Bispecifics in AL Amyloidosis

Dr Olga Motorna

Clinical Haematologist and Myeloma Lead, Box Hill Hospital

Clinical Haematologist, Alfred Hospital

Mrs NK, 81F

- HPC
  - Fatigue
  - LOW 10kg over 3 years > 36kg
  - Diarrhoea
  - Occ abdominal pain
  - Anorexia, dysphagia, early satiety
  - SOBOE
  - Occ chest tightness
  - No orthostatic sx
  - Peripheral neuropathy
- PMH
  - RA on prednisolone 2.5mg
  - Iron deficiency anaemia
  - Melanoma right leg 2006
  - Numerous BCCs and SCCs
  - OA
- SH
  - Retired councillor
  - Fully independent
  - Home with husband, 2 children, 4 grandchildren
  - Non-smoker, a glass of wine with dinner
  - Active social life!

Diagnosis

- Baseline LLC 5814 mg/L, KLC 19.4 mg/L, no intact paraprotein
- BMAT: 15% plasma cells, 1q+, Congo Red positive (lambda) in connective tissue
- Normal FBE, renal function, Ca, skeletal imaging
- No albuminuria/ proteinuria
- NT-proBNP 7313 ng/L, troponin 85 ng/L
- ECHO: IVS 17mm, PW 18mm, EF 55%, GLS -10%
- CMR c/w adv cardiac amyloidosis
- Scopes: amyloid in vessels of stomach, duodenum and colon, some amyloid in gastric lamina propria

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- Systemic light chain (AL) amyloidosis with cardiac, GI and autonomic involvement

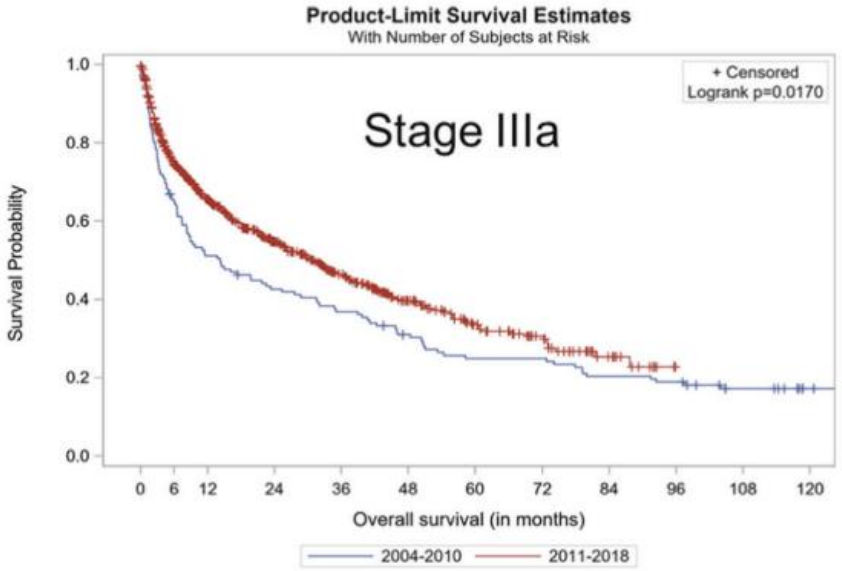
Table 1. Prognostic Models in AL Amyloidosis

Prognostic Model	NT-proBNP	Cardiac Troponin	dFLC	Stage	Median OS by Stage
Mayo 2004 model[43]	≥332 ng/L	cTnT ≥0.035 μg/L or cTnI ≥0.1 μg/L	NA	I: no marker above threshold II: 1 marker above threshold III: 2 markers above threshold	I: 26.4 mo (HR, ref) II: 10.5 mo (HR, 2.5 mo) III: 3.5 mo (HR, 6.7 mo)
European modification of Mayo 2004 model[28,44]	≥332 ng/L (>8,500 ng/L identifies higher risk)	cTnT ≥0.035 μg/L or cTnI ≥0.1 μg/L	NA	I: no marker above threshold II: 1 marker above threshold IIIa: 2 markers above threshold; NT-proBNP 332–8,500 ng/L IIIb: 2 markers above threshold and NT-proBNP >8,500 ng/L	I: Median OS, NR; 10-y OS, 57% (HR, ref) II: 67 mo (HR, 2.5 mo) IIIa: 15 mo (HR, 4.9 mo) IIIb: 4 mo (HR, 11.1 mo)
Mayo 2012 model[45]	≥1,800 pg/mL	cTnT ≥0.025 μg/L or cTnI ≥0.1 μg/L	≥18 mg/dL	I: no marker above threshold II: 1 marker above threshold III: 2 markers above threshold IV: 3 markers above threshold	I: 94.1 mo (HR, ref) II: 40.3 mo (HR, 1.7 mo) III: 14 mo (HR, 4.1 mo) IV: 5.8 mo (HR, 6.3 mo)

Diagnosis

- Baseline LLC 5814 mg/L, KLC 19.4 mg/L, no intact paraprotein
- BMAT: 15% plasma cells, 1q+, Congo Red positive (lambda) in connective tissue
- Normal FBE, renal function, Ca, skeletal imaging
- No albuminuria/ proteinuria
- NT-proBNP 7313 ng/L, troponin 85 ng/L
- ECHO: IVS 17mm, PW 18mm, EF 55%, GLS -10%
- CMR c/w adv cardiac amyloidosis
- Scopes: amyloid in vessels of stomach, duodenum and colon, some amyloid in gastric lamina propria

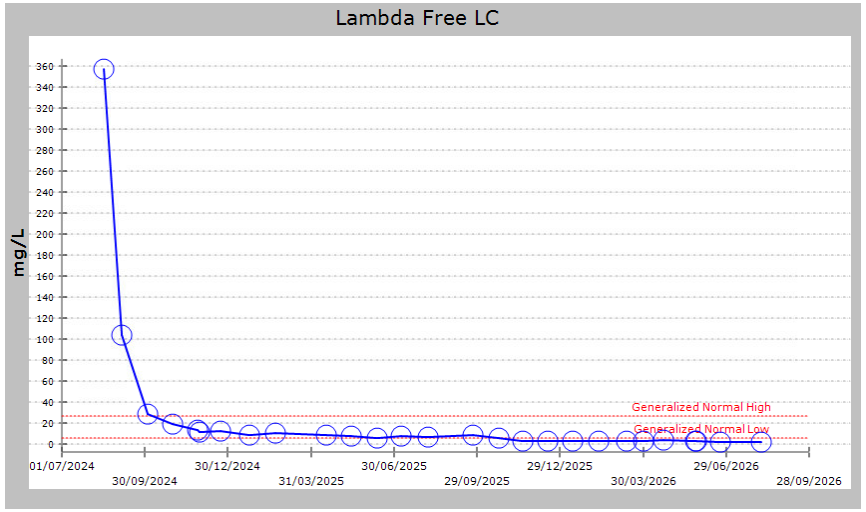
- Systemic light chain (AL) amyloidosis with cardiac, GI and autonomic involvement
- Mayo stage IIIa

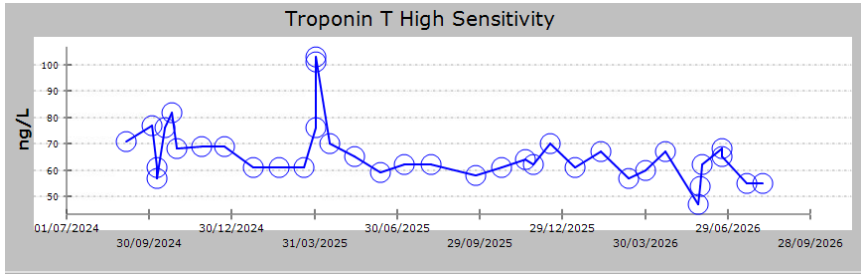


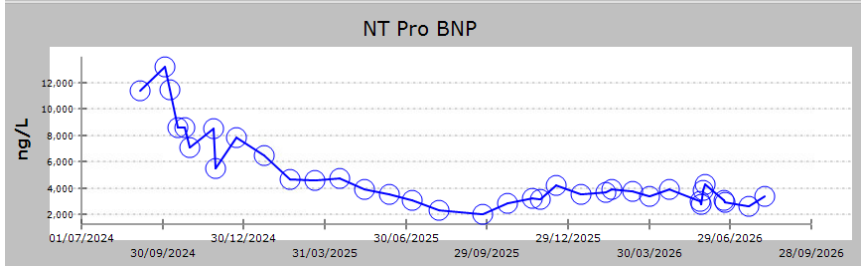
Palladini et al, Blood Cancer Journal , 2023

Treatment

1. D-VCD +/- CAEL-101 (mAb targeting amyloid fibrils) x 7 cycles → PR
2. PCD → MR, poorly tolerated (diarrhoea)
3. M24-209 clinical trial (BCMA-targeting bispecific etentamig) Aug 2024 – Aug 2026
    - Haematological response:
        - VGPR by C3
        - iFLC<20 by C4
        - dFLC<10 by C5
    - Cardiac response by C5
    - No CRS or ICANS
    - 3 LRTIs and 2 URTIs (in 2 years)







Why T-cell redirecting therapy in AL amyloidosis?

