3e CONGRÈS FRANCOPHONE MULTIDISCIPLINAIRE DE L'AMYLOSE

Progrès réalisés et à venir !

Jeudi 13 juin 2024

Fondation Biermans-Lapôtre ■ PARIS

ISA
INTERNATIONAL SOCIETY OF AMYLOIDOSIS

Best of de l'ISA

Hématologie

MAYO CLINIC

criBl ymphoprolifératifs contrôle réponse immune

Centre national de référence
Amylose AL
& autres maladies par dépôts d'immunoglobulines monoclonales

CHU Limoges

CHU de Poitiers

ifm

Principale cible: les plasmocytes

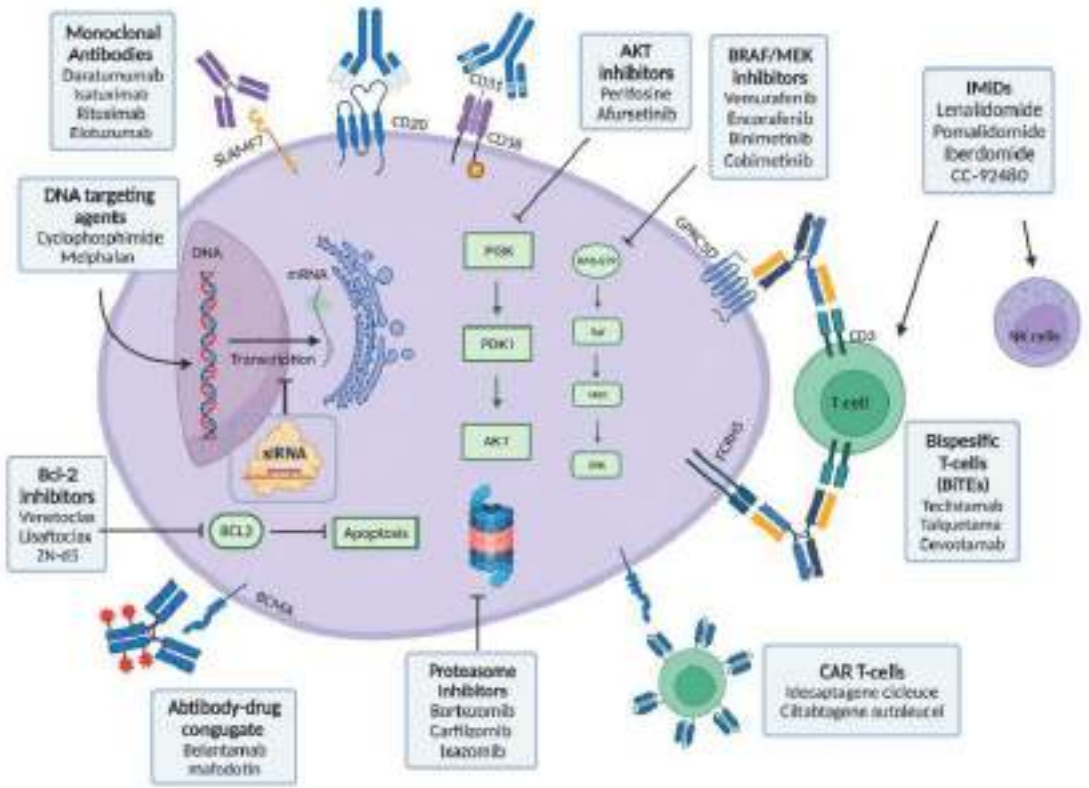


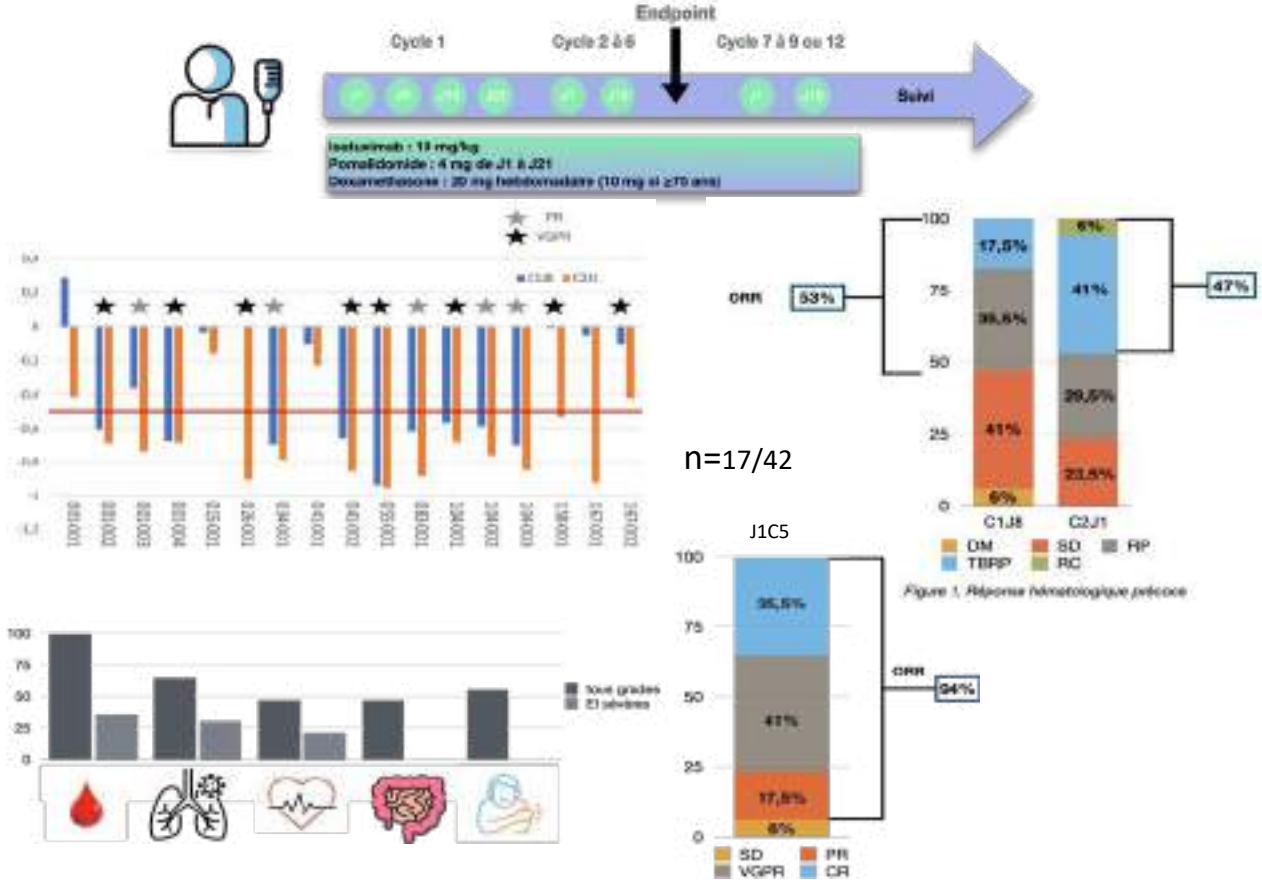
Figure 1. Actionable cellular molecules and signaling pathways to target plasma cells in AL amyloidosis. Created with BioRender.com (accessed on 10 November 2021).

Theodorakakou et al, Hemato 2022,3, 131–152.

