Real-World Healthcare Resource Utilization and Total Cost of Care among US Medicare Patients with Chronic Lymphocytic Leukemia Receiving First-Line Ibrutinib Vs. Chemoimmunotherapy

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BACKGROUND

- Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) is a malignancy in which the bone marrow produces excessive amounts of abnormal lymphocytes; CLL/SLL is the most frequent form of leukemia in Western countries and disproportionately affects older individuals[1]
- Despite their widespread use, anti-CD20-based chemoimmunotherapy (CIT) regimens have limited efficacy in those bearing *TP53* mutations or 17p deletions[2] and their use may pose safety risks for patients above 65 years of age[3]
- Ibrutinib (Imbruvica®; approved for the treatment of CLL/SLL as first-line [1L] therapy and in patients with ≥1 prior line of therapy[4]) is the only once-daily, oral inhibitor of Bruton's tyrosine kinase (BTK) with significant progression-free survival benefit demonstrated in 5 randomized phase 3 studies of patients with CLL/SLL,[5-9] with overall survival benefit in 3 of those studies[5,7,8]
- Moreover, it is the National Comprehensive Cancer Network (NCCN) guideline's only preferred Category 1 regimen for previously untreated CLL without 17p deletions across age and fitness types, and a preferred regimen in patients with 17p deletions[10]
- In a previous study of patients enrolled in Commercial managed care plans,[11] ibrutinib-treated patients had lower monthly total healthcare costs compared to CIT-treated patients over the first six months of 1L therapy and over the total observed duration of 1L therapy, with monthly savings in medical costs offsetting higher monthly pharmacy costs
- These results may or may not be generalizable to other insured populations such as Medicare due to differences in population characteristics and payment structure; therefore, there is a need to expand upon previous research by assessing the healthcare resource utilization (HRU) and costs of ibrutinib versus CIT in 1L therapy, specifically among Medicare patients with fee-for-service (FFS) or Medicare Advantage (MA) coverage

OBJECTIVE

- To compare HRU and corresponding healthcare costs of Medicare patients with CLL/SLL who received ibrutinib single agent versus CIT in 1L therapy

METHODS

Data Source

- For Medicare FFS data (Part A, B, and D), the Centers for Medicare and Medicaid Services' (CMS) 100% Medicare Research Identifiable Files (RIF) from 01/01/2005 to 12/31/2017 were used
  - RIF datasets included information on claims for durable medical equipment, inpatient (IP) and outpatient (OP) visits, home health agency, hospice, skilled nursing facility, carrier, and pharmacy dispensing, as well as beneficiary demographics (including date of death)
- For MA data (Part C), the Optum Clinformatics® Extended DataMart (Date of Death) De-Identified Databases from 01/01/2004 to 12/31/2017 were used
  - Optum Clinformatics® covers 13 million annual lives of UnitedHealth Group members in all census regions in the United States (US) and contains data on patient demographics, dates of eligibility, date of death, claims for IP and OP visits, and costs of services

