CLL-403

# Real-World Dosing Patterns and Time to Next Treatment for Previously Untreated Patients with Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma With or Without Ibrutinib Dose Reduction Following an Adverse Event

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## OBJECTIVE

Describe the dosing patterns and compare the TTNT following the first incident AE between patients with CLL/SLL who did and did not have DR of 1L ibrutinib

## CONCLUSIONS

In this real-world analysis, patients with DR following an incident AE had longer TTNT vs patients without DR
– These results are consistent for patients with cardiac AEs as well as those with non-cardiac AEs

Costs were lower among patients with DR relative to those without DR

Using TTNT as a marker for disease progression, these findings suggest that ibrutinib DR can be an effective strategy to manage AEs and maintain long-term treatment persistence while delaying disease progression

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## INTRODUCTION

- Ibrutinib, a once-daily oral Bruton's tyrosine kinase inhibitor (BTKi), is the only targeted therapy to demonstrate significant progression-free survival and overall survival benefit in multiple phase 3 studies for chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)[1-6]
- There is flexibility within the prescribing information for ibrutinib, with specific guidelines for dose reductions (DR) for management of different types of adverse events (AEs)
- In clinical trials, efficacy outcomes were similar for patients with DR compared to patients without DR;[7,8] however, real-world data on ibrutinib dosing patterns and the association between DR and outcomes remain scarce

## METHODS

### Data Source

- The data comprised inpatient and outpatient medical claims, pharmacy claims, and estimated costs of medical services, obtained through Optum's de-identified Clinformatics® Data Mart Database

### Study Design and Population

- Adults with CLL/SLL who initiated first-line (1L) single-agent ibrutinib at 420 mg on or after February 12, 2014, and had an AE after 1L treatment initiation were identified
- The sample was divided into 2 cohorts:
  - Patients with DR, defined as those who had a DR from the starting dose of 420 mg following the first incident AE
  - Patients without DR, defined as those who remained on 420 mg for the entire duration of 1L therapy

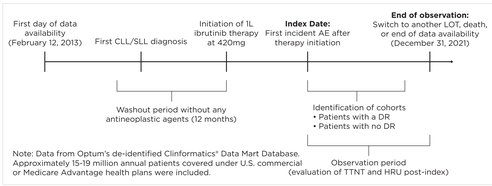
### Study Outcomes

- TTNT: time from the first incident AE to either first dose of a next treatment (any non-ibrutinib therapy), a gap of >90 days between the last day of supply of ibrutinib and the date of the next ibrutinib claim, or death
  - Evaluated for all patients analyzed and further stratified by those with and without cardiac AEs
- Patients without a next treatment or death were censored at the end of their continuous health insurance eligibility or the end of data availability
- All-cause and CLL-related comprehensive costs (patient + payer perspectives) and health resource utilization (HRU) were evaluated from the first incident AE to line of therapy (LOT) end and were reported per patient per month (PPPM)
  - Costs were adjusted to 2021 US dollar (USD) using the medical care component of the Consumer Price Index

### Statistical Analysis

- Baseline characteristics were reported using descriptive statistics
- TTNT was compared using univariate Cox proportional hazards models
- All-cause and CLL-related costs from incident AE to end of LOT were compared using t-tests
- Additional methods regarding study design, population, and outcomes are in the Supplement, accessible via QR code

### Study Design




Note: Data from Optum's de-identified Clinformatics® Data Mart Database. Approximately 15-19 million annual patients covered under U.S. commercial or Medicare Advantage health plans were included.

## RESULTS

- Among 658 patients and CLL/SLL with an incident AE included in this study, 95 (14%) had a DR and 563 (86%) did not have a DR following an AE (**Figure S1**)

