Caso clinico 2

Massimo Offidani

Clinica di Ematologia, AOU Ospedali Riuniti di Ancona

P.G., male, 62 years old:

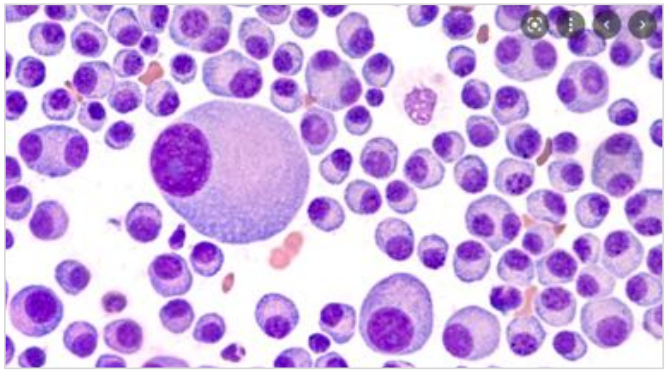
- **Diagnosis (Dec 2013):** k free light chain Multiple Myeloma, ISS: 1, R-ISS: 1, normal FISH, paraosseus plasmocytoma

- **Prior therapies:**

1. **VTD x 4 + 2 HSCT + left hip radiotherapy** (Jan 2014-Jan 2015)
2. Relapse Jun 2018 (FISH: del17p) → **Daratumumab-Lenalidomide-Dexamethasone (DRd) x 17**
3. Relapse October 2019 (FISH: del17p) →**Cyclophosphamide-Pomalidomide-Dexamethasone (CPd) x 6**
4. Relapse April 2020 (FISH: del17p): proteinuria 3 g/24h, BJ+, FLC kappa 1950 mg/l, lambda 14,1 mg/l, kappa/lambda 138, PLT 86.000/mcl, Creatinine 1.4 mg/dl, PLC 50%

- **Comorbidities** (69 yrs)**:** dislipidemia, diabetes mellitus type II, ischemic cardiopathy, steroide-related tremor, bortezomib-related peripheral neuropathy

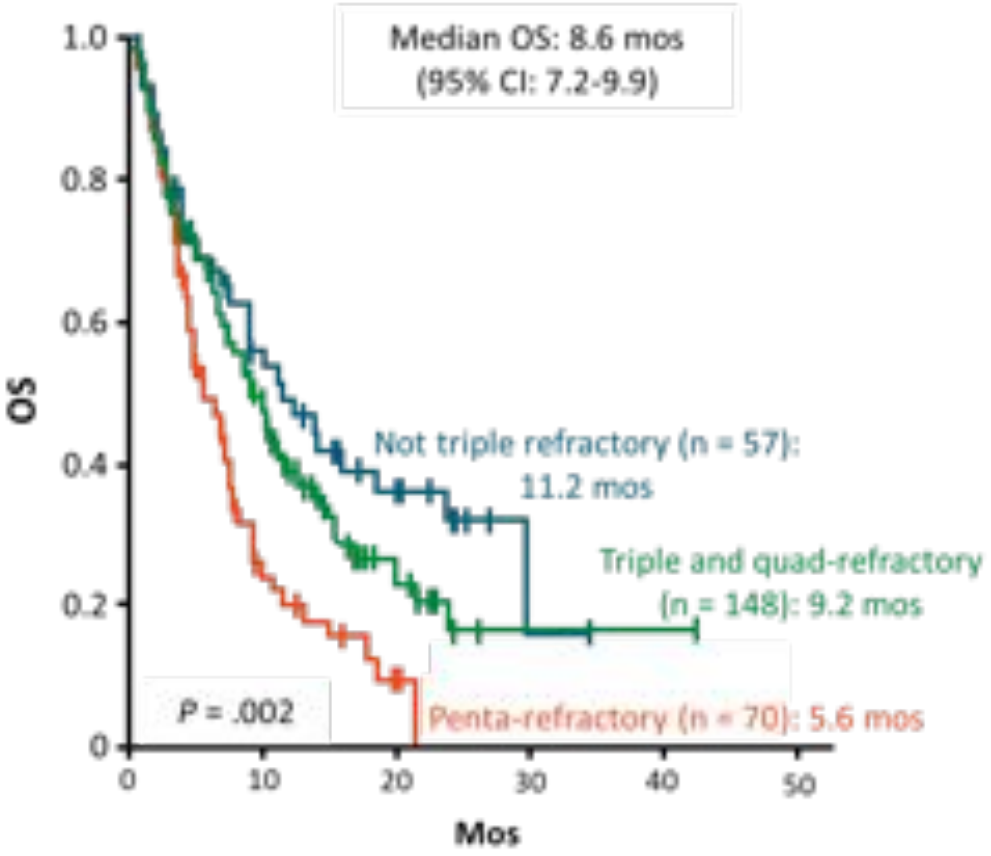
Triple/quad-class refractory MM?



R/R MM in the Modern Era: CD38 Antibody–Refractory Disease in MAMMOTH

- Retrospective study of patients with MM refractory to CD38 antibodies from 14 academic institutions (N = 275)
  - Triple refractory: CD38 antibody + 1 PI + 1 IMiD
  - Quad refractory: CD38 antibody + 1 PI + 2 IMiDs OR 2 PIs and 1 IMID
  - Penta-refractory: CD38 antibody + 2 PIs + 2 IMiDs
- 54% triple or quad refractory, 25% penta-refractory
- Median prior lines of therapy: 4 (range: 1-16)

Refractory, %	N = 275
Bortezomib	68.4
Carfilzomib	47.3
Lenalidomide	76.7
Pomalidomide	65.1

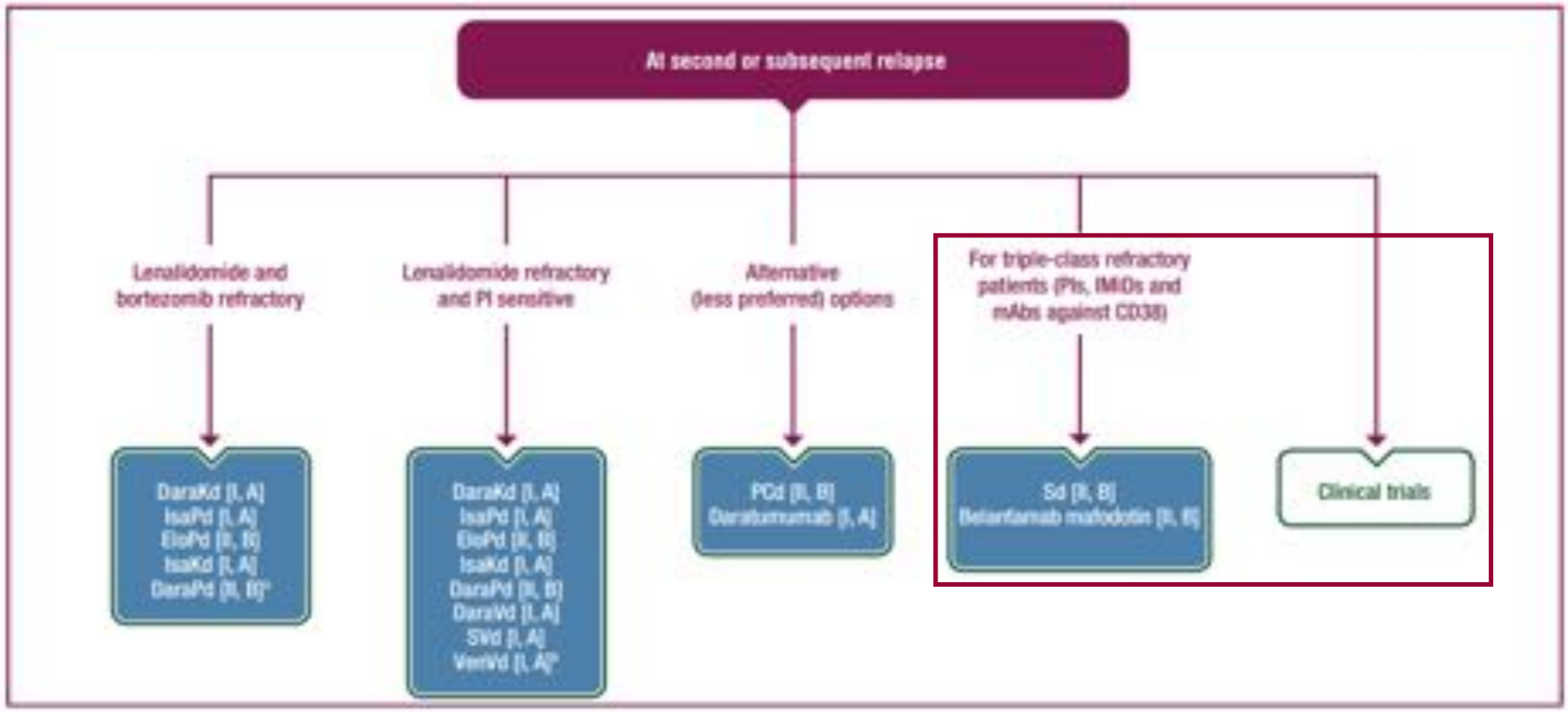


Gandhi. Leukemia. 2019; 33:2266.

