CLL-410

# Adherence and Discontinuation among Medicare Beneficiaries Initiating Venetoclax vs. BTKis for Relapsed/Refractory Chronic Lymphocytic Leukemia

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## OBJECTIVE

To examine real-world adherence and discontinuation of venetoclax vs. BTKis in older adults with relapsed/refractory (R/R) CLL

## CONCLUSIONS

Elderly (≥66 years) adults with R/R CLL treated with venetoclax had higher adherence and lower discontinuation rates relative to BTKi-treated patients over 12 months from initiation, despite having poorer clinical characteristics.

These differences in treatment pattern outcomes may reflect better tolerability or effectiveness (i.e., lack of progression) on venetoclax relative to BTKis (primarily ibrutinib) in a real-world population of elderly (≥66 years) patients.

These favorable results for venetoclax in this large real-world study are encouraging and support the goal of developing well-tolerated novel combinations for elderly (≥66 years) adults.

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## INTRODUCTION

- Compelling clinical trial data for BCL2 (i.e. venetoclax) and BTK inhibitors (BTKis) have led to a paradigm shift in chronic lymphocytic leukemia (CLL) treatment.
  - Venetoclax was first approved for previously treated relapsed/refractory CLL (with or without 17p deletion) in June 2018
- However, contemporary real-world studies comparing these oral medication classes remain limited, with real-world adherence and discontinuation in patients treated with venetoclax vs. BTKis uncertain.
- This evidence is particularly lacking in the Medicare population, a federally funded health insurance program for elderly (>65 years) or disabled individuals in the US
  - CLL is most prevalent in the elderly population, who primarily receive coverage through the Medicare program
  - Given the stringent eligibility criteria of clinical trials, elderly patients with multiple comorbidities may be excluded from participation

## METHODS

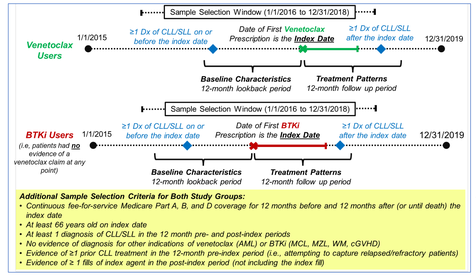
### Study Design

- Retrospective claims analysis using 2015-2019 100% Medicare claims data

### Sample Selection

- All fee-for-service Medicare beneficiaries age ≥66 years newly initiating venetoclax between 1/1/2016 and 12/31/2018 were identified
- From the remaining individuals during the same time period, we also identified patients newly initiating a BTKi
- See **Figure 1** for additional sample selection criteria

### Figure 1. Study Schematic




### Outcomes

- Treatment outcomes in the 12-month post-index period included:
  - *Adherence* (proportion of days covered [PDC] ≥ 0.80)
  - *Discontinuation* (evidence of a 90-day consecutive gap in treatment [sensitivity analyses: 60 and 120-day gaps]).

### Analysis

- Logistic regressions controlling for differences in sociodemographic and clinical characteristics between the two study groups were used to estimate adjusted outcomes.

## RESULTS

- The final sample contained 711 and 1,566 mutually exclusive groups of beneficiaries initiating venetoclax and BTKis, respectively

### Table 1. Sample Characteristics

| | Venetoclax Group | | BTKi Group* | | p-value |
|---|---|---|---|---|---|
| **Characteristic** | **N** | **%** | **N** | **%** | |
| N | 711 | 100% | 1566 | 100% | |
| Age, mean (SD) | 75.6 (6.0) | | 77.6 (6.9) | | <.0001 |
| Male | 424 | 59.6% | 932 | 59.5% | 0.957 |
| White | >631 | >88.7% | 1390 | 88.8% | 0.8368 |
| Urban | 601 | 84.5% | 1236 | 78.9% | 0.0017 |
| Receiving Full or Partial Part D Low-Income Subsidy (LIS) | 63 | 8.9% | 229 | 14.6% | 0.0001 |
| Number of Elixhauser comorbidities in the 12-month pre-index | | | | | 0.0003 |
| 0 | n<11 | <1.5% | 20 | 1.3% | |
| 1-2 | 69 | 9.7% | 170 | 10.9% | |
| 3-4 | 128 | 18.0% | 343 | 21.9% | |
| 5-7 | >223 | >31.4% | 557 | 35.6% | |
| 8-10 | 185 | 26.0% | 346 | 22.1% | |
| 11+ | 95 | 13.4% | 130 | 8.3% | |
| CLL treatments around index drug initiation in the 4-week pre-index and 8-weeks post-index periods | | | | | |
| None (i.e. venetoclax or BTK only and none of the drugs below) | 325 | 45.7% | 1079 | 68.9% | |
| Obinutuzumab | 49 | 6.9% | 66 | 4.2% | 0.0069 |
| Rituximab | 164 | 23.1% | 304 | 19.4% | 0.0456 |
| BTK Inhibitors | 181 | 25.5% | N/A | N/A | |
| Other CLL treatments (not listed above) | 79 | 11.1% | 213 | 13.6% | 0.0995 |
| Number of prior CLL agents in the 12-month pre-index period | | | | | |
| 1-2 | 599 | 84.2% | 1399 | 89.3% | |
| 3-4 | 93 | 13.1% | 144 | 9.2% | |
| 5+ | 19 | 2.7% | 23 | 1.5% | |
| Type of prior CLL treatments in the 12-month pre-index period | | | | | |
| Chemotherapy +/- CD20 | 155 | 21.8% | 814 | 52.0% | <.0001 |
| PI3K +/- CD20 | 82 | 11.5% | 58 | 3.7% | <.0001 |
| BTKi +/- CD20 | 493 | 69.3% | 0 | 0.0% | <.0001 |
| CD20 monotherapy | 74 | 10.4% | 677 | 43.2% | <.0001 |
| All-cause hospitalization in the 12-month pre-index period | 363 | 51.1% | 665 | 42.5% | 0.0001 |
| Index year | | | | | <.0001 |
| 2016 | 72 | 10.1% | 601 | 38.4% | |
| 2017 | 206 | 29.0% | 524 | 33.5% | |
| 2018 | 433 | 60.9% | 441 | 28.2% | |
| Died during follow-up | 155 | 21.8% | 315 | 20.1% | 0.3571 |

