La personalizzazione del trattamento: Il caso degli ADC

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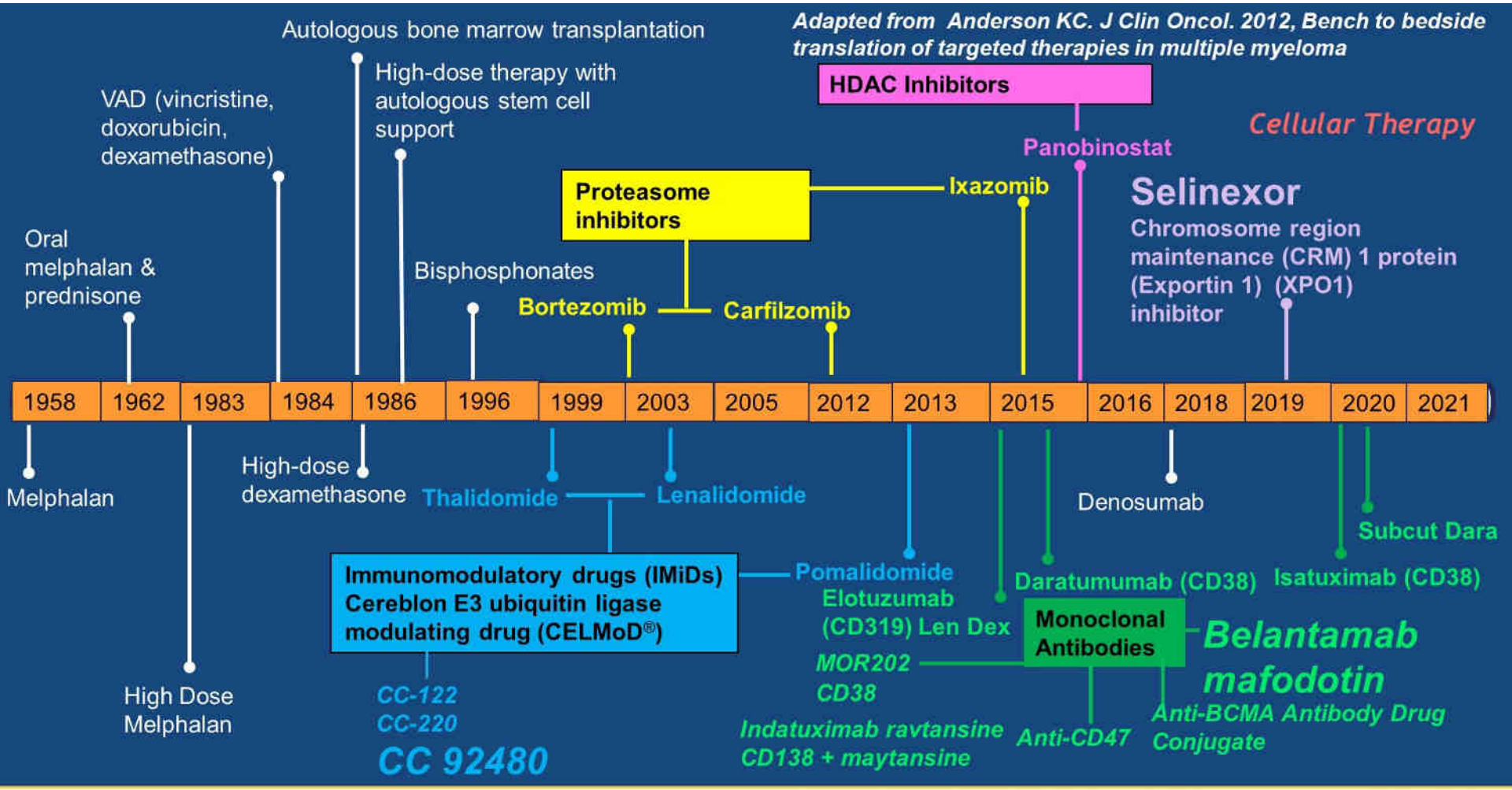
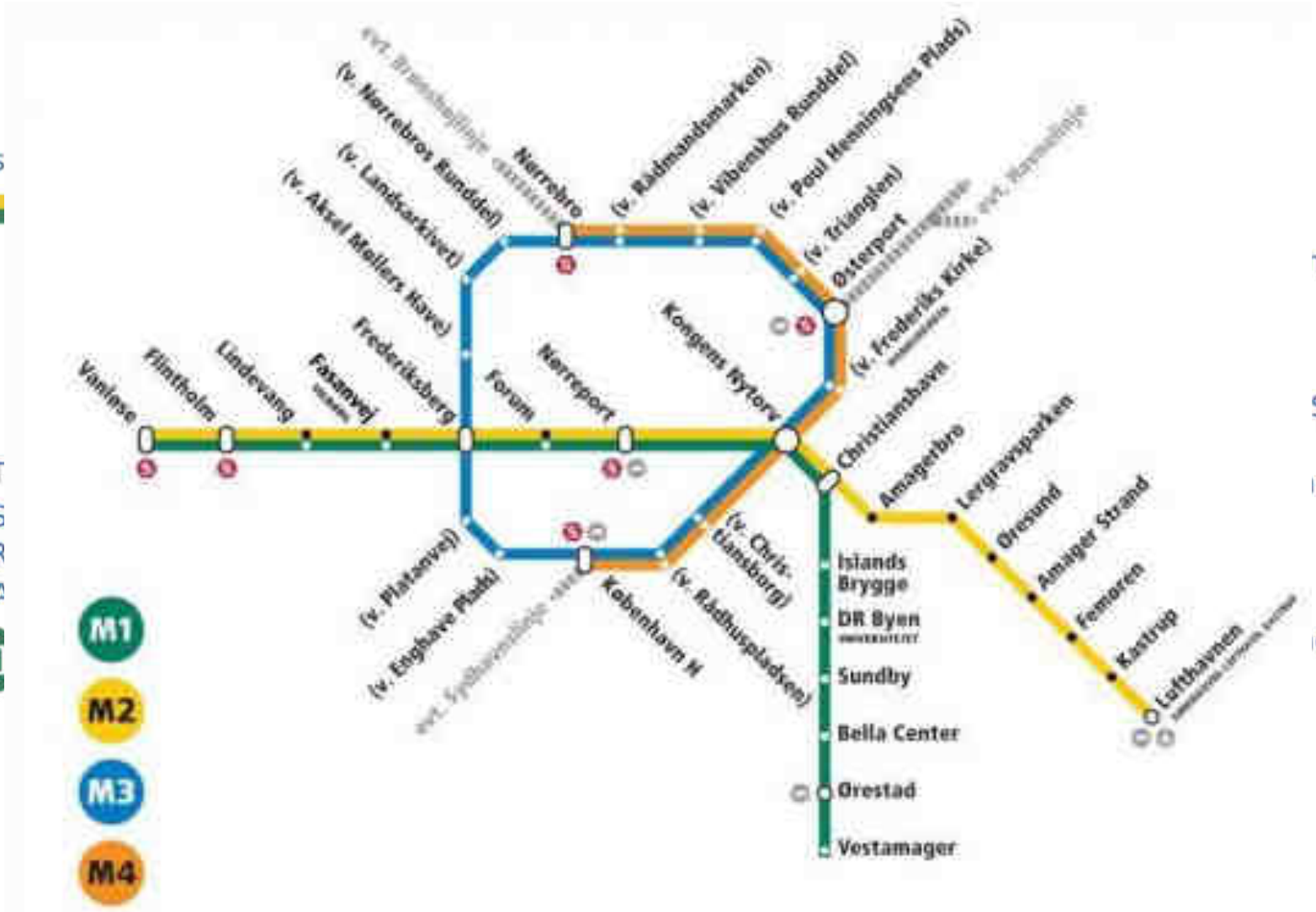



Bortezomib
Thalidomide
Pomalidomide
Allotransplant
Carfilzomib
Isatuximab
Elotuzumab
Ixazomib
Daratumumab
Autotransplant
Teclistamab
Talquetamab
Belantamab mafodotin
CAR-T
Lenalidomide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(v. Axel Møllers Have)
(v. Rådmandsmarken)
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(v. Poul Henningsens Plads)
(v. Trianglen)
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(v. Frederiks Kirke)
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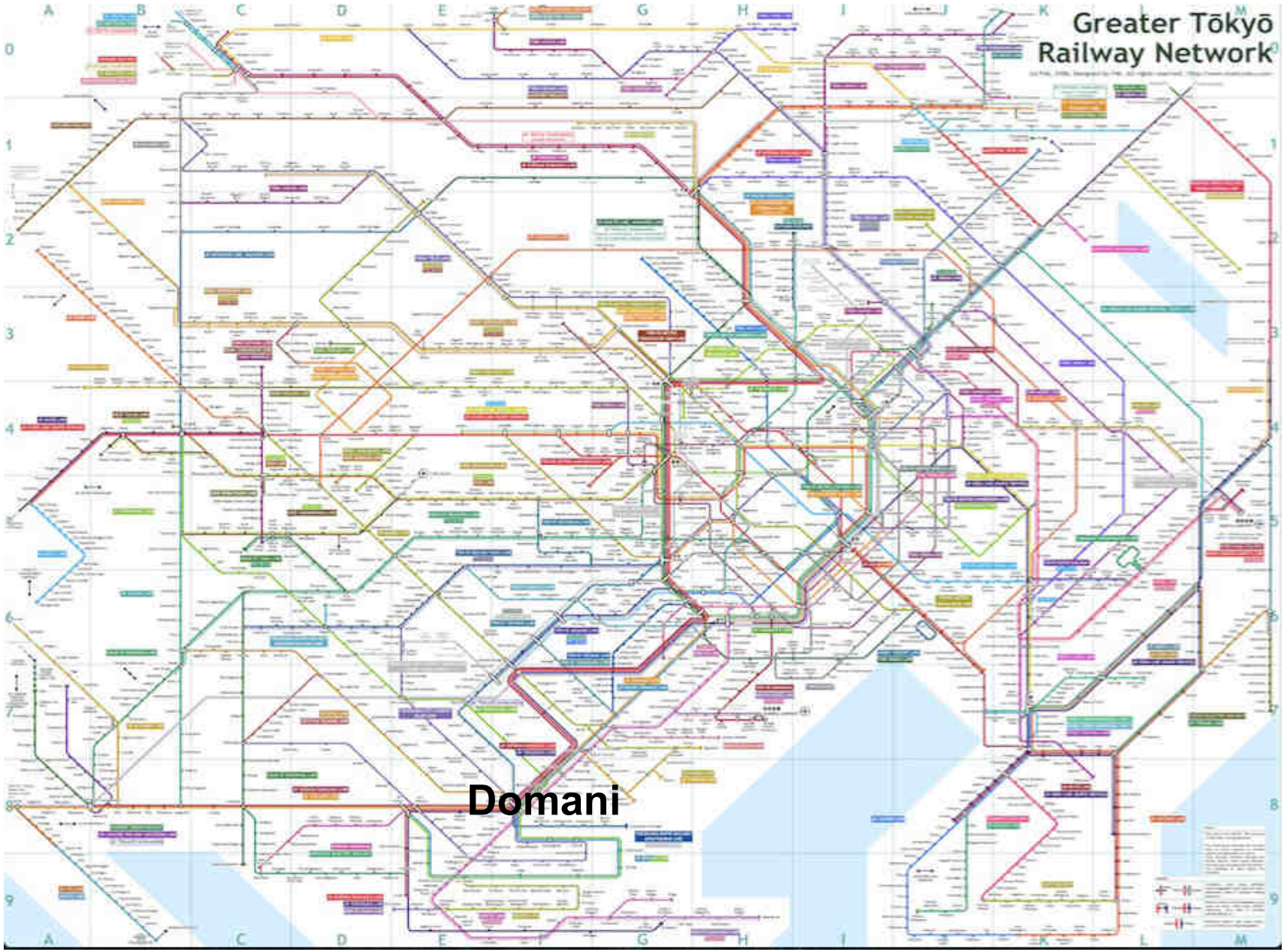
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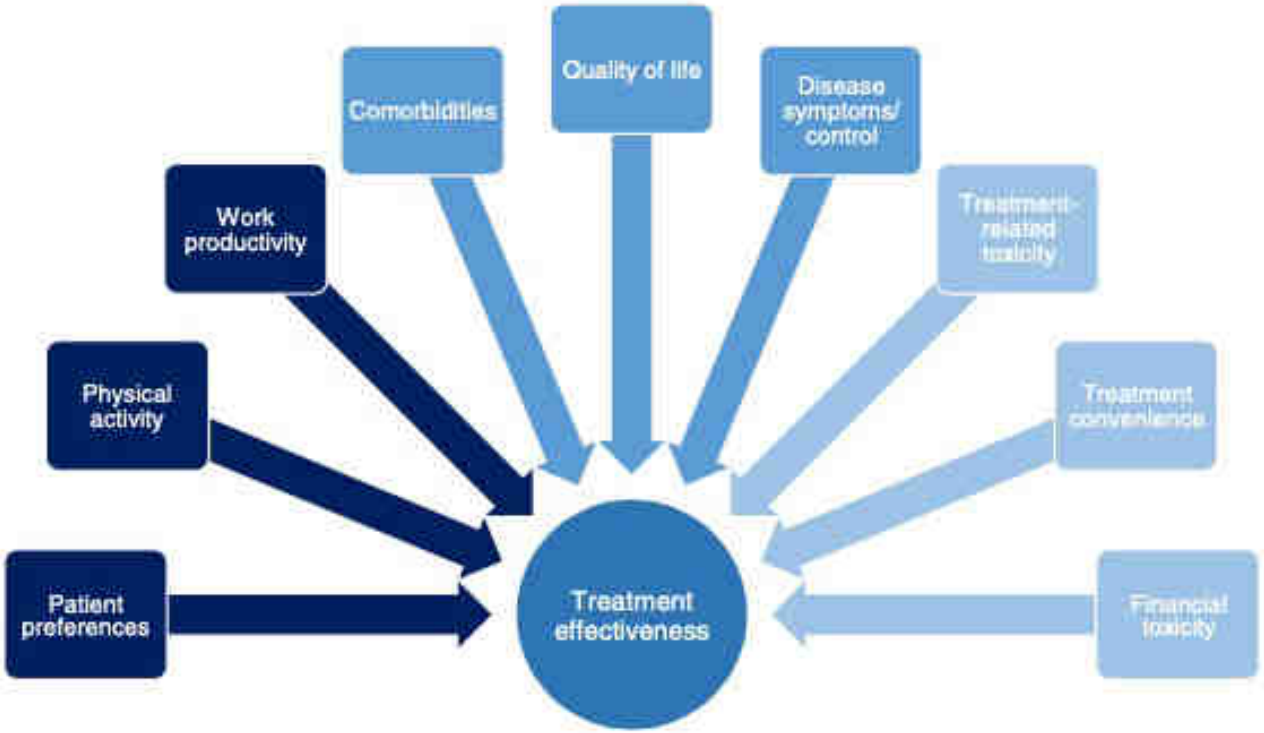
Terpos et al. *Blood Cancer Journal* (2021)11:40
https://doi.org/10.1038/s41408-021-00432-4

REVIEW ARTICLE Open Access

Management of patients with multiple myeloma beyond the clinical-trial setting: understanding the balance between efficacy, safety and tolerability, and quality of life

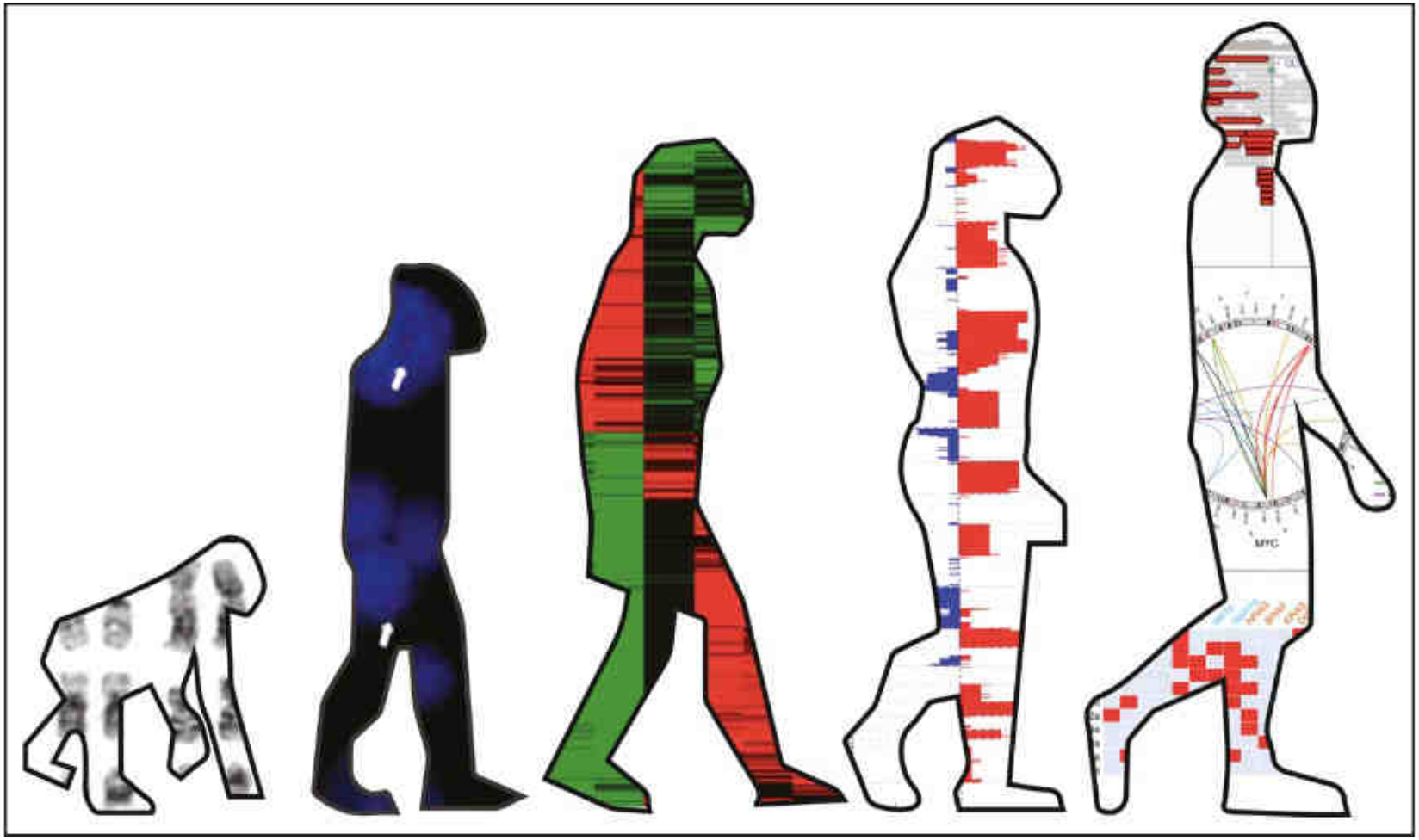
Evangelos Terpos[1], Joseph Mikhael[2], Roman Hajek[3], Ajai Chari[4], Sonja Zweegman[5], Hans C. Lee[6], María-Victoria Mateos[7], Alessandra Larocca[8], Karthik Ramasamy[9], Martin Kaiser[10], Gordon Cook[11], Katja C. Weisel[12], Caitlin L. Costello[13], Jennifer Elliott[14], Antonio Palumbo[14] and Saad Z. Usmani[15]



Toward personalized treatment in multiple myeloma based on molecular characteristics

Charlotte Pawlyn[1] and Faith E. Davies[2]

[1]The Institute of Cancer Research, London, United Kingdom; and [2]Myeloma Center, University of Arkansas for Medical Sciences, Little Rock, AR



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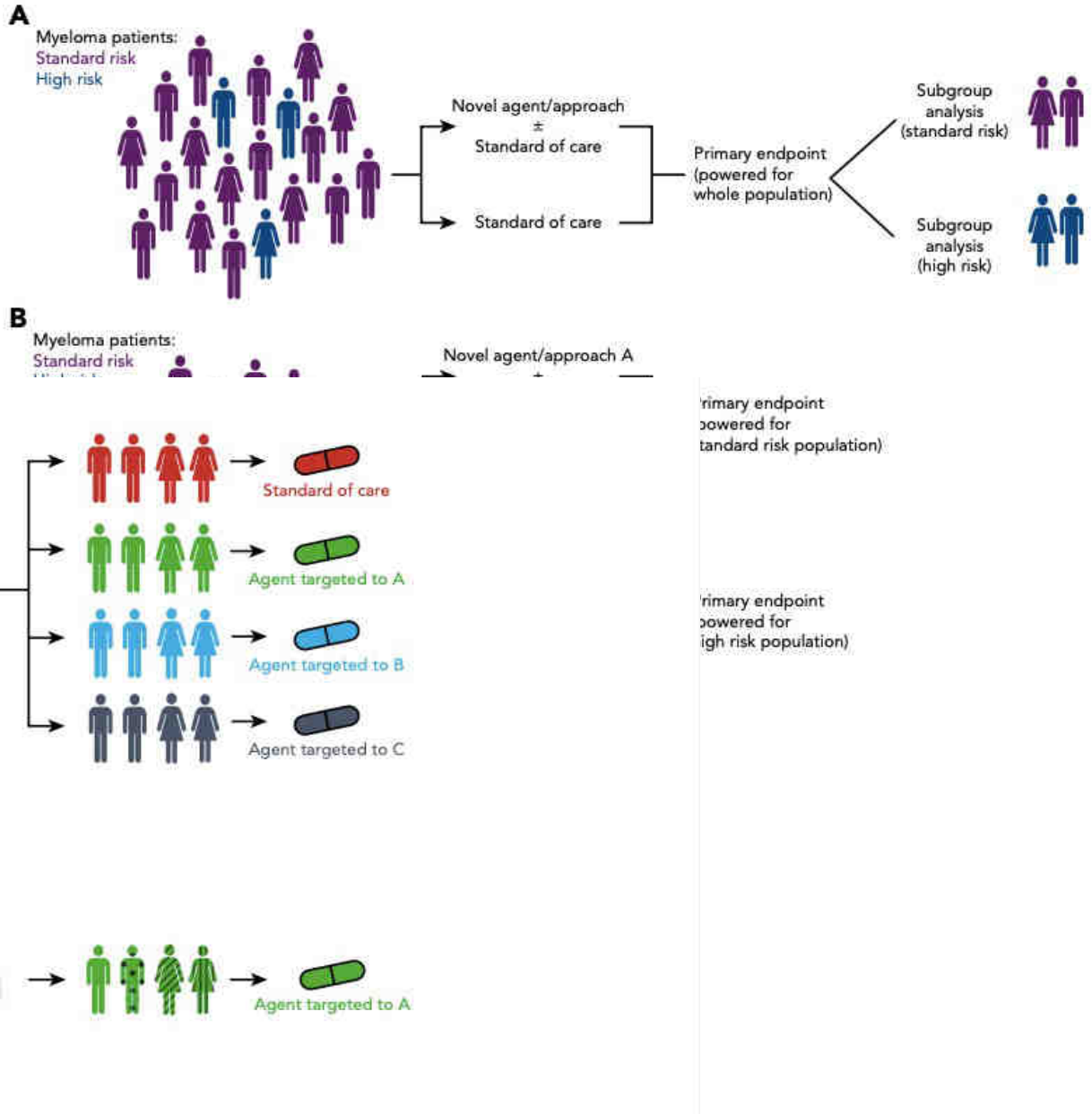
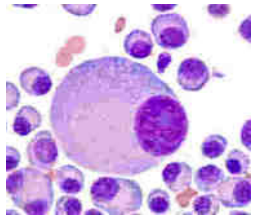


Personalised decision-making

- ✓ Prior therapies: which truly refractory?
- ✓ Toxicities
- ✓ Co-morbidities

Patient

Disease



- ✓ Cytogenetic subgroup
- ✓ Molecular risk at diagnosis

- ✓ Unresolved toxicity
- ✓ Frailty
- ✓ Ability to attend hospital
- ✓ Route of delivery

- ✓ Speed of relapse
- ✓ Associated end organ damage
- ✓ Extramedullary disease

- ✓ Availability/financial toxicity

ADC and «customization» of therapy

1. Switch of target
2. High-risk status
3. Managebility of administration
4. Safety profile and quality of life

ADC and «customization» of therapy

1. Switch of target

This real-world study identified EHR data of US patients treated in community practices demonstrated high heterogeneity in 2L and 3L treatment choices

Real-world treatment patterns in US patients who initiated 2L or 3L RRMM therapy

Introduction

Real-world evidence regarding treatment patterns and patient outcomes in RRMM are limited, especially in the 2L and 3L settings

Study design

Retrospective study using EHR data (Flatiron Health)

Prevalent cohorts: Pts with ≥1 MM agent[a] in 2L/3L from 2018-2020

Incident cohorts: MM 2L/3L treatment start date between January 1, 2018 and April 30, 2021

Key findings

- **Prevalent cohorts:** From 2018-2020, the most frequently used 2L and 3L regimens were bor/len/dex (10%-13%) and dara/pom/dex (8%-11%), respectively
- **Incident cohorts:** Patient characteristics were similar between the 2L and 3L groups except for higher prior dara use in 3L (16%) compared with 2L (1%)
- **Incident cohorts: len/dex** was the most common 2L regimen and DPd was the most common 3L regimen (10% for both)
- **Incident cohorts:** For both 2L and 3L, immunomodulatory drugs and PIs were common. Additionally, treatment with triplet regimens was a common approach (47% for both)

Triplet regimens were common in 2L and 3L in the community practices, but overall, there was a wide variety in regimens

[a]Must have been a nonmaintenance, nontransplant MM drug.

