Sponsor
Novartis Pharmaceuticals

Generic Drug Name
Tyrosine Kinase receptor

Trial Indication(s)
Chronic Myeloid Leukemia (CML)

Protocol Number
CABL001AUS07

Protocol Title
Real-World Treatment Patterns, Healthcare Resource Utilization and Associated Costs among Patients with Chronic Myeloid Leukemia in Later Lines of Therapy

Clinical Trial Phase
NA

Phase of Drug Development
NA

Study Start/End Dates
Study start date: 08/03/2021

Study Completion date: 15/10/2021

Reason for Termination

NA

Study Design/Methodology

A retrospective, non-interventional cohort study was used to address the study objectives. A cohort of adult patients with CML who were treated with TKIs were identified using the IBM® MarketScan® Commercial and Medicare Supplemental databases (commercial claims; the MarketScan database) to have a better understanding of real-world treatment patterns, HRU and healthcare costs among patients with CML treated with later lines of therapy (i.e., third line or later).

For Phase I, the IBM® MarketScan® Commercial Claims and Encounters and Medicare Supplemental Databases were used (commercial claims). The commercial claims covered the period from 01/01/2001 to 06/30/2019.

The study consisted of the following periods:

- The baseline period was defined as the 6-month period before the first line therapy initiation for CML.

- The observation period was defined as the period of at least 12 months from the first CML diagnosis to the end of data availability or end of health plan coverage, whichever occurs first; the observation period varied by patient.

Centers

Novartis Investigative Site

Objectives:

Primary objective(s)

- To evaluate treatment patterns in patients with CML who were previously treated with TKIs, who are relapsed/refractory to/intolerant of TKIs on third or later lines of therapy

- To evaluate HRU and costs among patients with CML who were previously treated with TKIs, who are relapsed/refractory to/intolerant of TKIs on third or later lines of therapy

Secondary objective(s)

- To estimate the prevalence of patients with CML who were previously treated with TKIs, who are relapsed/refractory to/intolerant of TKIs in second-line or third or later lines of therapy
- To estimate HRU and costs among patients with CML in first-line or second-line of therapy

Test Product (s), Dose(s), and Mode(s) of Administration

NA

Statistical Methods

A descriptive analysis was carried out to assess CML treatment patterns, HRU, and healthcare costs among patients who were relapsed/refractory to/intolerant of TKIs. These descriptive statistics consisted of frequencies, proportions, means, standard deviations, and medians. HRU and direct healthcare costs were reported as of third line therapy initiation, as well as during third and fourth line therapy.

Prevalence of patients with CML who had a third line therapy were reported from 2008 to 2018 (MarketScan databases).

In addition to primary and secondary outcomes, patient characteristics were reported for the overall study sample, patients with CML who initiated third line therapy. Continuous variables were summarized using means, standard deviations, and medians. Categorical variables were summarized using frequencies and proportions.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion criteria

Patients were selected for the analysis of later lines of therapy in commercial claims (i.e., were previously treated with TKIs, who are relapsed/refractory to/intolerant of TKIs) if they met the following criteria:

- Had at least one diagnosis for CML, with first CML diagnosis observed in claims on or after May 10, 2001, the date of FDA approval for imatinib
- Were at least 18 years of age as of the first CML diagnosis
- Started a first line therapy for CML with imatinib, dasatinib, nilotinib, or bosutinib (conditional on FDA-approval dates)
- Initiated first line therapy within a maximum of 1 month prior to the first diagnosis for CML or a maximum 3 months following the first diagnosis for CML
- Had continuous health plan enrollment (pharmacy and medical benefits) from the washout period to at least 12 months following the first CML diagnosis. Patients were further classified into CAR-T IP and CAR-T OP cohorts depending on where the administration occurred.

Exclusion criteria
- Patients had a diagnosis for CML remission or relapse any time prior to first line therapy
- Patients had a medical claim associated with a clinical trial during the washout period up to the end of the observation period
- Patients had an HSCT during the washout period up to the first line therapy initiation
- Patients had chemotherapy treatment (except hydroxyurea) during the washout period up to the first line therapy initiation

Participant Flow
The sample size included 3,234 patients who initiated at least one line of TKI therapy. Of these, 296 initiated third line TKI therapy.

