

Hepatic response criteria in light chain amyloidosis: a multicenter validation study

Eli Muchtar,¹ Giovanni Palladini,^{2,3} Stefan Schönland,⁴ Susan Geyer,⁵ Katharine E. Dooley,⁵ Angela Dispenzieri,¹ Brendan Wisniowski,⁶ Giampaolo Merlini,^{2,3} Paolo Milani,^{2,3} Ute Hegenbart,⁴ Tobias Dittrich,⁴ Efstathios Kastritis,⁷ Meletios A. Dimopoulos,⁷ Vaishali Sanchorawala,⁸ Raphael Szalat,⁸ Michaela Liedtke,⁹ Mani Gupta,⁹ Heather Landau,¹⁰ Suzanne Lentzsch,¹¹ Michael S. Hughes,¹¹ Maria Teresa Cibeira,¹² Joan Bladé,¹² Shaji K. Kumar,¹ Ashutosh Wechalekar⁶ and Morie A. Gertz¹

¹Division of Hematology, Mayo Clinic, Rochester, MN, USA; ²Department of Molecular Medicine, University of Pavia, Pavia, Italy; ³Amyloidosis Research and Treatment Center, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy; ⁴Medical Department V, Amyloidosis Center, University of Heidelberg, Heidelberg, Germany; ⁵Division of Clinical Trials and Biostatistics, Mayo Clinic, Rochester, MN, USA; ⁶National Amyloidosis Centre, University College London, Royal Free Hospital Campus, London, UK; ⁷Department of Clinical Therapeutics, National and Kapodistrian University of Athens, Athens, Greece; ⁸Section of Hematology and Oncology, Amyloidosis Center, Boston University Chobanian & Avedisian School of Medicine, Boston Medical Center, Boston, MA, USA; ⁹Stanford Amyloid Center, Stanford University School of Medicine, Stanford, CA, USA; ¹⁰Division of Hematologic Oncology, Memorial Sloan Kettering Cancer Center, New York, NY, USA; ¹¹Division of Hematology/Oncology, Columbia University Medical Center, New York, NY, USA and ¹²Department of Hematology, IDIBAPS, Hospital Clinic, Barcelona, Spain

Correspondence: E. Muchtar
muchtar.eli@mayo.edu

Received: September 20, 2025.
Accepted: December 24, 2025.
Early view: January 15, 2026.

<https://doi.org/10.3324/haematol.2025.289218>

©2026 Ferrata Storti Foundation
Published under a CC BY-NC license 

Supplemental material to:

Hepatic response criteria in light chain amyloidosis: A multicenter validation study. Muchtar E,

Supplementary Table 1. Alkaline phosphates normal reference values in the participating centers	
Center	Reference
Mayo Clinic, Rochester, MN	Men: 40-129 U/L Female: 35-104 U/L
Pavia, Italy	46-150 U/L
Heidelberg, Germany	40-130 U/L
National amyloidosis center, London, UK	40-129 U/L
Athens, Greece	40-124 U/L
Columbia, New York, NY	40-129 U/L
Boston University, Boston, MA	25-100 U/L
Memorial Sloan Kettering, New York, NY	45-129 U/L
Stanford University, Stanford, CA	35-105 U/L
Barcelona, Spain	46-116 U/L

Supplementary Table 2. Comparison of Baseline characteristics between ASCT and non-ASCT patients			
	ASCT (n=23)	Non-ASCT (n=93)	P-value
Age, years, Median (range)	58 (37-82)	62 (40-83)	0.08
Male sex, N (%)	14 (60.9%)	52 (57.8%)	0.66
Lambda restricted, N (%)	12 (52.2%)	57 (61.3%)	0.42
Intact immunoglobulin isotype, N (%)			
IgG	6 (26.1%)	29 (31.2%)	0.81
IgA	2 (8.7%)	4 (4.3%)	
IgM	1 (4.3%)	6 (6.4%)	
Light chain only	14 (60.9%)	54 (58.1%)	
dFLC, mg/L, median (IQR)	170 (17-494)	193 (93-539)	0.02
BMPCs %, median (IQR)	10 (5-17)	10 (7-15)	0.98
Serum alkaline phosphatase, U/L, median (IQR)	357 (247-593)	307 (238-548)	0.55
Serum alkaline phosphates, folds of the upper limit of institutional normal, median (IQR)	3.2 (2.0-4.9)	2.4 (1.8-4.3)	0.17
Serum total bilirubin, mg/dL, median (IQR)	0.6 (0.4-1.0)	0.6 (0.4-0.9)	0.63
Serum albumin, g/dL, median (IQR)	3.5 (3.0-4.1)	3.3 (2.4-4.0)	0.18
Concomitant heart involvement, N (%)	6 (26.1%)	59 (63.4%)	0.0011
Concomitant kidney involvement, N (%)	15 (65.2%)	59 (63.4%)	0.87

