

Presenting Author: Ehab L. Atallah, MD
eataallah@mcw.edu

Healthcare Resource Utilization and Associated Costs Among Patients with Chronic Myeloid Leukemia by Line of Therapy in the United States (US) from a Commercial Perspective

Ehab L. Atallah, MD¹; Rodrigo Maegawa, MD²;
Dominick Latremouille-Viau, MSc³; Carmine Rossi, PhD³;
Annie Guérin, MSc³; Pallavi Patwardhan, PhD²

¹Medical College of Wisconsin, Milwaukee, WI, USA; ²Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; ³Analysis Group, Inc., Montreal, QC, Canada



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CONCLUSIONS

- This study fills an important gap in knowledge by using claims data to characterize patients with CML-CP treated with TKIs over multiple LOTs; this population has unmet needs as failure on multiple TKIs limits further treatment options and has an adverse effect on long-term clinical outcomes
- While pharmacy costs accounted for the largest proportion of the total cost burden during treatment, medical costs PPPM became more important in later LOTs, with IP costs, particularly CML-related IP costs, and HSCT being the main drivers of this increase
 - This increasing trend in medical costs was also observed in the sensitivity analyses (after excluding HSCT cost and after generic imatinib availability [02/01/2016])
- Commercially insured patients with CML had increasing HRU and costs as they cycled through TKIs, highlighting the need for new treatments that can help to optimize disease management
- Cost of CML-related healthcare is substantial in the US, accounting for >90% of HRU for CML patients

