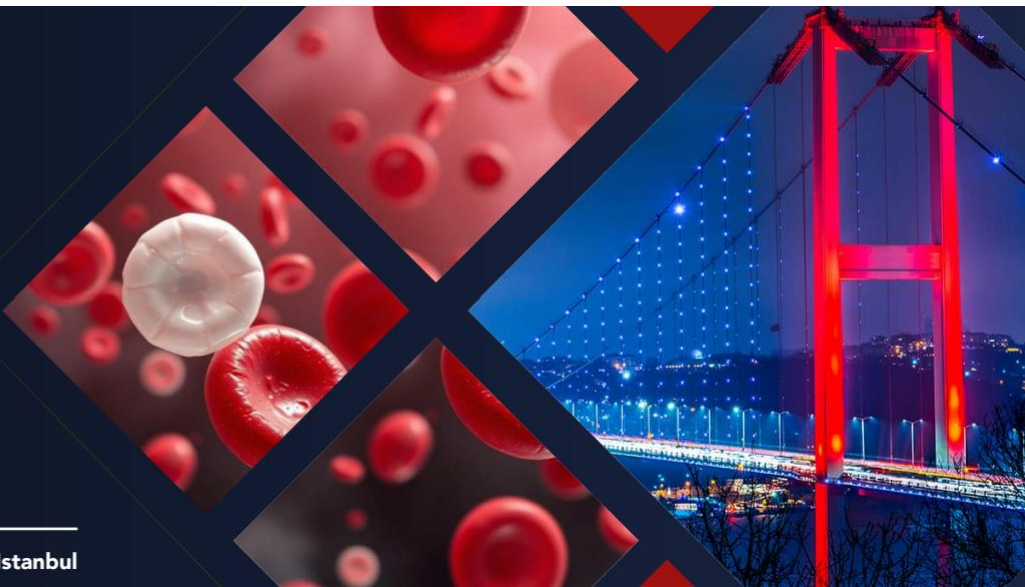


# BOSPHORUS MYELOMA FORUM 2026

*Treatment Sequencing in the Era of  
Cellular and Immune Therapies*



June 6, 2026 📍 The Ritz-Carlton Hotel, Istanbul



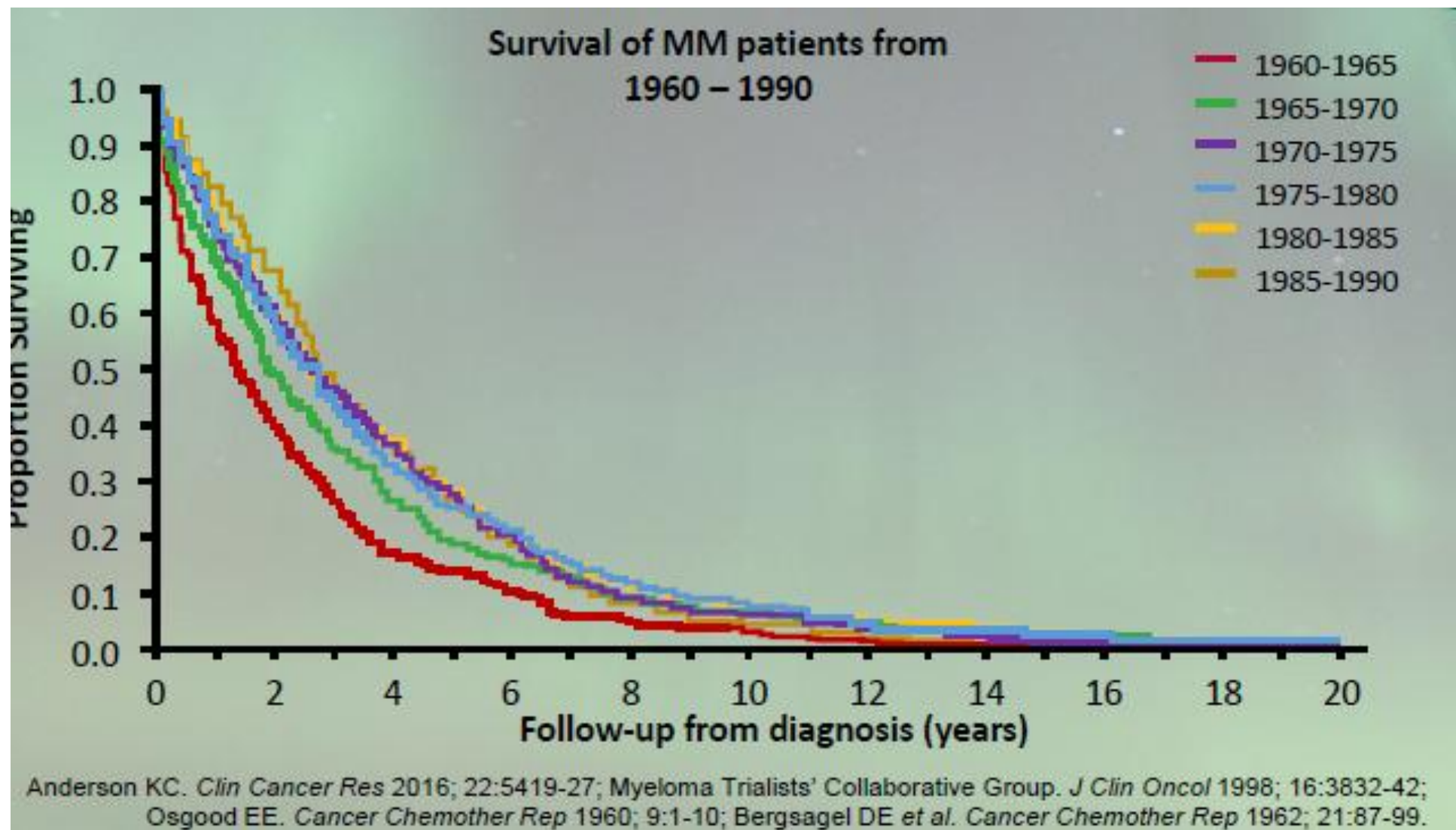
# The Role of XPO1 Inhibition and other Novel Agents

**Claudio Cerchione, MD, PhD**

Dirigente Medico Ricercatore and Lead of Multiple Myeloma in CCCRN Romagna

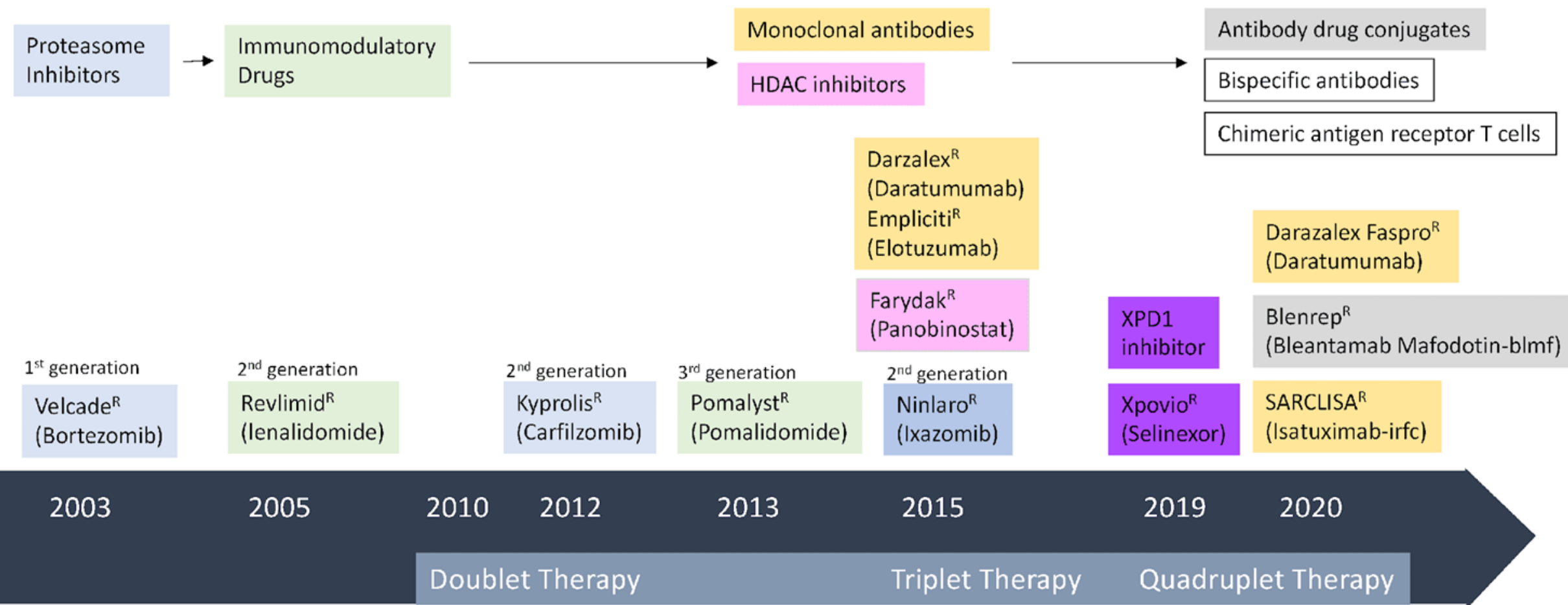
Hematology Unit - Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS Meldola (FC) – Italy

President of Society of Hematologic Oncology Italy (SOHO Italy)



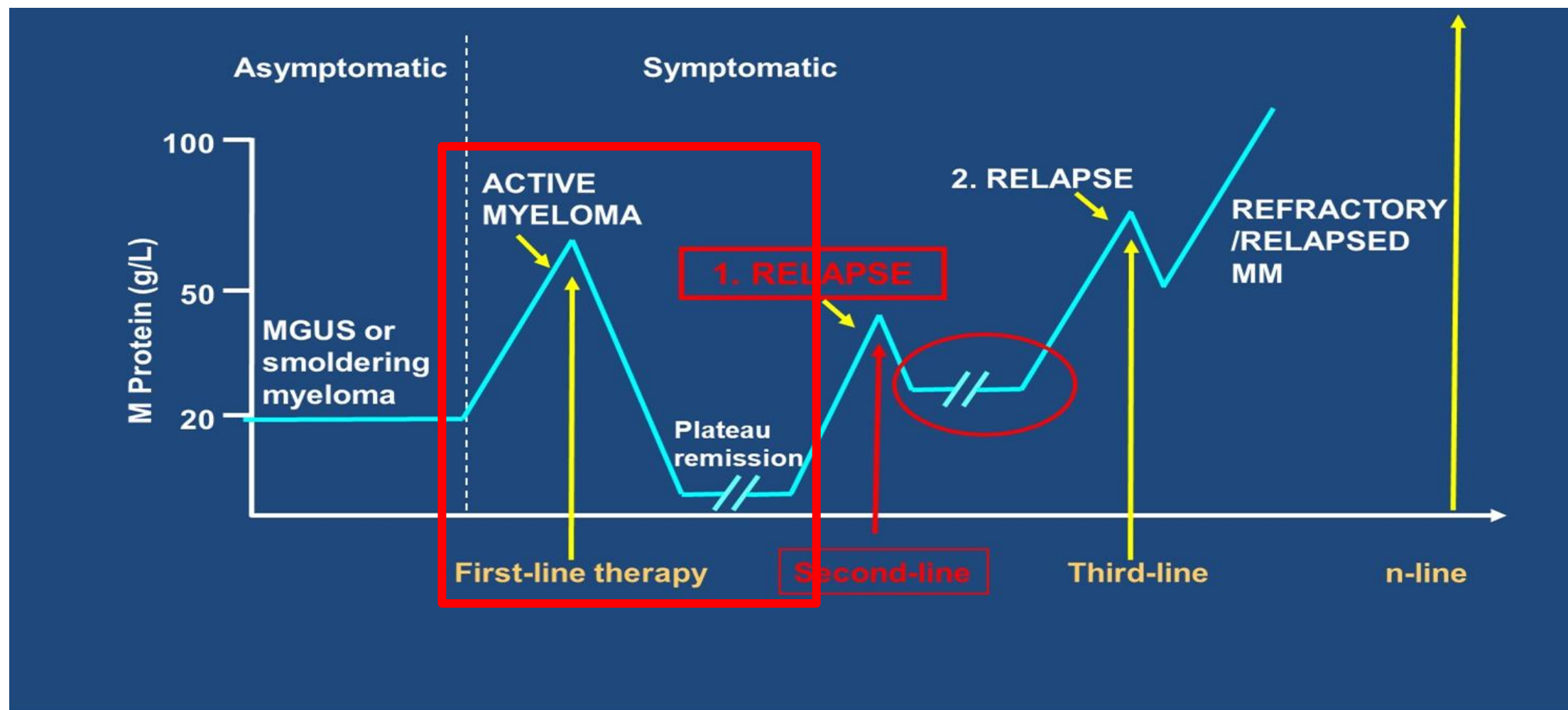


# The Therapeutic Revolution in Multiple Myeloma





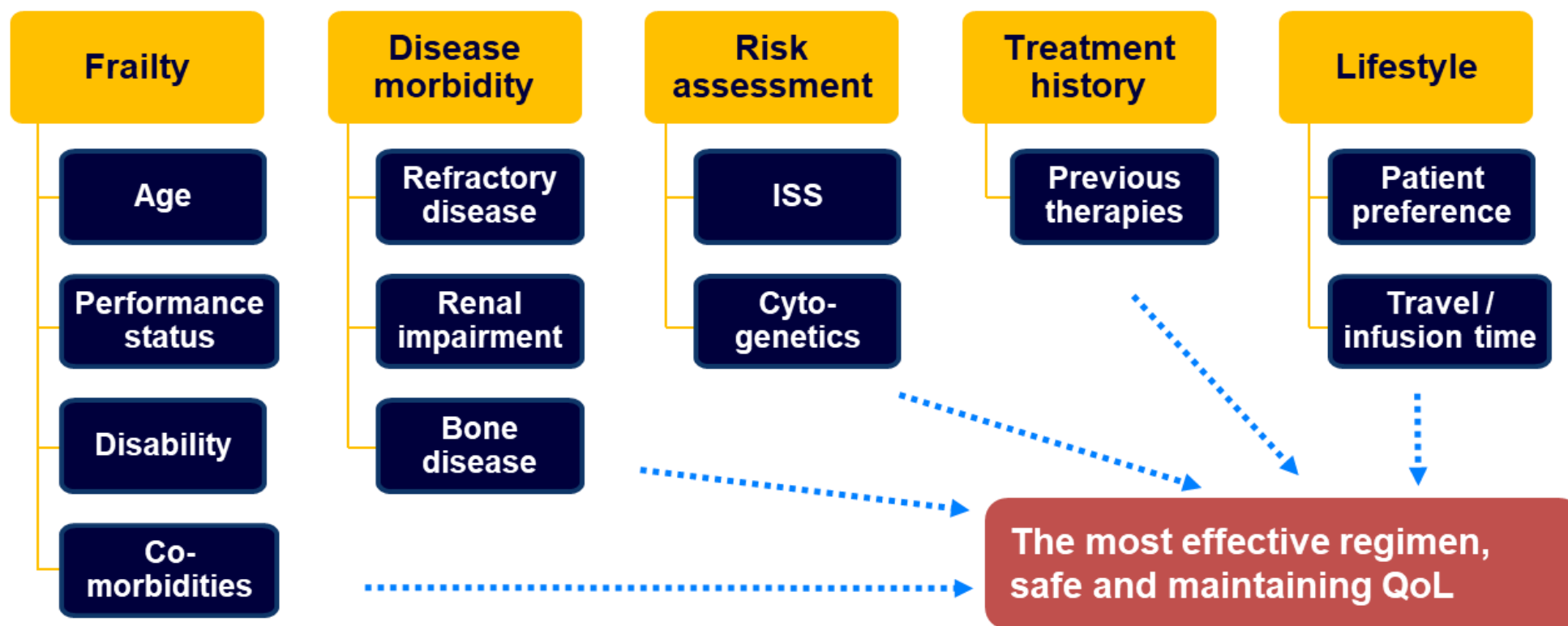
# The Natural History of Multiple Myeloma



