

# Cost-Savings Associated With Venetoclax-Obinutuzumab Versus Covalent Bruton's Tyrosine Kinase Inhibitor in Frontline Chronic Lymphocytic Leukemia: A Real-World Study

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## OBJECTIVE

To examine healthcare costs before and after completion of the fixed-duration treatment (FDT) period for venetoclax plus obinutuzumab (VenO) relative to continuous treat-to-progression therapies, like covalent Bruton's tyrosine kinase inhibitors (cBTKis), for frontline (1L) chronic lymphocytic leukemia (CLL)

## CONCLUSIONS

This real-world study of patients with CLL demonstrates a substantial reduction in monthly healthcare costs in the VenO group after the 12-month FDT period, largely driven by reduced CLL-related prescription drug costs

These findings, consistent with previous studies, support the economic benefits of VenO, which offers patients a treatment-free period, relative to treat-to-progression therapies like cBTKis (alone or in combination with anti-CD20 agents [cBTKi ± anti-CD20])

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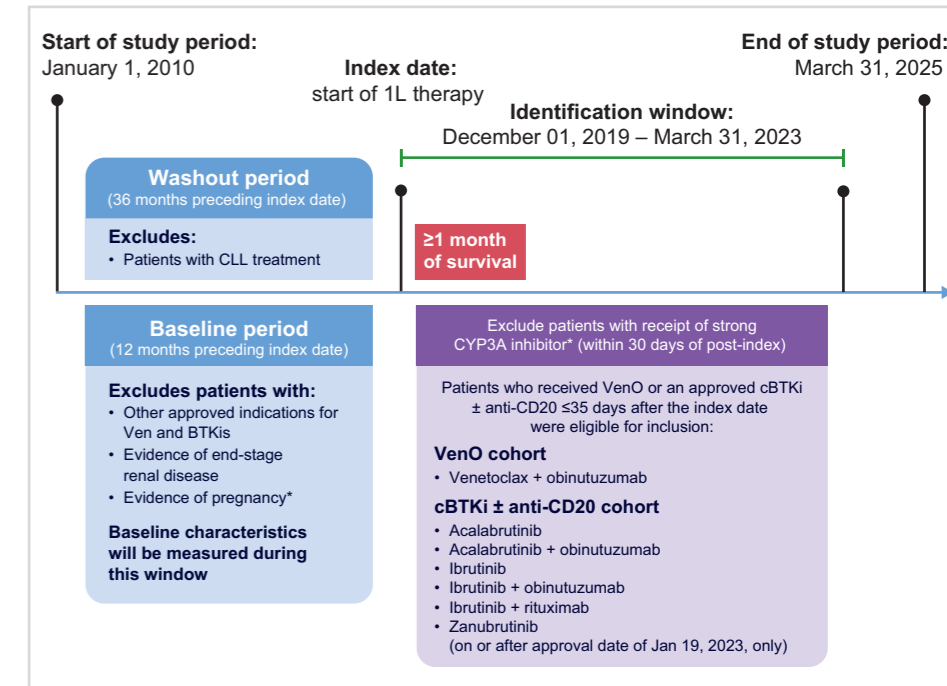
## INTRODUCTION

- CLL is the most common adult leukemia, with a median age at diagnosis ~ 70 years old<sup>1</sup>
- The treatment landscape for CLL has improved with the advancement of targeted therapies, including cBTKis (eg, first-generation ibrutinib or second-generation acalabrutinib and zanubrutinib) and B cell lymphoma-2 (BCL-2) inhibitors (eg, venetoclax monotherapy or in combination with the anti-CD20 agent obinutuzumab [VenO])<sup>2</sup>
  - Acalabrutinib in combination with venetoclax as a FDT was also recently approved for 1L CLL<sup>3,4</sup>
- Oral cBTKis as monotherapy or plus anti-CD20 agents are typically administered in a continuous “treat-to-progression” approach, requiring indefinite therapy until disease progression or intolerance, which extends treatment duration and can substantially increase cumulative costs<sup>5</sup>
- Unlike oral cBTKis, VenO is a fixed-duration, chemotherapy-free 1L regimen for CLL that has been shown to achieve deep remissions with a defined treatment period, typically 12 months<sup>5,6</sup>
  - FDT has the potential to reduce costs through the avoidance of continuous treatment exposure
- Here we report healthcare costs associated with VenO compared with cBTKi ± anti-CD20 for 1L CLL over a 24-month period, representing 12 month- on-treatment and off-treatment periods with VenO