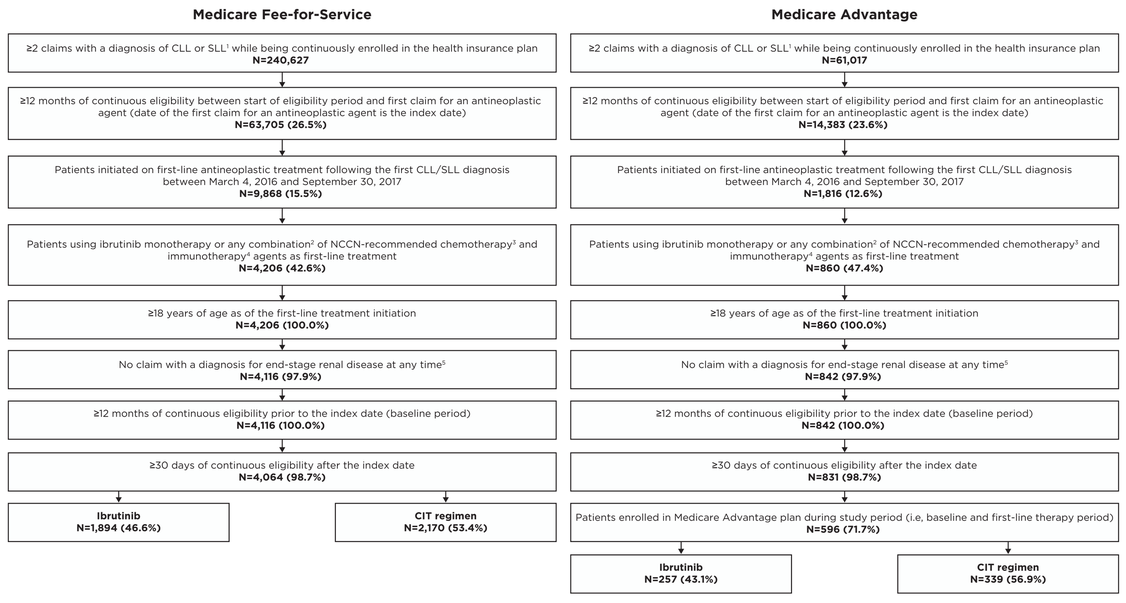
Study Design

- A retrospective cohort design was used to compare HRU and healthcare costs (Medicare spending) for patients receiving ibrutinib single agent (ibrutinib cohort) versus those receiving CIT (CIT cohort) as a 1L regimen
  - CIT regimen was defined as a combination of an NCCN-recommended chemotherapy agent with an NCCN-recommended immunotherapy agent with no claims for any other antineoplastic agent
- The index date (between 03/04/2016 and 09/30/2017; 03/04/2016 being the date of approval of ibrutinib in 1L for all patients) was defined as the date of initiation of 1L therapy with ibrutinib single agent or CIT
  - The start of the index period corresponded to the US approval date for ibrutinib in 1L therapy for all patients with CLL/SLL
  - The index period ended 3 months prior to the end of data availability to allow for ≥3 months of follow-up data accumulation by the end of study period
- The baseline period was defined as the 12-month period pre-index
- As per the prescribing information, continuous ibrutinib therapy is administered orally once daily until disease progression,[4] while CIT regimens containing anti-CD20 agents such as rituximab or obinutuzumab are typically given for up to six 28-day cycles (i.e., approximately six months)[12,13]; post-index, patients were evaluated during two different observation periods:
  - 1L Oncology Care Model (OCM) episode, defined as the period from 1L treatment initiation up to the earliest of six months post-initiation, end of continuous insurance eligibility, or lack of available follow-up data
    - The OCM was issued in 2016 by CMS to provide higher quality oncology care and offers a framework to evaluate healthcare costs as it monitors financial performance over a 6-month period (i.e., OCM episode) after treatment initiation[14]
  - 1L therapy period, defined as the total duration spanning from 1L treatment initiation up to the earliest of second-line treatment initiation, end of continuous insurance eligibility, or lack of available follow-up data; to represent an extended period beyond six months post-index, during which those in the ibrutinib cohort were expected to continue treatment while those in the CIT cohort should have completed planned treatment as indicated per prescribing guidelines[12,13]

Study Population

- Inclusion/exclusion criteria are shown in **Figure 1**

Figure 1. Study Population Selection — Medicare Fee-For-Service and Medicare Advantage



CIT=chemoimmunotherapy; CLL=chronic lymphocytic leukemia; NCCN=National Comprehensive Cancer Network; SLL=small lymphocytic lymphoma.

Notes:
[1]CLL diagnosis was identified using ICD-9 CM codes 204.1x and ICD-10 CM codes C91.1x. SLL diagnosis was identified using ICD-10 CM codes C83.0x.
[2]For combination therapy, the prescription date of each agent has to be within 30 days.
[3]Chemotherapy agents include bendamustine, chlorambucil, cyclophosphamide, cytarabine, doxorubicin, fludarabine, oxaliplatin, pentostatin, vincristine, lenalidomide, and cladribine.
[4]Immunotherapy agents include alemtuzumab, obinutuzumab, ofatumumab, and rituximab.
[5]End-stage renal disease diagnosis was identified using ICD-9 CM code 585.6, ICD-10 CM code N18.6, or the Medicare End-Stage Renal Disease Indicator.

Study Outcomes

- All-cause HRU and healthcare costs were evaluated during the 1L OCM episode and the 1L therapy period
  - For Medicare FFS, costs represented the amount paid by CMS Medicare. Since Part D plans are administered by private insurers, pharmacy costs from the CMS Medicare perspective were calculated as 68% of the gross drug cost above the out-of-pocket limit (GDCA) plus the amount paid for the drug by Part D low income subsidy, where 68% represents the average reinsurance amount paid by CMS in proportion of the GDCA in most recent years[15]
  - For MA, costs represented the amount paid by the private insurer

Statistical Analysis

- Differences in baseline characteristics between the ibrutinib and CIT cohorts were taken into account using inverse probability of treatment weighting (IPTW; see **Table 1** footnotes for the list of variables used in the propensity score calculation); characteristics with standardized differences <10% were considered as balanced when comparing the two study cohorts
- Comparisons of HRU and costs between the ibrutinib and CIT cohorts were conducted for Medicare FFS and MA populations, separately
- HRU were reported per-patient-per-month (PPPM) and compared between the two study cohorts using rate ratios (RRs) obtained from weighted generalized linear models (GLMs) with a Poisson distribution
- Healthcare costs were reported PPPM and compared between the two study cohorts using mean monthly cost differences (MMCDs) obtained from ordinary least square regressions
- Non-parametric bootstrap procedures were used to evaluate statistical significance and 95% confidence intervals (CIs) of RRs and MMCDs
- Cost outcomes were inflated to 2017 US dollars using the medical care component of the Consumer Price Index