1. **Depth and speed of clonal response are critical determinants of survival**
   - Ongoing tissue deposition of amyloid fibrils + direct toxicity of circulating free light chains
   - Achieving **≥VGPR, and ideally dFLC <10 mg/L / iFLC ≤20 mg/L** is associated with improved organ responses and survival

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2. **Unmet need in RR AL amyloidosis**
   - 40% of the patients will not achieve CR with D-VCd
   - Late line options are increasingly limited by organ toxicity, PBS constraints and absence of clinical trials

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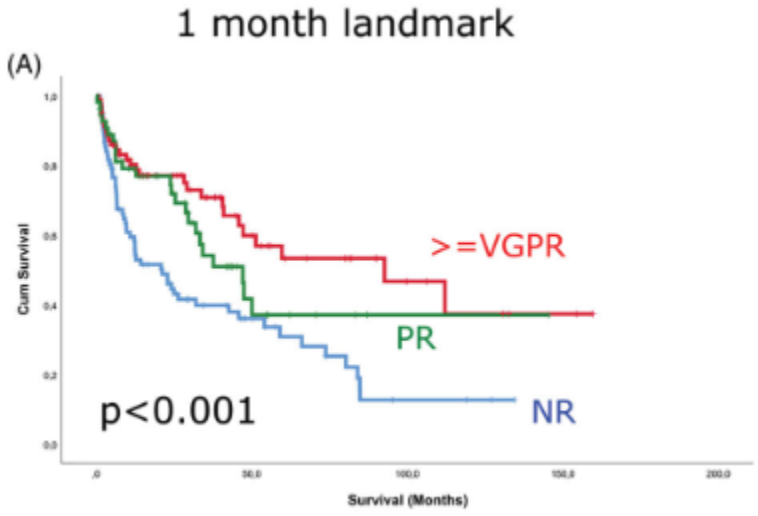
   - 40% of the patients will not achieve CR with D-VCd
   - Late line options are increasingly limited by organ toxicity, PBS constraints and absence of clinical trials
3. **Low tumour burden plasma cell clone may be more susceptible to TCE + translate to less risk of complications**

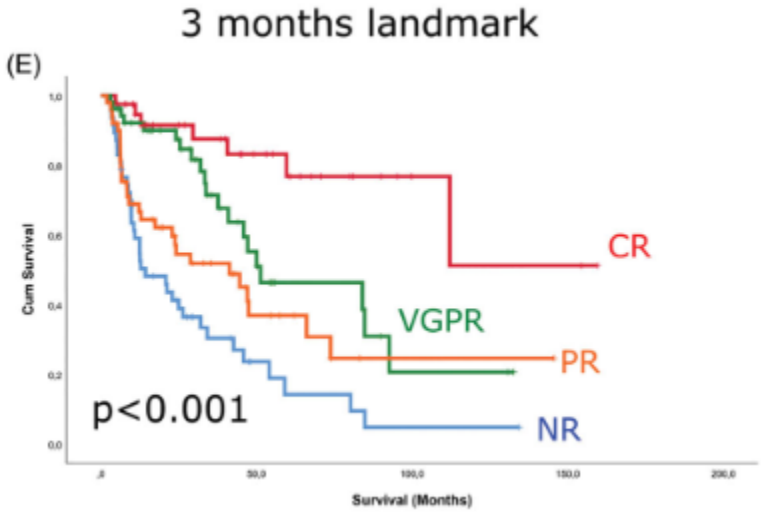
Table 2. Validated criteria for response assessment in light chain amyloidosis

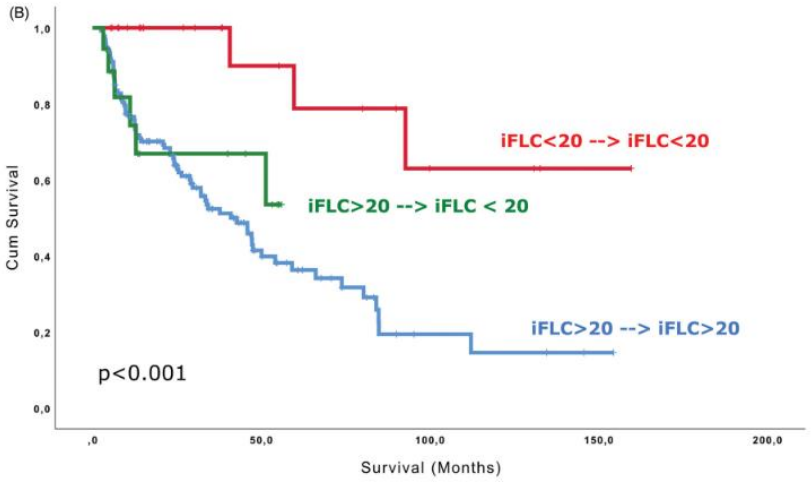
Response criteria	Definition
Hematologic response	
Complete response	Negative serum and urine immunofixation and normal FLC ratio
Very good partial response	dFLC <40 mg/L
Partial response	dFLC decrease >50% compared to baseline
No response	All other patients
Patients with dFLC <50 mg/l	
Complete response	Negative serum and urine immunofixation and normal FLC ratio
Low-dFLC-response	dFLC <10 mg/l
Cardiac response	Decrease of NT-proBNP by >30% and 300 ng/l (if baseline NT-proBNP >650 ng/l), or at least a 2-point decrease of NYHA class (if baseline NYHA class is III or IV)
Renal response	At least 30% decrease in proteinuria or drop below 0.5 g/24 h, in the absence of renal progression defined as a >25% decrease in eGFR

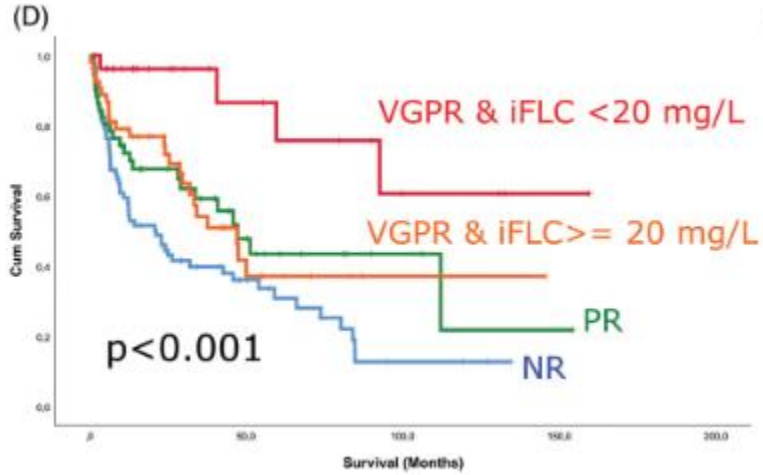
Milani et al, Kidney Int Reports , 2018

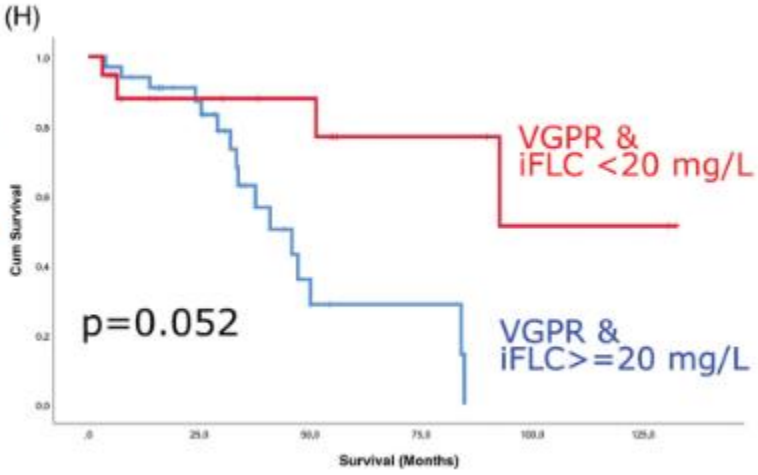
Timing and impact of a deep response on the outcome of patients with AL amyloidosis











If you haven't reached a VGPR by 1 month, you have only 25% chance of reaching it by 3 months

Kastritis et al, Amyloid, 2021

Guideline Article

Guidelines for non-transplant chemotherapy for treatment of systemic AL amyloidosis: EHA-ISA working group

Ashutosh D. Wechalekar, M. Teresa Cibeira, Simon D. Gibbs, Arnaud Jaccard, Shaji Kumar, Giampaolo Merlini, ...show all

Pages 3-17 | Received 14 Mar 2022, Accepted 21 Jun 2022, Published online: 15 Jul 2022

Recommendations on goals of clone directed treatments in AL amyloidosis:

- *Goal of treatment is to achieve a complete haematologic response (Grade B, Level IIb) with iFLC <20 mg/L or dFLC <10 mg/L (Grade B; Level III)*
- *Patients achieving less than a very good partial response by cycle 3 or less than a partial response by cycle 2 should be considered for treatment modification (Grade C; Level IV)*