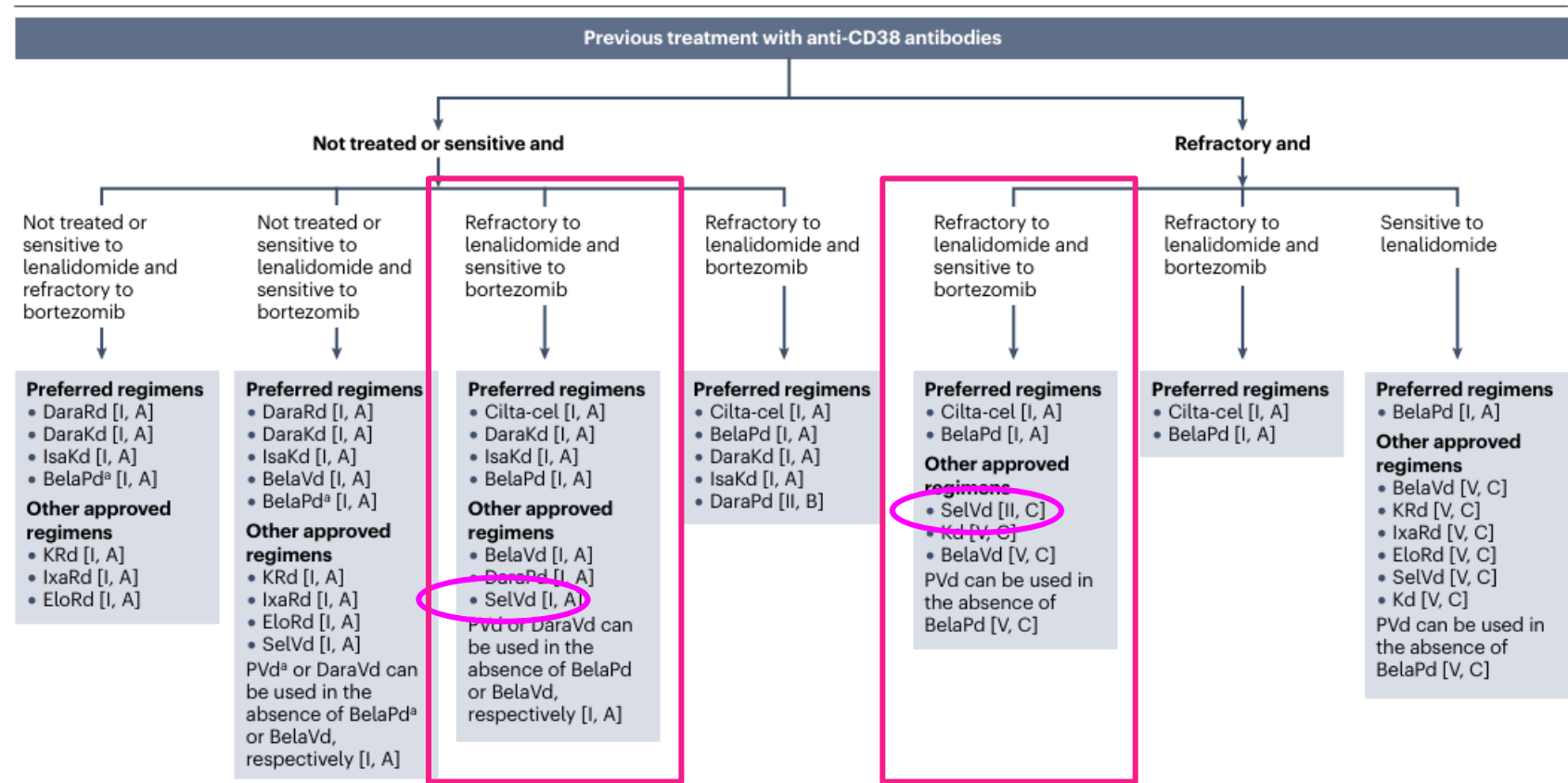




# Disease and Patient Factors Influence Treatment Choices in Relapsed Refractory MM



# EHA EMN Guidelines 2025



**SVd is recommended in the guidelines as an effective and safe treatment from the first relapse**

Dimopoulos MA, Terpos E, et al. Nat Rev Clin Oncol 2025

# TR National Guidelines: TREATMENT OPTIONS IN RELAPSED REFRACTORY MM

## AFTER 1 LINE OF TREATMENT

VRd in 1L	R-sensitive	KRd, D-Rd, PVd, D-Kd, IsaKd, IsaPd, IxaRd, Seli-Vd, KCd, KPd, PCd, EloRd
	R-refractory	PVd, D-Kd, IsaKd, IsaPd, Seli-Vd, KCd, KPd, PCd
	V-sensitive	KRd, D-Rd, EloRd, PVd, D-Kd, DVd, IsaKd, IsaPd, Seli-Vd, VenVd, KCd, KPd, PCd
	R/V-refractory	D-Kd, IsaKd, IsaPd, KCd, KPd, PCd
D-Rd in 1L	R-sensitive	PVd, Kd, EloRd, KRd, KCd, KPd, PCd, IxaRd, Seli-Vd, Seli-Pd, VenVd, VenKd
	R-refractory	PVd, Kd, Seli-Vd, Seli-Pd, VenVd, VenKd, KCd, KPd, PCd
D-VTd or D-VMP in 1L	V-sensitive	EloRd, KRd, IxaRd, VRd, Seli-Vd, Seli-Pd, Kd, VenVd, VenKd, PVd
	V-refractory	EloRd, KCd, KPd, PCd, Seli-Pd, VenKd

## ≥2 LINE OF TREATMENT

R/V-refractory	D-Kd, IsaPd, EloPd, IsaKd, D-Pd, Seli-Pd, VenKd
R-refractory, PI-sensitive	D-Kd, EloPd, IsaKd, IsaPd, D-Pd, D-Vd, Seli-Vd, Seli-Pd, VenVd, VenKd
Alternative (less preferred) options	PCd, daratumumab, panobinostat-based regimens
Triple class refractory patients	Clinical trials, Seli-d, belamaf, melflufen-deksa, venetoclax (Ven; if t(11;14) (+)), elranatamab, teclistamab, talquetamab, CAR-T



# REIMBURSED TREATMENT OPTIONS for RRMM in TR



1L

**ASCT Eligible:**  
Induction (4-6 cycles) – ASCT – Len Maintenance

**ASCT Ineligible:**  
Combination therapy according to risk stratification

2L

DRd / DVd

KRd / Kd

PVd

IxaRd

SVd

These are  
reimbursed 2L+

3L

DPd

IxaPd

Pd

These are  
reimbursed 3L+

5L

Elranatamab

• 25.03.2025 tarihli ve 32852 sayılı SUT Değişiklik Tebliğine göre uyarlanmıştır. Daha ayrıntılı bilgi için sağlık uygulama tebliğine bakınız. <https://www.sgk.gov.tr/>



# Len-Refractory Patients



## RRMM Reimbursed Treatment Options In Türkiye\*

1L

ASCT Eligible:  
Induction (4-6 cycles) – ASCT – Len Maintenance

ASCT Ineligible:  
Combination therapy according to risk stratification

2L

~~DRd~~ / DVd

KRd / Kd

PVd

lxaRd

SVd

These are  
reimbursed 2L+

3L

DPd


lxaPd

Pd


These are  
reimbursed 3L+

5L


Elranatamab



SERVIZIO SANITARIO REGIONALE  
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Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori  
Istituto di Ricerca e Cura e Centro Scientifico




ISTITUTO SCIENTIFICO ROMAGNOLO  
PER LO STUDIO E LA CURA  
DEI TUMORI



10  
anni

# Treatment Options for Len-ref Patients In Key Phase III Studies



BOSPHORUS  
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FORUM 2026  
Treatment Evolving in the Era of  
Cellular and Immune Therapies  
June 6-7, 2026 | The Bosphorus Hotel, Istanbul

mPFS in investigational arms for lenalidomide subgroups		CASTOR <sup>3,4</sup> DVd vs Vd	APOLLO <sup>6</sup> DPd vs Pd	ICARIA-MM <sup>9</sup> IsaPd-Pd	OPTMISMM <sup>2</sup> PVd vs Vd	ENDEAVOR <sup>5</sup> Kd vs Vd	BOSTON <sup>1,7</sup> SVd vs Vd
ITT	n	251	151	154	281	287	195
	mPFS	16.7 mo	12.4 mo	11.5 mo	11.2 mo	22.2 mo	13.9 mo
Len refractory	n	60	120	144	200	113	53
	mPFS	7.8 mo	9.9 mo	11.4 mo <sup>10</sup>	9.5 mo	8.6 mo	13.9* mo <sup>8</sup>

\*patients who were managed with dose reduction EHA 2025

In the absence of head-to-head studies, comparisons of efficacy and safety should not be made, or conclusions should ne be drawn.

The Role of XPO1 Inhibition and other Novel Agents

Bosphorus Myeloma Forum 2026 – 6 June 2026 - Istanbul

Dr. Claudio Cerchione, MD, PhD

IRST IRCCS Meldola (FC)

1. Grosicki S, et al. Lancet. 2020;396(10262):1563-1573. 2. Richardson PG, et al. Lancet Oncol 2019;20:781-94; 3. Weisel K, et al. ASH 2019, abstract 3192; 4. Usmani SZ, et al. ASH 2018, abstract 3288; 5. Moreau P, et al. Leukemia 2016;31:115-22; 6. Dimopoulos MA, et al. ASH 2020, abstract O412.; 7. Mateos MV, Engelhardt M, Leleu X, et al. Eur J Haematol. 2024;113(2):242-252. 8.Sosana Delimpasi Abstract: PF743 EHA Library. Delimpasi S. 06/13/2025; 4160150; Impact of selinexor dose reductions on selinexor, bortezomib, dexamethasone (SVd) outcomes in patients with lenalidomide with refractory multiple myeloma: BOSTON trial subgroup analysis 9. Richardson, P. G., Perrot, A., San-Miguel, J. F., Beksac, M., Spicka, I., Ocio, E. M. ICARIA-MM Study Group. (2022).



# Selinexor is a first in class treatment with a unique MOA<sup>1-4</sup>

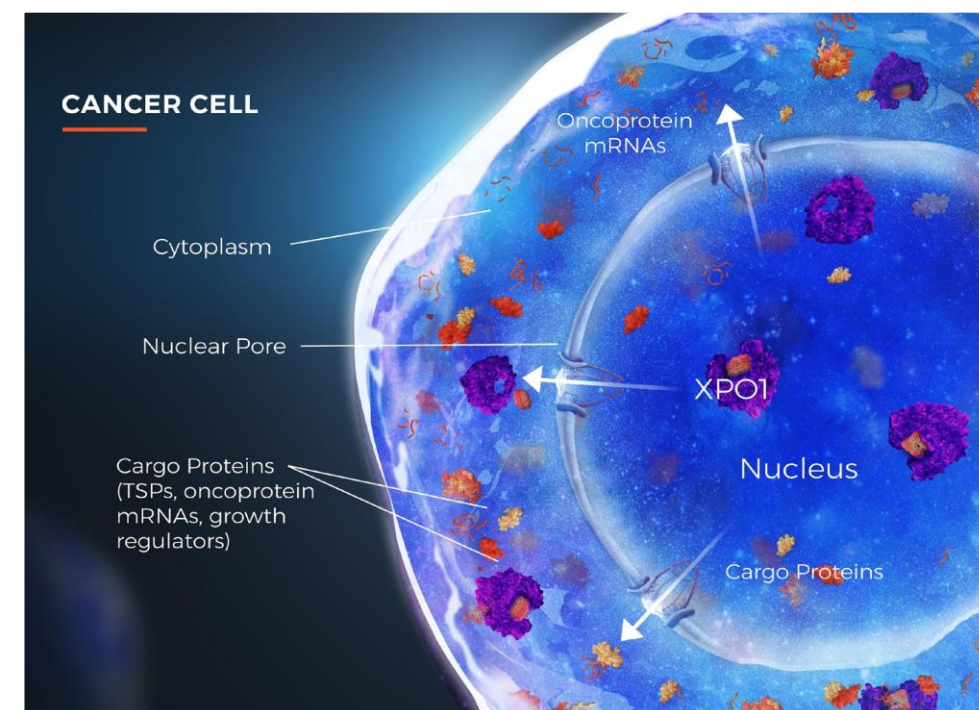


## XPO1 overexpression:<sup>5,6</sup>

- Inactivates tumour suppressor proteins
- Enhances proto-oncogene translation
- Disrupts growth regulation, promoting sustained cellular proliferation

## Selinexor:<sup>1-4</sup>

- Blocks XPO1 so that it cannot carry cargos out of the nucleus
- The cargos accumulate in the nucleus
- This accumulation causes cell cycle arrest and apoptosis

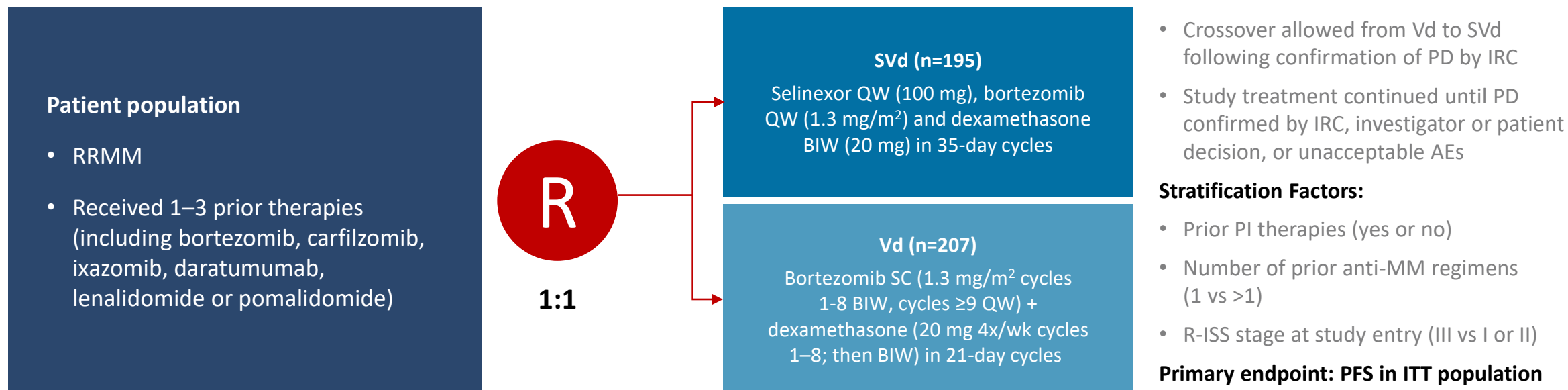


Adapted from Sun Q, et al. *Signal Transduct Target Ther.* 2016.