2L, second line; 3L, third line; bor, bortezomib; dara, daratumumab; dex, dexamethasone; EHR, electronic health records; len, lenalidomide; MM, multiple myeloma; PI, proteasome inhibitor; pom, pomalidomide; pt, patient; RRMM, relapsed/refractory multiple myeloma.

Boytsov N, et al. Presented at the 64th American Society of Hematology Annual Meeting & Exposition. December 10-13, 2022. New Orleans, LA. Publication only Abstract.

The efficacy and safety outcomes as well as the choice of 3L+ treatments in RRMM are heterogeneous, highlighting the lack of SOC in this setting

Goal of study

To explore efficacy and safety outcomes in 3L+ treatment of RRMM, including in patients who are refractory to anti-CD38 antibody

Study design

Searches were conducted on March 28, 2022, for publications (2008-2022) and unpublished/grey literature (2018-2020) reporting evidence from interventional studies in patients receiving RRMM treatment after ≥2 prior LOTs

Types of studies (N=147)	
RCT/single-arm trial, n	1
RCT, n	41
Single-arm trial, n	87
Non-RCT, n	12
Pooled analysis, n	6

Key findings

- Median PFS and OS varied widely across studies based on key modifiers of treatment outcomes. ORR and PFS were shortest in **len** refractory patients and OS was longest in patients who had received as few as 2 LOT and were not **len** refractory
- Due to heterogeneity in outcomes reported such as from fewer number of patients in a study, early phase trials, or reported in triple-class refractory patients and not from anti-CD38 refractory patients, efficacy of subsequent LOT in anti-CD38-refractory patients are unclear
- Overall rates of reported adverse events were high (94%-100%), with anemia, thrombocytopenia, and neutropenia being the most frequently reported

Identifying an SOC in 3L+ is challenging given the heterogeneity in populations evaluated, subgroups analysed, and outcomes reported. Outcomes of patients refractory to anti-CD38 antibody on subsequent LOT are lacking

The table has been independently created by GSK from original data presented in Hanna M at ASH. December 2022.

3L, third-line; len, lenalidomide; LOT, line of therapy; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; RCT, randomised, controlled trial; RRMM, relapsed/refractory multiple myeloma; SOC, standard of care.

Hanna M, et al. Presented at the 64th American Society of Hematology Annual Meeting & Exposition. December 10-13, 2022. New Orleans, LA. Publication Only Abstract.

Outcomes of a majority of patients with RRMM remain suboptimal potentially due to retreatment with prior therapies

STUDY POPULATION

RRMM Patients

- Longitudinal, retrospective cohort study using COTA de-identified database (11/16/2015 to 9/12/2022; N=1662)
- Final 2L+ population was **1118 patients** (544 patients excluded d/t stem cell therapy during index LOT or in the prior 100 days)
- Patients must have had active RRMM and received ≥1 prior line of treatment
- Time-to-event outcomes, including PFS, DOT, and TTNT, were evaluated with Kaplan-Meier survival analysis
- The following overlapping sub-cohorts were created based on patients' prior exposure and refractory status:

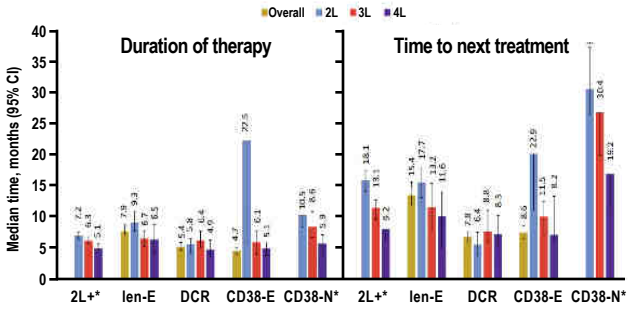
CD38-N (n=757)	len-E (n=1123)	CD38-E (n=764)	DCR (n=713)
(no prior exposure to an anti-CD38 agent)	(prior exposure to lenalidomide)	(prior exposure to an anti-CD38 agent)	(refractory to a PI and an immunomodulatory therapy)

After 2L+ index LOT, 57.3% of the overall population progressed to a subsequent LOT

Despite prior exposure, many were retreated with an anti-CD38 agent both during and after index LOT (49.0% and 33.7%, respectively)

Median PFS and TTNT in the overall 2L+ cohort were 21.8 and 18.1 months; shortest in DCR (6.7 and 7.8 months) and CD38-E cohorts (5.6 and 8.6 months)

Median DOT was short across overall 2L+ patients (7.2 months at 2L) and sub-cohorts, and generally remained consistent across LOTs



The figure was first presented in Richter J. ASH. December 2022. Poster presentation 1891.

*Overall category is not included for the 2L+ population and CD38-N since LOTs are not mutually exclusive; individual patients could have multiple index dates and appear in multiple LOTs. This does not apply to the **len** E, DCR, and CD38 E sub cohorts in which patients had a single index date following the exposure or refractory status of interest. DOT was measured from the initiation of index line of therapy to the stop of index line of therapy; TTNT was measured from the initiation of index line of therapy to initiation of the following line of therapy. These figures were first presented in Richter J at ASH. December 2022. Poster presentation 1891.

These findings support the need for increased uptake of new treatments with novel mechanisms of action earlier in the patient journey

2L, second line; 3L, third line; 4L, fourth line; bor, bortezomib; CI, confidence interval; DCR, double-class refractory; dex, dexamethasone; DOT, duration of treatment; d/t, due to; E, exposed; len, lenalidomide; LOT, line of treatment; N, naïve; PFS, progression-free survival; PI, proteasome inhibitor; RRMM, relapsed/refractory multiple myeloma; TTNT, time to next therapy.

Richter J, et al. Presented at the 64th American Society of Hematology Annual Meeting & Exposition. December 10-13, 2022. New Orleans, LA. Poster 1891.

Many patients at 3L were treated with the same agent class used in prior line, and len-based regimens were most common in Germany and Italy

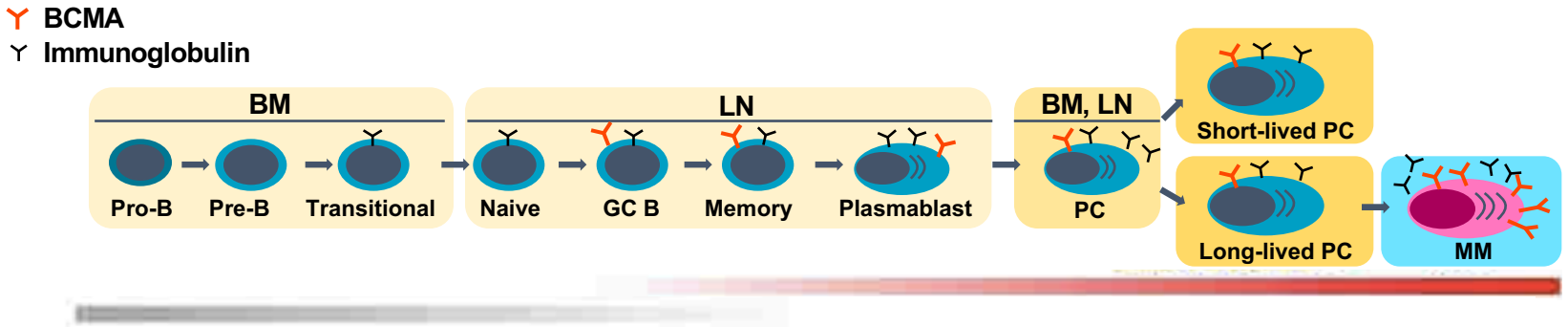
- **Real-world treatment utilisation in patients from European claims data sets who initiated 3L treatment for RRMM**

Background	Study design	Key findings
Real-world evidence on treatment patterns can complement clinical trial data, provide valuable insights on clinical practice in different countries, and help identify and address unmet medical needs	Claims data from the German AOK PLUS health insurance fund and Italian Local Health Units (2012-2020) were used Patients initiating 3L treatment from 2016-2020 (index date) were identified	Following **len**-based regimens, which were most common, high proportions of cfz- and pom-based regimens were observed in 3L in Germany and Italy, respectively Use of pom/dex in 3L in Italy was higher than in Germany (12% vs 4%, respectively), whereas use of cfz- (10% vs 21%) and dara-based regimens in 3L was lower (9% vs 29%) Many 3L patients were re-treated with the same agent class used in a prior line bor use in 3L was prominent for retreatment in Germany and Italy, which may reflect bor's prior use in a fixed-duration regimen. Retreatment with **len** in 3L was also common in Italy

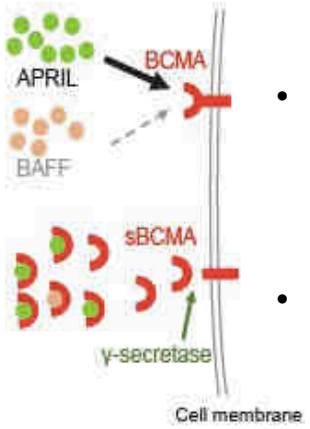
3L, third line; bor, bortezomib; cfz, carfilzomib; dara, daratumumab; dex,dexamethasone len, lenalidomide; dex, dexamethasone; pom, pomalidomide; RRMM, r elapsed or refractory multiple myeloma.

Lehne M, et al. Presented at the 64th American Society of Hematology Annual Meeting & Exposition. December 10-13, 2022. New Orleans, LA. Publication only abstract.

BCMA, a good target



Cho SF, et al. Front Immunol. 2018;9:1821. Moreaux J, et al. Blood. 2004;103:3148-57. Sanchez E, et al. Br J Haematol. 2012;158:727-38.

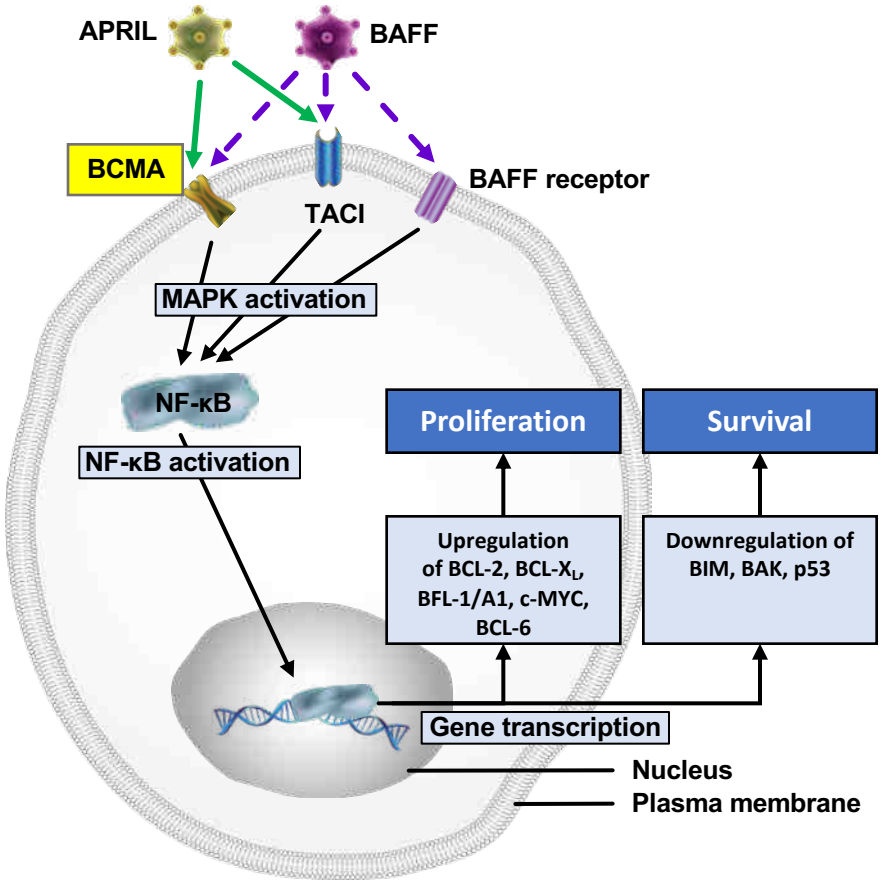


- **BCMA is an antigen expressed specifically on PCs and myeloma cells**
  - **higher expression in myeloma cells than normal PCs**
  - **promotes myeloma cell growth, chemoresistance and immunosuppression**
- **BCMA expression increases as the disease progresses from MGUS to advanced myeloma**

Cho S-F. et al.; Front Immunol. 2018; 9:1821
Sanchez E. et al.; Br J Haematol. 2012; 158:727-738

The BCMA signalling pathway

- BCMA is a member of the TNF receptor superfamily and its expression is highly restricted to plasma cells[1]
- BCMA is expressed in multiple myeloma cells at relatively higher levels than observed on normal plasma cells[2]
- Interaction of BCMA with APRIL or BAFF induces activation of the MAPK pathway and NF-κB to promote proliferation and survival[1,3]
- Elevated serum BCMA in multiple myeloma correlates with disease status, response to therapy, and overall survival[4]
- Inhibition of BCMA may present a novel therapeutic approach for multiple myeloma

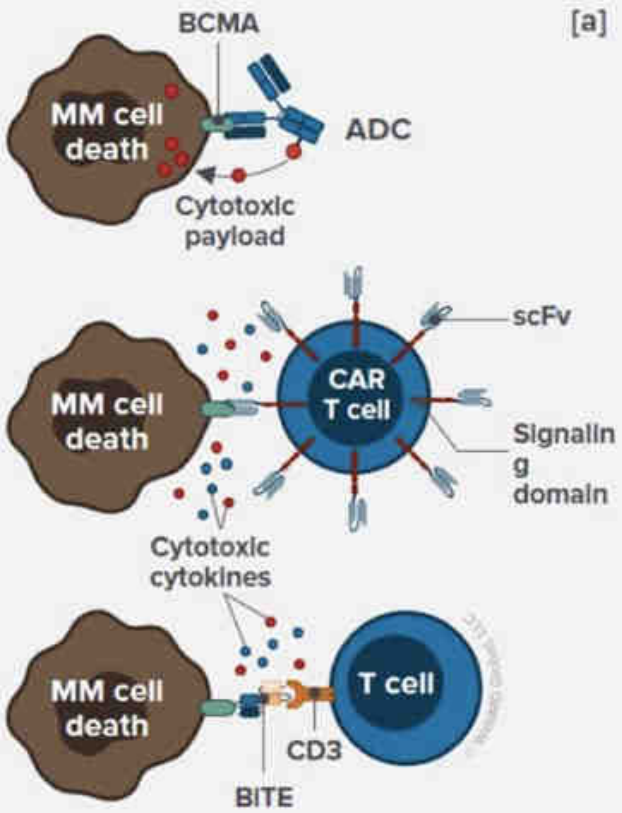


APRIL, a proliferation-inducing ligand;
BCMA, B-cell maturation antigen;
MAPK, mitogen-activated protein kinase;
TACI, transmembrane activator and CAML interactor;
TNF, tumour necrosis factor.

Figure adapted from Yang S, et al. Crit Rev Oncol Hematol 2014;91:113–22.

1. Coquery CM, et al. Crit Rev Immunol 2012;32:287–305;
2. Zhao C, et al. Oncogene 2008;27:63–75;
3. Hatzoglou A, et al. J Immunol 2000;165:1322–30;
4. Sanchez E, et al. Br J Haematol 2012;158:727–38.

EMA-Approved BCMA-Targeted Therapies in MM



Antibody-Drug Conjugates

- Belantamab mafodotin[b]

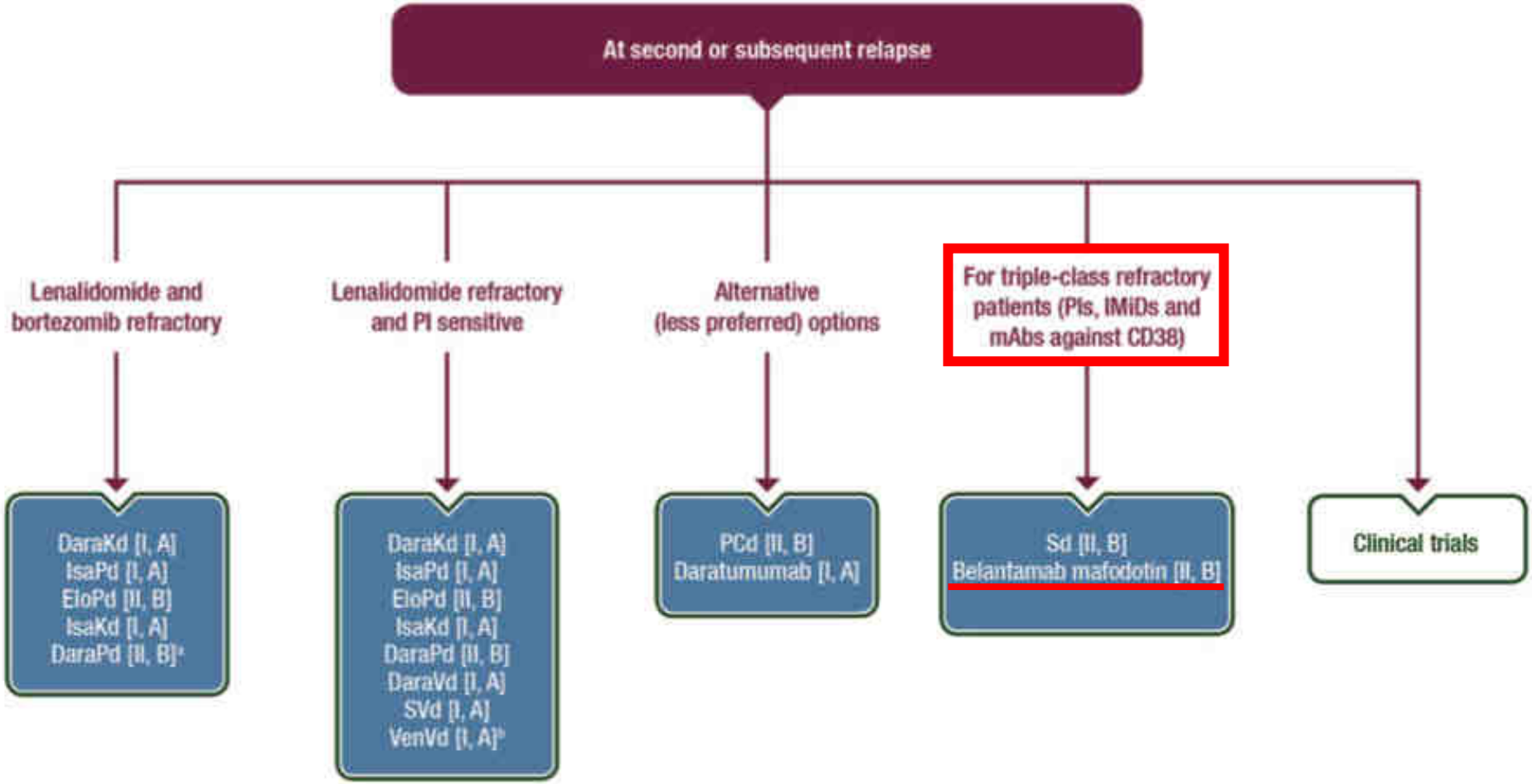
CAR T-Cell Therapies

- Idecabtagene vicleucel (ide-cel)[c]
- Ciltacabtagene autoleucel (cilta-cel)
- P-BCMA-101

Bispecific Antibodies

- CC-93269
- Teclistamab
- Elranatamab
- REGN5458

ADC, antibody-drug conjugate; BITE, bi-specific T-cell engager; scFv, single-chain variable fragment.
a. Yu B, et al. J Haematol Oncol. 2020;13:125; b. Belantamab mafodotin. Product information. European Medicines Agency (EMA). Published July 2020. Updated March 2021. Accessed October 13, 2021. https://www.ema.europa.eu/en/documents/product-information/blenrep-epar-product-information_en.pdf; c. Idecabtagene vicleucel. Product information. European Medicines Agency (EMA). Published June 2021. Updated 12 October 2021. Accessed September 22, 2021. https://www.ema.europa.eu/en/documents/product-information/abecma-epar-product-information_en.pdf.


At second or subsequent relapse
Lenalidomide and bortezomib refractory
Lenalidomide refractory and PI sensitive
Alternative (less preferred) options
For triple-class refractory patients (PIs, IMiDs and mAbs against CD38)
Clinical trials
DaraKd [I, A]
IsaPd [I, A]
EloPd [II, B]
IsaKd [I, A]
DaraPd [II, B]a
DaraKd [I, A]
IsaPd [I, A]
EloPd [II, B]
IsaKd [I, A]
DaraPd [II, B]
DaraVd [I, A]
SVd [I, A]
VenVd [I, A]b
PCd [II, B]
Daratumumab [I, A]
Sd [II, B]
Belantamab mafodotin [II, B]

DREAMM-2: belantamab mafodotin monotherapy demonstrated deep and durable activity with a manageable profile in TCR patients[1,2]

Primary analysis data cutoff: January 31, 2020[3]

Belantamab mafodotin 2.5mg/kg Q3W
Overall population N=97

Patient characteristics[1,3]

- **Median age, years** (range): **65** (60-70)
- **Median prior lines of therapy** (range): **7** (3-21)
  - All patients (N=97, 100%) were **triple-class refractory**

Efficacy outcomes[3,4]

ORR, n (%)	**31 (32)**
≥VGPR, n (%)	18 (19)
mDOR, months	**11.0**
mPFS, months	2.8
mOS, months	**13.7**

AEs*

	Any grade, n (%)[2]	Grade ≥3, n (%)[4]
Any	93 (98)	80 (84)
Keratopathy†	67 (71)	44 (46)‡
Thrombocytopenia§	23 (24)	21 (22)
Anemia	26 (27)	20 (21)

*Events reported based on CTCAE v4.03 (with the exception of MECs) in the safety population (all patients who received ≥1 dose of study treatment).[4] †Keratopathy is a pathological exam finding, including superficial keratopathy and/or microcyst-like epithelial changes (MECs).[1,2] ‡Represents severe MECs based on corneal examination findings and changes in BCVA from baseline (does not include patient-reported symptoms).[1] §Includes preferred terms thrombocytopenia, decreased platelet count, and cerebral hemorrhage (2 cases within the 3.4mg/kg group only).[4]
Please see slide notes for abbreviations and references.

DREAMM-2: efficacy

Median follow-up: 6 months

Response in ITT Population

	2.5 mg/kg	3.4 mg/kg
ORR, %	31	34
≥ CR, %	3	3
mDOR	NR	NR
mPFS, mo	2.9	4.9

Recommended Dose: 2.5 mg/kg

Activity in Heavily Pretreated MM

	ORR at 2.5 mg/kg
≤ 4 prior lines of therapy	37.5
> 4 prior lines of therapy	29.6
Refractory to:	
Any PI	30.5
Any IMiD	31.6
Any Anti-CD38	30.9

CR, complete response; IMiD, immunomodulatory drug; ITT, intention to treat; mDOR, median duration of response; mPFS, median progression-free survival; PI, proteasome inhibitor.

a. Lonial S, et al. Lancet Oncol. 2020;21:207-221; b. Belantamab mafodotin. Product information. European Medicines Agency. Approved July 2020. Revised March 2021. Accessed October 13, 2021. https://www.ema.europa.eu/en/documents/product-information/blenrep-epar-product-information_en.pdf

DREAMM-2 and RWE patient characteristics

	DREAMM-2 2.5mg/kg cohort (Lonial)[1,2]	GSK expanded access (Shragai)[3]	Mayo Clinic efficacy and safety (Vaxman)[4]	Mayo Clinic 2022 (Abeykoon)[5]
N	97	67	36	38
Patient demographics				
Female, n (%)	46 (47)	29 (43)	13 (36)	13 (34)
Age, years (range)	65 (60-70)*	70 (36-88)*	61 (37-83)‡	67 (49-90)*
High-risk cytogenetics, n (%)	41 (42)	18 (47)	14 (41)	32 (89)
With extramedullary disease, n (%)	22 (23)	7 (10)	5 (14)	N/A
Prior treatment				
Median prior LOT (range)	7 (3-21)	5 (4-7)†	8 (7-11)†	8 (2-15)
% of patients previously treated with an immunomodulatory agent, a PI, and an anti-CD38 mAb, n (%)	97 (100)	44 (67)	36 (100)	N/A
% of patients with prior ASCT, n (%)	73 (75)	34 (51)	27 (75)	N/A
% of patients previously treated with an anti-BCMA targeted agent, n (%)	0	N/A	N/A	4 (11)
CAR-T therapy, n (%)	0	N/A	7 (19)	4 (11)

***Median age.[1,3,5] †Interquartile range.[3,4] ‡Mean age.[4]**
ASCT, autologous stem cell transplant; BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T cell; CD, cluster of differentiation; LOT, lines of therapy; mAb, monoclonal antibody; N/A, not available; PI, proteasome inhibitor;
RWE, real-world evidence.