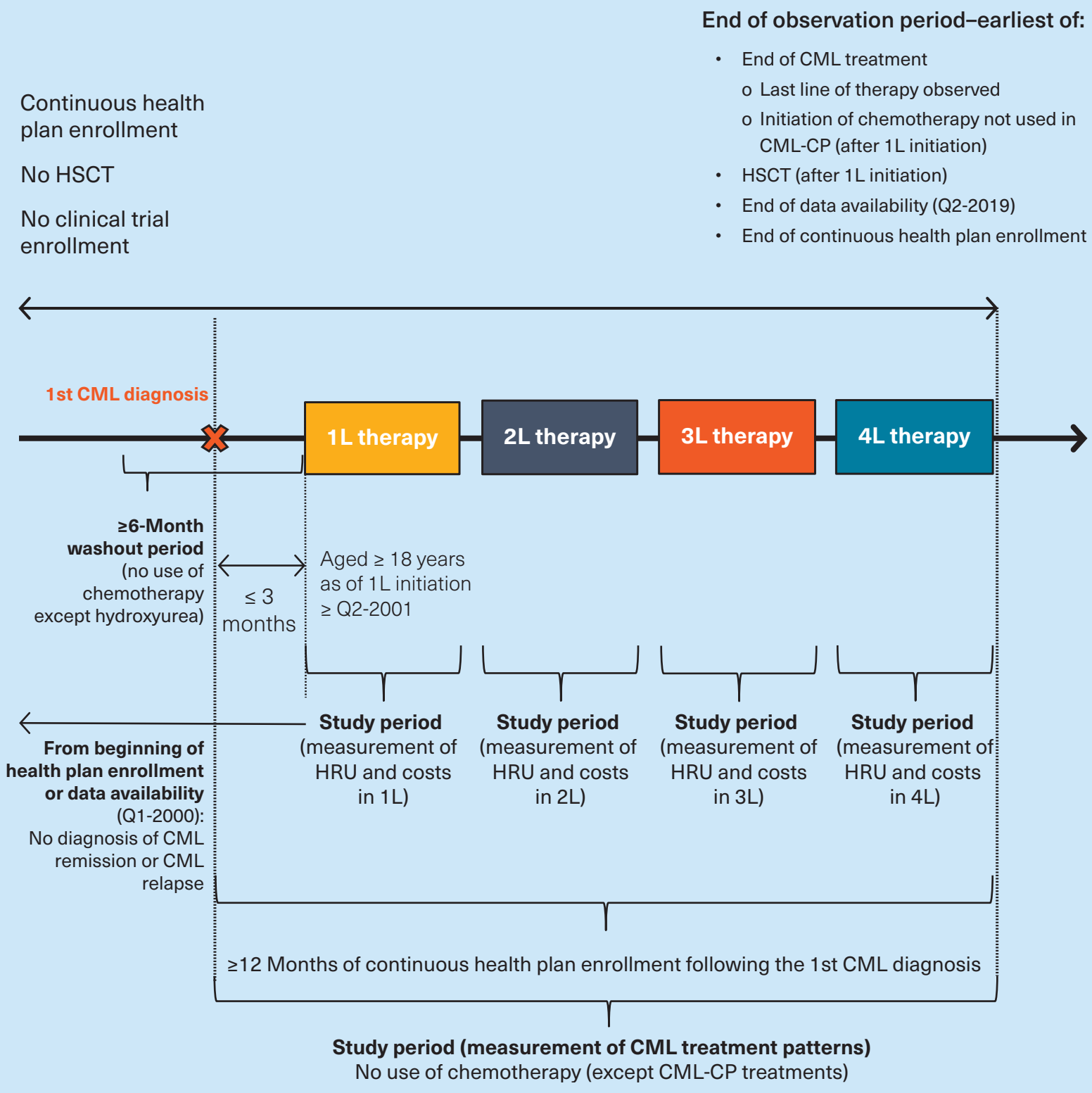
BACKGROUND

- Chronic myeloid leukemia (CML) is a rare leukemia with an incidence of ~1–2 cases per 100,000 in the United States (US)¹. In approximately 95% of CML cases, a balanced chromosomal translocation between chromosomes 9 and 22 results in an abnormal *BCR-ABL1* gene²
- Currently, tyrosine kinase inhibitors (TKIs) that target the resultant BCR-ABL1 oncoprotein are the standard of care for CML³; these include 1st generation (1G; imatinib), 2nd generation (2G; dasatinib, nilotinib, and bosutinib), and 3rd generation (3G; ponatinib) TKIs
- Despite the use of TKIs, a proportion of patients with CML in the chronic phase (CML-CP) is refractory/intolerant to these medications and cycle through multiple lines of therapy (LOTs), reaching third line (3L) or later. There is currently limited information available on the costs of care among these patients from CML-CP treatment initiation to later LOTs

METHODS (CONT...)

- The study period spanned each LOT (1L, 2L, 3L, and 4L), beginning at the first claim for a given CML-CP treatment (i.e., index date) and ending at the earliest among the following: treatment discontinuation (i.e., gap of ≥ 90 days), switch to another CML-CP treatment (i.e., TKIs, omacetaxine), initiation of chemotherapy not used in CML-CP, or hematopoietic stem cell transplantation (HSCT)
 - Short-term use of transition treatment (e.g., hydroxyurea) was not considered as an LOT

Figure 1: STUDY DESIGN



Outcomes and Statistical Analysis

- Treatment patterns were described from 1L to 4L
- During each LOT from 1L to 4L, all-cause and CML-related healthcare resource utilization (HRU: number of inpatient [IP] admissions, IP days, days with outpatient [OP] services, and emergency department [ED] visits) were reported as annual incidence rates (IR)
 - CML-related HRU was defined as medical claims with a diagnosis for CML or a procedure for CML-CP treatment
- During each LOT from 1L to 4L, all-cause and CML-related direct healthcare costs (2019 USD, payer's perspective), including medical and pharmacy costs, were reported as mean costs per patient per month (PPPM)
 - In addition to costs from medical claims for CML-related HRU, pharmacy claims for CML-CP treatment were also included in CML-related costs
 - Costs were stratified by HSCT status at each LOT (i.e., including and excluding medical services with an HSCT-related code [diagnosis or procedure code for HSCT])
- Sensitivity analysis was performed after generic imatinib availability (02/01/2016) for the treatment pattern and cost analyses