Nouvelles associations: anti CD38 + pomalidomide

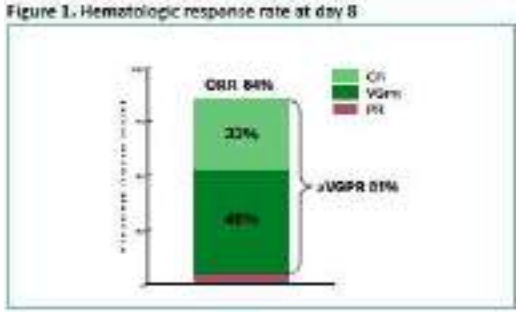
Efficacy and safety of isatuximab, pomalidomide and dexamethasone (IPd) in relapsed AL amyloidosis: interim results of the IsaMYP study

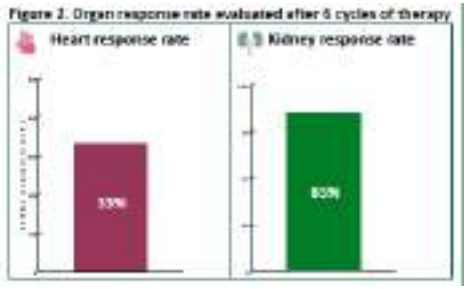
K. Queru (1) ; L. Tabone (2) ; S. Bender (3) ; B. Royer (4), M. Macro (5), G. Olombel (3) ; V. Pascal (3) ; MO. Petillon (2) ; J. Corre (6); F. Bridoux (3,7); A. Jaccard (1,3) ; M. Roussel (1,3)



Patients received up to 6 cycles of daratumumab (1800 mg sc once weekly for 3 cycles and subsequently every other week), pomalidomide (4 mg from day 1-21, on 28 days cycles) and weekly dexamethasone (20+20 mg).

A total of 27 patients were enrolled and 3 of them were still on treatment at the time of data lock. Twenty (74%) patients completed the planned treatment.





GRADE ≥ 3	N (%)
Overall	33
Neutropenia	20 (74)
Pulmonary infection	4 (15)
Cutaneous rash	3 (11)
Fluid retention	2 (7)
Thrombocitopenia	1 (3)
Emottisis	1 (3)
Atrio-ventricular block	1 (3)

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Efficacy and safety of daratumumab monotherapy in newly diagnosed patients with stage 3B light-chain amyloidosis: A phase 2 study by the European Myeloma Network

Kastritis E[1], Minnema MC[2], Dimopoulos MA[1], Merlini G[3], Theodorakakou F[1], Fotiou D[1], Huart A[4], Belhadj K[5], Ninos I[6], Psarros G[6], Sonneveld P[7], Palladini G[3]

[1]Department of Clinical Therapeutics, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece; [2]Department of Hematology, University Medical Center Utrecht, Utrecht, Netherlands; [3]Amyloidosis Research and Treatment Center, University of Pavia, Pavia, Italy, [4]Department of Nephrology and Transplantation, Rangueil University Hospital, Toulouse; [5]Lymphoid Malignancies Unit, Henri Mondor Hospital, Créteil, France; [6]Health Data Specialists, Dublin, Ireland; [7]Erasmus MC Cancer Institute, Rotterdam, Netherlands

OBJECTIVE

- To evaluate the efficacy and safety of daratumumab (dara) monotherapy in newly diagnosed (ND) patients with stage 3B systemic light chain (AL) amyloidosis

BACKGROUND

- Patients with Mayo2004/European stage 3B systemic AL amyloidosis have a high risk of early death, mainly due to severe cardiac dysfunction[1,2]
- The ANDROMEDA study showed that in ND patients with AL amyloidosis, dara plus bortezomib / cyclophosphamide / dexamethasone (D-VCd) induced high rates of hematologic complete response (CR);[3,4] however, patients with Mayo stage 3B were excluded
- Single-agent dara has shown efficacy with a favorable toxicity profile in patients with AL amyloidosis, thus representing a possible treatment option for stage 3B AL amyloidosis patients[5]

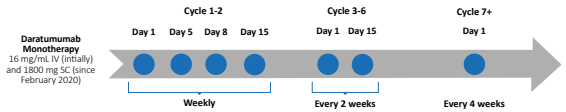
METHODS

- EMN22 is an ongoing, prospective, phase 2, open-label, multicenter study in ND patients with stage 3B AL amyloidosis from Greece, the Netherlands, Italy, and France
- **Primary endpoint: Overall survival (OS) rate at 6 months**
- Secondary endpoints include the overall response rate (ORR) at 3 and 6 months; the organ response rate; and the safety and tolerability of dara monotherapy

Abbreviations: CA, cytogenetic abnormality; dFLC, difference between involved and uninvolved free light chains; FISH, fluorescence in situ hybridization; HS Troponin T, high-sensitivity troponin T; ITT, intention-to-treat; IV, intravenous; LVEF, Left ventricular ejection fraction; NT-proBNP, N-terminal pro b-type natriuretic peptide; NYHA, New York heart association; ORR, overall response rate; PR, partial response; SAE, serious adverse event; SC, subcutaneous; TEAE, treatment-emergent adverse event; VGPR, very good partial response.

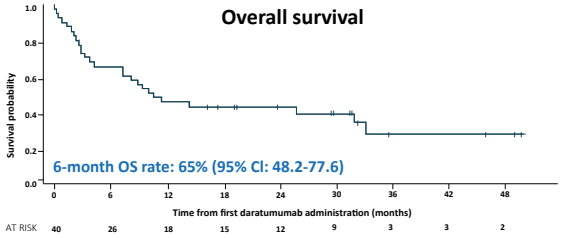
References: [1]Basset M, et al. Blood. 2022;140(18):1964-71; [2]Wechalekar AD, et al. Lancet. 2016;387(10038):2641-54; [3]Kastritis E, et al. N Engl J Med. 2021;385(1):46-58; [4]Minnema MC, et al. JACC CardioOncol. 2022;4(4):474-87; [5]Cohen OC, et al. Amyloid. 2020;27(3):200-5; [6]Eckhert E, et al. Br J Haematol. 2019;186(1):144-6; [7]Wechalekar AD, et al. Blood. 2013;121:3420-7; [8]Vaxman I, et al. Leukemia. 2021;35(12):3604-7.

STUDY DESIGN



*Subjects not achieving a hematologic very good partial response or better OR a hematologic partial response with a major organ response by Cycle 4 may also receive weekly bortezomib (1.3 mg/m² for a maximum of 6 cycles) and low-dose dexamethasone at the investigator's discretion

KEY RESULT



CONCLUSIONS

- In ND patients with stage 3B AL amyloidosis, dara monotherapy induced deep hematologic responses with a 6-month OS of 65.0%, higher than the historical 6-month OS (41-45%)[7,8]
- No new safety signals were observed
- Based on these outcomes, dara monotherapy may be considered as a treatment option for these patients.