What can we do?

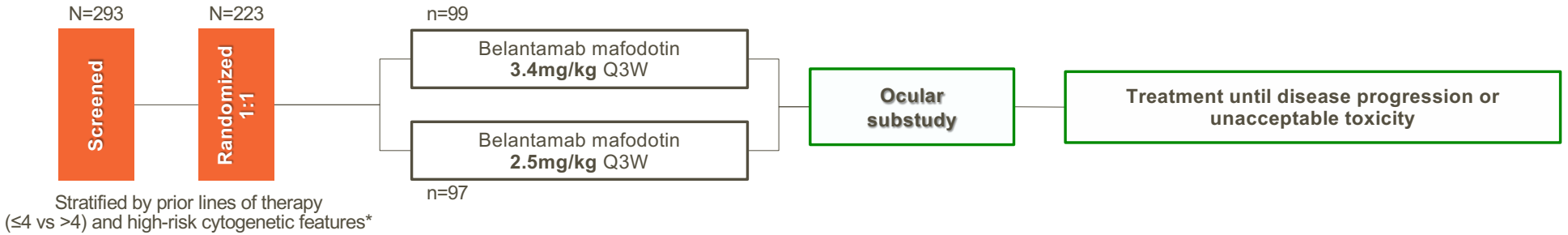
Multiple myeloma: EHA-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

M. A. Dimopoulos[1], P. Moreau[2], E. Terpos[1], M. V. Mateos[3], S. Zweegman[4], G. Cook[5], M. Delforge[6], R. Hájek[7], F. Schjesvold[8,9], M. Cavo[10], H. Goldschmidt[11], T. Facon[12], H. Einsele[13], M. Boccadoro[14], J. San-Miguel[15], P. Sonneveld[16] & U. Mey[17], on behalf of the EHA Guidelines Committee* and ESMO Guidelines Committee*



DREAMM-2: study design

A phase II, open-label, randomized, 2-dose study in patients with RRMM who were refractory to an immunomodulatory drug and a PI and refractory and/or intolerant to an anti-CD38 mAb



Inclusion criteria

- ≥3 prior lines of MM therapy
- Refractory to prior immunomodulatory agents, proteasome inhibitors, and refractory and/or intolerant to an anti-CD38 monoclonal antibody
- BCMA-targeted therapy naïve
- Prior ASCT allowed
- ECOG PS 0-2

Primary endpoint

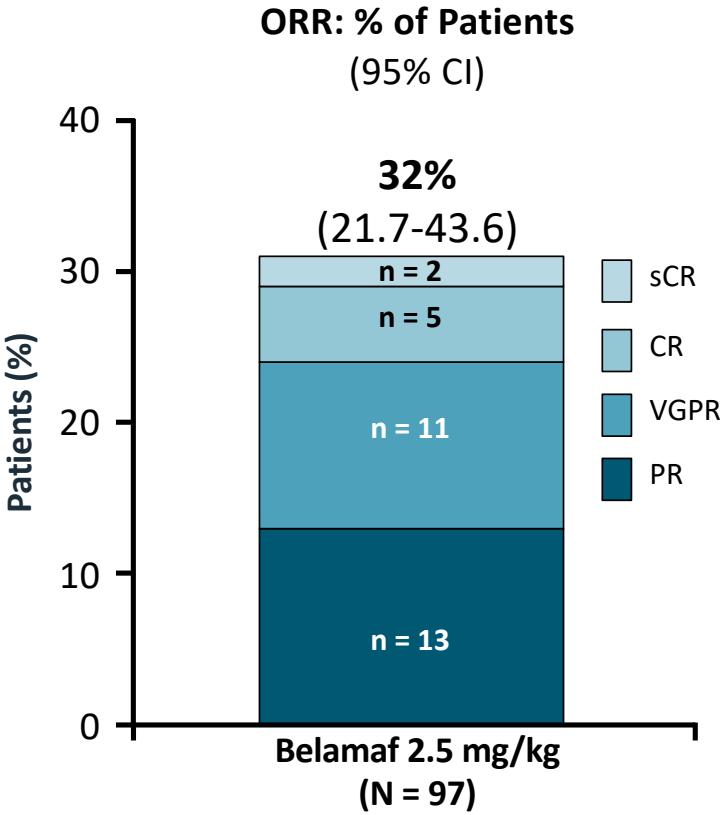
- ORR (IRC)

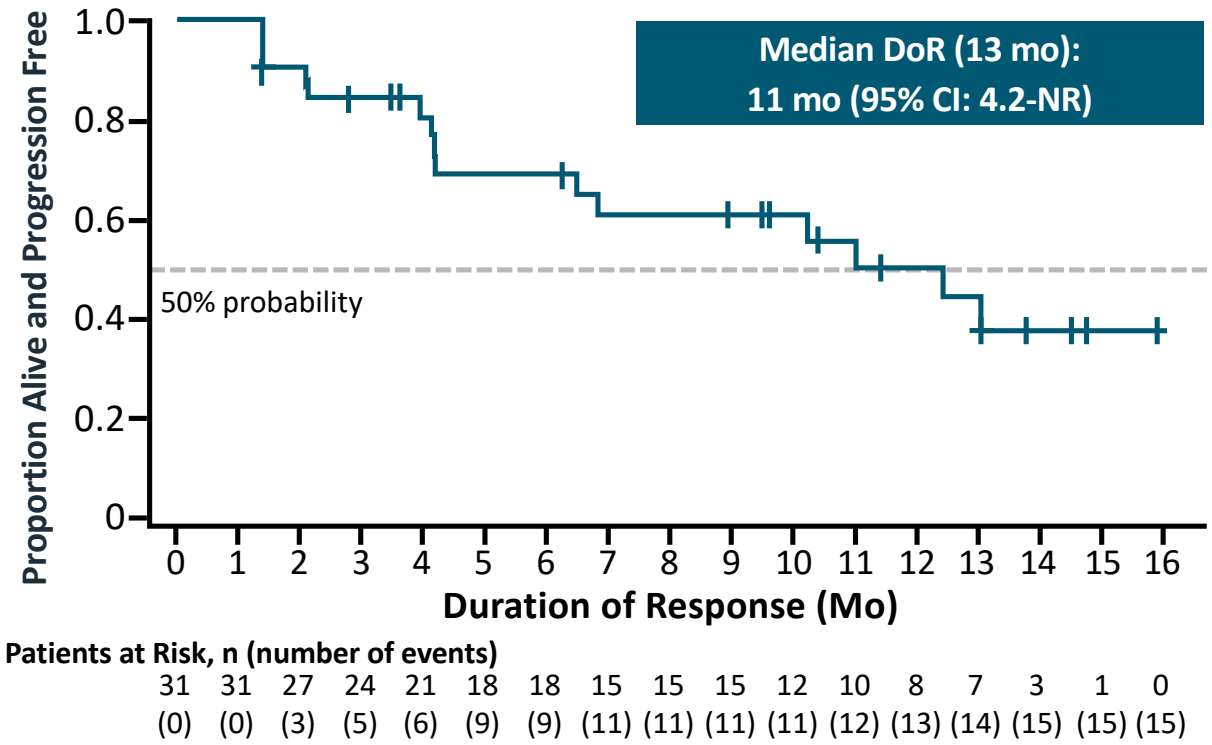
Secondary endpoints

- DOR, PFS, OS, CBR
- Safety
- ORR assessed by investigator,† TTR,† TTP†
- ADA activities†
- PK profiles†
- PROs†
- HRQOL†