OBJECTIVE

- This study assessed treatment patterns and economic outcomes among commercially insured patients with CML by LOT, from first line (1L) through fourth line (4L)

METHODS

Data source

- Data for adult patients with CML were extracted from the IBM® MarketScan® Commercial Claims and Medicare Supplement Databases (01/01/2000–06/30/2019)
- This included combined claims from over 130 payers from all census regions in the US with information on health plan enrollment, demographics, claims for medical services with diagnosis and procedure codes, and claims for pharmacy services

Study Design / Sample Selection

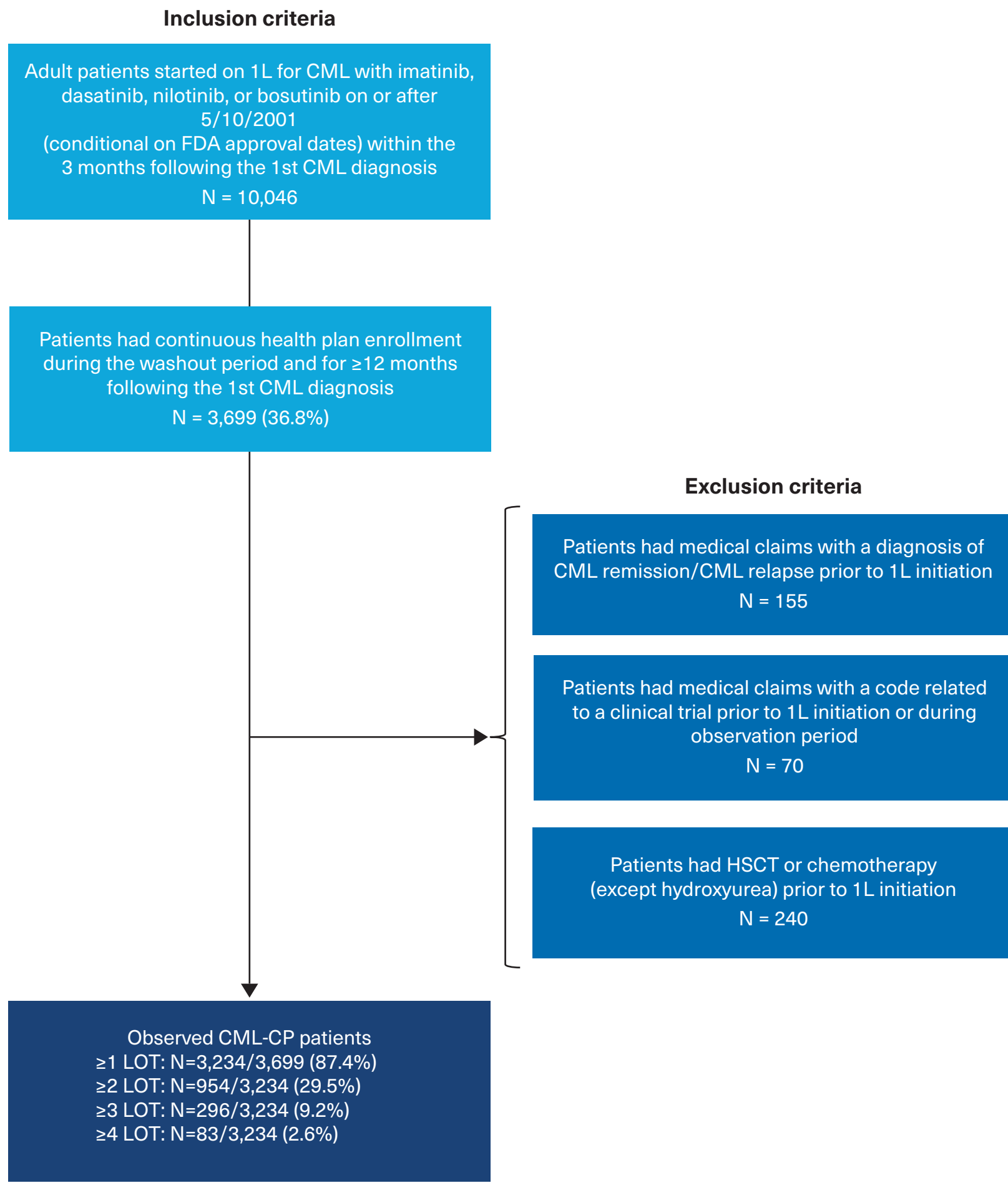
- A retrospective cohort study design was used (**Figure 1**)
- Adult patients with 1L for CML-CP (imatinib, dasatinib, nilotinib, or bosutinib) on or after 5/10/2001 (conditional on FDA approval dates) within the 3 months following the first CML diagnosis observed in medical claims, for whom there was no evidence of CML treatment for ≥6 months prior to 1L initiation (i.e., washout period of ≥6 months, with all data prior to 1L initiation reviewed) were included in the analysis
 - Among these patients with 1L, patients with subsequent LOTs for CML-CP (TKIs: imatinib, bosutinib, nilotinib, or ponatinib; or omacetaxine) were also reported
- The index date was defined as the date of initiation of 1L or of 2L, 3L, or 4L for patients who were previously treated with TKIs