OTHER RESULTS

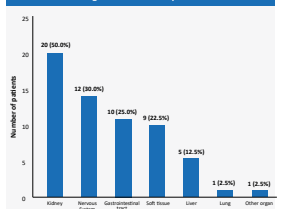
Patient characteristics and treatment details

- All planned patients (N=40) have been enrolled in the study
- By the cutoff date (15/12/2023), 10 (25.0%) completed study treatment, 4 (10.0%) are continuing with treatment, and 26 have discontinued (progressive disease: 7; safety event: 3; death: 14; consent withdrawal: 1; physician's decision: 1)

Patient characteristics at baseline (N=40)	
Age	70.5 (45.0–86.0)
Male	22 (55.0)
NYHA classification II/IIIA*	16 (40.0) / 24 (60.0)
NT-proBNP (pg/mL)*	14,353.0 (8,516.0–72,522.0)
HS Troponin T (pg/mL)*	136.0 (55.1–692.0)
dFLC (mg/L)*	427.0 (36.0–2,823.0)
LVEF value (%)*	44.5 (26.0-68.0)
Revised Mayo 2012 stage III / IV	10 (25.0) / 30 (75.0)
Patients with isolated heart involvement	7 (17.5)
Patients with organ involvement apart from the heart	33 (82.5)
Patients with more than 2 organs involved apart from heart†	17 (51.5)
Number of organs involved apart from heart†	2.0 (1.0-5.0)
Patients with at least one CA*‡	15 (46.9)
Patients with t (11;14)*‡	11 (40.7)

Data are median (range) or n (%) patients. *Assessed at screening. †Percentages and median (range), are based on the 33 patients with at least one organ involved, apart from heart (n=33). ‡CAs assessment was not mandatory as per protocol and was performed as per standard of care at each site. The assessment was performed by FISH for the following CAs: 17p13, 1q21, t (4;14), t (11;14), and t (14;16). Percentages are based on the number of patients that had evaluable assessments (CAs: n=32, t (11;14): n=27).

Patients with organ involvement apart from the heart*



*Proportions are calculated using the intention-to-treat population (N=40) as the denominator.

- **Number of daratumumab infusions**, median (range): **18** (1–36)
- **Duration of therapy**, median (range): **6.6** (<1–25.3) months
- **Follow-up**, median (range): **10.3** (<0.1–50.1) months

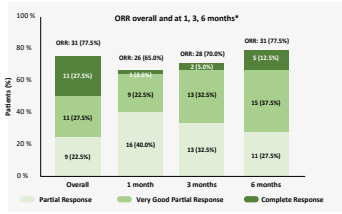
Further survival information

- 12-month OS rate: 45.0% (95% CI: 29.3-59.5)
- Median survival time (months): 10.3 (95% CI: 4.1-32.1)

Early mortality rates

- 15 days following C1D1: 7.5% (3 deaths)
- 1 month following C1D1: 10.0% (4 deaths)

Hematologic response

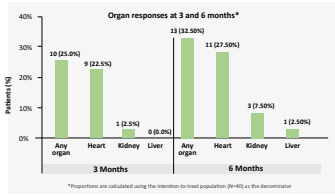


- **Time to first PR or better response** (median [range]): **7 (6–125)** days
- **Time to first VGPR or better response** (median [range]): **1.8 (0.2–7.3) months**

Best responses observed at each timepoint are presented.

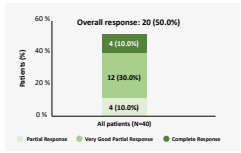
*Proportions are calculated using the ITT population (N=40) as the denominator.

Organ response



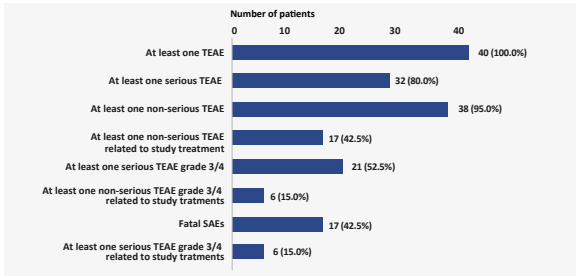
*Proportions are calculated using the intention-to-treat population (N=40) as the denominator

Best cardiac response

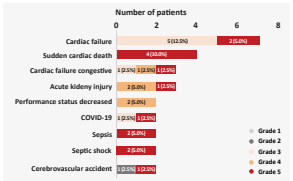


Best cardiac response was evaluated using the minimum NT-proBNP post-baseline value. PR, 30–59% NT-proBNP reduction from baseline; VGPR, ≥60% NT-proBNP reduction from baseline; CR, NT-proBNP <450 pg/mL[6]

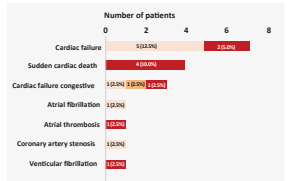
Safety overview



Most common* SAEs



Cardiac SAEs



*SAEs observed at a rate of at least 5%. Percentages are calculated over the ITT population (40 patients). SAE, serious adverse event; TEAE, treatment-emergent adverse event.

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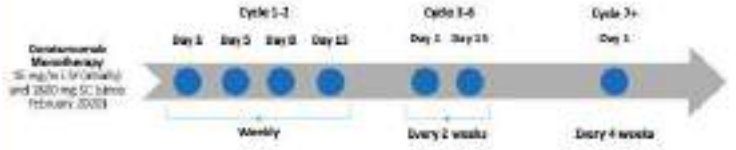
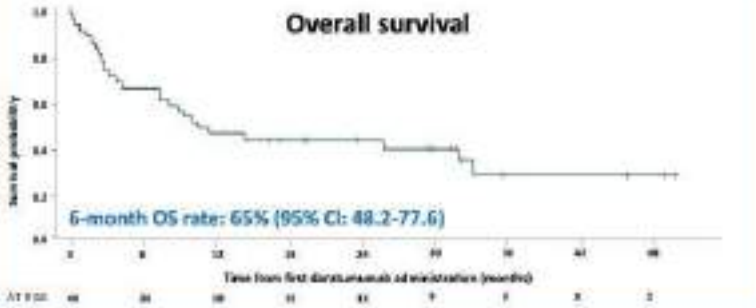
STUDY DESIGN



Until disease progression according to major organ deterioration progression-free survival criteria, start of new therapy, or for a maximum of 2 years

KEY RESULT



CONCLUSIONS

- In ND patients with stage 3B AL amyloidosis, dara monotherapy induced deep hematologic responses with a 6-month OS of 65.0%, higher than the historical 6-month OS (41-45%)[7,8]
- No new safety signals were observed
- Based on these outcomes, dara monotherapy may be considered as a treatment option for these patients.