Screening occurred between June 18, 2018, and January 2, 2019.
*Presence or absence of t(4;14), t(14;16), 17p13del, or 1q21+. †Will be reported separately.
ADA, anti-drug antibody; ASCT, autologous stem cell transplant; BCMA, B-cell maturation antigen; CBR, clinical benefit rate; CD, cluster of differentiation; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HRQOL, health-related quality of life; IRC, independent review committee; mAb, monoclonal antibody; MM, multiple myeloma; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetic; PI, proteasome inhibitor; PRO, patient-reported outcome; Q3W, every 3 weeks; RRMM, relapsed/refractory multiple myeloma; TTP, time to progression; TTR, time to response.
Lonial S et al. *Lancet Oncol.* 2020;21(2):207-221.

Phase II DREAMM-2: Response and DoR at 13 Mo of Follow-up, Belantamab Mafodotin 2.5 mg/kg



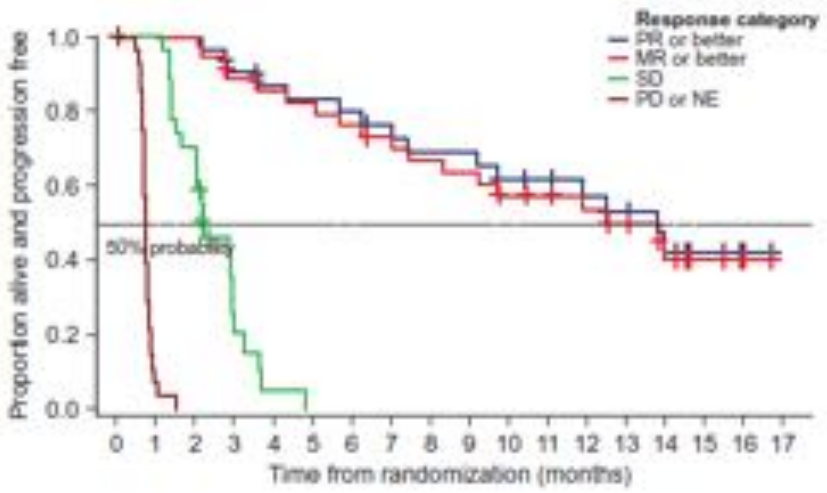


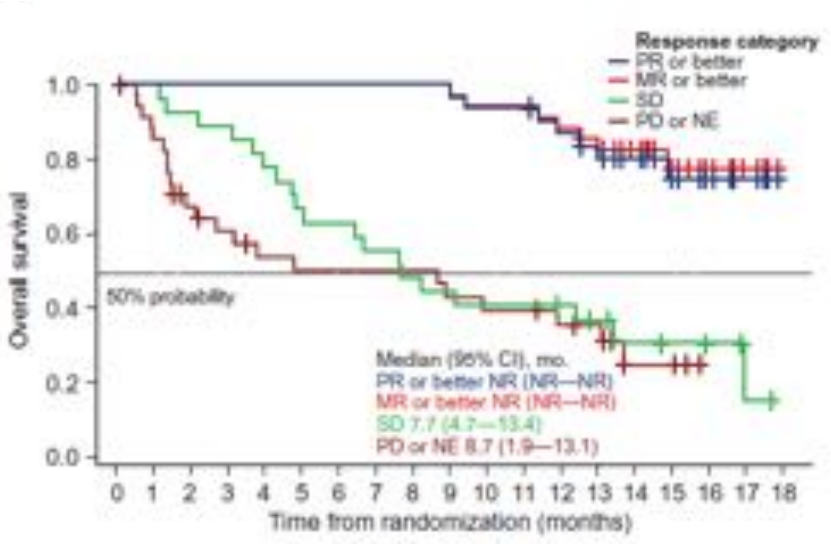
Patients at Risk, n (number of events)

31	31	27	24	21	18	18	15	15	15	12	10	8	7	3	1	0
(0)	(0)	(3)	(5)	(6)	(9)	(9)	(11)	(11)	(11)	(11)	(12)	(13)	(14)	(15)	(15)	(15)

Lonial. Cancer 2021;[Epub].

Outcomes according to response to therapy





DREAMM-2 Study: 13-Month Follow-Up/Lonial et al
Cancer Month 0, 2021

P.G. started Belantamab-Mafodotin (EAP use) 2,5 mg/kg on **April 30, 2020 (C1d1)**

Baseline disease evaluation:
Severe RI, high FLC, thrombocytopenia

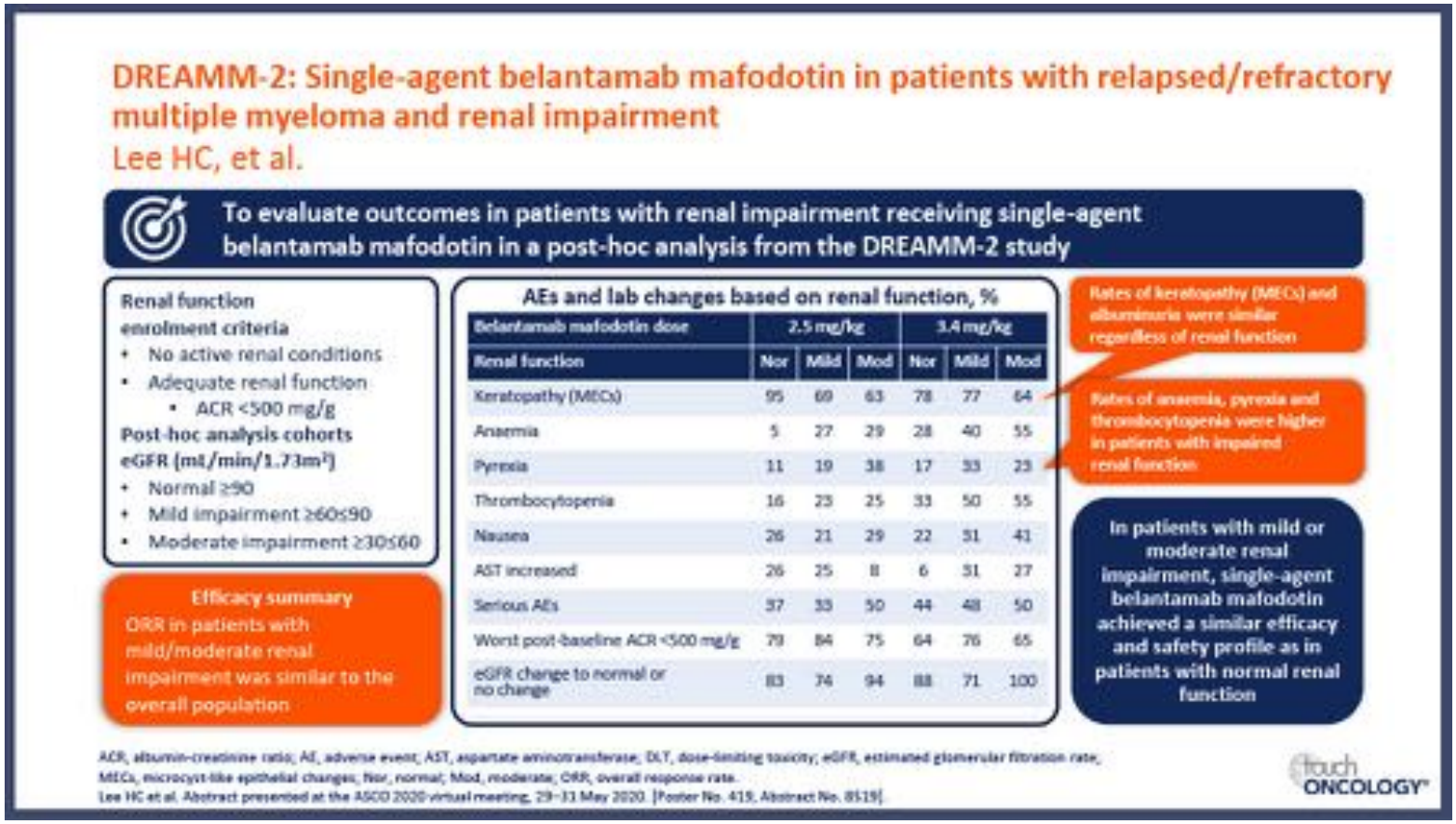
PROTEINE URINARIE	3,50 g/24h
PROTEINA BJ (Immunofissazione)	POSITIVA: presenza di catene leggere libere monoclonali di tipo kappa
PROTEINE URINARIE	1,75 g/l
PROTEINE URINE 24 h	3,50 g/24h
ELETTROFORESI URINE	Tracce di albumina Presenza di banda anomala di aspetto omogeneo
IMMUNOFISSAZIONE DEL SIERO	Presenza in zona gamma di componente monoclonale costituita da catene leggere libere di tipo kappa.
CATENE LEGGERE K LIBERE SIERO	6.620,0 mg/l
CATENE LEGGERE L LIBERE SIERO	14,6 mg/l
RAPPORTO K/L LIBERE SIERO	453,42

