The impact of cost sharing on adherence to ibrutinib for patients with diffuse large B-cell lymphoma

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Abstract

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Purpose: Nonadherence with ibrutinib, an oral treatment for diffuse large B-cell lymphoma (DLBCL), has been associated with disease progression. We examined the relationship between out-of-pocket (OOP) ibrutinib costs and adherence to ibrutinib among new users with DLBCL.
Patients and Methods: We conducted a retrospective study using MarketScan® commercial and Medicare supplemental claims to identify adults with DLBCL who initiated ibrutinib therapy between October 1, 2015 and December 31, 2018 with ≥ 6 months of insurance coverage before and after initiation. Primary outcomes were adherence (proportion of days covered [PDC] ≥ 80%) and persistence at 180 days. We used multivariable logistic regression to estimate the odds of adherence and persistence at 180 days for patients with zero, low (below median of non-zero OOP costs) and high (above median of non-zero OOP costs) OOP costs.

Results: A total of 113 patients were included in the study. Monthly OOP costs for ibrutinib averaged $245 (median: $26, range: $0-$3765), and the mean PDC for ibrutinib was 67%. The odds of ibrutinib adherence trended lower for patients with higher OOP costs (adjusted odds ratio [aOR]: 0.8; 95% CI: 0.5, 1.3) following initiation, although findings failed to reach statistical significance. The odds of ibrutinib persistence at 180 days were similar across OOP cost groups (aOR: 1.0, 95% CI: 0.6-1.7).

Conclusion: Patients with higher OOP costs may be more likely to be nonadherent to ibrutinib. Persistence with ibrutinib was similar across OOP cost categories. Further research with larger sample sizes is warranted to evaluate this important relationship.

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Introduction

Ibrutinib is an oral Bruton's tyrosine kinase inhibitor taken for diffuse large B-cell lymphoma (DLBCL) and has been shown to increase survival in patients with non-germinal center B-cell-like (GCB) DLBCL.[1-5] However, previous studies have demonstrated that ibrutinib nonadherence is associated with disease progression and inferior survival outcomes.[6,7] An observational study evaluating the impact of nonadherence (proportion of days covered [PDC] < 80%) on survival outcomes found that nonadherence was associated with significantly worse progression-free (PFS) and overall survival in patients with non-Hodgkin's lymphoma. Of note, DLBCL is the most common subtype of non-Hodgkin's lymphoma, representing approximately 40% of cases.[6,8,9]

Treatment with ibrutinib is costly due to both drug price and treatment until progression.[5] Using average wholesale price (AWP), the estimated monthly cost of ibrutinib is $16,680, or more than $200,000 annually.[10] While these estimates do not reflect out-of-pocket (OOP) costs paid by patients, insurance plans are increasing cost-sharing measures as a means to control prescription drug costs.[11,12] Previous studies have shown that increased cost sharing reduces the use of and adherence to oral anticancer drugs.[13-16] However, no studies have evaluated the relationship between OOP costs and adherence to oral anticancer drugs in patients with DLBCL. This is despite DLBCL being a cancer in which roughly 40% of patients develop relapsed or refractory disease, leading to increased morbidity and mortality.[17-19] The objectives of our study were to examine variation in patient OOP costs for ibrutinib and estimate the association between OOP costs for ibrutinib and both adherence to and persistence with ibrutinib during the first 180 days of treatment for patients with DLBCL.

Methods

Study Design, Data Source, and Sample

We conducted a retrospective cohort study using insurance claims data to describe OOP ibrutinib costs. We then measured adherence to and persistence with ibrutinib during the first 180 days of treatment and evaluated whether there is an association between OOP ibrutinib costs and initial ibrutinib use.

