

COMPARATIVE ASSESSMENT OF MEASURABLE RESIDUAL DISEASE DETECTION AND IMMUNOLOGICAL EFFECTS IN RELAPSED CLL PATIENTS TREATED WITH RITUXIMAB- VENETOCLAX IN THE REAL WORLD: INSIGHTS FROM THE “DEDALUS” PROTOCOL

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INTRODUCTION

The fixed-duration treatment rituximab (R) and venetoclax (Ven) has revolutionized chronic lymphocytic leukemia (CLL) therapy, achieving a 7-year overall survival rate of 69.6% and enabling measurable residual disease (MRD) eradication. Sensitive techniques are essential for accurate MRD evaluation and response assessment.

AIM

The "Dedalus" protocol evaluates MRD using flow cytometry (MFC) and next-generation sequencing (NGS) in patients with relapsed/refractory CLL treated with fixed-duration R-Ven therapy and correlates MRD status with clinical and immunological outcomes.

METHOD

Twenty-two patients were analyzed using European Research Initiative on CLL (ERIC)-compliant flow cytometry and the Lymphotrack NGS panel, which detects immunoglobulin heavy chain (IgH) clonality with 10^{-5} sensitivity. Advanced ultrasound techniques were used to assess response. Immunological profiles and MRD were analyzed at 1, 6, 12, and 18 months, or at the time of treatment discontinuation.

CONCLUSIONS

This study underscores the efficacy of R-Ven and highlights the superior accuracy of NGS over MFC for MRD detection. While MFC remains cost-effective and widely used, NGS provides deeper insights into residual disease. Future studies may explore digital polymerase chain reaction for IgH rearrangements as a noninvasive MRD biomarker, alongside investigations into Ven's immunomodulatory effects in larger cohorts.

RESULTS

Twenty patients achieved a complete response, with MRD undetectable in 15 at the first checkpoint using both methods; two patients remained in partial response. In these, NGS detected residual IgH clonality (3–45 clonal cell equivalents/ 10^6 cells) when flow cytometry was negative. Detection limits were 10^{-4} for MFC and up to 10^{-5} for NGS (15% of tests). Venetoclax induced significant and sustained B-cell depletion and cluster of differentiation (CD) 4^{+} T-cell reduction, altering the CD4/CD8 ratio in 25% of cases.

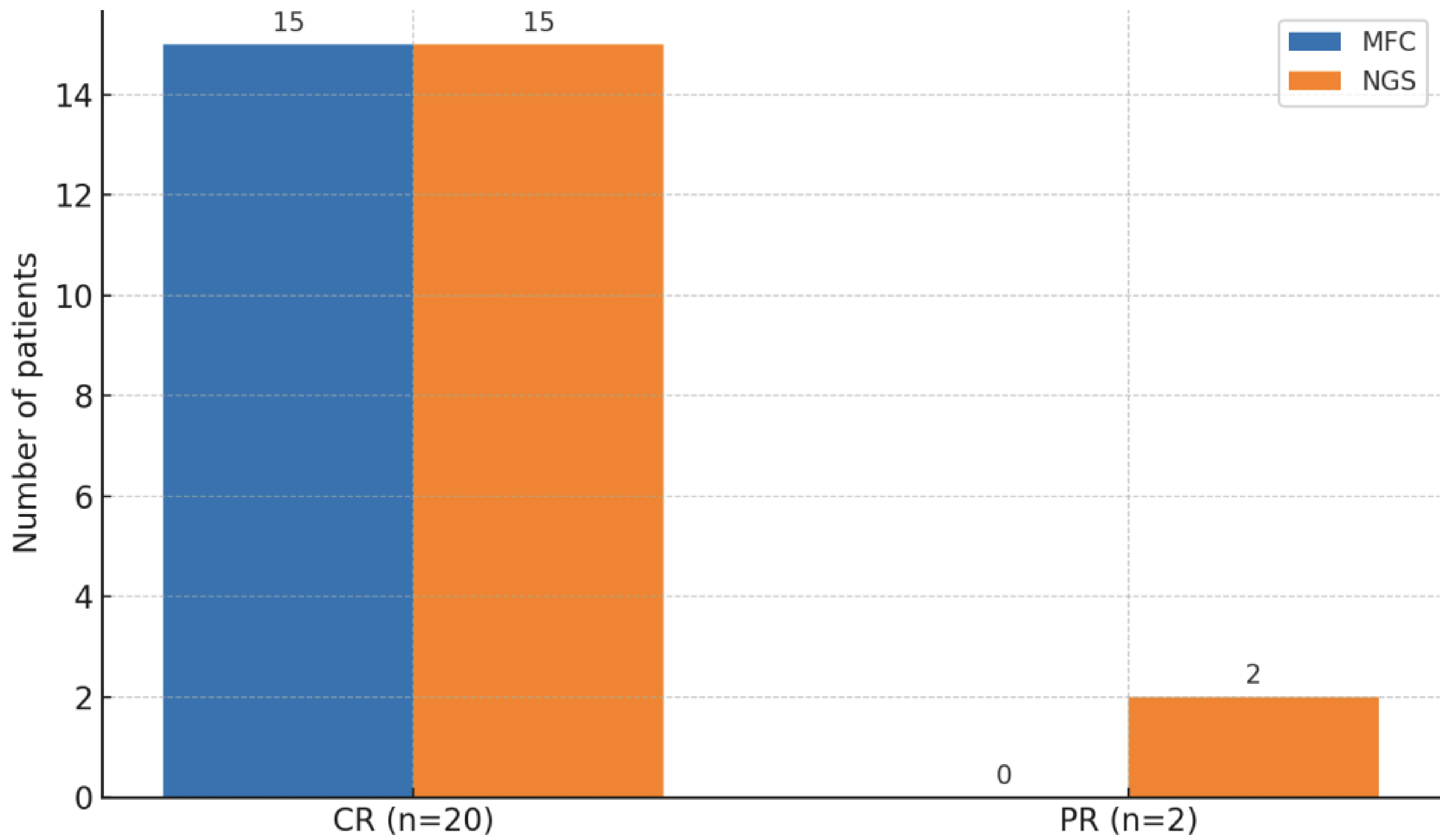


Figure 1: Comparison between MFC and NGS MRD in CLL patients treated with R-Ven

ACKNOWLEDGEMENTS

Previously presented at IwCLL Congress 2025, Krakow, 12–15 September, 2025.

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