RESULTS

Baseline Demographic and Clinical Characteristics

- In the Medicare FFS population, the weighted sample sizes (after IPTW) of the ibrutinib and CIT cohorts were 2,014 and 2,050, respectively (**Table 1**)
  - After IPTW, the cohorts were well-balanced with respect to baseline characteristics; in the weighted cohorts, the mean age was 75 years and approximately 40% of patients were females
- In the MA population, the weighted sample sizes (after IPTW) of the ibrutinib and CIT cohorts were 293 and 303, respectively (**Table 1**)
  - After IPTW, the cohorts were well-balanced with respect to baseline characteristics; in the weighted cohorts, the mean age was 75 years and approximately 45% of patients were females

Table 1. Demographic and Clinical Characteristics During the 12-Month Baseline Period - Weighted Populations

	Medicare Fee-for-Service[1]			Medicare Advantage[2]		
	Ibrutinib Weighted N = 2,014	CIT Weighted N = 2,050	Standardized difference (%)	Ibrutinib Weighted N = 293	CIT Weighted N = 303	Standardized difference (%)
Demographics						
Gender, female, n (%)	794 (39.4)	809 (39.5)	0.1%	131 (44.8)	135 (44.6)	0.5%
Age[3], mean ± SD [median]	74.6 ± 8.1 [74.1]	74.5 ± 7.8 [74.1]	1.9%	75.2 ± 6.8 [75.0]	74.7 ± 6.9 [74.0]	7.4%
Year and quarter of index date, n (%)						
2016	1,000 (49.6)	1,022 (49.9)	0.5%	117 (39.8)	117 (38.7)	2.3%
Q1	89 (4.4)	90 (4.4)	0.1%	8 (2.7)	5 (1.7)	7.4%
Q2	340 (16.9)	348 (17.0)	0.3%	36 (12.2)	42 (13.8)	4.7%
Q3	288 (14.3)	293 (14.3)	0.0%	30 (10.3)	33 (10.8)	1.5%
Q4	282 (14.0)	290 (14.2)	0.4%	43 (14.6)	38 (12.5)	6.0%
2017	1,015 (50.4)	1,028 (50.1)	0.5%	176 (60.2)	186 (61.3)	2.3%
Q1	346 (17.2)	354 (17.2)	0.2%	54 (18.3)	63 (20.7)	6.0%
Q2	322 (16.0)	326 (15.9)	0.3%	59 (20.2)	60 (19.9)	0.8%
Q3	346 (17.2)	348 (17.0)	0.5%	63 (21.6)	63 (20.7)	2.2%
Race, n (%)						
White	1,811 (89.9)	1,844 (90.0)	0.1%	-	-	-
African American	128 (6.4)	129 (6.3)	0.4%	-	-	-
Other/unknown	75 (3.7)	77 (3.8)	0.3%	-	-	-
Region, n (%)						
South	706 (35.1)	715 (34.9)	0.4%	130 (44.5)	133 (43.8)	1.5%
West	365 (18.1)	371 (18.1)	0.0%	56 (19.2)	61 (20.1)	2.3%
Midwest	513 (25.5)	521 (25.4)	0.1%	73 (25.0)	73 (24.0)	2.3%
Northeast	430 (21.4)	441 (21.5)	0.4%	32 (11.0)	36 (11.8)	2.5%
Unknown	0 (0.0)	0 (0.0)	-	1 (0.3)	1 (0.3)	0.2%
Medicaid dual eligibility status[3], n (%)						
Non-dual	1,745 (86.7)	1,777 (86.7)	0.2%	-	-	-
Partial-dual	84 (4.2)	85 (4.1)	0.1%	-	-	-
Full-dual	185 (9.2)	187 (9.1)	0.2%	-	-	-
Other/unknown	0 (0.0)	< 11 (< 0.5)	2.2%	-	-	-
Clinical characteristics						
Time between the first observed CLL/SLL diagnosis and the index date, months, mean ± SD [median]	32.9 ± 35.4 [20.5]	33.2 ± 38.2 [19.3]	0.9%	20.3 ± 20.9 [15.6]	18.8 ± 21.0 [12.6]	7.3%
Use of corticosteroids[4], n (%)	891 (44.2)	906 (44.2)	0.0%	112 (38.3)	117 (38.7)	0.8%
Quan-Charlson comorbidity index score[4], mean ± SD [median]	4.2 ± 2.3 [4.0]	4.2 ± 2.3 [4.0]	0.6%	4.3 ± 2.2 [4.0]	4.2 ± 2.2 [4.0]	1.1%

CIT=chemoimmunotherapy; CLL=chronic lymphocytic leukemia; SD=standard deviation; SLL=small lymphocytic lymphoma

Notes:
[1]For Medicare fee-for-service, variables used in the propensity score calculation included the following baseline characteristics: age category, gender, region, dual status, race, quarter of the index date, time from CLL/SLL diagnosis to the index date, Quan-Charlson comorbidity index score, baseline use of proton pump inhibitors, baseline use of corticosteroids, and comorbidities (lymphoma, hypertension, deficiency anemia, diabetes, coagulation deficiency, chronic pulmonary disease).
[2]For Medicare Advantage, variables used in the propensity score calculation included the following baseline characteristics: age, gender, region, year and quarter of index date, time from first CLL/SLL diagnosis to initiation of first-line therapy, Quan-Charlson comorbidity index score, comorbidities (neutropenia, lymphoma, atrial fibrillation, enlarged lymph nodes, thrombocytopenia, peripheral vascular disorder, liver disease, valvular disease, coagulation deficiency, sleep-wake disorders, and substance-related and addictive disorders), baseline use of corticosteroids, and baseline use of proton pump inhibitors.
[3]Evaluated at the index date.
[4]Evaluated during the 12-month baseline period.