## METHODS

- This US-based retrospective cohort study utilized the Optum Clinformatics DataMart from 01/2010–03/2025 and included adult patients with CLL who received 1L VenO or cBTKi ± anti-CD20 regimens between 12/2019–03/2023 and had continuous enrollment ≥24 months after 1L initiation (**Figure 1**)
  - Cohorts were balanced (standardized mean difference [SMD] ≤0.1) using stabilized inverse probability of treatment weighting (IPTW)
    - Demographic and clinical variables in the propensity score (PS) model included age at index, Charlson comorbidity index, region, atrial fibrillation, sex, hypertension, insurance, race, time to 1L initiation, arrhythmias, and baseline all-cause costs
  - Healthcare cost measures included all-cause and CLL-related per-patient-per-month (PPPM) total, prescription, and medical costs
  - PPPM costs were captured during Months 1–12 (on-treatment period for VenO) and Months 13–24 (off-treatment period for VenO) after 1L initiation
    - PPPM all-cause and CLL-related costs were compared between cohorts using a weighted generalized estimating equation (GEE) model
    - Imbalanced variables in the PS model (Northeast [SMD=0.11] and age at index [SMD=−0.10]) were included in the weighted GEE model

Figure 1. Study Design



\*Required to keep study consistent with label. 1L, frontline; CLL, chronic lymphocytic leukemia.

## RESULTS

### Baseline characteristics and demographics

- The final sample included 915 patients (VenO: n=154; cBTKi ± anti-CD20: n=761), with similar baseline characteristics between groups (**Table 1**)

Table 1. Unweighted baseline characteristics and demographics overall and among VenO- and cBTKi ± anti-CD20–treated groups

	VenO (n=154)	cBTKi ± anti-CD20 (n=761)	Total (N=915)
Mean age at 1L initiation, years (SD)	69.3 (9.8)	75.4 (7.9)	74.4 (8.6)
Mean time to 1L, months (SD)	32.4 (27.3)	37.3 (34.4)	36.5 (33.4)
Sex			
Female	45 (29.2)	322 (42.3)	367 (40.1)
Male	109 (70.8)	439 (57.7)	548 (59.9)
Race and ethnicity			
White	117 (76.0)	584 (76.7)	701 (76.6)
Black/African-American	10 (6.5)	87 (11.4)	97 (10.6)
Asian	3 (1.9)	10 (1.3)	13 (1.4)
Unknown/missing	24 (15.6)	80 (10.1)	104 (11.4)
US region <sup>a</sup>			
South	64 (41.6)	258 (33.9)	322 (35.2)
West	32 (20.8)	244 (32.1)	276 (30.2)
Midwest	46 (29.9)	190 (25.0)	236 (25.8)
Northeast	12 (7.8)	68 (8.9)	80 (8.7)
Type of insurance			
Commercial	47 (30.5)	85 (11.2)	132 (14.4)
Medicare	107 (69.5)	676 (88.8)	783 (85.6)
Year of 1L initiation			
2019	3 (1.9)	19 (2.5)	22 (2.4)
2020	28 (18.2)	214 (28.1)	242 (26.4)
2021	49 (31.8)	242 (31.8)	291 (31.8)
2022	54 (35.1)	219 (28.8)	273 (29.8)
2023	20 (13.0)	67 (8.8)	87 (9.5)
Cardiovascular disorders			
Atrial fibrillation	17 (11.0)	88 (11.6)	105 (11.5)
Other cardiac arrhythmias	15 (9.7)	86 (11.3)	101 (11.0)
Hypertension	105 (68.2)	534 (70.2)	639 (69.8)
Charlson Comorbidity Index			
0	0 (0.0)	9 (1.2)	9 (1.0)
1	0	0	0
2	77 (50.0)	308 (40.5)	385 (42.1)
3+	77 (50.0)	444 (58.3)	521 (56.9)
1L therapy			
Acalabrutinib	0 (0.0)	319 (41.9)	319 (34.9)
Acalabrutinib + obinutuzumab	0 (0.0)	30 (3.9)	30 (3.3)
Ibrutinib	0 (0.0)	369 (48.5)	369 (40.3)
Ibrutinib + obinutuzumab	0 (0.0)	6 (0.8)	6 (0.7)
Ibrutinib + rituximab	0 (0.0)	23 (3.0)	23 (2.5)
Venetoclax + obinutuzumab	154 (100)	0 (0.0)	154 (16.8)
Zanubrutinib	0 (0.0)	14 (1.8)	14 (1.5)