We used data from the IBM MarketScan® Commercial Claims and Encounters and Medicare Supplemental database from 2015 to 2018, which contain the annual medical utilization and expenditures for inpatient, outpatient and prescription claims for over 41.2 million employees, their spouses, and their dependents who are covered under employer-sponsored private health insurance or Medicare supplemental insurance in the United States.[20]

We included adult patients with DLBCL who were new ibrutinib users between October 1, 2015 and December 31, 2018 (**Figure 1**). Patients with DLBCL were defined as having either ≥ 1 inpatient or ≥ 2 outpatient claims at least 30 days apart with an International Classification of Diseases, 10th revision (ICD-10) code for DLBCL. The first observed DLBCL claim was considered the diagnosis date. Ibrutinib use was defined as ≥ 1 outpatient prescription claim on or after the DLBCL diagnosis date. The first observed ibrutinib dispensing date was considered the index date. We defined new users of ibrutinib as those with no prior prescription claim in the 6-months prior to the index date. Patients were required to be ≥ 18 years at the index date and

have continuous enrollment with medical and prescription insurance ≥ 6 months before (pre-index period) and after index date (follow-up period).

Primary Outcomes

The primary outcomes were adherence to and persistence with ibrutinib therapy during the first 180 days following ibrutinib initiation. Adherence was defined as proportion of days covered (PDC). This measure represents the number of days that a patient had a medication available divided by the number of days in the study period, with an upper limit of 100%. Patients were considered adherent to ibrutinib if they had ≥ 80% of days with ibrutinib available during the 180-day follow-up period after initiating ibrutinib. A 180-day follow-up period was selected to balance two key considerations: the recommended chronic treatment for ibrutinib therapy and sample size.[5] Persistence was defined as the duration of time (days) from initiation to discontinuation of therapy. This measure is defined as the proportion of patients with ibrutinib available at the end of the 180-day follow-up period after initiating ibrutinib. We defined non-persistence as the first occurrence of a 30-day gap in ibrutinib availability for our primary analysis. A 60-day gap was employed in a sensitivity analysis.

Primary Independent Variable

The primary independent variable was OOP cost per 30-day supply of ibrutinib. We estimated OOP cost per 30-day supply of ibrutinib by dividing the total OOP costs for ibrutinib by the total days of supply within 180 days of initiation and then multiplied that value by 30 to standardize OOP cost to a 30-day supply of ibrutinib. We estimated OOP costs by summing copayments, coinsurance, and deductibles paid by the patient for ibrutinib prescriptions filled. Patients were

characterized as having zero, low (below median of non-zero OOP costs) and high (above median of non-zero OOP costs) OOP costs based on the distribution of the data. Costs were adjusted for inflation to 2018 dollars using the medical care component of the Consumer Price Index.[21]

Covariates

We included age, sex, health plan type (preferred provider organization [PPO] vs other), number of concomitant unique medication classes, and Charlson comorbidity index (CCI) as additional covariates. Clinical and demographic characteristics were assessed at the index date. The pre-index period was used to identify the number of concomitant unique medication classes and CCI for patients.[22-24] History of hematopoietic stem cell transplant (HSCT) was identified using claims starting from January 1, 2007, which was the earliest data available at the time of analysis.

Statistical Analysis

Demographic and clinical characteristics were summarized using descriptive statistics. Categorical variables were expressed using frequencies and percentages, and continuous variables using means and standard deviations. Unadjusted differences between zero, low, and high OOP cost groups were assessed using chi-squared tests for categorical variables and unpaired t-tests with unequal variances for continuous variables. We also created box plots of OOP cost per 30-day supply of ibrutinib by OOP cost groups. We used a multivariable logistic regression model to evaluate the association between OOP cost per 30-day supply of ibrutinib, and adherence and persistence at 180 days. Findings were presented as unadjusted and adjusted

odds ratios (ORs) with corresponding 95% confidence intervals (95% CIs) and p-values. For all statistical comparisons, we used a two-sided 5% significance level.

Sensitivity Analyses

To test the robustness of our findings, we conducted sensitivity analyses. First, we excluded deductibles from our OOP cost calculations. We excluded deductible payments to avoid overestimating OOP payment requirements since deductibles represent one-time payments that may not apply to subsequent fills and may primarily affect enrollees whose index date is at the start of the calendar year. Second, we varied our cut point for defining adherence from a PDC value of 80% to 70% and 90% to more fully understand how the choice for a cut point might have affected our results. Third, we calculated persistence with a discontinuation gap duration of 60 days or more.