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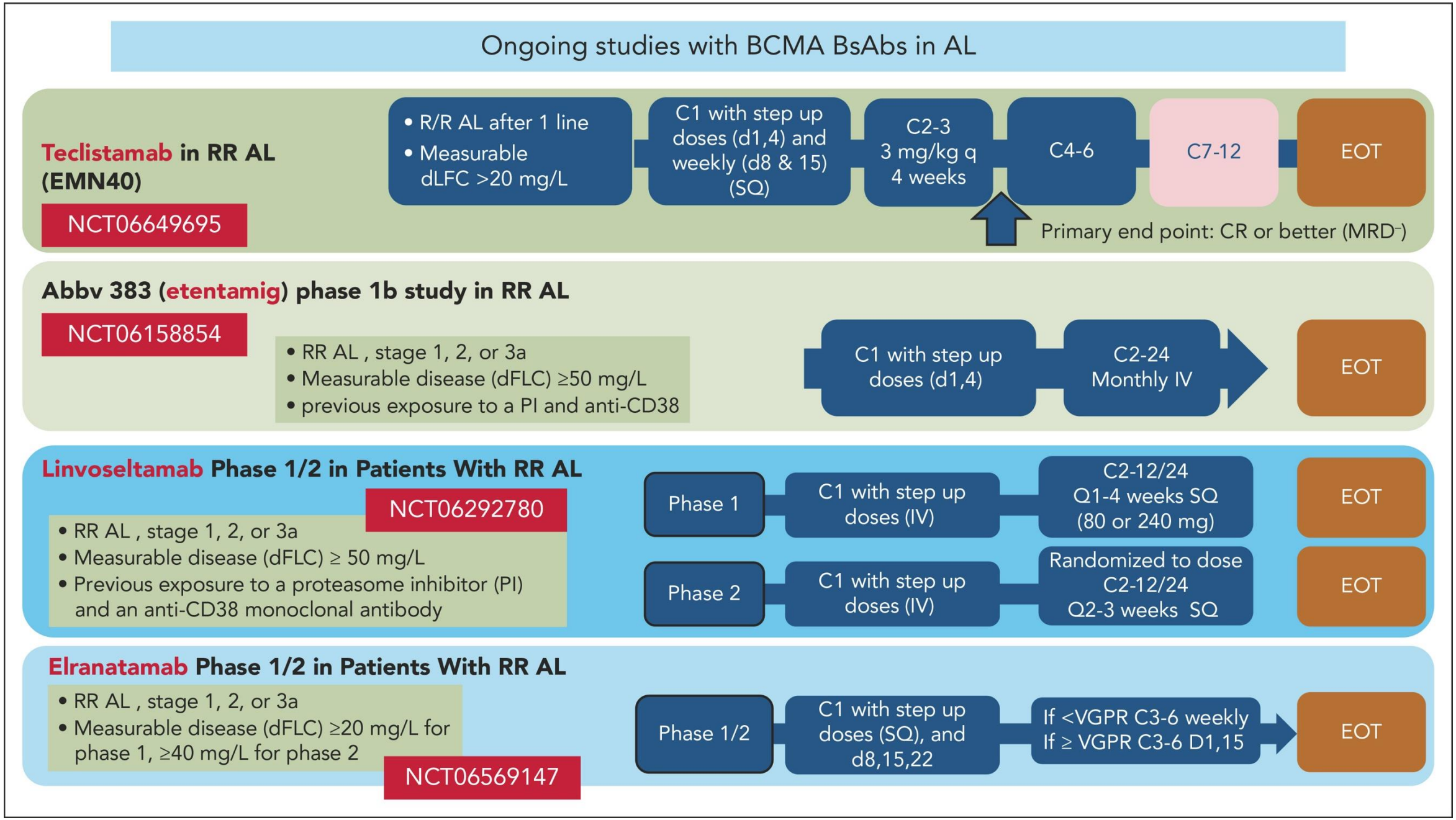
A UK consensus algorithm for early treatment modification in ND AL amyloidosis:

In a multivariate model, difference in involved amyloidogenic and uninvolved serum free light chains (dFLC) at diagnosis (dFLC >400 mg/l, odds ratio [OR] 4.051, $p < 0.005$) and no response at 1 month (OR 4.787, $p < 0.005$) were significant predictors of no improvement in response. Only 5% of patients with a dFLC of >400 mg/l and no response at 1 month improved their response ($p < 0.005$). We suggest that these patients should switch treatment early, subject to their functional status.

Ravichandran et al, BJH , 2022

Rapid and deep haematological responses are fundamental to achieving organ recovery and improving survival in AL amyloidosis


Ongoing studies with BCMA BsAbs in AL
Teclistamab in RR AL (EMN40)
NCT06649695
• R/R AL after 1 line
• Measurable dLFC >20 mg/L
C1 with step up doses (d1,4) and weekly (d8 & 15) (SQ)
C2-3 3 mg/kg q 4 weeks
C4-6
C7-12
EOT
Primary end point: CR or better (MRD⁻)
Abbv 383 (etentamig) phase 1b study in RR AL
NCT06158854
• RR AL , stage 1, 2, or 3a
• Measurable disease (dFLC) ≥50 mg/L
• previous exposure to a PI and anti-CD38
C1 with step up doses (d1,4)
C2-24 Monthly IV
EOT
Linvoseltamab Phase 1/2 in Patients With RR AL
NCT06292780
• RR AL , stage 1, 2, or 3a
• Measurable disease (dFLC) ≥ 50 mg/L
• Previous exposure to a proteasome inhibitor (PI) and an anti-CD38 monoclonal antibody
Phase 1
C1 with step up doses (IV)
C2-12/24 Q1-4 weeks SQ (80 or 240 mg)
EOT
Phase 2
C1 with step up doses (IV)
Randomized to dose C2-12/24 Q2-3 weeks SQ
EOT
Elranatamab Phase 1/2 in Patients With RR AL
• RR AL , stage 1, 2, or 3a
• Measurable disease (dFLC) ≥20 mg/L for phase 1, ≥40 mg/L for phase 2
NCT06569147
Phase 1/2
C1 with step up doses (SQ), and d8,15,22
If <VGPR C3-6 weekly
If ≥ VGPR C3-6 D1,15
EOT

Phase 1/2 Dose Escalation and Expansion Study of Etentamig in Patients With Relapsed or Refractory Light Chain Amyloidosis

Efstathios Kastritis[1], Antoine Huart[2], Rajshekhar Chakraborty [3], Arnaud Jaccard[4], Heather J Landau[5], Shinsuke Iida[6], Olga Motorna[7], Tadao Ishida[8], Yawara Kawano[9], Manisha Bhutani[10], Anita D'Souza[11], Andrew J Cowan[12], James E Hoffman[13], Chetasi Talati[14], Tanya S Rosenberg[14], Ross La Motte-Mohs[14], Fan Wang[14], David M Hoffman[14], Mingwei Fei[14], Emma L Arriola[14], Faisal Rahman[14], Cara Rosenbaum[14], Jovian Yu[14], Shaji Kumar[15], Angela Dispenzieri[16], Giovanni Palladini[17,18], Vaishali Sanchorawala[19]

[1]Department of Clinical Therapeutics, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece; [2]Department of Nephrology and Organ Transplantation, University Hospital Toulouse, Toulouse, France; [3]Multiple Myeloma and Amyloidosis Program, Herbert Irving Comprehensive Cancer Center, Columbia University Irving Medical Center, New York, NY, USA; [4]Hematology Department, French Reference Center for AL Amyloidosis (Limoges-Poitiers), CHU Limoges, Limoges, France; [5]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [6]Department of Hematology and Oncology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan; [7]Department of Haematology, Eastern Health, and Eastern Clinical School, Monash University; [8]Department of Hematology, Japanese Red Cross Medical Center, Tokyo, Japan; [9]Department of Hematology, Rheumatology, and Infectious Disease, Kumamoto University Graduate School of Medicine, Kumamoto, Japan; [10]Division of Hematology, Atrium Health Levine Cancer Institute, Wake Forest University School of Medicine, Charlotte, NC, USA; [11]Division of Hematology/Oncology, Department of Medicine, Froedtert & Medical College of Wisconsin Cancer Center, Milwaukee, WI, USA; [12]University of Washington and Fred Hutchinson Cancer Center, Seattle, WA, USA; [13]University of Miami Health System, Miami, FL, USA; [14]AbbVie Inc., North Chicago, IL, USA; [15]Division of Hematology, Department of Internal Medicine, Mayo Clinic, Rochester, MN, USA; [16]Division of Hematology, Mayo Clinic, Rochester, MN, USA; [17]Department of Molecular Medicine, University of Pavia, Pavia, Italy; [18]Amyloidosis Research and Treatment Center, Foundation "Istituto di Ricovero e Cura a Carattere Scientifico Policlinico San Matteo," Pavia, Italy; [19]Amyloidosis Center, Boston University School of Medicine and Boston Medical Center, Boston, MA, USA

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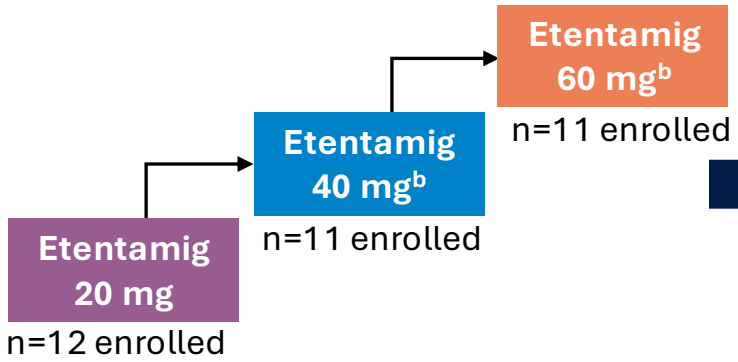
Global phase 1/2 study evaluating safety and efficacy of etentamig monotherapy in patients with RR AL amyloidosis

Phase 1 dose escalation

Key eligibility

- RR AL amyloidosis after ≥1 prior therapy (including PI and anti-CD38 mAb)
- No prior BCMA-targeted therapy
- ≥1 baseline organ involved
- Cardiac risk Mayo stage 1–3a[a]
- eGFR ≥ 20 mL/min
- Measurable hematologic disease: dFLC ≥50 mg/L

Dose escalation (N=34; fully enrolled)



Dosing

- Etentamig monotherapy Q4W from the start
- Single SUD of 2 mg incorporated in 40 mg and 60 mg cohorts in Cycle 1
- Fixed 24 months of etentamig
- Premedication with dexamethasone in Cycle 1[c]

Phase 2 dose expansion

Dose expansion (N=40)

Etentamig 40 mg[b]

Phase 1 endpoints

Primary endpoints

- Safety/tolerability, PK, and RP2D

Secondary endpoints

- Efficacy as measured by hematologic (ORR, CR) and organ response[d]

Ongoing study has fully enrolled to both dose escalation and expansion phases

[a]European Modification of the Mayo Stage (2013). [b]Cohorts with SUD incorporated on C1D1 and full dose on C1D4. [c]Dexamethasone can be tapered after C1 if no CRS or ICANS are observed. [d]Responses are investigator assessed per consensus guidelines (Comenzo, et al. *Leukemia*. 2012; 26(11):2317–2325; Palladini G, et al. *Amyloid*. 2021[Epub];28(1):1–2). AL, amyloid light-chain; BCMA, B-cell maturation antigen; C, cycle; CR, complete response; CRS, cytokine release syndrome; D, day; dFLC, difference between the involved and uninvolved free light chains; eGFR, estimated glomerular filtration rate; ICANS, immune effector cell-associated neurotoxicity syndrome; mAb, monoclonal antibody; ORR, overall response rate; PI, protease inhibitors; PK, pharmacokinetic; Q4W, every 4 weeks; RP2D, recommended phase 2 dose; RR, relapsed/refractory; SUD, step-up dosing.

