EE365

COST-MINIMIZATION AND BUDGET IMPACT ANALYSIS OF VENETOCLAX PLUS OBINUTUZUMAB COMPARED WITH ACALABRUTINIB IN THE FIRST LINE AND R/R CHRONIC LYMPHOCYTIC LEUKEMIA FROM THE BRAZILIAN PRIVATE HEALTHCARE PERSPECTIVE

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Presented at the ISPOR Europe 2022, Nov 06-09

INTRODUCTION

Chronic Lymphocytic Leukemia (CLL) is a lymphproliferative disease caracterized by the persistency of a minimum of 5 × 10^9/L type B monoclonal lymphocytes, which can accumulate in periferal blood, lymph nodes, blood marrow and spleen. More frequent in elders and considered a rare disease, CLL has a global incidence between <1 and 5.5 cases per 100,000 inhabitants. (1,2)

CLL is an indolent disease, in which about 60% of patients at the time of diagnosis may be assymtomatic, while other 40% may have several inespecific clinical and laboratory changes. (3,4) Patients with IGHV unmutated may present faster disease progression compared to IGHV mutated and presence of 17p deletion, TP53 mutation may indicate worse clinical results specially when treated with immuno chemotherapy.(1)

Among therapies available for untreated CLL, venetoclax in combination with obinutuzumab is an oral administered, fixed duration therapy that targets the BCL-2 (B-Cell Leukemia/Lymphoma 2 Gene) inhibitor, exhibiting significant apoptotic activity, while acalabrutinib is also an oral administered, inhibitor of Bruton's tyrosine kinase, continuous treatment until disease progression or unacceptable toxicity. (5)

According to the recently ANS RoI (Brazilian mandatory coverage list), CLL patients are contemplated with ibrutinib and acalabrutinib, as well as venetoclax in first line for untreated CLL and R/R patients. This provides more treatment options for the patient and enables the physician to evaluate the best therapeutic strategy ensuring the best outcome for the patient and the healthcare system.

OBJECTIVE

To perform a cost-minimization and budget impact (BI) analysis of venetoclax + obinutuzumab (VenO), venetoclax + rituximab (VenR), versus acalabrutinib monotherapy (acala) in the 1L and relapse or refractory (R/R) chronic lymphocytic leukemia (CLL) treatment from the Brazilian Private Healthcare perspective.

METHODS

The network meta-analysis from (6) presented similar overall survival (OS) and progression-free survival (PFS) between VenO and acalabrutinibe in 1L-CLL. The head-to-head trial comparing acalabrutinib and ibrutinib (7) and the indirect comparison of VenR with B-cell receptor inhibitors (8) were used as assumption of similar efficacy between VenR and acala in R/R-CLL.

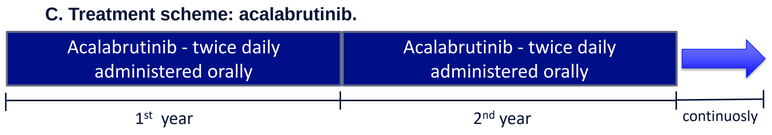
In a systematic review developed by authors, it was not found any direct-comparison between venetoclax and acalabrutinib. Therefore it was developed a cost-minimization analysis assuming equivalency in therapeutic efficacy between VenR and acalabrutinib.

Considering the similar efficacy, a cost-minimization model was developed, and it included only the drug acquisition costs based on 2022 Brazilian list price (9). Total treatment cost over 5 years were compared. The BI model was performed for the treatments included in this study and considering the total estimated patients in the private market over 5 years.

Figure 1 A. Treatment scheme: venetoclax + obinutuzumab

B. Treatment scheme: venetoclax + rituximab

C. Treatment scheme: acalabrutinib.



Obinutuzumab starts with 100mg on Day 1, ramping up to 900mg on Day 2 and 1000mg on Day 8 and 15 (cycle 1) and continue the same dose in each Day 1 until end of the 6th month (cicles 2 to 6).(10) The daily oral venetoclax regimen was initiated on day 22 of cycle 1, starting with a 5-week dose ramp-up (1 week each of 20, 50, 100, and 200 mg, then 400 mg daily for 1 week), thereafter continuing at 400 mg daily until completion of cycle 12 (Figure 1). The initial dose of venetoclax is 20mg (02 tablets of 10mg), weekly ramping-up untill reaching 400mg (04 tablets of 100mg) at the begining of week 5. From that point on patient will follow the maintenance 400mg dosage per day until the end of the 12th month. Rituximab dose calculation was based on patients body surface area, defined according to Mosteller formula, based on Brazilian antropometric data, weight: 67.2 kg, hight:164.5 cm, body surface area: 1.75 m². (11) Acalabrutinib dose is 100 mg, twice daily (equivalent to a total daily dose of 200 mg) (12, 13).