SAS version 9.4 (SAS Institute Inc., Cary, NC) was used for constructing the analytic dataset and R version 3.5.2 (R Foundation for Statistical Computing, Vienna, Austria) for the statistical analyses.

Results

We started with 12,724 patients diagnosed with DLBCL on or after October 1, 2015. After applying eligibility criteria, 12,611 patients were excluded, resulting in 113 patients newly initiating ibrutinib included in the analysis (**Table 1**).

Patient characteristics are summarized in **Table 2**. The mean age was 63 years (standard deviation [SD], 16), and 38% were female. Mean PDC for the sample was 67% (SD, 29%). The proportion of patients who were adherent (PDC ≥80%) was 47%, and the proportion of patients who were persistent at 180 days was 50%. Patients in each OOP cost group were similar on most measured characteristics, although the mean age in the high OOP cost group was lower than in the zero and low OOP cost groups (58.7 years vs 66.5 vs 63.6, respectively). In addition, a greater proportion of patients in the zero OOP cost group were enrolled in PPO plans than in the low and high OOP cost groups (71.8% vs 45.9% vs 45.9%, respectively).

The majority of OOP costs were due to coinsurance (42.4%), despite only 21.2% of patients paying coinsurance. Conversely, the majority of patients (52.2%) paid copayments, which only comprised 30.4% of total OOP costs. Deductibles were paid by 15.9% of patients and made up 27.4% of total OOP costs.

Over the study period, mean OOP cost per 30-day supply of ibrutinib was $245 (SD, $568; median, $26; interquartile range [IQR], $126). There was little variation in OOP costs across the sample, with two-thirds of patients paying less than the non-zero median of $82 (**Figure 2**). However, OOP costs in the high OOP cost group varied widely (mean, $716; SD, $814; median, $576; IQR, $649).

Among new users of ibrutinib, approximately 54% of patients of the zero OOP cost group, 49% of the low OOP cost group, and 38% of the high OOP cost group were adherent during the first 180 days following initiation of ibrutinib (**Table 2**). For patients with higher OOP costs, the odds

of ibrutinib adherence were 19% lower (adjusted odds ratio [aOR]: 0.81; 95% CI: 0.49, 1.32), although this did not reach statistical significance (**Table 3**). Conversely, the odds of ibrutinib persistence at 180 days were similar across OOP cost groups (aOR: 1.02, 95% CI: 0.62-1.70). A test of heterogeneity indicated similar trends as demonstrated by a grouped linear model for both adherence and persistence, although these results did not reach statistical significance.

Sensitivity Analyses

Results from the sensitivity analyses in which we (1) excluded deductibles from the OOP cost calculations, (2) varied the definition of adherence to a PDC value ≥ 70% or ≥ 90%, and (3) changed the definition of a gap to more than 60 days of no ibrutinib availability were consistent with the primary analysis (**Supplemental Tables 1-3**).

Discussion

We conducted a retrospective cohort study using insurance claims data from 2015 through 2018 and found little variation in OOP costs per 30-day supply of ibrutinib across our sample; approximately two-thirds of patients paid less than $82. However, OOP costs in the high OOP cost group varied widely (median, $576; IQR, $649). We also found that higher OOP costs may be associated with lower adherence to ibrutinib, although statistical significance was not reached. We found no difference across OOP cost groups in persistence at 180 days. Of note, while adherence and persistence were both dichotomous variables, persistence is a cruder measure than adherence (e.g. using our discontinuation gap definition of 30 days, a nonadherent patient with a PDC of 52% can remain persistent). These findings should be interpreted in the context of likely limited power due to sample size. Nevertheless, our finding that higher OOP costs may be

associated with lower adherence to ibrutinib is important because insurance plans are increasingly using cost-sharing measures to control rising prescription drug costs. Thus, there could be unintentional negative health outcomes associated with employing cost-sharing measures since nonadherence to ibrutinib is associated with disease progression and poor survival outcomes.[6,7,11,12]

