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156 | MURANO: FINAL 7 YEAR FOLLOW UP AND RETREATMENT ANALYSIS IN VENETOCLAX-RITUXIMAB (VENR)-TREATED PATIENTS WITH RELAPSED/REFRACTORY CHRONIC LYMPHOCYTIC LEUKEMIA (*R/R* CLL)

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Introduction: Fixed-duration (FD) VenR treatment (tx) in patients (pts) with *R/R* CLL in the Phase 3 MURANO trial (NCT02005471) resulted in superior progression-free survival (PFS) and overall survival (OS), versus bendamustine (B)R. This was sustained at 5 years (y) median (m) follow up (FU): PFS, 53.6 months [mo] with VenR versus 17.0 mo with BR; 5 y OS rates, 82.1% with VenR versus 62.2% with BR; $p < 0.0001$ for both. We report the final analyses of MURANO at 7 y mFU: specifically, updated PFS and OS, with minimal

residual disease (MRD) evaluation, in pts treated in the main study, and in VenR-retreated pts in the substudy.

Methods: Pts with *R/R* CLL were randomized to VenR (Ven 400 mg daily for 2 y + monthly R for the first 6 mo) or BR (6 mo). In the substudy (2018 onwards), pts with progressive disease (PD) received VenR (to the main study regimen) as re-tx or as crossover from BR. PFS was investigator assessed. Peripheral blood MRD was measured centrally by ASO-PCR and/or flow cytometry. Undetectable (u)MRD was defined as $<10^{-4}$.

Results: Baseline characteristics are shown in the Table. At the final data cut (3 August 2022), mPFS (95% confidence interval [CI]) in VenR-treated pts ($n = 194$) was 54.7 mo (52.3, 59.9) versus 17.0 mo (15.5, 21.7) in BR-treated pts ($n = 195$; hazard ratio [HR] 0.25). Seven y PFS rates (95% CI) were 23.0% (16.1, 29.9) with VenR (no BR-treated pts were progression free at this time point); 7 y OS rates (95% CI) were 69.6% (62.8, 76.5) with VenR and 51.0% (43.3, 58.7) with BR (HR 0.53). M time to next tx with VenR was 63.0 mo versus 24.0 mo with BR (HR 0.30); 37.1% of VenR-treated pts have not had further anti-CLL tx.

Among VenR-treated pts who had uMRD at end of tx (EOT) without PD ($n = 83/118$; 70.3%), mPFS (95% CI) from EOT was 52.5 mo (44.5, 61.5) versus 18.0 mo (8.5, 29.3; $p < 0.0001$) in pts who were MRD+ at EOT ($n = 35$; 29.7%). At 7 y FU, 14 (16.9%) pts had no PD nor confirmed MRD conversion; in the 63 (75.9%) pts with MRD conversion, m time to conversion (95% CI) was 19.4 mo (8.7, 28.0). Among 63 pts who converted, 39 subsequently had PD or died; m time from conversion to PD (95% CI) was 28.3 mo (23.2, 35.0).

In the substudy ($n = 34$), 25 pts received VenR re-tx (Table), 92.0% of whom had ≥1 of the following high-risk features: *IGHV*-unmutated disease, genomic complexity, del(17p) and/or *TP53* mutations; despite this, 14/25 (56.0%) achieved uMRD at EOT in the main study. Best overall response rate (ORR) to re-tx was 72.0% and mPFS (95% CI) was 23.3 mo (15.6, 24.3). M (range) time from the last Ven dose in the main study to Ven ramp-up in the substudy was 2.3 y (1.2–3.1). Eight (32.0%) pts achieved uMRD at the re-tx end of combination tx, but no pts retained uMRD at the re-tx EOT.

No new safety findings were observed.

Conclusions: PFS and OS benefits for VenR versus BR were sustained and uMRD was associated with prolonged PFS. In the high risk VenR-retreated pts, ORR was high and uMRD was attainable. These data support FD VenR in *R/R* CLL, and suggest that VenR re-tx is a viable option for pre-treated pts.

Encore Abstract - previously submitted to EHA 2023

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	Main study		Substudy
	Pts treated with VenR (n=194)	**Pts treated with BR (n=195)**	**Pts retreated with VenR (n=25)**
Baseline characteristics			
Mean age, years (SD)	63.9 (10.5)	64.4 (9.6)	65.8 (8.3)
Number of prior cancer therapy, n (%)			
1	111 (57.2)	117 (60.0)	0 (0.0)
2	58 (29.9)	43 (22.1)	20 (80.0)
≥3	25 (12.9)	35 (17.9)	5 (20.0)
del(17p) and/or *TP53* mutation (aCGH), n (%)			
mutated	53 (27.3)	55 (28.2)	14 (56.0)
unmutated	104 (53.6)	98 (50.3)	9 (36.0)
unknown	37 (19.1)	42 (21.5)	2 (8.0)
Genomic complexity, n (%)	n=48	n=46	n=20
3–4	34 (70.8)	29 (63.0)	3 (15.0)
≥5	14 (29.2)	17 (37.0)	8 (40.0)
IGHV, n (%)	n=180	n=180	n=23
mutated	53 (29.4)	51 (28.3)	2 (8.7)
unmutated	123 (68.3)	123 (68.3)	21 (91.3)
unknown	4 (2.2)	6 (3.3)	0 (0.0)
Efficacy results			
Median follow-up, months	85.7	85.7	33.4
Best ORR, %	93.3	67.7	72.0
uMRD at EOCT of main study, n (%)	121 (62.4)	26 (13.3)	16 (64.0)
uMRD at EOCT of substudy, n (%)	N/A	N/A	8 (32.0)
uMRD at EOT of main study, n (%)	83 (70.3)*	N/A	14 (56.0)
uMRD at EOT of substudy, n (%)	N/A	N/A	0 (0.0)
Median PFS, months (95% CI)	54.7 (52.3, 59.9)	17.0 (15.5, 21.7)	23.3 (15.6, 24.3)
3 year OS rate, % (95% CI)	88.4 (83.8, 93.0)	78.9 (72.8, 84.9)	53.1 (25.1, 81.0)

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Keywords: Chronic Lymphocytic Leukemia (CLL), Combination Therapies

Conflicts of interests pertinent to the abstract

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