### Baseline Characteristics[a] Were Similar Between Patients With and Without DR

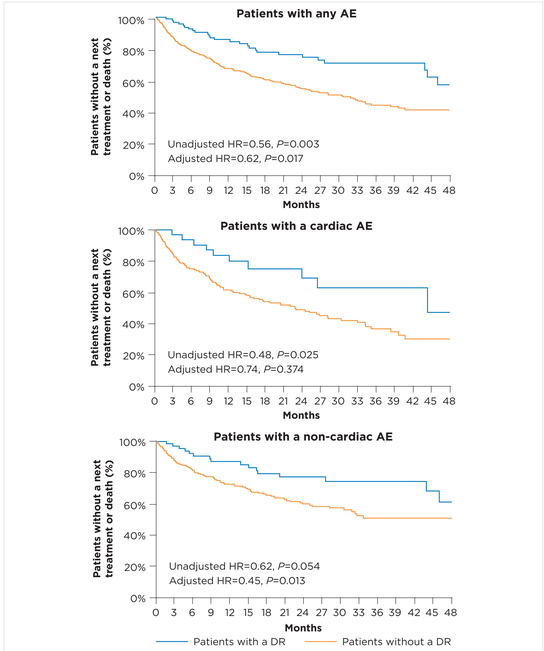
| | Patients With DR N=95 | Patients Without DR N=563 |
|---|---|---|
| Female, n (%) | 38 (40) | 206 (37) |
| Age[b], mean ± SD [median], years | 74 ± 10 [75] | 72 ± 10 [73] |
| Region[b], n (%) | | |
| *South* | 31 (33) | 196 (35) |
| *Midwest* | 28 (30) | 146 (26) |
| *West* | 19 (20) | 156 (28) |
| *Northeast/unknown* | 17 (18) | 65 (12) |
| Race[b], n (%) | | |
| *White* | 77 (81) | 418 (74) |
| *Non-White* | 18 (19) | 145 (26) |
| | Total Population (N=658)[c] | |
| *Hispanic* | 73 (11) | |
| *Black* | 39 (6) | |
| *Asian* | 12 (2) | |
| *Unknown* | 39 (6) | |
| Insurance plan type[b], n (%) | | |
| *Medicare Advantage* | 80 (84) | 461 (82) |
| *Commercial insurance* | 15 (16) | 102 (18) |
| Year of initiation of 1L therapy, n (%) | | |
| *2014-2016* | 11 (12) | 80 (14) |
| *2017* | 20 (21) | 77 (14) |
| *2018* | 21 (22) | 115 (20) |
| *2019* | 23 (24) | 146 (26) |
| *2020-2021* | 20 (21) | 145 (26) |
| Time between first CLL diagnosis observed in the data and initiation of 1L therapy, mean ± SD [median], months | 33 ± 35 [23] | 25 ± 27 [17] |
| Quan-Charlson comorbidity index, mean ± SD [median] | 4 ± 2 [4] | 4 ± 2 [3] |
| Elixhauser comorbidities, n (%) | | |
| *Renal failure* | 28 (30) | 94 (17) |
| *Solid tumor without metastasis* | 19 (20) | 62 (11) |
| DSM-5 mental comorbidities, n (%) | 31 (33) | 246 (44) |
| CLL-related and ibrutinib/acalabrutinib–related AEs and other events, n (%) | | |
| *Infections* | 53 (56) | 271 (48) |
| *Musculoskeletal pain (including arthralgia)* | 45 (47) | 224 (40) |
| *Fatigue/weakness* | 36 (38) | 164 (29) |
| *Abdominal pain* | 21 (22) | 71 (13) |
| Any gastrointestinal event or use of an antacid, n (%) | 25 (26) | 142 (25) |
| Corticosteroid use, n (%) | 35 (37) | 188 (33) |
| Use of proton pump inhibitors, n (%) | 22 (23) | 122 (22) |
| All-cause HRU PPPM, mean ± SD [median] | | |
| *Number of outpatient visits* | 1.84 ± 1.26 [1.50] | 1.69 ± 1.06 [1.42] |
| *Number of inpatient admissions* | 0.02 ± 0.05 [0.00] | 0.02 ± 0.05 [0.00] |
| Total all-cause costs, comprehensive perspective, 2021 USD, mean ± SD [median] | 2368 ± 2860 [1442] | 2219 ± 2872 [1276] |

DSM-5, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; SD, standard deviation.
[a]Baseline characteristics were evaluated during the 12 months preceding the index therapy line. [b]Evaluated at initiation of 1L therapy. [c]Categories with <11 patients were combined with other categories to ensure patient confidentiality.

### Duration of 1L Therapy and Time Between First Incident AE and End of 1L Therapy, but not Time to First Incident AE, Were Longer Among Patients With DR

| | Patients With DR | Patients Without DR |
|---|---|---|
| Duration of 1L therapy, mean (median), days | 922 (842) | 735 (606) |
| Time to the first incident AE, mean (median), days | 161 (51) | 227 (119) |
| Time between first incident AE and end of 1L therapy, mean (median), days | 761 (725) | 508 (352) |

### Patients With a DR After an AE Had a Longer TTNT Than Patients Without a DR




HR, hazard ratio.