Our findings are consistent with the body of literature on adherence and OOP costs, but there are some notable differences between our study populations.[13,14,25,26] First, most of these studies were in the front-line setting.[13,14] Previous studies in other cancer types have shown that adherence worsened as line of therapy increased.[27,28] Similarly, we found low adherence overall (mean PDC = 67%) to ibrutinib, a second-line and subsequent therapy in DLBCL.[5,29] Second, most of these studies were in chronic myeloid leukemia (CML), which is an indolent cancer.[13,14] Patients may exhibit different behavior and price elasticity in a relapsed or refractory setting of a more aggressive cancer like DLBCL. Research focused on the price elasticity of specialty oncology drugs in metastatic cancers has found that cost sharing had a minimal effect on initiation and continuation of cancer therapy.[30,31] However, our study adds to a limited body of literature on cost sharing and adherence in the relapsed or refractory setting of DLBCL in which there is currently no standard of care and healthcare resource utilization is high.[29,32]

This study has several limitations. First, our measures of adherence and persistence were based on pharmacy claims, which represent an imperfect proxy for actual medication ingestion, similar to other claims-based adherence analyses. Second, our results may not be generalizable to other insured populations since our sample represents patients with employer-sponsored private health

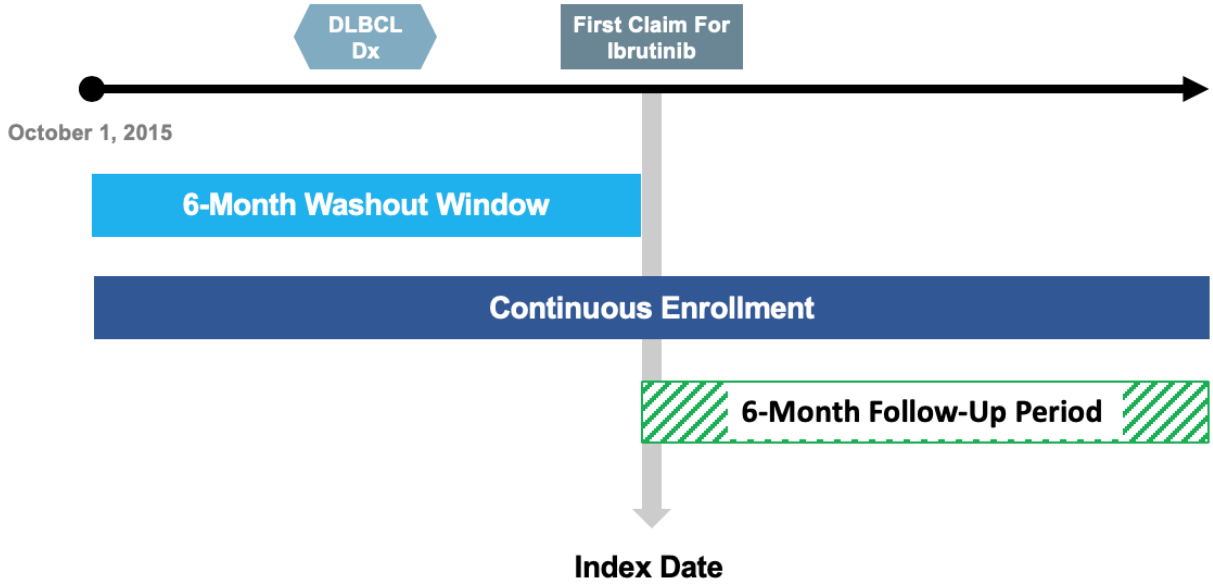
insurance or Medicare supplemental insurance. Our sample may represent a best-case scenario (i.e. generous insurance coverage) when evaluating the potential association between cost sharing and adherence. Over 99% of Medicare Part D stand-alone prescription drug plans and Medicare Advantage prescription drug plans charge an average coinsurance of 30% for imatinib, which is an oral anticancer agent used in CML.[13] In our analysis, the majority of OOP ibrutinib costs were due to coinsurance (42.4%), despite only 21.2% of patients in the sample paying coinsurance. Therefore, it is likely that fee-for-service Medicare and Medicare Advantage beneficiaries are at higher risk of cost-related discontinuation since OOP costs are likely to increase further among patients facing coinsurance requirements. Third, we were unable to determine reasons for nonadherence or non-persistence to ibrutinib. There are a variety of factors beyond OOP costs that may impact patient adherence to ibrutinib. Prior literature showed that reasons for interruptions in ibrutinib therapy typically included intolerance, disease progression, patient requests, and economic reasons.[33-37] A recent observational study showed that a monitoring program led by clinical pharmacists was able to address many of these factors and consequently, improve survival and tolerance to ibrutinib therapy. The program consisted of patient education for management of toxicities, adherence monitoring, interventions to reduce drug-drug interactions, and follow-up across the transition from hospital to community.[38] Continued testing of and scaling up effective programs like this will be important to improve adherence to oral cancer treatments, like ibrutinib, in order to improve patient outcomes. Fourth, we were unable to account for line of treatment as a potential effect modifier due to the shorter window of our analysis. However, we do not expect this to have significantly impacted our results since a recent retrospective claims analysis, also using MarketScan® claims data, found that ibrutinib was primarily used in the third-line setting of DLBCL.[29] Fifth, our study had a