Baseline Characteristics

Patient characteristics	At first line initiation N = 3,234	At third line initiation N = 296
Demographic characteristics		
Age, years; mean ± SD [median]	55.11 ± 14.43 [56.00]	58.52 ± 13.88 [58.00]
18-24 years old, N (%)	87 (2.7)	4 (1.4)
25-34 years old, N (%)	192 (5.9)	10 (3.4)
35-44 years old, N (%)	398 (12.3)	30 (10.1)
45-54 years old, N (%)	816 (25.2)	67 (22.6)
55-64 years old, N (%)	1,013 (31.3)	97 (32.8)
65+ years old, N (%)	728 (22.5)	88 (29.7)
65-74 years old, N (%)	389 (12.0)	46 (15.5)
75+ years old, N (%)	339 (10.5)	42 (14.2)
Female, N (%)	1,442 (44.6)	147 (49.7)
Census region of residence, N (%)		
South	1,276 (39.5)	120 (40.5)
Midwest/North Central	894 (27.6)	81 (27.4)
Northeast	537 (16.6)	44 (14.9)
West	498 (15.4)	51 (17.2)
Unknown	29 (0.9)	0 (0.0)
Health plan type, N (%)		
Preferred provider organization	1,702 (52.6)	148 (50.0)
Medicare supplemental coverage	749 (23.2)	89 (30.1)
Comprehensive	509 (15.7)	56 (18.9)
Home maintenance organization	433 (13.4)	43 (14.5)
Point of service	258 (8.0)	16 (5.4)
Uncapitated	226 (7.0)	16 (5.4)
Partially or fully capitated	32 (1.0)	0 (0.0)
Consumer driven health plan	154 (4.8)	17 (5.7)
High deductible health plan	90 (2.8)	9 (3.0)
Unknown	58 (1.8)	5 (1.7)
Exclusive provider organization	30 (0.9)	2 (0.7)
Calendar year of first CML diagnosis, N (%)		
2001	21 (0.6)	0 (0.0)
2002	51 (1.6)	1 (0.3)
2003	71 (2.2)	1 (0.3)
2004	116 (3.6)	7 (2.4)
2005	141 (4.4)	15 (5.1)
2006	150 (4.6)	13 (4.4)
2007	168 (5.2)	12 (4.1)
2008	224 (6.9)	15 (5.1)
2009	260 (8.0)	23 (7.8)
2010	249 (7.7)	26 (8.8)
2011	318 (9.8)	39 (13.2)
2012	283 (8.8)	32 (10.8)
2013	271 (8.4)	27 (9.1)
2014	245 (7.6)	22 (7.4)
2015	217 (6.7)	30 (10.1)
2016	192 (5.9)	15 (5.1)
2017	172 (5.3)	16 (5.4)
2018	85 (2.6)	2 (0.7)
2019	0 (0.0)	0 (0.0)

Description of patient clinical characteristics

Patient characteristics	At first line initiation N = 3,234	At third line initiation N = 296
Modified Quan-CCI, excluding CML		
Mean ± SD [median]	1.20 ± 1.45 [1.00]	1.64 ± 1.69 [2.00]
0, N (%)	1,580 (48.9)	118 (39.9)
1, N (%)	225 (7.0)	19 (6.4)
2, N (%)	1,036 (32.0)	88 (29.7)
≥3, N (%)	393 (12.2)	71 (24.0)
Darkow disease complexity index, N (%)		
Mild	1,556 (48.1)	106 (35.8)
Moderate	1,089 (33.7)	104 (35.1)
Severe	589 (18.2)	86 (29.1)
Patients unfit for HSCT, N (%)	457 (14.1)	61 (20.6)
75+ years old	339 (10.5)	42 (14.2)
Congestive heart failure	160 (4.9)	32 (10.8)
Cirrhosis	9 (0.3)	1 (0.3)
End-stage renal disease	7 (0.2)	0 (0.0)
Observation period duration, months, mean ± SD [median]	46.68 ± 32.43 [36.96]	57.79 ± 36.31 [47.99]
≥1 year	3,234 (100.0)	296 (100.0)
≥2 years	2,307 (71.3)	263 (88.9)
≥3 years	1,664 (51.5)	203 (68.6)

Primary Outcome Result(s)