**BTKi group consisted almost exclusively of patients treated with ibrutinib, though some patients were using acalabrutinib.*

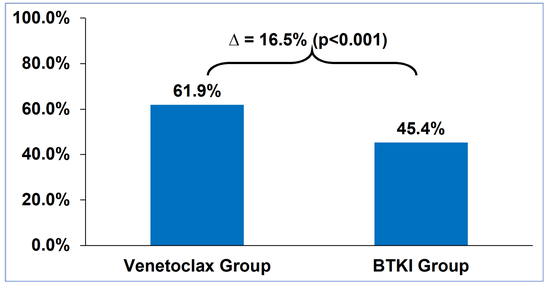
- Compared to BTKi initiators, those initiating venetoclax tended to be slightly younger but had poorer clinical characteristics (for example, 39.4% vs. 30.4% with ≥8 comorbidities, 15.8% vs.10.7% with ≥ 3 prior CLL agents and 51.5% vs. 42.5% with any hospitalization in the 12-months pre-index). (**Table 1**)
- **Table 2** displays unadjusted treatment pattern outcomes
  - The mean number of 30-day refills was 8.5 (SD 4.0) for venetoclax patients and 7.8 (SD 4.0) for BTKi patients.
  - Compared to the BTKi group, the venetoclax group had a higher unadjusted rate of adherence (57.9% vs. 47.3%) and a lower unadjusted rate of discontinuation (32.8% vs. 45.1%).
  - Sensitivity analyses using a 60-day gap (38.5% vs. 50.5%) and 120-day gap (27.8% vs. 40.2%) to define discontinuation also showed a lower rate in the venetoclax vs. BTKi group.

### Table 2. Unadjusted Treatment Pattern Outcomes

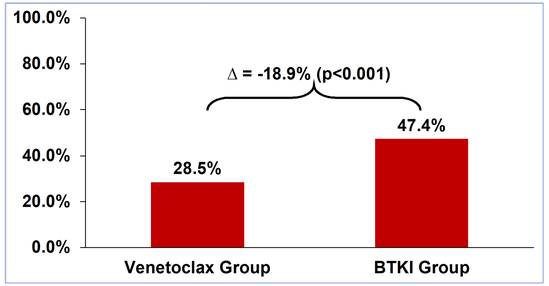
| | Venetoclax Group | | BTKi Group | |
|---|---|---|---|---|
| | **N** | **%** | **N** | **%** |
| N | 711 | 100% | 1566 | 100% |
| Number of 30-day refills, mean (SD) | 8.5 (4.0) | | 7.8 (4.0) | |
| 2 fills | 75 | 10.5% | 172 | 11.0% |
| 3 to 5 fills | 127 | 17.9% | 402 | 25.7% |
| 6 to 8 fills | 99 | 13.9% | 236 | 15.1% |
| 9 to 11 fills | 134 | 18.8% | 287 | 18.3% |
| 12 fills | 135 | 19.0% | 233 | 14.9% |
| 13 fills | 120 | 16.9% | 209 | 13.3% |
| 14 or more fills | 21 | 3.0% | 27 | 1.7% |
| | | | | |
| Adherent (PDC ≥0.80) | 412 | 57.9% | 741 | 47.3% |
| Discontinuation (≥90-day gap) - primary definition | 233 | 32.8% | 706 | 45.1% |
| Discontinuation (≥60-day gap) - sensitivity analysis definition | 274 | 38.5% | 791 | 50.5% |
| Discontinuation (≥120-day gap) - sensitivity analysis definition | 198 | 27.8% | 629 | 40.2% |

- **Figure 2** and **Figure 3** display the risk-adjusted outcomes.
  - After risk-adjustment, the venetoclax group had an even higher adherence rate than the BTKi group (61.9% vs. 45.4%, p<.0001).
  - Similarly, the risk-adjusted rate of discontinuation (90-day gap) was even lower for the venetoclax group compared to the BTKi group (28.5% vs. 47.4%, p<0.001).

### Figure 2. Risk-Adjusted* Rate of Adherence




### Figure 3. Risk-Adjusted* Rate of Discontinuation




** Risk-adjusted outcomes estimated from logistic regressions controlling for the following factors: age, sex, race, census region, metropolitan status, Part D low income subsidy status, Part D drug benefit type, number of Elixhauser comorbidities, use of CD20 therapy, number of prior CLL agents, all-cause hospitalization, index year, and death during follow-up.*

## LIMITATIONS

- Claims-based measure of adherence/discontinuation only captured medication filled at pharmacy; cannot be certain patient took as directed
- Despite risk adjustment, there could still be unobserved confounders between the the venetoclax and BTKI groups that could bias results