limited sample size resulting in low statistical power and wide confidence intervals. In order to assess the power available in our study, we conducted separate post hoc power calculations for each pairwise comparison (three total) of unadjusted associations between OOP cost groups (zero, low, high) and prevalence of adherence (PDC ≥ 80%). All power calculations indicated insufficient power (range: 6.6% - 28.5%) to detect the ORs we observed in our study. In order to detect statistical significance of an OR as small as what we observed (β set to 80% and α set to 0.05), we conservatively estimated that we would have needed 1,450 patients in each OOP cost group. Lastly, because our study was observational, residual confounding may remain. Nevertheless, to the best of our knowledge, our study represents the first examination of the association between OOP costs and adherence to and persistence with ibrutinib among new users with DLBCL.

In summary, we conducted a retrospective cohort study using insurance claims data and found that higher OOP ibrutinib costs may be associated with lower adherence to ibrutinib in patients with DLBCL newly initiating ibrutinib therapy. Future research is needed with larger sample sizes and in more representative samples.

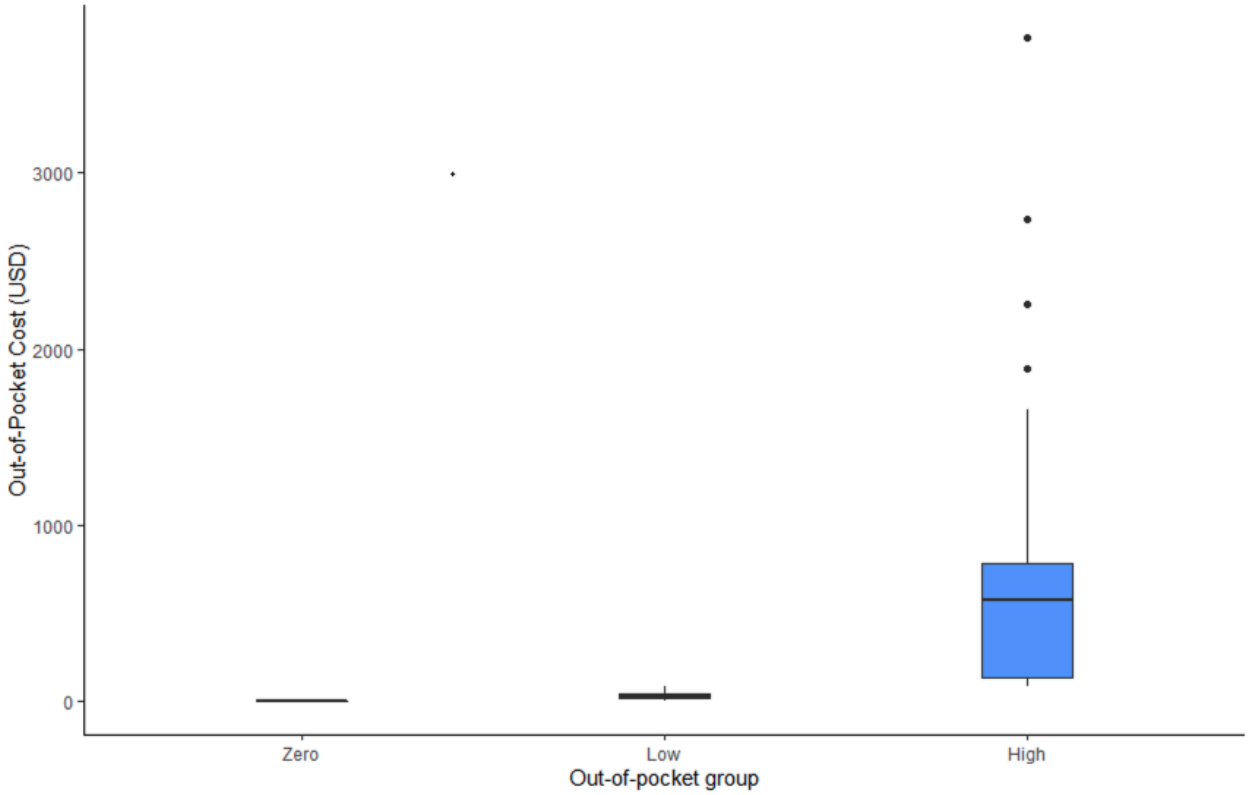
Figures

