THE DEDALO PROTOCOL: AN INTEGRATED APPROACH TO MRD IN CLL PATIENTS RECEIVING VENETOCLAX PLUS RITUXIMAB

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Introduction

In previous analyses, the MURANO study demonstrated significant progression-free survival (PFS) and overall survival (OS) benefit for fixed-duration venetoclax-rituximab treatment compared with bendamustine-rituximab in relapsed/refractory chronic lymphocytic leukemia (CLL) patients. Furthermore, the study demonstrated that deep responses with undetectable minimal residual disease (uMRD) were associated with favorable PFS.[1,2] We designed the "Dedalo" study to test MRD from a multidisciplinary point of view (flow cytometry, molecular biology, and ultrasound) and of assessing MRD's predictive/prognostic value.

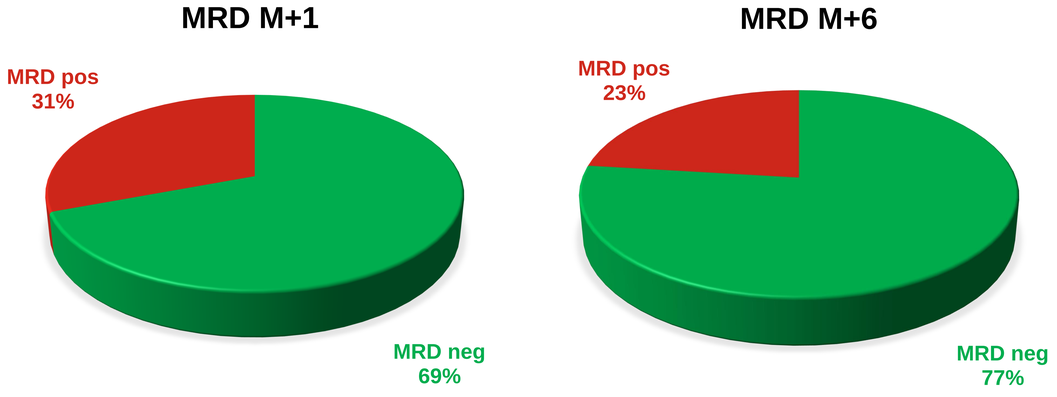
Up today 19 patients have been enrolled in the protocol; all were characterized by IgHV mutational status and TP53/del(17p) presence. MRD status was assessed by flow cytometry in peripheral blood from 13 patients after the first cycle (M1) and after the sixth cycle (M6) of Rituximab-Venetoclax, with a sensitivity of 10^{-4}.

Parameter	Patients
Age, median, y	65.1
age </= 65 y, N (%)	9 (47.4)
Male sex, N (%)	17 (89.5)
Binet stage N (%)	
B	15 (79)
C	4 (21)
Previous Treatment, N (%)	
1	12 (63.2)
2	2 (10.5)
3	5 (26.3)
IGHV mutational status, N (%)	
mutated	2 (10.5)
unmutated	12 (63.2)
Del(17p)/TP53 mut	
yes	5 (26.3)
no	13 (68.4)

Results

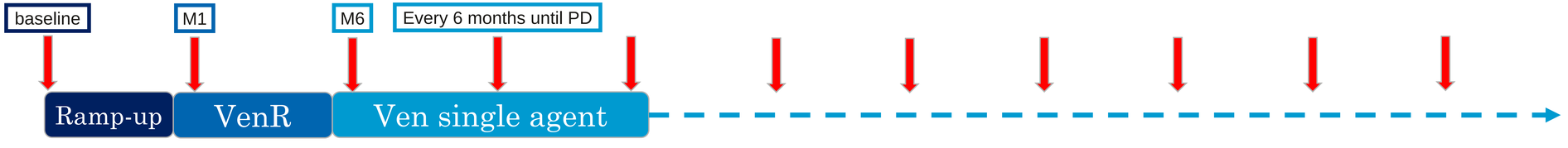
The median age of the patients is 65.1 years, with nine individuals under the age of 65 (47.4%). Seventeen of them are males (89.5%). 63.2% of patients had unmutated IGHV status, while five patients have a TP53 mutation or del(17p) (26.3%).

Out of the 19 enrolled patients, until now only one had to discontinue the treatment and 12 patients reached the twelfth month of therapy. After the first cycle, MRD status was assessed in 13 patients, with a 69% rate of PB undetectable MRD (less than 10^{-4}) and a 31% rate of low MRD positivity (defined as 10^{-4} to < 10^{-2}) and with 0% of high MRD positivity (defined as ≥ 10^{-2}). After the sixth cycle, MRD status was assessed in 13 patients, with an 77% rate of uMRD. Among the 5 patients carrying TP53 mutation and/or del(17p), 3 patient reached uMRD after the first cycle, 1 patient has achieved a low MRD positivity after the first cycle, and 1 patient remained MRD positive after the sixth cycle.



Conclusion

With all patients still on treatment, favorable MRD kinetics was observed in the venetoclax-rituximab setting. The majority of patients achieved PB uMRD after the first cycle of the treatment, with a higher percentage after the sixth cycle. These results are superimposable to those from the Murano trial (at 4 months, uMRD 60%, low MRD positivity 20%, 78% at 6 months).[1,2] The durability of uMRD rates, their role in the prediction of PFS in a real-life experience, and the effect of genetic characteristics on the MRD kinetics are still under investigation.



References

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