Based on results from the Phase 3 BOSTON study, SVd is indicated for adults with RRMM who have received at least one prior therapy<sup>1,7</sup>

Tumour suppressor proteins include p53, p73, FOXO3a, IKB, pRb and BRCA1. Additional cargo exported by XPO1 include growth regulators (glucocorticoid receptors), and oncoprotein mRNA (c-Myc, cyclin D, Bcl-2, Bcl-6).<sup>1,4,5,8,9</sup> Bcl, B-cell lymphoma; BRCA1, breast cancer gene 1; c-Myc, c-mycelocytomatosis oncogene product; FOXO3a, forkhead box O3; MOA, mechanism of action; mRNA, messenger ribonucleic acid; pRb, retinoblastoma protein; RRMM, relapsed/refractory multiple myeloma; SVd, selinexor + bortezomib + dexamethasone; TSP, tumour suppressor protein; XPO1, exportin-1. 1. NEXPOVIO (selinexor) Summary of Product Characteristics. May 2022; 2. Yang J, et al. *PLoS One.* 2014;9(7):e102983; 3. Gupta A, et al. *J Thorac Oncol.* 2017;12(9):1446–1450; 4. Ben-Barouch S, Kuruvilla J. *Expert Opin Investig Drugs.* 2020;29(1):15–21; 5. Sun Q, et al. *Signal Transduct Target Ther.* 2016;1:16010; 6. Tai Y-T, et al. *Leukemia.* 2014;28(1):155–165; 7. Grosicki S, et al. *Lancet.* 2020;396:1563–1573. 8. Gravina GL, et al. *J Hematol Oncol.* 2014;7:85; 9. Gandhi UH, et al. *Clin Lymphoma Myeloma Leuk.* 2018;18(5):335–345.

# The BOSTON trial investigated SVd in RRMM patients treated with 1–3 prior therapies<sup>1,2</sup>



**LANCET publication was based on Feb 18 2020 data cut-off<sup>1</sup>**

- Median follow up 13.2 vs 16.5 months, SVd vs Vd<sup>1</sup>

**Here we report efficacy analyses based on Feb 2021 data cut and safety analyses on Jun 2022 data cut<sup>2,3</sup>**

- Median follow up 28.7 and 28.6 months, SVd vs Vd<sup>3</sup>

AE, adverse event; BIW, twice weekly; IRC, independent review committee; ITT, intention to treat; MM, multiple myeloma; PD, progressive disease; PFS, progression-free survival; PI, proteasome inhibitor; QW, once weekly; R, randomised; R-ISS, revised international staging system; RRMM, relapsed or refractory multiple myeloma; SC, subcutaneous; SVd, selinexor + bortezomib + dexamethasone; Vd, bortezomib + dexamethasone. 1. Grosicki S, et al. *Lancet*. 2020;395(10262):1563–1573. 2. Mateos MV, et al. Poster P917. Presented at EHA2023 Hybrid Congress, 8–11 June 2023, Frankfurt, Germany. 3. Mateos MV, et al. Poster P886. Presented at EHA2023 Hybrid Congress, 8–11 June 2023, Frankfurt, Germany.

# The BOSTON trial included difficult-to-treat patients with MM refractory to lenalidomide and previously treated with anti-CD38 therapies<sup>1</sup>



## Baseline characteristics in the BOSTON trial<sup>1</sup>

\*15 (8%) of patients were not assessed for cytogenetic abnormalities. Fluorescence in-situ hybridisation was performed at central laboratories to assess cytogenetic risk status [del(17p), t(14;16), or (4;14), or amp 1q21 with three or more copies].

ECOG, Eastern Cooperative Oncology Group; R-ISS, revised international staging system; SVd, selinexor + bortezomib + dexamethasone; Vd, bortezomib + dexamethasone.

1. Grosicki S, et al. *Lancet*. 2020;369(10262):1563–1573.

	SVd (n=195)	Vd (n=207)
Median age, years	66 (59–72)	67 (61–74)
Male	115 (59%)	115 (56%)
Female	80 (41%)	92 (44%)
ECOG performance status		
0	69 (35%)	77 (37%)
1	106 (54%)	114 (55%)
2	20 (10%)	16 (8%)
Cytogenetic abnormalities*	97 (50%)	95 (46%)
R-ISS disease stage at screening		
I–II	173 (89%)	177 (86%)
III	12 (6%)	16 (8%)
Unknown	10 (5%)	14 (7%)
Time since initial diagnosis, years	3.8 (2.5–5.4)	3.6 (2.1–5.6)

Adapted from Grosicki, et al. 2020.

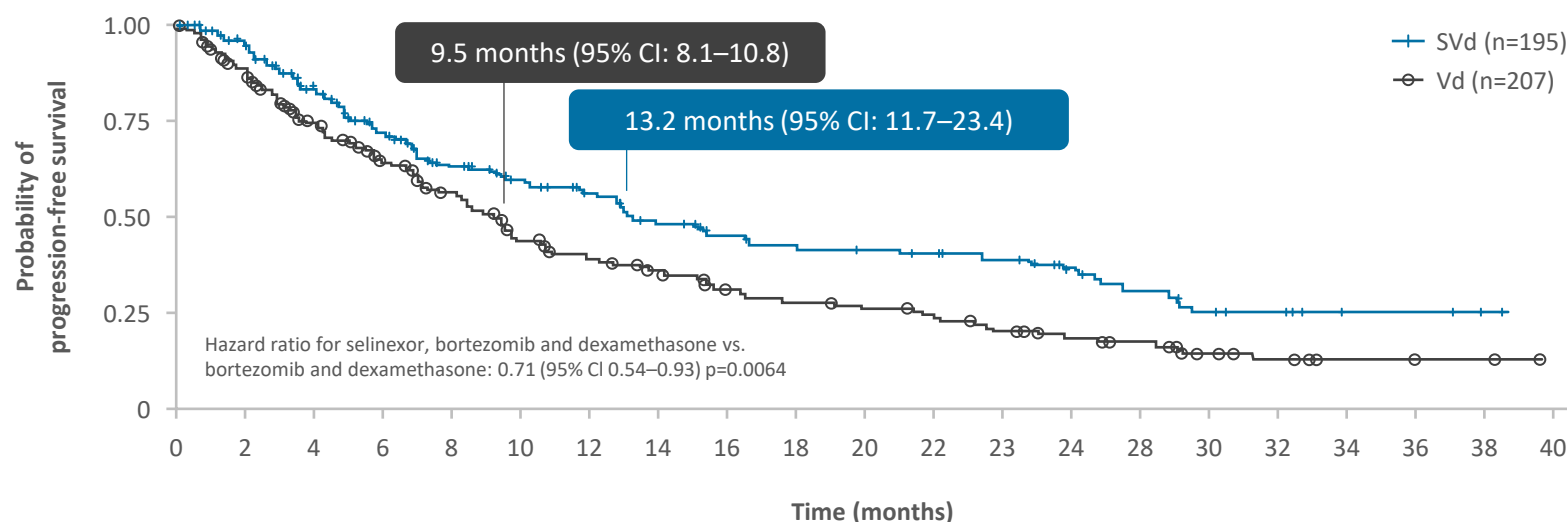
	SVd (n=195)	Vd (n=207)
Number of previous lines of therapy		
One	99 (51%)	99 (48%)
Two	65 (33%)	64 (31%)
Three	31 (16%)	44 (21%)
Previous stem-cell transplantation	76 (39%)	63 (30%)
Previous therapy		
Bortezomib	134 (69%)	145 (70%)
Carfilzomib	20 (10%)	21 (10%)
Ixazomib	6 (3%)	3 (1%)
Daratumumab	11 (6%)	6 (3%)
Lenalidomide	77 (39%)	77 (37%)
Pomalidomide	11 (6%)	7 (3%)



# BOSTON trial: SVd showed a statistically significant improvement in mPFS vs Vd<sup>1</sup>



## PFS in the ITT population<sup>1</sup>



Adapted from Selinexor Summary of Product Characteristics.

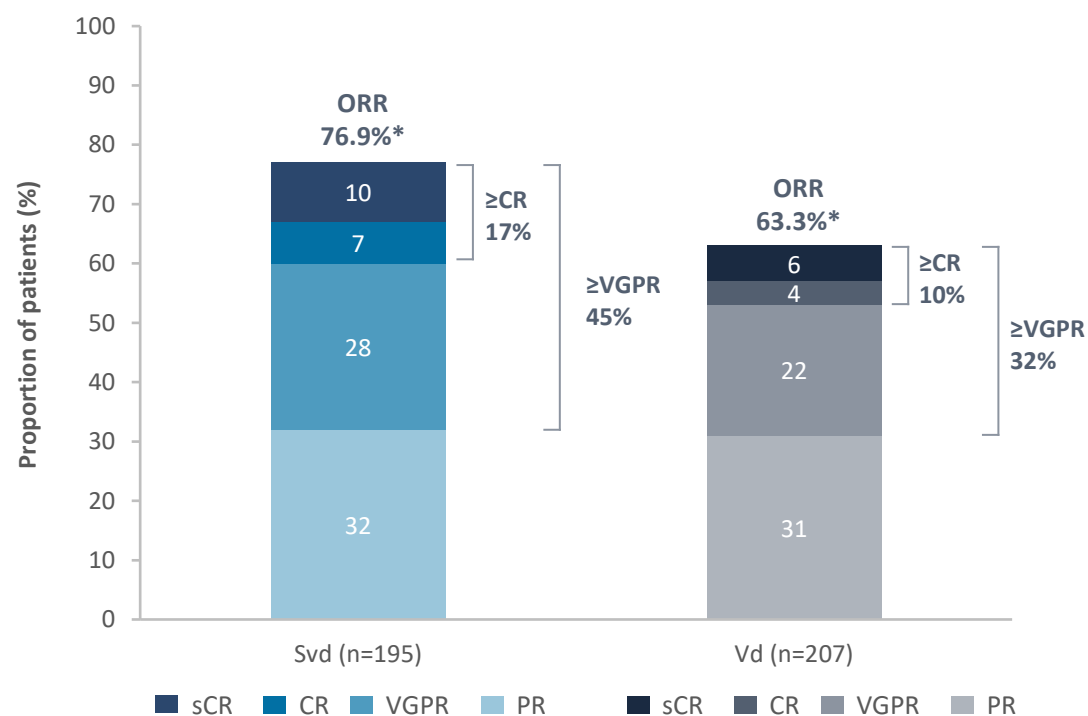
CI, confidence interval; mPFS, median progression-free survival; PFS, progression-free survival; SVd, selinexor + bortezomib + dexamethasone; Vd, bortezomib + dexamethasone.

1. NEXPOVIO® (selinexor) Summary of Product Characteristics. May 2022.

# BOSTON trial: SVd showed a statistically significant improvement in response vs Vd<sup>1</sup>



## Overall response rate in the ITT population<sup>1</sup>



Adapted from Selinexor Summary of Product Characteristics.

\*p=0.0012.

	SVd arm (n=195)	Vd arm (n=207)
Median time to response, months (95% CI) <sup>1</sup>	1.4 (1.4–1.5)	1.6 (1.5–2.1)
Median duration of response, months (95% CI) <sup>1</sup>	17.3 (12.6–26.3)	12.9 (9.3–15.8)

Adapted from NEXPOVIO® (selinexor) Summary of Product Characteristics.

# Stratified efficacy analyses were performed in BOSTON trial subgroups<sup>1,2</sup>



## PI-naïve patients<sup>1</sup>

- At the time of the analysis, median follow-up was 28.7 months for SVd arm and 28.6 for Vd arm<sup>2</sup>
- SVd n=47; Vd n=48

## Lenalidomide-refractory patients<sup>2</sup>

- At the time of the analysis, median follow-up was 28.7 months for SVd arm and 28.6 for Vd arm
- Post-hoc stratified analysis (with crossover adjustment using the two stage method)
- SVd n=53; Vd n=53

## Limitations of subgroup analysis<sup>1</sup>

- These subgroup analyses were not included in the study objectives, and do not control for type 1 error
- These subgroup analyses were not powered or adjusted for multiplicity

PI, proteasome inhibitor; SVd, selinexor + bortezomib + dexamethasone; Vd, bortezomib + dexamethasone.