Figure 1. Study design



Abbreviations: DLBCL = diffuse large B-cell lymphoma; Dx = diagnosis

Figure 2. Out-of-pocket costs per 30-day supply of ibrutinib by out-of-pocket cost group



Note: Out-of-pocket costs are calculated by summing copayments, coinsurance and deductibles paid for ibrutinib fills standardized to a 30-day supply and adjusted for medical care inflation to 2018 dollars. Patients are characterized as having zero, low (below median of non-zero out-of-pocket costs) and high (above median of non-zero out-of-pocket costs).

Tables

Table 1. Cohort selection flowchart

Step	Inclusion Criteria	No. of observations	No. excluded
1	Patients diagnosed with DLBCL on or after October 1, 2015	12,724	
2	Patients who received ibrutinib after DLBCL diagnosis	238	12,486
3	Patients continuously enrolled in a medical and prescription plan for 6 months before and after index date[a]	135	103
4	Patients without ibrutinib use for 6 months before index date (washout period)	135	0
5	Patients with ibrutinib claims filled for 0-day supply	113	22

[a]Index date is defined as the first observed ibrutinib dispensing date within study period (October 1, 2015 to December 31, 2018)

Abbreviations: DLBCL = diffuse large B-cell lymphoma

Table 2. Characteristics of new ibrutinib users stratified by out-of-pocket cost group (n=113)