EMOCROMO	
WBC LEUCOCITI	8,28 x 10^3 /mmc
RBC ERITROCITI	2,78 x 10^6 / mmc
Hgb EMOGLOBINA	9,2 g/dl
Hct EMATOCRITO	29,3 %
MCV Volume globul.medio	105 fl
MCH Contenuto medio Hgb	33,1 pg
MCHC Conc.Corp.Media Hgb	31,4 g/dl
Ampiezza Dis. Er. (RDW-CV)	18,6 %
PIASTRINE	81 x 10^3 / mmc
Neutrofili %	69,60 %
Linfociti %	16,80 %
Monociti %	13,30 %
Eosinofili %	0,10 %
Basofili %	0,20 %
Luc %	
Blasti %	
Plasmacel. %	
Promiel. %	
Mielo+Metamielociti %	
Neutrofili	5,76 x 10^3 /mmc
Linfociti	1,39 x 10^3 /mmc
Monociti	1,10 x 10^3 /mmc
Eosinofili	0,01 x 10^3 /mmc

CREATININA	2,69 mg/dl
CKD-EPI eGFR	24 ml/min/1,73 mq
CKD-EPI eGFR	
CALCIO	9,3 mg/dl
SODIO	145 mEq/l
POTASSIO	4,5 mEq/l

Is Belamaf safe in patients with renal failure? **Yes**

Belantamab Mafodotin in renal failure setting



Timing of best response

- **VGPR (-95%) after 2 cycles** of therapy
- Great improvement of renal function (24 ml/min →82 ml/min) and of anemia (9.2 → 15.1 g/dl)

C1d1
30-apr-2020

C3d1
6-jul-2020

PROTEINE URINARIE	1,05 g/24h
PROTEINA BJ (Immunofissazione)	Positiva: presenza di catene leggere libere monoclonali di tipo kappa
PROTEINE URINARIE	0,51 g/l
PROTEINE URINE 24 h	1,05 g/24h
ELETTROFORESI URINE	Glomerulare mediamente selettivo
	Presenza di banda anomala di aspetto omogeneo
IMMUNOFISSAZIONE DEL SIERO	Presenza in zona gamma di componente monoclonale costituita da catene leggere libere di tipo kappa
CATENE LEGGERE K LIBERE SIERO	322,0 mg/l
CATENE LEGGERE L LIBERE SIERO	7,6 mg/l
RAPPORTO K/L LIBERE SIERO	42,37

CALCIO	9,2 mg/dl
SODIO	141 mEq/l
POTASSIO	4,3 mEq/l
	Risultato sovrastimato per emolisi
CREATININA	1,02 mg/dl
CREATININA URINARIA	59,00 mg/dl
CREATININA CLEARANCE	82 ml/min

EMOCROMO	
WBC LEUCOCITI	5,37 x 10^3 /mmc
RBC ERITROCITI	4,50 x 10^6 / mmc
Hgb EMOGLOBINA	15,1 g/dl
Hct EMATOCRITO	46,5 %
MCV Volume globul.medio	103 fl
MCH Contenuto medio Hgb	33,6 pg
MCHC Conc.Corp.Media Hgb	32,5 g/dl
Ampiezza Dis. Er. (RDW-CV)	14,9 %
PIASTRINE	43 x 10^3 / mmc
Neutrofili %	66,90 %
Linfociti %	21,00 %
Monociti %	11,40 %
Eosinofili %	0,00 %
Basofili %	0,70 %
Luc %	
Blasti %	
Plasmacel. %	
Promiel. %	
Mielo+Metamielociti %	
Neutrofili	3,59 x 10^3 /mmc
Linfociti	1,13 x 10^3 /mmc
Monociti	0,61 x 10^3 /mmc
Eosinofili	0,00 x 10^3 /mmc

Progression free survival

- **Biochemical relapse?** **(only proteinuria increase)**
- Normal FLC, renal and bone marrow functions

C1d1
30-apr-2020

PFS = 6 months?

C8d1
9-nov-2020

PROTEINE URINARIE	2,69 g/24h
PROTEINA BJ (Immunofissazione)	Positiva: presenza di catene leggere libere monoclonali di tipo kappa
PROTEINE URINARIE	1,79 g/l
PROTEINE URINE 24 h	2,69 g/24h
ELETTROFORESI URINE	Glomerulare non selettivo
IMMUNOFISSAZIONE DEL SIERO	Non evidenti ispessimenti omogenei monoclonali a carico di immunoglobuline e/o catene leggere
CATENE LEGGERE K LIBERE SIERO	23,8 mg/l
CATENE LEGGERE L LIBERE SIERO	8,1 mg/l
RAPPORTO K/L LIBERE SIERO	2,94

CALCIO	8,9 mg/dl
SODIO	141 mEq/l
POTASSIO	3,6 mEq/l
CREATININA	1,00 mg/dl
CREATININA URINARIA	84,00 mg/dl
CREATININA CLEARANCE	87 ml/min

EMOCROMO	
WBC LEUCOCITI	6,36 x 10^3 /mmc
RBC ERITROCITI	4,65 x 10^6 / mmc
Hgb EMOGLOBINA	15,0 g/dl
Hct EMATOCRITO	46,0 %
MCV Volume globul.medio	99 fl
MCH Contenuto medio Hgb	32,3 pg
MCHC Conc.Corp.Media Hgb	32,6 g/dl
Ampiezza Dis. Er. (RDW-CV)	15,7 %
PIASTRINE	66 x 10^3 / mmc
Neutrofili %	62,00 %
Linfociti %	21,40 %
Monociti %	15,40 %
Eosinofili %	0,60 %
Basofili %	0,60 %
Luc %	
Blasti %	
Plasmacel. %	
Promiel. %	
Mielo+Metamielociti %	
Neutrofili	3,94 x 10^3 /mmc
Linfociti	1,36 x 10^3 /mmc
Monociti	0,98 x 10^3 /mmc
Eosinofili	0,04 x 10^3 /mmc

Duration of Response

- **Clinical relapse**
- **Renal failure (82 ml/min →25 ml/min) and thrombocytopenia**

C1d1
30-Apr-2020

DoR = 10 months

C12d1
4-Mar-2021

STOP THERAPY

PROTEINE URINARIE	7,04 g/24h
PROTEINA BJ (Immunofissazione)	Positiva: presenza di catene leggere libere monoclonali di tipo kappa
PROTEINE URINARIE	4,02 g/l
PROTEINE URINE 24 h	7,04 g/24h
ELETTROFORESI URINE	Glomerulare non selettivo
IMMUNOFISSAZIONE DEL SIERO	Presenza di banda anomala di aspetto omogeneo Presenza in zona beta di componente monoclonale costituita da catene leggere libere di tipo kappa.
CATENE LEGGERE K LIBERE SIERO	6.360,0 mg/l
CATENE LEGGERE L LIBERE SIERO	10,8 mg/l
RAPPORTO K/L LIBERE SIERO	588,88