Treatment sequences

	All patients N = 3,234
Had one line of therapy, N (%)	2,280 (70.5)
Imatinib	1,513 (46.8)
Dasatinib	499 (15.4)
Nilotinib	267 (8.3)
Bosutinib	1 (0.0)
Ponatinib	0 (0.0)
Had two lines of therapy, N (%)	658 (20.3)
Imatinib + Dasatinib	293 (9.1)
Imatinib + Nilotinib	129 (4.0)
Dasatinib + Imatinib	71 (2.2)
Dasatinib + Nilotinib	67 (2.1)
Nilotinib + Dasatinib	29 (0.9)
Nilotinib + Imatinib	27 (0.8)
Dasatinib + Bosutinib	14 (0.4)
Imatinib + Bosutinib	11 (0.3)
Nilotinib + Bosutinib	7 (0.2)
Dasatinib + Ponatinib	6 (0.2)
Imatinib + Ponatinib	2 (0.1)
Nilotinib + Ponatinib	2 (0.1)
Had at least three lines of therapy, N (%)	296 (9.2)
Imatinib + Dasatinib + Nilotinib	60 (1.9)
Imatinib + Nilotinib + Dasatinib	33 (1.0)
Imatinib + Dasatinib + Imatinib	18 (0.6)
Dasatinib + Imatinib + Nilotinib	13 (0.4)
Imatinib + Dasatinib + Bosutinib	12 (0.4)
Dasatinib + Nilotinib + Imatinib	11 (0.3)
Nilotinib + Dasatinib + Imatinib	9 (0.3)
Imatinib + Dasatinib + Nilotinib + Dasatinib	8 (0.2)
Nilotinib + Imatinib + Dasatinib	8 (0.2)
Dasatinib + Imatinib + Dasatinib	6 (0.2)
Imatinib + Dasatinib + Nilotinib + Imatinib	6 (0.2)
Imatinib + Nilotinib + Bosutinib	6 (0.2)
Imatinib + Dasatinib + Nilotinib + Bosutinib	5 (0.2)
Imatinib + Nilotinib + Dasatinib + Bosutinib	5 (0.2)
Nilotinib + Dasatinib + Bosutinib	5 (0.2)
Dasatinib + Nilotinib + Bosutinib	4 (0.1)
Dasatinib + Nilotinib + Dasatinib	3 (0.1)
Dasatinib + Nilotinib + Ponatinib	3 (0.1)
Imatinib + Dasatinib + Imatinib + Dasatinib	3 (0.1)
Imatinib + Dasatinib + Imatinib + Nilotinib + Imatinib	3 (0.1)
Imatinib + Nilotinib + Imatinib + Dasatinib	3 (0.1)
Nilotinib + Dasatinib + Imatinib + Bosutinib	3 (0.1)
Imatinib + Nilotinib + Dasatinib + Ponatinib	0 (0.0)
Nilotinib + Dasatinib + Ponatinib + Omacetaxine + Bosutinib	0 (0.0)
Dasatinib + Bosutinib + Imatinib + Nilotinib + Ponatinib	0 (0.0)
Nilotinib + Bosutinib + Ponatinib	0 (0.0)
Other	69 (2.1)

Treatment patterns, by line of therapy, among patients with three lines of therapy or more