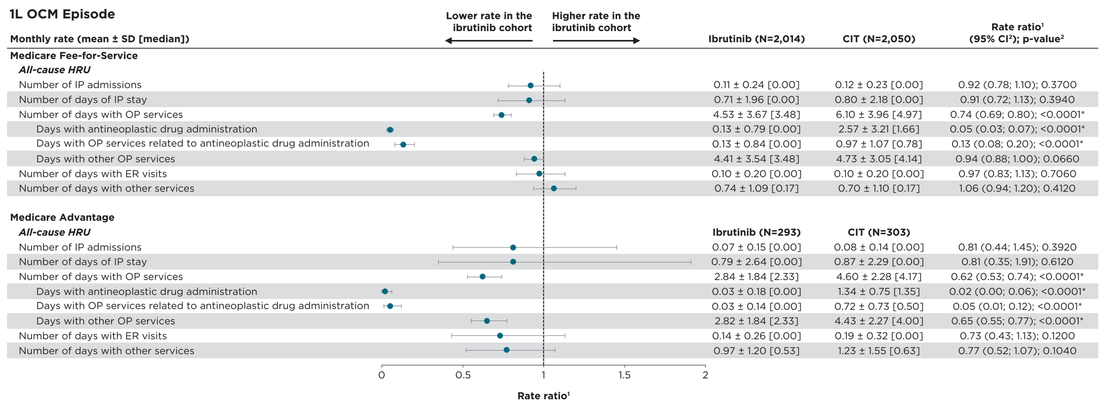
Comparison of HRU

- During the 1L OCM episode, patients in the ibrutinib cohort had significantly fewer days with OP services PPPM compared to those in the CIT cohort (FFS: RR=0.74, p<0.0001; MA: RR=0.62, p<0.0001), driven by fewer days with antineoplastic drug administration and OP services related to antineoplastic drug administration (**Figure 2**)
  - Additionally, MA beneficiaries in the ibrutinib cohort had fewer days with other OP services (i.e., unrelated to antineoplastic drug administration)
- Similarly, during the 1L therapy period, patients in the ibrutinib cohort had significantly fewer days with OP services PPPM compared to those in the CIT cohort (FFS: RR=0.86, p<0.0001; MA: RR=0.72, p<0.0001), driven by fewer days with antineoplastic drug administration and OP services related to antineoplastic drug administration (**Figure 2**)
  - Additionally, MA beneficiaries in the ibrutinib cohort had fewer days with other OP services

Figure 2. Comparison of HRU Between Ibrutinib Single Agent and CIT During the 1L OCM Episode and 1L Therapy Period among Medicare Fee-For-Service and Medicare Advantage Beneficiaries

