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EFFICACY AND TOLERABILITY OF VENETOCLAX PLUS RITUXIMAB IN RELAPSED OR REFRACTORY CHRONIC LYMPHOCYTIC LEUKEMIA – REAL-WORLD ANALYSIS OF POLISH ADULT LEUKEMIA STUDY GROUP

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AIM: TO ASSESS THE CLINICAL EFFICACY AND SAFETY PROFILE OF VEN-R TREATMENT IN PATIENTS WITH RR-CLL OUTSIDE OF CLINICAL TRIALS.

Table 1 Characteristics of patients in the entire cohort.

	PALG	MURANO (VEN-R)
N	**363**	194
Age at the start of treatment [median, (range)]	**69 (32-91)**	64.5 (28–83)
Gender [n, (%)]		
F	**148 (40.8)**	58 (29.9)
M	**215 (59.2)**	136 (70.1)
Del17p(+) [n, (%)]	**48 (14.5)**	46 (26.6)
TP53mut [n, (%)]	**33 (19.3)**	48 (25.0)
ECOG [n, (%)]		
N	**358**	194
0	**50 (14.0)**	111 (57.2)
1	**251 (70.0)**	82 (42.3)
2	**55 (15.4)**	1 (0.5)
3	**2 (0.6)**	0 (0)
Number of treatment lines prior to VEN-R [n,(%)]		
N	**362**	194
1	**151 (41.7)**	111 (57.2)
2	**102 (28.2)**	57 (29.4)
3	**57 (15.7)**	22 (11.3)
4	**30 (8.3)**	4 (2.1)
≥5	**22 (6.1)**	

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INTRODUCTION

The prognosis of patients with relapsed/refractory chronic lymphocytic leukemia (RR-CLL) has improved following the introduction of venetoclax into clinical practice. Since MURANO trial [1], the regimen of venetoclax and rituximab (VEN-R) has become firmly established in the standard therapeutic landscape for RR-CLL and is widely used in clinical practice.

METHODS

We conducted a retrospective analysis of RR-CLL patients treated with VEN-R at hematology centers affiliated with the Polish Adult Leukemia Study Group (PALG) between 2019 and 2024 to assess the clinical efficacy and safety profile of VEN-R treatment in patients with RR-CLL outside of clinical trials.

RESULTS

Clinical data of 363 RR-CLL patients treated with VEN-R were collected. Detailed characteristics of patients are presented in Table 1. The features with the highest importance were: the median eastern cooperative oncology group (ECOG) performance status of 1 (range 0 - 3) with 57 patients with ECOG status 2 or higher; patients had received a median of 2 (range 1–10) prior lines of therapy; 50 (50/362, 13.8%) recipients had previously received BTKi and 12 (12/362, 3.3%) PI3Ki-based therapies. Among evaluable patients, 48 of 331 (14.5%) had 17p deletion, whereas TP53 mutation was identified in 33 of 172 patients (19.2%).

EFFICACY

The median follow-up was 22.8 months. Response was assessed according to iwCLL 2018 criteria. The overall response rate (ORR) was 97.1% with 121 of 312 patients (38.8%) achieving complete remission (CR) and 182 (58.3%) partial remission (PR), in just 1 patient (0.3%) disease progression was the best obtained response. In the whole cohort the median PFS and the median OS were not reached. The estimated 3y-PFS rate was 62.1% (95%CI 54.9%-70.2%), and the 3y-OS rate was 69.0% (95%CI 62.3%–76.4%).

In addition, we analysed the impact of prior BTKi/PI3Ki treatment on OS and PFS. While the data obtained for PI3Ki therapy history were not statistically significant, we were able to identify the adverse impact of BTKi treatment history on both the OS and PFS (Figure 3, Figure 4).

We also assessed the impact of the type of the reimbursement programme (new - requirement of at least one previous line of treatment; older/strict - high cytogenetic and/or molecular risk/history of treatment refractoriness/early relapse (<12 months) after first-line treatment) on treatment outcomes. According to our statistical analysis, the change in the drug programme significantly affected OS, but not PFS (Figure 5, Figure 6).

SAFETY

Six cases of Richter transformation (1.8%) were diagnosed during the follow-up period. There were 72 deaths recorded during observation: 24 (33.3%) due to infection and 11 (15.3%) due to disease progression. At last follow-up, 85 (23.5%) patients completed their scheduled chemotherapy regimen, therapy was discontinued in 106 (29.4%) cases, while 170 patients (47.1%) remained on treatment. Reasons for therapy discontinuation included mainly patient's death (n=36, 34%) and treatment-related cytopenias (n=17,16.0%). The adverse events of VEN-R treatment were reported during the study are presented in Table 3.