1. Mateos MV, et al. Poster P917. Presented at EHA2023 Hybrid Congress, 8–11 June 2023, Frankfurt, Germany.

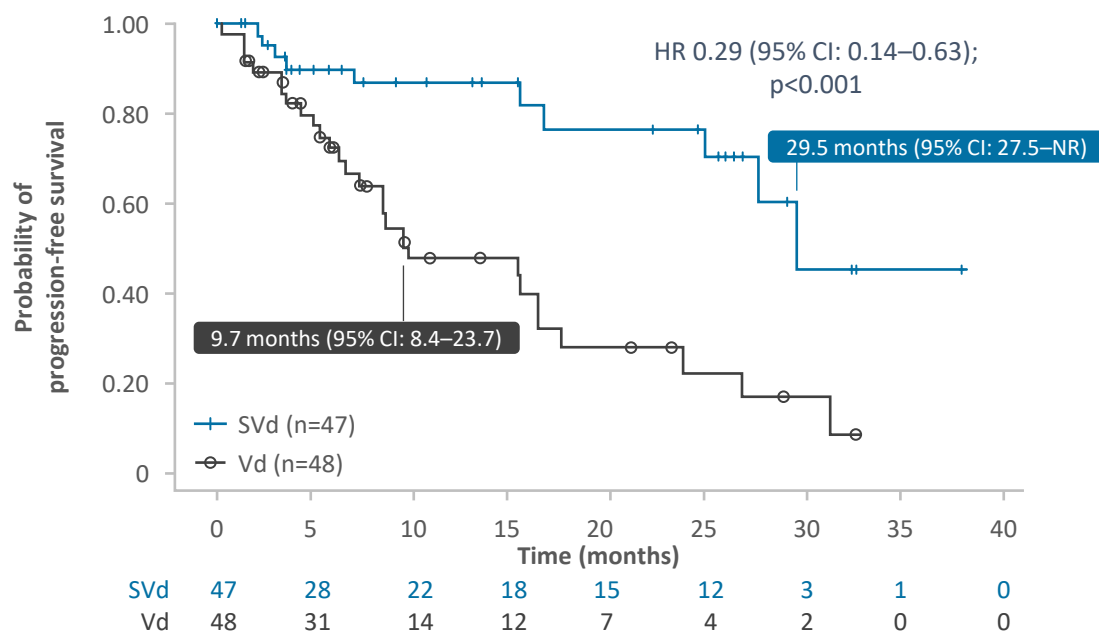
2. Mateos MV, et al. Poster P886. Presented at EHA2023 Hybrid Congress, 8–11 June 2023, Frankfurt, Germany.



# BOSTON trial: SVd showed a statistically significant improvement in PFS in PI-naïve patients vs Vd<sup>1</sup>

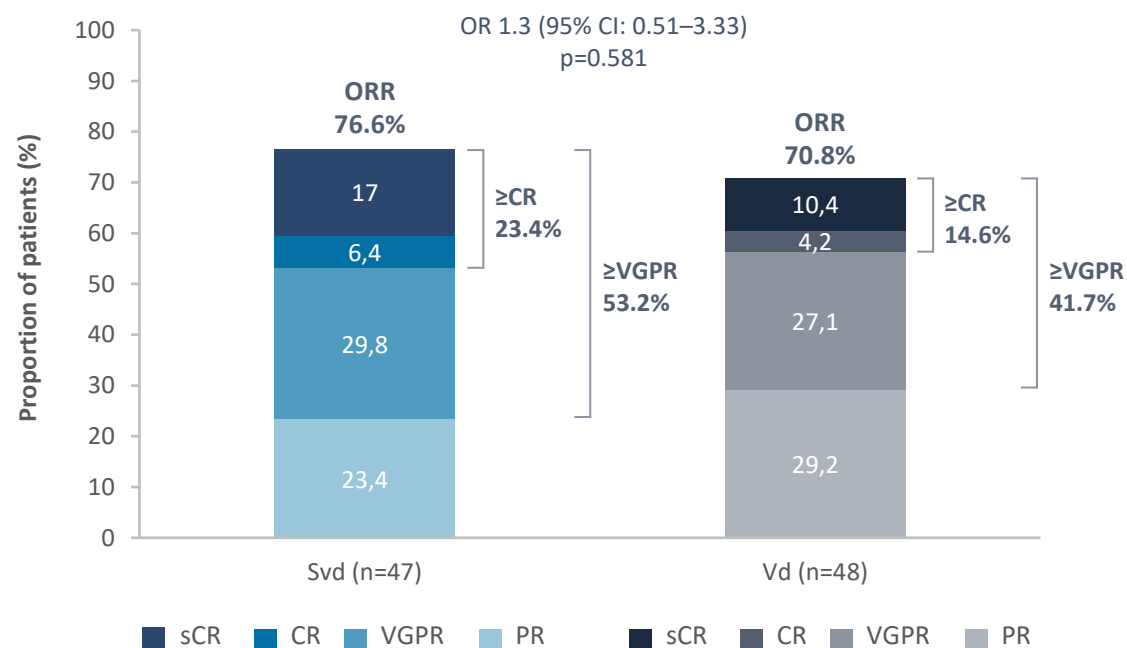


## PFS in PI-naïve patients<sup>1</sup>



Adapted from Mateos MV, et al. EHA2023. Poster P917.

## Overall response rate in PI-naïve patients<sup>1</sup>



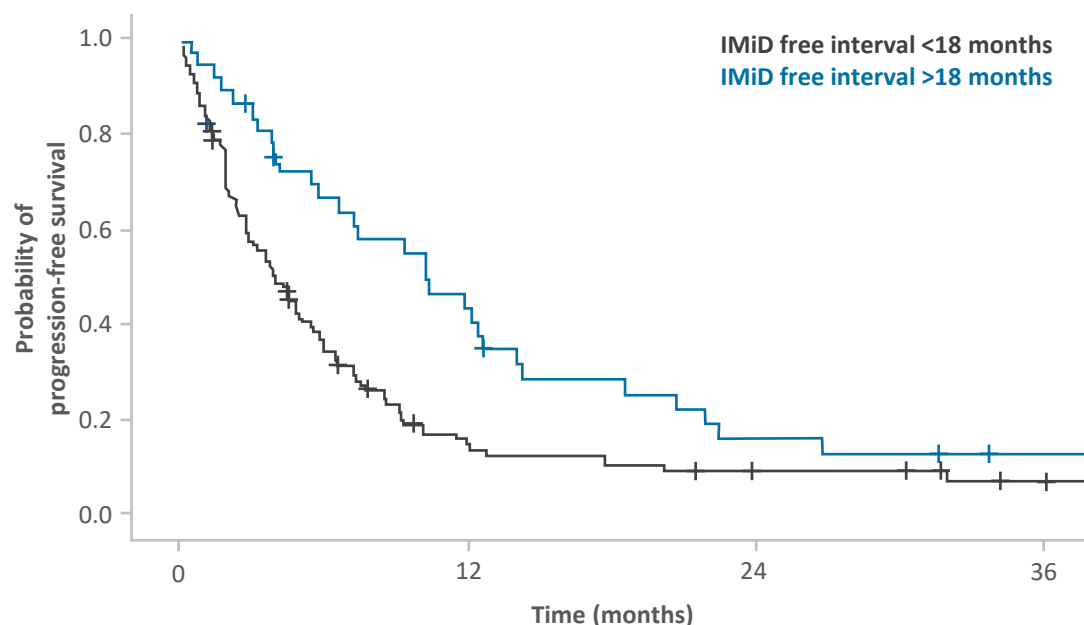
Adapted from Mateos MV, et al. EHA2023. Poster P917.

Treatment with SVd provided a statistically significant and clinically meaningful ~20-month mPFS improvement vs Vd<sup>1</sup>

# A longer duration of prior lenalidomide therapy and longer IMiD-free interval results in a statistically significant improvement in PFS and OS, irrespective of number of prior lines of therapy<sup>1</sup>



## PFS according to IMiD free interval<sup>1</sup>



Adapted from Kastiris E, et al. *Blood Adv.* 2019.

Single centre, real-world study of 147 consecutive patients with RRMM treated with IMiDs, pomalidomide and dexamethasone (median, 3 prior lines of treatment)<sup>1</sup>

## Multivariate analysis for PFS and OS (final models)<sup>1</sup>

		95% CI for HR		
	HR	Lower	Upper	P
<b>PFS</b>				
Duration of last lenalidomide regiment <12 mo	1.485	1.009	2.186	.045
Time since last lenalidomide dose <18 mo	1.970	1.271	3.054	.002
<b>OS</b>				
Duration of last lenalidomide regiment <12 mo	1.661	1.102	2.503	.015
Time since last lenalidomide dose <18 mo	1.775	1.107	2.845	.017

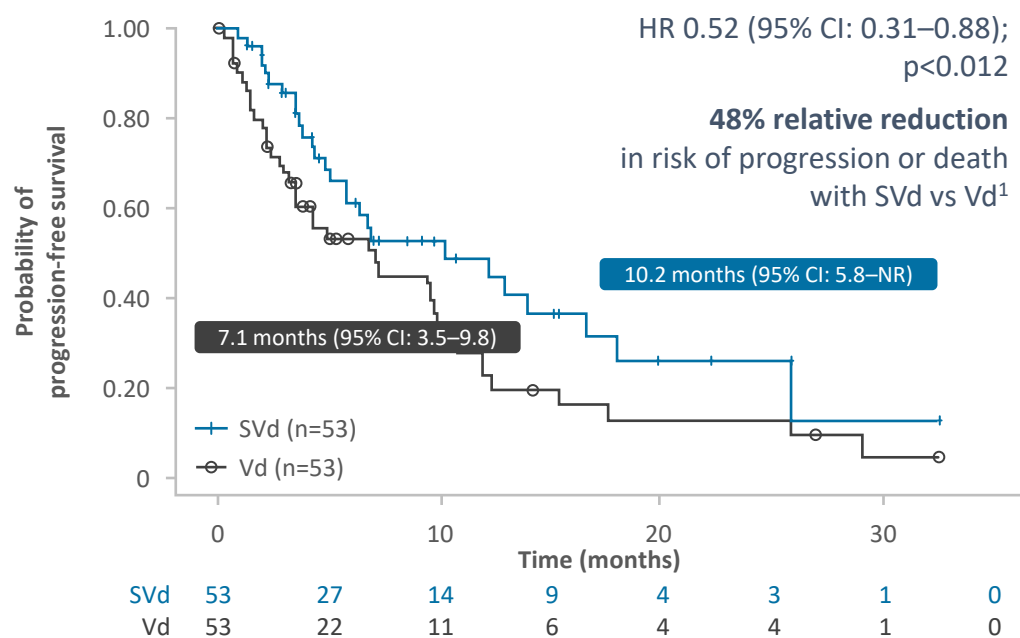
Adapted from Kastiris E, et al. *Blood Adv.* 2019.

An IMiD-free interval of >18 months was associated with a PFS of 10.3 vs 3.9 months ( $p=0.003$ )<sup>1</sup>

# BOSTON trial: SVd showed a statistically significant improvement in PFS and OS in lenalidomide-refractory patients vs Vd<sup>1</sup>

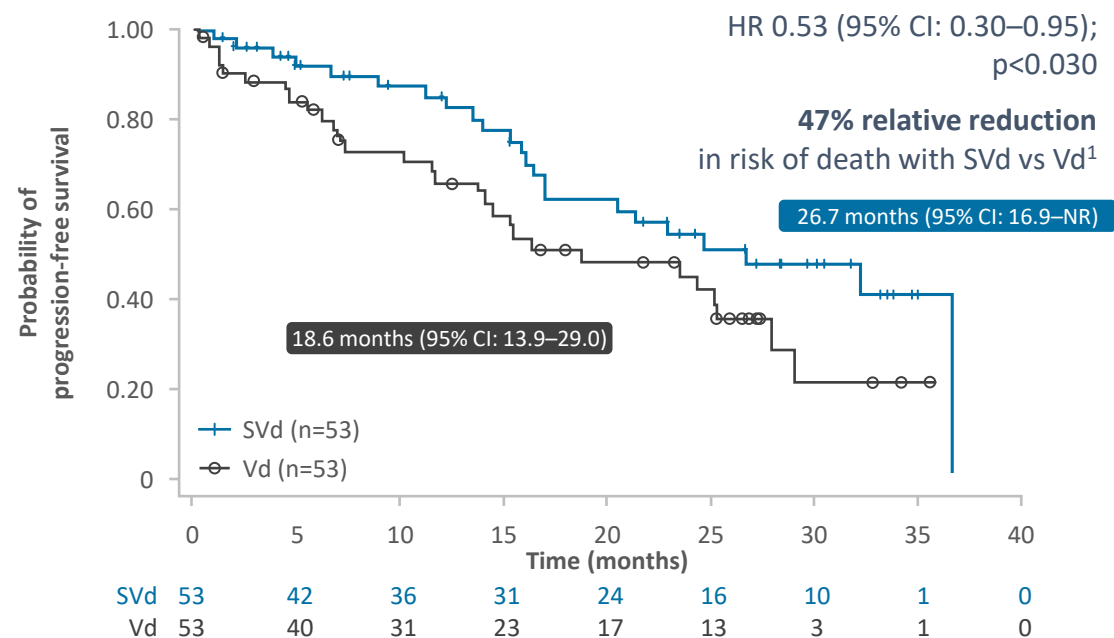


## PFS in lenalidomide-refractory patients\*<sup>1</sup>



Adapted from Mateos MV, et al. EHA2023. Poster P886.

## OS in lenalidomide-refractory patients<sup>1</sup>

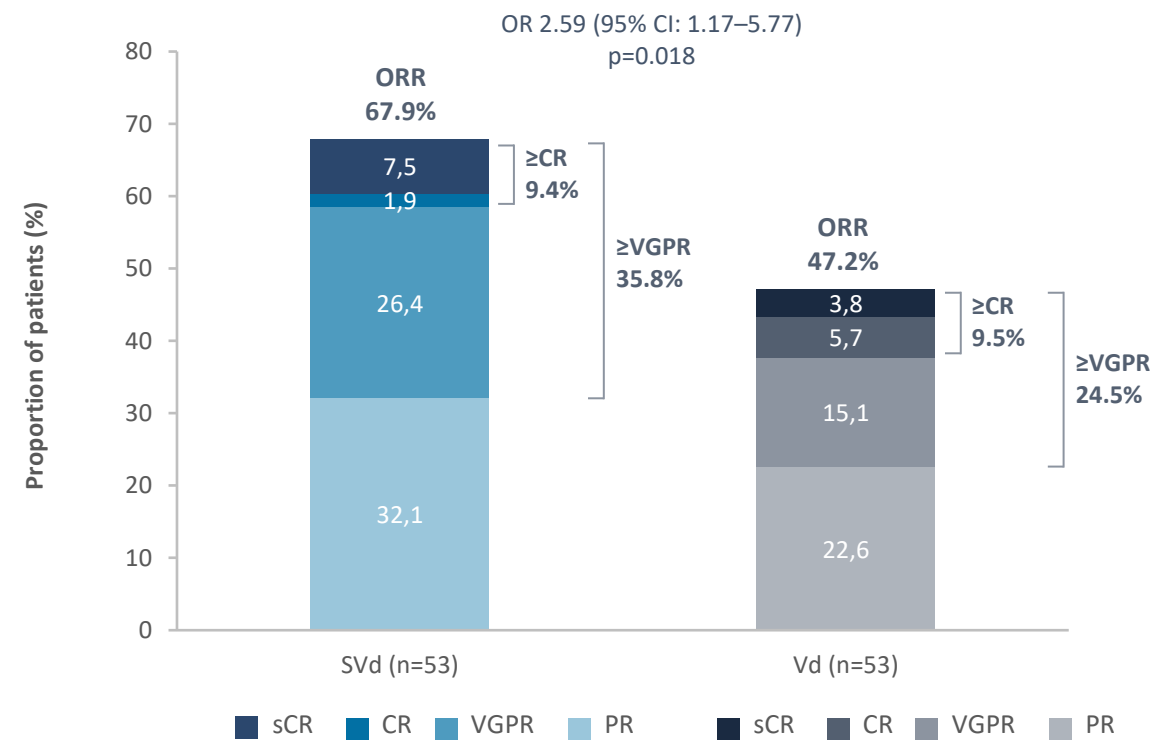


Adapted from Mateos MV, et al. EHA2023. Poster P886.