Baseline characteristics were generally well-balanced

	20 mg Q4W (n=12)	40 mg Q4W (n=11)	60 mg Q4W (n=11)	Total (N=34)
Age, median years (range)	72 (56–85)	74 (49–82)	66 (54–84)	70 (49–85)
Sex, Male	5 (41.7)	9 (81.8)	4 (36.4)	18 (52.9)
Race, n (%)				
White	6 (54.5)	10 (90.9)	9 (81.8)	25 (75.8)
Black	1 (9.1)	0	1 (9.1)	2 (6.1)
Asian	4 (36.4)	1 (9.1)	1 (9.1)	6 (18.2)
Time from initial diagnosis, median years (range)	3.6 (0–12)	5.2 (0–13)	4.8 (0–21)	4.5 (0–21)
Number of prior LoT, median (range)	2 (1–6)	2 (1–8)	2 (1–4)	2 (1–8)
Prior Dara-CyBorD, n (%)	6 (50.0)	8 (72.7)	9 (81.8)	23 (67.6)
Daratumumab refractory, n (%)	8 (66.7)	7 (63.6)	8 (72.7)	23 (67.6)
Had prior SCT (yes), n (%)	4 (33.3)	2 (18.2)	1 (9.1)	7 (20.6)
dFLC, median mg/L (range)	110.5 (56.6–617.5)	91.4 (55.9–345.3)	118.8 (49.0–862.5)	108.9 (49.0–862.5)
Organ involvement at enrollment, n (%)				
Cardiac	10 (83.3)	9 (81.8)	9 (90.0)	28 (84.8)
Renal	3 (25.0)	6 (54.5)	4 (40.0)	13 (39.4)
Hepatic	1 (8.3)	2 (18.2)	0	3 (9.1)
Other[a]	4 (33.3)	3 (27.3)	0	8 (24.2)
Cardiac Risk Stage 3a at enrollment, n (%)	3 (25.0)	2 (18.2)	3 (27.3)	8 (23.5)
NT-proBNP, median ng/L (range)	548.1 (158.0–6827.2)	665.0 (118.4–1658.2)	414.5 (101.5–4982.9)	595.6 (101.5–6827.2)
Renal Risk Stage III at enrollment, n (%)	1 (9)	0	1 (9)	2 (5.6)

[a]In the 20 mg cohort, 1 patient each involving GI tract, gallbladder, GI/autonomic nervous system, lymph node/macroglossia; In the 40 mg cohort, 1 patient with GI tract and 2 patients with neurological involvement. Dara-CyBorD; daratumumab-cyclophosphamide, bortezomib, and dexamethasone; dFLC, difference between the involved and uninvolved free light chains; ECOG-PS, Eastern Cooperative Oncology Group performance status; GI, gastrointestinal; LoT, line of therapy; NT-proBNP, N-terminal pro-brain natriuretic peptide; Q4W, every 4 weeks; SCT, stem cell transplant. **(Data cut 22 Nov 2025)**

Promising safety profile of etentamig is observed with longer follow-up

	20 mg Q4W (n=12)		40 mg Q4W (n=11)		60 mg Q4W (n=11)		Total (N=34)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Any TEAE (≥15%)	12 (100.0)	7 (58.3)	10 (90.9)	5 (45.5)	11 (100.0)	6 (54.5)	33 (97.1)	18 (52.9)
Hypogammaglobulinemia	4 (33.3)	0	2 (18.2)	0	4 (36.4)	0	10 (29.4)	0
Upper respiratory tract infection	4 (33.3)	1 (8.3)	2 (18.2)	0	3 (27.3)	0	9 (26.5)	1 (2.9)
Cough	3 (25.0)	0	3 (27.3)	0	2 (18.2)	0	8 (23.5)	0
AST elevation	1 (8.3)	0	2 (18.2)	1 (9.1)	3 (27.3)	0	6 (17.6)	1 (2.9)
Blood creatinine increased	2 (16.7)	0	1 (9.1)	0	3 (27.3)	0	6 (17.6)	0
Diarrhea	1 (8.3)	0	3 (27.3)	0	2 (18.2)	0	6 (17.6)	0
Peripheral edema	2 (16.7)	0	3 (27.3)	0	1 (9.1)	0	6 (17.6)	0
Any Infection TEAEs	9 (75.0)	1 (8.3)	8 (72.7)	**1 (9.1)**	9 (81.8)	0	26 (76.5)	2 (5.9)
Hematologic TEAE (≥2%)								
Anemia	0	0	0	**0**	4 (36.4)	1 (9.1)	4 (11.8)	1 (2.9)
Neutropenia[a]	1 (8.3)	1 (8.3)	1 (9.1)	**1 (9.1)**	2 (18.2)	1 (9.1)	4 (11.8)	3 (8.8)
Lymphopenia[b]	1 (8.3)	1 (8.3)	0	**0**	2 (18.2)	2 (18.2)	3 (8.8)	3 (8.8)
Thrombocytopenia[c]	1 (8.3)	0	0	**0**	0	0	1 (2.9)	0

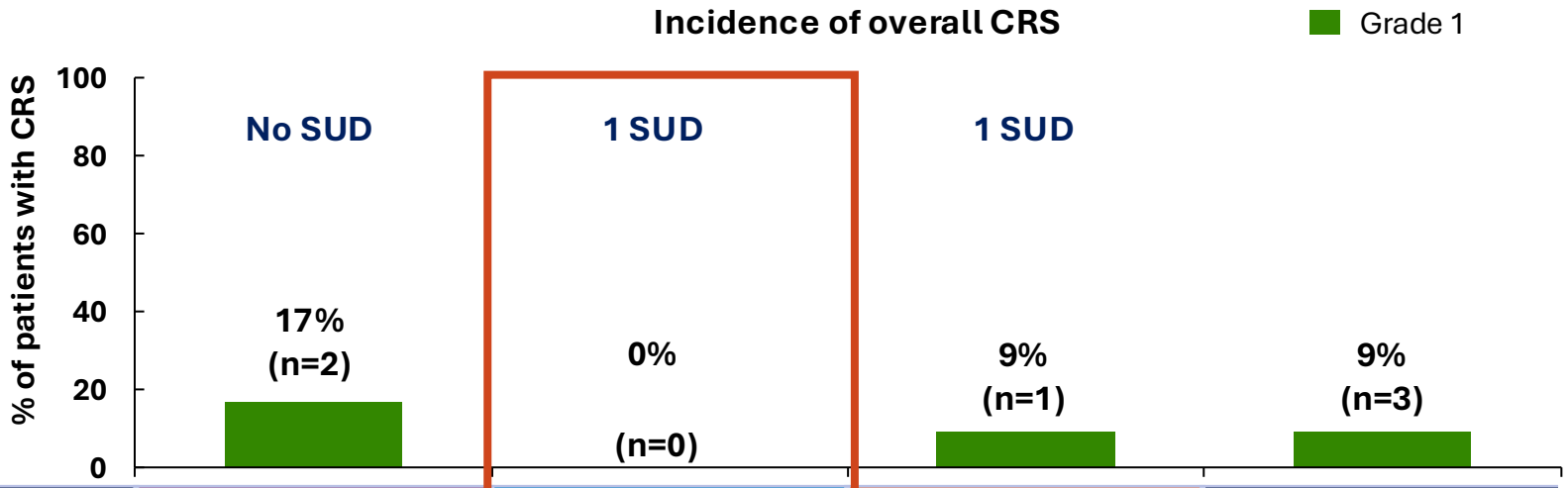
At 40 mg, 1 patient experienced a Grade 3 infection (No Grade 4)
No fatal events occurred across dosing cohorts

Data are displayed as n (%) unless stated otherwise. No new DLTs.
[a]Combined neutropenia and neutrophil count reduced.
[b]Combined lymphopenia and lymphocyte count reduced.
[c]Combined thrombocytopenia and platelet count reduced.
AST, aspartate aminotransferase; DLT, dose limiting toxicity; Q4W, every 4 weeks; TEAE, treatment emergent adverse event.

(Data cut 22 Nov 2025)

No case of CRS or ICANS occurred at RP2D of 40 mg

Across all cohorts:
- CRS incidence was 9%, all Grade 1
- No CRS recurrence
- No ICANS



	20 mg Q4W (n=12)	40 mg Q4W[a] (n=11)	60 mg Q4W[a] (n=11)	Total (N=34)
Time to CRS onset,[b] median (range) hours	6.8 (6.7–6.9)	0	12.4[d]	6.9 (6.7–12.4)
Time to CRS resolution,[c] median (range) hours	79.4 (8.8–150.0)	0	48.0[d]	48.0 (8.8–150.0)
Tocilizumab for management of CRS, n (%)	1 (8.3)	0	0	1 (2.9)
Rate of CRS recurrence, n (%)	0	0	0	0

At 40 mg with 1 SUD, NO CRS was observed without use of prophylactic tocilizumab

[a]SUD on Day 1 was implemented for 40 mg and 60 mg cohorts during Cycle 1. [b]Time to onset of AE is calculated by (start date/time of AE – date/time of last previous dose). [c]Time to resolution of AE is calculated as (end date/time of AE – start data/time of AE). [d]n=1; individual value presented as median (range) not calculable.