	First line N = 296	Second line N = 296	Third line N = 296	Fourth line N = 83
Use of pre-treatment hydroxyurea, N (%)	101 (34.1)	47 (15.9)	21 (7.1)	7 (8.4)
Treatment received*, N (%)				
Imatinib	192 (64.9)	45 (15.2)	62 (20.9)	17 (20.5)
Initial dose				
<400 mg	3 (1.6)	0 (0.0)	13 (21.0)	5 (29.4)
400 mg	140 (72.9)	43 (95.6)	41 (66.1)	10 (58.8)
>400 mg	49 (25.5)	2 (4.4)	8 (12.9)	2 (11.8)
Dasatinib	64 (21.6)	145 (49.0)	73 (24.7)	24 (28.9)
Initial dose				
<100 mg	1 (1.6)	9 (6.2)	17 (23.3)	6 (25.0)
100 mg	57 (89.1)	106 (73.1)	44 (60.3)	15 (62.5)
>100 mg	6 (9.4)	30 (20.7)	12 (16.4)	3 (12.5)
Nilotinib	40 (13.5)	92 (31.1)	107 (36.1)	12 (14.5)
Initial dose				
<600 mg	2 (5.0)	6 (6.5)	15 (14.0)	2 (16.7)
600 mg	31 (77.5)	52 (56.5)	43 (40.2)	8 (66.7)
>600 mg	7 (17.5)	34 (37.0)	49 (45.8)	2 (16.7)
Bosutinib	0 (0.0)	13 (4.4)	41 (13.9)	22 (26.5)
Initial dose				
<400 mg	0 (0.0)	0 (0.0)	8 (19.5)	3 (13.6)
400 mg	0 (0.0)	2 (15.4)	8 (19.5)	4 (18.2)
>400 mg	0 (0.0)	11 (84.6)	25 (61.0)	15 (68.2)
Ponatinib	0 (0.0)	1 (0.3)	13 (4.4)	6 (7.2)
Initial dose				
<45 mg	0 (0.0)	0 (0.0)	4 (30.8)	3 (3.6)
45 mg	0 (0.0)	1 (100.0)	8 (61.5)	3 (3.6)
>45 mg	0 (0.0)	0 (0.0)	1 (7.7)	0 (0.0)
Omacetaxine mepesuccinate	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.4)
Calendar year of line of therapy initiation, N (%)				
2001	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2002	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2003	2 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
2004	8 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)
2005	12 (4.1)	0 (0.0)	0 (0.0)	0 (0.0)
2006	15 (5.1)	3 (1.0)	1 (0.3)	0 (0.0)
2007	12 (4.1)	13 (4.4)	3 (1.0)	1 (1.2)
2008	16 (5.4)	11 (3.7)	7 (2.4)	2 (2.4)
2009	22 (7.4)	19 (6.4)	13 (4.4)	2 (2.4)
2010	24 (8.1)	24 (8.1)	18 (6.1)	4 (4.8)
2011	39 (13.2)	42 (14.2)	29 (9.8)	2 (2.4)
2012	33 (11.1)	36 (12.2)	39 (13.2)	11 (13.3)
2013	28 (9.5)	30 (10.1)	38 (12.8)	14 (16.9)
2014	21 (7.1)	34 (11.5)	29 (9.8)	5 (6.0)
2015	26 (8.8)	23 (7.8)	24 (8.1)	13 (15.7)
2016	20 (6.8)	25 (8.4)	32 (10.8)	9 (10.8)
2017	16 (5.4)	29 (9.8)	28 (9.5)	10 (12.0)
2018	2 (0.7)	5 (1.7)	25 (8.4)	8 (9.6)
2019	0 (0.0)	2 (0.7)	10 (3.4)	2 (2.4)

	First line N = 296	Second line N = 296	Third line N = 296	Fourth line N = 83
Duration of the line of therapy, months, mean ± SD [median]	14.92 ± 18.70 [8.47]	10.43 ± 15.19 [4.24]	15.61 ± 18.49 [8.32]	14.34 ± 15.43 [8.39]
Patients with one prescription fill, N (%)	31 (10.5)	73 (24.7)	45 (15.2)	13 (15.7)
Patients with ≤3 months duration, N (%)	78 (26.4)	128 (43.2)	87 (29.4)	25 (30.1)
Patients with >3 to ≤ 6 months duration, N (%)	50 (16.9)	43 (14.5)	37 (12.5)	8 (9.6)
Patients with >6 months duration, N (%)	168 (56.8)	125 (42.2)	172 (58.1)	50 (60.2)
Patients with >12 months duration, N (%)	116 (39.2)	83 (28.0)	118 (39.9)	33 (39.8)
Treatment-free period among those with an observed subsequent line of therapy, months, mean ± SD [median]	1.28 ± 4.08 [0.13]	2.56 ± 5.45 [0.44]	1.54 ± 3.02 [0.30]	1.67 ± 2.69 [0.07]
≤1 month, N (%)	225 (76.0)	181 (61.1)	56 (18.9)	15 (18.1)
>1 to ≤ 6 months, N (%)	59 (19.9)	77 (26.0)	22 (7.4)	6 (7.2)
>6 months, N (%)	12 (4.1)	38 (12.8)	5 (1.7)	3 (3.6)
>12 months, N (%)	5 (1.7)	14 (4.7)	2 (0.7)	0 (0.0)
Reason for ending the line of therapy, N (%)				
Discontinued treatment (treatment-free period)	0 (0.0)	0 (0.0)	30 (10.1)	13 (15.7)
HSCT following the end of the line of therapy	0 (0.0)	0 (0.0)	5 (1.7)	0 (0.0)
Chemotherapy following the end of the line of therapy	0 (0.0)	0 (0.0)	1 (0.3)	1 (1.2)
Switch to another TKI or omacetaxine	296 (100.0)	296 (100.0)	83 (28.0)	24 (28.9)
Chemotherapy	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)
HSCT	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
End of continuous health plan enrollment/data availability	0 (0.0)	0 (0.0)	182 (61.5)	45 (54.2)
HSCT following the end of the line of therapy	0 (0.0)	0 (0.0)	12 (4.1)	1 (1.2)
Chemotherapy following the end of the line of therapy	0 (0.0)	0 (0.0)	16 (5.4)	2 (2.4)

Note: Treatments for CML-CP: bosutinib, dasatinib, imatinib, nilotinib, ponatinib, and omacetaxine mepesuccinate. The list of selected treatments was based on observations from the clinical practice for CML-CP. Short-term transition treatments (i.e, pre-treatment with/short-term hydroxyurea use) were not included as a line of therapy. There was only 1 patient with 1 medical claim with a procedure code for interferon alfa.