# BOSTON trial: SVd showed a statistically significant improvement in ORR in lenalidomide-refractory patients vs Vd<sup>1</sup>



## Overall response rate in lenalidomide-refractory patients<sup>1</sup>



Adapted from Mateos MV, et al. EHA2023. Poster P886.

# BOSTON trial: SVd may provide improved, durable outcomes, and reduced incidence of PN in patients with RRMM and renal impairment vs Vd<sup>1</sup>



## PFS in patients with renal impairment<sup>1</sup>

	<40 mL/min			40-60 mL/min			>60 mL/min		
	SVd (n=21)	Vd (n=26)	P value	SVd (n=35)	Vd (n=44)	P value	SVd (n=139)	Vd (n=137)	P value
Median PFS (months)	7.62	4.30	0.129	16.62	7.62	0.028	13.24	9.66	0.019
HR	0.62				0.49			0.71	
ORR, %	81.0	53.8	0.027	80.0	59.1	0.024	74.8	65.0	0.037
OR		3.64			2.77			1.60	
≥VGPR, %	38.1	26.9	0.210	48.6	27.3	0.053	44.6	35.0	0.053
OR		1.67			2.52			1.49	
Median DOR, months (95% CI)	20.27	NR	0.660	NR	12.58	0.211	15.34	12.68	0.053
HR		1.32			0.69			0.71	
Median OS, months (95% CI)	NR	19.06	0.264	NR	21.22	0.080	NR	24.97	0.446
HR		0.74			0.55			0.97	
Median TTNT, months (95% CI)	NR	19.06	0.137	NR	20.93	0.040	15.34	10.97	0.007
HR		0.65			0.56			0.67	

Adapted from Delimpasi S, et al. *Am J Hematol.* 2022.

Renal impairment was defined as CrCL <40 or 40–60 mL/min. In the BOSTON trial, 56 patients in the SVd arm and 70 patients in the Vd arm had renal impairment<sup>1</sup>

PFS of patients with CrCl 40–60 mL/min showed a statistically significant improvement in patients treated with SVd compared to Vd (16.62 vs 7.26 months;  $P=0.028$ )<sup>1</sup>

ORR showed a statistically significant improvement in patients treated with SVd compared to Vd across all levels of renal function (CrCl <40 mL/min:  $P=0.027$ ; CrCl 40–60 mL/min:  $P=0.024$ ; CrCl >60 mL/min:  $P=0.037$ )<sup>1</sup>

Selinexor-based regimens are well tolerated and effective in patients with renal impairment<sup>2</sup>



# Selinexor's safety profile and management strategies



# BOSTON trial: AEs were generally self-limiting, reversible and manageable<sup>1</sup>

## Haematological TEAEs in ≥10% of either group (ITT population)

AEs, n (%)	SVd arm (n=195)		Vd arm (n=204)*	
	Any Grade <sup>†</sup>	Grade 3/4	Any Grade <sup>‡</sup>	Grade 3/4
Thrombocytopenia	117 (60)	77 (39)	55 (27)	35 (17)
Anaemia	71 (36)	31 (16)	47 (23)	20 (10)
Neutropenia	29 (15)	17 (9)	12 (6)	7 (3)

Adapted from Grosicki S, et al. *Lancet*. 2020.

**The most common Grade 3/4 AEs were thrombocytopenia, fatigue, anaemia, and pneumonia**

\*Three patients from this group who did not receive any doses of study drug were excluded from the safety population.

<sup>†</sup>Includes four Grade 5 events: three (2%) cases of pneumonia and one (1%) case of bronchitis.

<sup>‡</sup>Includes four Grade 5 events: three (1%) cases of pneumonia and one (<1%) case of anaemia.

<sup>§</sup>Includes high-level MedDRA term “peripheral neuropathies NEC”.

<sup>¶</sup>Includes pneumonia, lung infection, *Haemophilus* infection, pulmonary sepsis, pneumonia respiratory syncytial viral, pneumonia pneumococcal, pneumonia influenza viral, pneumonia parainfluenza viral, pneumonia bacterial, and pneumonia fungal infections.

Adapted from Grosicki S, et al. *Lancet*. 2020.

## Non-haematological TEAEs in ≥10% of either group (ITT population)

AEs, n (%)	SVd arm (n=195)		Vd arm (n=204)*	
	Any Grade <sup>†</sup>	Grade 3/4	Any Grade <sup>‡</sup>	Grade 3/4
Fatigue	82 (42)	26 (13)	37 (18)	2 (1)
Nausea	98 (50)	15 (8)	20 (10)	0
Diarrhoea	63 (32)	12 (6)	51 (25)	1 (<1)
Peripheral neuropathy <sup>§</sup>	63 (32)	9 (5)	96 (47)	18 (9)
Decreased appetite	69 (35)	7 (4)	11 (5)	0
Weight loss	51 (26)	4 (2)	25 (12)	2 (1)
Asthenia	48 (25)	16 (8)	27 (13)	9 (4)
Constipation	33 (17)	0	35 (17)	3 (1)
Cough	35 (18)	1 (1)	30 (15)	0
Insomnia	31 (16)	2 (1)	32 (16)	4 (2)
Back pain	30 (15)	1 (1)	29 (14)	2 (1)
Pneumonia <sup>¶</sup>	35 (18)	24 (12)	34 (17)	21 (10)
Pyrexia	30 (15)	3 (2)	22 (11)	2 (1)
Cataract	42 (22)	17 (9)	13 (6)	3 (1)
Vomiting	40 (21)	8 (4)	9 (4)	0
Peripheral oedema	23 (12)	1 (1)	26 (13)	0
Dyspnoea	18 (9)	1 (1)	27 (13)	5 (2)
Bronchitis	24 (12)	3 (2)	20 (10)	1 (<1)
URTI	35 (18)	5 (3)	30 (15)	1 (<1)



# BOSTON trial: Discontinuation due to adverse events<sup>1</sup>

Treatment discontinuations due to AEs were similar between the two treatment groups (ITT population)<sup>1</sup>

	SVd (n=195)	Vd (n=204)
<b>Discontinuation due to TEAEs, n (%)</b>	41 (21)	32 (16)
Of which patients >70 years old, n (%)	19 (46)	16 (50)
<b>Median time to discontinuation, days (IQR)</b>	194 (100–332)	184 (106–276)
<b>Deaths due to adverse events, n (%)</b>	12 (6)	11 (5)
Unrelated to treatment	8 (67)	10 (91)

- Peripheral neuropathy was the most common TEAE leading to treatment discontinuation in both treatment arms (SvD arm 5%; Vd arm 7%)<sup>1</sup>
- Deaths due to AEs were of similar frequency in the SVd and Vd group<sup>1</sup>

AE, adverse event; IQR, interquartile range; ITT, intention-to-treat; SVd, selinexor + bortezomib + dexamethasone; TEAE, treatment-emergent adverse event; Vd, bortezomib + dexamethasone.

1. Grosicki S, et al. *Lancet*. 2020;396:1563–1573.

Adapted from Grosicki S, et al. *Lancet*. 2020.



# Selinexor dose can be reduced to help manage AEs without compromising on efficacy<sup>1-3</sup>

Selinexor dose has been optimised through trials and dose reductions to help manage AEs<sup>1-3</sup>

## STORM trial<sup>1</sup>

160 mg (80 mg twice weekly) + d

## BOSTON trial<sup>2</sup>

100 mg (100 mg once weekly) + Vd

## BOSTON dose reduction subgroup<sup>3</sup>

71 mg (median dose) + Vd

i

**65% of patients** in the Selinexor + Vd arm **had a dose reduction** (126/195 patients)<sup>3</sup>

The **median dosage** of Selinexor patients who had a dose reduction was **71 mg (29.7–101.4 mg) per week**<sup>3</sup>

# Differences in toxicity by the change in dosing from twice weekly to once weekly dosing across trials<sup>1</sup>



Most Frequent TEAEs (%)	STORM, ITT population (Selinexor dose – 80 mg twice weekly) <sup>1</sup>	
	Sd All Grades	Sd Grade 3/4
Neutropenia	36.6	18.7
Anaemia	48	29.3
Thrombocytopenia	67.5	53.7
Leucopenia	29.3	13.0
Nausea	69.1	9.8
Fatigue	56.1	18.7
Decreased appetite	52.0	3.3
Weight loss	47.2	0.8
Diarrhoea	33.3	6.5
Upper RTI	5.7	3.3
Vomiting	35.0	3.3
Asthenia	13.8	4.9

Most Frequent TEAEs (%)	BOSTON, ITT population (Selinexor dose – 100 mg once weekly) <sup>1</sup>			
	SVd All Grades	SVd Grade 3/4	Vd All Grades	Vd Grade 3/4
Neutropenia	14.9	8.7	5.9	3.4
Anaemia	36.4	15.9	23.0	9.8
Thrombocytopenia	60.0	39.5	27.0	17.2
Leucopenia	NR	NR	NR	NR
Nausea	50.3	7.7	9.8	0.0
Fatigue	42.1	13.3	18.1	1.0
Decreased appetite	35.4	3.6	5.4	0.0
Weight loss	26.2	2.1	12.3	1.0
Diarrhoea	32.3	6.2	25.0	0.5
Upper RTI	29.2	3.6	21.6	1.5
Vomiting	20.5	4.1	4.4	0.0
Asthenia	24.6	8.2	13.2	4.4

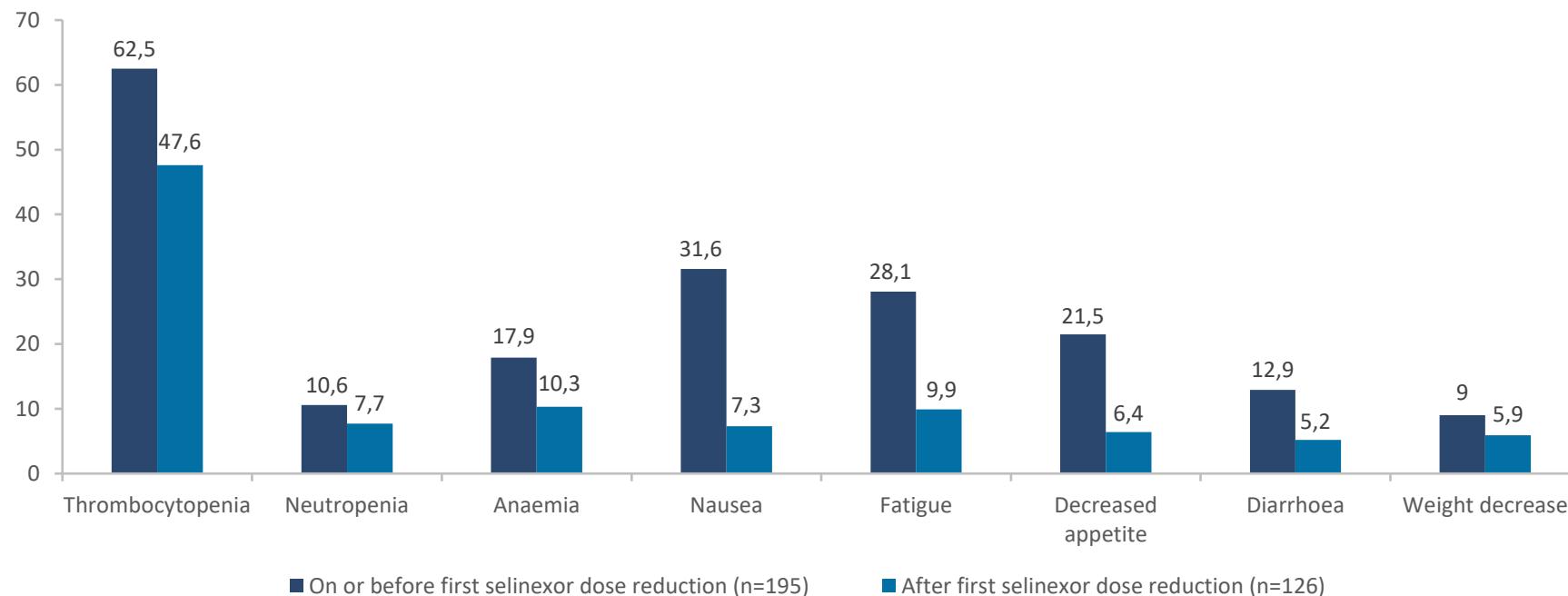
Adapted from Nooka AK et al. Clin Lymphoma Myeloma Leuk. 2022





# BOSTON trial: Dose reductions reduced AE incidence<sup>1</sup>

## Duration-adjusted\* incidence of adverse events of clinical interest for all grades with SVd<sup>1</sup>



Adapted from Jagannath S, et al. ASH. 2021.