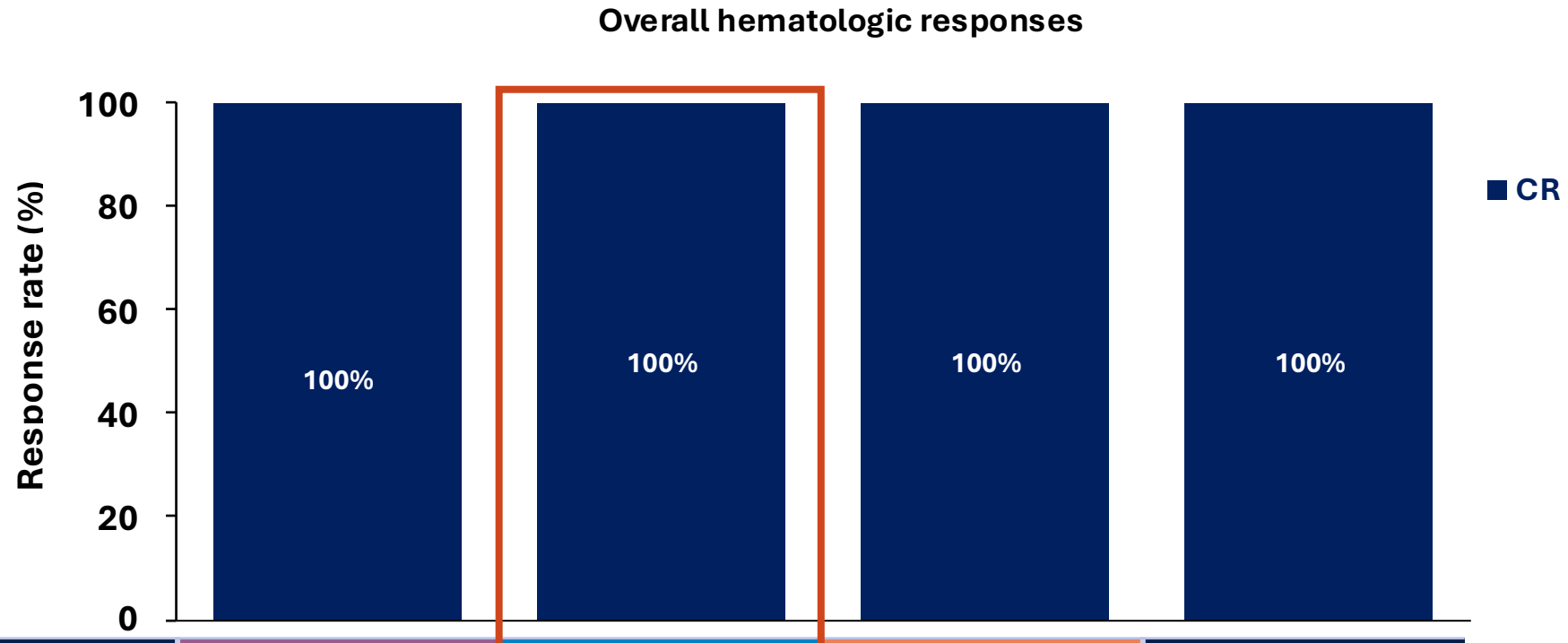
AE, adverse event; CRS, cytokine release syndrome; ICANS, immune effector-cell associated neurotoxicity syndrome; Q4W, every 4 weeks; RP2D, recommended phase 2 dose; SUD, step-up dosing.

(Data cut 22 Nov 2025)

Etentamig led to deep hematologic responses across all dose levels

As of May 1, 2026:

- 100% of patients have achieved hematologic CR across all cohorts
- In 40 mg cohort, 100% achieved MRD negativity at 10^{-5} in those that were MRD evaluable



	20 mg Q4W (n=12)	40 mg Q4W (n=11)	60 mg Q4W (n=11)	Total (n=34)
Time to first hematologic CR (TTCR), median (range) months	0.9 (0.2–15.7)	1.0 (0.2–13.0)	1.8 (0.2–10.1)	1.5 (0.2–15.7)

Overall hematologic CR rate was 100% with no cases of hematologic progression

CR assessed per IACC criteria (Palladini G, et al. *Amyloid*. 2021[Epub];28(1):1–2): Normalization of free light chain levels and ratio; and negative serum and urine immunofixation.
CR, complete response; MRD, minimal residual disease; Q4W, every 4 weeks.

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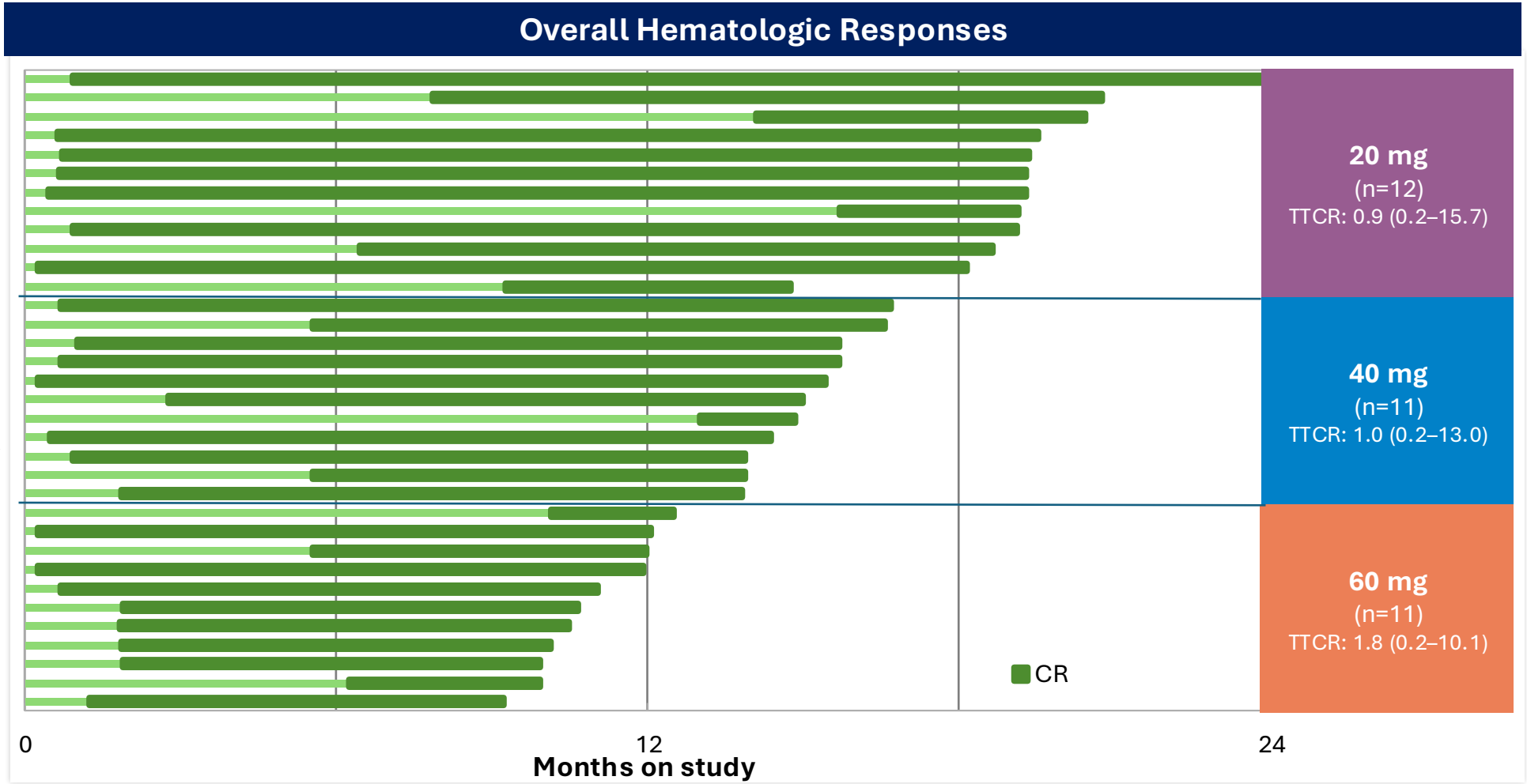

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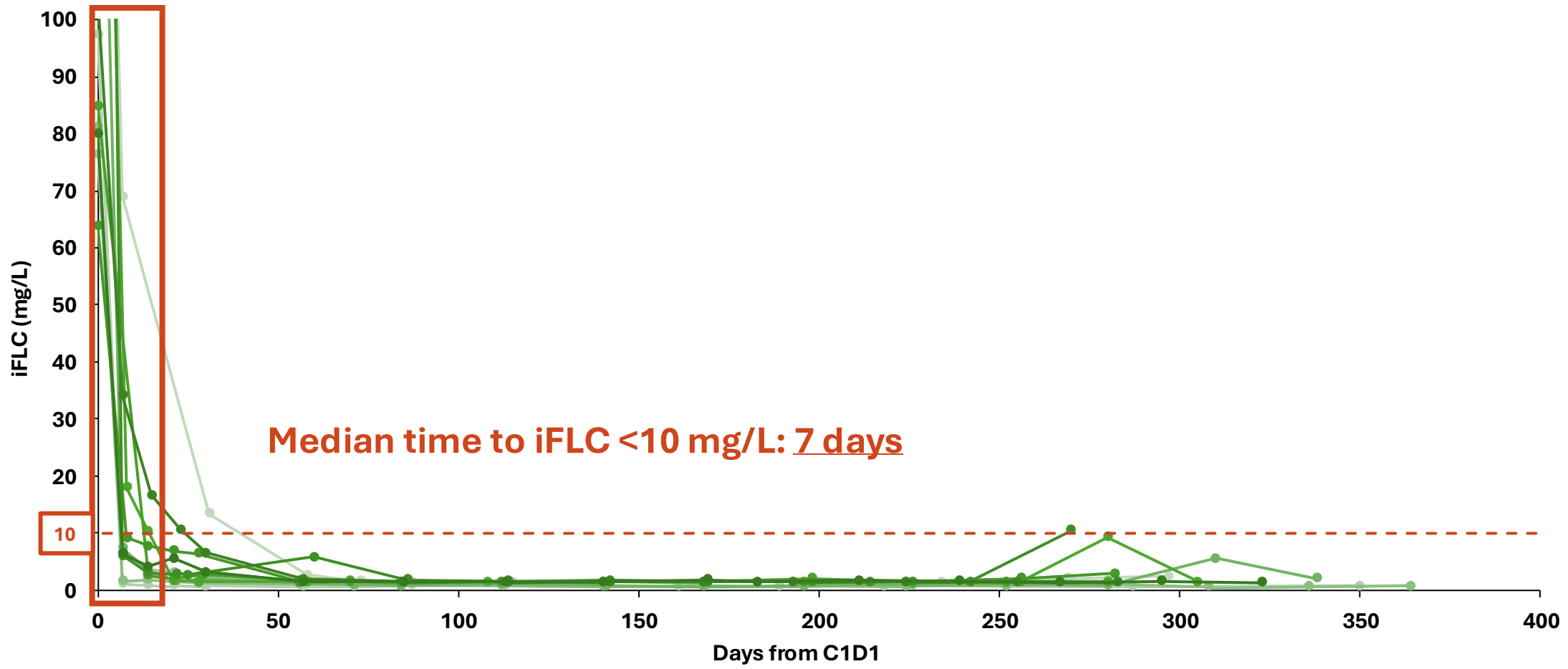
Etentamig 40 mg led to rapid decrease of iFLC to <10 mg/L