OTHER RESULTS

Patient characteristics and treatment details

- All planned patients (N=40) have been enrolled in the study
- By the cutoff date (15/12/2023), 10 (25.0%) completed study treatment, 4 (10.0%) are continuing with treatment, and 26 have discontinued (progressive disease: 7; safety event: 3; death: 14; consent withdrawal: 1; physician's decision: 1)

Patient characteristics at baseline (N=40)	
Age	[illegible]
Male	[illegible]
[illegible]	[illegible]
[illegible]	[illegible]
[illegible]	[illegible]
[illegible]	[illegible]
[illegible]	[illegible]
[illegible]	[illegible]
[illegible]	[illegible]
[illegible]	[illegible]
[illegible]	[illegible]
[illegible]	[illegible]
[illegible]	[illegible]
[illegible]	[illegible]

- **Number of daratumumab infusions**, median (range): 18 (1–36)
- **Duration of therapy**, median (range): 6.6 (<1–25.3) months
- **Follow-up**, median (range): 10.3 (<0.1–50.1) months

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- 12-month OS rate: 45.0% (95% CI: 29.3-59.5)
- Median survival time (months): 10.3 (95% CI: 4.5-32.1)

Early mortality rates

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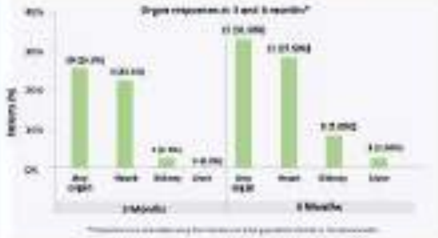
- 1 month following C1D1: 10.0% (4 deaths)

Hematologic response

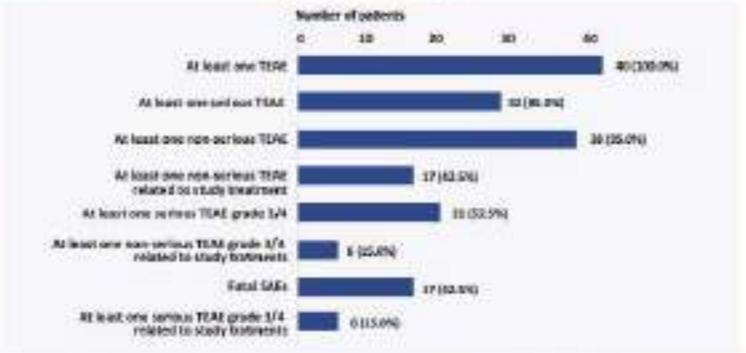
- Time to first PR or better response (median [range]): 7 (6–125) days
- Time to first VGPR or better response (median [range]): 1.8 (0.2–7.3) months

Organ response



Best cardiac response

Safety overview



Most common* SAEs

Cardiac SAEs

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Efficacy and Safety of Belantamab Mafodotin Monotherapy in Patients with Relapsed or Refractory Light-Chain Amyloidosis: A Phase 2 Study by the European Myeloma Network

Kastritis E[1], Palladini G[2], Dimopoulos MA[1], Jaccard A[3], Merlini G[2], Theodorakakou F[1], Fotiou D[1], Minnema MC[4], Wechalekar A[5], Ninos I[6], Psarros G[6], Sonneveld[7], Schönland S[8]

[1]Department of Clinical Therapeutics, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece;[2] Amyloidosis Research and Treatment Center, University of Pavia, Pavia, Italy;[3] Referral Center for AL Amyloidosis, Limoges, France;[4] Department of Hematology, University Medical Center Utrecht, Utrecht, Netherlands;[5] Clinical Haematology, Cancer Division, University College London Hospital, London, UK;[6] Health Data Specialists, Dublin, Ireland;[7] Erasmus MC Cancer Institute, Rotterdam, Netherlands;[8] University of Heidelberg, Heidelberg, Germany

BACKGROUND

- Currently, no standard treatments exist for patients with relapsed/refractory (RR) systemic light chain (AL) amyloidosis, and the options for daratumumab- and bortezomib-exposed patients are limited[1]
- Belantamab mafodotin (belamaf), a multi-modal antibody-drug conjugate targeting the B-cell maturation antigen which is expressed on plasma cells, has shown single agent activity in RR multiple myeloma (MM)[2]
- As the clonal plasma cells in AL amyloidosis and MM are phenotypically similar, belamaf could be a novel treatment option in AL amyloidosis[1]

OBJECTIVE

- To present an updated analysis of the EMN27 study assessing the efficacy and safety of belamaf monotherapy in patients with RRAL amyloidosis

STUDY DESIGN

- EMN27 is an ongoing prospective, open-label, multinational, phase 2 study aiming to enroll 36 patients with RRAL amyloidosis

Eligibility criteria
- Diagnosis for AL amyloidosis
- Previous systemic treatment
- Adequate organ function
- Mayo2004/European cardiac stage I-IIIA
- ECOG PS 0-2

Study treatment
Belamaf 2.5 mg/kg (or 1.92 mg/kg for toxicity)
C1-C8: Q6W IV until disease progression, start of subsequent therapy, or a maximum of 8 cycles

Primary objective
To evaluate the efficacy of belamaf in patients with RRAL amyloidosis
Other objectives
- Belamaf safety profile
- Secondary efficacy evaluations
- Belamaf PK profile

- The study design included pre-planned safety run-in and interim efficacy analyses

Abbreviations: AL, systemic light chain; C, cycle; CR, complete response; dara; daratumumab; dFLC, difference between involved and uninvolved free light chains; ECOG PS, Eastern Cooperative Oncology Group performance status; GI, gastrointestinal; Gr, grade; IV, intravenous; N/n, number of patients; NT-proBNP, N-terminal pro b-type natriuretic peptide; NYHA, New York Heart Association; PR, partial response; Q6W/Q8W/Q12W, once every 6/8/12 weeks; SAE, serious adverse event; TEAE, treatment-emergent adverse event; VGPR, very good PR. **References:** [1]Kastritis et al., HemaSphere 2022;6:804-5; [2]Lonial et al., Lancet Oncol 2020;21:207-21.

RESULTS

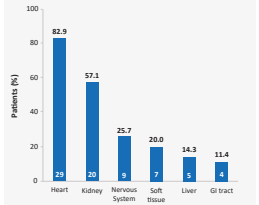
Patient characteristics and belamaf treatment details

- Thirty-five patients were enrolled (enrollment completed)
- By the cutoff date (15 December 2023), 4 patients (11.4%) completed study treatment, 5 patients (14.3%) are continuing with treatment, and 26 patients have discontinued (progressive disease or inadequate response: 13; adverse event: 8; death: 3; consent withdrawal: 1; physician's decision: 1)

Patient characteristics at baseline

Age (years)	65.0 (46.0-80.0)
Male sex	20 (57.1)
NYHA class I / II	8 (22.9) / 27 (77.1)
Mayo2004/European*	
I	5 (14.3)
II	19 (54.3)
IIIA	11 (31.4)
NT-proBNP (pg/mL)	1,268.5 (90.0-7,270.0)
High-sensitivity troponin T (pg/mL)	37.9 (3.0-1,280.0)
dFLC (mg/L)	117.1 (3.5-2,791.0)
Previous AL amyloidosis treatments	3.0 (1.0-10.0)
Previous daratumumab exposure	26 (74.3)
Previous bortezomib exposure	30 (85.7)

Organ involvement*

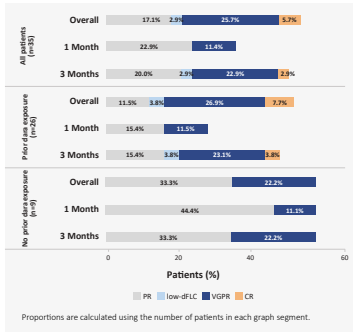


*Patients could have >1 organ involved. Numbers within the bars indicate the number of patients. Proportions are calculated using the total number of patients (N=35) as the denominator.

Data are median (range) or n (%) patients. *Assessed at screening.

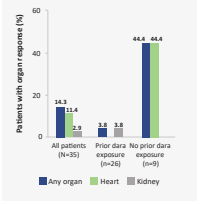
- The median (range) treatment duration with belamaf was 3.3 months (<0.1-16.8) and the median (range) follow-up was 12.7 months (3.2–25.9)

Clinical response – Primary endpoint

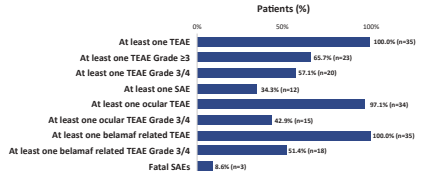


Proportions are calculated using the number of patients in each graph segment.