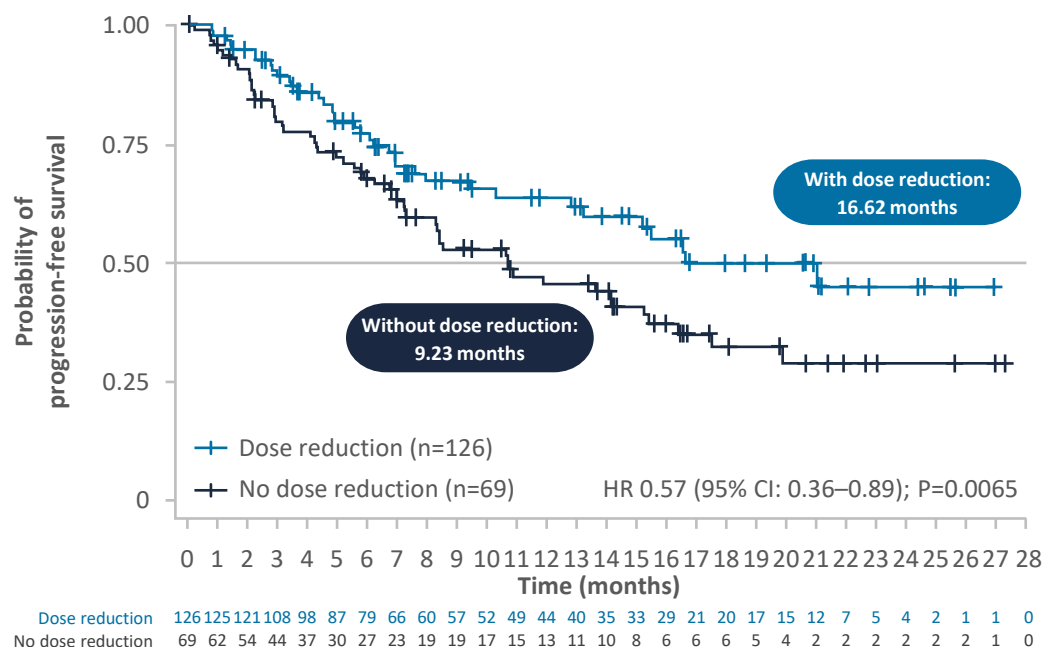
- In the BOSTON trial, **126 patients underwent a dose reduction<sup>1</sup>**
- In patients who underwent a dose reduction, **median dose was 71 mg selinexor** vs 100 mg selinexor per week in the patients who did not undergo a dose reduction<sup>1,2</sup>

Patients who underwent dose reduction experienced fewer AEs than patients who did not undergo dose reduction<sup>1</sup>

# BOSTON trial: Dose reductions improved tolerability and optimised treatment outcomes by extending the duration of SVd treatment<sup>1</sup>

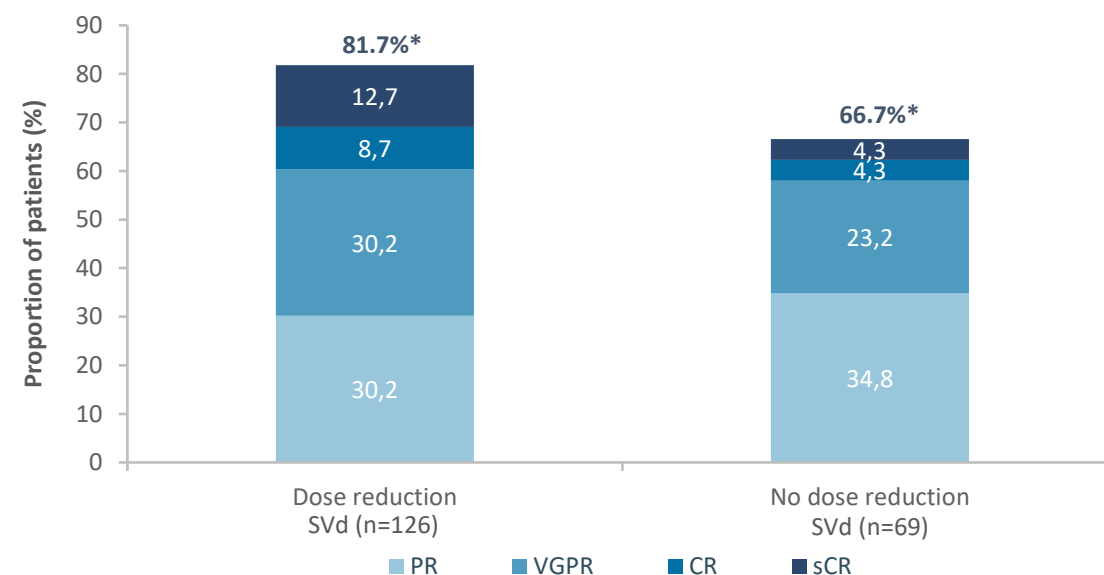


**PFS by dose reduction in patients in the SVd arm<sup>1</sup>**



Adapted from Jagannath S, et al. ASH 2021.

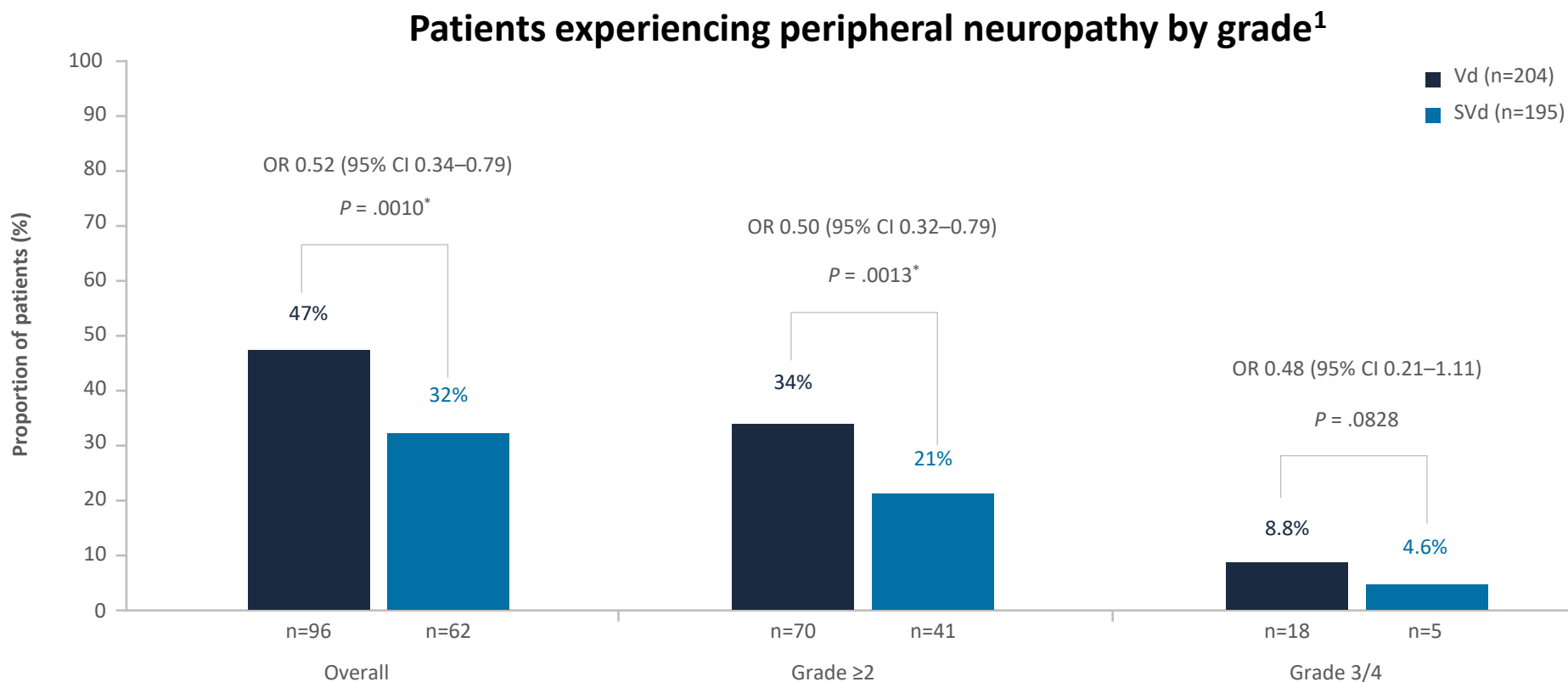
**ORR by dose reduction of selinexor in the SVd arm<sup>1\*</sup>**



Adapted from Jagannath S, et al. ASH 2021.

Average duration of therapy with dose reduction was 44.4 weeks vs 30.5 weeks without dose reduction<sup>1</sup>

# BOSTON trial: Statistically significant lower rates of bortezomib-induced peripheral neuropathy were observed with once-weekly SVd vs twice-weekly Vd<sup>1</sup>

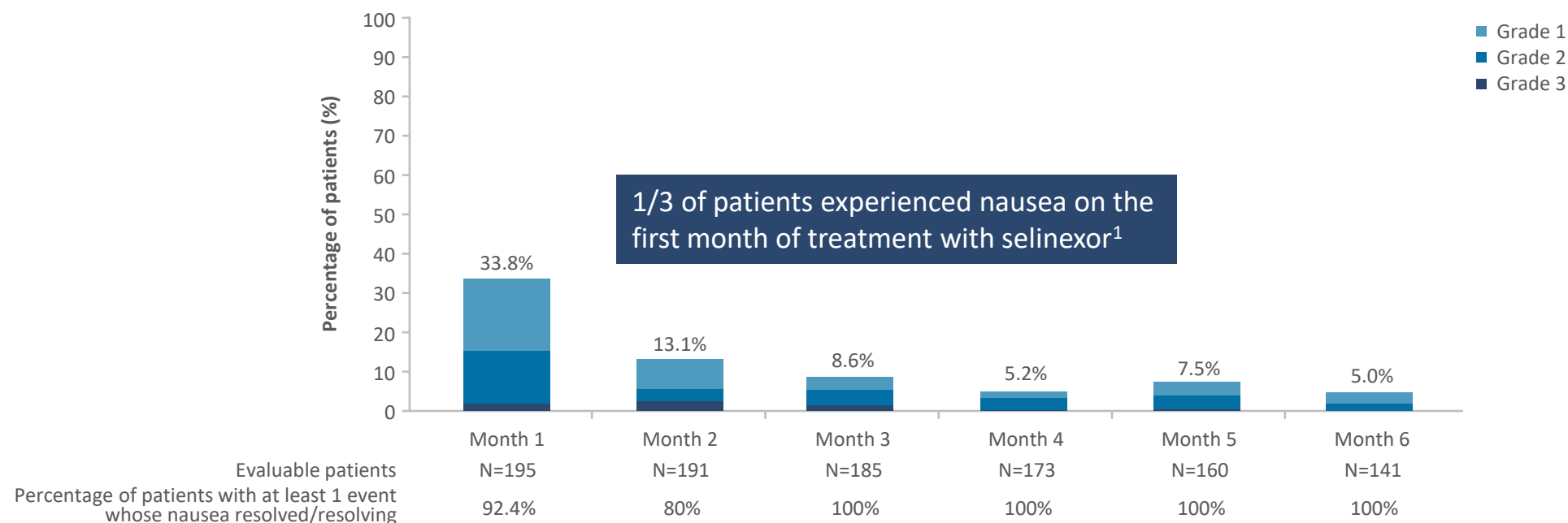


Adapted from Grosicki S, et al. *Lancet*. 2020.

# In the BOSTON trial, SVd treatment-related nausea was transient with decreasing incidence after the first month of therapy<sup>1</sup>



## Percentage of patients experiencing nausea events per month in the SVd arm of the BOSTON trial



Adapted from Nooka AK, et al. *Clin Lymphoma Myeloma Leuk.* 2022.

Patients in the BOSTON trial were administered 5-HT3 receptor antagonists and other anti-nausea agents prior to and during treatment with selinexor<sup>1-3</sup>



# Selinexor: Toxicity and monitoring considerations<sup>1</sup>

Select AEs to access	<ul style="list-style-type: none"> <li><b>Thrombocytopenic events</b> were frequently reported in patients receiving selinexor which can be severe (Grade 3/4). Grade 3/4 thrombocytopenia can sometimes lead to clinically significant bleeding and in rare cases may lead to potentially fatal haemorrhage</li> <li><b>Neutropenia</b> including severe neutropenia (Grade 3/4) has been reported with selinexor. In a few cases concurrent infections occurred in patients with Grade 3/4 neutropenia</li> <li><b>Nausea, vomiting, diarrhoea</b>, which sometimes can be severe and require the use of anti-emetic and anti-diarrhoeal medicinal products</li> <li>Selinexor can cause <b>weight loss and anorexia</b></li> </ul>	
Monitoring	<ul style="list-style-type: none"> <li>Patients should have their <b>CBC</b> assessed at baseline, during treatment, and as clinically indicated. Monitor more frequently during the first two months of treatment</li> <li>Patients with <b>neutropenia</b> should be monitored for signs of infection and evaluated promptly</li> <li>Patients should have their <b>body weight, nutritional status and volume</b> checked at baseline, during treatment, and as clinically indicated. Monitoring should be more frequent during the first two months of treatment</li> <li>Patients should have their <b>sodium levels</b> checked at baseline, during treatment, and as clinically indicated. Monitoring should be more frequent during the first two months of treatment</li> <li>Patients at a high risk for <b>TLS</b> should be monitored closely</li> </ul>	
Dose reductions	<b>Starting dose (SVd): 100 mg once weekly</b> <ul style="list-style-type: none"> <li>First: 80 mg once weekly</li> <li>Second: 60 mg once weekly</li> <li>Third: 40 mg once weekly</li> <li>Discontinue after third reduction</li> </ul>	<b>Starting dose (Sd): 80 mg Days 1 and 3 (160 mg total)</b> <ul style="list-style-type: none"> <li>First: 100 mg once weekly</li> <li>Second: 80 mg once weekly</li> <li>Third: 60 mg once weekly</li> <li>Discontinue after third reduction</li> </ul>
Prophylactic treatments	<ul style="list-style-type: none"> <li>Patients should be advised to maintain adequate <b>fluid and caloric intake</b> throughout treatment. <b>Intravenous hydration</b> should be considered for patients at risk of dehydration</li> <li>Prophylactic concomitant treatment with a <b>5-HT3 antagonist</b> and/or other anti-nausea agents should be provided prior to and during treatment</li> </ul>	

Adapted from NEXPOVIO® (selinexor) Summary of Product Characteristics.