HRU among patients with three lines of therapy or more

HRU Outcomes	Third line or later			Third line			Fourth line		
	N (%)	Events	Monthly IR per 100 patients	N (%)	Events	Monthly IR per 100 patients	N (%)	Events	Monthly IR per 100 patients
Number of patients	**N = 296**			**N = 296**			**N = 83**		
Duration, months, mean ± SD [median]	24.52 ± 23.41 [17.34]			15.61 ± 18.49 [8.32]			14.34 ± 15.43 [8.39]		
Total patient-time, months		7,258.6			4,620.3			1,190.6	
All-cause HRU									
Inpatient admissions	110 (37.2)	255	3.5	78 (26.4)	156	3.4	22 (26.5)	41	3.4
Inpatient days	110 (37.2)	2,084	28.7	78 (26.4)	978	21.2	22 (26.5)	241	20.2
Hospice admissions	7 (6.4)	11	0.2	4 (5.1)	6	0.1	2 (9.1)	2	0.2
Hospice days	7 (6.4)	80	1.1	4 (5.1)	34	0.7	2 (9.1)	14	1.2
Days with outpatient services	289 (97.6)	18,653	257.0	286 (96.6)	11,702	253.3	82 (98.8)	3,140	263.7
Emergency department visits	151 (51.0)	727	10.0	124 (41.9)	472	10.2	25 (30.1)	76	6.4
CML-related HRU									
Inpatient admissions	102 (34.5)	212	2.9	74 (25.0)	129	2.8	18 (21.7)	31	2.6
Inpatient days	102 (34.5)	1,803	24.8	74 (25.0)	838	18.1	18 (21.7)	192	16.1
Days with outpatient services	282 (95.3)	6,402	88.2	275 (92.9)	4,081	88.3	79 (95.2)	1,008	84.7
Omacetaxine-related	1 (0.3)	5	0.1	0 (0.0)	0	0.0	0 (0.0)	0	0.0
CML-related	282 (95.3)	6,402	88.2	275 (92.9)	4,081	88.3	79 (95.2)	1,008	84.7
Emergency department visits	68 (23.0)	179	2.5	48 (16.2)	103	2.2	11 (13.3)	21	1.8

Healthcare costs among patients with three lines of therapy or more

Healthcare Cost (2019 $USD)	Third line or later	Third line	Fourth line
Number of Patients	N = 296	N = 296	N = 83
Duration, months, mean ± SD [median]	24.52 ± 23.41 [17.34]	15.61 ± 18.49 [8.32]	14.34 ± 15.43 [8.39]
All-cause total costs, PPPM, mean ± SD [median]			
Total cost	19,073 ± 40,407 [11,102]	15,537 ± 15,210 [12,238]	19,916 ± 42,541 [12,127]
Payers' cost	18,784 ± 40,373 [10,849]	15,206 ± 15,140 [12,037]	19,546 ± 42,167 [11,990]
Beneficiaries' cost	288 ± 348 [200]	331 ± 534 [201]	370 ± 824 [175]
Medical costs			
Total cost	9,732 ± 39,412 [1,559]	4,960 ± 13,046 [1,261]	9,285 ± 42,150 [1,005]
Payers' cost	9,564 ± 39,373 [1,425]	4,760 ± 12,989 [1,144]	9,113 ± 41,756 [891]
Beneficiaries' cost	168 ± 286 [90]	200 ± 485 [86]	173 ± 442 [87]
Inpatient admissions			
Total cost	7,296 ± 37,681 [0]	2,563 ± 12,069 [0]	6,904 ± 42,002 [0]
Payers' cost	7,258 ± 37,638 [0]	2,528 ± 12,037 [0]	6,847 ± 41,603 [0]
Beneficiaries' cost	38 ± 214 [0]	36 ± 166 [0]	56 ± 412 [0]
Outpatient			
Total cost	2,217 ± 4,006 [882]	2,096 ± 3,988 [833]	2,189 ± 5,182 [681]
Payers' cost	2,103 ± 3,971 [782]	1,952 ± 3,854 [696]	2,094 ± 5,177 [593]
Beneficiaries' cost	114 ± 175 [70]	144 ± 446 [68]	95 ± 129 [57]
Emergency department			
Total cost	218 ± 575 [2]	300 ± 1,349 [0]	193 ± 488 [0]
Payers' cost	203 ± 548 [2]	280 ± 1,309 [0]	171 ± 435 [0]
Beneficiaries' cost	15 ± 48 [0]	20 ± 99 [0]	21 ± 80 [0]
Pharmacy costs			
Total cost	9,341 ± 5,275 [8,815]	10,577 ± 5,528 [9,985]	10,631 ± 5,954 [10,032]
Payers' cost	9,221 ± 5,249 [8,667]	10,446 ± 5,480 [9,842]	10,434 ± 5,999 [9,850]
Beneficiaries' cost	120 ± 188 [76]	132 ± 199 [81]	198 ± 673 [72]
Event cost (Total), PPPM, mean ± SD [median]			
Inpatient	N = 255; 51,815 ± 114,564 [15,551]	N = 156; 35,951 ± 61,293 [15,695]	N = 41; 29,293 ± 58,113 [13,624]
Outpatient	N = 18,653; 492 ± 1,984 [121]	N = 11,702; 471 ± 1,809 [119]	N = 3,140; 379 ± 1,202 [115]
Emergency department	N = 727; 2,169 ± 3,276 [993]	N = 472; 2,310 ± 3,302 [1,161]	N = 76; 2,240 ± 3,278 [1,023]