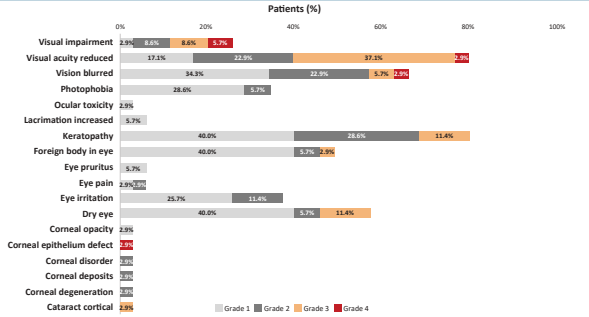
Organ responses at 3 months



Adverse events



Ocular adverse events

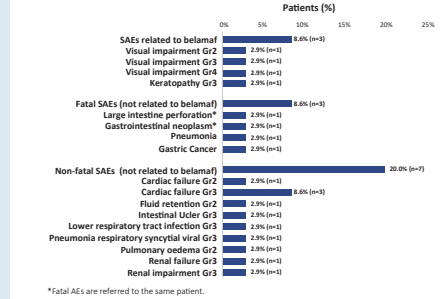


Other efficacy assessments

		All patients N=35	Prior dara exposure N=26	No prior data exposure N=9
Overall	**PR or better**	**18 (51.4)**	**13 (50.0)**	**5 (55.6)**
	Time to PR or better (months)	0.5 (0.2-4.9)	1.0 (0.3-4.9)	0.3 (0.2-0.5)
	VGPR or better	**11 (31.4)**	**9 (34.6)**	**2 (22.2)**
	Time to VGPR or better (months)	1.4 (0.5-9.0)	1.4 (0.5-9.0)	1.7(0.5-2.8)
1 Month	**PR or better**	**12 (34.3)**	**7 (26.9)**	**5 (55.6)**
	Low dFLC response/VGPR or better	4 (11.4)	3 (11.5)	1 (11.1)
3 Months	**PR or better**	**17 (48.6)**	**12 (46.2)**	**5 (55.6)**
	Low dFLC response/VGPR or better	10 (28.6)	8 (30.8)	2 (22.2)

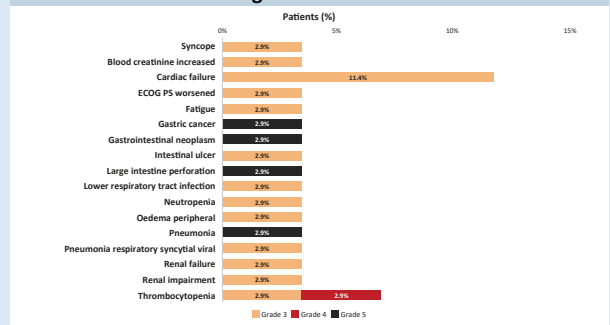
Data are median (range) or n (%) patients. Proportions are calculated using the number of patients in each group.

Serious adverse events



*Fatal AEs are referred to the same patient.

Non-ocular grade ≥3 adverse events



CONCLUSIONS

- Belamaf monotherapy is active in heavily pretreated patients with RRAL without unexpected toxicity
- Belamaf could be a valid treatment option for this difficult-to-treat patient population
- Combinations of belamaf with standard-of-care systemic treatments could allow for longer belamaf dosing intervals (Q8W/Q12W), thus reducing ocular toxicity while maintaining or improving efficacy

XIX International Symposium on Amyloidosis, 26-30 May 2024, Rochester, Minnesota, USA

RESULTS

Patient characteristics and belamaf treatment details

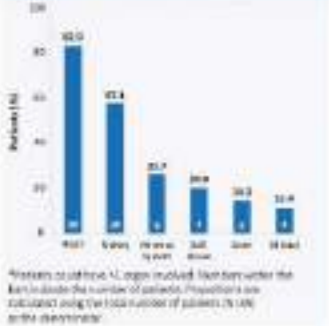
- Thirty-five patients were enrolled (enrollment completed)
- By the cutoff date (15 December 2023), 4 patients (11.4%) completed study treatment, 5 patients (14.3%) are continuing with treatment, and 26 patients have discontinued (progressive disease or inadequate response: 13; adverse event: 8; death: 3; consent withdrawal: 1; physician's decision: 1)

Patient characteristics at baseline

Age (years)	[illegible]
Male sex	20 (57.1)
NYHA class I/II	[illegible]
Mayo 2004/European stage*	
I	[illegible]
II	[illegible]
IIIA	[illegible]
NT-proBNP (pg/mL)	[illegible]
High sensitivity troponin T (pg/mL)	[illegible]
dFLC (mg/L)	[illegible]
Previous AL amyloidosis treatments	[illegible]
Previous daratumumab exposure	[illegible]
Previous bortezomib exposure	[illegible]

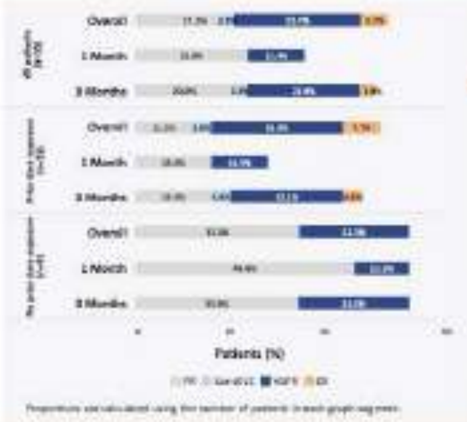
Data are median (range) or n (%) patients. *Assessed at screening

Organ involvement*

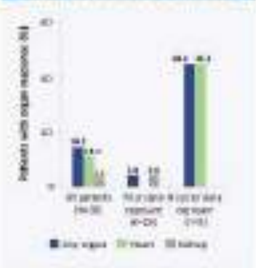


- The median (range) treatment duration with belamaf was 3.3 months (<0.1-16.8) and the median (range) follow-up was 12.7 months (3.2–25.9)