RESULTS

Sample Selection

- From 01/01/2000-06/30/2019, among the 3,234 patients with 1L, 954 (29.5%) had ≥ 2 LOTs, 296 (9.2%) had ≥ 3 LOTs, and 83 (2.6%) had ≥ 4 LOTs (**Figure 2**)
- The median age of patients and proportion of females at LOT initiation were as follows:
 - 1L: 56 years and 44.6% female
 - 2L: 57 years and 47.3% female
 - 3L: 58 years and 49.7% female
 - 4L: 62 years and 48.2% female

Figure 2: SAMPLE SELECTION OF PATIENTS WITH CML



1/2/3/4L = first/second/third/fourth line; CML-CP = chronic myeloid leukemia (chronic phase); FDA = United States Food and Drug Administration; HSCT = hematopoietic stem cell transplantation; LOT = line of therapy; TKI = tyrosine kinase inhibitor.

Treatment Patterns

- From 01/01/2001-06/30/2019, the 1G TKI was most prevalent in the 1L setting ([n=3,234]; 66.2%) while 2G TKIs were most prevalent in 2L ([n=954]; 83.9%), 3L ([n=296]; 74.7%), and 4L ([n=83]; 69.9%) (**Table 1**)
 - After 02/01/2016, 2G TKIs were most prevalent in 1L ([n=440]; 57.7%), 2L ([n=208]; 72.6%), 3L ([n=90]; 77.8%), and 4L ([n=29]; 69.0%)