Healthcare Cost (2019 $USD)	Third line or later	Third line	Fourth line
Number of Patients	**N = 296**	**N = 296**	**N = 83**
Among patients who initiated a line of TKI therapy on or after 2/1/2016, N (%)	**90 (30.4)**	**90 (30.4)**	**29 (34.9)**
All-cause total costs, PPPM, mean ± SD [median]			
Total cost	17,561 ± 22,293 [13,659]	17,477 ± 17,314 [14,706]	31,410 ± 69,702 [17,409]
Payers' cost	17,277 ± 22,280 [13,476]	17,128 ± 17,280 [14,508]	30,840 ± 69,090 [17,165]
Beneficiaries' cost	285 ± 269 [252]	350 ± 444 [225]	569 ± 1,298 [233]
Medical costs			
Total cost	6,513 ± 20,490 [1,329]	4,871 ± 15,698 [1,087]	19,365 ± 70,009 [1,237]
Payers' cost	6,352 ± 20,466 [1,287]	4,660 ± 15,669 [992]	19,120 ± 69,340 [1,132]
Beneficiaries' cost	161 ± 179 [106]	211 ± 344 [86]	245 ± 703 [91]
Pharmacy costs			
Total cost	11,048 ± 5,745 [10,395]	12,607 ± 5,637 [12,509]	12,045 ± 6,540 [12,172]
Payers' cost	10,925 ± 5,749 [10,357]	12,468 ± 5,586 [12,345]	11,720 ± 6,714 [12,111]
Beneficiaries' cost	123 ± 194 [76]	139 ± 238 [79]	325 ± 1,060 [85]

Secondary Outcome Result(s)

Prevalence of later lines of therapy, second line of therapy

	Later lines of therapy (3+)			Sensitivity analysis: Later lines of therapy (3+) among patients who initiated a first line of TKI therapy		Second line of therapy (2L)			Sensitivity analysis: Second line of therapy (2L) among patients who initiated a first line of TKI therapy	
Prevalence	Numerator	Denominator	Prevalence (%)	Denominator	Prevalence (%)	Numerator	Denominator	Prevalence (%)	Denominator	Prevalence (%)
Year										
2006	1	5,339	0.02%	463	0.22%	10	5,339	0.19%	463	2.16%
2007	4	6,321	0.06%	585	0.68%	40	6,321	0.63%	585	6.84%
2008	10	9,114	0.11%	743	1.35%	63	9,114	0.69%	743	8.48%
2009	19	10,722	0.18%	905	2.10%	98	10,722	0.91%	905	10.83%
2010	29	11,211	0.26%	1,002	2.89%	144	11,211	1.28%	1,002	14.37%
2011	52	12,893	0.40%	1,209	4.30%	232	12,893	1.80%	1,209	19.19%
2012	81	13,717	0.59%	1,358	5.96%	273	13,717	1.99%	1,358	20.10%
2013	95	12,111	0.78%	1,358	7.00%	260	12,111	2.15%	1,358	19.15%
2014	96	12,221	0.79%	1,326	7.24%	264	12,221	2.16%	1,326	19.91%
2015	94	8,275	1.14%	1,218	7.72%	250	8,275	3.02%	1,218	20.53%
2016	104	7,929	1.31%	1,236	8.41%	246	7,929	3.10%	1,236	19.90%
2017	101	6,816	1.48%	1,106	9.13%	234	6,816	3.43%	1,106	21.16%
2018	85	6,148	1.38%	876	9.70%	186	6,148	3.03%	876	21.23%
Average annual growth rate		51.7%		45.5%			35.0%		28.8%	
Compound annual growth rate		43.1%		37.3%			26.1%		21.0%	
Linear coefficient (percentage point per year)		0.13%		0.86%			0.27%		1.49%	
P-value		<0.001		<0.001			<0.001		<0.001	