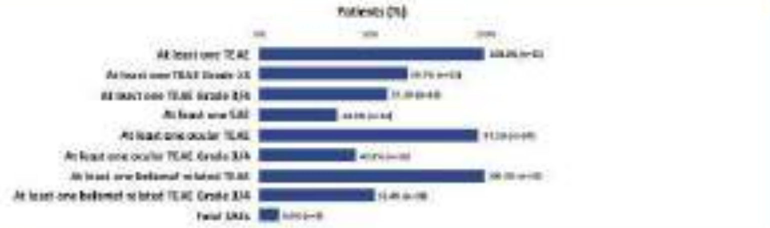
Clinical response – Primary endpoint



Organ responses at 3 months



Adverse events



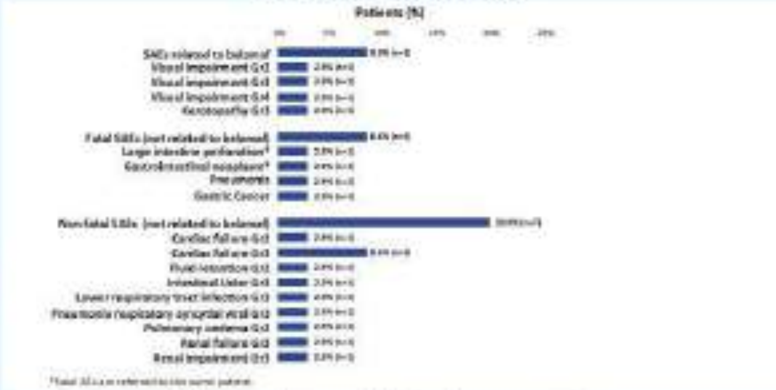
Ocular adverse events

Other efficacy assessments

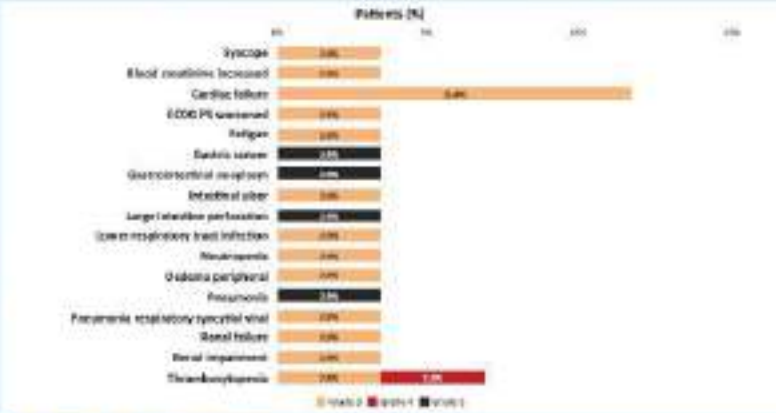
		All patients N=35	Prior dara exposure N=26	No prior dara exposure N=9
Overall	PR or better	18 (51.4)	13 (50.0)	5 (55.6)
	Time to PR or better (months)	0.5 (0.1-4.9)	[illegible]	[illegible]
	VGPR or better	11 (31.4)	9 (34.6)	[illegible]
	Time to VGPR or better (months)	1.4 (0.5-5.0)	1.4 (0.5-5.0)	[illegible]
1 Month	PR or better	12 (34.3)	7 (26.9)	5 (55.6)
	Low dFLC response/VGPR or better	4 (11.4)	3 (11.5)	1 (11.1)
3 Months	PR or better	17 (48.6)	12 (46.2)	5 (55.6)
	Low dFLC response/VGPR or better	[illegible]	8 (30.8)	2 (22.2)

Data are median (range) or n (%) patients. Proportions are calculated using the number of patients in each group.

Serious adverse events



Non-ocular grade ≥3 adverse events



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Jeudi 13 juin 2024

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ISA INTERNATIONAL SOCIETY OF AMYLOIDOSIS

The 2024 International Symposium on Amyloidosis

HADASSAH UNIVERSITY MEDICAL CENTER

BRING THEM HOME NOW!

Efficacy and Safety of Anti-BCMA Chimeric Antigen Receptor T-Cell (CART) for the Treatment of Relapsed and Refractory AL amyloidosis

E. Lebel[1,2]*, S. Kfir Erenfeld[1]*, N. Asherie[1]*, S. Grisariu[1], B. Avni[1], S. Elias[1], M. Assayag[1], T. Dubnikov[1], N. Zalcman[1], M. Pick[2], E. Zimran[2], C. Cohen[3], P. Stepensky[1]†, M.E. Gatt[2]†

[1]Department of Bone Marrow Transplantation and Cancer Immunotherapy, Hadassah Medical Center, Faculty of Medicine,Hebrew University of Jerusalem, Jerusalem, Israel. [2]Department of Hematology, Hadassah Medical Center, Faculty of Medicine, Hebrew University of Jerusalem, Jerusalem, Israel. [3] Laboratory of Tumor Immunology and Immunotherapy, The Mina and Everard Goodman Faculty of Life Sciences, Bar-Ilan University, Ramat Gan, Israel.

[*Equally contributed as first authors ; †Equally contributed as last authors]

INTRODUCTION

- In AL amyloidosis (AL), deep hematologic responses are crucial for the achievement of organ responses, leading to improved survival and quality of life.
- As in multiple myeloma (MM) deep responses were indeed observed with anti-BCMA chimeric antigen receptor T-cell (CART), this therapy may be a great opportunity for AL as well. However, CART treatment poses great challenges: 1. BCMA expression is lower in AL plasma cells compared to MM; 2. Many AL patients are frail, with multi-organ involvement, including heart and kidney disease.
- HBI0101 is a novel anti-BCMA CART, developed at Hadassah Medical Center, Jerusalem, Israel, for MM and AL treatment. The first four treated patients with AL were previously reported[1]. Albeit having multi-organ and severe cardiac involvement, these patients have endured the treatment safely, with manageable toxicities, and with remarkable efficacy. This proof-of-concept has promoted the further usage of HBI0101 in AL amyloidosis. **Herein, reported is the safety and efficacy of 13 patients treated with HBI0101 to date.**

METHODS

- HBI0101 is a second generation anti-BCMA CART, with 4-1BB co-stimulatory domain.
- The clinical study phase 1a/b-2 with HBI0101 (NCT04720313) started on March 2021, enrolling MM and AL patients with ≥3 prior lines of therapy, including a PI, IMiD and anti-CD38 antibody.
- **It is the first CART clinical trial including AL Amyloidosis patients**
- The inclusion criteria for organ function were relatively permissive, with 30,000x10^9/l platelets as the threshold, creatinine clearance of 20ml/min, ejection fraction of 40% and ECOG-performance status of 2.
- Planned manufacturing time was 10 days for fresh product and 16 days for frozen product
- Lymphodepletion included fludarabine 25mg/m^2 and cyclophosphamide 250mg/m^2 on days -5 to -3 before infusion (bendamustine for patients with creatinine clearance <30ml/min).

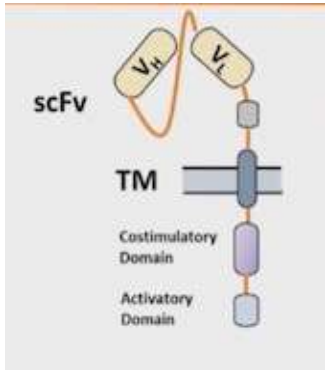

Table 1- Key characteristics of the 13 AL patients infused

Age- median (range), years		64 (55-82)
Males (n) ; Females (n)		8 ; 5
Time since diagnosis- median (range), years		4.2 (0.8-19)
Concurrent clinical MM- n/N (%)		2 (15)
FISH karyotype- n/N (%)	t(11:14)	6/13 (46)
	17p-	2/13 (15)
	1q+	3/13 (23)
Involved organs – n/N (%)	Heart	11/13 (85)
	Kidneys	10/13 (77)
	Soft tissue	6/13 (46)
	PNS	5/13 (38)
	Liver	4/13 (31)
	GI	3/13 (23)
Cardiac Mayo-stage- n/N (%)	1-2	8/13 (61)
	3a	4/13 (31)
	3b	1/13 (8)
ECOG-PS, n/N (%)	0-1	10/13 (77)
	2	2/13 (15)
	3-4	1/13 (8)
No. of prior lines of therapy, median (range)		4 (3-10)
Triple drug refractory- n/N (%)		11/13 (85)
Belantamab refractory- n/N (%)		6/13 (46)