	Zero OOP Cost (n=39)	Low OOP Cost (n=37)	High OOP Cost (n=37)	P-value
Age, years				0.084
Mean	66.5	63.6	58.7	
SD	15.3	11.3	18.8	
Sex, n (%)				0.497
Male	27 (69.2%)	21 (56.8%)	22 (59.5%)	
Female	12 (30.8%)	16 (43.2%)	15 (40.5%)	
Region, n (%)				< 0.001
Northeast	25 (64.1%)	6 (16.2%)	3 (8.1%)	
North Central	3 (7.7%)	12 (32.4%)	8 (21.6%)	
South	9 (23.1%)	12 (32.4%)	20 (54.1%)	
West	2 (5.1%)	6 (16.2)	6 (16.2%)	
Unknown	0 (0.0%)	1 (2.7%)	0 (0.0%)	
Plan type, n (%)				0.032
PPO	28 (71.8%)	17 (45.9%)	17 (45.9%)	
Other and unknown[a]	11 (28.2%)	20 (54.1%)	20 (54.1%)	
Year of ibrutinib initiation, n (%)				0.502
2015	8 (20.5%)	2 (5.4%)	4 (10.8%)	
2016	11 (28.2%)	13 (35.1%)	12 (32.4%)	
2017	13 (33.3%)	16 (43.2%)	12 (32.4%)	
2018	7 (17.9%	6 (16.2%)	9 (24.3%)	
History of HSCT, n (%)	1 (2.6%)	5 (13.5%)	4 (10.8%)	0.214
No. of medications 3-months before index date				0.271
Mean	4.3	6.7	5.9	
SD	6.4	7.0	6.2	
Charlson comorbidity index, n (%)				0.239
0	13 (33.3%)	15 (40.5%)	17 (45.9%)	
1	8 (20.5%)	13 (35.1%)	11 (29.7%)	
2	13 (33.3%)	6 (16.2%)	4 (10.8%)	
3 or more	5 (12.8%)	3 (8.1%)	5 (13.5%)	
Out-of-pocket costs per 30-day supply of ibrutinib ($)				< 0.001
Mean	0	32.14	716.43	
SD	0	19.91	814.94	
Median	0	28.22	576.29	
Proportion of days covered (PDC)				0.948
Mean	0.68	0.66	0.67	
SD	0.31	0.30	0.28	
Adherence, n (%)				0.364
PDC ≥ 80%	21 (53.8%)	18 (48.6%)	14 (37.8%)	
PDC < 80%	18 (46.2%)	19 (51.4%)	23 (62.2%)	
Mean duration on ibrutinib (days)[b]				0.914
Mean	131.7	127.2	132.8	
SD	60.5	61.7	58.6	
Persistence at 180 days, n (%)				0.965
Persistent	19 (48.7%)	18 (48.6%)	19 (51.4%)	
Non-persistent	20 (51.3%)	19 (51.4%)	18 (48.6%)	

[a]Other and unknown plan type includes CDHP, HDHP, HMO, and POS
[b]Mean duration on ibrutinib is capped at 180 days
Note: Adherence is defined as having ≥ 80% of days with ibrutinib available during the 180-day period after ibrutinib initiation. Discontinuation is defined as having a gap of more than 30 days after the exhaustion of drug supply. Out-of-pocket costs are calculated by summing copayments, coinsurance and deductibles paid for ibrutinib fills standardized to a 30-day supply and adjusted for medical care inflation to 2018 dollars. Patients are characterized as having zero, low (below median of non-zero out-of-pocket costs) and high (above median of non-zero out-of-pocket costs).
Abbreviations: CDHP = consumer-driven health plan; HDHP = high-deductible health plan; HMO = health maintenance organization; HSCT = hematopoietic stem cell transplant; OOP = out-of-pocket; POS = point-of-service; PPO = preferred provider organization; SD = standard deviation

Table 3. Association between out-of-pocket cost, adherence, and persistence during the first 180 days after ibrutinib initiation

	Adherence				Persistence at 180 days			
Primary analysis	**OR**	**aOR[a]**	**95% CI**	**P-value**	**OR**	**aOR[a]**	**95% CI**	**P-value**
Grouped linear model	0.72	0.81	0.49, 1.32	0.400	0.89	1.02	0.62, 1.70	0.925
Test for heterogeneity								
Zero OOP group		1.00 (reference)				1.00 (reference)		
Low OOP group	0.81	1.01	0.38, 2.75	0.979	1.00	1.48	0.54, 4.16	0.452
High OOP group	0.52	0.66	0.24, 1.77	0.407	1.11	1.60	0.59, 4.46	0.363

