

Immunoglobulin Remission Kinetics as Prognostic Markers in Lymphoplasmacytic Lymphoma / Waldenström Macroglobulinemia

Peirou Yan^{1,2*}, Wenjie Xiong^{1,2*}, Yuting Yan^{1,2}, Tingyu Wang^{1,2}, Weiwei Sui^{1,2}, Ying Yu^{1,2}, Tengpeng Yu^{1,2}, Rui Lyu^{1,2}, Yi Wang^{1,2}, Wei Liu^{1,2}, Huimin Liu^{1,2}, Gang An^{1,2}, Yan Xu^{1,2}, Wenyang Huang^{1,2}, Dehui Zou^{1,2}, Lugui Qiu^{1,2#}, Shuhua Yi^{1,2#}

¹State Key Laboratory of Experimental Hematology, National Clinical Research Center for Blood Diseases, Haihe Laboratory of Cell Ecosystem, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin 300020, China

²Tianjin Institutes of Health Science, Tianjin 301600, China

#Correspondence:

Dr. Lugui Qiu, MD

¹State Key Laboratory of Experimental Hematology, National Clinical Research Center for Blood Diseases, Haihe Laboratory of Cell Ecosystem, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin 300020, China

²Tianjin Institutes of Health Science, Tianjin 301600, China

No. 288, Nanjing Road, Tianjin 300020, China

E-mail: qiulg@ihcams.ac.cn

Telephone number: 86-13821266636

Dr. Shuhua Yi, MD

¹State Key Laboratory of Experimental Hematology, National Clinical Research Center for Blood Diseases, Haihe Laboratory of Cell Ecosystem, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin 300020, China

Background:

Response evaluation in LPL/WM is dominated by static best-response categories that capture peak IgM reduction but not the tempo, magnitude, or durability of decline. Identical response grades may therefore conceal heterogeneous IgM kinetic patterns with different survival implications. Whether time to best response (TBR), maximal IgM reduction, and duration of best response (DBR) independently predict outcome remains unclear.

Objective:

To evaluate whether TBR, maximal IgM reduction, and DBR predict progression-free survival (PFS) and overall survival (OS) in LPL/WM.

Methods:

We retrospectively analyzed 235 patients with LPL/WM treated from 2007 to 2024 who had complete kinetic data. A total of 198 patients achieving minor response or better ($\geq$ MR) constituted the core analytical cohort. Cutoffs for kinetic parameters were defined from cohort data: TBR of 4 months, maximal IgM reduction of 80.45%, and DBR of 24 months. Patients were stratified by TBR alone and by combined TBR–DBR and TBR–IgM reduction depth groups to compare outcomes across distinct response-kinetic phenotypes. PFS and OS were the primary endpoints. Survival was estimated by the Kaplan–Meier method and compared with the log-rank test; landmark survival rates at 3, 5, and 10 years were calculated. Multivariable Cox proportional hazards models were used to identify independent prognostic factors for PFS and OS after adjustment for confounding variables.

Results:

A total of 235 patients were included. Median age was 60.00 (54.00–66.00) years, median IgM was 31.00 (17.15–55.70) g/L, and the MYD88 mutation rate was 84.3%. Among patients who received systemic therapy, median PFS was 56.50 months (range, 1.77–161.37) and median OS was 165.24 months (range, 2.56–219.78). Deep responders had a median PFS of 105.85 months, and median OS was not reached. Compared with PR/MR

or SD, CR+VGPR was associated with significantly longer PFS (median PFS for CR+VGPR vs PR+MR vs SD: 105.85 vs 52.76 vs 33.61 months; $P<0.001$); corresponding median OS values were not reached, 190.64, and 128.88 months ($P=0.055$).

Among patients achieving $\geq$ PR, delayed response (TBR ≥ 4 months) was associated with longer PFS and OS than early response (TBR < 4 months): median PFS was 96.39 vs 56.50 months, with 3-/5-/10-year PFS rates of 80.1%/64.0%/35.5% vs 74.6%/45.0%/9.6% ($P=0.046$); median OS was not reached vs 122.93 months, with 3-/5-/10-year OS rates of 96.6%/94.0%/87.3% vs 90.2%/83.7%/64.3% ($P=0.007$).

