Acceptance Code: EE430

Evaluating the cost benefit of fixed-duration targeted therapy in first line (1L) in (CLL): A Real-World Analysis Using Hungarian Claims Data

Jeskó J[1], Hegyi R[1], Nagy B[1]

[1] *Healthware Consulting Ltd., Budapest, Hungary*

OBJECTIVE

In chronic lymphocytic leukemia (CLL) fixed-duration treatment is available with itemized reimbursement from 2022 in Hungary. This research clarifies the saving potential associated with novel fixed-duration targeted 1L therapies in CLL based on claims data in Hungary.

CONCLUSIONS

The Hungarian real-world data demonstrate that chemotherapy followed by ibrutinib monotherapy is clearly being replaced by fixed-length regimens at the end of the research period.

This research has shown that the per protocol using of fixed-duration CLL therapy of venetoclax-obinutuzumab in 1L provides robust savings for the Payer in Hungary, which can ensure access for further patients to new innovative therapies.

The results have approached the comparison of treatments from a cost perspective, it would be important to investigate whether similar or better outcomes in terms of patient survival can be achieved with the new types of fixed length therapies.

Healthware Ltd. collaborated with the local Abbvie department in the capacity of an external consultancy firm

INTRODUCTION

- CLL is the most common type of leukemia in Western countries with an incidence of 4.2/100,000 population/year1. The disease typically occurs in elderly patients and has a highly variable clinical course[2].
- Venetoclax in combination with obinutuzumab is indicated for the treatment of adult patients with previously untreated CLL received European Commission approval in 2020[3].
- Several studies on the economic evaluation of fixed-duration targeted therapy in CLL first line (1L) have been published in recent years, demonstrating the cost-effectiveness of these therapies.[4,5,6]
- The aim of this research is to clarify the cost-saving potential of novel fixed-duration targeted 1L therapies in CLL based on the Payer's claims database in Hungary.

METHODS

- The analysis of the National Health Insurance Fund (NHIF) claims database was conducted using anonymized data.
- The database covers all reimbursement events and the main demographic data of the patients on all level of public healthcare
- The analysis of the NHIF (National Health Insurance Fund) claims database was conducted using anonymized data.
- The database covers all reimbursement events and the main demographic data of the patients on all level of public healthcare
- The research period was from 1 January 2017 to 30 September 2023.
- The results were summarized using descriptive, unadjusted statistics using PL/SQL Developer 14.0.
- Fees of healthcare services were calculated using the official list prices of the NHIF database and adjusted to the average euro (€) exchange rate from January to December 2023 (€1 = 381.9 HUF). Note that the fees do not include any potential discounts or rebates.
- The identification of the relevant patient group was based on the reported ICD-10 code C91. This was determined by at least one relevant prescription fulfilment, hospital event or outpatient event with an associated ICD-10 code. In cases where the patient did not have a detailed record of their drug-related events, the most recent pharmacy fulfilment was used to determine the patient's indication category.
- Limitation: No patient level data can be provided. Instead, it provides only aggregated data.

RESULTS

Detection of relevant 1L mono- and combination therapies

One of the most significant challenge of the research was the identification of 1L treatment protocols in a real-world claim database during a period of notable change in CLL treatment patterns in Hungary. The following set of criteria was employed for the purpose of detecting treatments:

- ibrutinib monotherapy (continuous therapy): ibrutinib therapy is continuous and there is no other relevant treatment within +/-30 days of the ibrutinib dispense (monotherapy). The duration of the therapy is outlined in the SmPC.
- venetoclax–obinutuzumab combination (fixed treatment duration): venetoclax therapy is continuous in 12 cycles and there is at least one obinutuzumab dispense within +/- 30 days
- ibrutinib-rituximab (continuous therapy): ibrutinib therapy is continuous and there is at least one rituximab dispense within +/-90 days
- ibrutinib-obinutuzumab (continuous therapy): ibrutinib therapy is continuous and there is at least one obinutuzumab dispense within +/-90 days

Nevertheless, these combination patterns do not precisely align with the recommended protocols. It is conceivable that patient identification in the Payer database could be achieved through the aforementioned method, and the monotherapy duration is not contingent on the rules governing combination therapies.