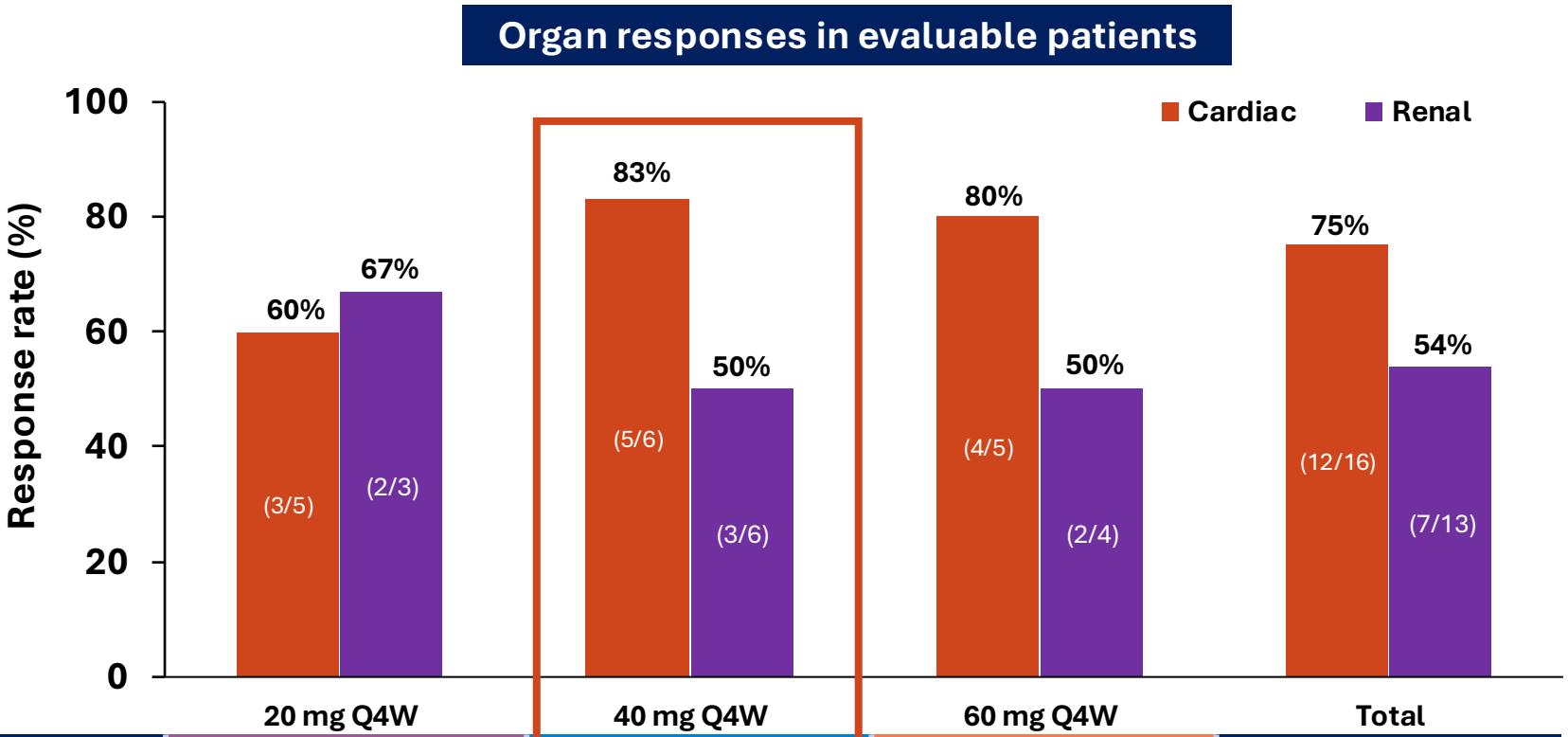


Rapid and profound iFLC reduction can be achieved in 1 week after the initial 40 mg dose

Range for time to iFLC is 7–58 days.
iFLC <10 mg/L threshold per Godara A et al. *Am J Hematol*. 2020 96(1):E20-23.
C, cycle; D, day; iFLC, involved free light chain.

(Data cut 22 Nov 2025)

Etentamig led to rapid and robust organ responses



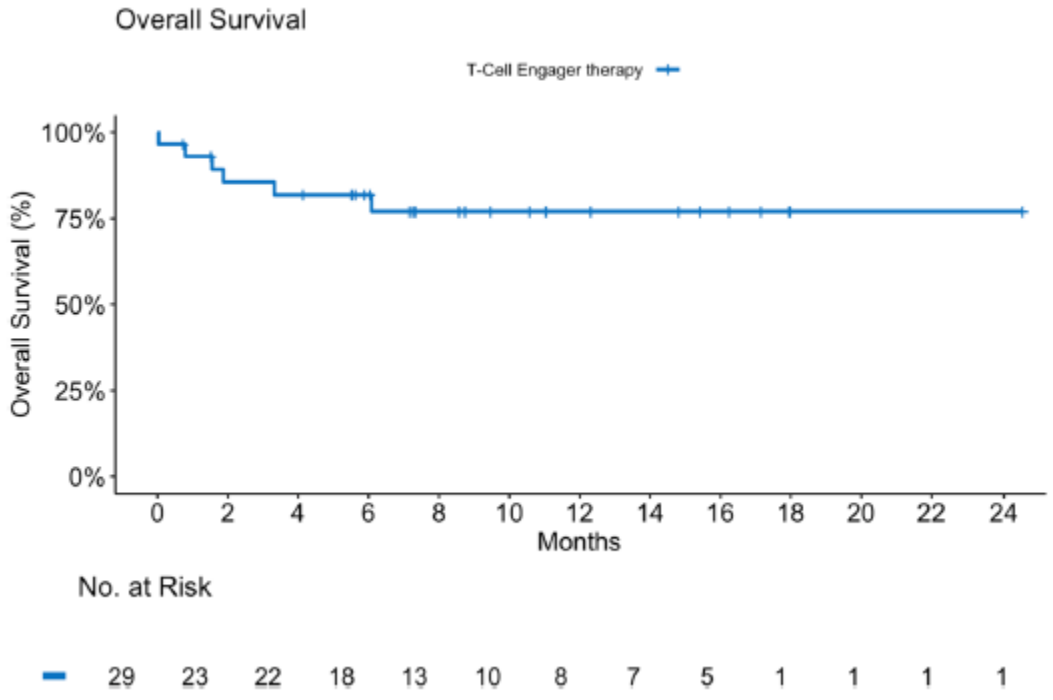
Response outcomes	20 mg Q4W	40 mg Q4W	60 mg Q4W	Total
Time to cardiac response, median (range) months	4.7 (2.8-7.5)	1.0 (0.5–5.6)	1.5 (0.9–3.7)	2.5 (0.5–7.5)
Time to renal response, median (range) months	1.4 (0.9–1.9)	1.9 (1.0–8.9)	1.4 (1.0–1.8)	1.8 (0.9–8.9)

Median duration of follow up was 10.1 (5.9–18.6) months.
Q4W, every 4 week.

(Data cut 22 Nov 2025)

In conclusion

- TCEs are highly effective, tolerable and feasible in RR AL amyloidosis
- Real-world data are a little more sobering
- Optimal treatment duration, sequencing and combination strategies remain to be worked out
- Frontline studies upcoming:
  - Enlight: elranatamab monotherapy
  - M25-586: etentamig v D-VCD



Rees et al, AJH 2025

“As the light chains are now at remission levels, I am looking forward to getting stronger, being the gardener I once was and rejoining our walking group.

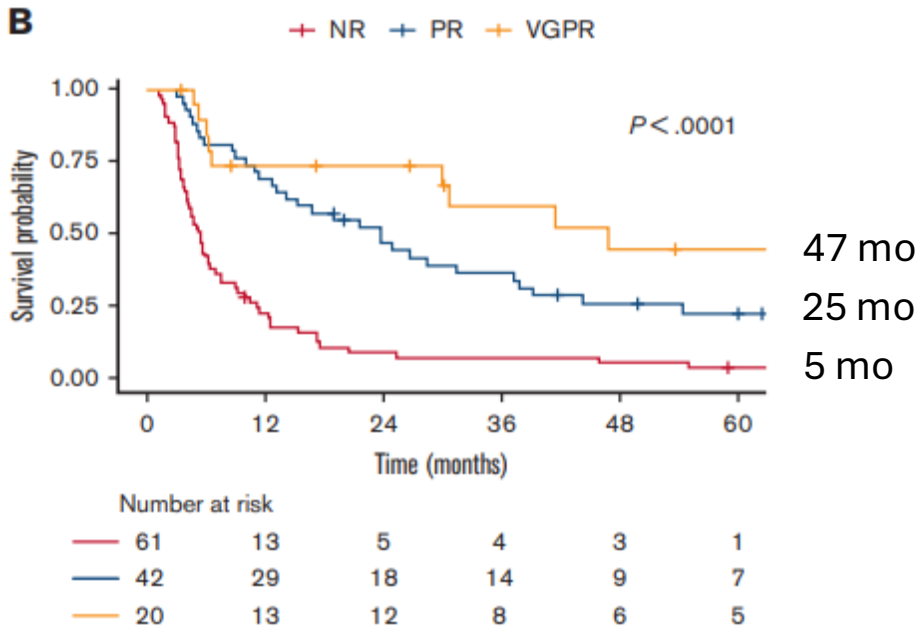
I recently walked up the steep rocky slope to the top of Mt Tinbeerwah in Queensland - and I must say, I was very pleased with myself!