# Summary of Mount Sinai School of Medicine recommended supportive care guidelines with selinexor\*1

Mount Sinai School of Medicine (MSSM) used the STORM protocol to assess supportive care strategies used at the centre. Of 123 patients enrolled in the STORM trial, 28 were enrolled at MSSM<sup>1</sup>

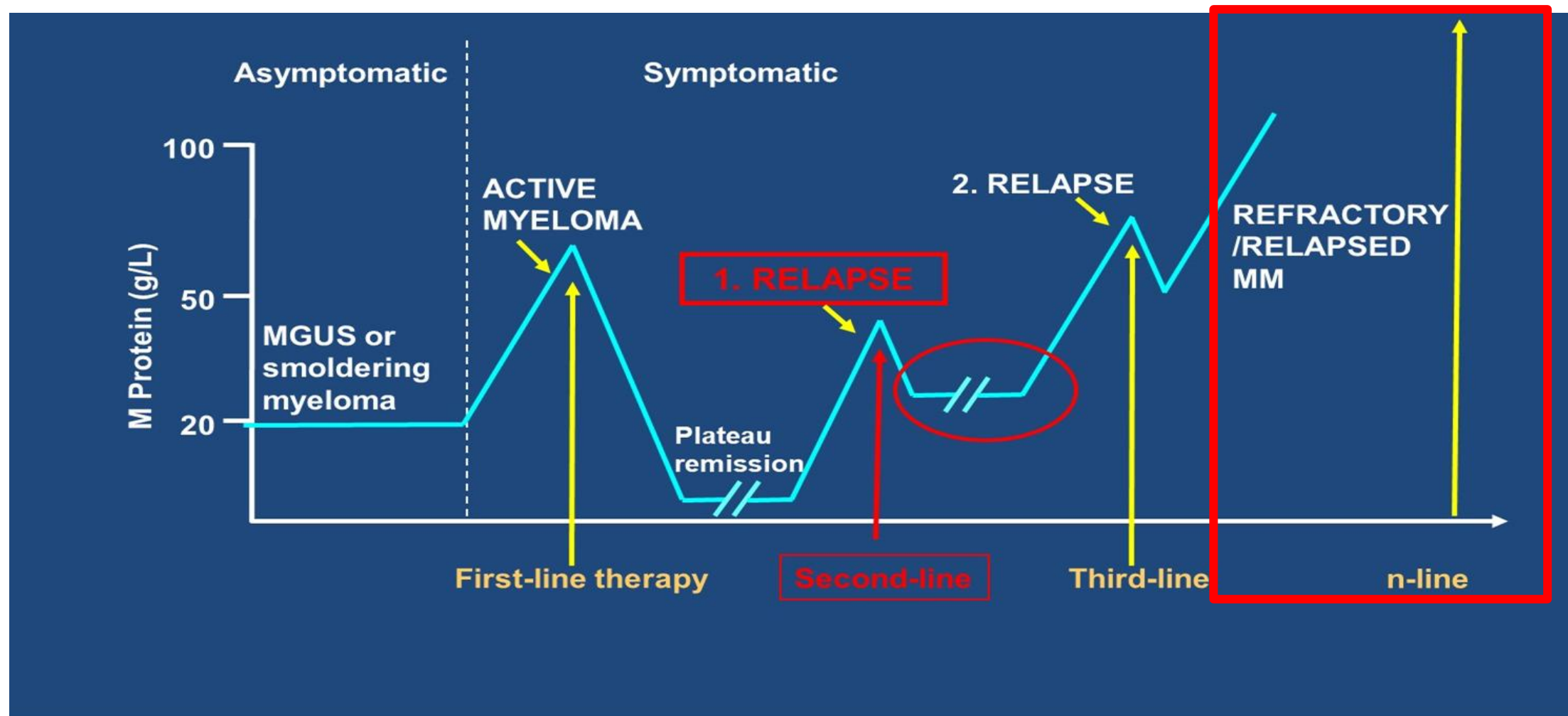
## MSSM supportive care algorithm<sup>1</sup>

Identification/Implementation	<ul style="list-style-type: none"><li>Educate patients regarding selinexor side-effects, prophylactic and responsive measures, and nutrition</li><li>Call patients once weekly</li><li>Weights at least weekly for the first 8 weeks, then as needed</li><li>CBC and chemistry at least weekly for the first 8 weeks, then as needed</li></ul>
Nausea/Emesis Prophylaxis Treatment Preferred Second Antiemetic	<ul style="list-style-type: none"><li>Begin with 5-HT3 antagonist and 1 or 2 additional antiemetics on first day of selinexor in most patients*</li><li>Rapidly add second or third antiemetic if nausea occurs after the first selinexor dose: 70% received second antiemetic with early initiation (day 2–3)</li><li>Recommend NK-1 antagonist as second agent for nausea/emesis</li></ul>
Fatigue/Asthenia	<ul style="list-style-type: none"><li>Rule out hypovolemia, anaemia, hypothyroidism, and adrenal insufficiency</li><li>Treat with methylphenidate (≥10 mg/d); monitor food and fluid intake</li></ul>
Thrombocytopenia	<ul style="list-style-type: none"><li>When platelets are &lt;50,000/μL, begin weekly romiplostim 10 mcg/kg subcutaneously after each once-weekly dose of selinexor</li></ul>

Adapted from Chari A, et al. *Clin Lymphoma Myeloma Leuk.* 2021.



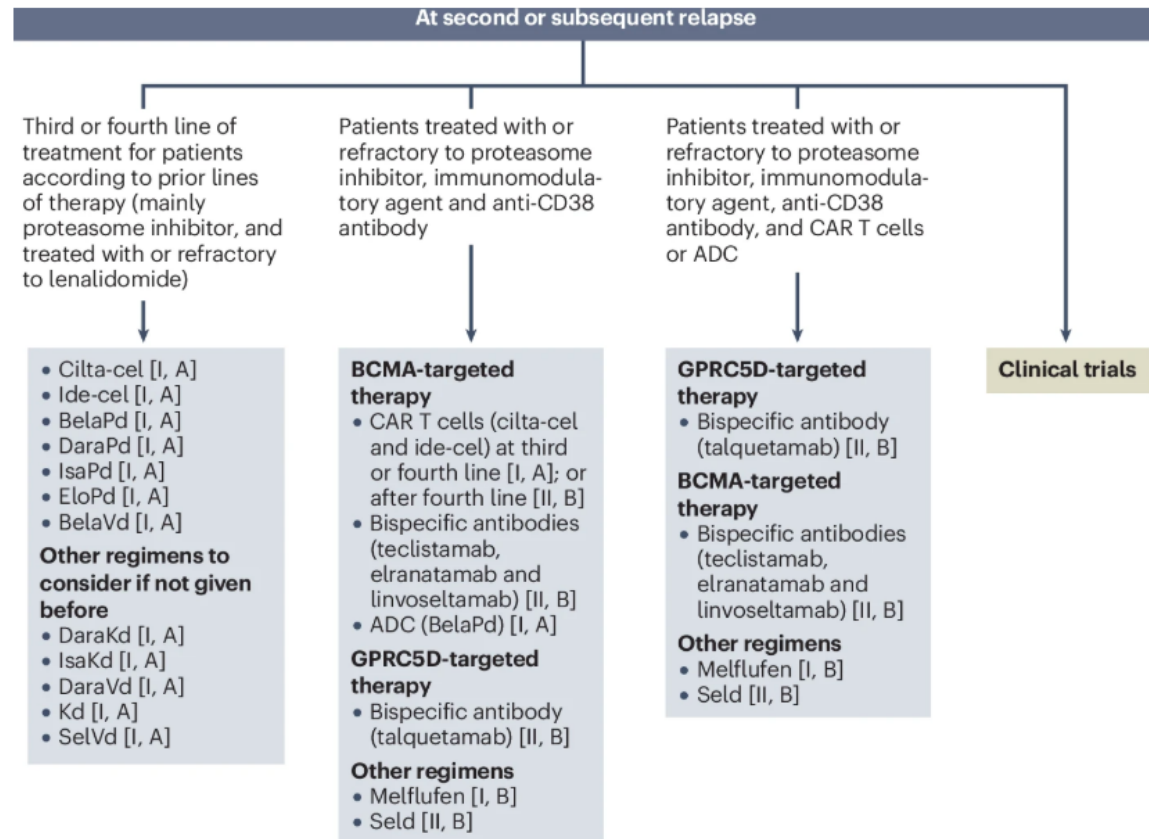
# The Natural History of Multiple Myeloma





**Fig. 3: Recommendations for the treatment of patients with relapsed and/or refractory multiple myeloma at third line and beyond.**

From: [EHA-EMN Evidence-Based Guidelines for diagnosis, treatment and follow-up of patients with multiple myeloma](#)



Recommendations include supporting levels of evidence and have been graded<sup>170</sup> (Supplementary Table 1). ADC, antibody–drug conjugate; Bela, belantamab mafodotin; CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; d, dexamethasone; Dara, daratumumab; Elo, elotuzumab; ide-cel, idecabtagene vicleucel; Isa, isatuximab; K, carfilzomib; P, prednisone; Sel, Selinexor; V, bortezomib.

# IMWG Recommendations for Post-T-cell Redirecting Therapy

## *Post T-cell Redirecting Therapy*



**Non-TCRT approaches, including selinexor, may salvage relapses after BCMA-targeted CAR-T cell therapy\***

### **Based on preclinical data, XPO1 inhibitors:<sup>1</sup>**

- Have less detrimental and more potentiating effect on T cells
- May promote T-cell fitness and reduce markers of T-cell exhaustion by modulating the immune microenvironment

### **In the STOMP clinical trial:**

- Selinexor-based triplet or quadruplet combination induced responses in 7 of 11 patients (64%) with prior BCMA-targeted therapy<sup>2</sup>
- Selinexor or selinexor-based combinations induced objective responses in 6 of 7 patients with relapse post BCMA-targeted CAR-T cells<sup>3</sup>

## **RECOMMENDATION<sup>1</sup>**

**Use a therapy with a different mechanism of action or immunotherapy targeting a different antigen for patients progressing while receiving, or shortly after receiving, BCMA-targeting TCE**

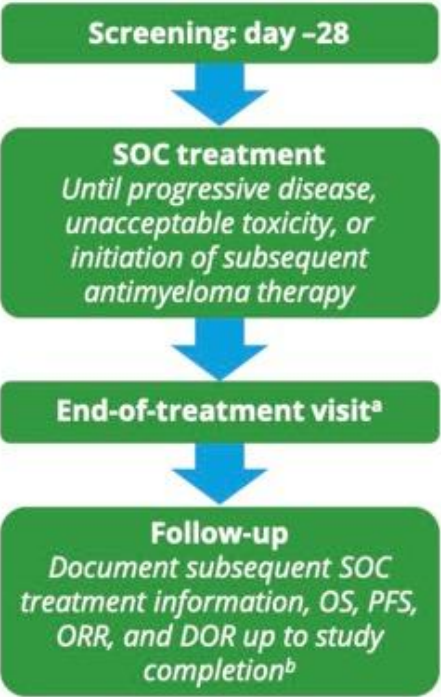
\*Selinexor and selinexor-based combinations were one of five therapeutic options described by the authors. Post-TCRT salvage with non-TCRT therapies has not been systematically investigated.

BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T cell; IMWG, International Myeloma Working Group; MM, multiple myeloma; TCE, T-cell engager; TCRT, T-cell redirecting therapies.

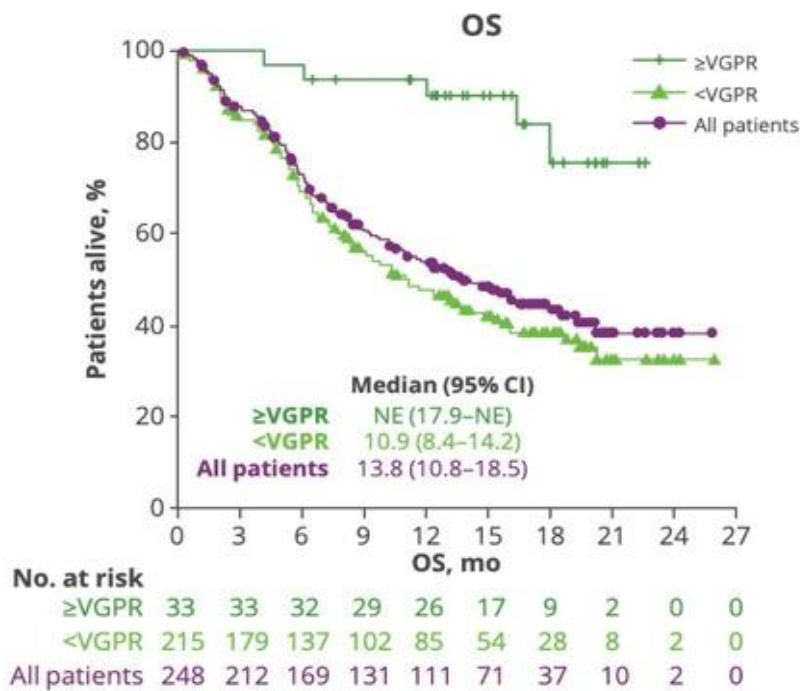
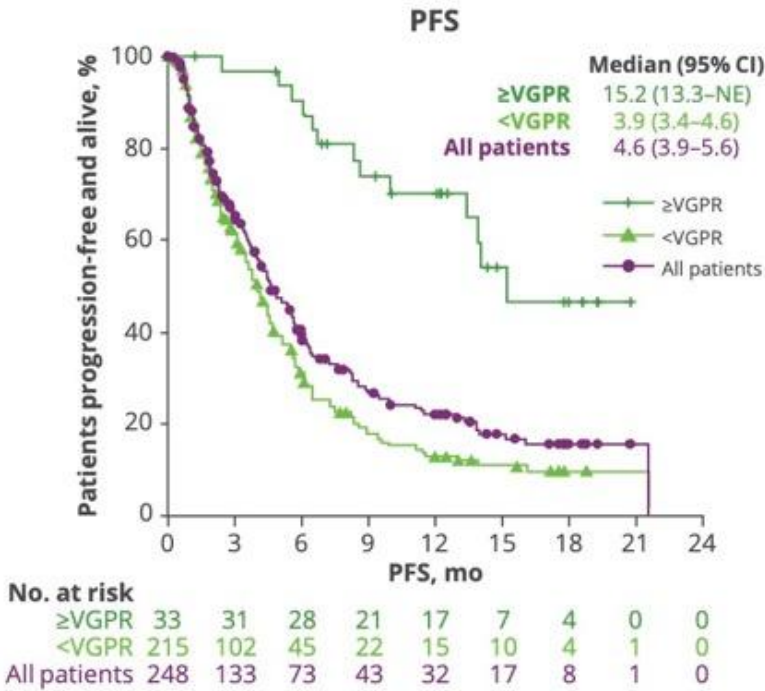
1. Costa LJ, et al. Leukemia. 2025;39(3):543–554; 2. Baljevic M, et al. EJHaem. 2022;3(4):1270–1276; 3. Chari A, et al. Br J Haematol. 2020;189(4):e126–e130.



# LocoMMotion: Real-life current standards of care in patients with RRMM who received ≥3 prior lines of therapy



<sup>a</sup>End-of-treatment visit is defined as ~30 days after completion of the last dose of the first SOC therapy used within the study. <sup>b</sup>End of the study is defined as 24 months after the first dose of SOC treatment for the last patient included in the study, except in cases of patient death that would end the study early. DOR, duration of response.