	Later lines of therapy (3+)			Sensitivity analysis: Later lines of therapy (3+) among patients who initiated a first line of TKI therapy		Second line of therapy (2L)			Sensitivity analysis: Second line of therapy (2L) among patients who initiated a first line of TKI therapy	
Prevalence	**Numerator**	**Denominator**	**Prevalence (%)**	**Denominator**	**Prevalence (%)**	**Numerator**	**Denominator**	**Prevalence (%)**	**Denominator**	**Prevalence (%)**
Year										
2006	1	5,339	0.02%	463	0.22%	10	5,339	0.19%	463	2.16%
2007	4	6,321	0.06%	585	0.68%	40	6,321	0.63%	585	6.84%
2008	10	9,114	0.11%	743	1.35%	63	9,114	0.69%	743	8.48%
2009	19	10,722	0.18%	905	2.10%	98	10,722	0.91%	905	10.83%
2010	29	11,211	0.26%	1,002	2.89%	144	11,211	1.28%	1,002	14.37%
2011	52	12,893	0.40%	1,209	4.30%	232	12,893	1.80%	1,209	19.19%
2012	81	13,717	0.59%	1,358	5.96%	273	13,717	1.99%	1,358	20.10%
2013	95	12,111	0.78%	1,358	7.00%	260	12,111	2.15%	1,358	19.15%
2014	96	12,221	0.79%	1,326	7.24%	264	12,221	2.16%	1,326	19.91%
2015	94	8,275	1.14%	1,218	7.72%	250	8,275	3.02%	1,218	20.53%
2016	104	7,929	1.31%	1,236	8.41%	246	7,929	3.10%	1,236	19.90%
2017	101	6,816	1.48%	1,106	9.13%	234	6,816	3.43%	1,106	21.16%
2018	85	6,148	1.38%	876	9.70%	186	6,148	3.03%	876	21.23%
Average annual growth rate		51.7%		45.5%			35.0%		28.8%	
Compound annual growth rate		43.1%		37.3%			26.1%		21.0%	
Linear coefficient (percentage point per year)		0.13%		0.86%			0.27%		1.49%	
P-value		<0.001		<0.001			<0.001		<0.001	

HRU among patients with earlier lines of therapy

HRU Outcomes	First line			Second line		
	N (%)	Events	Monthly IR per 100 patients	N (%)	Events	Monthly IR per 100 patients
Number of patients	**N = 3,234**			**N = 954**		
Duration, months, mean ± SD [median]	31.19 ± 30.28 [21.69]			19.98 ± 22.93 [11.69]		
Total patient-time, months		100,878.9			19,056.8	
All-cause HRU						
Inpatient admissions	917 (28.4)	1,696	1.7	249 (26.1)	156	2.5
Inpatient days	917 (28.4)	11,046	10.9	249 (26.1)	978	16.3
Hospice admissions	66 (7.2)	91	0.1	17 (6.8)	6	0.1
Hospice days	66 (7.2)	625	0.6	17 (6.8)	34	0.8
Days with outpatient services	3,216 (99.4)	194,304	192.6	931 (97.6)	11,702	220.7
Emergency department visits	1,509 (46.7)	5,004	5.0	400 (41.9)	472	6.0
CML-related HRU						
Inpatient admissions	729 (22.5)	1,156	1.1	214 (22.4)	129	1.9
Inpatient days	729 (22.5)	7,646	7.6	214 (22.4)	838	13.3
Days with outpatient services	3,135 (96.9)	67,638	67.0	900 (94.3)	4,081	80.3
Omacetaxine-related	0 (0.0)	0	0.0	0 (0.0)	0	0.0
CML-related	3,135 (96.9)	67,638	67.0	900 (94.3)	4,081	80.3
Emergency department visits	536 (16.6)	1,039	1.0	162 (17.0)	103	1.6