Figure1: Incident patient number by mono- and combination 1L CLL therapies

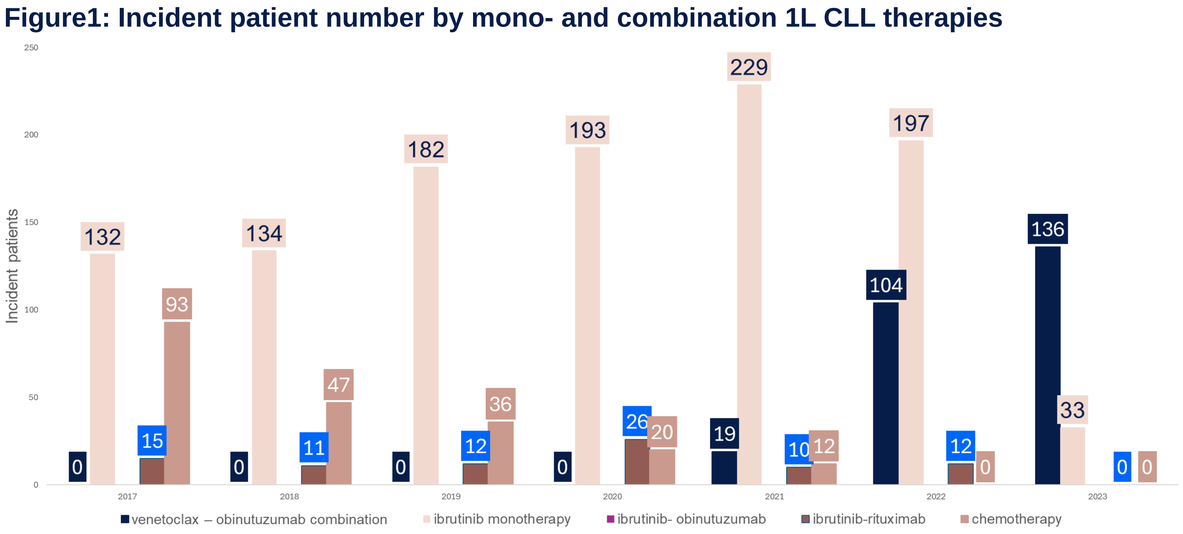

Figure 1 illustrates the unadjusted incident patient number by mono and combination therapies among patients with CLL. During the research period, there have been notable shifts in the landscape of 1L CLL treatment. The predominant trends can be summarized as follows:

- The use of chemotherapy has been gradually discontinued from clinical practice.
- Until 2022, ibrutinib monotherapy was the most prevalent treatment approach (TP53-aberrated and IGHVunmutated CLL), with nearly 70% of 1L CLL patients receiving this therapy between 2018 and 2021.
- Venetoclax–obinutuzumab combination became the preferred option in December 2022. In 2023, this fixed therapy was administered to over 60% of all first-line patients.

Table 1 – Threshold calculation

	Total mg amount during the fix term therapy	Gross wholesaler price/mg	All costs per patient
venetoclax	117 390	0,41 €	48 130 €
obinutuzumab	8 000	2,81 €	22 473 €
Total costs of fixed-length therapy			70 603 €
	Ibrutinib monotherapy weekly dose (mg)	**Gross wholesaler price/mg**	**Ibrutinib weekly costs**
Ibrutinib	2 940	0,38 €	1 114 €
Venetoclax-obinutuzumab fixed cost/ibrutinib weekly cost			63,4
Threshold			**64**

To determine the threshold, the total cost of venetoclax-obinutuzumab therapy was calculated at the wholesale price of mg per protocol. This was compared to the weekly mg dose per protocol and the wholesale price of ibrutinib monotherapy. If the average duration of treatment for patients starting 1L ibrutinib exceeds 64 weeks, fixed-dose therapy has a cost advantage.

Figure2: Comparison of per protocol venetoclax-obinutuzumab and unadjusted average length* of ibrutinib monotherapy among 1L CLL patients

