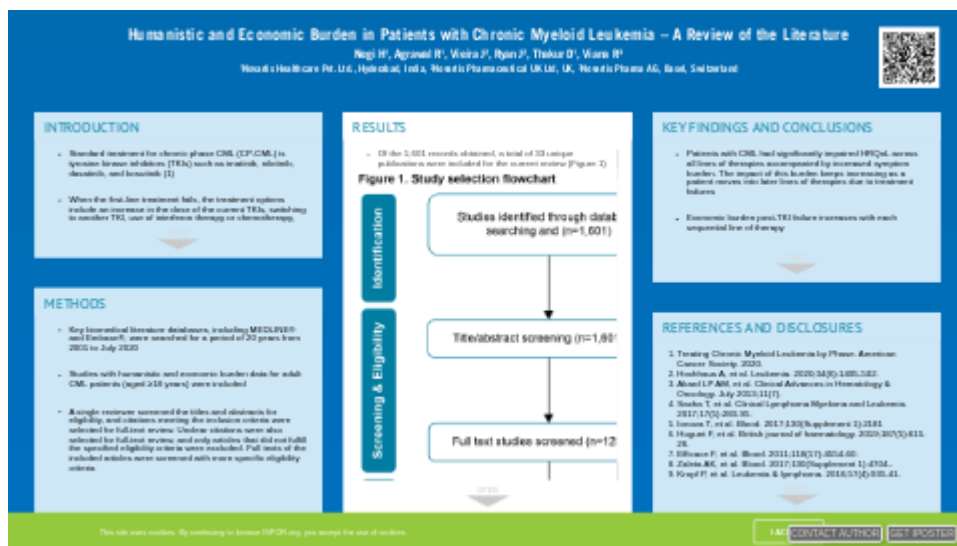


Humanistic and Economic Burden in Patients with Chronic Myeloid Leukemia – A Review of the Literature



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PRESENTED AT:



INTRODUCTION

- Standard treatment for chronic phase CML (CP-CML) is tyrosine kinase inhibitors (TKIs) such as imatinib, nilotinib, dasatinib, and bosutinib (1)
- When the first-line treatment fails, the treatment options include an increase in the dose of the current TKIs, switching to another TKI, use of interferon therapy or chemotherapy, and stem cell transplantation (1, 2)
- The rates of treatment failure increase from 50% in patients receiving second-line treatments to 75%-80% in patients receiving third-line treatments (3)
- As there is still an unmet need for novel treatments for heavily pre-treated CP-CML patients therefore we conducted the targeted literature review to understand the published evidence on humanistic and economic burden in patients with CML, receiving different lines of TKIs

