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UNVEILING THE JOURNEY OF CHRONIC LYMPHOCYTIC LEUKEMIA PATIENTS IN PORTUGAL

INSIGHTS INTO THE RITUXIMAB-VENETOCLAX PROTOCOL

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OBJECTIVES

Multicenter retrospective analysis of the implementation and outcomes of Rituximab-Venetoclax regímen across 12 Portuguese centers.

- **Primary endpoints**: progression-free survival (PFS) and overall survival (OS).
- **Secondary endpoints:** time to next treatment or death (TTNTD), response rates, feasibility and safety outcomes, assessed per iwCLL criteria.

CONCLUSIONS

- RV regimen yielded high overall and complete response rates
- There were **no impact of established high-risk features on response rates or PFS**.
- Prior BTKi exposure did not affect response rates but was associated with **inferior OS**
- Our findings support the feasibility of outpatient venetoclax ramp-up, with no compromise in safety or efficacy.

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INTRODUCTION

Rituximab-Venetoclax (RV) has emerged as the standard of care for relapsed/refractory Chronic Lymphocytic Leukemia (CLL), following the phase III MURANO trial, which demonstrated its superiority over chemoimmunotherapy. (SeymorJF, 2018)

This combination was approved in Europe in 2018 for patients with previously treated CLL, and its use in Portugal expanded rapidly thereafter.

Despite its widespread adoption, real-world, population-level evidence characterizing its use in routine clinical practice remains limited. In particular, data are scarce regarding the practical implementation of the ramp-up phase, the effectiveness of the regimen outside clinical trial settings, and the incidence and severity of adverse events.

METHODS

Inclusion criteria: Patients aged ≥18 years who received RV treatment between January 1, 2019, and December 31, 2023, with a data cut off on April 30, 2025.

Exclusion criteria: Patients who were still in the ramp-up phase of the treatment protocol.

Table 1.Baseline clinical characteristics

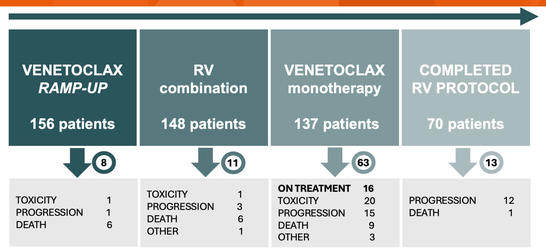
	n (%)
Gender,male (n=156)	96 (61.5%)
Mean age, years (n=156) (SD)	70 (10.4)
ECOG-PS (n=148)	
0-1	139 (93.9%)
2-3	9 (6.1%)
Number of prior cancer therapies (n=156)	
1	100 (64.1)
2	36 (23.1)
≥3	20 (12.8)
Previous lines of therapy (n=156)	
Chemotherapy	133 (85.3)
BTKi	47 (30.1)
PI3Ki	6 (29.8)
del(17p) and/or TP53 mutation	
mutated	47 (30.1)
unmutated	106 (67.9)
unknown	3 (1.9)
IGHV status	
mutated	9 (5.8)
unmutated	47 (30.1)
inconclusive	3 (1.9)
unknown	97 (62.2)
Binet stage	
A	28 (20.7)
B	45 (33.3)
C	62 (45.9)
CLL-IPI (n=78)	
low risk	5 (6.4)
intermediate risk	23 (29.5)
high risk	40 (51.3)
very high risk	10 (12.8)

RESULTS

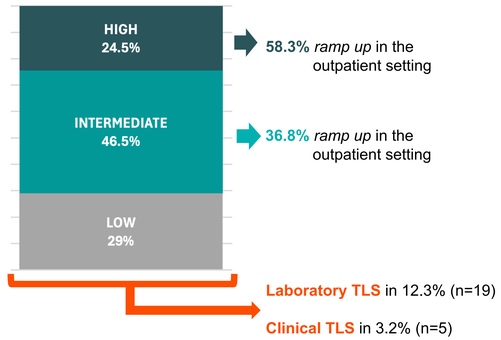
156 patients included → median follow-up time of 28.5 months.

Indications for treatment initiation:

- Bone marrow failure (48.4%)
- Progressive lymphocytosis (49.0%)
- Progressive lymphadenopathy (54.2%)
- B symptoms (23.1%).



Tumor lysis syndrome risk assessment



Adverse events

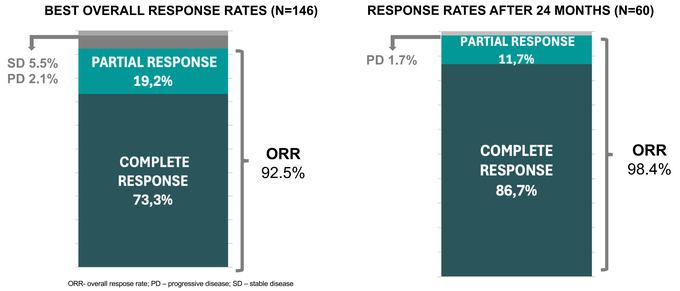
	ANY GRADE n (%)	GRADE ≥3 n (%)
Hematologic toxicity (N=156)	138 (88.5%)	92 (59%)
Anemia	62 (40,3%)	17 (11%)
Neutropenia	118 (76,1%)	80 (48.4%)
Thrombocytopenia	96 (61,9%)	30 (19.4%)
Infections (N=156)	86 (55,5%)	nd
Recurrent infections (N=155)	26 (16,8%)	nd
Febrile neutropenia (N=156)	26 (16,7%)	nd
Hypogammaglobulinemia (N=103)	16 (15,5%)	nd
Gastrointestinal toxicity	nd	8 (5,2%)
Other toxicity	nd	20 (12,9%)

nd – not determined

Temporary venetoclax interruptions (≥14 days) in 28.2%

→ 59% due to AE.

Response rates



ORR- overall respose rate; PD – progressive disease; SD – stable disease

Progression

Disease progression in 26.3%

Richter's transformation in 9 patients

Deaths

42 deaths (26.9%)

- 40.5% disease progression
- 19.5% toxicity
- 19.5% not related to therapy / CLL
- 19.5% unknown cause

Survival analysis