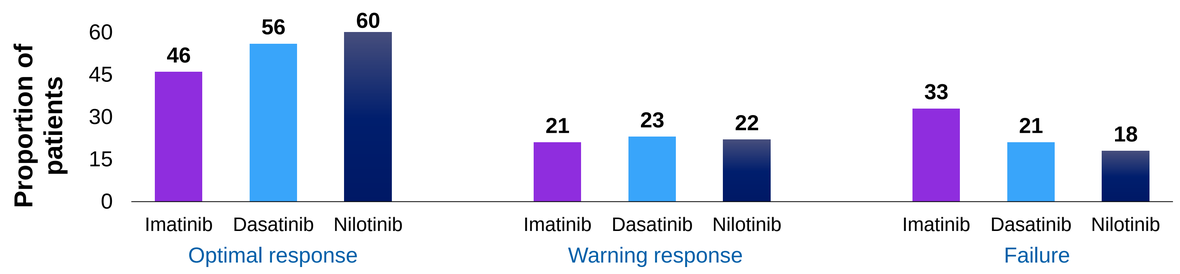
- A French study of 253 CP-CML patients found that 7.9% lost their complete cytogenetic response (CCyR) and 20.9% lost their major molecular response (MMR) after a median of 2.6 and 5.0 years from the start of 1L TKI therapy, respectively and developed resistance to the treatment (3).
- Another study from the USA and Europe reported that 1L dasatinib and nilotinib had more optimal response (BCR-ABL1 ≤0.1%) than imatinib at 12 months. However, imatinib experienced more failure response (BCR-ABL1 >1% and/or Ph+ >0%), while warning response (BCR-ABL1 >0.1-1%) was equivalent across TKI cohorts (**figure 4**) (4).

Treatment free remission (TFR) (n=8)

- At 12 and 24 months, TFR was maintained in 60% to 80% and 57% to 68% of patients, respectively after discontinuing TKI treatment (5, 6).
- A French population-based study of 507 CML patients diagnosed between 2006 and 2016 received TKI as 1L treatment. After a median follow-up of 5.1 years from TKI initiation, 26 of 507 patients were in TFR following 1L treatment (7).

The definition of TFR eligibility was not reported in the included studies.

Figure 4. Proportion of 1L CML patients with optimal, warning and failure responses at 12 months according to 2013 ELN guidelines



The definitions of optimal, warning, and failure responses for CML patients remain the same in the 2020 ELN guidelines (optimal response: BCR-ABL1 ≤ 0.1% in PCR test, warning response: BCR-ABL1 > 0.1% to 1% in PCR test, failure response: BCR-ABL1 > 1% in PCR test).

Humanistic burden (n=24)

- A wide variety of instruments were employed in the studies to elicit quality of life (QoL) data for patients with CML.
- Oncology-specific instruments were used in 7 studies, generic measures in 16 studies, and the CML-specific instruments MDASI-CML and EORTC QLQ-CML24 were used in one study each.
- The EORTC QLQ-C30 and SF-36 were the most frequently administered instruments.
- Fatigue, dyspnea, appetite loss, anxiety, depression, and gastrointestinal symptoms were the most common and burdensome symptoms.
- A study of 422 Italian CML patients reported that women and younger patients on 1L therapy had worse HRQoL on the SF-36 measure compared to their peers in the general population, while patients aged 60 or older showed almost identical HRQoL scores (8).
- The TIGER Phase 3 trial found that HRQoL in CML patients was comparable to the German general population on the EORTC QLQ-30 measure.
- Notable negative impacts were observed in women and younger patients, particularly in role (unable to perform usual activities), social (unable to engage in social activities and maintain relationships), and emotional functioning (adverse impacts on emotional well-being: anxiety, depression, irritability, and overall mood), as well as symptoms like appetite loss, fatigue, and dyspnea at diagnosis (9, 10).
- Poor QoL was correlated with intolerance due to AEs and lower treatment adherence.
- None of the studies evaluated caregiver burden.

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Disclosures

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