Prognostic markers in patients with chronic lymphocytic leukemia on anti-CD20 chemoimmunotherapy: A systematic review & meta-analysis of prognostic factors

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INTRODUCTION

- Chemoimmunotherapy (CIT) consisting of anti-CD20 monoclonal antibodies (mAbs) have improved progression-free survival (PFS) and overall survival (OS) in patients with chronic lymphocytic leukaemia (CLL).
- We performed a synthesis of prognostic factors in patients with CLL on CIT with anti-CD20 mAbs compared with standard chemotherapy alone or novel targeted therapy.

OBJECTIVE(S)

- To assess evidence for treatment of patients with CLL with anti-CD20 mAbs and novel targeted therapy.
- To provide evidence-based prognostic factors associated with poor survival in patients with CLL on CIT with anti-CD20 mAbs.

METHODOLOGY

MeSH terms

Chronic lymphocytic leukemia
Rituximab
Ofatuzumab
Obinutuzumab
Ibrutinib
Acalabritunib
Venetoclax
Idelalisib
Anti-CD20 & prognosis

Inclusion criteria

- P: Patients with CLL
- I: CLL-IPI, GCLLSG, MDACC
- C: Additional prognostic factors
- O: PFS/OS
- T: RCTs at any time point & setting

Data sources

PubMed.gov
NIH ClinicalTrials.gov
EBSCOhost

Risk of bias assessment

- Quality In Prognostic Studies (QUIPS) tool.

Statistical analysis

- Inter-rater reliability - The Cohen's kappa
- The hazard ratios (HR) and 95% confidence interval (CI) were pooled to estimate the survival increases in OS and PFS.
- The random-effects model meta-analysis was performed.
- Prognostic factors were confirmed based on the robustness of the overall direction of the effect across all eligible studies.

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RESULTS

A total of 17 studies (7 349 patients) published between 2010 – 2021 in Europe, Americas, Australia and Asia were included in the analysis (fig 1).

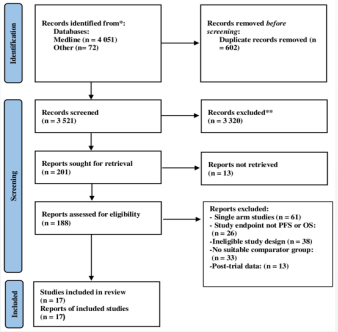

Fig 1: Study selection diagram

We judged the overall quality of these trials as low (n = 10), moderate (n = 5) and high (n = 2). Overall, the included studies were scored as low risk for study participation, moderate risk for study attrition and confounding measurement and high risk for prognostic factor measurement and statistical analysis and reporting

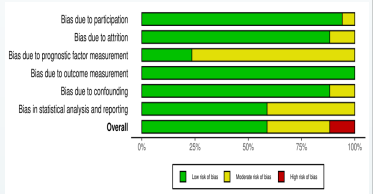

Fig 2: Risk of bias assessment

CIT with anti-CD20 mAbs was associated with improved PFS when compared to standard chemotherapy alone (HR = 0.50 CI [0.35–0.65], p<0.01). Targeted therapy was associated with improved OS (HR = 0.56 CI [[0.33–0.80], p = 0.05)

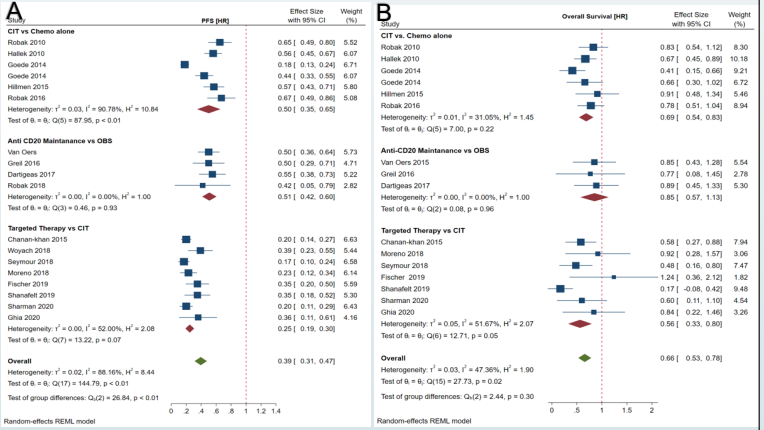

Fig 3: Meta-analysis of the HR for **a)** PFS and **b)** OS

RESULTS *continued*

Table 1: Confirmed prognostic factors included in a meta-analysis

Prognostic factors	Studies	Pooled HR
Deletion 17p	3	3.39
IGHV status	2	0.96
β_2 microglobulin	2	1.41

CONCLUSIONS

- The value of β_2-microglobulin as an independent prognostic marker has not been extensively assessed in patients with CLL on CIT and novel targeted therapy.
- Future studies comprising of diverse patient populations are needed especially in minority ethnic groups to allow for validation of this prognostic marker in the era of CIT and novel targeted therapy.
- Findings from this study are mainly derived from American and European populations. This limits the extrapolation of these findings into other low-to-middle income countries.

Disclosures: No relevant conflicts of interest to declare.

Trial registration: International Prospective Register of Systematic Reviews (PROSPERO) registry (CRD42021218997).

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