Table 1 shows SKU, list price (9), dosage and treatment monthly cost of venetoclax, obinutuzumab, rituximab and acalabrutinib. For the calculation of monthly costs, it was considered that one month had 30 days. All costs are presented in reais (RBL) and american dollars (USD). Currency exchange rate used was R$5.20 to USD 1.00, according to last 60 days average-price (08/12/2022 to 10/11/2022).(14)

Table 1. Price of drugs and monthly treatment costs.

Drugs	SKU	List Price (PF18%)	Dosage	Monthly treatment costs
Venetoclax	10mg, 50mg and 100mg tablets (start-kit)	US$ 1,821.46 RBL 9,471.60	1st month (start-kit)	US$ 1,821.46
Venetoclax	100 mg x 120 tablets	US$ 8,439.20 RBL 43,883.82	400 mg (maintenance dosage)	US$ 8,439.20
Obinutuzumab	1000 mg IV x 40ml per bottle	US$ 4,861.30 RBL 25,278.74	1st Cicle: 3,000 mg (month 1) 2-6 Cicles: 1,000 mg (months 2-6)	US$ 14,583.90 $ 4,861.30
Rituximab	10 mg/mL x 10 mL per bottle	US$ 615.65 RBL 3,201.39	1st Cicle: 375 mg/m² 2-6 Cicles: 500 mg/m²	1st Cicle: US$ 4,044.99 2-6 Cicles:US$ 5,393.33
Acalabrutinibe	100 mg x 60 tablets	US$ 9,166.70 RBL 47,666.82	200 mg (fixed dose)	US$ 7,252.71

An alternative comparison of treatment costs in 60 months has been developed according to ANS's appraisal of acalabrutinib in 1L CLL patients (15).

A budget–impact analysis was also carried out. Eligible population for Venetoclax + Obinutuzumab (VenO) and acalabrutinib, and Venetoclax + Rituximab (VenR) and acalabrutinib were estimated based on epidemiological premises according the flow presented on Figure 3 and specified in Table 2. A sub-analysis of high risk patients was also included.

Table 2. Epidemiological parameters for defining eligible population (2022).

Parameter	Value
HMOs' beneficiaries	47,031,971 (16)
CLL incidence (per 100 thousand inhabitants)	4.7 (17)
Patients who need treatment (no watch & wait indication)	66.7% (18)
Presence of 17p deletion (with 17p Del) or IGVH non-mutated	62% (19)
Brazilian population growth (20)	
2022-2023	0.68%
2023-2024	0.65%
2024-2025	0.62%
2025-2026	0.59%
2027-2028	0.56%

Based on parameters defined in Table 2, the projection of CLL population elegible for treatment with venetoclax + obinutuzumab and acalabrutinib is shown in Table 3.The projection of CLL population elegible for treatments vs acalabrutinib is shown in Table 2.

Table 3. Projection of eligible population for 1L CLL treatment with venetoclax + obinutuzumab and acalabrutinib (2022-2026)

Year	2022	2023	2024	2025	2026
General population	2,031	2,044	2,057	2,069	2,081
With 17p deletion or IGVH non-mutated	1,259	1,268	1,275	1, 283	1,290
Without 17p deletion or IGVH mutated	772	777	782	786	791

Table 4. Projection of eligible population for R/R CLL treatment with venetoclax + rituximab and acalabrutinib (2022-2026)

Year	2022	2023	2024	2025	2026
General population	908	914	920	925	930
Post relapsed treatment with 17p deletion	272	274	276	277	279
Post relapsed treatment Without 17p deletion	636	640	644	647	651