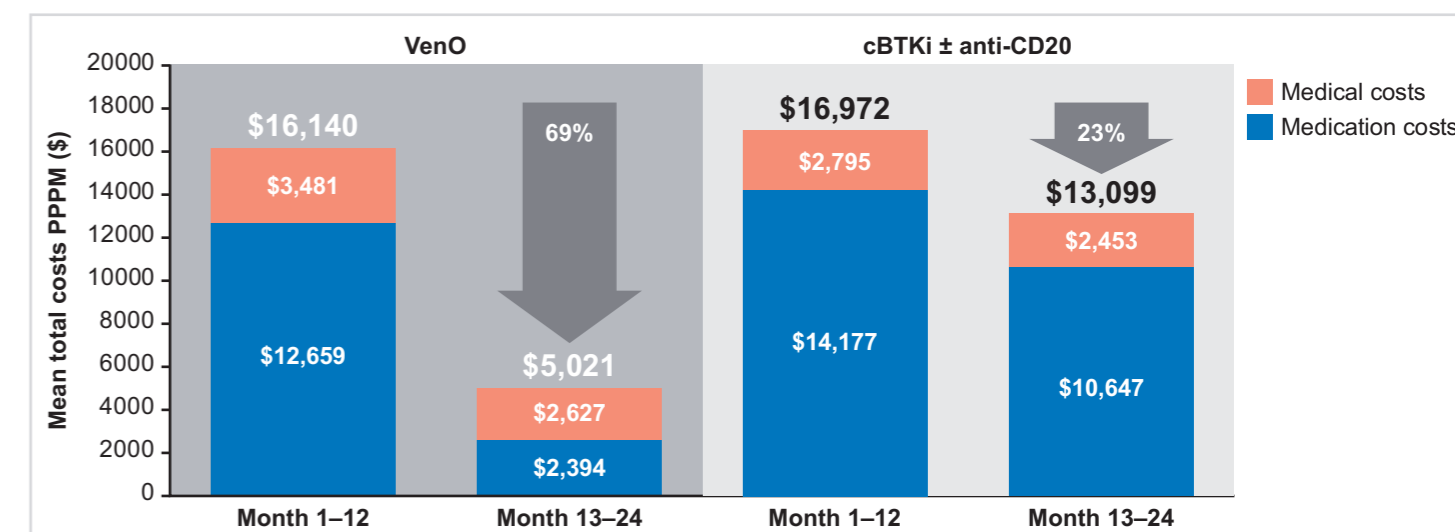
<sup>a</sup>Baseline was defined as the 12 months preceding 1L initiation.

<sup>b</sup>1 patient missing from the cBTKi ± anti-CD20 group.

1L, frontline; cBTKi, covalent Bruton's tyrosine kinase inhibitors; VenO, venetoclax plus obinutuzumab.

### Healthcare resource utilization and costs

Figure 2. Threefold greater relative reduction in unweighted all-cause total costs (PPPM) for VenO vs cBTKi ± anti-CD20 from Month 1–12 to Month 13–24