RESULTS

- 13 AL patients were infused, 11 in the study and 2 on a compassionate basis. 1 patient received 150x10^6 CART cells, 2 patients received 450x10^6 CART cells and 10 patients received 800x10^6 CART cells. Manufacturing success rate was 100%.
- Patients' characteristics are detailed in **Table 1**

Safety:

- Grade 3-4 cytopenias were less severe than is seen in MM (0/13 thrombocytopenia, 3/13 anemia, 7/13 neutropenia), and resolved early (by day +28 : no anemia in 12/13, neutrophils of ≥1x10^9/L in 11/12, (excluding a patient with severe MDS))
- CRS was observed in 11/13, including 2 patients with grade 3 CRS, but no grade 4/5.
- Tocilizumab was used in 9/11 with CRS, steroids in 2/11
- There were no cases of ICANS or other neurotoxicity
- 3 cases of heart failure exacerbations were seen, all of grade 3-4, all managed successfully with supportive care
- 4 cases of acute on chronic kidney injury were seen, all of grade 1-2 and reversible with supportive care
- No treatment related death were observed and no irreversible toxicities

Efficacy:

- Responses are detailed in **Table 2 + Figure and Swimmers plot**
- 7 patients died on follow-up, 5 due to heart disease.
- Of note, 3 patients died while in hematological response

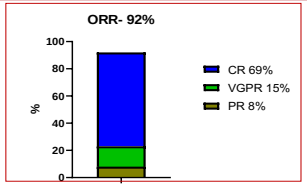

Table 2- Responses

Overall hematological response rate- n/N (%)		**12/13 (92)**
Best hematological response- n/N (%)	CR	9/13 (69)
	VGPR	2/13 (15)
	PR	1/13 (8)
	No response	1/13 (8)
MRD negativity, 10^{-5}- n/N evaluable (%)		7/11 (64)
iFLC at best response (mg/L)- median (range), days		1 (0.1-56)
Time to best response- days		27
Organ response- n/N evaluable (%)	Cardiac	4/10
	Renal	2/9
Improvement in NYHA scale- n/N evaluable (%)		5/9 (56)

CONCLUSIONS

- CART can be given safely in AL, including in frail and severe cardiac patients, with remarkable responses.
- Due to the deep and quick reduction of light chain toxicity, organ response is observed quickly
- Deaths due to cardiac disease in the first year were frequent. Usage earlier in the disease may provide better organ responses and survival
- **HBI0101 is the first clinical trial with anti-BCMA CART therapy. It provides a proof that this therapy is safe enough and highly efficacious for the treatment of AL amyloidosis patients, even frail and heavily pretreated patients.**

References:

1. **Feasibility of a Novel Academic BCMA-CART (HBI0101) for the Treatment of Relapsed and Refractory AL Amyloidosis.** Kfir-Erenfeld S, Asherie N, Grisariu S, Avni B, Zimran E, Assayag M, Sharon TD, Pick M, Lebel E, Shaulov A, Cohen YC, Avivi I, Cohen CJ, Stepensky P, Gatt ME. Clin Cancer Res. 2022 Dec 1;28(23):5156-5166.

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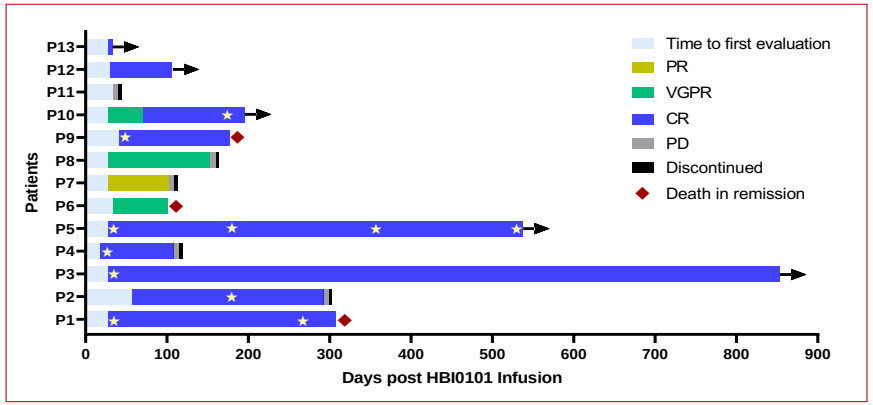
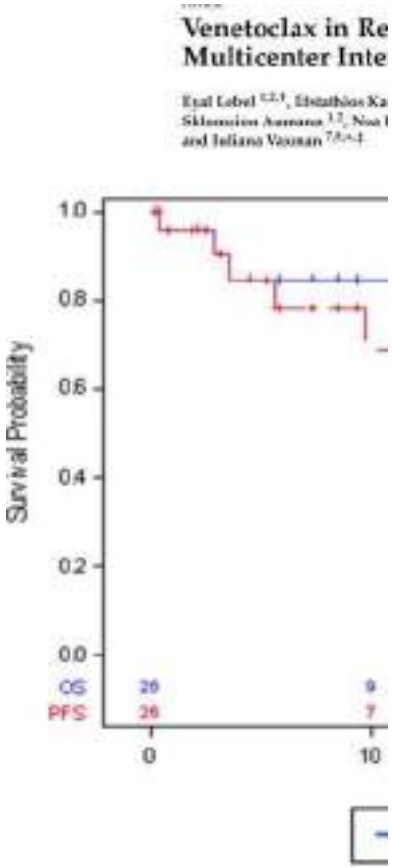


venetoclax in AL



Upcoming joint trial (France and Greece)

Frontline venetoclax consolidation in t(11;14) AL amyloidosis patients not in CR by the end of cycle 3 of Dara-CyBorD: the VENAMY trial

Standard of care	Cycle 1	Cycle 2	Cycle 3	Cycle 4 Study	Cycle 5 Study	Cycle 6 Study	Cycle 7-12 Study
Daratumumab 1800 mg	w	w	2w	2w	2w	2w	m
Bortezomib 1,3mg/m2	w	W	w	w	w	w	
Cyclophosphamide 300 mg/m2	w	w	w	Stop			
Dexamethasone 20 mg	w	w	w	w	w	w	
Venetoclax 400 mg				J1-28	J1-28	J1-28	J1-28

The number of patients to be allocated to the trial is 60 (45 in France and 15 in Greece).
The sample size is calculated according to an exact single-stage binomial distribution and based on the primary endpoint CR at 3 months of treatment with venetoclax plus Dara-BorD.
We expect that replacing cyclophosphamide by venetoclax in the Dara-BorD regimen in the non-CR subjects will provide 50% CR rate after 3 months of therapy.