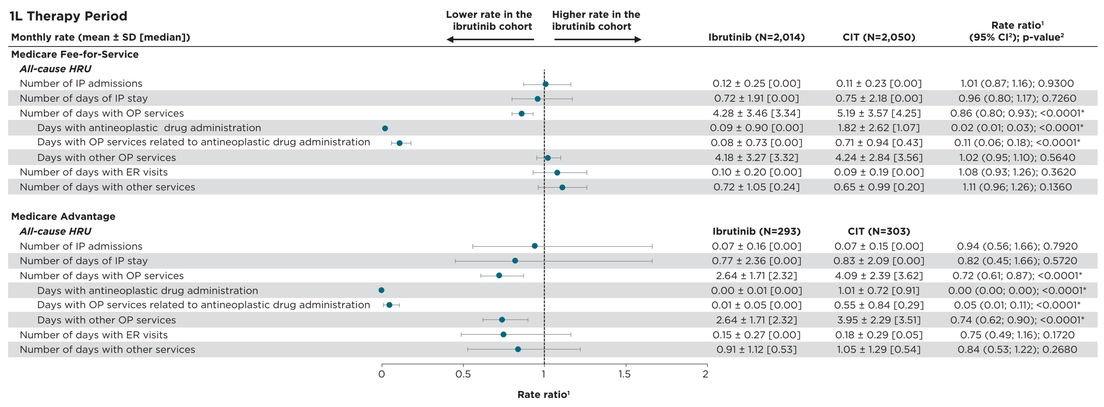
1L OCM Episode

Monthly rate (mean ± SD [median])	Ibrutinib (N=2,014)	CIT (N=2,050)	Rate ratio[1] (95% CI[2]); p-value[2]
Medicare Fee-for-Service			
All-cause HRU			
Number of IP admissions	0.11 ± 0.24 [0.00]	0.12 ± 0.23 [0.00]	0.92 (0.78; 1.10); 0.3700
Number of days of IP stay	0.71 ± 1.96 [0.00]	0.80 ± 2.18 [0.00]	0.91 (0.72; 1.13); 0.3940
Number of days with OP services	4.53 ± 3.67 [3.48]	6.10 ± 3.96 [4.97]	0.74 (0.69; 0.80); <0.0001*
Days with antineoplastic drug administration	0.13 ± 0.79 [0.00]	2.57 ± 3.21 [1.66]	0.05 (0.03; 0.07); <0.0001*
Days with OP services related to antineoplastic drug administration	0.13 ± 0.84 [0.00]	0.97 ± 1.07 [0.78]	0.13 (0.08; 0.20); <0.0001*
Days with other OP services	4.41 ± 3.54 [3.48]	4.73 ± 3.05 [4.14]	0.94 (0.88; 1.00); 0.0660
Number of days with ER visits	0.10 ± 0.20 [0.00]	0.10 ± 0.20 [0.00]	0.97 (0.83; 1.13); 0.7060
Number of days with other services	0.74 ± 1.09 [0.17]	0.70 ± 1.10 [0.17]	1.06 (0.94; 1.20); 0.4120
Medicare Advantage			
All-cause HRU	**Ibrutinib (N=293)**	**CIT (N=303)**	
Number of IP admissions	0.07 ± 0.15 [0.00]	0.08 ± 0.14 [0.00]	0.81 (0.44; 1.45); 0.3920
Number of days of IP stay	0.79 ± 2.64 [0.00]	0.87 ± 2.29 [0.00]	0.81 (0.35; 1.91); 0.6120
Number of days with OP services	2.84 ± 1.84 [2.33]	4.60 ± 2.28 [4.17]	0.62 (0.53; 0.74); <0.0001*
Days with antineoplastic drug administration	0.03 ± 0.18 [0.00]	1.34 ± 0.75 [1.35]	0.02 (0.00; 0.06); <0.0001*
Days with OP services related to antineoplastic drug administration	0.03 ± 0.14 [0.00]	0.72 ± 0.73 [0.50]	0.05 (0.01; 0.12); <0.0001*
Days with other OP services	2.82 ± 1.84 [2.33]	4.43 ± 2.27 [4.00]	0.65 (0.55; 0.77); <0.0001*
Number of days with ER visits	0.14 ± 0.26 [0.00]	0.19 ± 0.32 [0.00]	0.73 (0.43; 1.13); 0.1200
Number of days with other services	0.97 ± 1.20 [0.53]	1.23 ± 1.55 [0.63]	0.77 (0.52; 1.07); 0.1040



1L Therapy Period

Monthly rate (mean ± SD [median])	Ibrutinib (N=2,014)	CIT (N=2,050)	Rate ratio[1] (95% CI[2]); p-value[2]
Medicare Fee-for-Service			
All-cause HRU			
Number of IP admissions	0.12 ± 0.25 [0.00]	0.11 ± 0.23 [0.00]	1.01 (0.87; 1.16); 0.9300
Number of days of IP stay	0.72 ± 1.91 [0.00]	0.75 ± 2.18 [0.00]	0.96 (0.80; 1.17); 0.7260
Number of days with OP services	4.28 ± 3.46 [3.34]	5.19 ± 3.57 [4.25]	0.86 (0.80; 0.93); <0.0001*
Days with antineoplastic drug administration	0.09 ± 0.90 [0.00]	1.82 ± 2.62 [1.07]	0.02 (0.01; 0.03); <0.0001*
Days with OP services related to antineoplastic drug administration	0.08 ± 0.73 [0.00]	0.71 ± 0.94 [0.43]	0.11 (0.06; 0.18); <0.0001*
Days with other OP services	4.18 ± 3.27 [3.32]	4.24 ± 2.84 [3.56]	1.02 (0.95; 1.10); 0.5640
Number of days with ER visits	0.10 ± 0.20 [0.00]	0.09 ± 0.19 [0.00]	1.08 (0.93; 1.26); 0.3620
Number of days with other services	0.72 ± 1.05 [0.24]	0.65 ± 0.99 [0.20]	1.11 (0.96; 1.26); 0.1360
Medicare Advantage			
All-cause HRU	**Ibrutinib (N=293)**	**CIT (N=303)**	
Number of IP admissions	0.07 ± 0.16 [0.00]	0.07 ± 0.15 [0.00]	0.94 (0.56; 1.66); 0.7920
Number of days of IP stay	0.77 ± 2.36 [0.00]	0.83 ± 2.09 [0.00]	0.82 (0.45; 1.66); 0.5720
Number of days with OP services	2.64 ± 1.71 [2.32]	4.09 ± 2.39 [3.62]	0.72 (0.61; 0.87); <0.0001*
Days with antineoplastic drug administration	0.00 ± 0.01 [0.00]	1.01 ± 0.72 [0.91]	0.00 (0.00; 0.00); <0.0001*
Days with OP services related to antineoplastic drug administration	0.01 ± 0.05 [0.00]	0.55 ± 0.84 [0.29]	0.05 (0.01; 0.11); <0.0001*
Days with other OP services	2.64 ± 1.71 [2.32]	3.95 ± 2.29 [3.51]	0.74 (0.62; 0.90); <0.0001*
Number of days with ER visits	0.15 ± 0.27 [0.00]	0.18 ± 0.29 [0.05]	0.75 (0.49; 1.16); 0.1720
Number of days with other services	0.91 ± 1.12 [0.53]	1.05 ± 1.29 [0.54]	0.84 (0.53; 1.22); 0.2680