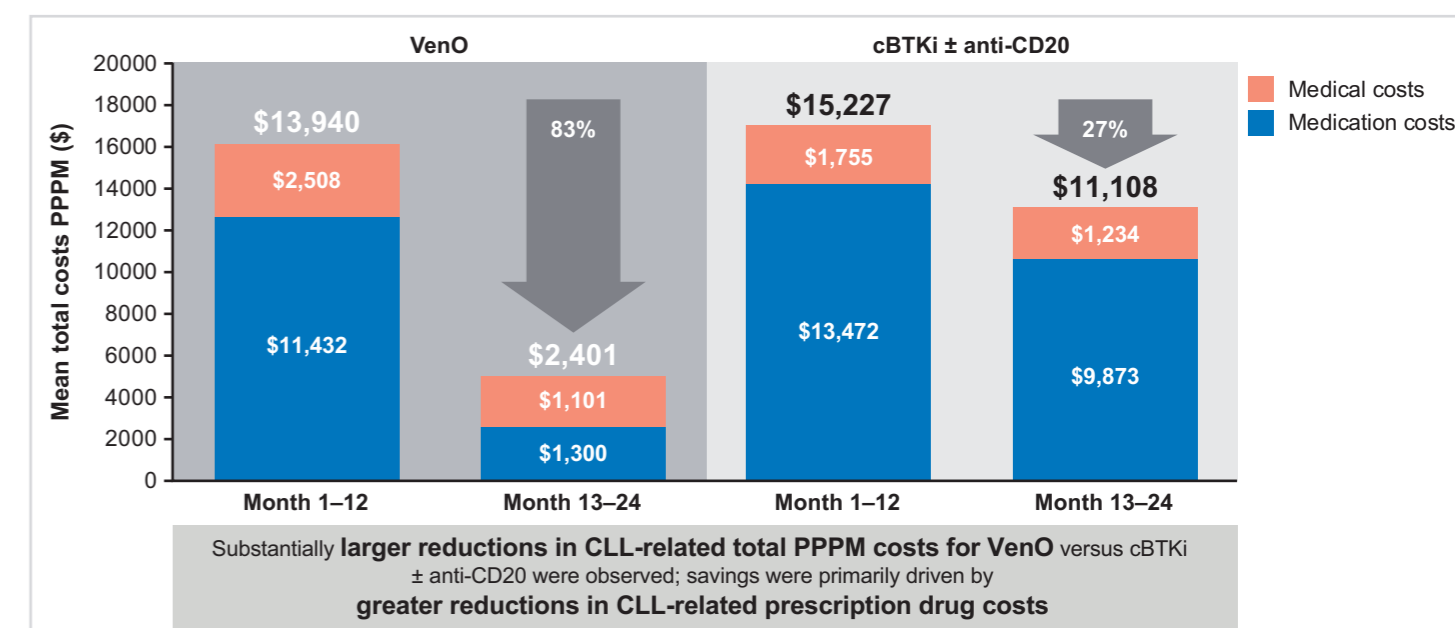


cBTKi, covalent Bruton's tyrosine kinase inhibitors; PPPM, per patient per month; VenO, venetoclax plus obinutuzumab.

- Between Months 1–12, unweighted mean all-cause total costs PPPM were slightly lower for VenO (\$16,140) than cBTKi ± anti-CD20 patients (\$16,972) (**Figure 2**)
- During Months 13–24, unweighted all-cause total costs PPPM declined by 69% for VenO patients (\$16,140 to \$5,021) and 23% for cBTKi ± anti-CD20 patients (\$16,972 to \$13,099)

The **weighted estimated cost savings PPPM** during the off-treatment period for patients treated with VenO versus cBTKi ± anti-CD20 was **\$6,430** (95% CI: \$7,843–\$5,018; p<0.0001)

Figure 3. Threefold greater relative reduction in unweighted CLL-related costs (PPPM) for VenO vs cBTKi ± anti-CD20 from Month 1–12 to Month 13–24



cBTKi, covalent Bruton's tyrosine kinase inhibitors; PPPM, per patient per month; VenO, venetoclax plus obinutuzumab.

- Between Months 1–12, unweighted mean CLL-related costs PPPM were also slightly lower for VenO (\$13,940) than cBTKi ± anti-CD20 patients (\$15,227) (**Figure 3**)
- During Months 13–24, unweighted CLL-related costs PPPM declined by 83% for VenO patients (\$13,940 to \$2,401) and 27% for cBTKi ± anti-CD20 patients (\$15,227 to \$11,107)

### Limitations

- Claims data are subject to limitations including coding errors, incomplete clinical details or unmeasured confounders, and baseline differences between cohorts that could bias results; however, PS-derived stabilized IPTW was applied to balance observed covariates
- Requirement for ≥24 months of continuous enrollment may limit generalizability, as patients with shorter follow-up were excluded
  - However, this approach was necessary to evaluate treatment-cost outcomes during/after the VenO FDT period
- Other 1L fixed-duration combinations (eg, Ven + ibrutinib) were not assessed