Cardiac stage, % I / II / IIIA/ IIIB	65.2/34.8/0/0	15.6/40.0/31.1/13.3	<0.001
Renal stage, % I/II/III	68.2/27.3/4.5	42.0/39.8/18.2	0.05
Best hematological response			
CR	19 (82.6%)	30 (32.3%)	<0.001
VGPR	3 (13.0%)	28 (30.1%)	
PR	1 (4.4%)	35 (37.6%)	

Abbreviations: AL, light chain amyloidosis; ASCT, autologous stem-cell transplantation; BMPC, Bone marrow plasma cells; CR, complete response; dFLC, difference between involved and uninvolved light chains; HR, hazard ratio; IQR, Interquartile range; NR, no response; PR, partial response; VGPR, very good partial response

Bold signifies statistical significance (P-value <0.05)

Supplementary Table 3. 6-month landmark univariate and multivariate analysis for overall survival using binary 6-month hepatic response				
	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P
Age≥65 years (vs age <65)	2.75 (1.45 to 5.22)	0.002	1.8 (0.9 – 3.6)	0.1
ASCT as primary therapy	0.36 (0.13 to 1.01)	0.053	0.7 (0.2 - 2.1)	0.5
dFLC ≥ 180 mg/L	1.58 (0.83 to 3.02)	0.16	n\	a
Cardiac stage Stage IIIA + IIIB (vs Stage I + II)	1.72 (0.89 to 3.35)	0.11	1.5 (0.7 - 3.0)	0.28
Best hematological response Hematological CR/VGPR (vs hematological PR)	0.32 (0.17 to 0.62)	<0.001	0.4 (0.2 - 0.8)	0.011
Hepatic response Response (vs non-response)	0.8 (0.3 - 1.9)	0.62	0.6 (0.2 – 1.6)	0.34

Abbreviations: ASCT, autologous stem-cell transplantation; CI, Confidence interval; CR, complete response; dFLC, difference between involved and uninvolved light chains; HR, hazard ratio; PR, partial response; VGPR, very good partial response

Bold signifies statistical significance (P-value <0.05)

Supplementary Table 4. 12-month landmark univariate and multivariate analysis for overall survival using binary 12-month hepatic response				
	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P
Age≥65 years (vs age <65)	2.67 (1.31 to 5.43)	0.007	1.8 (0.8 – 3.9)	0.14
ASCT as primary therapy	0.43 (0.15 to 1.24)	0.12	0.6 (0.2 – 1.9)	0.37
dFLC ≥ 180 mg/L	1.43 (0.70 to 2.90)	0.32	n\	a
Cardiac stage Stage IIIA + IIIB (vs Stage I + II)	1.52 (0.72 to 3.23)	0.27	0.9 (0.4 – 2.2)	0.81
Best hematological response Hematological CR/VGPR (vs hematological PR)	0.25 (0.12 to 0.51)	<0.001	0.2 (0.1 - 0.5)	<0.001
Hepatic response Response (vs non-response)	0.3 (0.1 – 0.75)	0.009	0.2 (0.1 – 0.5)	<0.001

Abbreviations: ASCT, autologous stem-cell transplantation; CI, Confidence interval; CR, complete response; dFLC, difference between involved and uninvolved light chains; HR, hazard ratio; PR, partial response; VGPR, very good partial response

Bold signifies statistical significance (P-value <0.05)