### Patients With a DR Had Significantly Lower Costs (All-Cause and CLL-Related) Compared With Patients Without a DR

| | Patients with DR N=95 | Patients without DR N=563 | *P*-value |
|---|---|---|---|
| Duration of time period of interest, mean ± SD [median], months | 25.4 ± 16.6 [24.2] | 17.0 ± 15.5 [11.8] | - |
| HRU PPPM, mean ± SD [median] | | | |
| All-cause HRU | | | |
| *Number of outpatient visits* | 2.71 ± 1.68 [2.43] | 2.87 ± 3.24 [2.08] | 0.457 |
| *Number of inpatient admissions* | 0.05 ± 0.10 [0.00] | 0.14 ± 0.41 [0.00] | <0.001* |
| *Number of ED visits* | 0.10 ± 0.15 [0.04] | 0.22 ± 1.41 [0.00] | 0.043* |
| *Number of visits for other services*[a] | 0.58 ± 0.68 [0.34] | 0.73 ± 1.70 [0.37] | 0.153 |
| CLL-related HRU[b] | | | |
| *Number of outpatient visits* | 1.14 ± 1.13 [0.95] | 1.33 ± 2.43 [0.76] | 0.237 |
| *Number of inpatient admissions* | 0.04 ± 0.08 [0.00] | 0.09 ± 0.29 [0.00] | <0.001* |
| *Number of ED visits* | 0.03 ± 0.09 [0.00] | 0.04 ± 0.30 [0.00] | 0.398 |
| *Number of visits for other services*[a] | 0.20 ± 0.35 [0.04] | 0.24 ± 0.66 [0.00] | 0.333 |
| Costs PPPM, mean ± SD [median] | | | |
| All-cause costs, 2021 USD | | | |
| *Total* | 14,558 ± 6236 [14,602] | 19,992 ± 29,150 [15,076] | <0.001* |
| *Medical* | 3960 ± 5800 [1822] | 10,592 ± 29,072 [2325] | <0.001* |
| *Outpatient* | 1848 ± 2348 [983] | 2778 ± 11,820 [858] | 0.093 |
| *Inpatient* | 1878 ± 4316 [0] | 7174 ± 25,983 [0] | <0.001* |
| *ED* | 152 ± 265 [33] | 431 ± 3325 [0] | 0.051 |
| *Other services*[a] | 82 ± 145 [28] | 210 ± 1228 [26] | 0.018* |
| *Pharmacy* | 10,598 ± 3883 [11,945] | 9400 ± 5921 [12,510] | 0.012* |
| CLL-related costs, 2021 USD | | | |
| *Total* | 12,698 ± 5124 [13,071] | 16,006 ± 23,594 [14,028] | 0.003* |
| *Medical* | 2335 ± 4167 [644] | 6884 ± 23,260 [924] | <0.001* |
| *Outpatient* | 766 ± 1626 [335] | 1185 ± 4786 [217] | 0.111 |
| *Inpatient* | 1492 ± 3659 [0] | 5540 ± 22,675 [0] | <0.001* |
| *ED* | 60 ± 186 [0] | 125 ± 1092 [0] | 0.188 |
| *Other services*[a] | 17 ± 43 [2] | 34 ± 185 [0] | 0.058 |
| *Pharmacy* | 10,363 ± 3831 [11,624] | 9122 ± 5928 [12,144] | 0.008* |

*$P \leq 0.05$. ED, emergency department.
[a]Other services include durable medical equipment and dental and vision care. [b]CLL-related HRU and medical costs were defined as the subset of claims and costs for claims with a diagnosis for CLL in any position. CLL-related pharmacy costs were defined as costs for claims for agents used in the treatment of CLL.

- DR was significantly associated with a lower risk of starting a next treatment or death both in patients with cardiac and non-cardiac AEs, although this difference did not reach statistical significance for the cardiac AE subgroup after adjusting for baseline and time-varying covariates
- Patients with a DR had a lower mean number of all-cause inpatient admissions (0.05 vs 0.14; $P<0.001$) and lower mean number of ED visits (0.10 vs 0.22; $P=0.043$) compared with patients without a DR

### Limitations

- Causal association between an AE and subsequent DR cannot be inferred from the claims database due to the cross-sectional nature of this study
- Reasons for DR were not available in the Optum database
- A claim for a medication did not necessarily indicate its use
- As DR occurred post-index date, patients with a DR may have been subject to immortal time bias. Time-varying Cox proportional hazard models were used to mitigate potential bias introduced by this method
- Multivariable model adjustment may have been subject to residual confounding due to unmeasured confounders

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