Efficacy and Safety of Fixed-Duration Venetoclax-Based Therapy in Chronic Lymphocytic Leukemia: A Systematic Review and Meta-Analysis

Basil Joy[1], Anusree Haridas[2], Manu Antony[3], Subodh Mathew[4]
[1] Government Medical College, Kozhikode, India
[2] Government Medical College, Trivandrum, India
[3] Jubilee Mission Medical College, Thrissur, India
[4] Government Medical College, Kottayam, India

INTRODUCTION

- Fixed-duration venetoclax-based regimens offer chemotherapy-free, time-limited treatment in CLL.
- They can achieve deep remissions and treatment-free intervals.
- However, pooled evidence across treatment settings remains limited.

AIM

To evaluate the efficacy, survival outcomes, MRD response, and safety of fixed-duration venetoclax-based therapy in adults with CLL/SLL.Method

METHOD

- Databases: PubMed, Embase, Cochrane CENTRAL & major conference databases.
- Search period: Inception–May 2026.
- Included phase 2/3 trials and prospective cohorts with ≥100 patients.
- 18 studies were included.
- Outcomes: PFS, OS, uMRD, and grade ≥3 adverse events.
- Hazard ratios were pooled using random-effects meta-analysis; proportions were pooled after logit transformation.
- Heterogeneity assessed using I^2.

CONCLUSIONS

- Fixed-duration venetoclax-based therapy provides deep, durable remissions across CLL settings.
- It is superior to chemoimmunotherapy and noninferior to continuous BTK inhibition.
- Significant survival benefit is demonstrated in relapsed/refractory CLL.
- uMRD is a strong, setting-independent predictor of disease control.
- The efficacy and safety profile supports fixed-duration venetoclax-based therapy as a preferred treatment framework in CLL.

RESULTS

Treatment-naïve CLL

•**67% reduction** in progression/death vs chemoimmunotherapy
HR 0.33 (95% CI 0.22–0.50)
•**OS benefit:** HR **0.67 (95% CI 0.48–0.94)**
•Pooled **uMRD: 78.4%** vs **8–37%** with comparators.

Versus continuous ibrutinib

•Noninferior PFS: **HR 0.87 (98.3% CI 0.54–1.41)**
•uMRD: **73.3% vs 0%**

Relapsed/Refractory CLL

•Venetoclax–rituximab reduced progression risk by **77%**
HR 0.23 (95% CI 0.18–0.29)
•Reduced mortality by **47%** at 7 years
HR 0.53 (95% CI 0.37–0.74)

MRD & Safety

•Achieving uMRD reduced subsequent progression risk by **76%**
HR 0.24 (95% CI 0.17–0.35)
•Grade ≥3 neutropenia: **38.4% vs 42.6%**
•Clinical tumor lysis syndrome: **<1%** with standard ramp-up.

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CONTACT INFORMATION

Email: drbjoe@gmail.com