Healthcare costs among patients with earlier lines of therapy

Healthcare Cost (2019 $USD)	First line	Second line
Number of Patients	**N = 3,234**	**N = 954**
Duration, months, mean ± SD [median]	31.19 ± 30.28 [21.69]	19.98 ± 22.93 [11.69]
All-cause total costs, PPPM, mean ± SD [median]		
Total cost	10,660 ± 10,345 [9,201]	14,324 ± 12,143 [11,724]
Payers' cost	10,340 ± 10,263 [8,910]	14,016 ± 12,090 [11,438]
Beneficiaries' cost	320 ± 486 [196]	309 ± 501 [197]
Medical costs		
Total cost	2,724 ± 9,439 [925]	4,262 ± 11,013 [1,088]
Payers' cost	2,578 ± 9,370 [808]	4,111 ± 10,947 [962]
Beneficiaries' cost	146 ± 254 [86]	151 ± 218 [90]
Inpatient admissions		
Total cost	1,208 ± 8,370 [0]	2,146 ± 9,175 [0]
Payers' cost	1,184 ± 8,317 [0]	2,125 ± 9,132 [0]
Beneficiaries' cost	25 ± 173 [0]	22 ± 105 [0]
Outpatient		
Total cost	1,369 ± 3,546 [663]	1,855 ± 4,395 [717]
Payers' cost	1,259 ± 3,500 [570]	1,742 ± 4,350 [628]
Beneficiaries' cost	110 ± 163 [71]	113 ± 158 [71]
Emergency department		
Total cost	147 ± 630 [0]	260 ± 1,250 [0]
Payers' cost	135 ± 596 [0]	244 ± 1,224 [0]
Beneficiaries' cost	11 ± 64 [0]	17 ± 69 [0]
Pharmacy costs		
Total cost	7,936 ± 3,714 [7,387]	10,062 ± 4,789 [10,240]
Payers' cost	7,762 ± 3,681 [7,223]	9,905 ± 4,775 [10,045]
Beneficiaries' cost	174 ± 390 [79]	157 ± 449 [76]
Event cost (Total), PPPM, mean ± SD [median]		
Inpatient	N = 1,696; 30,233 ± 47,806 [15,704]	N = 468; 34,540 ± 54,082 [17,834]
Outpatient	N = 194,304; 444 ± 2,252 [118]	N = 42,066; 475 ± 2,186 [119]
Emergency department	N = 5,004; 1,583 ± 2,523 [720]	N = 1,148; 2,037 ± 4,083 [800]

Healthcare Cost (2019 $USD)	First line	Second line
Number of Patients	**N = 3,234**	**N = 954**
Among patients who initiated a line of TKI therapy on or after 2/1/2016, N (%)	**440 (13.6)**	**208 (21.8)**
All-cause total costs, PPPM, mean ± SD [median]		
Total cost	13,706 ± 10,488 [12,673]	15,326 ± 11,478 [13,500]
Payers' cost	13,312 ± 10,395 [12,266]	14,983 ± 11,471 [13,163]
Beneficiaries' cost	394 ± 613 [200]	343 ± 791 [196]
Medical costs		
Total cost	2,896 ± 9,063 [799]	3,028 ± 8,851 [808]
Payers' cost	2,766 ± 8,978 [707]	2,907 ± 8,801 [747]
Beneficiaries' cost	129 ± 224 [80]	122 ± 150 [80]
Medical costs		
Total cost	10,811 ± 4,372 [10,883]	12,298 ± 6,572 [12,235]
Payers' cost	10,546 ± 4,358 [10,421]	12,076 ± 6,569 [11,897]
Beneficiaries' cost	265 ± 573 [72]	221 ± 777 [66]

Safety Results
NA

Other Relevant Findings
None

Conclusion
This study characterized Chronic Myeloid Leukemia patients receiving later lines of therapy, a clinical population which has not been previously well studied with important unmet treatment needs as they repetitively fail Tyrosine Kinase Inhibitor (TKI) therapy.
Although the majority of patients were likely fit for Stem Cell Transplant (SCT), SCT was rare. In addition, patients quickly switched to the subsequent line of therapy, both facts suggesting that an important proportion of patients were intolerant to previous TKIs.
While pharmacy costs accounted for nearly half of the total cost burden during third line, the proportion of medical costs Per-Patient-Per-Month (PPPM) took more importance following third line therapy, with Inpatient costs being the primary cost drivers for this increase.
These findings support the need for better treatment options in pts with Chronic Myeloid Leukemia undergoing later lines of therapy.

Date of Clinical Study Report
30 June 2021