1. Lonial S et al. *Cancer.* 2021;127(22):4198-4212. 2. Lonial S et al. *Lancet Oncol.* 2020;21:207-221. 3. Shragai T et al. Presented at: European Hematology Association Congress; June 9-17, 2021. Poster 2853. Accessed August 4, 2021. library.ehaweb.org/eha/2021/eha2021-virtual-congress/324746/tamir.shragai.belantamab.mafodotin.treatment.for.patients.with.relapsed.html 4. Vaxman I et al. *Blood Cancer J.* 2021;11(12):196. doi:10.1038/s41408-021-00592-3
5. Abeykoon JP et al. *Br J Haematol*. 2022. doi:10.1111/bjh.18298

DREAMM-2 and RWE patient characteristics

	DREAMM-2 2.5mg/kg cohort (Lonial)[1,2]	MSKCC (Hultcrantz)[3]	University of Kansas Health System (Atieh)[4]	Spain compassionate use (Alegre)[5]	MD Anderson Cancer Center (Becnel)[6]	Dana-Farber Cancer Institute (Marzouk)[7]
N	97	50	28	33	39	40
Patient demographics						
Female, n (%)	46 (47)	25 (50)	8 (29)	18 (55)	13 (33)	17 (42)
Age, years (range)	65 (60-70)†	67 (37-87)	67 (42-85)†	70 (46-79)†	66 (39-89)†	66 (43-86)†
High-risk cytogenetics, n (%)	41 (42)	32 (74)	20 (71)	10 (30)	14 (38)§	13 (33)¶
With extramedullary disease, n (%)	22 (23)	N/A	13 (46)	N/A	14 (38)	10 (25)
Prior treatment						
Median prior LOT (range)	7 (3-21)	7 (3-14)	5 (3-15)	5 (3-8)	7 (3-16)	5 (2-14)
% of patients previously treated with an immunomodulatory agent, a PI, and an anti-CD38 mAb,* n (%)	97 (100)	50 (100)	28 (100)	≥29 (≥88)	37 (95)	36 (90)
% of patients with prior ASCT, n (%)	73 (75)	34 (68)‡	21 (75)	N/A	N/A	N/A
% of patients previously treated with an anti-BCMA targeted agent, n (%)	0	13 (26)	8 (29)	N/A	8 (21)‖	N/A
CAR-T therapy, n (%)	0	9 (18)	N/A	N/A	2 (5)	N/A

*All the patients in DREAMM-2 and the University of Kansas Health System study were also triple-class refractory.[1,3-7] †Median age.[1,4-7] ‡With high-dose melphalan; six patients had two prior ASCTs.[3] §High-risk FISH is defined as del 17p, t(4;14), and/or t(14;16). The high-risk status of two patients were not available.[6] ‖BCMA-refractory patients; prior BCMA therapy included antibody-drug conjugates (n=2), bispecifics (n=4), and CAR-Ts (n=2).[6] ¶The cytogenetic status of 9 (23%) patients was unknown.[7]

1. Lonial S et al. *Cancer*. 2021;127(22):4198-4212. 2. Lonial S et al. *Lancet Oncol*. 2020;21:207-221. 3. Hultcrantz M et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 11-14, 2021; Atlanta, GA. Poster 1644. 4. Atieh T et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 11-14, 2021; Atlanta, GA. Poster 1642. 5. Alegre A et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 11-14, 2021; Atlanta, GA. Poster 3775. 6. Becnel MR et al. Presented at: American Society of Clinical Oncology Annual Meeting; June 3-7, 2022; Chicago, IL. Poster 3060. 7. Marzouk O et al. Presented at: Hematology/Oncology Pharmacy Association Annual Conference; March 30-April 2, 2022; Boston, MA.
Please refer to slide notes for abbreviations.

DREAMM-2 and RWE efficacy

	DREAMM-2 2.5mg/kg cohort (Lonial)[1]	GSK expanded access (Shragai)[2]	Mayo Clinic efficacy and safety (Vaxman)[3]	Mayo Clinic 2022 (Abeykoon)[4,5]
N	97	67	36	38
Median follow-up, months	12.4	16.1	6	11
Response rates				
ORR, %	32	54	33	29
sCR	2	N/A	N/A	0
CR	5	6	6	0
VGPR	11	23	8	8
PR	13	25	19	21
MR	4	11	N/A	N/A
SD	28	14	28	N/A
PD	N/A	21	36	N/A
Survival outcomes				
Median PFS, months	2.8	4.4	2	2
Median OS, months	13.7	14	6.5	7.2
Median DOR, months	11*	N/A	5	3 (95% CI, 0.5-NR)

***For patients who achieved ≥PR.[1]**
CR, complete response; DOR, duration of response; MR, minimal response; N/A, not available; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; RWE, real-world evidence; sCR, stringent complete response; SD, stable disease; VGPR, very good partial response.

1. Lonial S et al. *Cancer*. 2021;127(22):4198-4212. 2. Shragai T et al. Presented at: European Hematology Association Congress; June 9-17, 2021. Poster 2853. Accessed August 4, 2021. library.ehaweb.org/eha/2021/eha2021-virtual-congress/324746/tamir.shragai.belantamab.mafodotin.treatment.for.patients.with.relapsed.html 3. Vaxman I et al. *Blood Cancer J*. 2021;11(12):196. doi:10.1038/s41408-021-00592-3 4. Abeykoon JP et al. *Br J Haematol*. 2022. doi:10.1111/bjh.18298 5. Abeykoon JP et al. Supplemental appendix. *Br J Haematol*. 2022. doi:10.1111/bjh.18298

DREAMM-2 and RWE efficacy

	DREAMM-2 2.5mg/kg cohort (Lonial)[1]	MSKCC (Hultcrantz)[2]	University of Kansas Health System (Atieh)[3]	Spain compassionate use (Alegre)[4]	MD Anderson Cancer Center (Becnel)[5]	Dana-Farber Cancer Institute (Marzouk)[6]
N	97	50	28	33	39	40
Median follow-up, months	12.4	8.5	7.4	11	10.1	N/A
Response rates						
ORR, %	32	54	46	42	27	38
sCR	2	N/A	0	N/A	0	N/A
CR	5	16	14	18†	0	N/A
VGPR	11	24	4	N/A	3	N/A
PR	13	14	29	N/A	24	N/A
MR	4	N/A	N/A	N/A	8	N/A
SD	28	16	25	N/A	N/A	N/A
PD	N/A	30	29	N/A	N/A	N/A
Survival outcomes						
Median PFS, months	2.8	6	4.9	3	1.8	9.1
Median OS, months	13.7	NR	7.4	14	9.2	9.1
Median DOR, months	11*	11*	N/A	N/A	NR	7.2

*Includes patients who achieved a ≥PR.[1,2] †Includes patients who achieved a ≥VGPR.[4]

1. Lonial S et al. *Cancer*. 2021;127(22):4198-4212. 2. Hultcrantz M et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 11-14, 2021; Atlanta, GA. Poster 1644. 3. Atieh T et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 11-14, 2021; Atlanta, GA. Poster 1642. 4. Alegre A et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 11-14, 2021; Atlanta, GA. Poster 3775.
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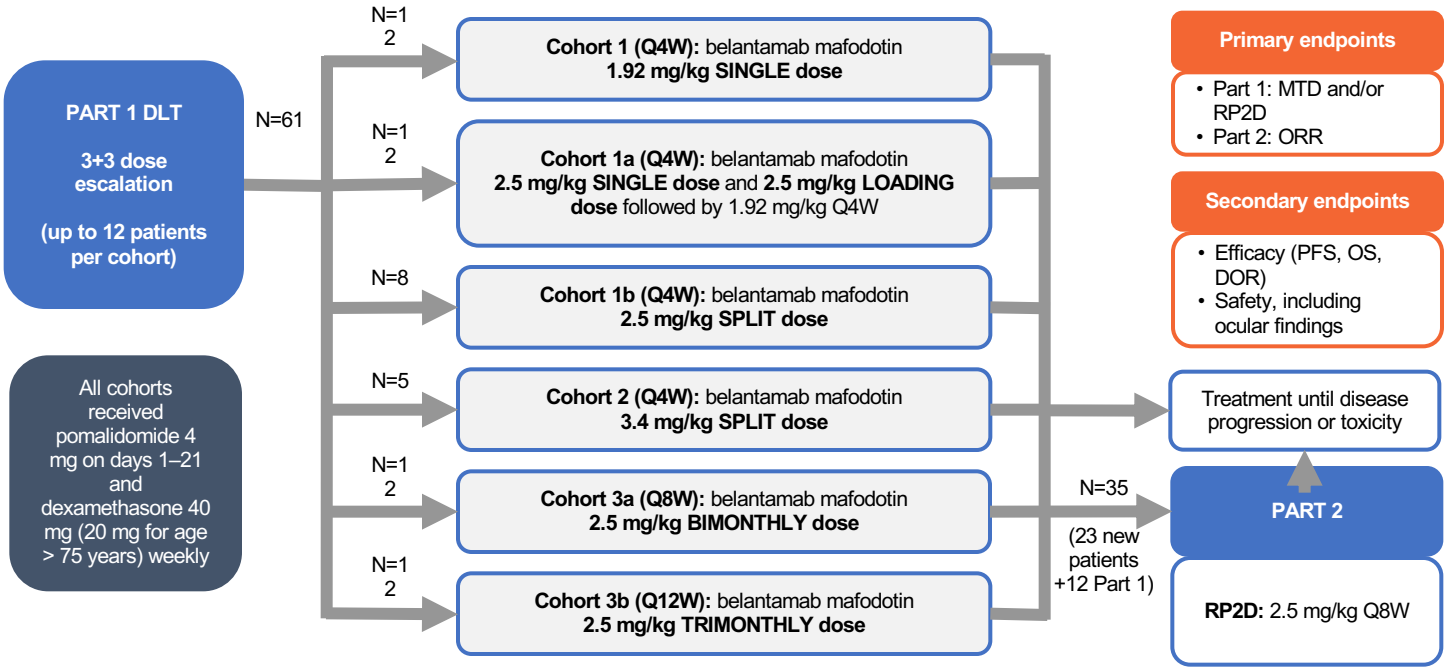
Please refer to slide notes for abbreviations.

The Algonquin study is a two-part phase 1/2 trial evaluating the safety and efficacy of different doses and schedules of belantamab mafodotin + pom/dex in patients with RRMM

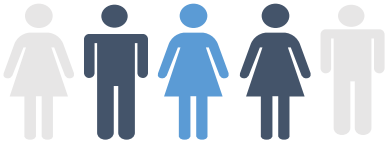


Part 1 of the Algonquin study established an RP2D of 2.5mg/kg Q8W

DLT, dose limiting toxicity; DOR, duration of response; MTD, maximum tolerated dose; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; pom/dex, pomalidomide/dexamethasone; QXW, every X weeks; RP2D, recommended phase 2 dose; RRMM, relapsed/refractory multiple myeloma.

Trudel S et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 10-13, 2022; New Orleans, LA. Poster 3248.

The Algonquin study enrolled patients with RRMM, including those with triple-class exposed/refractory (TCE/R*) MM



KEY ELIGIBILITY CRITERIA

Adult patients ≥18 years

- Confirmed diagnosis of multiple myeloma and relapsed and/or refractory disease
- Undergone stem cell transplant, or have been considered transplant ineligible
- ECOG performance status 0–2
- ≥1 prior line of treatment that must have included len and a proteasome inhibitor
- Refractory to len and exposed or refractory to a proteasome inhibitor

Patients were required to have measurable disease, defined as having at least one of the following:

Serum M-protein concentrations	Urine M-protein concentrations	Serum FLC assay
5 g/L or higher	200 mg per 24 hours or higher	FLC level 100 mg/L or higher and abnormal serum FLC ratio (<0.26 or >1.65)

This analysis consists of updated safety and efficacy data for the subgroup of TCE/R MM patients treated at doses of 1.92 or 2.5 mg/kg belantamab mafodotin + pom/dex

*TCE/R patients were exposed/refractory to len a proteasome inhibitor and an anti-CD38 agent.

ECOG, Eastern Cooperative Oncology Group; FLC, free light chain; M-protein, myeloma protein; len, lenalidomide; MM, multiple myeloma; pom/dex, pomalidomide/dexamethasone; RRMM, relapsed/refractory multiple myeloma; TCE/R, triple-class exposed or refractory

Trudel S et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 10-13, 2022; New Orleans, LA. Poster 3248.

Responses remained deep and durable in hard-to-treat double and triple refractory patients

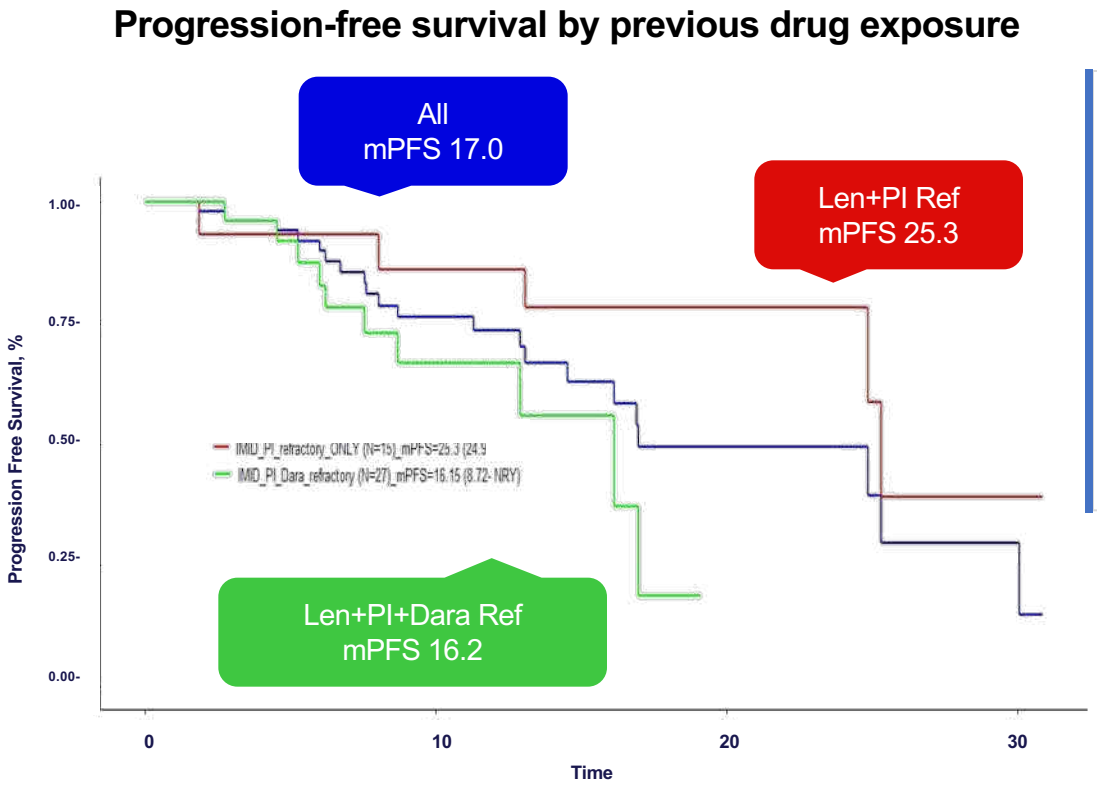
Outcome (months)	All N=56	Len+PI Refractory N=15	Len+PI+Dara Refractory N=27
ORR (≥PR) / VGPR	88.9/72.2	86.7/86.7	92.3/69.2
mPFS (95% CI)	17 (14.5-NYR)	25.3 (24.9-NYR)	16.2 (8.7-NYR)
Follow-up, median (range)	11 (0.5-30.9)	14.0 (1.9-30.9)	7.7 (0.5-19.1)

A 16.2 month PFS was observed in triple refractory patients

Dara = daratumumab; Len = lenalidomide; mPFS = median progression-free survival; ; NYR = not yet reached; ORR = overall response rate; OS = overall survival; PFS = progression-free survival; PI = proteasome inhibitor; PomDex = pomalidomide/dexamethasone; PR = partial response; RRMM = relapsed/refractory multiple myeloma; VGPR = very good partial response

Trudel S et al. Presented at the 63rd American Society of Hematology Annual Meeting 2021.

Higher numbers of Dara refractory patients in some cohorts may have impacted the mPFS



Dara refractory groups were associated with a short PFS, which is is expected

- In the MAMMOTH study, the mPFS of patients that received at least one additional line after becoming refractory to daratumumab was 3.4 months[2]

— All cohort (N=56) mPFS = 17 (14.5-NYR)

— Immunomodulatory and PI refractory only (N=15) mPFS = 25.3 (24.9-NYR)

— Immunomodulatory, PI, and DARA refractory (N=27) mPFS =16.15 (8.72-NYR)

Figures first presented in Trudel S et al. ASH. 2021.

Dara = daratumumab; Len = lenalidomide; mPFS = median progression-free survival; ; NYR = not yet reached; ORR = overall response rate; PFS = progression-free survival; PI = proteasome inhibitor; Pom/Dex = pomalidomide/dexamethasone; PR = partial response; QXW = every X weeks; RRMM = relapsed/refractory multiple myeloma

1. Trudel S et al. Presented at the 63rd American Society of Hematology Annual Meeting 2021; 2. Gandhu UH, et al. *Leukemia*. 2019

61 TCE patients were enrolled in dose cohorts received either 1.92 or 2.5 mg/kg belantamab mafodotin + pom/dex*

Patient Disposition (N=61)	n (%)
Ongoing	33 (54.1%)
Discontinued	28 (45.9%)
Progressive disease	20 (32.7%)
Adverse event (AE)	2 (3.3%)
Death†	4 (6.6%)
Patient withdrawal	2 (3.3%)

Median age was 67 years and median prior LOT was 3 (2-5)

Characteristics (N=61)	
Age, median (range), years	67 (36–85)
Previous LOT, median (range)	3 (2–5)
Stem cell transplant (%)	37 (60.7%)
len exposed/refractory (%)	61 (100%) / 60 (98.4%)
PI exposed/refractory (%)	61 (100%) / 61 (100%)
dara exposed/refractory (%)	61 (100%) / 60 (98.4%)
len and PI exposed/refractory (%)	61 (100%) / 60 (98.4%)
len, PI, and dara exposed/refractory (%)	61 (100%) / 60 (98.4%)
ISS Stage I/II/III/Unknown (%)	23.0% / 39.3% / 23.0% / 14.8%
High-risk cytogenetics [del17p13, t(4;14), t(14;16)] (%)	14/34 (41.2%)

These tables were independently created by GSK from original data first presented in Trudel S et al. ASH. 2022.

Consistent with inclusion criteria, 100% of patients were len refractory and PI exposed, 100% were TCE, and 98% were dara, len, and PI refractory (TCR)

*As of Oct 01, 2022. †4 fatal events occurred: 2 upper respiratory tract infections (1 COVID-19), 1 myelodysplastic syndrome (MDS), 1 not specified.
dara, daratumumab; ISS, International Staging System; len, lenalidomide; LOT, line of therapy; PI, proteasome inhibitor; pom/dex, pomalidomide/dexamethasone; TCE, triple-class exposed; TCR, triple-class refractory.

Trudel S et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 10-13, 2022; New Orleans, LA. Poster 3248.

The combination of belantamab mafodotin + pom/dex resulted in deep and durable responses in high unmet need TCE patients

- 55 patients were evaluable for response with median follow-up of 10.2 (0–30.5) months
- Across all dosing cohorts, the ORR(≥PR)/VGPR rates were 85%/56% for TCE patients
- The ORR/VGPR for patients treated at the RP2D (2.5 mg/kg Q8W) (n=33) was 82%/55%

- The **PFS** and **OS** for patients treated at the RP2D was 21.2 months and NYR, respectively
- **Median follow-up** was 10.2 months (0–30.5)

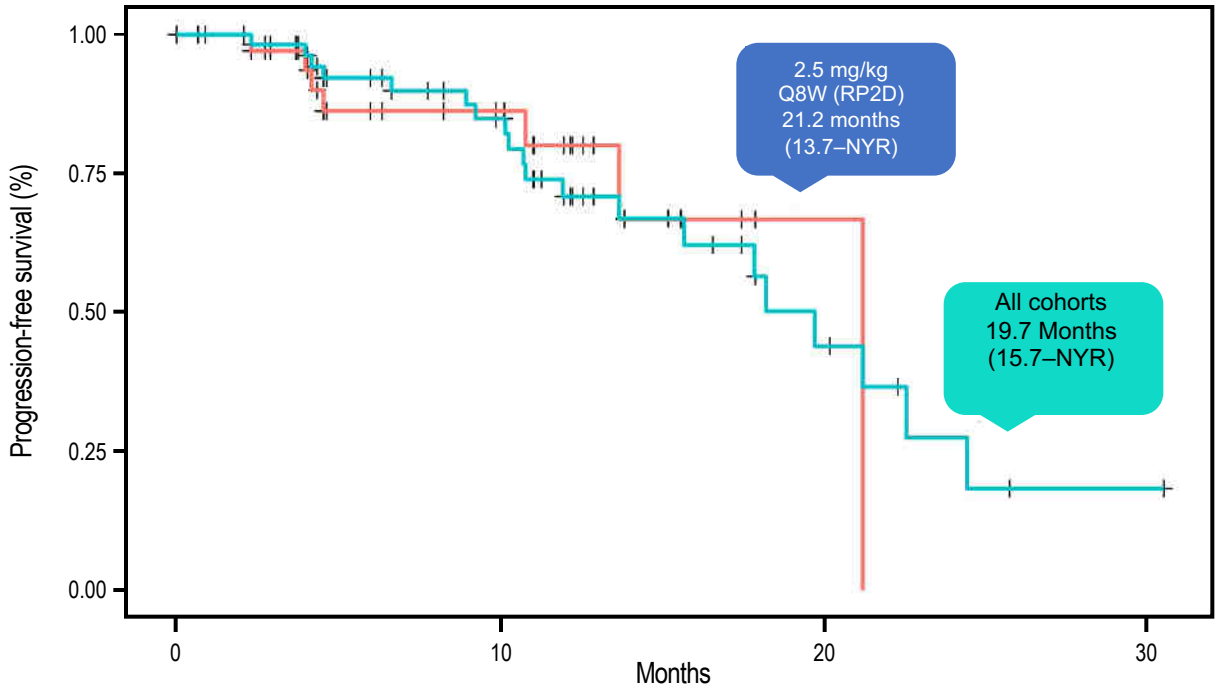
Efficacy Outcomes	Belantamab mafodotin 1.92 mg/kg Q4W N=6	Belantamab mafodotin 2.5 mg/kg Q4W N=6	Belantamab mafodotin 2.5 mg/kg Q8W N=38	Belantamab mafodotin 2.5 mg/kg Q12W N=11
ORR	4/6 (66.7%)	6/6 (100%)	27/33 (82%)	10/10 (100%)
sCR/CR	1/6 (16.7%)	1/6 (16.7%)	4/33 (12.1%)	3/10 (30%)
VGPR	2/6 (33.3%)	3/6 (50%)	14/33 (42.4%)	3/10 (30%)
PR	1/6 (16.7%)	2/6 (33.3%)	9/33 (27.3%)	4/10 (40%)
mPFS (95% CI), months	16.8 (10.2–NYR)	24.4 (11.9–NYR)	21.2 (13.67–NYR)	22.5 (10.2–NYR)
mOS (95% CI), months	21.4 (15.7–NYR)	NYR (24.4–NYR)	NYR (NYR–NYR)	22.5 (NYR–NYR)
Median follow-up, months	16.8 (9.2–21.4)	18.6 (6.6–30.5)	6.2 (0–21.2)	11.3 (0.9–22.5)

CR, complete response; mOS, median overall survival; mPFS, median progression-free survival; NYR, not yet reached; ORR, overall response rate; PR, partial response; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; RP2D, recommended phase 2 dose; sCR, stringent complete response; TCE, triple-class exposed; VGPR, very good partial response.

Trudel S et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 10-13, 2022; New Orleans, LA. Poster 3248.