CREATININA	2,64 mg/dl
CKD-EPI eGFR	25 ml/min/1,73 mq
CKD-EPI eGFR	

ENOCROMO	
WBC LEUCOCITI	5,76 x 10^3 /mmc
RBC ERITROCITI	3,99 x 10^6 / mmc
Hgb EMOGLOBINA	12,7 g/dl
Hct EMATOCRITO	38,0 %
MCV Volume globul.medio	95 fl
MCH Contenuto medio Hgb	31,8 pg
MCHC Conc.Corp.Media Hgb	33,4 g/dl
Ampiezza Dis. Er. (RDW-CV)	16,8 %
PIASTRINE	16 x 10^3 / mmc
Neutrofili %	45,30 %
Linfociti %	29,30 %
Monociti %	15,80 %
Eosinofili %	0,00 %
Basofili %	1,60 %
Luc %	
Blasti %	
Plasmacel. %	
Promiel. %	
Mielo+Metamielociti %	8,00 %
Neutrofili	2,61 x 10^3 /mmc
Linfociti	1,69 x 10^3 /mmc
Monociti	0,91 x 10^3 /mmc
Eosinofili	0,00 x 10^3 /mmc

Ocular Monitoring

Ocular baseline evaluation

C1d1
30-Apr-2020

C2d1
22-May-2020

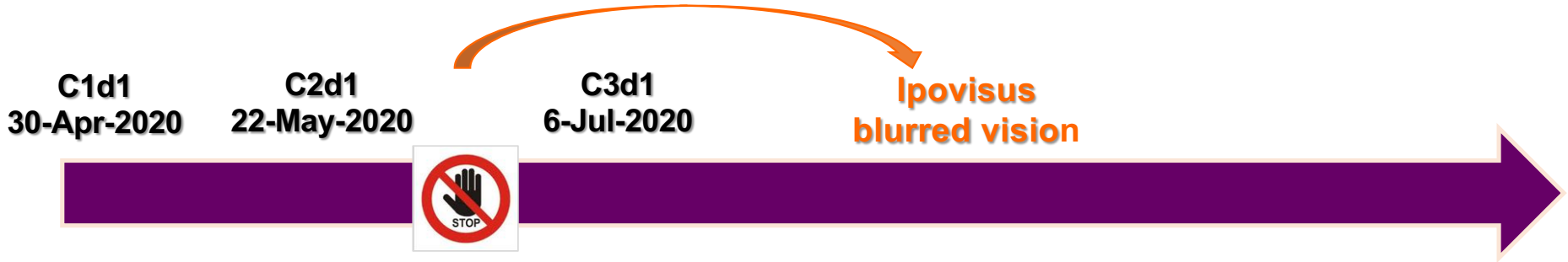
Visita oculistica (29/04/2020): VOD 10/10, VOS 8/10. No cheratopatia. Iniziale cataratta occhio sx.
Fundus oculi: nella norma dx, pucker maculare con iniziale foro a sx.

Visita oculistica (18/05/2020, post-I ciclo): VOD 10/10, VOS 7/10. No cheratopatia. Iniziale cataratta occhio sx.
Fundus oculi: nella norma dx, foro maculare a sx.

Grade 1 ocular toxicity: decline of 1 line on Snellen Visual Acuity → What should we have done?

Continue Belantamab full dose

Ocular Monitoring



Visita oculistica (11/06/2020, post-II ciclo): VOD 6/10, VOS 5/10 (baseline: VOD 10/10, VOS 8/10). Disepitelizzazione corneale severa superficiale, con notevole calo del visus. Utile visita oculistica a breve

Grade 3 ocular toxicity: STOP Belantamab C3d1 (12-Jun-2021)

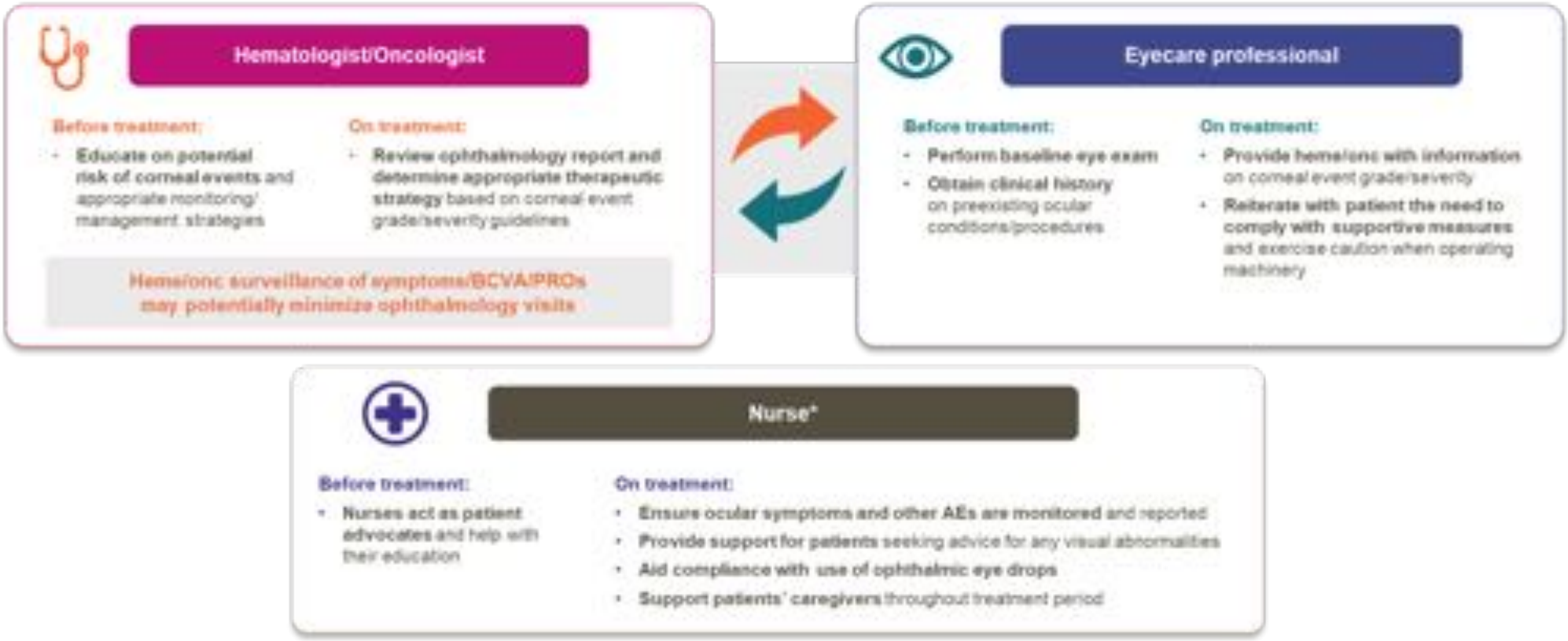
Visita oculistica (24/06/2020): VOD 6/10, VOS 6/10. Permane moderata disepitelizzazione corneale

Visita oculistica (01/07/2020): VOD 8/10, VOS 7/10. Lieve disepitelizzazione corneale

Visita oculistica (06/07/2020): VOD 9/10, VOS 8/10. In risoluzione disepitelizzazione corneale

Grade 1 ocular toxicity: restart infusion at reduced dose (06-Jul-2021)

A multidisciplinary team approach to treating patients on belantamab mafodotin



*This content is based on Dr. Popat's clinical opinion/experience.

AE, adverse event; BCVA, best-corrected visual acuity; heme/onc, hematologist/oncologist; PRO, patient-reported outcome.

Lonial S et al. *Blood Cancer J.* 2021;11:103.

Key roles of the hematologist-oncologist in managing corneal AEs with belantamab mafodotin

1 Advise patients

Corneal AEs may occur during treatment

Avoid contact lenses until the end of treatment

Use caution when driving or operating machinery as treatment may affect their vision

Ophthalmic examinations will be performed

2 Help identify patients who need additional monitoring and/or management by an eye care professional

AE, adverse event.