DOR

French Cohort

Relapsed
Frontline

mos

Relapsed
Frontline

nos

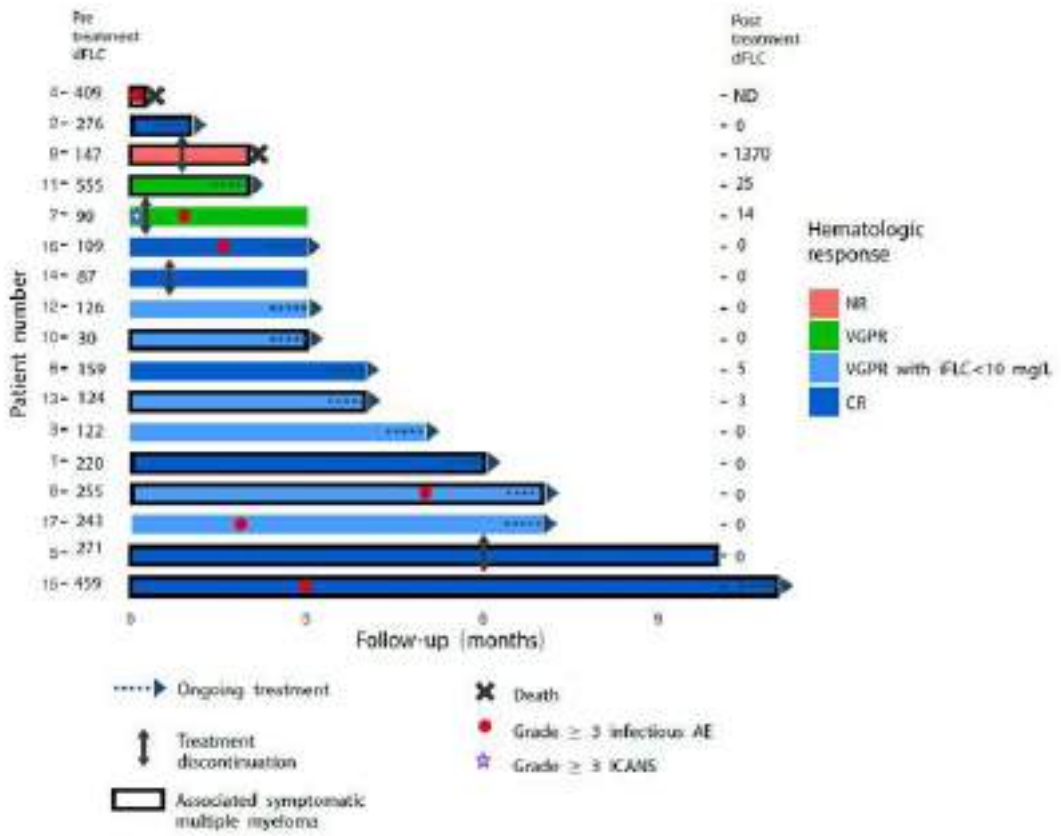
In frontline patients (n=16), with a median follow-up of 17·6 months, the estimated 2-year PFS and OS were 85·9% (95%CI, 69·5-100·0) and 93·7% (95%CI, 82·6-100·0), respectively

LETTER | DECEMBER 14, 2023

Teclistamab in relapsed or refractory AL amyloidosis, a multinational retrospective case series

Nathalie Forgeard, Dikelele ELESSA, Alexander Carpinteiro, Karim Belhadj, Monique C. Minnema, Murielle Roussel, Antoine Huart, Vincent Javeugue, Laurent Pascal, Bruno Royer, Alexis Talbot, Romain Gounot, Ute Hegenbart, Stefan Schonland, Lionel Karlin, Stephanie Hanel, Efstathios Kastritis, Frank Bridoux, Arnaud Jaccard, Bertrand Arnulf ✉

Blood Mond 2023002937
https://doi.org/10.1182/blood.2023022937
Article history



TECLISTAMY

9 sites in 6 countries

DOSING REGIMEN
teclistamab. Up to six 28-day cycles, 1.5 mg/kg SC,
C1, teclistamab will be administered at days 1, 3, 8 then weekly at days 15, and 22 according to MM ramp-up schedule.
C 2-3, teclistamab will be administered at days 1 and 15
C 4-6, teclistamab will be administered at day 1

After cycle 6, teclistamab will be administered according to treating physician with Janssen approval

LIMOGES, center of the world….

French Amyloidosis Network founded in 2007

initially 2 constitutive centres, 3 since 2023:

Limoges, Pr A. Jaccard, hematologist

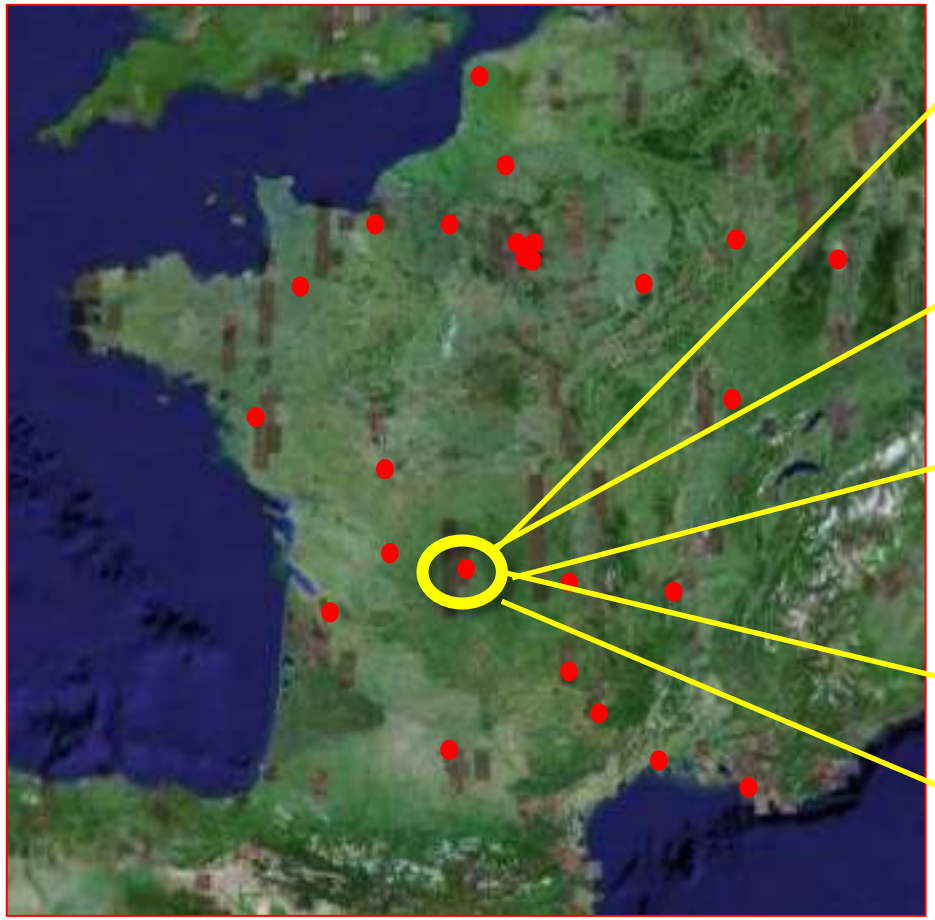
Poitiers, Pr F. Bridoux, nephrologist

Paris Saint-Louis, Pr B. Arnulf, immunologist




And 24 referral centres

Virtual MDT meetings every other weeks: >1500 patients referred since 2014



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cnrs Inserm Université de Limoges

Centre national de référence
Amylose AL
& autres maladies par dépôts d'immunoglobulines monoclonales

CHU CHU de Poitiers

criBL lymphoprolifération

ANR

FRM Fondation Recherche Médicale

FFRMG

La Ligue contre le cancer

sfh Société Française d'Hématologie

Association Française contre l'Amylose

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