Table 1: TREATMENT PATTERNS AMONG PATIENTS WITH CML, BY LOT

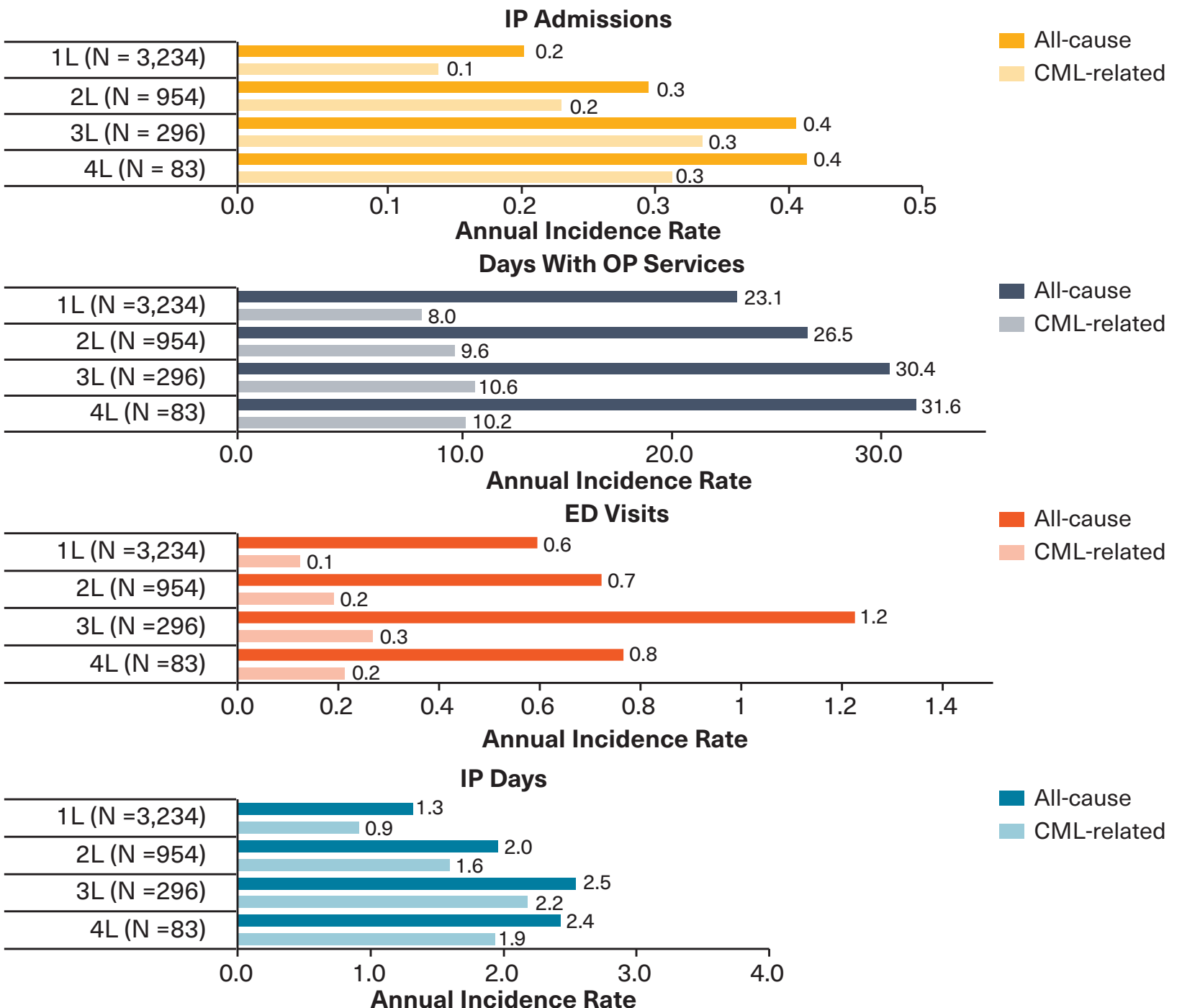
Study period 2001–2019	1L (N = 3,234)	2L (N = 954)	3L (N = 296)	4L (N = 83)
Duration of LOT, months; Mean ± SD [Median]	31.19 ± 30.28 [21.69]	19.98 ± 22.93 [11.69]	15.61 ± 18.49 [8.32]	14.34 ± 15.43 [8.39]
Treatment received, N (%)				
Imatinib	2140 (66.2%)	143 (15.0%)	62 (20.9%)	17 (20.5%)
Dasatinib	721 (22.3%)	467 (49.0%)	73 (24.7%)	24 (28.9%)
Nilotinib	372 (11.5%)	288 (30.2%)	107 (36.1%)	12 (14.5%)
Bosutinib	1 (0.0%)	45 (4.7%)	41 (13.9%)	22 (26.5%)
Ponatinib	0 (0.0%)	11 (1.2%)	13 (4.4%)	6 (7.2%)
Omacetaxine	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.4%)
HSCT ¹	53 (1.6%)	35 (3.7%)	18 (6.1%)	1 (1.2%)
Study period 2016–2019	1L (N = 440)	2L (N = 208)	3L (N = 90)	4L (N = 29)
Treatment received, N (%)				
Imatinib	186 (42.3%)	53 (25.5%)	15 (16.7%)	6 (20.7%)
Dasatinib	199 (45.2%)	71 (34.1%)	23 (25.6%)	9 (31.0%)
Nilotinib	54 (12.3%)	56 (26.9%)	27 (30.0%)	2 (6.9%)
Bosutinib	1 (0.2%)	24 (11.5%)	20 (22.2%)	9 (31.0%)
Ponatinib	0 (0.0%)	4 (1.9%)	5 (5.6%)	1 (3.4%)
Omacetaxine	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.9%)