Supplementary Table 5. 24-month landmark univariate and multivariate analysis for overall survival using 24-month binary hepatic response				
	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P
Age≥65 years (vs age <65)	2.65 (1.11 to 6.30)	0.028	1.6 (0.6 – 4.2)	0.34
ASCT as primary therapy	0.65 (0.22 to 1.95)	0.45	0.7 (0.2 – 2.7)	0.63
dFLC ≥ 180 mg/L	1.31 (0.55 to 3.08)	0.54	n\	a
Cardiac stage Stage IIIA + IIIB (vs Stage I + II)	1.20 (0.45 to 3.16)	0.72	1.0 (0.3 – 2.9)	0.95
Best hematological response Hematological CR/VGPR (vs hematological PR)	0.31 (0.13 to 0.73)	0.008	0.2 (0.1 - 0.7)	0.01
Hepatic response Response (vs non-response)	0.5 (0.2 – 1.2)	0.1	0.25 (0.1 – 0.7)	0.007

Abbreviations: ASCT, autologous stem-cell transplantation; CI, Confidence interval; CR, complete response; dFLC, difference between involved and uninvolved light chains; HR, hazard ratio; PR, partial response; VGPR, very good partial response

Bold signifies statistical significance (P-value <0.05)

Supplementary Table 6. 6-month landmark univariate and multivariate analysis for overall survival using the best graded (3-level) hepatic response criteria by 6 months

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P
Age≥65 years (vs age <65)	2.75 (1.45 to 5.22)	0.002	1.8 (0.9 – 3.7)	0.089
ASCT as primary therapy	0.36 (0.13 to 1.01)	0.053	0.7 (0.2 - 2.2)	0.55
dFLC ≥ 180 mg/L	1.58 (0.83 to 3.02)	0.16	n\	a
Cardiac stage Stage IIIA + IIIB (vs Stage I + II)	1.72 (0.89 to 3.35)	0.11	1.35 (0.7 - 2.7)	0.4
Best hematological response Hematological CR/VGPR (vs hematological PR)	0.32 (0.17 to 0.62)	<0.001	0.4 (0.2 - 0.8)	0.009
Graded hepatic response				
HepNR	Reference		Reference	
HepPR	1.4 (0.7 – 2.7)	0.34	1.6 (0.8 – 3.2)	0.1
HepVGPR/CR	0.7 (0.2 – 2.2)	0.5	0.6 (0.1 – 2.5)	0.45

Abbreviations: ASCT, autologous stem-cell transplantation; CI, Confidence interval; CR, complete response; dFLC, difference between involved and uninvolved light chains; Hep, hepatic; HR, hazard ratio; NR, No response; PR, partial response; VGPR, very good partial response

Bold signifies statistical significance (P-value <0.05)

Supplementary Table 7. 12-month landmark univariate and multivariate analysis for overall survival using best graded (3-level) hepatic response criteria by 12-months				
	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P
Age≥65 years (vs age <65)	2.67 (1.31 to 5.43)	0.007	1.5 (0.7 – 3.4)	0.33
ASCT as primary therapy	0.43 (0.15 to 1.24)	0.12	0.8 (0.2 – 2.6)	0.67
dFLC ≥ 180 mg/L	1.43 (0.70 to 2.90)	0.32	n\^a	
Cardiac stage Stage IIIA + IIIB (vs Stage I + II)	1.52 (0.72 to 3.23)	0.27	1.1 (0.5 – 2.6)	0.76
Best hematological response Hematological CR/VGPR (vs hematological PR)	0.25 (0.12 to 0.51)	<0.001	0.25 (0.1 - 0.6)	0.001
Graded hepatic response				
HepNR	Reference		Reference	
HepPR	1.1 (0.5 – 2.4)	0.81	0.8 (0.3 – 1.8)	0.56
HepVGPR/CR	0.5 (0.2 – 1.5)	0.21	0.3 (0.1 – 1.01)	0.051