PFS for TCE patients compares favorably when compared to historical data from the LocoMMotion study and to anti-CD38 antibody/pom/dex regimens

PFS for all cohorts and for 2.5 mg/kg Q8W (RP2D) cohort[1]



LocoMMotion is a prospective study of real-life SOC in TCE NDMM[2]

- Patients (N=248) were treated with median 4.0 (range, 1–20) cycles of SOC therapy
- Primary endpoint was ORR
- Secondary clinical assessments included ScR, CR, VGPR, DOR, PFS and OS

A PFS of 4.6 months was reported in the LocoMMotion study[2*]

mPFS of 11.5 - 12.4 months has been reported in anti-CD38 antibody/pom/dex regimens in anti-CD38 naïve patients at first or later relapse[3]

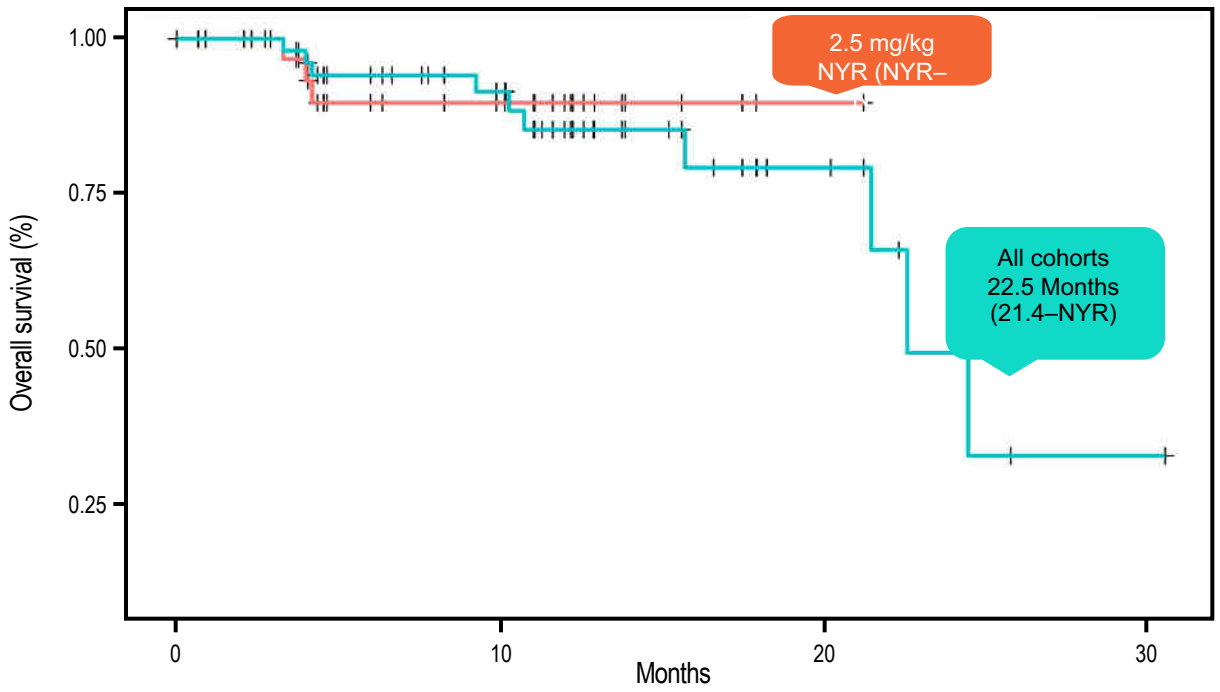
*Median follow-up was 11.01 months (range, 0.1–19.2) with a data cut-off date of May 21, 2021.

CR, complete response; DOR, duration of response; NDMM, newly diagnosed multiple myeloma; mPFS, median progression-free survival; NYR, not yet reached; OS, overall survival; PFS, progression-free survival; Q8W, every 8 weeks; RP2D, recommended phase 2 dose; sCR, stringent complete response; SOC, standard of care; TCE, triple-class exposed; VGPR, very good partial response.

1. Trudel S et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 10-13, 2022; New Orleans, LA. Poster 3248. **2**. Mateos MV et al. *Leukemia*. 2022. **3.** Dimopoulos M, et al. *Lancet Oncol*. 2021.

OS for TCE patients from all cohorts compares favorably to historical data from the LocoMMotion study*

OS for all cohorts and for 2.5 mg/kg Q8W (RP2D) cohort[1]



An OS of 12.4 months was reported in the LocoMMotion study[2]

*Data from different trials cannot be directly compared.

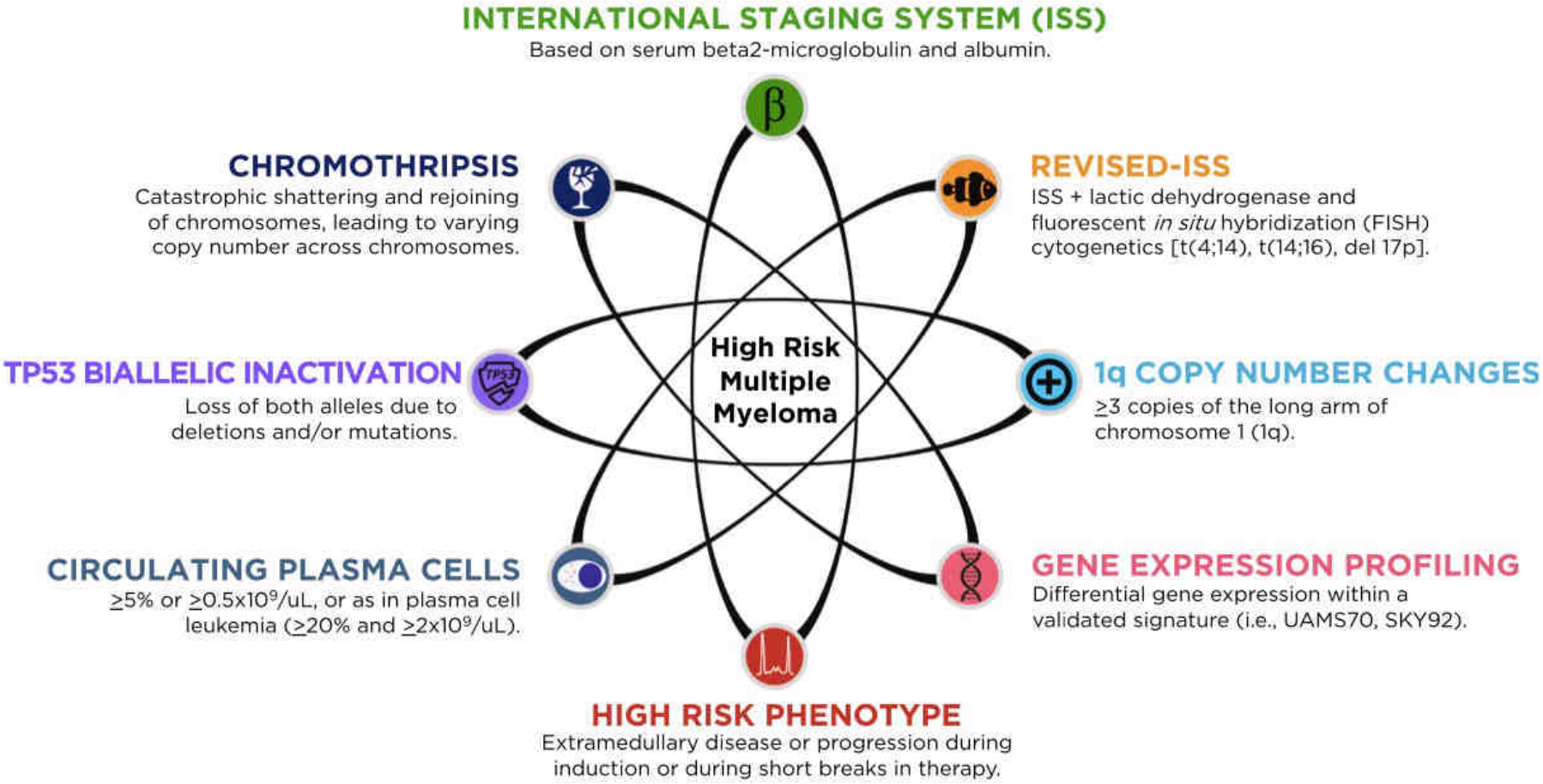
NYR, not yet reached; OS, overall survival; Q8W, every 8 weeks; RP2D, recommended phase 2 dose; TCE, triple-class exposed; VGPR, very good partial response.

1. Trudel S et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 10-13, 2022; New Orleans, LA. Poster 3248. **2**. Mateos MV et al. Leukemia. 2022.

ADC and «customization» of therapy

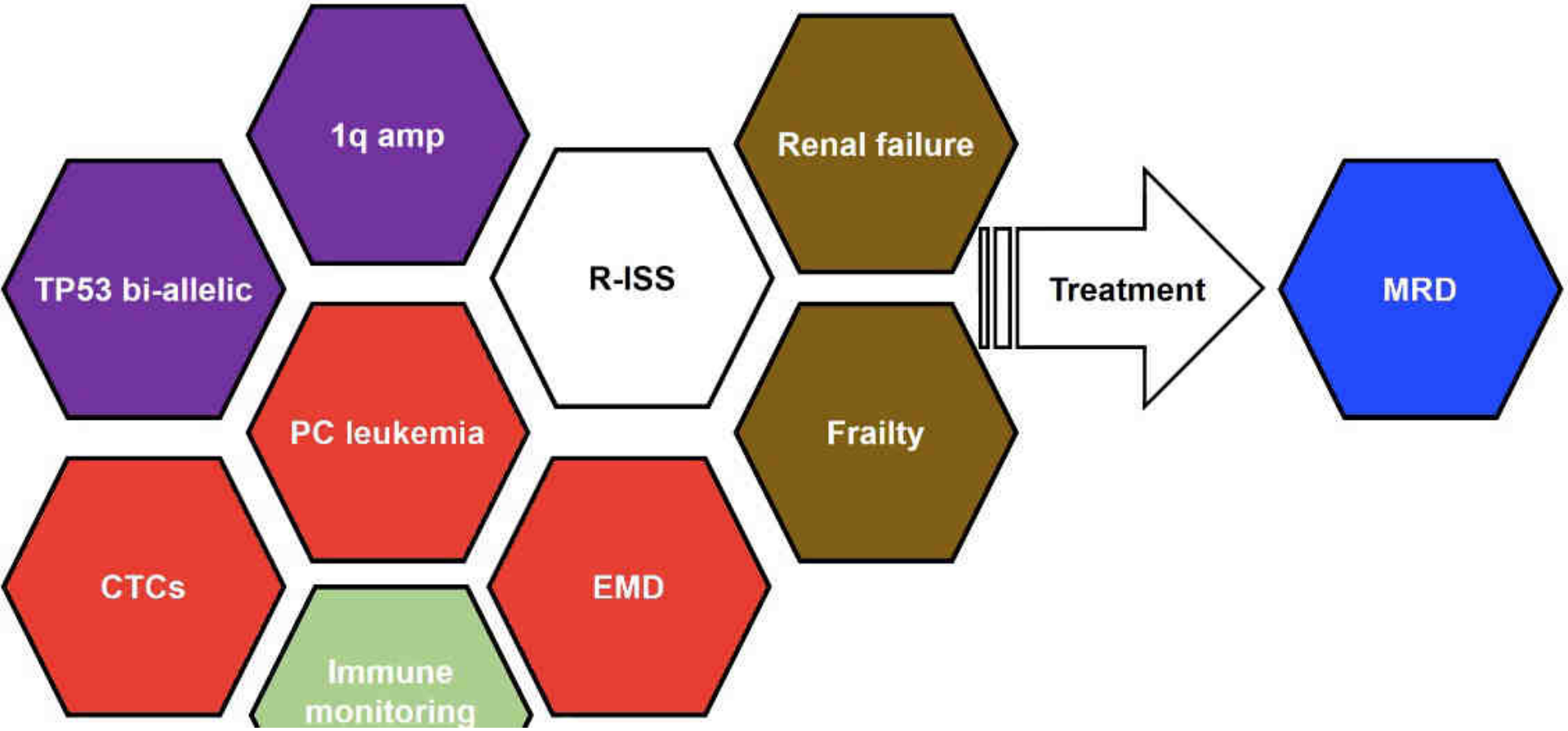
2. High-risk status

The Many Facets of High Risk Multiple Myeloma

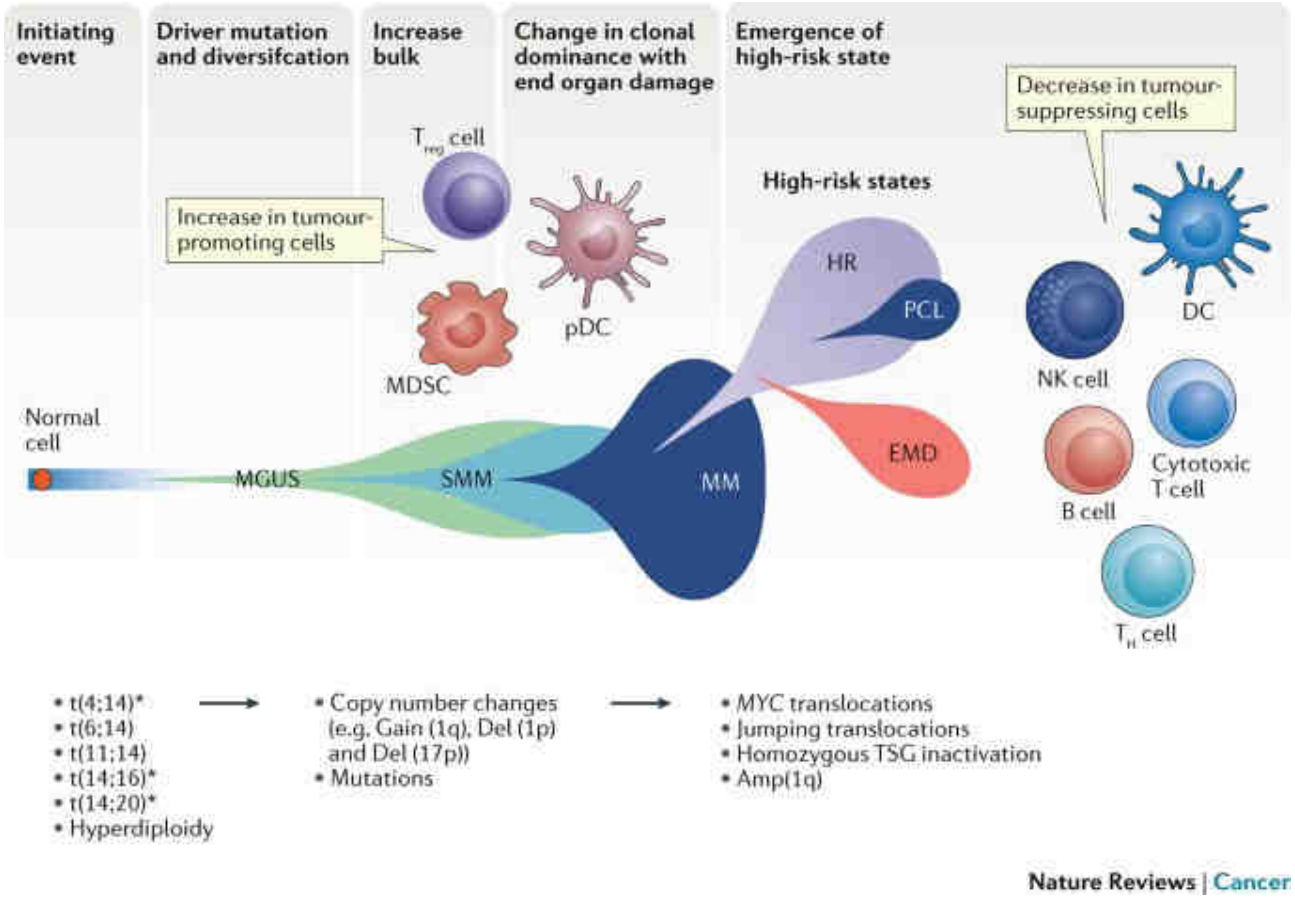


Derman B.A. et al Blood Reviews 51 (2022) 100887

Comprehensive patient characterization for precision medicine

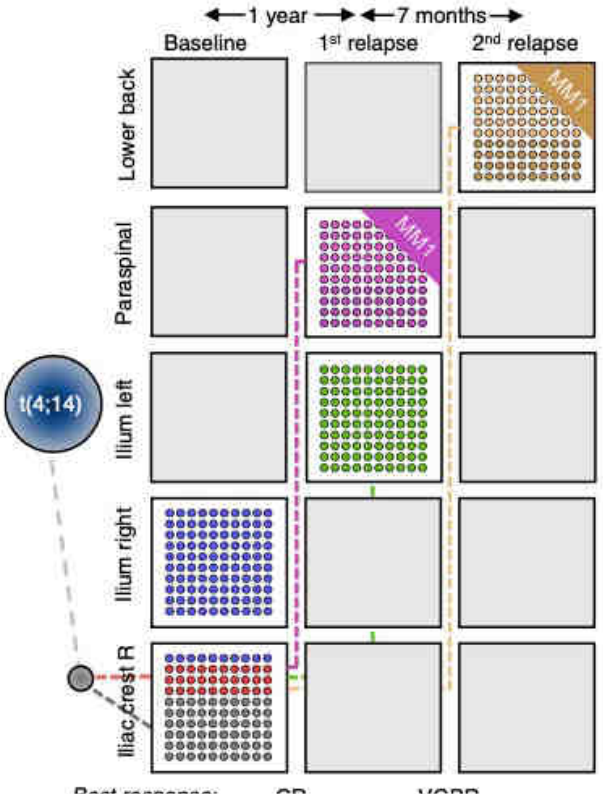


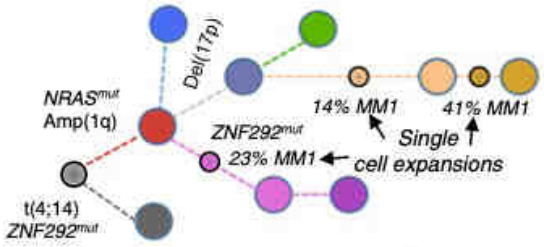
Disease evolution at relapse

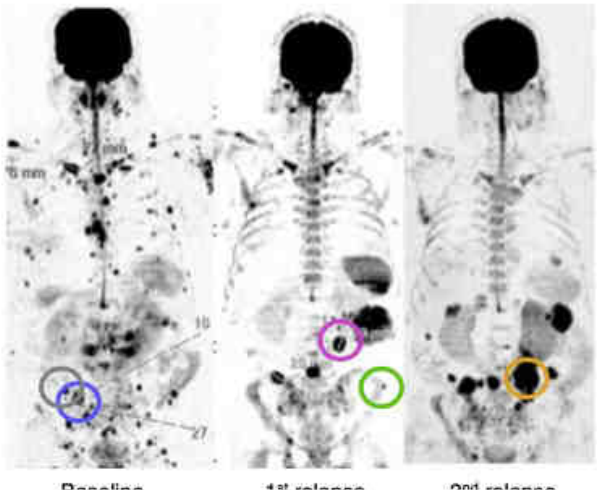


Nature Reviews | Cancer

Alternating spatial clonal dominance pattern







nature communications

Article

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The spatio-temporal evolution of multiple myeloma from baseline to relapse-refractory states

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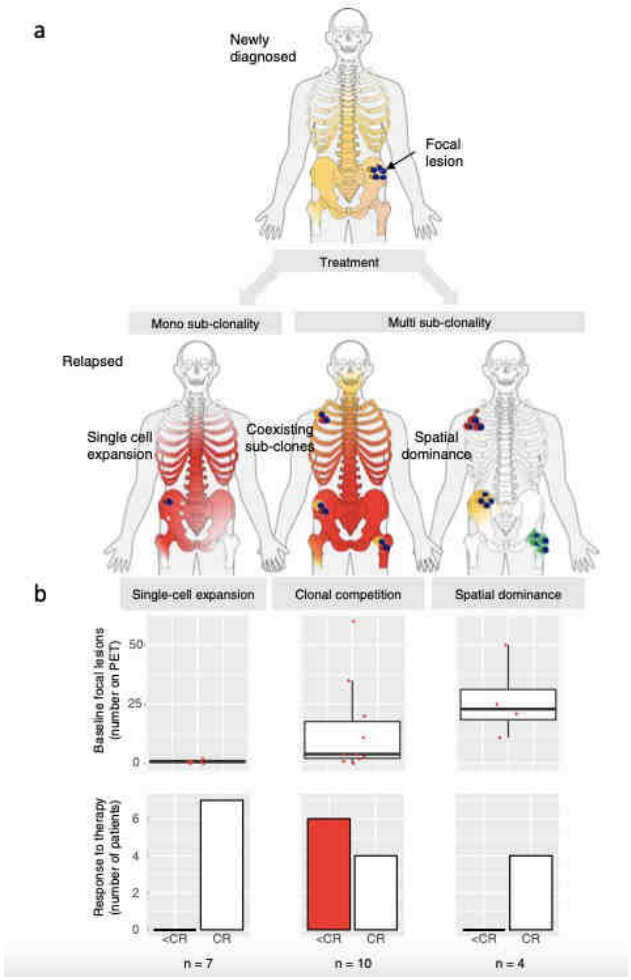
Leo Rasche[1,2,3], Carolina Schinke[1], Francesco Maura[4], Michael A. Bauer[1], Cody Ashby[1], Shayu Deelpande[1], Alexandra M. Poos[5], Maurizio Zangari[1], Shanmilan Thanendrarajan[1], Faith E. Davies[6], Brian A. Walker[6,7], Bart Barlogie[1], Ola Landgren[4], Gareth J. Morgan[4], Frits van Rhee[1] & Niels Weinhold[1,8]



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Article

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The spatio-temporal evolution of multiple myeloma from baseline to relapse-refractory states

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Leo Rasche[1,2,3], Caroline Schinke[1], Francesco Maura[2], Michael A. Bauer[1], Cody Ashby[1], Shayu Deshpande[1], Alexandra M. Poos[3], Maurizio Zangari[1], Shammilan Thanendrarajan[1], Faith E. Davies[1], Brian A. Walker[1], Bart Barlogie[1], Ola Landgren[1], Gareth J. Morgan[1], Frits van Rhee[1] & Niels Weinhold[1]

Evolutionary patterns and association with clinical feature: in a the three evolutionary patterns, which we observed in this study, are illustrated. These include (1) expansion and sweep driven by single tumor cells, (2) coexisting expanding subclones, and (3) site-unique expansions of distinct subclones, with the main difference between the second and the third pattern being the anatomical location of subclones. In b, boxplots are shown for the association between these patterns and (1) the number of PET-positive focal lesions at baseline (upper panel) and (2) the response to first-line therapy (lower panel), respectively. The boxplots show the median and the interquartile range, while the upper and lower whiskers show the highest and lowest values (excluding outliers), respectively. CR complete remission

Summary of the spatial-temporal evolution of Multiple Myeloma

nature communications

Article

The spatio-temporal evolution of multiple myeloma from baseline to relapse-refractory states

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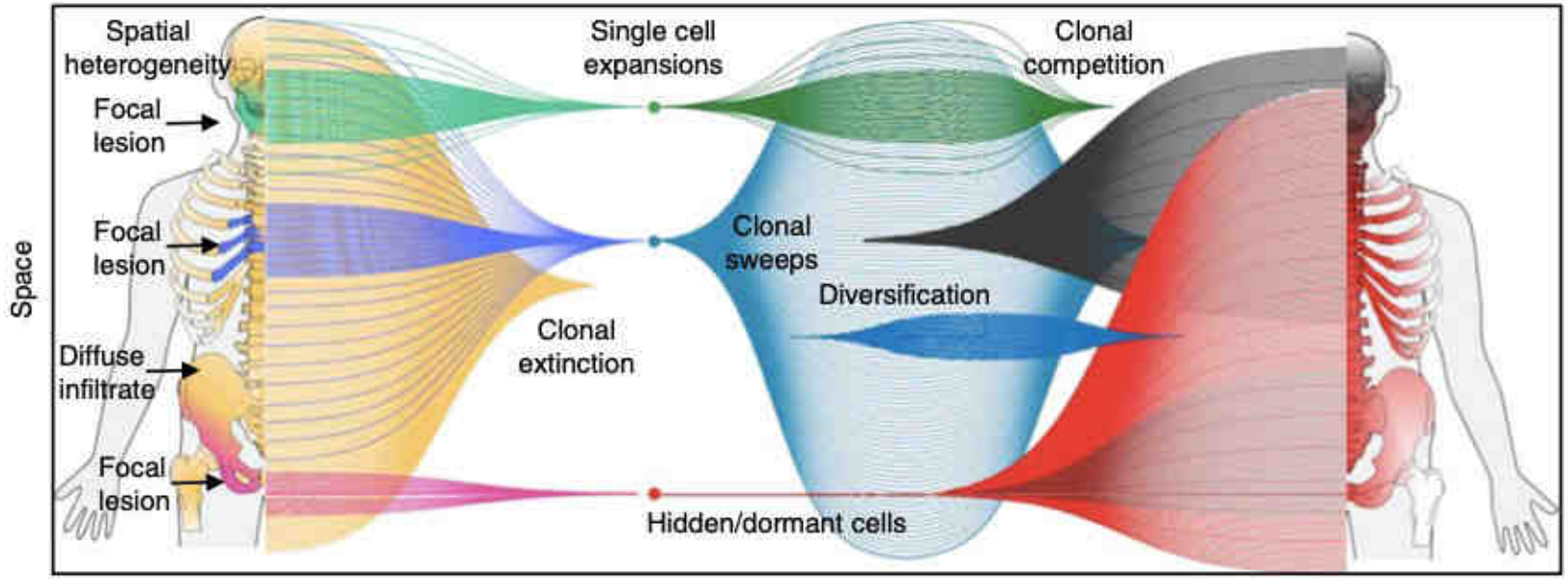


DREAMM-2 : belantamab mafodotin monotherapy showed deep and durable activity with mangeable safety in a broad patient population

Belantamab Mafodotin 2.5mg/kg Q3W (N=97)			
	HR-cytogenetic (N=41)†	Mild renal impairment (N=48)¶	Moderate renal impairment (N=24)#
Patient Characteristics			
Median age, years (range)	67.0 (42–85)	66.0 (40–85)	68.0 (45–85)
Median Prior lines therapy(range)	6 (3–11)	7 (3–12)	7 (3–21)
Triple-refractory, n (%)	3 (1–17)	3 (1–14)	3 (1–15)
Efficacy Outcomes			
ORR, n (%)††	12 (29)	16 (33)	8 (33)
(97.5%/95% CI)‡‡	(16.1–45.5)	(20.4–48.4)	(15.6–55.3)
sCR	1 (2)	0 (0)	1 (4)
CR	3 (7)	2 (4)	3 (13)
VGPR	5 (12)	6 (13)	4 (17)
Median DoR (95% CI)	10.3 (1.4-13.1)	12.5 (2.2-NR)	13.1 (4.2-NR)
Median PFS (95% CI)	2.1 (0.8-3.7)	2.2 (2.0-3.6)	3.7 (1.0-12.5)
Median estimated OS (95% CI)	13.1 (8.2-NR)	13.7 (11.4-NR)	NR (5.1-NR)

Safety Data		
Event	Any Grade	Grade ≥3
Keratopathy, n (%)	68 (72)	44 (46)
Thrombocytopenia, n (%)	36 (38)	21 (22)
Anemia , n (%)	26 (27)	20 (21)

Lonial Cancer 2021, follow up 13 months

DREAMM-2: Single-agent belantamab mafodotin (GSK2857916) in patients with relapsed/refractory multiple myeloma (RRMM) and high-risk (HR) cytogenetics.

