Outcomes of Venetoclax Retreatment After Prior Frontline Venetoclax-Based Therapy in Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: A Systematic Review and Meta-Analysis

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INTRODUCTION

Fixed-duration venetoclax-based regimens have improved outcomes in chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL). With increasing use of frontline venetoclax, relapse after prior exposure is becoming more common. However, evidence supporting venetoclax retreatment remains limited and consists largely of small clinical trials and observational cohorts with variable patient populations and retreatment approaches.

AIM

To evaluate the efficacy and safety of venetoclax retreatment or rechallenge in adults with CLL/SLL previously treated with frontline venetoclax-based therapy.

METHODS

Study design

Systematic review and random-effects meta-analysis conducted according to PRISMA guidelines.

Search strategy

PubMed/MEDLINE, Embase, Scopus, Web of Science, Cochrane Library, and major hematology conference proceedings (ASH, ASCO, and EHA) were searched.

Eligibility

Adults with CLL/SLL who received venetoclax retreatment/rechallenge in a later line after prior frontline venetoclax-based therapy.

Outcomes

Primary: Overall response rate (ORR) and complete response (CR)
Secondary: MRD negativity, progression-free survival (PFS), overall survival (OS), tumor lysis syndrome (TLS), grade ≥3 cytopenias, and toxicity-related treatment discontinuation

Analysis

Random-effects meta-analysis was used because heterogeneity across study designs, populations, and retreatment strategies was anticipated.

RESULTS

Included evidence

- 6 studies were included.
- 143 patients received venetoclax retreatment/rechallenge.
- Patient populations and retreatment strategies varied between cohorts.

EFFICACY*

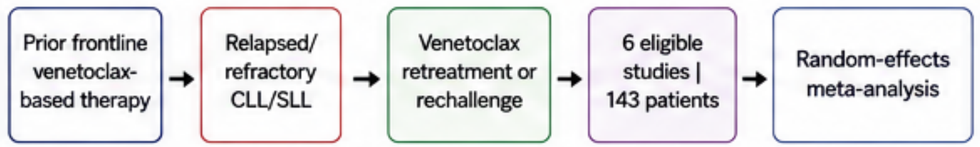
Outcome	Pooled estimate	95% CI
Overall response rate (ORR)	91.6%	(86.0% – 95.2%)
Partial response (PR)	73.7%	(66.0% – 80.4%)
Complete response (CR)	17.9%	(12.9% – 23.8%)
Peripheral-blood MRD negativity*	65.9%	(56.7% – 74.1%)
Bone-marrow MRD negativity*	59.4%	(49.6% – 68.4%)

*MRD outcomes were evaluated in 122 patients.

SAFETY

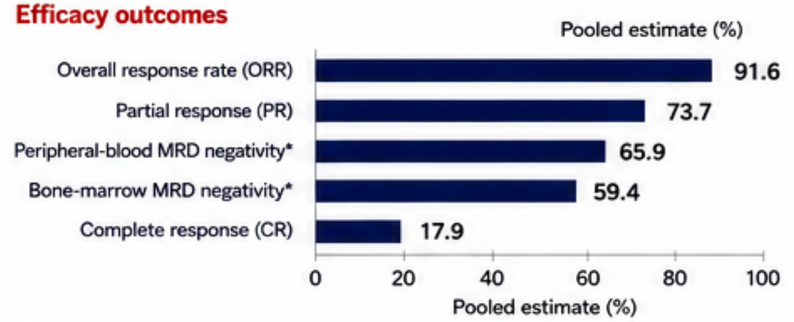
Outcome	Pooled estimate	95% CI
Grade ≥3 neutropenia	30.0%	(23.0% – 38.0%)
Grade ≥3 thrombocytopenia	6.9%	(3.1% – 11.5%)
Toxicity-related discontinuation	5.9%	(2.6% – 10.0%)
Tumor lysis syndrome (TLS)	2.7%	(1.1% – 5.5%)

Methods schematic

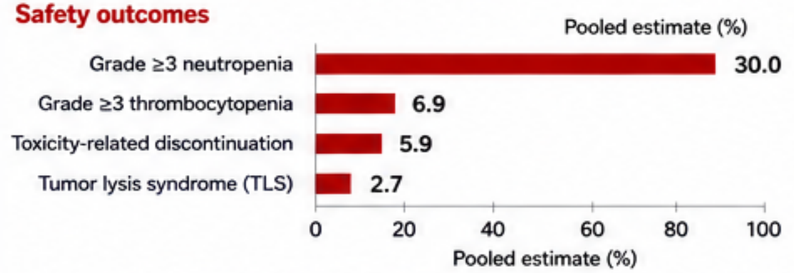


RESULTS (Graphical summary)

Efficacy outcomes



Safety outcomes



CONCLUSIONS

- Venetoclax retreatment after prior frontline venetoclax-based therapy produced a high pooled ORR (91.6%) in relapsed/refractory CLL/SLL.

ABBREVIATIONS

BM, bone marrow; CI, confidence interval; CLL, chronic lymphocytic leukemia; CR, complete response; EHA, European Hematology Association; MRD, measurable residual disease; ORR, overall response rate; OS, overall survival; PB, peripheral blood; PFS, progression-free survival; PR, partial response; SLL, small lymphocytic lymphoma; TLS, tumor lysis syndrome.

DISCLOSURES

The authors have no relevant conflicts of interest to disclose.

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