Table 5. Market share – reference and projected scenarios for 1L or R/R CLL

Year	2023	2024	2025	2026	2027
Reference scenario 1L CLL					
Venetoclax + Obinutuzumabe	0%	0%	0%	0%	0%
Acalabrutinib	100%	100%	100%	100%	100%
Projected scenario 1L CLL					
Venetoclax + Obinutuzumabe	100%	100%	100%	100%	100%
Acalabrutinib	0%	0%	0%	0%	0%
Reference scenario R/R CLL					
Venetoclax + rituximabe	0%	0%	0%	0%	0%
Acalabrutinib	100%	100%	100%	100%	100%
Projected scenario R/R					
Venetoclax + rituximabe	100%	100%	100%	100%	100%
Acalabrutinib	0%	0%	0%	0%	0%

A yearly discontinuation rate of 10.5% was applied from 2023 to 2027 to acalabrutinib continuous therapy, based on IBTKs phase III randomized trial. (21) Discontinuation rate was applied for VenO once the treatment duration is 12 months and authors opted for a more conservative approach on VenO and VenR costs.

RESULTS

Table 6. Annual treatment cost (RBL/USD).

Drugs	Treatment costs of 1st year		Treatment costs of 2nd year	
1L CLL				
Venetoclax + obinutuzumab	RBL 650,539.71	$ 125,103.79	-	
Acalabrutinib	RBL 572,001.85	$ 110,000.36	RBL 572,001.85	$ 110,000.36
R/R CLL				
Venetoclax + rituximab	RBL 452,341.47	$86,988.74	RBL 413,227.60	$ 79,466.85
Acalabrutinib	RBL 448,849.85	$86,317.28	RBL 448,849.85	$ 86,317.28

The cost-minimization analysis in a 24-month period demonstrates VenO as the most economic alternative compared to Acalabrutinib in 1L CLL treatment, with savings of about USD 94,896.92 per patient (43%). In the same period VenR compared to Acalabrutinib in R/R CLL the costs savings were $ 53,545.12 per pacient (24%).

Table 7. Results of cost-minimization analysis (per patient) – 24 months.

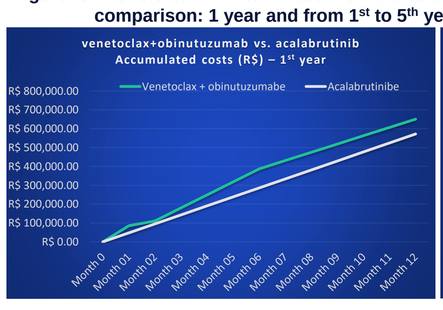
Drugs	Accumulated treatment costs of 2 years		Incremental	% of savings
CLL 1L				
Venetoclax + obinutuzumab	RBL 650,539.71	$125,103.79	- $ 94,896.92	43%
Acalabrutinib	RBL 1,144,003.70	$ 220,000.71		
R/R CLL				
Venetoclax + rituximab	RBL 865,569.07	$ 166,455.59	- $ 53,545.12	24%
Acalabrutinib	RBL 1,144,003.70	$ 220,000.71		

Considering the alternative scenario, in an 60 month period VenO demonstrates savings of about $ 424,897.98 per patient (-77%) compared to Acalabrutinib, which means that the cost of treating 1 1L CLL patient with Acalabrutinib is the same as treating about 4 patients with VenO.

Table 8. Results of cost-minimization analysis (per patient) – 60 months.

	Venetoclax + obinutuzumab		acalabrutinib		Incremental	% of savings
Cost of treatment	RBL650,539.71	$ 125,103.79	RBL 2,860,009.23	$ 550,001.78	- $ 424,897.98	77%

Figure 3. Venetoclax + rituximabe vs Acalabrutinib in CLL 1L - accumulated costs (USD) comparison: 1 year and from 1st to 5th year.



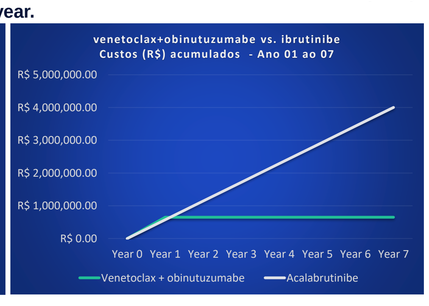
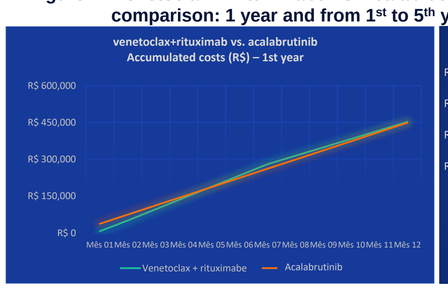
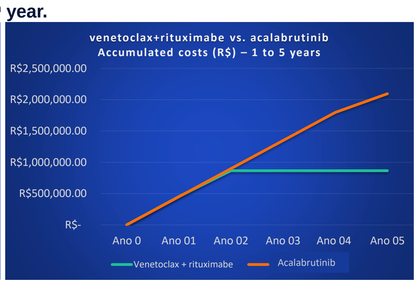


Figure 4. Venetoclax + rituximabe vs Acalabrutinib in CLL R/R - accumulated costs (RBL) comparison: 1 year and from 1st to 5th year.