Cohen A.D. et al.

2020 ASCO Annual Meeting -Abstract 8541

	2.5 mg/kg (n = 97)[a]	3.4 mg/kg (n = 99)[b]
ORR (≥PR), % (95% CI)	27 (14.2–42.9)	40 (25.8–54.7)
Median DoR (95% CI), months	NR (1.4–NR)	6.2 (4.8–NR)
Probability of DoR at 9 months, (95% CI[c]), %	52 (20–77)	47 (23–68)
Median PFS (95% CI), months	2.1 (0.8–3.7)	5.8 (1.5–6.9)
Probability of PFS ≥6 months, (95% CI[c]), %	30 (16–45)	46 (31–60)
Median OS (95% CI), months	9.4 (4.3–13.1)	13.8 (NE–NE)
Probability of OS at 12 months, (95% CI[c]), %	45 (27–61)	68 (25–80)

Efficacy outcomes in patients with HR-cytogenetics

[a]n = 41 on study, n = 8 on study treatment; [b]n = 48 on study, n = 11 on study treatment; [c]95% CI estimate. NE, not evaluable; NR, not reached.

DREAMM-2 and RWE patient characteristics

	DREAMM-2 2.5mg/kg cohort (Lonial)[1,2]	GSK expanded access (Shragai)[3]	Mayo Clinic efficacy and safety (Vaxman)[4]	Mayo Clinic 2022 (Abeykoon)[5]
N	97	67	36	38
Patient demographics				
Female, n (%)	46 (47)	29 (43)	13 (36)	13 (34)
Age, years (range)	65 (60-70)*	70 (36-88)*	61 (37-83)‡	67 (49-90)*
High-risk cytogenetics, n (%)	41 (42)	18 (47)	14 (41)	32 (89)
With extramedullary disease, n (%)	22 (23)	7 (10)	5 (14)	N/A
Prior treatment				
Median prior LOT (range)	7 (3-21)	5 (4-7)†	8 (7-11)†	8 (2-15)
% of patients previously treated with an immunomodulatory agent, a PI, and an anti-CD38 mAb, n (%)	97 (100)	44 (67)	36 (100)	N/A
% of patients with prior ASCT, n (%)	73 (75)	34 (51)	27 (75)	N/A
% of patients previously treated with an anti-BCMA targeted agent, n (%)	0	N/A	N/A	4 (11)
CAR-T therapy, n (%)	0	N/A	7 (19)	4 (11)

***Median age.[1,3,5] †Interquartile range.[3,4] ‡Mean age.[4]**
ASCT, autologous stem cell transplant; BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T cell; CD, cluster of differentiation; LOT, lines of therapy; mAb, monoclonal antibody; N/A, not available; PI, proteasome inhibitor;
RWE, real-world evidence.

1. Lonial S et al. *Cancer.* 2021;127(22):4198-4212. 2. Lonial S et al. *Lancet Oncol.* 2020;21:207-221. 3. Shragai T et al. Presented at: European Hematology Association Congress; June 9-17, 2021. Poster 2853. Accessed August 4, 2021. library.ehaweb.org/eha/2021/eha2021-virtual-congress/324746/tamir.shragai.belantamab.mafodotin.treatment.for.patients.with.relapsed.html 4. Vaxman I et al. *Blood Cancer J.* 2021;11(12):196. doi:10.1038/s41408-021-00592-3
5. Abeykoon JP et al. *Br J Haematol*. 2022. doi:10.1111/bjh.18298

DREAMM-2 and RWE patient characteristics

	DREAMM-2 2.5mg/kg cohort (Lonial)[1,2]	MSKCC (Hultcrantz)[3]	University of Kansas Health System (Atieh)[4]	Spain compassionate use (Alegre)[5]	MD Anderson Cancer Center (Becnel)[6]	Dana-Farber Cancer Institute (Marzouk)[7]
N	97	50	28	33	39	40
Patient demographics						
Female, n (%)	46 (47)	25 (50)	8 (29)	18 (55)	13 (33)	17 (42)
Age, years (range)	65 (60-70)†	67 (37-87)	67 (42-85)†	70 (46-79)†	66 (39-89)†	66 (43-86)†
High-risk cytogenetics, n (%)	41 (42)	32 (74)	20 (71)	10 (30)	14 (38)§	13 (33)¶
With extramedullary disease, n (%)	22 (23)	N/A	13 (46)	N/A	14 (38)	10 (25)
Prior treatment						
Median prior LOT (range)	7 (3-21)	7 (3-14)	5 (3-15)	5 (3-8)	7 (3-16)	5 (2-14)
% of patients previously treated with an immunomodulatory agent, a PI, and an anti-CD38 mAb,* n (%)	97 (100)	50 (100)	28 (100)	≥29 (≥88)	37 (95)	36 (90)
% of patients with prior ASCT, n (%)	73 (75)	34 (68)‡	21 (75)	N/A	N/A	N/A
% of patients previously treated with an anti-BCMA targeted agent, n (%)	0	13 (26)	8 (29)	N/A	8 (21)‖	N/A
CAR-T therapy, n (%)	0	9 (18)	N/A	N/A	2 (5)	N/A

*All the patients in DREAMM-2 and the University of Kansas Health System study were also triple-class refractory.[1,3-7] †Median age.[1,4-7] ‡With high-dose melphalan; six patients had two prior ASCTs.[3] §High-risk FISH is defined as del 17p, t(4;14), and/or t(14;16). The high-risk status of two patients were not available.[6] ‖BCMA-refractory patients; prior BCMA therapy included antibody-drug conjugates (n=2), bispecifics (n=4), and CAR-Ts (n=2).[6] ¶The cytogenetic status of 9 (23%) patients was unknown.[7]

1. Lonial S et al. *Cancer*. 2021;127(22):4198-4212. 2. Lonial S et al. *Lancet Oncol*. 2020;21:207-221. 3. Hultcrantz M et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 11-14, 2021; Atlanta, GA. Poster 1644. 4. Atieh T et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 11-14, 2021; Atlanta, GA. Poster 1642. 5. Alegre A et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 11-14, 2021; Atlanta, GA. Poster 3775. 6. Becnel MR et al. Presented at: American Society of Clinical Oncology Annual Meeting; June 3-7, 2022; Chicago, IL. Poster 3060. 7. Marzouk O et al. Presented at: Hematology/Oncology Pharmacy Association Annual Conference; March 30-April 2, 2022; Boston, MA.
Please refer to slide notes for abbreviations.

Characteristic	Lyophilised belantamab mafodotin 3.4 mg/kg (*N* = 25)
Renal impairment per eGFR (mL/min/1.73 m^2)	
Normal (≥90)	6 (24)
Mild (≥60 to <90)	13 (52)
Moderate (≥30 to <60)	6 (24)
Time from initial diagnosis, median (range), years	5.37 (1.92–10.28)
ISS disease stage at screening	
Stage I	7 (28)
Stage II	8 (32)
Stage III	10 (40)
Cytogenetic abnormalities	
t(11;14)	3 (12)
Del 13	6 (24)
Other[a]	9 (36)
High-risk cytogenetics[b]	7 (28)
17p13del	5 (20)
t(4;14)	1 (4)
t(14;16)	1 (4)
1q21+	5 (20)
Extramedullary disease	6 (24)

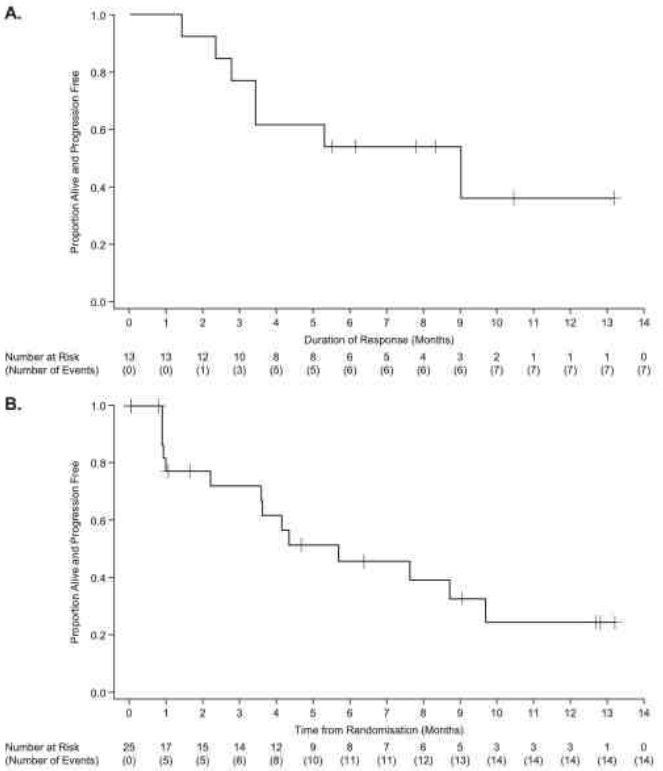
[b]High-risk cytogenetics defined as having any of the following cytogenetic features: *t*(4;14), *t*(14;16), 17p13del or 1q21+.

Richardson et al. *Blood Cancer Journal* (2020)10:106
https://doi.org/10.1038/s41408-020-00369-0

ARTICLE Open Access

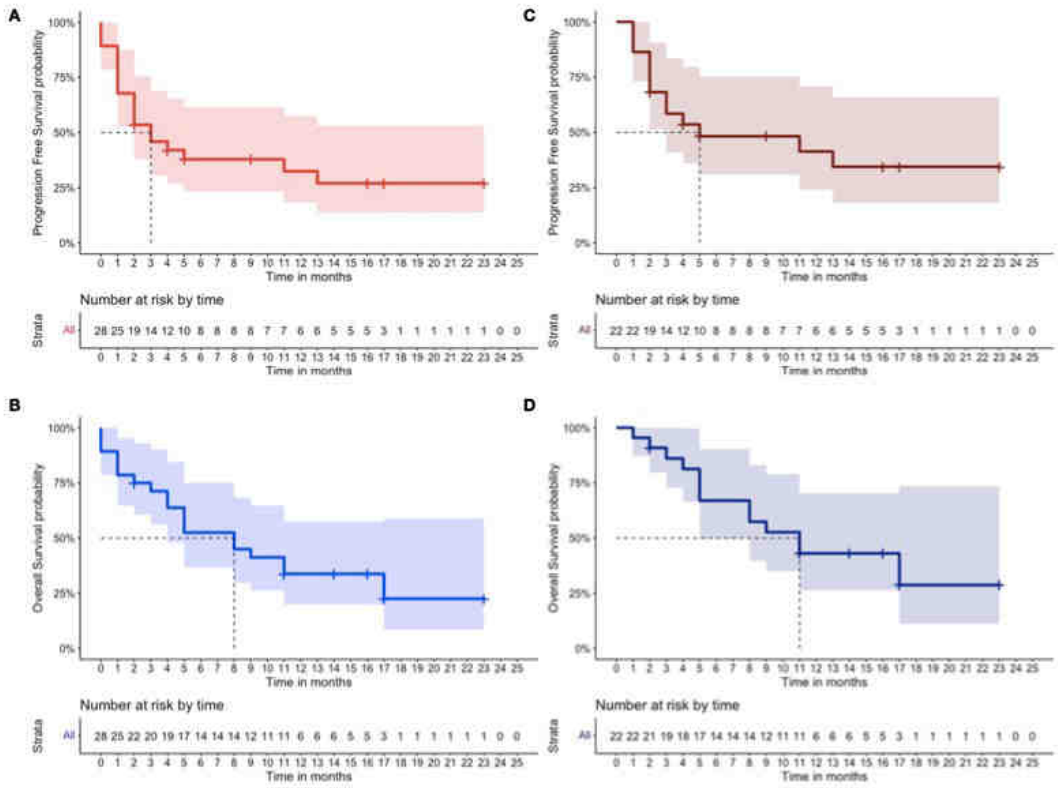
Single-agent belantamab mafodotin for relapsed/refractory multiple myeloma: analysis of the lyophilised presentation cohort from the pivotal DREAMM-2 study

Paul G. Richardson[1], Hans C. Lee[2], Al-Ola Abdallah[3], Adam D. Cohen[4], Prashant Kapoor[5], Peter M. Voorhees[6], Axel Hoos[7], Karrie Wang[7], January Baron[7], Trisha Piontek[7], Julie Byrne[7], Scott Richmond[8], Roxanne C. Jewell[9], Joanna Opalinska[7], Ira Gupta[7] and Sagar Lonial[10]



Duration of response (A) and progression-free survival (B) full analysis population. Responses were assessed by an independent review committee according to International Myeloma Working Group criteria[20].

Characteristics	Total cohort N = 28	Evaluable cohort* N = 22
Extramedullary disease	8 (28)	5 (23)
Median GFR, mL/min (range)	71 (8-125)	85 (8-125)
GFR ≥90 ml/min, n (%)	8 (29)	7 (32)
60 ≤GFR <90 ml/min, n (%)	8 (29)	8 (36)
30 ≤GFR <60 ml/min, n (%)	8 (29)	5 (23)
GFR <30 ml/min, n (%)	4 (13)	2 (9)



Efficacy and safety of belantamab-mafodotin in triple-refractory multiple myeloma patients: A multicentric real-life experience

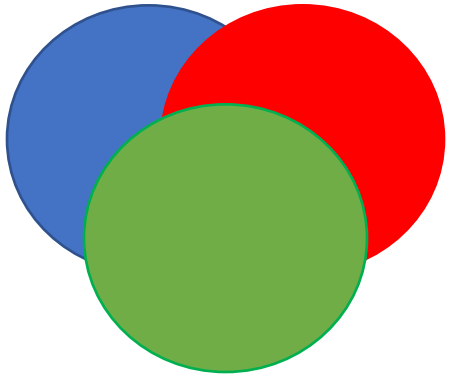
Rossella Iula[1†], Danilo De Novellis[2,3†], Fabio Trastulli[4], Roberta Della Pepa[1], Raffaele Fontana[2], Angela Carobene[2], Maria Di Perna[5], Alessandro D'Ambrosio[1], Martina Romano[2], Aldo Leone[3], Laura De Fazio[1], Alfonso Fiumarella[1], Giuseppe Gaeta[1], Violetta Marafioti[1], Serafina Barbato[1], Salvatore Palmieri[1], Stefano Rocco[4], Bianca Serio[5], Catello Califano[5], Fabrizio Pane[1], Felicetto Ferrara[4], Valentina Giudice[2,3*], Carmine Selleri[2,3] and Lucio Catalano[1]

ADC and «customization» of therapy

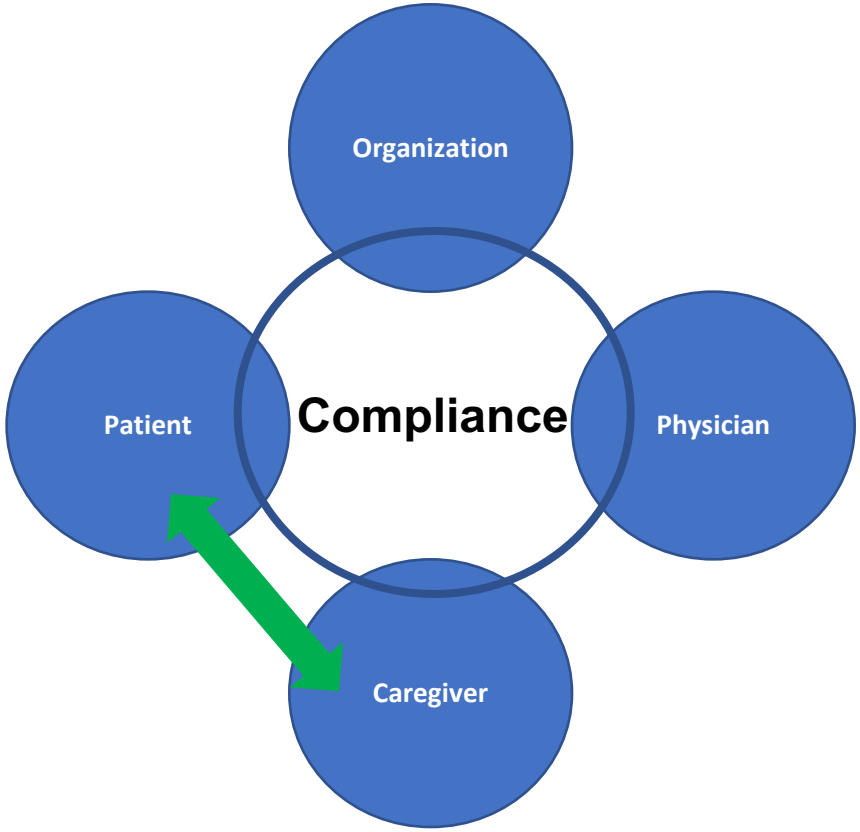
3. Manageability of administration

Dancing partners at the ball:

1. Compliance and adherence
2. Manageability
3. Safety



Compliance: different point of view



Compliance: Patient and caregiver point of view

All oral philosophy

PRO

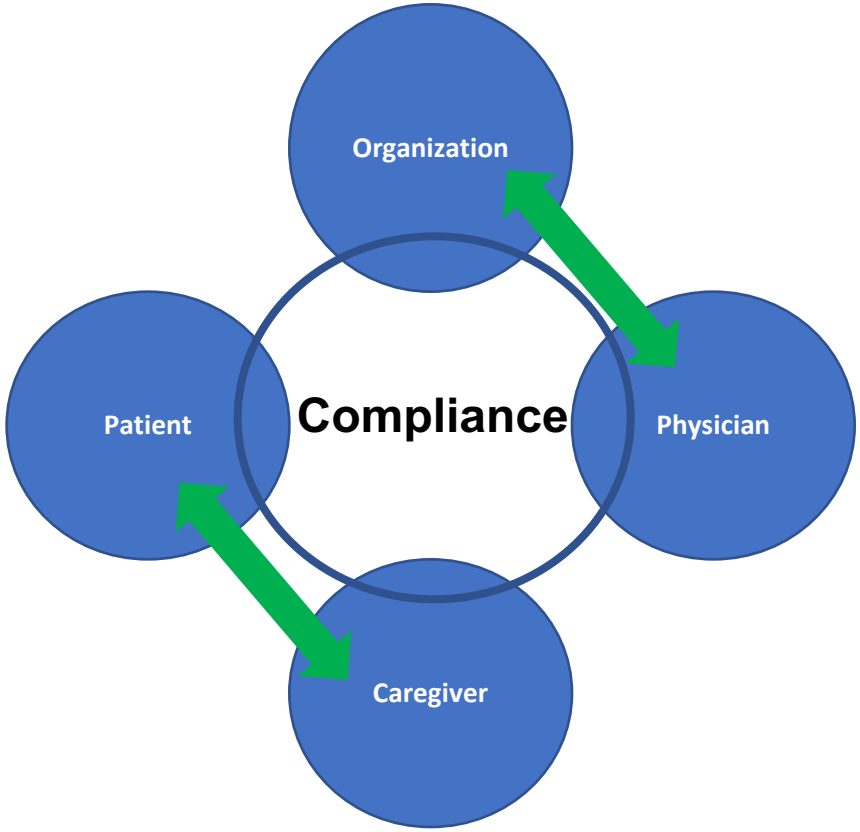
Treating cancer at home

CONTRA

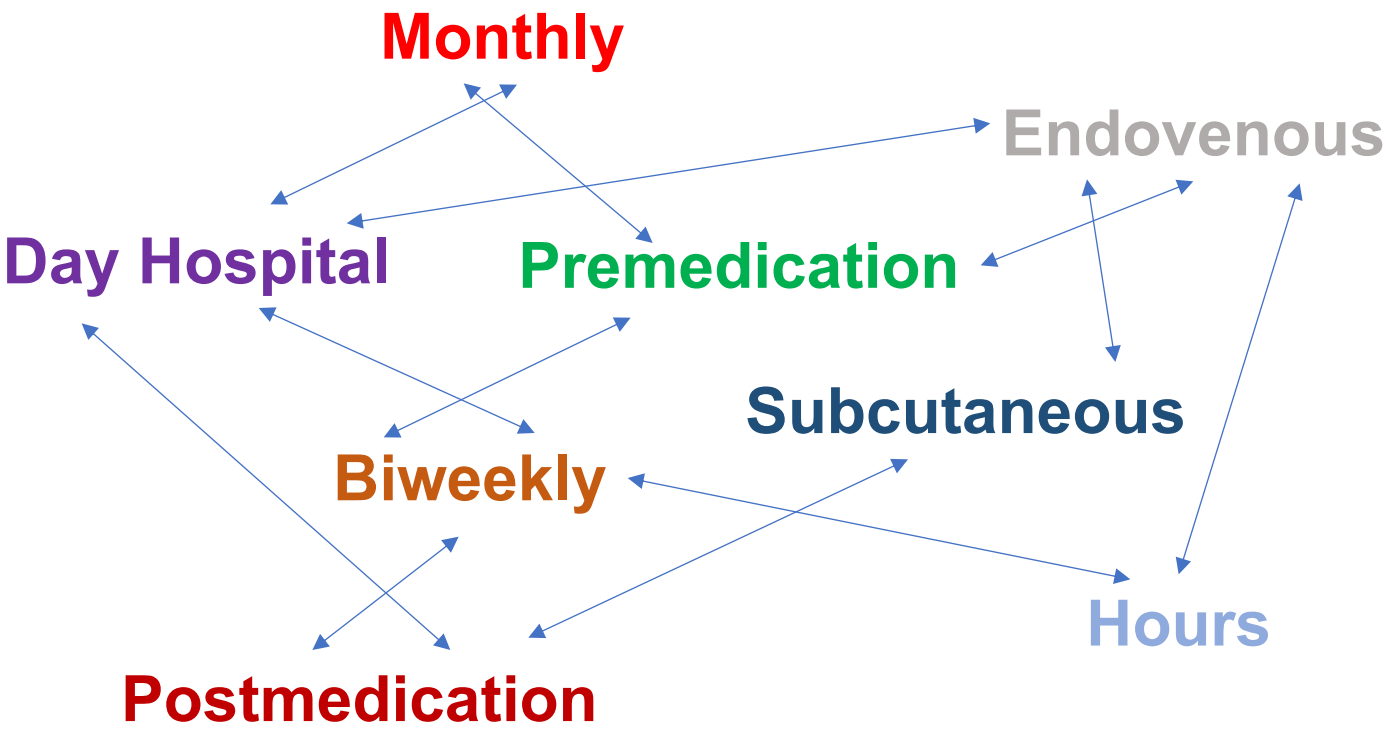
Shift in control and responsability from the healtcare provider to the patient

Treatment adherence
Poor adherence can make even the best treatments not affective

Compliance: different point of view



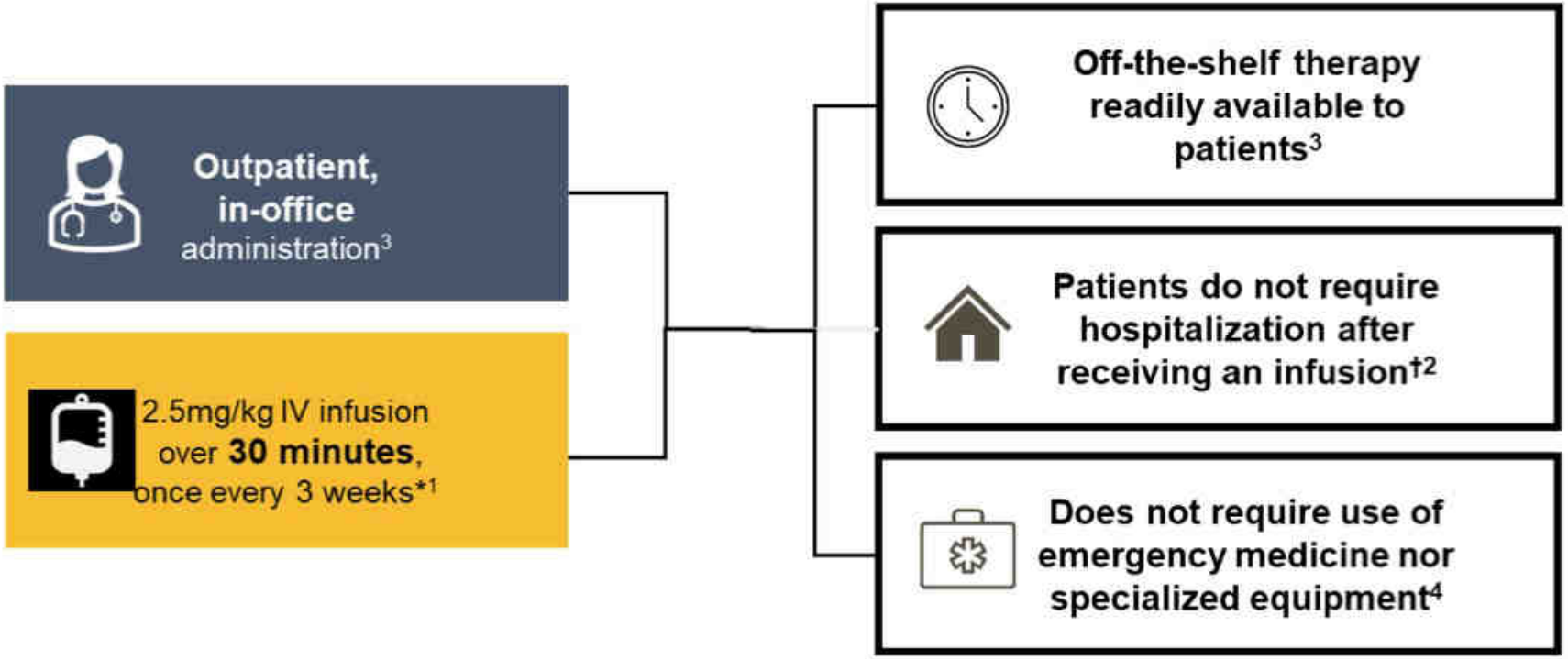
Compliance: Physician, Organization point of view



EFFECTIVENESS

TOLERABILITY
ADHERENCE
COMPLIANCE
SAFETY

Belantamab mafodotin is administrated through a 30-minute IV and does not require hospitalization[1,2]



1. BLENREP. Prescribing Information. GlaxoSmithKline; 2020. 2. Lonial S et al. OncLive. February 1, 2021. Accessed December 2, 2021. www.onclive.com/view/influencing-factors-to-initially-targeting-bcma-in-mm
3. Becnel MR, Lee HC. *Ther Adv Hematol*. 2020;11. doi:10.1177/2040620720981344. Accelerating our oncology pipeline: belantamab mafodotin (GSK'916) DREAMM-2 data. GSK. December 17, 2019. Accessed January 31. www.gsk.com/media/5771/gsk-dreamm2-17dec19_transcript.pdf 20215. Nooka A et al. Poster presented at: American Society of Hematology Annual Meeting and Exposition; December 5-8, 2020. Poster 3221.
6. Vaxman I et al. *Blood Cancer J*. 2021;11(12):196. doi:10.1038/s41408-021-00592-3
Please see slide notes for abbreviations and footnotes.