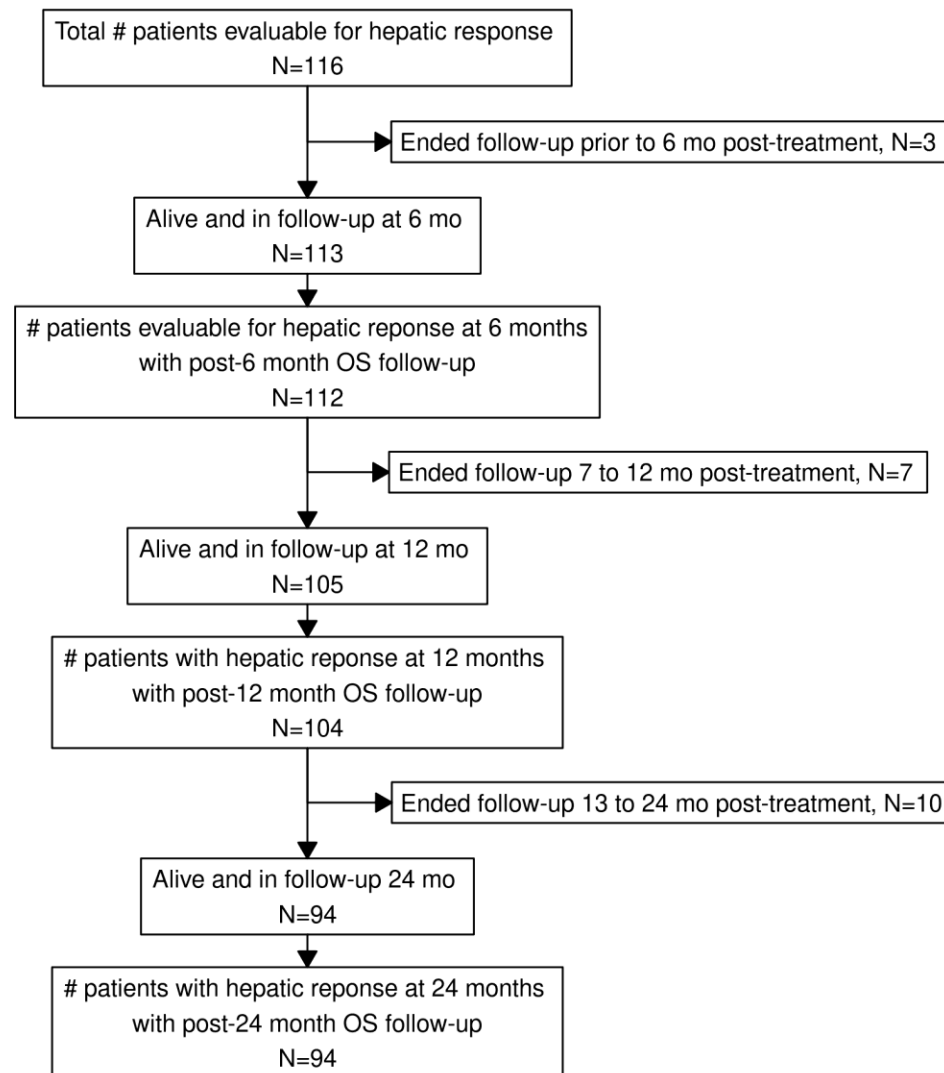
Abbreviations: ASCT, autologous stem-cell transplantation; CI, Confidence interval; CR, complete response; dFLC, difference between involved and uninvolved light chains; Hep, hepatic; HR, hazard ratio; NR, No response; PR, partial response; VGPR, very good partial response

Bold signifies statistical significance (P-value <0.05)

Supplementary Table 8. 24-month landmark univariate and multivariate analysis for overall survival using best graded (3-level) hepatic response criteria by 24-months				
	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P
Age≥65 years (vs age <65)	2.65 (1.11 to 6.30)	0.028	1.4 (0.5 – 3.7)	0.54
ASCT as primary therapy	0.65 (0.22 to 1.95)	0.45	1.0 (0.3 – 3.5)	0.95
dFLC ≥ 180 mg/L	1.31 (0.55 to 3.08)	0.54	n\	a
Cardiac stage Stage IIIA + IIIB (vs Stage I + II)	1.20 (0.45 to 3.16)	0.72	1.1 (0.4 – 3.2)	0.89
Best hematological response Hematological CR/VGPR (vs hematological PR)	0.31 (0.13 to 0.73)	0.008	0.3 (0.1 - 0.8)	0.016
Graded hepatic response				
HepNR	Reference		Reference	
HepPR	0.7 (0.2 – 2.1)	0.54	0.4 (0.1 – 1.4)	0.16
HepVGPR/CR	0.4 (0.1 – 1.3)	0.12	0.2 (0.05 – 0.7)	0.014

Abbreviations: ASCT, autologous stem-cell transplantation; CI, Confidence interval; CR, complete response; dFLC, difference between involved and uninvolved light chains; Hep, hepatic; HR, hazard ratio; NR, No response; PR, partial response; VGPR, very good partial response

Bold signifies statistical significance (P-value <0.05)



Supplementary Figure 1: Flow diagram for landmark analysis cohorts