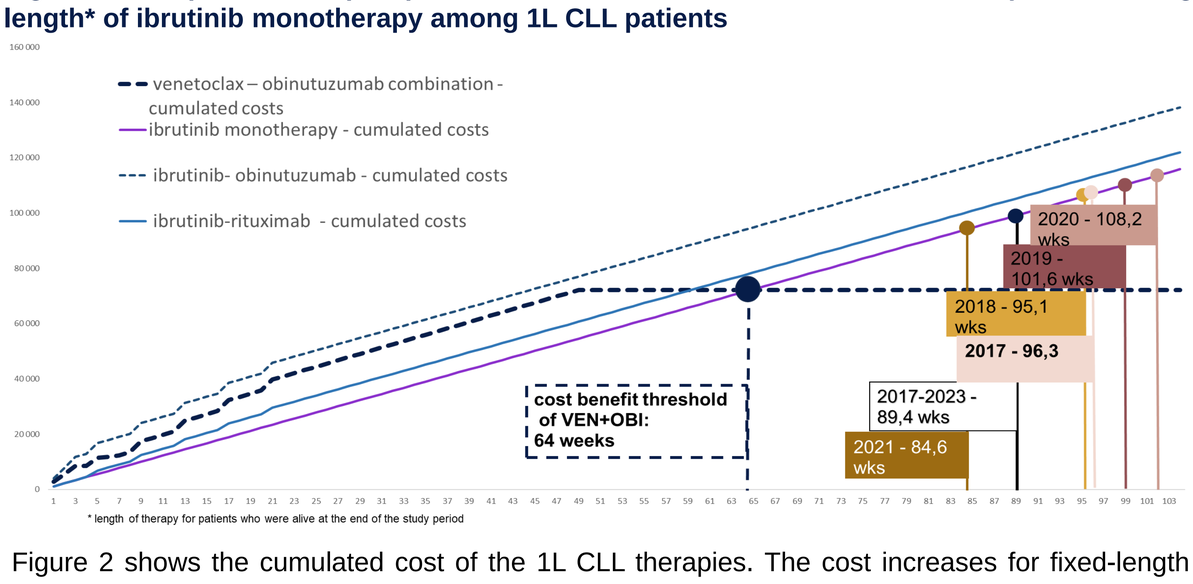

Figure 2 shows the cumulated cost of the 1L CLL therapies. The cost increases for fixed-length therapies cease at week 49, and the threshold (from week 64) represents the cost saving potential. Figure 2 also represents the unadjusted average length of ibrutinib monotherapy of incident patients per year and the whole research period.

Table 2 – Cost saving potential

Research period	venetoclax – obinutuzumab patient number	Venetoclax – Obinutuzumab cost benefit threshold (weeks)	Ibrutinib monotherapy avg length (weeks)	Ibrutinib monotherapy weekly dose (mg)	Ibrutinib Gross wholesaler price/mg	Cost saving potential
2017-2023	264	64	89,4	2 940	0,38 €	7 461 913 €
2017-2020			98,0			9 985 444 €

The research calculates the cost-savings potential that could be achieved using venetoclax–obinutuzumab combination (12 cycle fixed treatment duration). The time difference between the threshold (64 weeks) and the average length of ibrutinib monotherapy during the entire period (89.4 weeks) represents a significant cost saving potential, which amounts to 7,46 million euros.

For ibrutinib monotherapies, the values are spread over a constant range of 95-101 weeks. The lower value of the 2021 data is presumably due to the research period limitation, and it is expected that these values for this patient population will still be close to the average treatment duration of previous years (2017-2020).

[1] Kipps, T.J., et al.: Chronic lymphocytic leukaemia. Nat. Rev. Dis. Primers 3, 16096 (2017) - https://pubmed.ncbi.nlm.nih.gov/28102226/
[2] Hallek, M.: Chronic lymphocytic leukemia: 2020 update on diagnosis, risk stratifcation and treatment. Am. J. Hematol. 94(11), 1266–1287 (2019) - https://pubmed.ncbi.nlm.nih.gov/31364186/
[3] https://ec.europa.eu/health/documents/community-register/html/h1138.htm
[4] A Chatterjee et al.: EE12 A Probabilistic Cost-Effectiveness Analysis of Venetoclax and Obinutuzumab as a First-Line, 12-Month, Fixed Duration Therapy in Chronic Lymphocytic Leukemia (CLL) in Canada - https://www.valueinhealthjournal.com/article/S1098-3015(22)00465-X/fulltext?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS1098301522004 65X%3Fshowall%3Dtrue#%20
[5] Beenish S Manzoor et al: Real-World Comparison of Healthcare Costs of Venetoclax-Obinutuzumab Vs. Btki Use Among Elderly U.S. Medicare Beneficiaries with Chronic Lymphocytic Leukemia in the Front-Line (1L) Setting - https://ashpublications.org/blood/article/142/Supplement%201/5085/500772/Real-World-Comparison-of-Healthcare-Costs-of
[6] Anuja Chatterjee et al: Cost-effectiveness of a 12-month fixed-duration venetoclax treatment in combination with obinutuzumab in first-line, unfit chronic lymphocytic leukemia in the United States - https://pubmed.ncbi.nlm.nih.gov/34714110/
[7] Hungarian NHIF official prices - https://www.neak.gov.hu/pupha