1L=first-line; CI=confidence interval; CIT=chemoimmunotherapy; ER=emergency room; HRU=healthcare resource utilization; IP=inpatient; OCM=Oncology Care Model; OP=outpatient; SD=standard deviation.

Notes:
[1]Rate ratios were calculated using weighted generalized linear models with Poisson distribution.
*[2]CIs and p-values were obtained from non-parametric bootstrap procedures using 500 replicates. * indicates a p-value <0.05.*

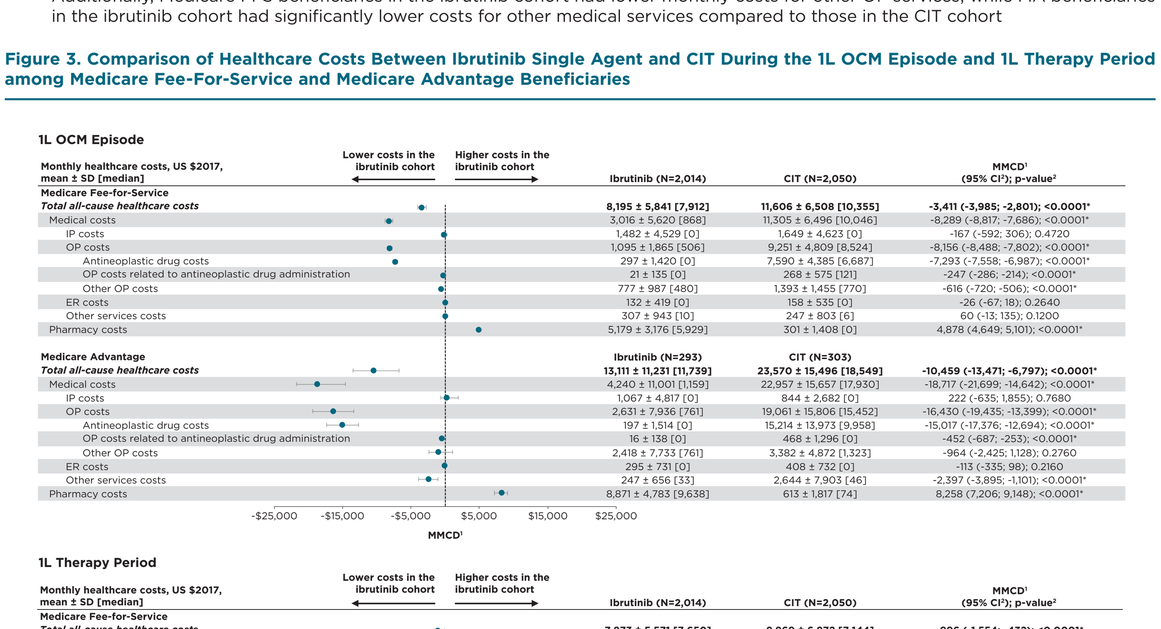
Comparison of Costs

- During the 1L OCM episode, total monthly all-cause cost savings were observed among patients in the ibrutinib cohort relative to the CIT cohort (FFS: -$3,411 PPPM, p<0.0001; MA: -$10,459 PPPM, p<0.0001), with lower monthly medical costs fully offsetting higher monthly pharmacy costs (**Figure 3**)
  - Lower monthly medical costs were driven by lower OP costs for antineoplastic drugs and their administration
  - Additionally, Medicare FFS beneficiaries in the ibrutinib cohort had lower monthly costs for other OP services
- During the 1L therapy period, total monthly all-cause cost savings were observed among patients in the ibrutinib cohort relative to the CIT cohort (FFS: -$996 PPPM, p<0.0001; MA: -$5,492 PPPM, p=0.0040), with lower monthly medical costs fully offsetting higher monthly pharmacy costs (**Figure 3**)
  - Lower monthly medical costs were driven by lower OP costs for antineoplastic drugs and their administration
  - Additionally, Medicare FFS beneficiaries in the ibrutinib cohort had lower monthly costs for other OP services, while MA beneficiaries in the ibrutinib cohort had significantly lower costs for other medical services compared to those in the CIT cohort

Figure 3. Comparison of Healthcare Costs Between Ibrutinib Single Agent and CIT During the 1L OCM Episode and 1L Therapy Period among Medicare Fee-For-Service and Medicare Advantage Beneficiaries