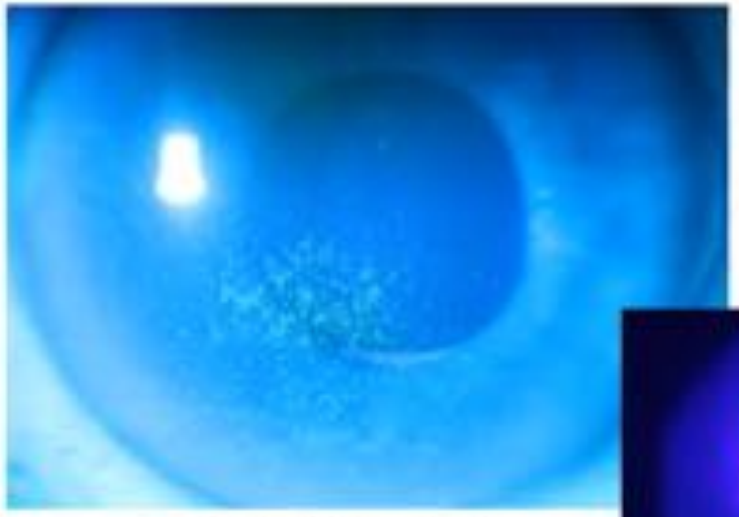
BLENREP. Corneal guide for eye care professionals. GlaxoSmithKline; 2020.

Corneal exam findings (keratopathy*), together with BCVA changes, guide dose modifications of belantamab mafodotin

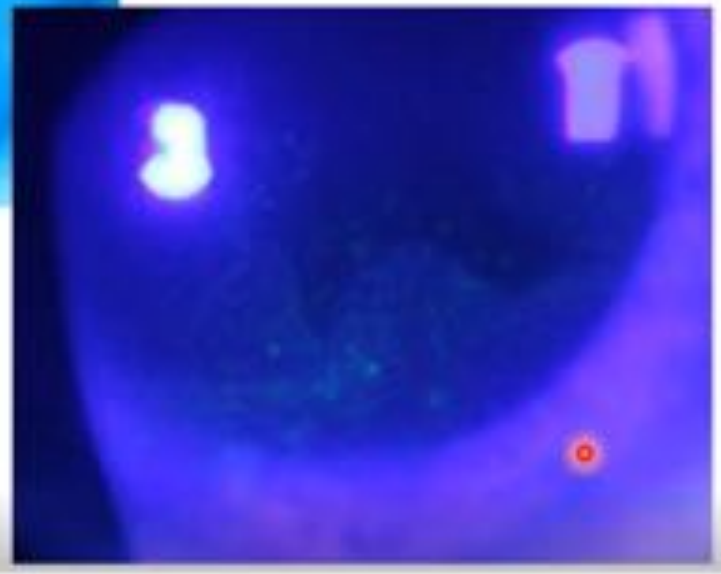
Severity[†]	Corneal examination finding(s)[‡]		Presentation of MECs[‡,¶]	Corneal AE management
	Change in BCVA	Description	Example schematics by severity	Recommended dose modifications
Grade 1/ Mild	Decline from baseline of 1 line on Snellen VA test	**Mild superficial keratopathy*[§]** (documented worsening from baseline), with or without symptoms		**Continue treatment** at current dose
Grade 2/ Moderate	Decline from baseline of 2 or 3 lines (and Snellen VA not worse than 20/200)	**Moderate superficial keratopathy*[§]** with or without patchy MECs, subepithelial haze (peripheral), or a new peripheral stromal opacity	 Dots represent MECs	**Withhold treatment** until improvement and BCVA reduction is of mild severity or better Resume at reduced dose of 1.9mg/kg
Grade 3/ Severe	Decline from baseline of more than 3 lines (and Snellen VA not worse than 20/200)	**Severe superficial keratopathy*[§]** with or without diffuse MECs involving the central cornea, subepithelial haze (central), or a new central stromal opacity		**Withhold treatment** until improvement and BCVA reduction is grade 1/mild Resume at reduced dose of 1.9mg/kg[‖]
Grade 4/ Severe	Snellen VA worse than 20/200	**Corneal epithelial defect,** including corneal ulcers. These should be managed promptly and as clinically indicated by an eyecare professional	N/A	**Withhold treatment** until improvement and BCVA reduction is of mild severity or better. For worsening symptoms, **consider discontinuing** Resume at reduced dose of 1.9mg/kg[‖]

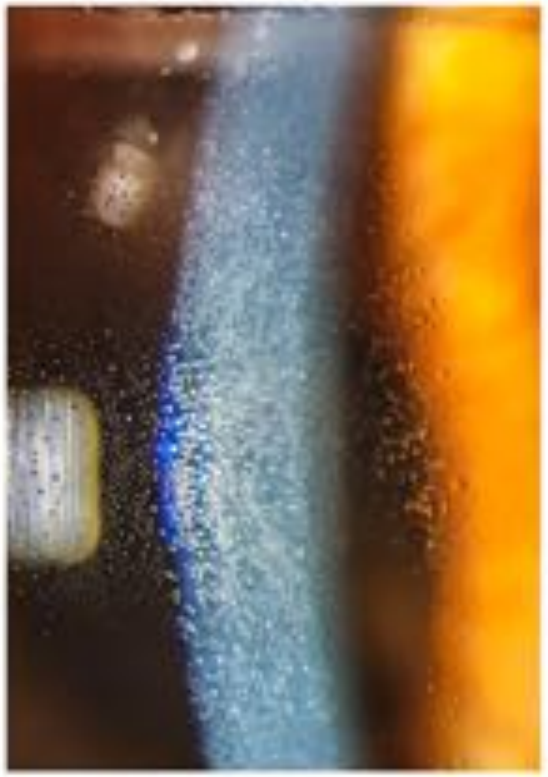
Lonial S, Nooka AK, Thulasi P, et al. Management of belantamab mafodotin-associated corneal events in patients with relapsed or refractory multiple myeloma (RRMM). *Blood Cancer J*. 2021;11:103.

Changes in the corneal epithelium treated pt



Punctate keratopathy





Microcyst-like epithelial changes

DREAMM-2 Results: Safety from 13-month Follow-up

The Most Frequent Ocular Symptoms Were Dry Eye, Blurred Vision or a Decline in BCVA

Adverse Events (any grade) of Special Interest*	Belantamab Mafodotin 2.5 mg/kg (N = 95)
Thrombocytopenia†	36 (38)
IRRs**	20 (21)
Keratopathy (MECs) ‡	68 (72)

BCVA and Other Ocular Symptoms	Belantamab Mafodotin 2.5 mg/kg (N = 95)
Change in BCVA	51 (54)
Other Ocular Symptoms	
Blurred vision§	24 (25)
Dry eye¶	14 (15)

These charts have been independently created by GSK from original data first presented in Lonial S et al. Cancer. 2021.

*Values expressed as n (%) unless otherwise noted.
†Thrombocytopenia (considered an adverse event of special interest) includes preferred terms thrombocytopenia and platelet count decreased.
**Infusion-related reactions (considered an adverse event of special interest) includes preferred terms infusion-related reaction, pyrexia, chills, diarrhea, nausea, asthenia, hypertension, lethargy, and tachycardia occurring within 24 hours of infusion.
‡Changes in the corneal epithelium observed on eye examination. Graded per protocol defined scale which was renamed as the Keratopathy and Visual Acuity scale.
§Blurred vision includes preferred terms vision blurred, diplopia, visual acuity reduced, and visual impairment.
¶Dry eye includes preferred terms dry eye, ocular discomfort, and eye pruritus.

AE = adverse event; BCVA = best-corrected visual acuity; IRR = infusion-related reaction; MEC = microcyst-like epithelial change.