ADC and «customization» of therapy

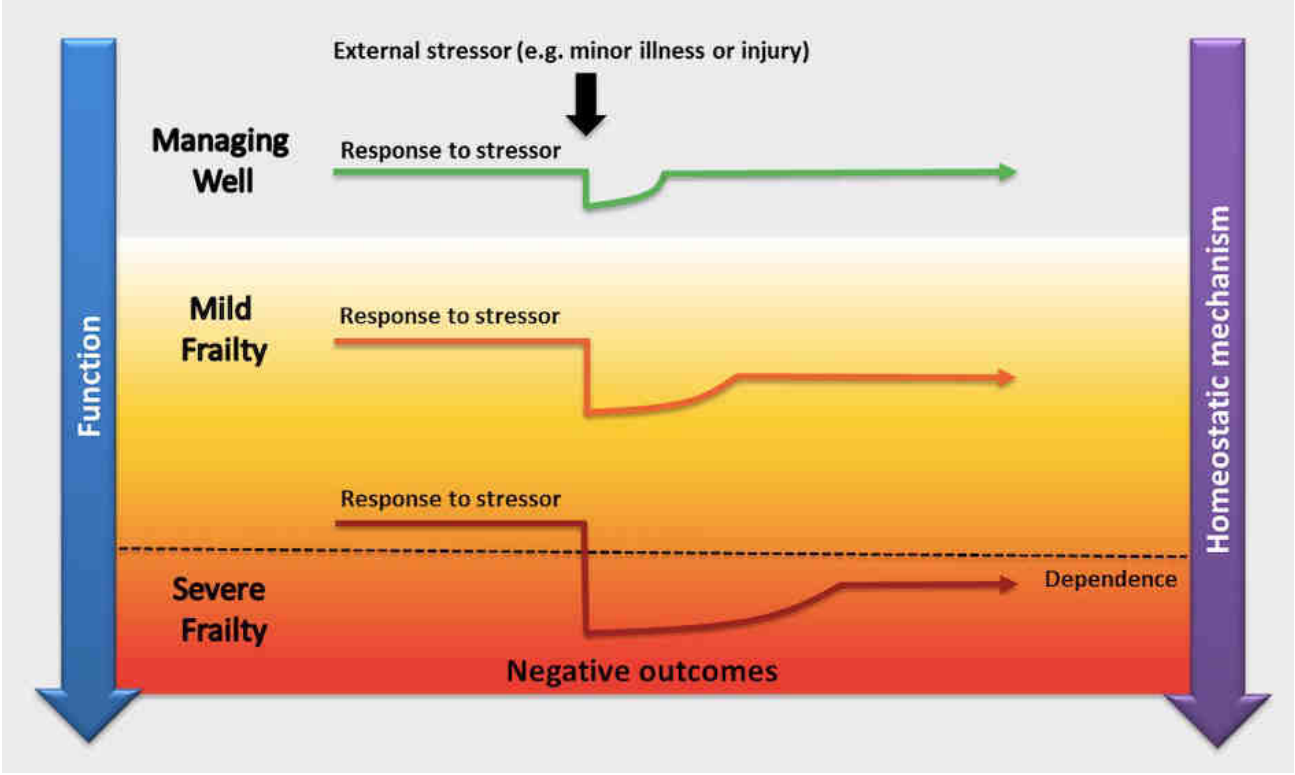
4. Safety profile and quality of life

Frailty ≠ Normal aging

- **Progressive decline in all physiological systems with age**

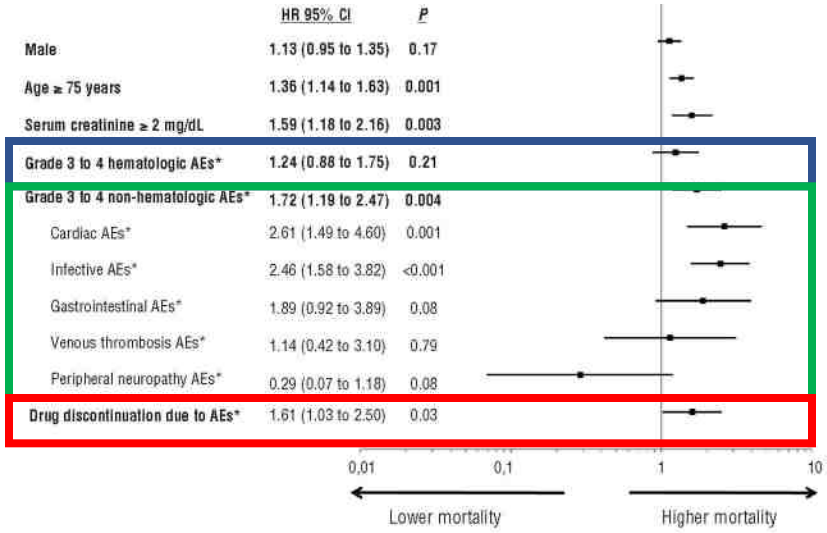
- **After ~age 75 our systems are less able to compensate for insult**

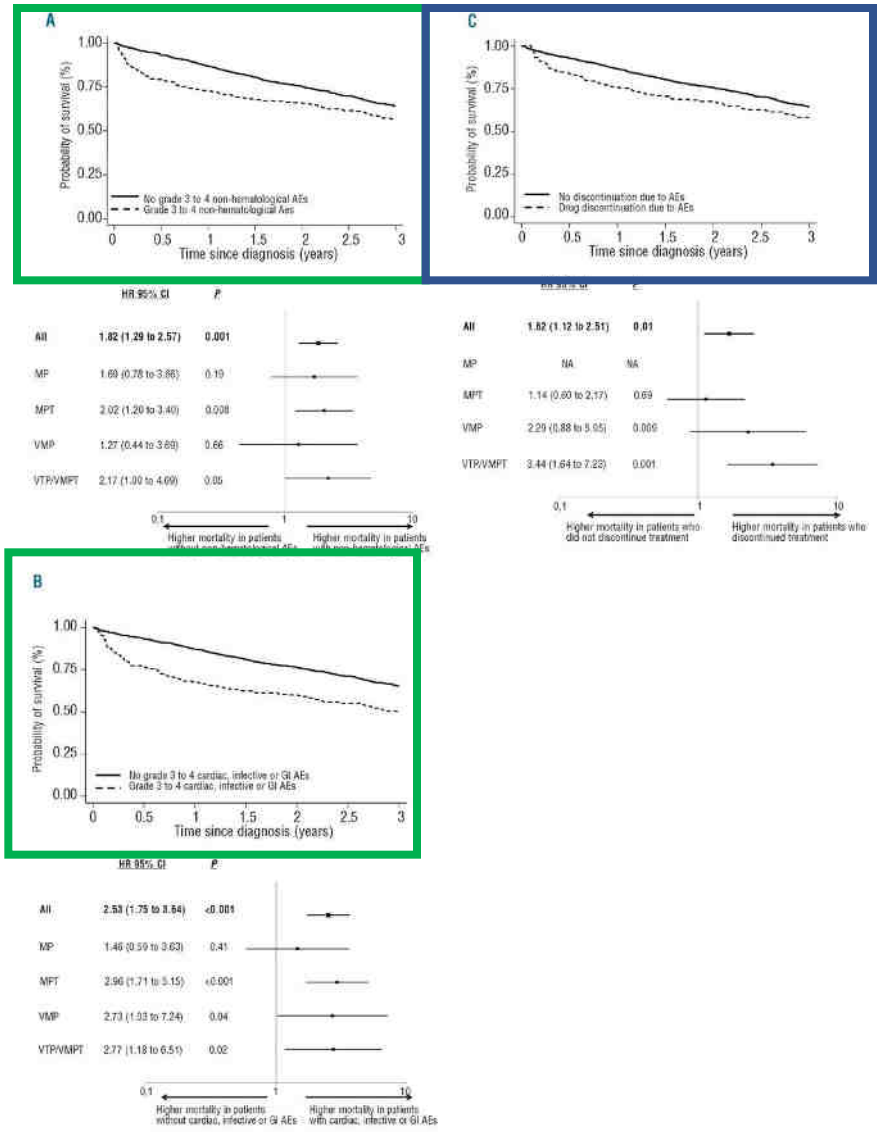
- **Frailty - minor insult may lead to disproportionate changes in health status, typically a fall or delirium**



Age and organ damage correlate with poor survival in myeloma patients: meta-analysis of 1435 individual patient data from 4 randomized trials

Sara Bringhen,[1] Maria Victoria Mateos,[2] Sonja Zweegman,[3] Alessandra Larocca,[1] Antonietta Pia Falcone,[4] Albert Oriol,[5] Davide Rossi,[6] Maide Cavalli,[7] Pierre Wijermans,[8] Roberto Ria,[9] Massimo Offidani,[10] Juan Jose Lahuerta,[11] Anna Marina Liberati,[12] Roberto Mina,[1] Vincenzo Callea,[13] Martijn Schaafsma,[14] Chiara Cerrato,[1] Roberto Marasca,[15] Luca Franceschini,[16] Andrea Evangelista,[17] Ana-Isabel Teruel,[18] Bronno van der Holt,[19] Vittorio Montefusco,[20] Giovannino Ciccone,[17] Mario Boccadoro,[1] Jesus San Miguel,[2] Pieter Sonneveld,[19] and Antonio Palumbo[1]





Leukemia (2018) 32:1542–1560
https://doi.org/10.1038/s41375-018-0040-1

REVIEW ARTICLE

Multiple myeloma, gammopathies

Prevention and management of adverse events of novel agents in multiple myeloma: a consensus of the European Myeloma Network

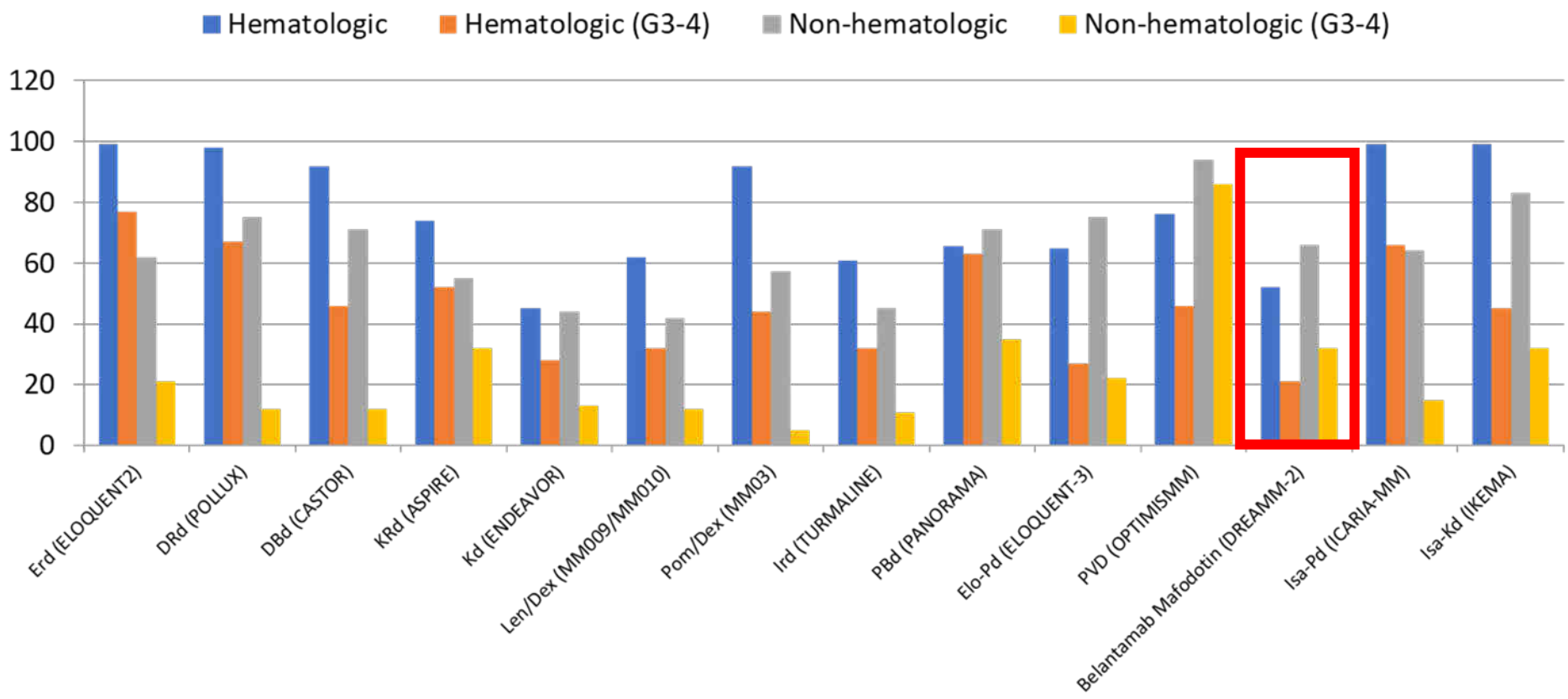
Heinz Ludwig[1] · Michel Delforge[2] · Thierry Facon[3] · Hermann Einsele[4] · Francesca Gay[5] · Philippe Moreau[6] · Hervé Avet-Loiseau[7] · Mario Boccadoro[8] · Roman Hajek[9] · Mohamad Mohty[10] · Michele Cavo[11] · Meletios A Dimopoulos[12] · Jesús F San-Miguel[13] · Evangelos Terpos[12] · Sonja Zweegman[14] · Laurent Garderet[10] · Maria-Victoria Mateos[15] · Gordon Cook[16] · Xavier Leleu[17] · Hartmut Goldschmidt[18] · Graham Jackson[19] · Martin Kaiser[20] · Katja Weisel[21] · Niels W. C. J. van de Donk[14] · Anders Waage[22] · Meral Beksac[23] · Ulf H. Mellqvist[24] · Monika Engelhardt[25] · Jo Caers[26] · Christoph Driessen[27] · Joan Bladé[28] · Pieter Sonneveld[29]

Received: 10 October 2017 / Revised: 23 November 2017 / Accepted: 30 November 2017 / Published online: 2 May 2018

Special warnings and precautions with regards to toxicities of novel agents as per USPI/EU SmPC

		Teratogenicity	Peripheral neuropathy	Cardiac toxicity	Seizures	Thromboembolic events/DVT	Thrombocytopenia	Hemorrhage	Neutropenia	Anemia	Amenorrhea	Infections	Viral reactivation	Somnolence/drowsiness	Dizziness	Hypotension	Hypertension	Nausea	Vomiting	Diarrhea	Constipation	SPM	Syncope/bradycardia	Infusion reaction	Severe skin reactions	Allergic/hypersensitivity reactions	Hepatic toxicity	Renal toxicity	Edema	Tumor lysis syndrome	Thyroid disorders	Cataract	Pulmonary disorders	Dyspnoea	PML	PRES
IMiDs	Thalidomide	•	•	•	•	•	•		•		•	•	•[a]	•	•							•	•		•	•			•	•						
	Lenalidomide	•	•[b]	•		•	•		•			•										•			•	•			•		•					
	Pomalidomide	•	•[c]	•		•	•		•	•		•			•							•				•	•		•			•				
PIs	Bortezomib	•	•	•	•		•		•	•			•[d]			•		•	•	•	•						•			•		•		•	•	•
	Carfilzomib	•		•		•[e]	•	•									•							•			•	•		•			•	•		•
	Ixazomib	•	•				•											•	•	•	•				•		•		•							
HDACi	Panobinostat	•		•			•	•	•	•		•						•	•	•	•						•				•					
mABs	Elotuzumab											•										•		•			•									
	Daratumumab						•		•				•											•												

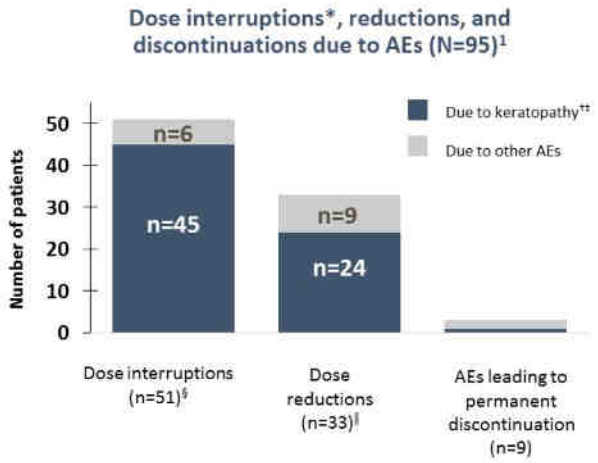
Toxicity in RRMM

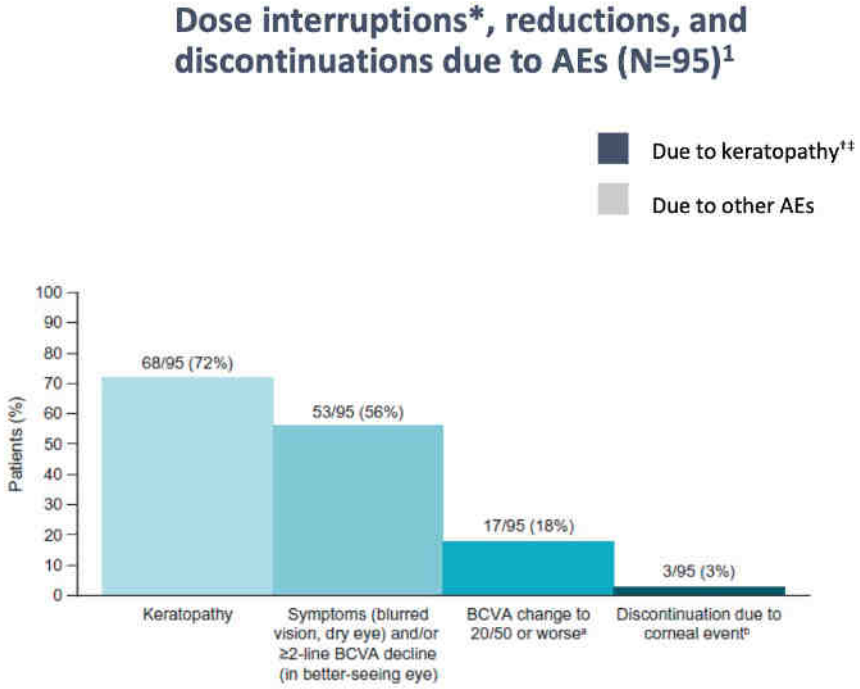


DREAMM-2: safety

AE*	Any grade, n (%)[2]	Grade ≥3, n (%)[3]
Any	93 (98)	80 (84)
Keratopathy[†‡]	67 (71)	44 (46)
Thrombocytopenia[§]	23 (24)	21 (22)
Anemia	26 (27)	20 (21)

Median time to onset (gr≥2): 37 days (19-147)
Recovered from first occurrence: 77%
Median time to resolution: 86.5 days (8-358)





Lonial S et al. Lancet Oncol. 2020; Lonial S et al. Cancer 2021

DREAMM-2 results: Safety from 13-month follow-up
Belantamab Mafodotin was generally tolerated with supportive care and dose modification

Event	Belamaf 2.5 mg/kg, N = 95: No. of Patients (%)	
	Any Grade	Grade ≥3
Any event	93 (98)	80 (84)
Eye examination finding		
Keratopathy[b]	68 (72)	44 (46)
Change in BCVA	51 (54)	29 (31)
Thrombocytopenia[c]	36 (38)	21 (22)
Anemia	26 (27)	20 (21)
Blurred vision[d]	24 (25)	4 (4)
Nausea	24 (25)	0 (0)
Pyrexia[e]	22 (23)	4 (4)
Aspartate aminotransferase increased	20 (21)	2 (2)
Infusion-related reaction[f]	20 (21)	3 (3)
Fatigue	15 (16)	2 (2)
Neutropenia[g]	14 (15)	10 (11)
Dry eye[h]	14 (15)	1 (1)
Hypercalcemia	14 (15)	7 (7)
Lymphocyte count decreased	13 (14)	12 (13)
Pneumonia	9 (9)	6 (6)

80 (84%) of patients in the safety population experienced Grade ≥3 events and these events were treatment-related in 54 (57%) of patients.