CONCLUSION

The results we obtained were similar to those of the registration study. During the observation period, we did not observe any new concerns regarding treatment side effects. We identified a group of patients who may respond less favourably to VEN-R treatment – patients with a history of BTKi. It seems that the lack of similar conclusions in the group of patients treated with PI3Ki may be explained by the small representation of patients in the cohort; this is subject to further evaluation. In the domestic treatment landscape, we were able to confirm that the introduction of VEN-R into the treatment routine for patients with RR-CLL has a significant positive impact on their overall survival.

Figure 1. PFS – whole cohort

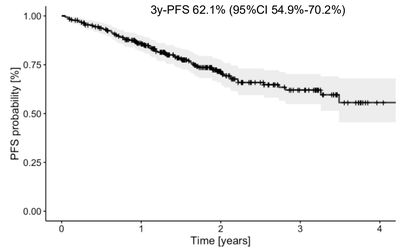


Figure 2. OS – whole cohort

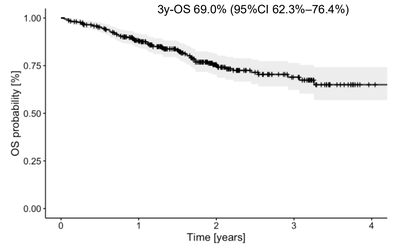


Figure 3. History of BTKi - PFS

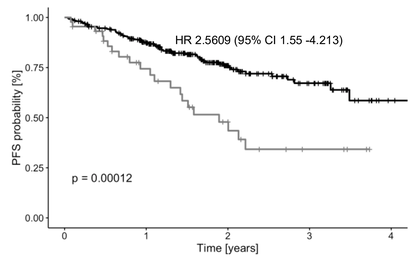
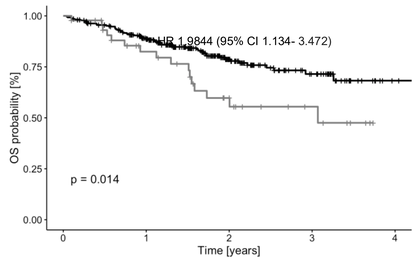


Figure 4. History of BTKi - OS



--- - no history of BTKi; ---history of previous treatment with BTKi

Figure 5. Type of the programme - PFS

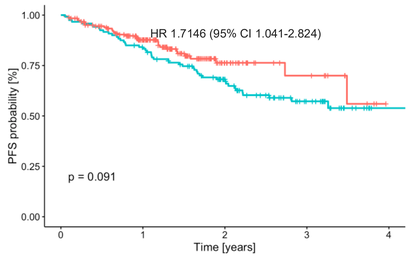
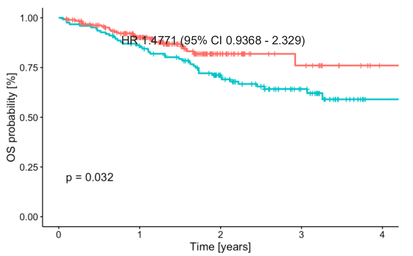


Figure 6. Type of the programme - OS



- New - requirement of at least one previous line of treatment
- Older/strict - high cytogenetic and/or molecular risk/history of treatment refractoriness/early relapse (<12 mos.) after first-line treatment

Table 2 Treatment efficacy.

Tratment efficacy	n	%
Response (defined as the best response obtained during observation)	312	100.0
ORR	303/312	97.1
➢ CR	121/312	38.8
➢ PR	182/312	58.3
➢ SD	8/312	2.6
➢ PD	1/312	0.3

Table 3 Most common adverse events in the whole cohort.

Adverse event	n	%
➢TLS		
▪Laboratory TLS	37/358	10.3
▪Clinical TLS	3/360	0.8
➢Cytopenia		
▪Neutropenia (during dose escalation) G≥3	104/33 1	31.4 40.3
▪Neutropenia (after dose escalation) G≥3	139/34 5	11.6 17.4
▪Anemia G≥3	38/328	
▪Thrombocytopenia G≥3	57/328	
Pneumonia	66/351	18.8
Neutropenic fever	14/351	4.0
Diarrhea G≥3	15/349	4.3

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