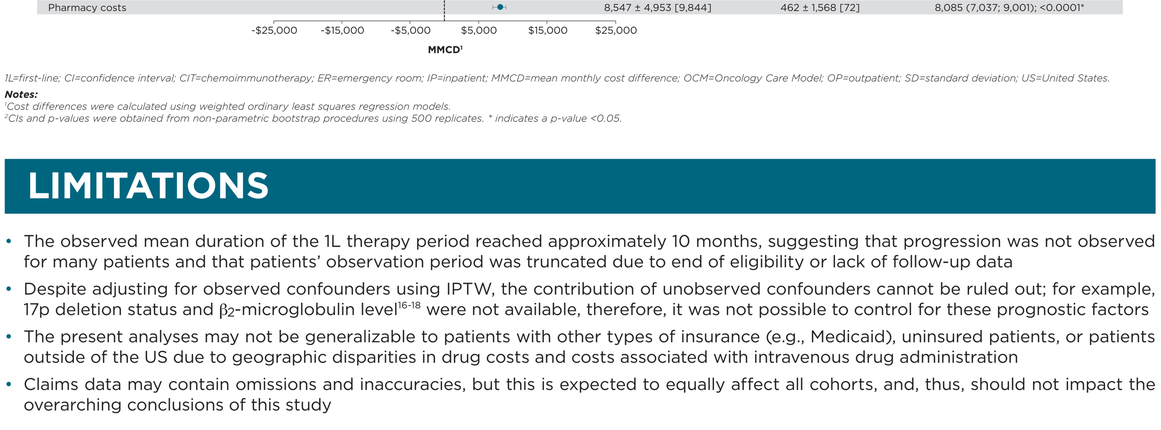
1L OCM Episode

Monthly healthcare costs, US $2017, mean ± SD [median]	Ibrutinib (N=2,014)	CIT (N=2,050)	MMCD[1] (95% CI[2]); p-value[2]
Medicare Fee-for-Service			
Total all-cause healthcare costs	**8,195 ± 5,841 [7,912]**	**11,606 ± 6,508 [10,355]**	**-3,411 (-3,985; -2,801); <0.0001***
Medical costs	3,016 ± 5,620 [868]	11,305 ± 6,496 [10,046]	-8,289 (-8,817; -7,686); <0.0001*
IP costs	1,482 ± 4,529 [0]	1,649 ± 4,623 [0]	-167 (-592; 306); 0.4720
OP costs	1,095 ± 1,865 [506]	9,251 ± 4,809 [8,524]	-8,156 (-8,488; -7,802); <0.0001*
Antineoplastic drug costs	297 ± 1,420 [0]	7,590 ± 4,385 [6,687]	-7,293 (-7,558; -6,987); <0.0001*
OP costs related to antineoplastic drug administration	21 ± 135 [0]	268 ± 575 [121]	-247 (-286; -214); <0.0001*
Other OP costs	777 ± 987 [480]	1,393 ± 1,455 [770]	-616 (-720; -506); <0.0001*
ER costs	132 ± 419 [0]	158 ± 535 [0]	-26 (-67; 18); 0.2640
Other services costs	307 ± 943 [10]	247 ± 803 [6]	60 (-13; 135); 0.1200
Pharmacy costs	5,179 ± 3,176 [5,929]	301 ± 1,408 [0]	4,878 (4,649; 5,101); <0.0001*
Medicare Advantage	**Ibrutinib (N=293)**	**CIT (N=303)**	
Total all-cause healthcare costs	**13,111 ± 11,231 [11,739]**	**23,570 ± 15,496 [18,549]**	**-10,459 (-13,471; -6,797); <0.0001***
Medical costs	4,240 ± 11,001 [1,159]	22,957 ± 15,657 [17,930]	-18,717 (-21,699; -14,642); <0.0001*
IP costs	1,067 ± 4,817 [0]	844 ± 2,682 [0]	222 (-635; 1,855); 0.7680
OP costs	2,631 ± 7,936 [761]	19,061 ± 15,806 [15,452]	-16,430 (-19,435; -13,399); <0.0001*
Antineoplastic drug costs	197 ± 1,514 [0]	15,214 ± 13,973 [9,958]	-15,017 (-17,376; -12,694); <0.0001*
OP costs related to antineoplastic drug administration	16 ± 138 [0]	468 ± 1,296 [0]	-452 (-687; -253); <0.0001*
Other OP costs	2,418 ± 7,733 [761]	3,382 ± 4,872 [1,323]	-964 (-2,425; 1,128); 0.2760
ER costs	295 ± 731 [0]	408 ± 732 [0]	-113 (-335; 98); 0.2160
Other services costs	247 ± 656 [33]	2,644 ± 7,903 [46]	-2,397 (-3,895; -1,101); <0.0001*
Pharmacy costs	8,871 ± 4,783 [9,638]	613 ± 1,817 [74]	8,258 (7,206; 9,148); <0.0001*