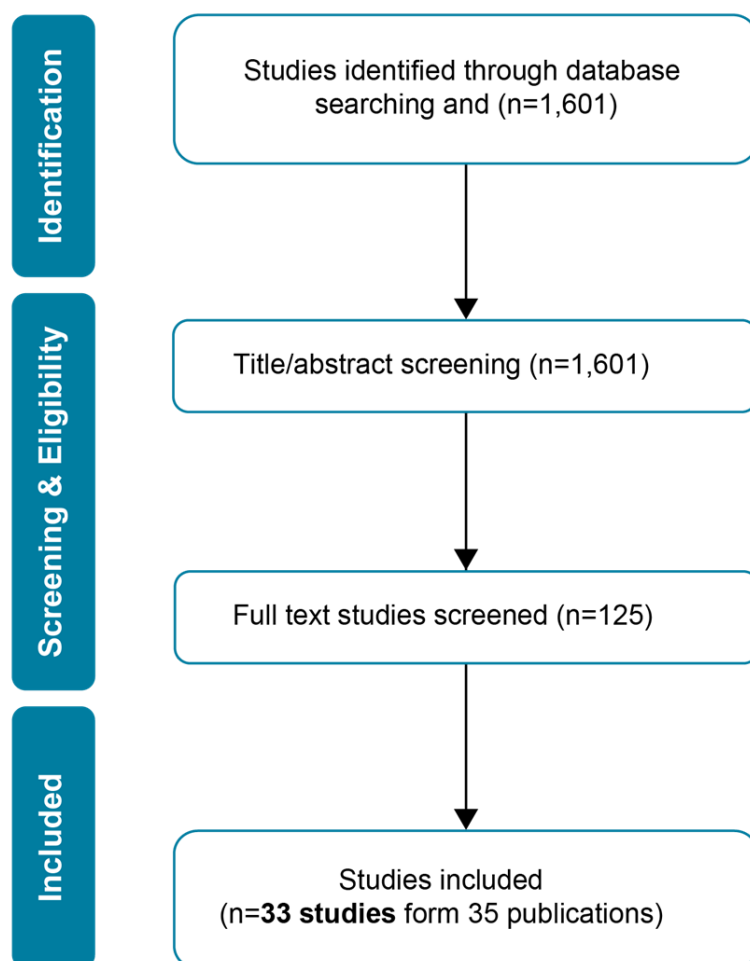
METHODS

- Key biomedical literature databases, including MEDLINE® and Embase®, were searched for a period of 20 years from 2001 to July 2020
- Studies with humanistic and economic burden data for adult CML patients (aged ≥ 18 years) were included
- A single reviewer screened the titles and abstracts for eligibility, and citations meeting the inclusion criteria were selected for full-text review. Unclear citations were also selected for full-text review, and only articles that did not fulfill the specified eligibility criteria were excluded. Full texts of the included articles were screened with more specific eligibility criteria
- Studies which met the inclusion criteria were extracted in a pre-defined extraction grid

RESULTS

- Of the 1,601 records obtained, a total of 33 unique publications were included for the current review (Figure 1)

Figure 1. Study selection flowchart



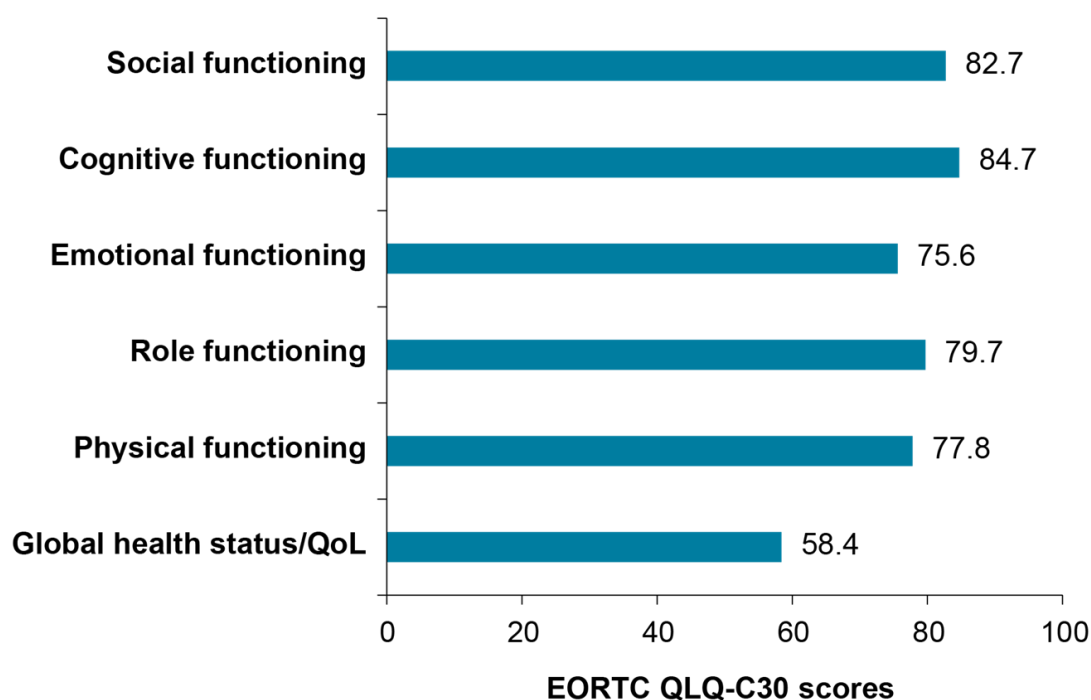
- Of the 33 studies included in this review, 11 were journal articles and 22 were conference abstracts. Of these eleven studies were from Europe and ten were from USA
- Sample size varied largely in these studies, and ranged from 30 to 4,541 patients
- The mean/median age ranged from 48.3 to 76.2 years and 63% of the studies had male predominance

Humanistic burden

- Twenty-three studies reported the health related quality of life (HRQoL) and five studies reported the symptom burden associated with CML in patients receiving different lines of therapy
- SF-36 and EORTC QLQ-C30 were the two most commonly used QoL instruments

- Physical function and emotional function were the most severely impacted QoL domains in most of the studies
- HRQoL of patients with CML was significantly impaired, irrespective of the use of earlier line of TKI therapy (Figure 2). (4)
- A real world study of CML patients treated with first line or second line TKIs reported 58% patients with mild QoL impairments, 11% with moderate and 31% with severe QoL impairments (5)
- Female patients reported worse HRQoL profile compared to the male patients (6, 7)