I believe I have been extremely fortunate to be on the clinical trial; the success it has been for me has enabled me to enjoy life again. One day at a time is my motto.”

Patient photographs and quotation used with permission

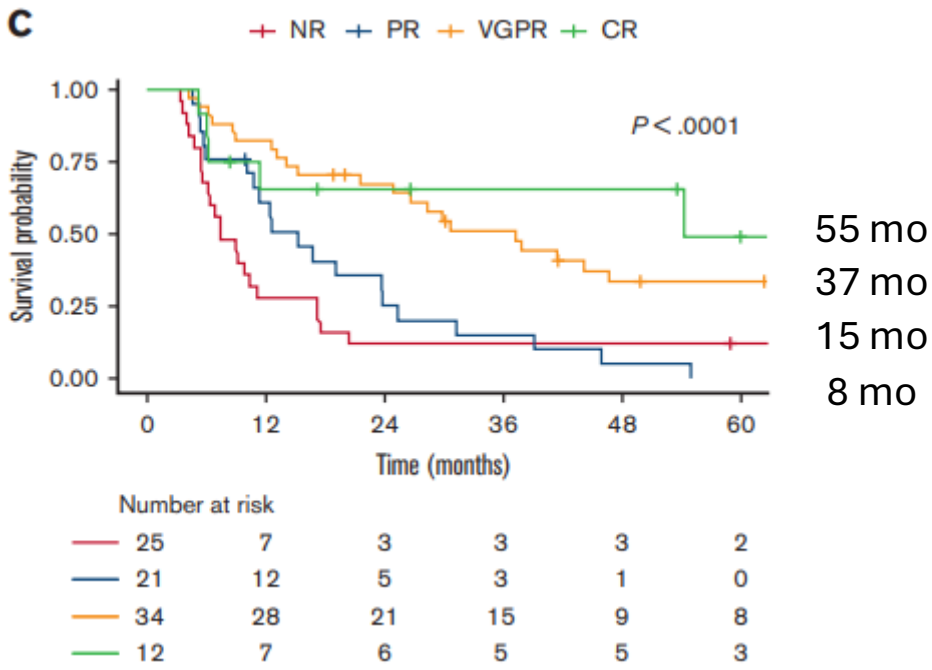
Impact of haematologic responses on survival in stage IIIb AL amyloidosis

Responses at 1 month



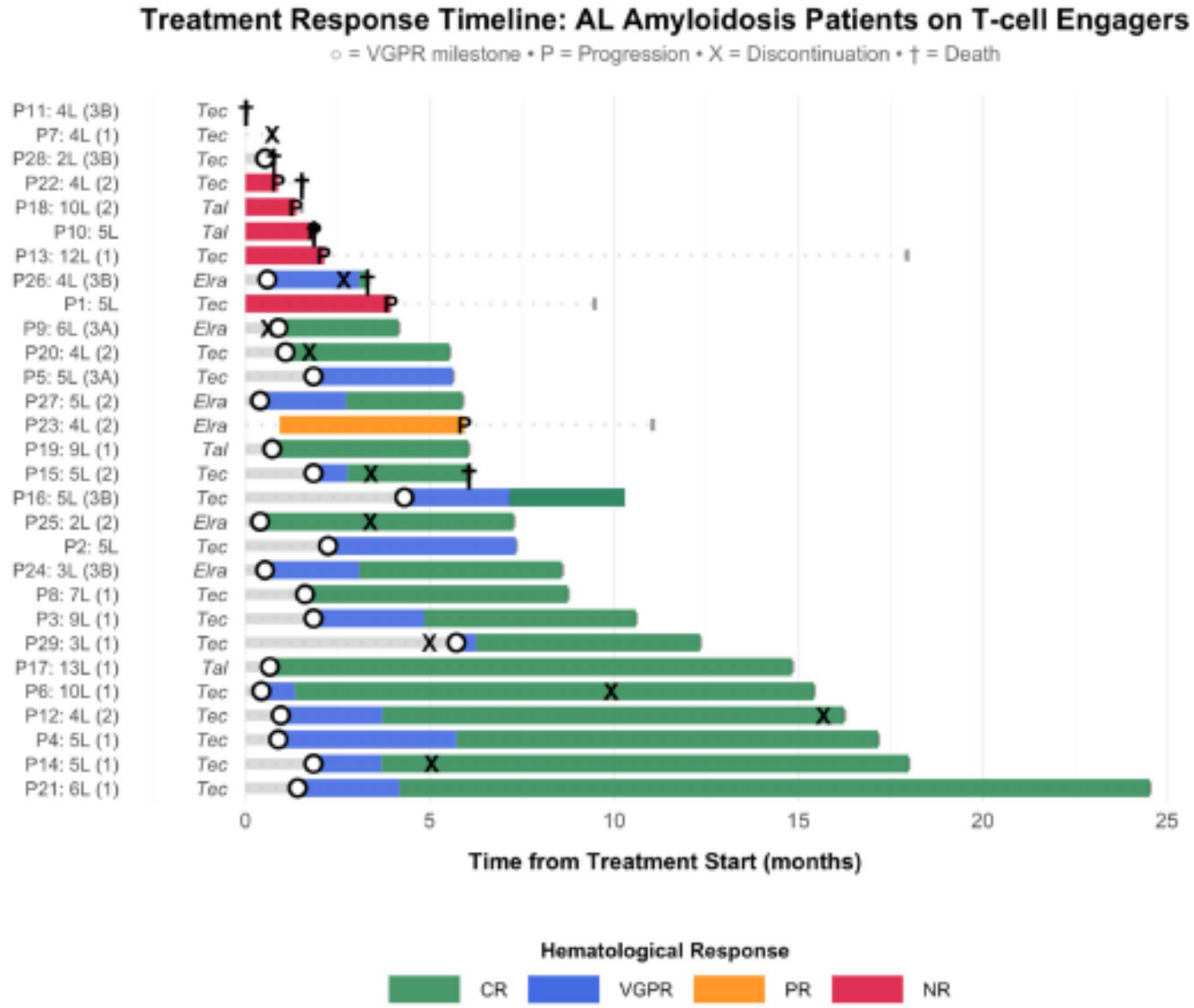
47 mo
25 mo
5 mo

Responses at 3 months



55 mo
37 mo
15 mo
8 mo

Gustine et al, Blood Adv , 2023



Rees et al, AJH 2025

Real-World Safety and Efficacy of BCMA Bispecific Antibodies in Relapsed AL Amyloidosis

Table. Baseline Characteristics

	N=20
Male, n (%)	9 (45)
Age at bispecific antibody initiation, median (range)	73 (60–83)
Involved light chain (κ/λ), n (%)	4/16 (20)
Plasma cell BM involvement, %	10
dFLC at bispecific antibody initiation, median (range)	68.5 (1.8–963.5)
Prior LOT, median (range)	4 (3–10)
Cardiac involvement, n (%)	14 (70)
Stage I	2 (10)
Stage II	0
Stage IIIA	9 (45)
Stage IIIB	3 (15)
Bispecific antibody received, n (%)	
Teclistamab	11 (55)
Elranatamab	9 (45)

Mico et al, ASH 2025

Real-World Safety and Efficacy of BCMA Bispecific Antibodies in Relapsed AL Amyloidosis

Table. Adverse Events

n (%)	N=20
Neutropenia	3 (15)
Infections	5 (25)
Cardiac AEs	2 (10)
CRS	10 (50)
Grade 1	6 (30)
Grade 2	3 (15)
Grade 3	1 (5)
ICANS	3 (15)
Grade 1	1 (5)
Grade 2	1 (5)
Grade 3	1 (5)
Deaths	2 (10)