¹Patients observed with HSCT post LOT initiation. These patients were not included in subsequent LOTs. 1/2/3/4L = first/second/third/fourth line; CML = chronic myeloid leukemia; HSCT = hematopoietic stem cell transplantation; LOT = line of therapy; SD = standard deviation.

HRU by LOT

- All-cause annual IR increased between 1L and 4L: 1.3 to 2.4 for IP days, 23.1 for days with OP services, and 0.6 to 0.8 for ED visits (**Figure 3**)
- The proportion of CML-related IP days increased from 69% to 80% between 1L and 4L

FIGURE 3: ALL-CAUSE AND CML-RELATED HRU BY LOT¹

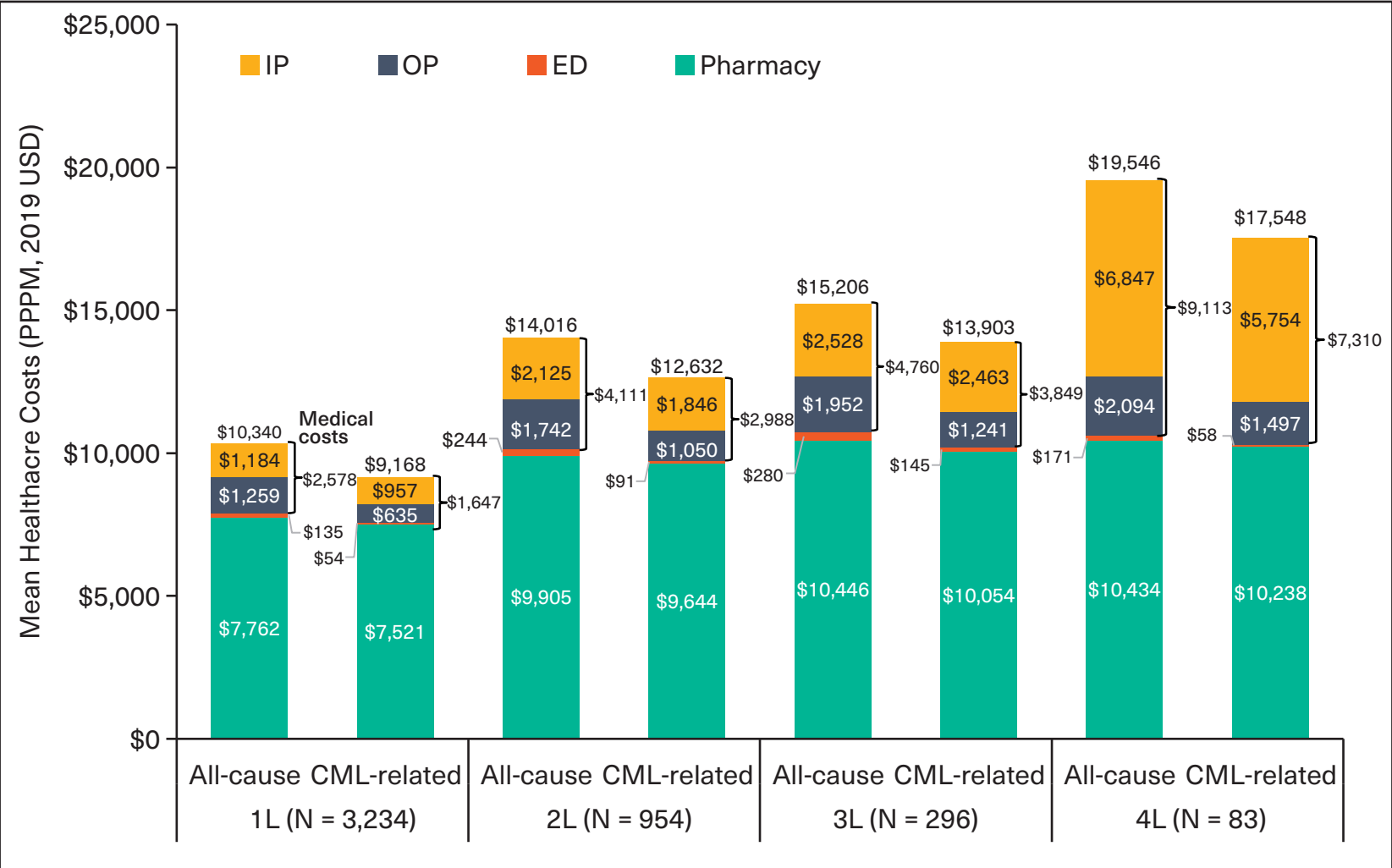


1/2/3/4L = first/second/third/fourth line; CML = chronic myeloid leukemia; ED = emergency department; HRU = health resource utilization; IP = inpatient; LOT = line of therapy; OP = outpatient.
¹Using data from 2001–2019.

Direct Healthcare Costs by LOT

- Mean all-cause total costs (medical+pharmacy) increased from \$10,340 (25% from medical) in 1L to \$19,546 PPPM (47% from medical) in 4L, with approximately 90% of costs from 1L through 4L being CML-related (**Figure 4**)
 - After excluding HSCT-related costs, cost results were consistent; mean all-cause total costs increased from \$10,322 (25% from medical) to \$15,073 PPPM (31% from medical)
- After 02/01/2016, all-cause total costs increased between 1L and 4L from \$13,312 (21% from medical) to \$18,379 PPPM (36% from medical)