Figure 2. QoL functions assessed using EORTC QLQ-C30 in patients receiving second-line therapy



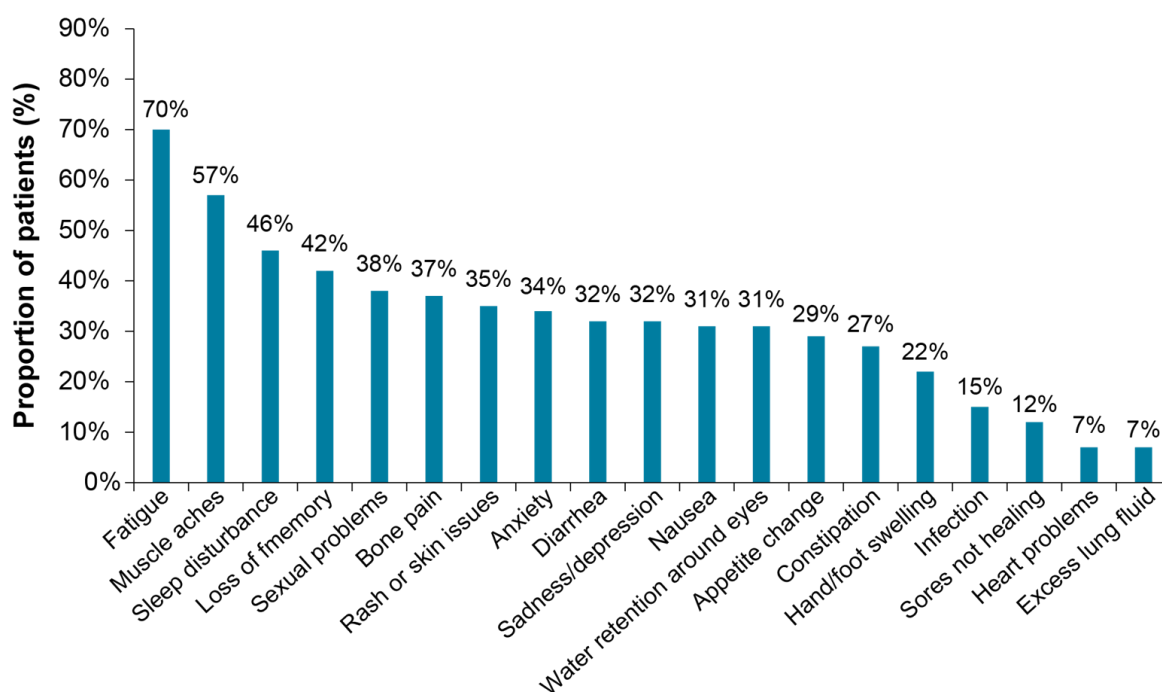
Source: *Sacha et al 2017 (4)*

EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life questionnaire, QoL: quality of life

- Fatigue, musculoskeletal pain, and disturbed sleep were the frequently reported symptoms in most of the studies
- Significant differences were found among male and female patients for fatigue, musculoskeletal pain and edema (7)

- A study from Community's Cancer Experience Registry reported 19 symptoms associated with the CML patients (Figure 3).

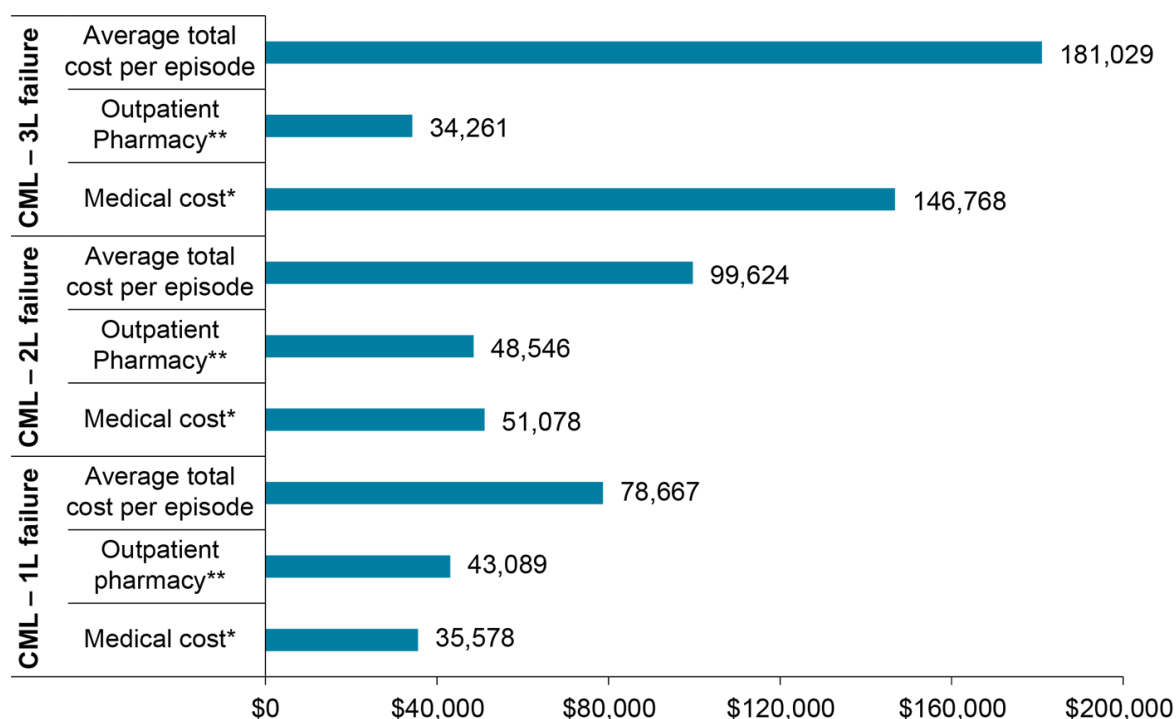
Figure 3. Symptom burden in patients with CML