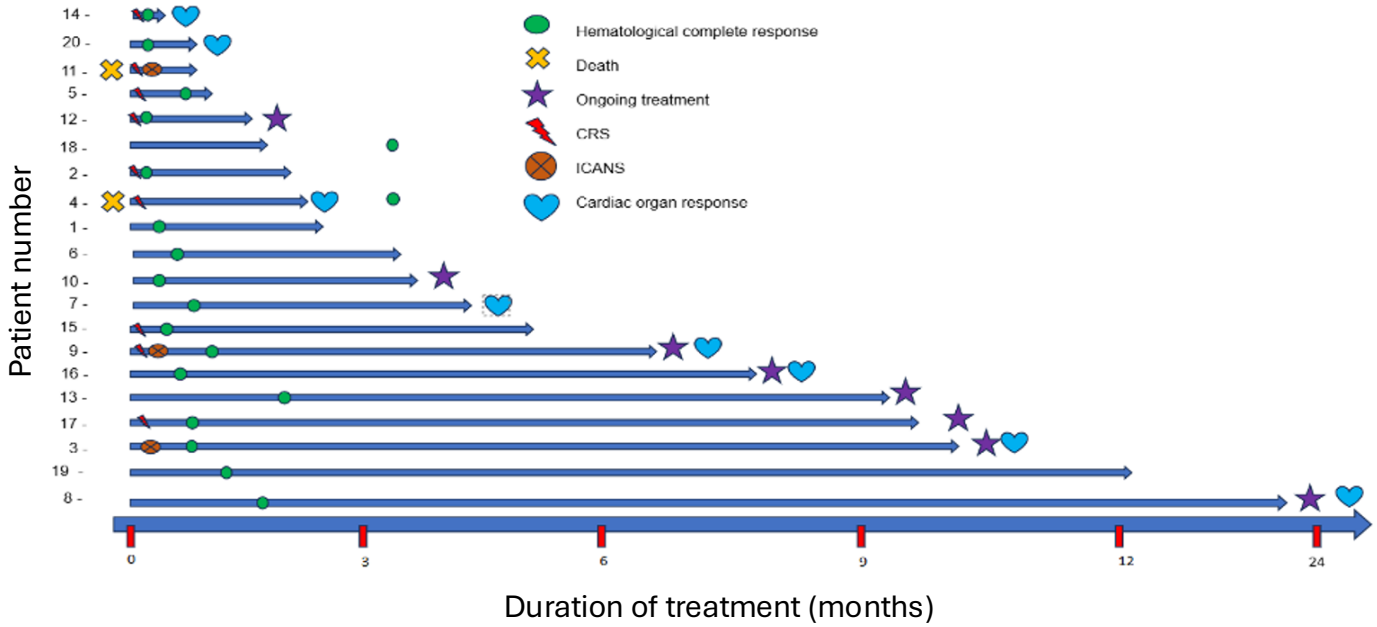
Mico et al, ASH 2025

Real-World Safety and Efficacy of BCMA Bispecific Antibodies in Relapsed AL Amyloidosis

Efficacy

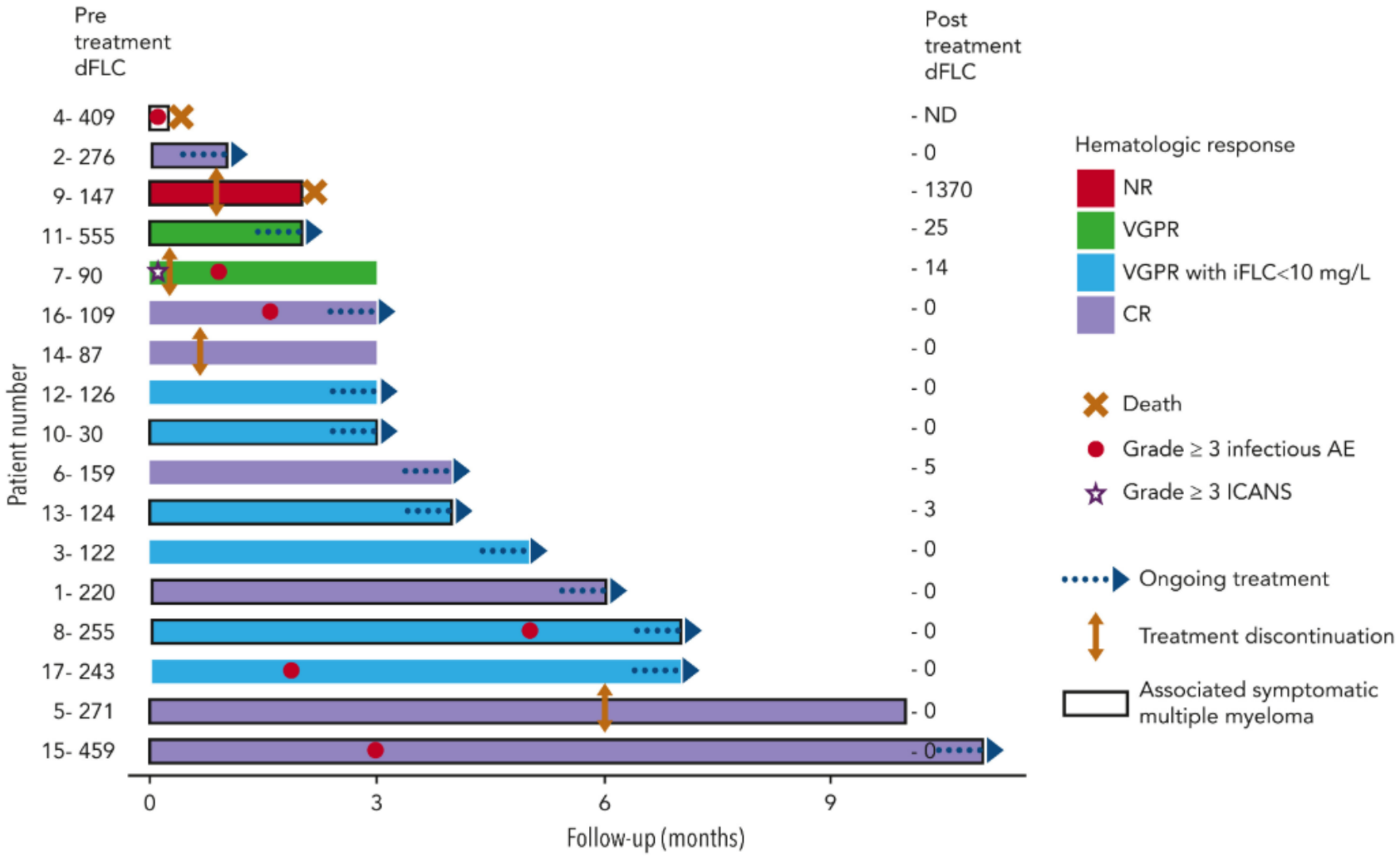
- Of the 19 patients evaluated:
  - ORR was 100%
  - hCR rate was 100%
- Median (range) time to first hematologic response and hCR were 0.5 (0.2–0.9) and 0.7 (0.2–1.9) months, respectively
- 8/14 patients with cardiac amyloid had evidence of organ recovery with a steady reduction in NT-proBNP
- Six patients with fixed-duration therapy stopped bispecific antibody treatment after achieving hCR and maintained disease control off treatment
  - Three patients were ~12 months from the last BCMA bispecific antibody dose

Longitudinal Follow-Up



Mico et al, ASH 2025

Teclistamab in RR AL amyloidosis

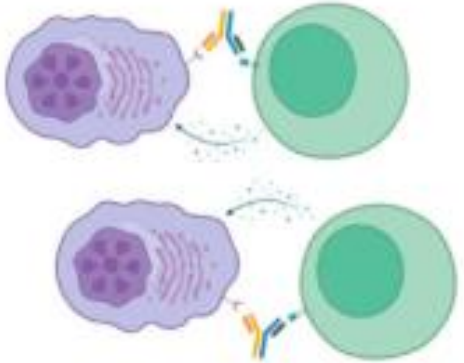


Forgeard et al, Blood 2024

Elranatamab, a BCMA×CD3 Bispecific T Cell Engager, in Patients with Relapsed and/or Refractory AL Amyloidosis

Context of Research:

- There are no FDA approved therapies for relapsed/refractory (RR) AL amyloidosis



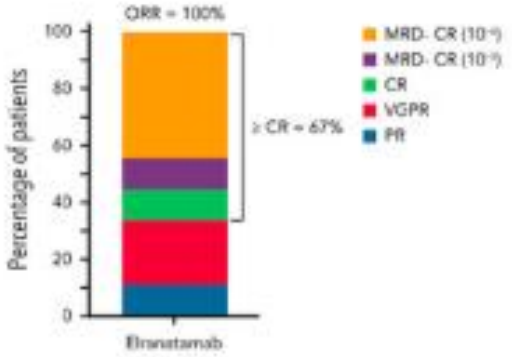
- Elranatamab is a BCMA×CD3 bispecific antibody that is effective in a related plasma cell disorder, multiple myeloma

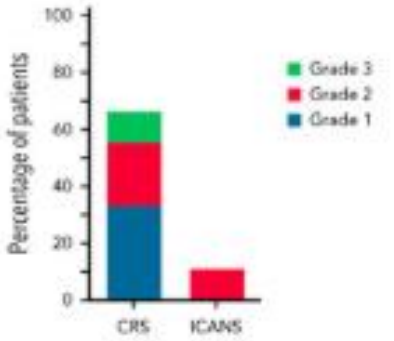
Methods

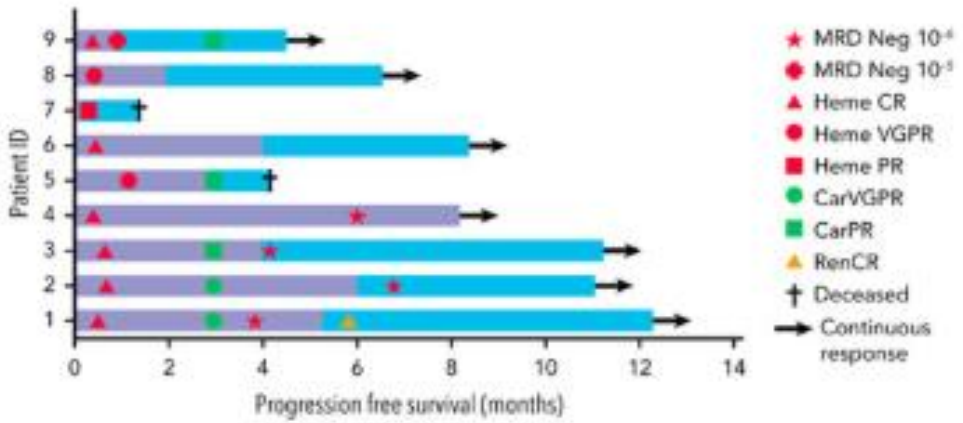
- We retrospectively report on safety and efficacy of elranatamab in 9 consecutive patients with RR AL amyloidosis treated at two large, multidisciplinary amyloidosis programs in the USA

Main Findings

- Elranatamab led to high rates of hematological and organ response







Vianna et al, Blood 2025