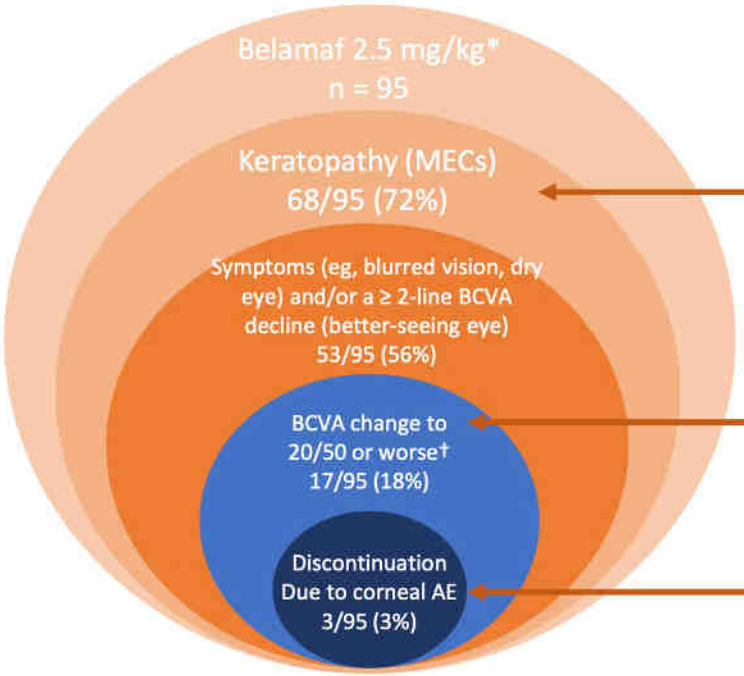
Only 3 (3%) SAEs were fatal (1 [1%] study treatment-related fatal events)

Lonial S et al. Cancer 2021

DREAMM-2: Outcomes due to ocular AES

1 patient experienced a worsening of BCVA to 20/200 in their better-seeing eye that recovered to baseline‡

1 patient developed a Grade 4 corneal ulcer¶



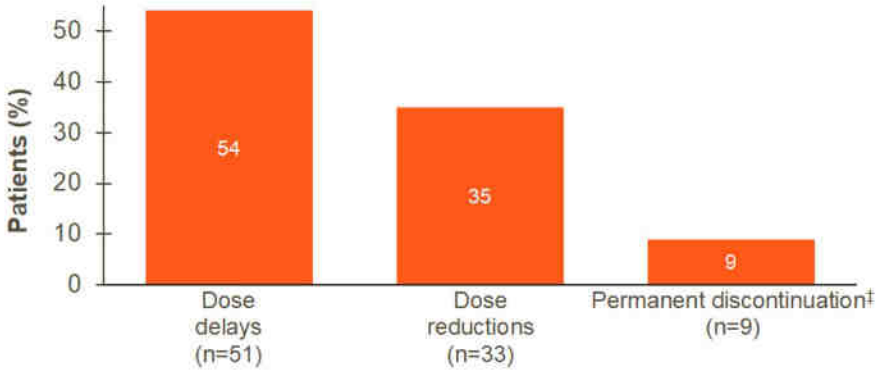
In patients with keratopathy (MECs) events Grade ≥ 2 per KVA, 48% (29/60) had > 1 event median time to onset: 37 days

Of these patients, 76% (13/17) had 1 event and 24% (4/17) had 2 events (no patients had > 2 events)

1 patient discontinued due to keratopathy (MECs), 1 due to blurred vision, and 1 due to reduced BCVA

DREAMM-2: dose delays and discontinuation

Dose delays,† reductions, and discontinuations due to any AE in the 2.5mg/kg arm (n=95)[1]



Clinical outcomes with first prolonged dose delays (>63 days) among patients treated with belantamab mafodotin 2.5mg/kg, n=16[3]	
Maintained a clinical benefit, n (%)	**14 (88)**
Deepened clinical response	6 (38)
Maintained the same response category	6 (38)
Did not meet progression criteria§	2 (13)
Developed progressive disease, n (%)	**2 (13)‖**

13-month analysis data cutoff[3]

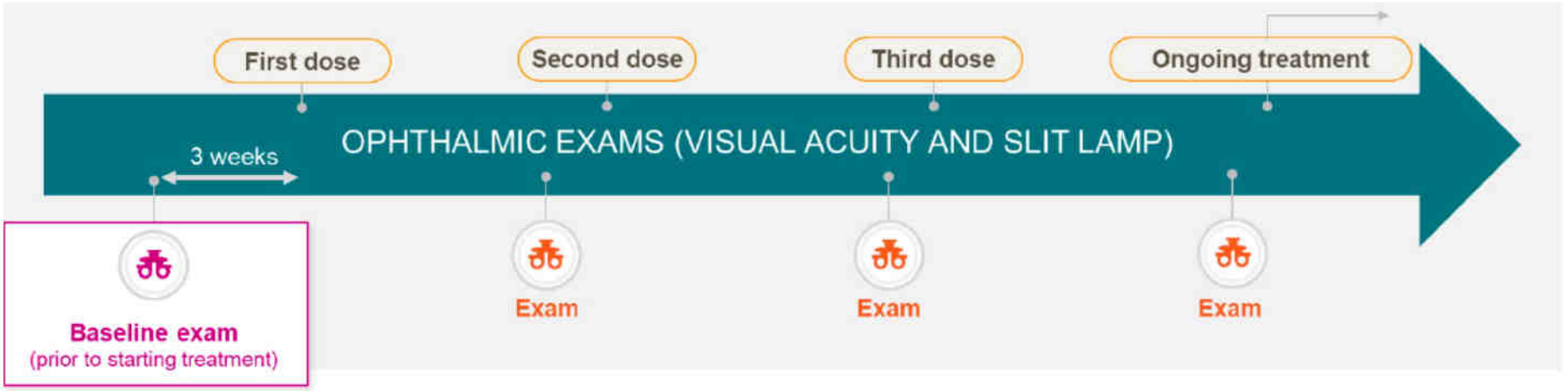
1. *Cohen AD et al. ASCO, 2020.* ***2.*** *Lonial S et al. Blood Cancer J.* ***3.*** *Lonial S et al.Cancer. 2021*

Characterization of Corneal Epitelial Findings: DREAMM-2 post-hoc analysis Recommended Monitoring, Diagnosis, and Management Techniques

Proposed paradigm for monitoring based on the post hoc analysis of DREAMM-2 and an objective literature review

Monitoring

Conduct eye examinations (visual acuity and slit lamp microscopy) at baseline (up to 3 weeks before), prior to each cycle (up to 2 weeks before), and promptly for worsening symptoms



DREAMM-2 and RWE safety: ocular AEs

	DREAMM-2 2.5mg/kg cohort (Lonial)[1]	GSK expanded access (Shragai)[2]	Mayo Clinic efficacy and safety (Vaxman)[3]	Mayo Clinic 2022 (Abeykoon)[4]
N	95	62	36	36
Ocular AEs, n (%)				
Keratopathy, any grade	68 (72)	41 (66)‡	16 (44)	25 (69)
Grade 1-2	24 (25)	21 (34)‡	13 (36)	20 (56)
≥Grade 3	44 (46)	20 (32)‡	3 (8)	5 (14)
% of patients who recovered from keratopathy	46 (77)*	46 (74)‡	N/A	N/A
Median time to recovery from keratopathy, days (range)	86.5 (8-358)	N/A	N/A	72 (15-126)
Reduction or change in BCVA, any grade	51 (54)	N/A	6 (17)	21 (58)
Grade 1-2	22 (23)	N/A	N/A	N/A
≥Grade 3	29 (31)	N/A	N/A	N/A
Time to resolution of ocular symptoms, days (range)	21.5 (7-64)†	N/A	N/A	3 mo (0.7-4)§

***Out of 60 patients who had data available and experienced keratopathy.[1] †Reported as median duration of decline in BCVA.[1] ‡Reported as ocular toxicity.[2] §Only includes patients who had a decrease in BCVA of 20/40 or worse in the better-seeing eye.[4]**

AE, adverse event; BCVA, best-corrected visual acuity; mo, months; RWE, real-world evidence.

1. Lonial S et al. *Cancer.* 2021;127(22):4198-4212. 2. Shragai T et al. Presented at: European Hematology Association Congress; June 9-17, 2021. Poster 2853. Accessed August 4, 2021. library.ehaweb.org/eha/2021/eha2021-virtual-congress/324746/tamir.shragai.belantamab.mafodotin.treatment.for.patients.with.relapsed.html 3. Vaxman I et al. *Blood Cancer J.* 2021;11(12):196. doi:10.1038/s41408-021-00592-3 4. Abeykoon JP et al. *Br J Haematol*. 2022. doi:10.1111/bjh.18298

DREAMM-2 and RWE safety: ocular AEs

	DREAMM-2 2.5mg/kg cohort (Lonial)[1]	MSKCC (Hultcrantz)[2]	University of Kansas Health System (Atieh)[3]	Spain compassionate use (Alegre)[4]	MD Anderson Cancer Center (Becnel)[5]	Dana-Farber Cancer Institute (Marzouk)[6]
N	95	50	28	33	33	40
Ocular AEs, n (%)						
Keratopathy, any grade	68 (72)	32 (64)	23 (82)	17 (52)	25 (76)	16 (41)
Grade 1-2	24 (25)	24 (48)	10 (36)	10 (30)	21 (64)	9 (23)
≥Grade 3	44 (46)	8 (16)	13 (56)	7 (21)	4 (12)	7 (18)
Patients who recovered from keratopathy	46 (77)*	N/A	N/A	N/A	13 (52)	N/A
Median time to recovery from keratopathy, days (range)	86.5 (8-358)*	N/A	N/A	N/A	67 (43-368)	23 (18-102)‖
Reduction or change in BCVA, any grade	51 (54)	24 (48)	N/A	10 (30)‡	25 (76)	14 (35)
Grade 1-2	22 (23)	20 (40)	N/A	N/A	23 (69)	8 (20)
≥Grade 3	29 (31)	3 (6)	N/A	N/A	2 (6)	6 (15)
Median time to resolution of BCVA changes, days (range)	21.5 (7-64)†	N/A	N/A	N/A	49 (27-116)	28 (28-126)¶

*Calculated for 60 patients who had data available and had recovered from first examination finding of grade ≥2 keratopathy according to the KVA scale.[1] †Reported as median duration of decline in BCVA.[1] ‡These patients experienced reduced visual acuity ≥0.4.[4] §The breakdown of patients who recovered from keratopathy or BCVA changes were not reported.[6] ‖Median time to resolution for patients with grade 3 keratopathy.[6] ¶Only representing patients who resolved from grade ≥3.[6]

AE, adverse event; BCVA, best-corrected visual acuity; KVA, Keratopathy and Visual Acuity; MSKCC, Memorial Sloan Kettering Cancer Center; N/A, not available; RWE, real-world evidence.

1. Lonial S et al. *Cancer.* 2021;127(22):4198-4212. 2. Hultcrantz M et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 11-14, 2021; Atlanta, GA. Poster 1644. 3. Atieh T et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 11-14, 2021; Atlanta, GA. Poster 1642. 4. Alegre A et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 11-14, 2021; Atlanta, GA. Poster 3775. 5. Becnel MR et al. Presented at: American Society of Clinical Oncology Annual Meeting; June 3-7, 2022; Chicago, IL. Poster 3060. 6. Marzouk O et al. Presented at: Hematology/Oncology Pharmacy Association Annual Conference; March 30-April 2, 2022; Boston, MA.

DREAMM-2 and RWE safety: dose reductions and delays

	DREAMM-2 2.5mg/kg cohort (Lonial)[1]	GSK expanded access (Shragai)[2]	Mayo Clinic 2022 (Abeykoon)[3]	MSKCC (Hultcrantz)[4]	University of Kansas Health System (Atieh)[5]	Dana-Farber Cancer Institute (Marzouk)[6]
N	95	67	36	50	28	40
Dose reduction, n (%)						
Due to ocular AE	N/A	65% of cycles	N/A	19 (38)	N/A	10 (25)†
Due to keratopathy	24 (25)	N/A	4 (11)	N/A	19 (68)*	N/A
Dose delay, n (%)						
Due to ocular AE	N/A	N/A	N/A	17 (34)	N/A	16 (40)
Due to keratopathy	45 (47)	N/A	9 (25)	N/A	19 (68)*	N/A
Treatment discontinuation, n (%)						
Due to ocular AE	2 (2)	4 (6)	N/A	6 (12)	N/A	9 (23)
Due to keratopathy	1 (1)	N/A	5 (14)	N/A	N/A	N/A

*A total of 19 patients experienced either a dose reduction or delay due to keratopathy.[5] †All patients who had dose reductions had dose delays.[6]

AE, adverse event; MSKCC, Memorial Sloan Kettering Cancer Center; N/A, not available; RWE, real-world evidence.

1. Lonial S et al. *Cancer.* 2021;127(22):4198-4212. 2. Shragai T et al. Presented at: European Hematology Association Congress; June 9-17, 2021. Poster 2853. Accessed August 4, 2021. library.ehaweb.org/eha/2021/eha2021-virtual-congress/324746/tamir.shragai.belantamab.mafodotin.treatment.for.patients.with.relapsed.html 3. Abeykoon JP et al. *Br J Haematol*. 2022. doi:10.1111/bjh.18298 4. Hultcrantz M et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 11-14, 2021; Atlanta, GA. Poster 1644. 5. Atieh T et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 11-14, 2021; Atlanta, GA. Poster 1642. 6. Marzouk O et al. Presented at: Hematology/Oncology Pharmacy Association Annual Conference; March 30-April 2, 2022; Boston, MA.

BELANTAMAB MAFODOTIN IN PATIENTS WITH RELAPSED AND REFRACTORY MULTIPLE MYELOMA WHO HAVE RECEIVED AT LEAST ONE PROTEASOME INHIBITOR, ONE IMMUNOMODULATORY AGENT AND ONE ANTI-CD38 MONOCLONAL ANTIBODY: A RETRO-PROSPECTIVE ITALIAN OBSERVATIONAL STUDY

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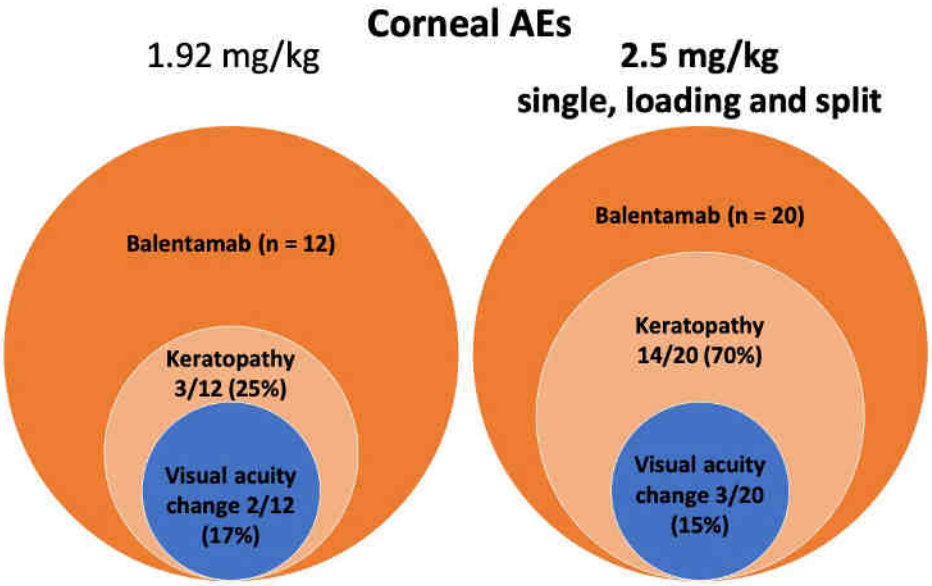
Adverse events	N (%)
Ocular	N=31
Keratopathy	23 (74)
Ocular symptoms	5 (16)
Change in BCVA	3 (10)
Grade 1	13 (42)
Grade 2	14 (45)
Grade 3	4 (13)
Dose reduction	4 (13)
Drug discontinuation	14 (45)
Hematological	N=16
Thrombocytopenia	14 (87.5)
Grade 1	5 (31)
Grade 2	3 (19)
Grade 3	8 (50)
Others	
Infections	N=8
Infusion reactions	N=4

- At last fu ocular adverse events recovered in 46% of cases, they requested drug discontinuation in 45% of cases and in 13% of cases drug was only reduction in dose.
- Thrombocytopenia was described in 87.5% of patients, 50% of them were grade 3, but reversible.
- Then, physicians reported 8 infections, 4 infusion reactions (clinically showing as fever) and one pulmonary embolism. Only one grade 5 secondary neoplasia was reported.

Belamaf was discontinued in 37 patients (55%, disease progression in 28, death in 3, toxicity in 5, other in 1 patient). Thirty patients (45%) are still receiving therapy.

BELANTAMAB - ALGONQUIN TRIAL

TEAE (Any Grade ≥ 25%) , n (%)	Any Grade	Grade ≥ 3
Keratopathy	28 (75.7)	19 (51.4)
Neutropenia	21 (56.8)	15 (40.5)
Thrombocytopenia	18 (48.6)	12 (32.4)
Decreased visual acuity	17 (45.9)	6 (16.2)
Fatigue	15 (40.5)	4 (10.8)
Fever	13 (35.1)	1 (2.7)
Cataract	13 (35.1)	1 (2.7)
Constipation	12 (32.4)	0
Diarrhea	11 (29.7)	0
Infusion-related reaction	11 (29.7)	2 (5.4)



- 1 patient discontinued treatment for grade 4 decreased visual acuity that recovered to grade 3 within 7 days

Trudel et al, ASH 2020

DREAMM-9 (BELA –VRD) Corneal AEs

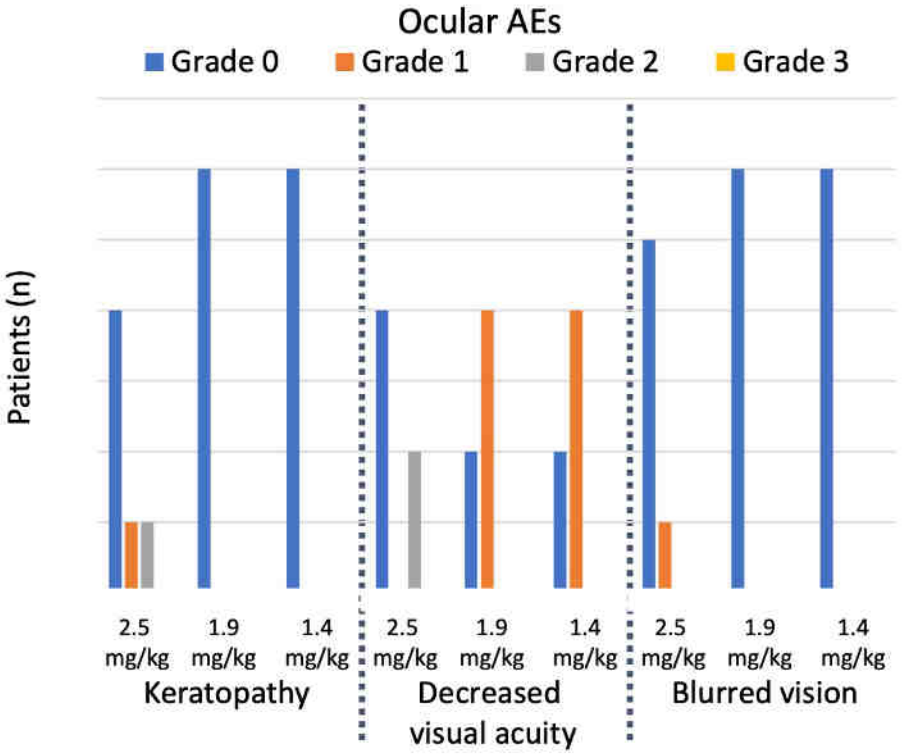
Corneal Events	1.9 mg/kg Q3/4W (n = 12)	1.4 mg/kg Q6/8W (n = 6)	1.9 mg/kg Q6/8W (n = 6)	1.0 mg/kg Q3/4W (n = 6)	1.4 mg/kg Q3/4W (n = 6)
Any corneal event, n (%)	12 (100)	3 (50)	4 (67)	4 (67)	5 (83)
Corneal AE leading to belantamab mafodotin dose reduction, n (%)	1 (8)	0	1 (17)	0	0
Corneal AE leading to belantamab mafodotin dose delay, n (%)	11 (92)	3 (50)	3 (50)	4 (67)	5 (83)
Grade ≥3 corneal events per KVA scale, n (%)	10 (83)	3 (50)	2 (33)	4 (67)	4 (67)
Median time to onset of grade ≥3 corneal event, days (range)	81.0 (63-383)	126.0 (85-197)	103.0 (84-122)	74.0 (42-145)	57.5 (22-107)
Worse case post baseline, n (%) ▪ ≥3-line decline in BCVA (better eye) ▪ ≥3-line decline in BCVA (worse eye)	 5 (42) 8 (67)	 1 (17) 1 (17)	 0 0	 1 (17) 1 (17)	 1 (17) 3 (50)

- No permanent treatment discontinuations of belantamab mafodotin due to corneal AEs
- Patients in cohort 2 and cohort 3 (Q6/8W dosing) had the lowest rate grade ≥3 corneal events per KVA scale

Usmani. ASH 2021. Abstr 2738

BELANTAMAB-RD IN NDMM- Ocular AEs

Baseline Ocular Characteristic, n	2.5 mg/kg (n = 6)	1.9 mg/kg (n = 6)	1.4 mg/kg (n = 6)
Cataract	Grade 1: 2 Grade 2: 4	Grade 1: 1 Grade 2: 2 Grade 3: 2	Grade 1: 4 Grade 2: 2
Normal corneal epithelium	2	2	3
Normal intraocular pressure	6	6	6
Normal dilated fundoscopic exam	0	0	1
Best corrected visual acuity 20/30 or better ▪ OD ▪ OS	 6 6	 5 4	 5 4



No grade ≥3 ocular toxicities

Terpos. ASH 2021

A low frequency of severe ocular TEAEs was observed

- Across all cohorts, no keratopathy higher than Grade 2 was observed
- Cohorts 2 and 3 showed no ocular symptoms higher than Grade 2
- Cohort 2 had a low occurrence of Grade 3-4 visual acuity reduction
- No Grade 4 ocular adverse events were observed

Ocular assessments	Cohort 1 belantamab mafodotin 2.5mg/kg Q8W + len/dex (n=12)	Cohort 2 belantamab mafodotin 1.9mg/kg Q8W + len/dex (n=12)	Cohort 3 belantamab mafodotin 1.4mg/kg Q8W + len/dex (n=12)
Ocular symptoms			
Grade 0-1	96 (73.8%)	123 (85.4%)	101 (79.5%)
Grade 2	32 (24.6%)	21 (14.6%)	26 (20.5%)
Grade 3-4	2 (1.5%)	0 (0.0%)	0 (0.0%)
Keratopathy			
Grade 0-1	115 (87.1%)	133 (91.1%)	117 (92.1%)
Grade 2	17 (12.9%)	13 (8.9%)	10 (7.9%)
Grade 3-4	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visual acuity reduced			
Grade 0-1	58 (44.3%)	94 (64.8%)	86 (67.7%)
Grade 2	59 (45.0%)	44 (30.3%)	31 (24.4%)
Grade 3-4	14 (10.7%)	7 (4.8%)	10 (7.9%)

This table was created independently by GSK from original data first presented in Terpos E., et al. ASH. 2022.

len/dex, lenalidomide/dexamethasone; Q8W, every eight weeks.

Terpos, E., et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 10-13, 2022; New Orleans, LA. Poster 1920.

The impact of belantamab mafodotin-associated ocular AEs on daily functioning for patients with TI-NDMM was evaluated

36 patients were followed for a median of 9.5 months (range 3.2-15.4)

Ocular assessments included BCVA using Snellen chart and manifest refraction and corneal exam using slit lamp biomicroscopy

Ocular symptoms were classified by CTCAEs, and dry eye disease severity and vision-related functioning were assessed with the patient-reported OSDI

In Part 1 of the study, severity of corneal events was assessed with the KVA scale

AE, adverse event; BCVA, best-corrected visual acuity; CTCAE, Common Terminology Criteria for Adverse Events; KVA, Keratopathy and Visual acuity; NDMM, newly diagnosed multiple myeloma; OSDI, Ocular Surface Disease Index; TI, transplant-ineligible.

Terpos, E., et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 10-13, 2022; New Orleans, LA. Poster 3234.

Most patients had ocular comorbidities at baseline[1,2]

	Cohort 1 belantamab mafodotin 2.5mg/kg Q8W + len/dex (n=12)	Cohort 2 belantamab mafodotin 1.9mg/kg Q8W + len/dex (n=12)	Cohort 3 belantamab mafodotin 1.4mg/kg Q8W + len/dex (n=12)
Baseline BCVA,* n (%)			
20/20	4 (33.3)	3 (25.0)	5 (41.7)
20/25	6 (50.0)	5 (41.7)	4 (33.3)
20/30	1 (8.3)	2 (16.7)	2 (16.7)
20/40	0 (0.0)	2 (16.7)	0 (0.0)
20/50	1 (8.3)	0 (0.0)	0 (0.0)
20/70	0 (0.0)	0 (0.0)	1 (8.3)
Ocular comorbidities, n (%)			
Cataract, any Grade	10 (83.3)	10 (83.3)	11 (91.7)
Grade 1	3 (25.0)	2 (16.7)	4 (33.3)
Grade 2	5 (41.7)	4 (33.3)	6 (50.0)
Grade 3	2 (16.7)	3 (25.0)	1 (8.3)
Grade 4	0 (0.0)	1 (8.3)	0 (0.0)
Abnormal fundoscopic findings	12 (100)	11 (91.7)	11 (91.7)
Abnormal intraocular pressure and/or glaucoma	1 (8.3)	3 (25.0)	2 (16.7)
Abnormal corneal epithelium†	1 (8.3)	0 (0.0)	0 (0.0)

*Best vision from either OD, OS, or OU is presented here. †No cases of punctate keratopathy of any Grade were reported at baseline; one case with stippled peripheral corneal staining.

Ocular assessments included BCVA using Snellen chart and manifest refraction and corneal exam using slit lamp biomicroscopy

AE, adverse event; BCVA, best-corrected visual acuity; len/dex, lenalidomide/dexamethasone; OD, oculus dexter (the right eye); OS, oculus sinister (the left eye); OU, oculus uterque (both eyes); Q8W, every eight weeks.

1. Terpos, E., et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 10-13, 2022; New Orleans, LA. Poster 1920. **2.** Terpos, E., et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 10-13, 2022; New Orleans, LA. Poster 3234

A low frequency (<11%) of ≤ Grade 3 ocular AEs were observed across cohorts of belantamab mafodotin + len/dex

Ocular examination	Cohort 1 (2.5mg/kg)	Cohort 2 (1.9mg/kg)	Cohort 3 (1.4mg/kg)
Number of assessments	132	146	127
Number (%) of assessments with maximum Grade 2 ocular AE*	60 (45.4%)	50 (34.2%)	31 (24.4%)
Number (%) of assessments with maximum Grade 3 ocular AE*	14 (10.6%)	7 (4.8%)	10 (7.9%)

This table was created independently by GSK from original data first presented in Terpos E., et al. ASH. 2022.