 - After excluding HSCT-related costs, mean all-cause total costs increased from \$13,275 (21% from medical) to \$18,092 PPPM (35% from medical)
 - Cost results were consistent from 2016–2019, with and without HSCT costs, despite the introduction of generic imatinib in February 2016

FIGURE 4: ALL-CAUSE AND CML-RELATED HEALTHCARE COSTS¹



1/2/3/4L = first/second/third/fourth line; CML = chronic myeloid leukemia; HSCT = hematopoietic stem cell transplantation; ED = emergency department; IP = inpatient; LOT = line of therapy; OP = outpatient; PPPM = per patient per month; USD = United States dollars.
¹Using data from 2001–2019; includes HSCT-related costs during the LOT.

Limitations

- Although administrative claims databases remain an important resource for assessing HRU and costs of CML management as they include diagnosis and procedure codes that are recorded for reimbursement purposes, laboratory test results, Sokal score, Eastern Cooperative Oncology Group Performance Status, CML phase, and reasons for terminating LOT were not available
- Pharmacy claims for a filled prescription do not guarantee actual consumption of the medication by the patient

Acknowledgments

Medical writing support was provided by a professional medical writer, Janice Imai, an employee of Analysis Group, Inc., which has received funding from Novartis Pharmaceuticals Corporation.

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