1L Therapy Period

Monthly healthcare costs, US $2017, mean ± SD [median]	Ibrutinib (N=2,014)	CIT (N=2,050)	MMCD[1] (95% CI[2]); p-value[2]
Medicare Fee-for-Service			
Total all-cause healthcare costs	**7,873 ± 5,571 [7,650]**	**8,869 ± 6,872 [7,144]**	**-996 (-1,554; -432); <0.0001***
Medical costs	2,792 ± 5,154 [991]	8,680 ± 6,800 [6,907]	-5,888 (-6,435; -5,313); <0.0001*
IP costs	1,497 ± 4,324 [0]	1,533 ± 4,510 [0]	-36 (-438; 400); 0.8360
OP costs	846 ± 1,073 [502]	6,781 ± 4,671 [5,670]	-5,935 (-6,222; -5,648); <0.0001*
Antineoplastic drug costs	65 ± 568 [0]	5,395 ± 4,114 [4,423]	-5,330 (-5,573; -5,085); <0.0001*
OP costs related to antineoplastic drug administration	13 ± 101 [0]	194 ± 476 [68]	-181 (-215; -153); <0.0001*
Other OP costs	768 ± 898 [492]	1,192 ± 1,295 [697]	-424 (-518; -327); <0.0001*
ER costs	131 ± 442 [0]	135 ± 412 [0]	-4 (-42; 40); 0.8340
Other services costs	317 ± 928 [16]	231 ± 745 [12]	86 (13; 159); 0.0240*
Pharmacy costs	5,081 ± 3,062 [5,664]	189 ± 1,123 [0]	4,892 (4,678; 5,103); <0.0001*
Medicare Advantage	**Ibrutinib (N=293)**	**CIT (N=303)**	
Total all-cause healthcare costs	**12,498 ± 11,037 [11,417]**	**17,990 ± 14,705 [14,049]**	**-5,492 (-8,351; -2,080); 0.0040***
Medical costs	3,952 ± 10,380 [1,199]	17,528 ± 14,776 [13,670]	-13,577 (-16,449; -10,092); <0.0001*
IP costs	842 ± 3,887 [0]	847 ± 2,980 [0]	-5 (-773; 1,231); 0.8840
OP costs	2,547 ± 7,950 [734]	14,663 ± 14,198 [11,328]	-12,117 (-14,782; -9,275); <0.0001*
Antineoplastic drug costs	3 ± 46 [0]	11,132 ± 11,634 [7,716]	-11,128 (-13,016; -9,042); <0.0001*
OP costs related to antineoplastic drug administration	13 ± 110 [0]	391 ± 1,734 [0]	-378 (-797; -153); <0.0001*
Other OP costs	2,531 ± 7,944 [734]	3,142 ± 5,265 [1,314]	-611 (-2,125; 1,378); 0.4280
ER costs	320 ± 853 [0]	378 ± 677 [41]	-58 (-294; 196); 0.5480
Other services costs	243 ± 611 [42]	1,641 ± 5,360 [44]	-1,398 (-2,322; -596); <0.0001*
Pharmacy costs	8,547 ± 4,953 [9,844]	462 ± 1,568 [72]	8,085 (7,037; 9,001); <0.0001*



1L=first-line; CI=confidence interval; CIT=chemoimmunotherapy; ER=emergency room; IP=inpatient; MMCD=mean monthly cost difference; OCM=Oncology Care Model; OP=outpatient; SD=standard deviation; US=United States.

Notes:
[1]Cost differences were calculated using weighted ordinary least squares regression models.
*[2]CIs and p-values were obtained from non-parametric bootstrap procedures using 500 replicates. * indicates a p-value <0.05.*

LIMITATIONS

- The observed mean duration of the 1L therapy period reached approximately 10 months, suggesting that progression was not observed for many patients and that patients' observation period was truncated due to end of eligibility or lack of follow-up data
- Despite adjusting for observed confounders using IPTW, the contribution of unobserved confounders cannot be ruled out; for example, 17p deletion status and β_2-microglobulin level[16-18] were not available, therefore, it was not possible to control for these prognostic factors
- The present analyses may not be generalizable to patients with other types of insurance (e.g., Medicaid), uninsured patients, or patients outside of the US due to geographic disparities in drug costs and costs associated with intravenous drug administration
- Claims data may contain omissions and inaccuracies, but this is expected to equally affect all cohorts, and, thus, should not impact the overarching conclusions of this study

CONCLUSIONS

- During the 1L OCM episode and the observed 1L therapy period, as well as for both Medicare FFS and MA beneficiaries, patients in the ibrutinib cohort had fewer monthly days with OP services and lower monthly total all-cause healthcare costs compared to patients in the CIT cohort, with savings in medical costs (driven by lower OP costs) fully offsetting higher pharmacy costs
- Therefore, HRU and cost reductions previously observed among US veterans and patients enrolled in commercial managed care plans[11,19,20] can also be generalized to both Medicare FFS and MA beneficiaries

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This study was supported by Janssen Scientific Affairs, LLC.