Grade 3 ocular AEs were observed only for reduced visual acuity, visual impairment, vision blurred, and cataracts; no Grade 4 ocular AEs were observed

Belantamab mafodotin doses skipped due to ocular AEs per the total number of planned administrations were 26/80 (32.5%), 18/86 (20.9%), and 16/81 (19.8%) in cohorts 1, 2, and 3, respectively

Keratopathy and BCVA changes from baseline were resolved by a median of ~3 months and ~2 months respectively; for each of the reported ocular AEs, similar times to resolution were recorded across all cohorts

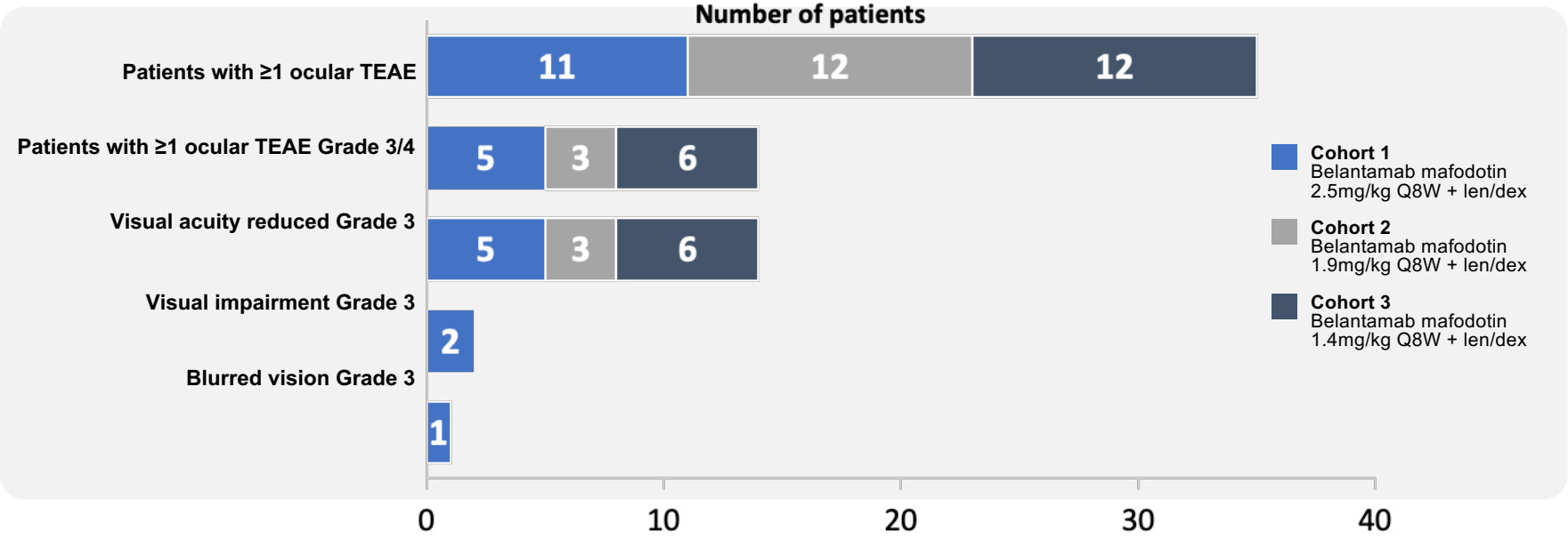
This analysis showed a lower frequency of ocular AEs, especially Grade 3, compared to previous belantamab mafodotin studies

*Ocular AE=BCVA change or keratopathy.

AE, adverse event; BCVA, best corrected visual acuity.

1. Terpos, E., et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 10-13, 2022; New Orleans, LA. Poster 3234.

Low frequency of Grade 3 ocular AEs was observed with no Grade 4 ocular AEs

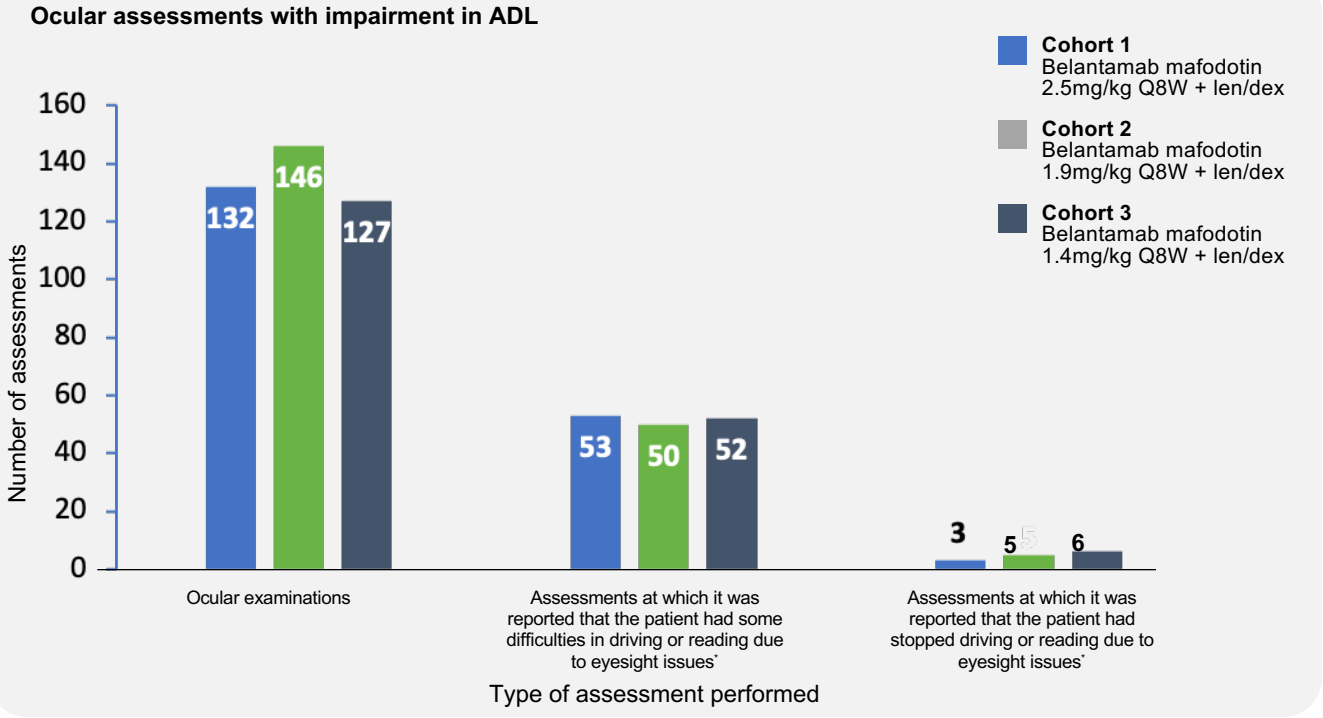


Although Grade 3 visual acuity reduced was observed in 14 patients, Grade 3 visual impairment and blurred vision, which represent the patients' perception of decreased vision, were noted in only 2 and 1 patients, respectively

AE, adverse event; len/dex, lenalidomide/dexamethasone; Q8W, every eight weeks; TEAE, treatment-emergent AE.

Terpos, E., et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 10-13, 2022; New Orleans, LA. Poster 323[4]

Very few patients had stopped activities of daily living due to ocular AEs



The percentage of assessments at which it was reported that the patient had some difficulties in driving or reading due to eyesight were **40.2%**, **34.2%** and **40.9%** in cohorts 1, 2, and 3, respectively

The percentage of assessments at which it was reported that the patient had stopped driving or reading due to eyesight issues were **<5% across all cohorts**

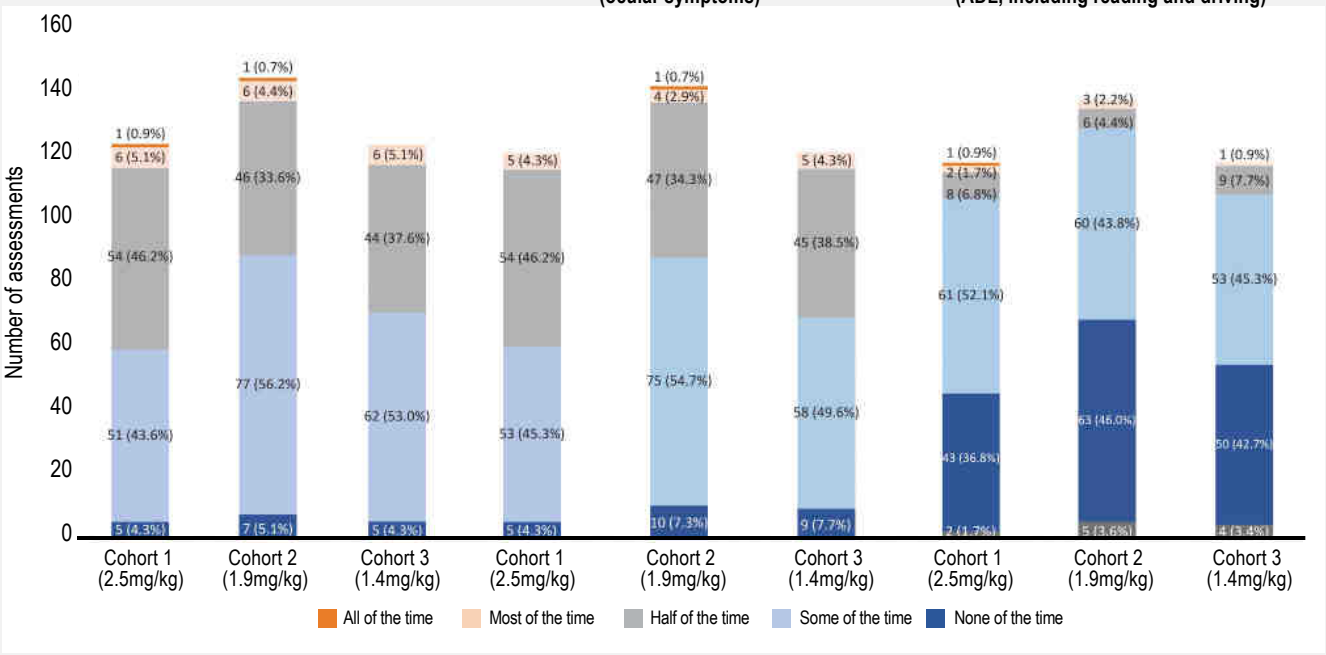
*Classified based on the worst reported degree between driving and reading; if for the same assessment some difficulties are reported for driving and stopped is reported for reading, then the assessment is counted only in the 'stopped' category.

AE, adverse event; ADL, activities of daily living; Q8W, every eight weeks.

1. Terpos, E., et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 10-13, 2022; New Orleans, LA. Poster 3234.

Belantamab mafodotin + len/dex had only a minor impact on activities of daily living across all cohorts

Less than 2.0% of OSDI assessment were observed where the impact in daily functioning was 'all' or 'most of the time'



ADL, activities of daily living; len/dex, lenalidomide/dexamethasone; OSDI, ocular surface disease index; Q, question.

Terpos, E., et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 10-13, 2022; New Orleans, LA. Poster 3234.

DREAMM-2 and RWE safety: non-ocular AEs

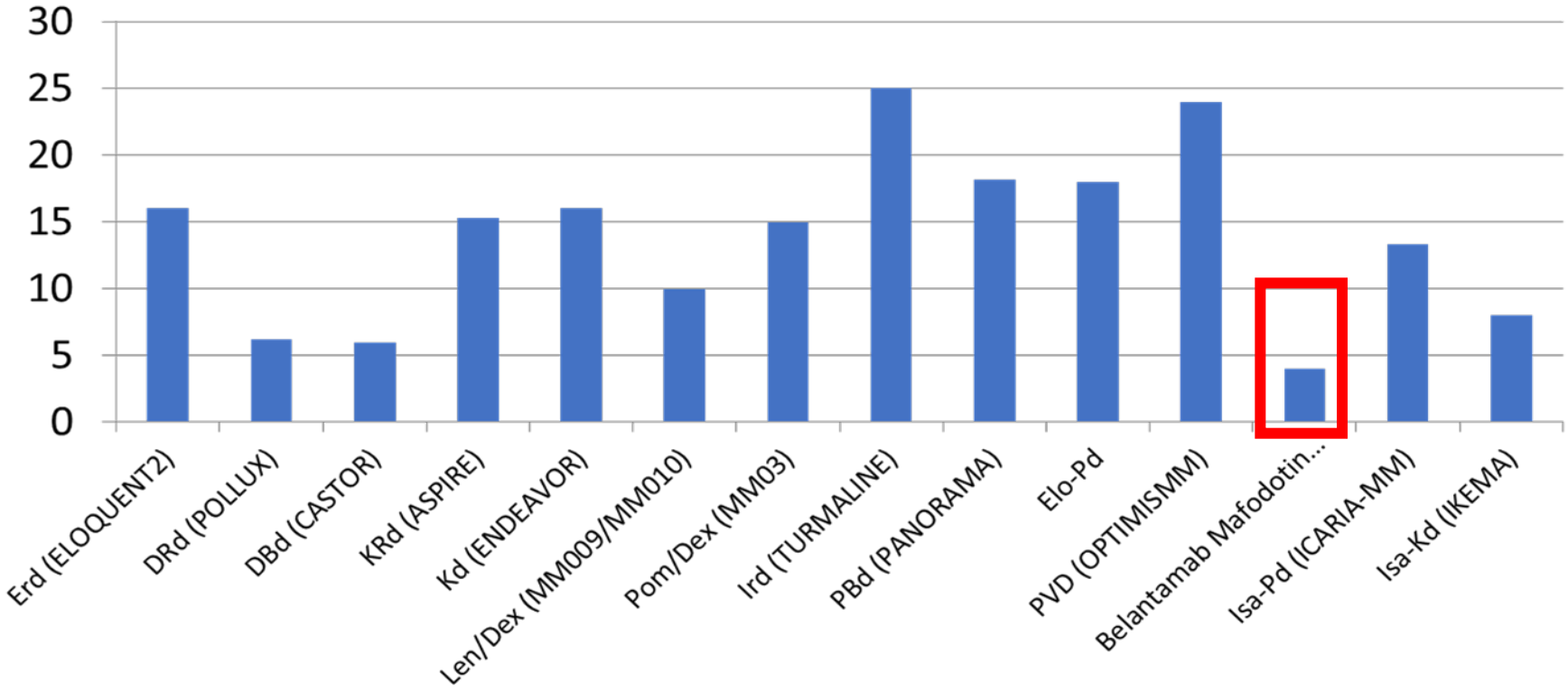
	DREAMM-2 2.5mg/kg cohort (Lonial)[1]	GSK expanded access (Shragai)[2]	Mayo Clinic efficacy and safety (Vaxman)[3]	University of Kansas Health System (Atieh)[4]	Spain compassionate use (Alegre)[5]
N	95	67	36	28	33
Non-ocular AEs, n (%)					
IRR	20 (21)*	N/A	2 (5)	N/A	N/A
Anemia	26 (27)	6 (9)	N/A	23 (83)	N/A
Thrombocytopenia	36 (38)†	26 (39)	3 (8)¶	19 (70)	7 (21)
Neutropenia	14 (15)‡	9 (13)	N/A	8 (30)	N/A
Elevated LFTs	20 (21)§	7 (10)	N/A	15 (53)	N/A
Infection	9 (9)‖	7 (10)	1 (3)¶	N/A	N/A

*Infusion-related reactions (considered AEs of special interest) include the preferred terms infusion-related reaction, pyrexia, chills, diarrhea, nausea, asthenia, hypertension, lethargy, and tachycardia occurring within 24 hours of infusion.[1] †Thrombocytopenia (considered an AE of special interest) includes the preferred terms thrombocytopenia and platelet count decreased.[1] ‡Neutropenia includes neutropenia and neutrophil count decreased.[1] §Increased levels of aspartate aminotransferase.[1] ‖Pneumonia of any grade.[1] ¶Includes patients hospitalized for thrombocytopenia or infections; however, this may not represent a full account of thrombocytopenia or infection events.[3]

AE, adverse event; IRR, infusion-related reaction; LFT, liver function test; N/A, not available; RWE, real-world evidence.

1. Lonial S et al. *Cancer.* 2021;127(22):4198-4212. 2. Shragai T et al. Presented at: European Hematology Association Congress; June 9-17, 2021. Poster 2853. Accessed August 4, 2021. library.ehaweb.org/eha/2021/eha2021-virtual-congress/324746/tamir.shragai.belantamab.mafodotin.treatment.for.patients.with.relapsed.html 3. Vaxman I et al. *Blood Cancer J.* 2021;11(12):196. doi:10.1038/s41408-021-00592-3 4. Atieh T et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 11-14, 2021; Atlanta, GA. Poster 1642. 5. Alegre A et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 11-14, 2021; Atlanta, GA. Poster 3775.

Discontinuation



DREAMM-2: Single-Agent Belantamab Mafodotin (Belamaf) Effects on Patient-Reported Outcome (PRO) Measures in Patients with Relapsed/Refractory Multiple Myeloma (RRMM)

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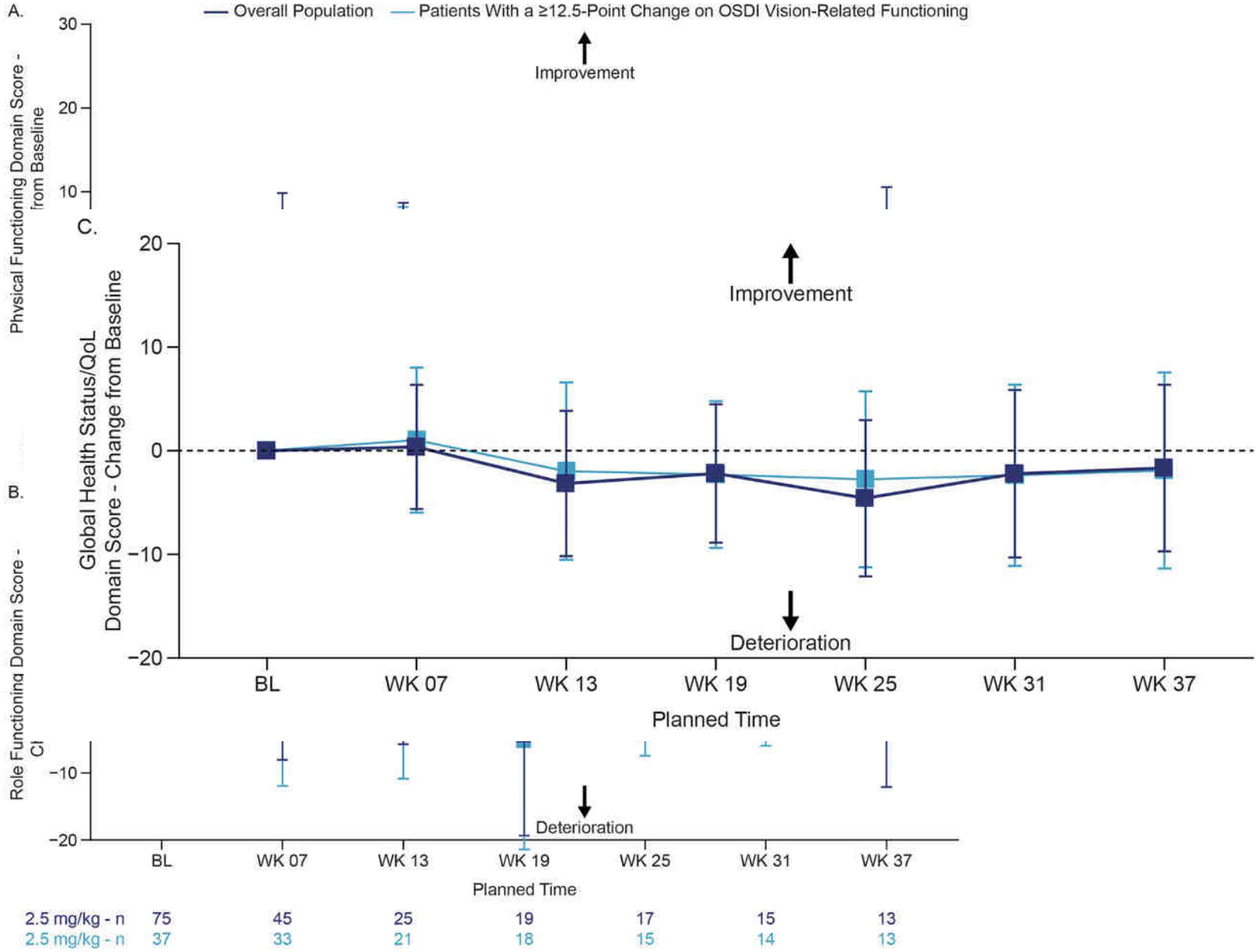
A.
Overall Population
Patients With a ≥12.5-Point Change on OSDI Vision-Related Functioning
Improvement
Physical Functioning Domain Score - from Baseline
30
20
10
C.
Improvement
Global Health Status/QoL Domain Score - Change from Baseline
20
10
0
−10
−20
Deterioration
B.
BL
WK 07
WK 13
WK 19
WK 25
WK 31
WK 37
Planned Time
Role Functioning Domain Score - Cl
−10
−20
Deterioration
BL
WK 07
WK 13
WK 19
WK 25
WK 31
WK 37
Planned Time
2.5 mg/kg - n 75 45 25 19 17 15 13
2.5 mg/kg - n 37 33 21 18 15 14 13

Single-Agent Belantamab Mafodotin in Patients with Relapsed or Refractory Multiple Myeloma (RRMM): Final Analysis of the DREAMM-2 trial

Poster No. 3246

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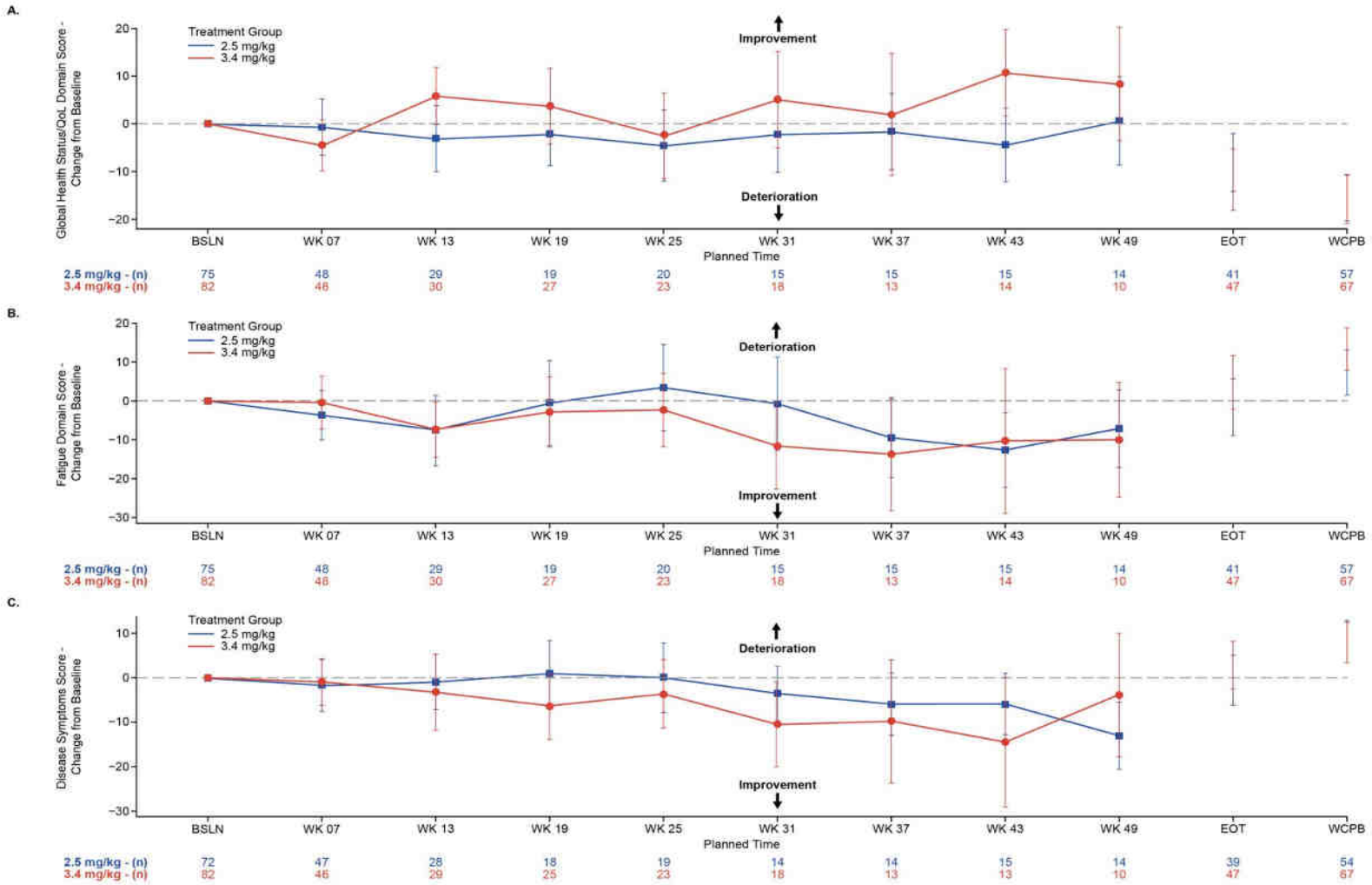
Figure 4. Global health status, fatigue, and disease symptoms



Conclusions

1. Single-agent Belantamab mafodotin showed rapid, deep, and durable responses in DREAMM-2, particularly in TCE/R and heavy pre-treated patients

2. These data were confirmed in RWE also in patients TCE/R

3. Belantamab mafodotin, as single agent and in association, seems to be effective in high-risk population

4. This drug is manageable and with an acceptable safety profile, in all the patients affected with Multiple Myeloma

Gruppo «Gammopatie Monoclonali»

Thank you