SERUM MONOCLONAL IMMUNOGLOBULIN PREDICTS INFERIOR PROGNOSIS IN PATIENTS TREATED FOR CHRONIC LYMPHOCYTIC LEUKEMIA

Martin Šimkovič[1,2], Filip Vyskočil[2], Pavel Vodárek[1,2], Dominika Écsiová[1,2], Lukáš Smolej[1,2]

[1] 4th Department of Internal Medicine – Hematology, University Hospital Hradec Králové, Czech Republic

[2] Charles University Faculty of Medicine in Hradec Králové, Czech Republic

1. Introduction

1. Chronic Lymphocytic Leukemia (CLL) prognosis is influenced by various markers (e.g. *TP53*, IGHV).
2. Previous research has highlighted the significance of paraproteins at CLL diagnosis.
3. Corbingi et al. (*BJH* 2020) discovered that serum monoclonal immunoglobulin (MIg) at diagnosis indicates a worsened prognosis.
4. The prognostic implications of MIg at the onset of therapy remain underexplored.

2. Objectives

- Analyze the prognostic relevance of MIg in CLL patients fulfilling IWCLL criteria for therapy (single-centre, retrospective study).
- Evaluate the prognostic relevance of MIg, including relationship to other known prognostic factors.
- Analyze data using the R software (v4.2.1).

3. Patients and methods

- Study Population: 220 CLL pts undergoing first-line treatment from 1996 to 2022 (see Table 1)
- Presence of serum monoclonal immunoglobulin :
  - 42 patients (19%) had detectable serum MIg.
  - IgM MIg: 23 patients (55%).
  - IgG MIg: 19 patients (45%).

Software Used: R software (version 4.2.1) | www.r-project.org. Proportion Differences: Determined using the chi-squared test. Survival Curves: Constructed via the Kaplan–Meier method. Survival Differences: Compared using the log-rank test. Independent Predictors: Determined by Cox regression analysis for time to event.

Tab. 1. Characteristics of Pts Treated for CLL Based on Monoclonal Immunoglobulin (MIg) Presence

Characteristics	MIg positive CLL	MIg negative CLL	*P*
Number of patients	42 (19%)	178 (81%)	
Age at CLL diagnosis in years, median	63	60	0.035
Age at administration of 1st line treatment in years, median	66	64	0.099
Male gender	24 (57%)	116 (65%)	NS
Median follow-up in months	131	162	NS
Time to first CLL treatment in months	33	36	NS
Prognostic markers			
Unmutated IGHV genes	27/39 (69%)	113/151 (75%)	NS
Del17p and/or *TP53* mutation	2/42 (5%)	10/178 (6%)	NS
Del11q	13/39 (33%)	53/167 (32%)	NS
Tris12	12/39 (39%)	21/173 (16%)	0.005
Del13q	20/39 (51%)	85/164 (52%)	NS
Complex karyotype	5/24 (21%)	20/119 (17%)	NS
Rai modified risk			
Low	4 (10%)	5 (1%)	0.049
Intermediate	7 (10%)	18 (10%)	NS
High	24 (35%)	66 (26%)	0.124
Treated with oral tyrosine kinase inhibitor	16 (38%)	90 (51%)	0.137
BCL-2 inhibitor	5 (12%)	28 (16%)	NS
PI3K inhibitor	4 (10%)	29 (16%)	NS
BTK inhibitor	12 (17%)	63 (35%)	NS

Abbreviations: CLL, chronic lymphocytic leukemia, MIg, monoclonal immunoglobulin, IGHV immunoglobulin heavy chain variable region, *TP53*, tumour protein p53, BCL-2, B-cell lymphoma 2, BTK, Bruton tyrosine kinase, PI3K, phosphatidyl inositol 3-kinase, NS, not significant

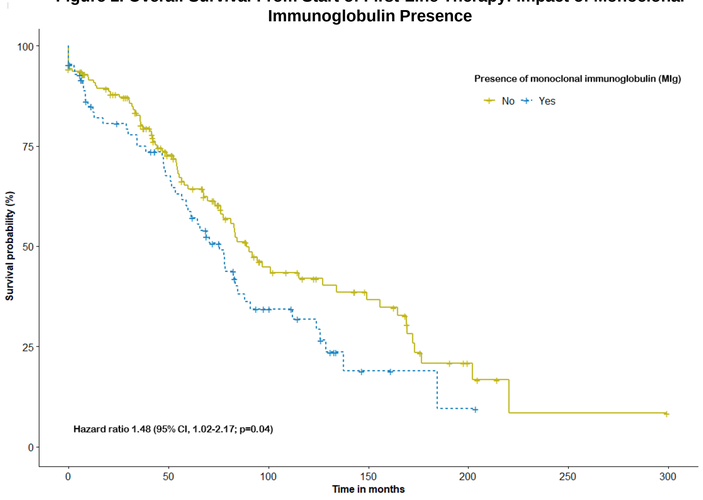
4. Results

•Survival Analysis:

•Overall survival with MIg: 78 months (95% CI, 61-94).

•Overall survival without MIg: 92 months (95% CI, 65-119) (Figure 1)

Figure 1. Overall Survival From Start of First-Line Therapy: Impact of Monoclonal Immunoglobulin Presence



5. Key Findings

- Presence of MIg correlated with shortened overall survival in univariate analysis: HR of 1.48 (95% CI 1.02-2.17; p=0.04).
- Chemoimmunotherapy without targeted inhibitors resulted in shorter survival: HR 1.72 (95% CI 1.08-2.74; p=0.02).
- Patients over 65 years had increased risk: HR 2.69, 95% CI 1.80-4.02; p<0.001.
- TP53 deletion/mutation was a negative indicator of OS: HR 2.95, 95% CI 1.01-8.59, p=0.05.

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