[a]aOR was adjusted for the following covariates: age, sex, health plan type, number of concomitant unique therapeutic classes, and Charlson comorbidity index

Note: Adherence is defined as having ≥ 80% of days with ibrutinib available during the 180-day period after ibrutinib initiation. Discontinuation is defined as having a gap of more than 30 days after the exhaustion of drug supply. Out-of-pocket costs are calculated by summing copayments, coinsurance, and deductibles paid for ibrutinib fills standardized to a 30-day supply. Patients are characterized as having zero, low (below median of non-zero out-of-pocket costs) and high (above median of non-zero out-of-pocket costs).

Abbreviations: aOR = adjusted odds ratio, CI = confidence interval, OOP = out-of-pocket, OR = odds ratio, PDC = proportion of days covered

Supplementary Materials

Table 1. Association between out-of-pocket cost, adherence and persistence during the first 180 days after ibrutinib initiation excluding deductibles

	Adherence				Persistence at day 180			
Out-of-pocket costs	**OR**	**aOR[a]**	**95% CI**	**P-value**	**OR**	**aOR[a]**	**95% CI**	**P-value**
Excluding deductibles	0.73	0.82	0.50, 1.34	0.429	1.05	1.29	0.78, 2.15	0.325

[a]aOR was adjusted for the following covariates: age, sex, health plan type, number of concomitant unique therapeutic classes, and Charlson comorbidity index

Note: Adherence is defined as having ≥ 80% of days with ibrutinib available during the 180-day period after ibrutinib initiation. Discontinuation is defined as having a gap of more than 60 days after the exhaustion of drug supply. Out-of-pocket costs are calculated by summing copayments and coinsurance paid for ibrutinib fills standardized to a 30-day supply.

Abbreviations: aOR = adjusted odds ratio, CI = confidence interval, OOP = out-of-pocket, OR = odds ratio, PDC = proportion of days covered

Table 2. Association between out-of-pocket cost and adherence during the first 180 days after ibrutinib initiation using alternate adherence cutoffs

	Adherence			
Adherence cutoff	**OR**	**aOR[a]**	**95% CI**	**P-value**
PDC ≥ 70%	0.95	1.08	0.65, 1.82	0.746
PDC ≥ 90%	0.83	0.93	0.55, 1.55	0.769

[a]aOR was adjusted for the following covariates: age, sex, health plan type, number of concomitant unique therapeutic classes, and Charlson comorbidity index

Note: Adherence is defined as having ≥ 70% or ≥ 90% of days with ibrutinib available during the 180-day period after ibrutinib initiation. Patients are characterized as having zero, low (below median of non-zero out-of-pocket costs) and high (above median of non-zero out-of-pocket costs). Out-of-pocket costs are calculated by summing copayments, coinsurance and deductibles paid for ibrutinib fills standardized to a 30-day supply.

Abbreviations: aOR = adjusted odds ratio, CI = confidence interval, OOP = out-of-pocket, OR = odds ratio, PDC = proportion of days covered

Table 3. Association between out-of-pocket cost and persistence during the first 180 days after ibrutinib initiation using alternate gap of 60 days for discontinuation

	Persistence at day 180			
Discontinuation gap duration	**OR**	**aOR[a]**	**95% CI**	**P-value**
60 days	1.05	1.26	0.76, 2.10	0.368

[a]aOR was adjusted for the following covariates: age, sex, health plan type, number of concomitant unique therapeutic classes, and Charlson comorbidity index

Note: Discontinuation is defined as having a gap of more than 60 days after the exhaustion of drug supply. Out-of-pocket costs are calculated by summing copayments, coinsurance, and deductibles paid for ibrutinib fills standardized to a 30-day supply. Patients are characterized as having zero, low (below median of non-zero out-of-pocket costs) and high (above median of non-zero out-of-pocket costs).

Abbreviations: aOR = adjusted odds ratio, CI = confidence interval, OOP = out-of-pocket, OR = odds ratio, PDC = proportion of days covered

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