As observed, the number of patients treated with VenO is stable over years, a consequence of its 12-month finite duration dosage, though representing a more predictable and cost-saving treatment option while acalabrutinib presents the cumulative effect related to a continuous treatment.

Table 9. Patients in treatment – total population.

Year	2023	2024	2025	2026	2027
Reference scenario 1L CLL					
Ibrutinib	2,031	3,862	5,514	7,004	8,349
Projected scenario 1L CLL					
Acalabrutinib	2,031	3,862	5,514	7,004	8,349
Venetoclax + Obinutuzumabe	2,031	2,044	2,057	2,069	2,081
Reference scenario R/R CLL					
Ibrutinib	908	1,699	2,389	2,992	3,518
Projected scenario R/R CLL					
Acalabrutinib	908	1,699	2,389	2,992	3,518
Venetoclax + rituximabe	908	1,672	2,316	2,330	2,344

The budget impact analysis, in 1L CLL, estimates a cumulative saving around 658 million in five years if eligible patients are treated with VenO instead of Acalabrutinib. The cost savings were more than 157 million in R/R CLL patients, in the same time (Table 9). If considered only the high-risk patients (with 17p Del/TP53 or IGVH non-mutated), cumulative savings are estimated at $ 165,736,169.28 and $101,229,369 in five years, in the 1L and R/R respectively (Table 10).

Table 10. Budget impact (in USD) – Total population

	2023	2024	2025	2026	2027
			1L CLL		
Projected	254,124,127.79	255,769,290.55	257,349,170.50	258,861,850.11	260,305,521.14
Reference	223,444,422.90	424,873,728.20	606,542,101.84	770,465,354.22	918,446,045.71
Incremental	30,679,704.89	-169,104,437.65	-349,192,931.34	-511,603,504.11	-658,140,524.58
			R/R CLL		
Projected	78,985,253.24	139,746,363.76	144,819,840.26	145,691,713.14	146,525,127.83
Reference	78,375,566.88	146,677,824.28	206,246,534.83	258,240,001.79	303,659,599.79
Incremental	609,686.37	-6,931,460.52	-61,426,694.57	-112,548,288.64	-157,134,471.96

Table 11. Budget impact (in USD) – High Risk Population

	2023	2024	2025	2026	2027
			1L CLL		
Projected	25,412,412.78	25,576,929.05	25,734,917.05	25,886,185.01	26,030,552.11
Reference	22,344,442.29	42,487,372.82	60,654,210.18	77,046,535.42	91,844,604.57
Incremental	3,067,970.49	-16,910,443.76	-34,919,293.13	-51,160,350.41	-65,814,052.46
			R/R CLL		
Projected	23,695,576	41,923,909	43,445,952	43,707,514	43,957,538
Reference	23,512,670	44,003,347	61,873,960	77,472,001	91,097,880
Incremental	182,906	-2,079,438	-18,428,008	-33,764,487	-47,140,342

References or footnote

CONCLUSIONS

Results of the analysis indicate VenO and VenR associated with lower treatments costs in both scenarios with a higher resource saving for 1L CLL budget impact for the Brazilian Private Healthcare System.

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DISCLOSURES

Marinato, André has served as speaker for AbbVie, Janssen and Astra Zeneca and as consultant for Takeda, Gilead and United Medical. Takao, Augusto has served as speaker for Takeda, MSD, Janssen, Bhoeringer, Roche, Astelas, Sanofi, AstraZeneca, BMS, Lilly and Merck. Silva, Rafael and Tanaka, Straus were AbbVie employees, elaborated the models and submitted abstract. Campos, Laura is an employee and stockholder of AbbVie. All authors contributed to the development of the publication and maintained control over the final content. Financial support was provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the poster.

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