Source: *Zaleta et al 2017 (8)*
CML: chronic myeloid leukemia

Economic burden

- Ten studies reporting cost data and five studies reporting resource use associated with CML were identified from the literature
- Medical services such as inpatient, emergency room (ER), ambulatory and lab tests were the primary drivers of increased cost burden associated with treatment failure in later lines of therapies
- Total healthcare costs per month increased significantly for patients who switched from first line to second line therapy (9)
- A study from US claims database reported that average cost (adjusted to 2012 US dollars) for patients with first-line treatment failure was \$78,677, which increased to \$99,624 for patients with second-line treatment failure and was the highest for patients with failure of third-line therapy (\$181,029) (Figure 4) (10)

Figure 4. Economic burden as per line of therapy failure

Source: McGarry *et al* 2016 (10)*

Costs for non-pharmacologic services; **Costs for pharmacy claims

CML: chronic myeloid leukemia

Costs were adjusted to 2012 US dollars

- Patients switching to second-line or later lines of therapies had more ER visits, hospital and outpatient visits per month than patients who did not switch and remained on initial line of TKI therapy (9)
- Outpatient prescription fills, hospitalizations, ER visits, physician office visits, and outpatient surgical center visits mainly contributed to resource utilizations (Table 1) (10)
- Overall resource utilization was higher for patients with failure of 2 lines of therapy compared with the those who failed one line of therapy

Table 1: Resource use in patients with CML

Patient population	Resource use item	Proportion of patients	Resource use, mean (SD)
CML – 1L failure	Outpatient prescription fills	100	37 (34.2)
CML – 1L failure	Hospitalizations	23.2	2 (1.6)
CML – 1L failure	ER visits	34.7	1.8 (1.4)
CML – 1L failure	Physician office visits	98.3	20 (18.3)
CML – 1L failure	Outpatient surgical center visits	59.3	2.2 (3.7)
CML – 1L failure	Laboratory tests and other services	98.8	107.8 (128.6)
CML – 2L failure	Outpatient prescription fills	100	44.2 (36.4)
	Hospitalizations	31.1	1.9 (1.5)
CML – 2L failure	ER visits	36.7	2 (1.5)
CML – 2L failure	Physician office visits	98.3	24.9 (20.7)
CML – 2L failure	Outpatient surgical center visits	63.3	3.5 (8)
CML – 2L failure	Laboratory tests and other services	97.8	148.2 (173.6)

Source: McGarry *et al* 2016 (10)

1L: first line, 2L: second line, CML: chronic myeloid leukemia, ER: emergency room, SD: standard deviation

KEY FINDINGS AND CONCLUSIONS

- Patients with CML had significantly impaired HRQoL across all lines of therapies accompanied by increased symptom burden. The impact of this burden keeps increasing as a patient moves into later lines of therapies due to treatment failures
- Economic burden post-TKI failure increases with each sequential line of therapy
- This literature review also suggests that both humanistic and economic burden are not widely studied in patients with CML especially for patients taking later line of TKI therapies. To fill this evidence gap, further research is warranted

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Conflict of Interest

Harish Negi, Rumjhum Agrawal, Joao Vieira, Jacqueline Ryan and Ricardo Viana are employees of Novartis. Deepika Thakur is former employee of Novartis.