Combined TBR–DBR stratification showed the best OS for TBR ≥ 4 and DBR ≥ 24 months ($n=47$; 3-/5-/10-year OS 100.0%/96.9%/90.4%), followed by TBR < 4 and DBR ≥ 24 months ($n=64$; 94.9%/87.3%/72.6%) and TBR ≥ 4 and DBR < 24 months ($n=40$; 89.9%/81.0%/81.0%); OS was worst for TBR < 4 and DBR < 24 months ($n=47$; 78.2%/78.2%/58.6%). Overall differences across the four groups were significant for both PFS and OS (PFS $P<0.001$; OS $P=0.049$).

Combined maximal IgM reduction depth and TBR stratification showed the best PFS and OS for high reduction with TBR ≥ 4 months ($n=47$; median PFS not reached; 3-/5-/10-year PFS 84.8%/74.1%/52.1%; 3-/5-/10-year OS 100.0%/100.0%/91.7%), followed by high reduction with TBR < 4 months ($n=52$; median PFS 59.79 months; 3-/5-/10-year PFS 80.0%/45.8%/22.9%; 3-/5-/10-year OS 98.0%/98.0%/65.8%) and low reduction with TBR ≥ 4 months ($n=40$; median PFS 51.15 months; 3-/5-/10-year PFS 75.9%/44.4%/13.3%; 3-/5-/10-year OS 93.1%/80.7%/80.7%). PFS and OS were worst for low reduction with TBR < 4 months ($n=59$; median PFS 50.72 months; 3-/5-/10-year PFS 57.3%/35.8%/0.0%; 3-/5-/10-year OS 82.6%/73.6%/64.5%). Overall differences were significant for PFS and OS (PFS $P<0.001$; OS $P=0.020$).

On multivariable Cox analysis, TBR < 4 months was an independent risk factor for PFS (HR=1.754, $P=0.028$), and each 10% increase in maximal IgM reduction was an independent protective factor (HR=0.782, $P<0.001$). Early IgM decline rates differed significantly across regimens, with bendamustine-containing regimens declining fastest.

Conclusions:

IgM remission kinetics add prognostic value beyond static response depth. A shorter TBR

is not inherently advantageous; deep, delayed, and durable responses are associated with the most favorable outcomes, whereas shallow or early but non-durable responses are associated with the poorest outcomes.

Keywords: lymphoplasmacytic lymphoma; Waldenström macroglobulinemia; immunoglobulin kinetics; time to best response; duration of response; prognosis

Form record received

From International Workshop on Waldenstrom's Macroglobulinemia <pattersonkent@outlook.com>

Date Sun 26-Jul-26 7:57 AM

To Patterson, Christopher <Christopher_Patterson@DFCI.HARVARD.EDU>

External Email - Use Caution

Record saved to database with ID: 202

Form ID: 1

Form title: Abstract Submission

Form name: Abstract_Submission

Submitted at: 2026-07-26 07:56:41

Submitter IP: 125.37.189.92

User-ID: 0

Username: -

User full name: -

Submitter provider: Unknown

Submitter browser: Mozilla/5.0 (Windows NT 10.0; Win64; x64) AppleWebKit/537.36 (KHTML, like Gecko)

Chrome/150.0.0.0 Safari/537.36 Edg/150.0.0.0

Submitter operating system: win

First Name: Peirou

Last Name: Yan

Email: yanpeirou86@qq.com

Phone Number (optional): 18811572021

Registration Type: Delegate in Training

Abstract Title: Immunoglobulin Remission Kinetics as Prognostic Markers in Lymphoplasmacytic Lymphoma / Waldenström Macroglobulinemia

Select abstract file to attach:

/home/dkwolfpk2016/public_html/waldenstromworkshop/media/breezingforms/uploads/abstractiwwm13peirouyan.docx

Additional file (optional):

/home/dkwolfpk2016/public_html/waldenstromworkshop/media/breezingforms/uploads/abstractiwwm13peirouyan.pdf

Please consider me for a YIA grant: YIA Grant Consideration

Conference: IWWM13