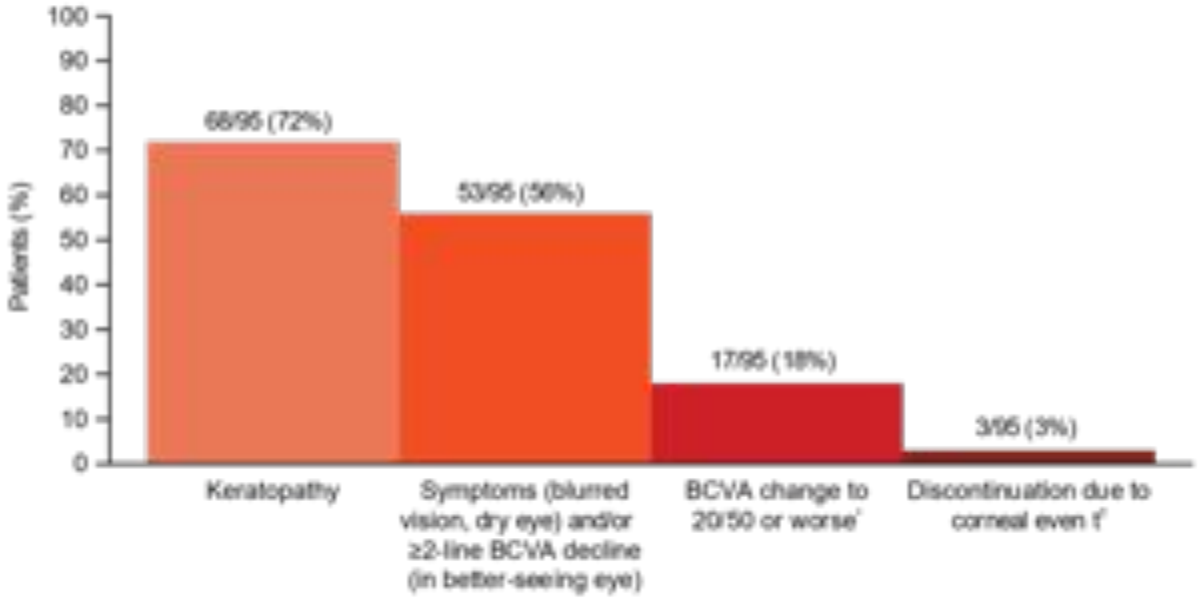
Lonial S et al. Cancer. 2021.

Grade 3/4 symptoms were less common. **This included dry eye (1%) and blurred vision (4%)**

DREAMM-2 Results: Safety from 13-month Follow-up

Keratopathy can occur with or without symptoms

Frequency of ocular symptoms in patients treated with belantamab mafodotin 2.5 mg/kg in DREAMM-2 (n=95)



- 82% of patients without clinically significant visual acuity change*
- No new safety signals observed at 13-month follow-up
- 1 patient developed a Grade 4 corneal ulcer¶

This figure has been independently created by GSK from data first presented in Lonial S et al. Cancer. 2021.

*Clinically meaningful BCVA change represents a BCVA of Snellen Visual Acuity 20/50 or worse in the better-seeing eye; †Discontinuation included 1 patient the keratopathy, 1 patient with blurred vision, and 1 patient with reduced visual acuity. ¶CTCAE scale event grading: 1 patient (with a history of cataract surgery in the right eye) developed a central corneal ulcer that resolved 9 days after onset with the use of topical antibiotics
BCVA = best-corrected visual acuity; MEC = microcyst-like epithelial change.
1. Lonial S et al. Presented at the 62nd American Society of Hematology Annual Meeting. 2020; 2. Lonial S et al. Cancer. 2021.

DREAMM-2 Results: Safety from 13-month Follow-up

Dose Modifications and Discontinuations

n (%)	Belantamab Mafodotin 2.5 mg/kg (N = 95)
AEs leading to dose delays*	**51 (54)**
Dose delays due to keratopathy (MECs)	45 (47)
AEs leading to dose reductions	33 (35)
Dose reductions due to keratopathy (MECs)	**24 (25)**
AEs leading to permanent treatment discontinuation	9 (9)
Discontinuation due to keratopathy (MECs†)	**1 (1)**
Discontinuation due to patient-reported AEs/symptoms	2 (2)‡

This chart has been independently created by GSK from original data first presented in Lonial S et al. Cancer 2021

*Dose delays of any duration, including but not limited to delays >63 days
†an eye examination finding
‡ Blurred vision or change in BCVA (n = 1 each)

Most dose delays and reductions were due to keratopathy (MECs). Ocular symptoms were **generally managed** with frequent application of preservative-free lubricant eye-drops, and by dose modification (reduction and/or delay) or treatment discontinuation

Ocular symptoms **continued to resolve** with additional patient follow-up

AE = adverse event; BCVA = best-corrected visual acuity; MEC = microcyst-like epithelial change

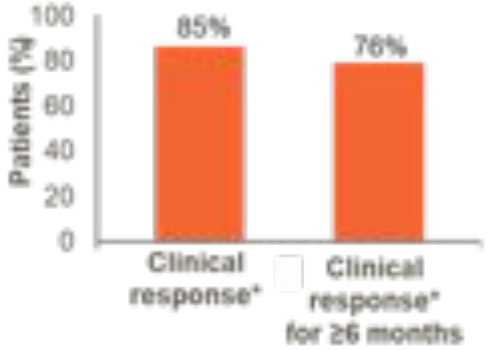
Lonial S et al. Cancer 2021

Patients in DREAMM-2 were effectively managed with dose modifications, allowing for continued clinical benefit with belantamab mafodotin treatment

14 patients were analyzed at a follow-up of ≥12 months in a post hoc analysis of DREAMM-2

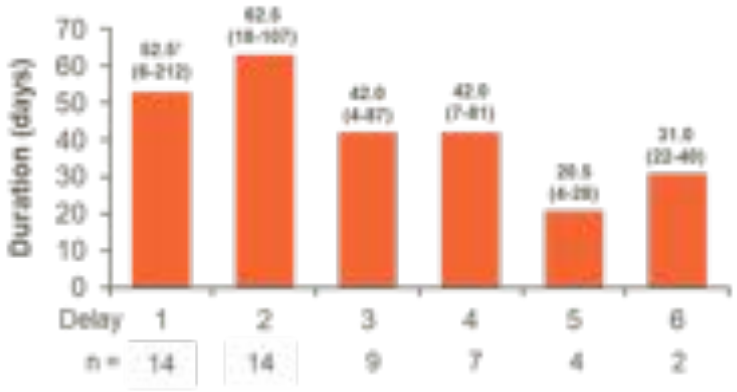
- All patients had **at least 2 dose holds,** 10 of whom had holds **lasting longer than 63 days**
- At the cutoff mark, the **mDOR was 12.5 months**

Percentages of patients with clinical response or clinical response ≥6 months



5 of the 10 patients with a dose delay >63 days had a VGPR or CR

Median duration of dose delays



Duration of delays tended to decrease over the course of treatment.
The median duration of delay was 42 days (range: 4-212).
The median latency until the first delay was 66.5 days (range: 22-213)

*Defined as a partial response or better. †Median (range).
CR, complete response; mDOR, median duration of response; VGPR, very good partial response.
Lonial S et al. Poster presented at: European Hematology Association Virtual Congress; June 9-17, 2021. Poster 1026.

Ocular Monitoring

C4d1 31-jul-2020	Visita oculistica (31/07): VOD 9/10, VOS 8/10. In risoluzione disepitelizzazione corneale. Stabile cataratta occhio sx
C5d1 17-aug-2020	Visita oculistica (17/08): VOD 9/10, VOS 8/10. In risoluzione disepitelizzazione corneale. Stabile cataratta occhio sx
C6d1 24-sep-2020	Visita oculistica (24/09): VOD 9/10, VOS 8/10. Non più disepitelizzazione corneale. Stabile cataratta occhio sx
C7d1 19-oct-2020	Visita oculistica (19/11): VOD 10/10, VOS 8/10. Cornea nei limiti. Cataratta in peggioramento occhio sx
C8d1 09-nov-2020	Visita oculistica (09/11): VOD 10/10, VOS 8/10. Cornea nei limiti. Cataratta occhio sx stabile
C9d1 31-nov-2020	Visita oculistica (31/11): VOD 10/10, VOS 8/10. Cornea nei limiti. Cataratta occhio sx stabile
C10d1 21-jan-2021	Visita oculistica (21/01/2021): VOD 10/10, VOS 8/10. Cornea nei limiti. Cataratta occhio sx stabile
C11d1 11-feb-2021	Visita oculistica (11/02/2021): VOD 10/10, VOS 8/10. Cornea nei limiti. Cataratta occhio sx stabile

Stable BCVA and ocular findings: continued Belantamab at reduced dose

When do we conduct ophtalmic examination?

Management of Corneal Symptoms

Recommended Monitoring, Diagnosis, and Management Techniques

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*

*Follow-up eye examination recommendations differ regionally. Eye examinations must be conducted before every dose in the U.S. but are required only before the first three treatment cycles in the E.U. Additional eye examinations are required as needed in both regions.

1. Farooq AV et al. Ophthalmol Ther. 2020; 2. Lonial S et al. Blood Cancer J. 2021.

Is prophylactic steroid drops useful? **No**

Recommendations on the use of prophylactic therapy and frequency of ophthalmic exams to manage corneal AEs

Prophylactic measure	Dose and administration	Interval
Preservative-free eye drops[1-3]	Administer in each eye at least 4 to 8 times daily	Administer daily beginning on cycle 1, day 1 until end of treatment
Cooling eye mask[2,3]	May apply to both eyes for approximately 1 hour or as long as tolerated	During belantamab mafodotin infusion administration in the first hour for up to 4 hours, as tolerated
Bandage contact lens[4]	Currently under evaluation in DREAMM-3*	

The DREAMM-2 ocular substudy reported **no benefit** from using **prophylactic corticosteroid drops** to the development of corneal epitheliopathy compared with lubricant eye drops alone, but a short pulse may help relieve symptoms and can be used at the discretion of the eye care professional[5]

Management of corneal AEs	Frequency
Ophthalmic exams[6]	Visual acuity and slit lamp exams should be performed at baseline, before the subsequent 3 treatment cycles, and as clinically indicated during treatment

*DREAMM-3 is a phase III study of belantamab mafodotin compared to pomalidomide/dexamethasone in RRMM.[4]

AE, adverse event; RRMM, relapsed/refractory multiple myeloma

1. BLENREP. Summary of Product Characteristics. GlaxoSmithKline (Ireland) Ltd; 2021. 2. BLENREP German Expanded Access Program. GlaxoSmithKline Research & Development Ltd; 2020. 3. BLENREP French cohort ATU/EAP SmPC. GlaxoSmithKline Research & Development Ltd; 2020. 4. Data on file. GlaxoSmithKline; 2020. 5. Popat R et al. Haematologica. 2020;105(5):e261-e263. 6. BLENREP. Patient corneal event guide. GlaxoSmithKline; 2020.

Belantamab Mafodotin: Select AEs in DREAMM-2

AEs of Special Interest

- Corneal events: 72% to 77%
  - Blurred vision, dry eyes, photophobia, changes in visual acuity
  - Reversible and manageable with ophthalmic consult, steroid eye drops, dose reduction
- Thrombocytopenia: 36% to 57%
  - Hematologic AEs common in MM
- **Infusion-related reaction: 16% to 21%**
  - Occurs at first dose without premedication
  - Does not recur with subsequent doses

Grade ≥ 3 AEs in ≥ 5% of Patients, %	Bela maf 2.5 mg/kg (n = 97)	Bela maf 3.4 mg/kg (n = 99)
Any	84	84
Keratopathy	46	42
Anemia	21	27
Thrombocytopenia	22	32
Decreased lymphocyte count	13	7
Neutropenia	11	17
Hypercalcemia	7	3
Pneumonia	7	13
GGT increase	3	9
Hypertension	4	7
AST increase	2	8
Fatigue	2	5

Is premedication required? **No**

Lonial. ASCO 2020. Abstr 8536.

Thrombocytopenia

Belantamab Mafodotin: Select AEs in DREAMM-2

AEs of Special Interest

- Corneal events: 72% to 77%
  - Blurred vision, dry eyes, photophobia, changes in visual acuity
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GGT increase	3	9
Hypertension	4	7
AST increase	2	8
Fatigue	2	5

Lonial. ASCO 2020. Abstr 8536.

baseline

WBC LEUCOCITI	10,86 x 10^3 /mmc
RBC ERITROCITI	2,79 x 10^6 / mmc
Hgb EMOGLOBINA	9,5 g/dl
Hct EMATOCRITO	29,3 %
MCV Volume globul.medio	105 fl
MCH Contenuto medio Hgb	34,1 pg
MCHC Conc.Corp.Media Hgb	32,4 g/dl
Ampiezza Dis. Er. (RDW-CV)	18,1 %
PIASTRINE	64 x 10^3 / mmc
Neutrofili %	80,00 %
Linfociti %	9,50 %
Monociti %	10,00 %
Eosinofili %	0,00 %
Basofili %	0,50 %

C1d1
30-Apr-2020

WBC LEUCOCITI	6,36 x 10^3 /mmc
RBC ERITROCITI	4,65 x 10^6 / mmc
Hgb EMOGLOBINA	15,0 g/dl
Hct EMATOCRITO	46,0 %
MCV Volume globul.medio	99 fl
MCH Contenuto medio Hgb	32,3 pg
MCHC Conc.Corp.Media Hgb	32,6 g/dl
Ampiezza Dis. Er. (RDW-CV)	15,7 %
PIASTRINE	66 x 10^3 / mmc
Neutrofili %	62,00 %
Linfociti %	21,40 %
Monociti %	15,40 %
Eosinofili %	0,60 %
Basofili %	0,60 %

C8d1
9-Nov-2020

C10d1
21-Jan-2021

WBC LEUCOCITI	6,39 x 10^3 /mmc
RBC ERITROCITI	5,18 x 10^6 / mmc
Hgb EMOGLOBINA	16,7 g/dl
Hct EMATOCRITO	51,6 %
MCV Volume globul.medio	100 fl
MCH Contenuto medio Hgb	32,2 pg
MCHC Conc.Corp.Media Hgb	32,4 g/dl
Ampiezza Dis. Er. (RDW-CV)	16,5 %
PIASTRINE	139 x 10^3 / mmc
Neutrofili %	62,10 %
Linfociti %	22,40 %
Monociti %	10,20 %
Eosinofili %	4,00 %
Basofili %	1,30 %

Resolution of thrombocytopenia

How to manage thrombocytopenia?

Adverse reaction	Severity	Recommended dosage modifications
Thrombocytopenia	Platelet count 25,000 to less than 50,000/mcL	**Consider withholding BLENREP and/or reducing the dose of BLENREP.**
	Platelet count less than 25,000/mcL	**Withhold BLENREP until platelet count improves to Grade 3 or better. Consider resuming at a reduced dose.**

C12d1
04-Mar-2021:
Clinical relapse

Return of severe thrombocytopenia

WBC LEUCOCITI	4,39 x 10^3 /mmc
RBC ERITROCITI	3,69 x 10^6 / mmc
Hgb EMOGLOBINA	12,6 g/dl
Hct EMATOCRITO	39,1 %
MCV Volume globul.medio	106 fl
MCH Contenuto medio Hgb	34,1 pg
MCHC Conc.Corp.Media Hgb	32,2 g/dl
Ampiezza Dis. Er. (RDW-CV)	17,4 %
PIASTRINE	23 x 10^3 / mmc
Neutrofili %	64,00 %
Linfociti %	20,00 %
Monociti %	14,50 %
Eosinofili %	1,00 %
Basofili %	0,50 %

11-Mar-2021

WBC LEUCOCITI	1,32 x 10^3 /mmc
RBC ERITROCITI	3,40 x 10^6 / mmc
Hgb EMOGLOBINA	10,8 g/dl
Hct EMATOCRITO	31,6 %
MCV Volume globul.medio	93 fl
MCH Contenuto medio Hgb	31,8 pg
MCHC Conc.Corp.Media Hgb	34,2 g/dl
Ampiezza Dis. Er. (RDW-CV)	16,1 %
PIASTRINE	5 x 10^3 / mmc
Neutrofili %	67,00 %
Linfociti %	26,00 %
Monociti %	6,00 %
Eosinofili %	0,00 %
Basofili %	0,00 %

Grazie