- Median age: 68 years
- Median prior lines: 4 (2–13)
- Triple-class refractory: 73.4%
- ORR: 31.5%
- mDOR: 7.7 months

Moreau P et al. IMS 2022;abstract P-264 (poster presentation)

mDOR, median duration of response; NE, not evaluable; SOC, standard of care





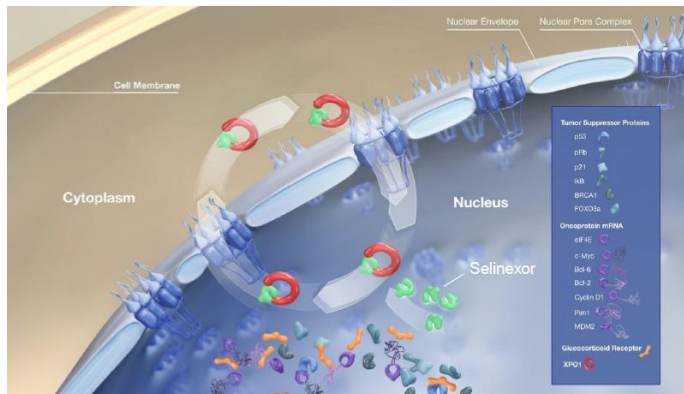
# Selinexor in Triple Class (IMiDs, PIs,CD38) RRMM

## • Inhibits XPO1

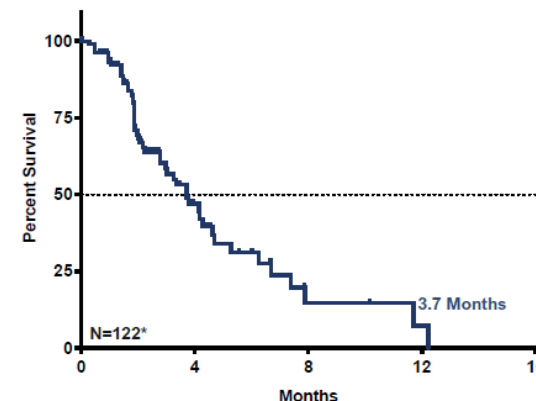
- XPO1 is the major nuclear export protein
- XPO1 is overexpressed in MM

## • STORM Study

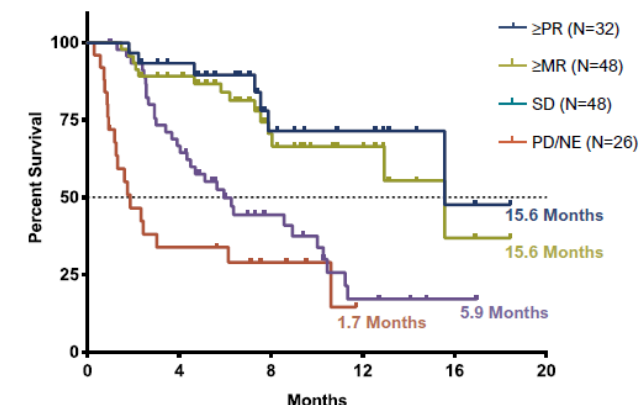
- N = 122; median 7 prior treatments
- 86% refractory to bortezomib, carfilzomib, lenalidomide, pomalidomide, and daratumumab
- Selinexor/Dex
- 19.7% PR, 4.9% VGPR, 1.6% sCR
- mDOR = 4.4 months
- Associated with hematologic and GI toxicity
- Aggressive supportive care needed



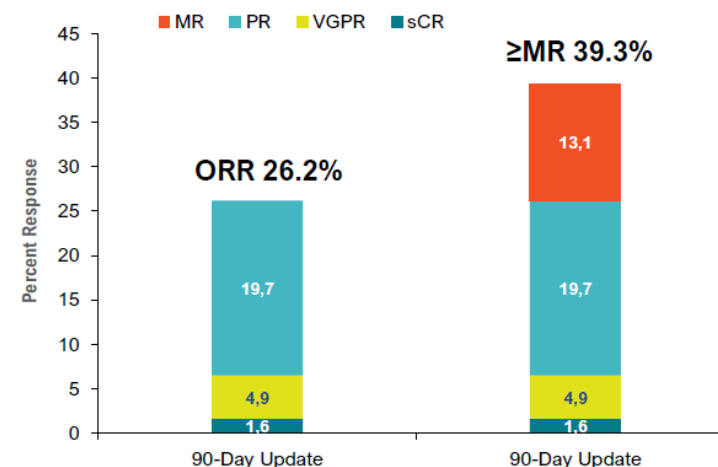
Progression-Free Survival – All



Overall Survival – Groups



Category	All Patients (N=122)	≥PR (N=32)	≥MR (N=48)	SD (N=48)	PD/NE (N=26)
Median PFS	3.7 Months	5.3 Months	4.6 Months	2.8 Months	1.1 Months
Median OS	8.6 Months	15.6 Months	15.6 Months	5.9 Months	1.7 Months



- Median of 7 prior treatment regimens
- Two patients with prior progression after CAR-T achieved a PR
- Median time to response was 1 month (range 1-14 weeks)
- Median duration of response was 4.4 months

Chari et al NEJM 2019; 381:727-38.



# Novel Selinexor Triplet and Quadruplet Regimens (SNd, SPed, SBd, SDPd): Results From the Phase 1b/2 STOMP Multiple Myeloma Trial

Sumit Madan,<sup>1</sup> Cristina Gasparetto,<sup>2</sup> Gary J Schiller,<sup>3</sup> Natalie S Callander,<sup>4</sup> Suzanne Lentzsch,<sup>5</sup> Sascha A Tuchman,<sup>6</sup> Noa Biran,<sup>7</sup> Tomer Mark,<sup>8</sup> Dane Van Domelen,<sup>8</sup> Jesus G Berdeja<sup>9</sup>

<sup>1</sup>Banner MD Anderson Cancer Center, Gilbert, AZ, USA; <sup>2</sup>Duke University Medical Center, Durham, NC, USA; <sup>3</sup>David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; <sup>4</sup>Carbone Cancer Center, University of Wisconsin-Madison, Madison, WI, USA; <sup>5</sup>Columbia University, New York, NY, USA; <sup>6</sup>University of North Carolina, Chapel Hill, NC, USA; <sup>7</sup>Hackensack Meridian Health, Hackensack University Medical Center, Teaneck, NJ, USA; <sup>8</sup>Karyopharm Therapeutics, Newton, MA, USA; <sup>9</sup>Tennessee Oncology, Nashville, TN, USA.

# Results: Treatment and Response

Parameter	SNd (n = 6)	SPEd (n = 5)	SBd (n = 7)	SDPd (n = 3)
Remain on treatment, n (%)	1 (16.7)	0	0	1 (33.3)
Duration of study treatment exposure (wk), median (min, max)	26.5 (8-148)	7.0 (4-81)	14.0 (4-50)	24.0 (16-118)
Average SEL dose (mg/week), median (min, max)	55.3 (41.9-61.0)	35.0 (21.8-40.0)	50.0 (24.0-60.0)	27.5 (14.7-31.3)
Relative SEL dose intensity (mg/week), median (min, max)	93.6 (88-117)	100.0 (73-120)	83.3 (40-100)	91.7 (49-100)
Dose reduction, n (%)				
Selinexor	0	0	4 (57.1)	0
Other co-drugs*	0	1 (20.0)	0	1 (33.3)
Dose interruption, n (%)				
Selinexor	4 (66.7)	2 (40.0)	2 (28.6)	2 (66.7)
Other co-drugs*	4 (66.7)	3 (60.0)	4 (57.1)	3 (100.0)
ORR, n (%)	1 (16.7)	1 (20.0)	5 (71.4)	2 (66.7)

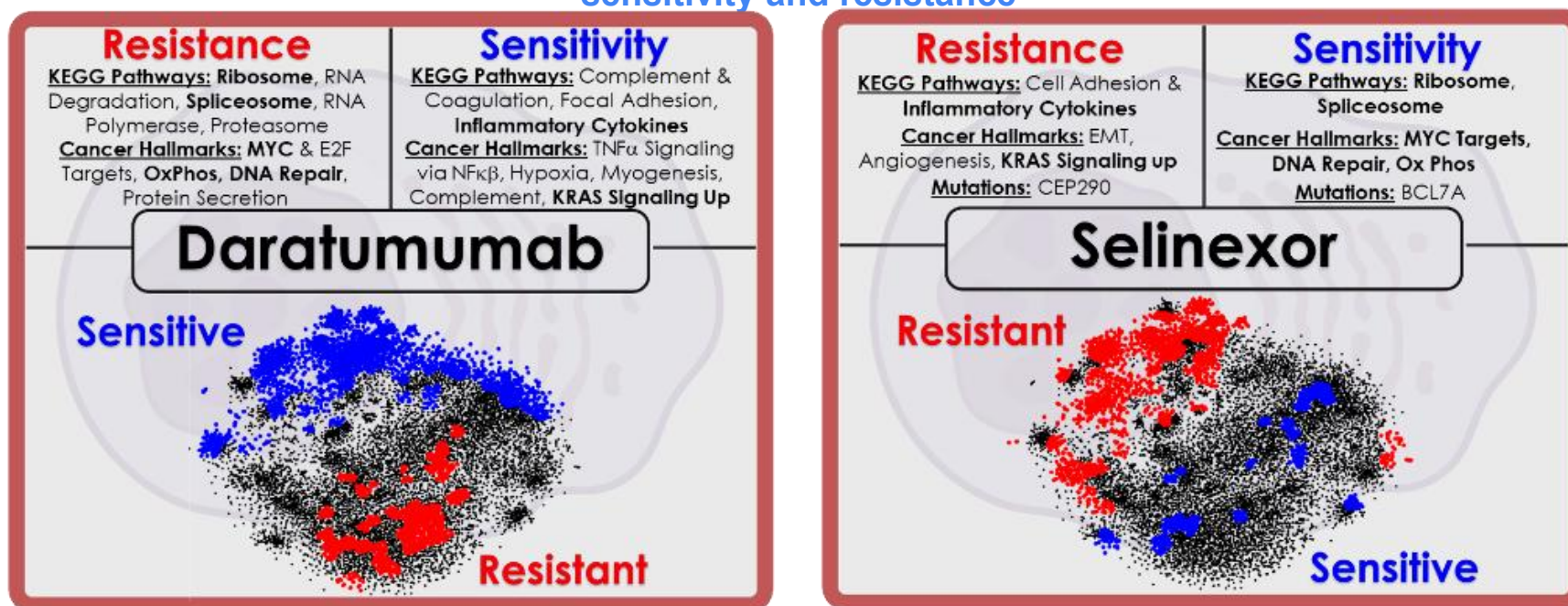
- Median duration of exposure ranged from 7 to 26.5 weeks.
- Overall response rates (ORR) ranged from 16.7% to 71.4%.

\*Includes any of pomalidomide, elotuzumab, daratumumab, ixazomib, or belantamab.

ORR, overall response rate; SBd, selinexor + belantamab mafodotin + dexamethasone; SDPd, selinexor + daratumumab + pomalidomide + dexamethasone; SEL, selinexor; SNd; selinexor + ixazomib + dexameth + elotuzumab + dexamethasone; STD, standard deviation.

# Gene Clusters Correlated With ex-vivo Sensitivity/Resistance to Selinexor Showed Patterns Opposing Those of Daratumumab

MM transcriptomic profile overlayed with gene clusters correlated with treatment sensitivity and resistance



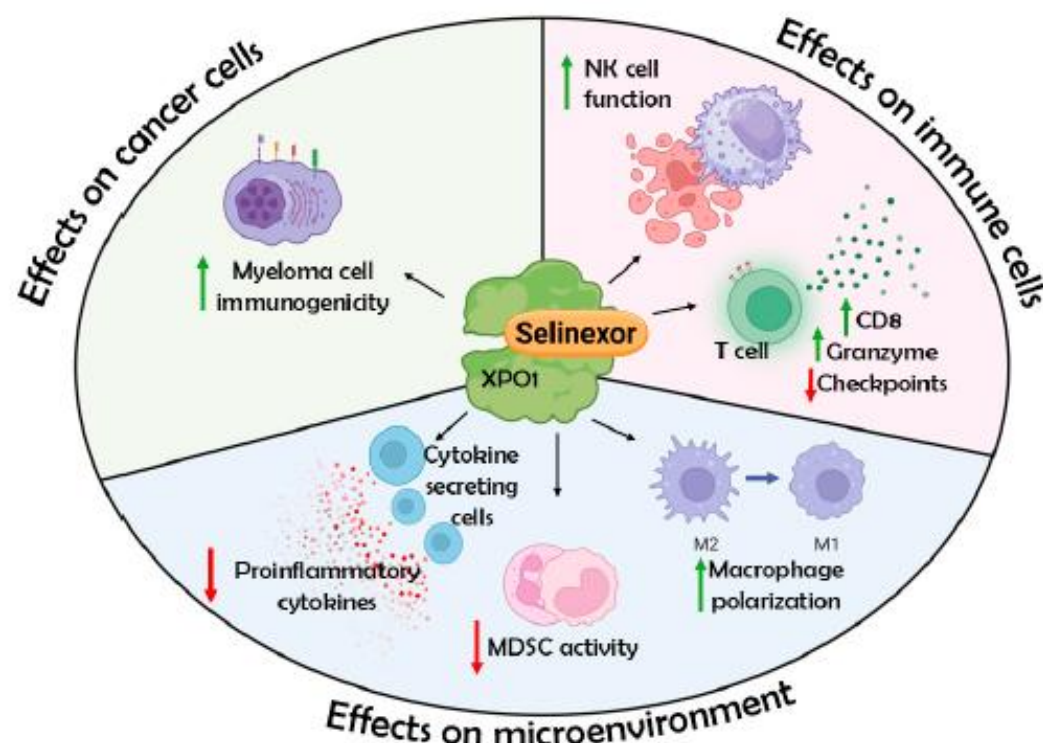
Genes associated with resistance to daratumumab were found to be associated with sensitivity to selinexor and vice versa

Sudalagunta, Praneeth Reddy et al. Cancer research vol. 85,2 (2025): 378-398.



# Selinexor influences multiple-immune cell pathways

Schematic illustration of selinexor's influences on immune cells and immunotherapy<sup>1</sup>



XPO1 inhibitors have the potential to promote T-cell fitness and reduce T-cell exhaustion, and different studies have demonstrated the effect of selinexor on T-cell fitness.

*XPO1 inhibitors may modulate the immune microenvironment to promote T-cell fitness and reduce markers of T-cell exhaustion”<sup>2</sup>*

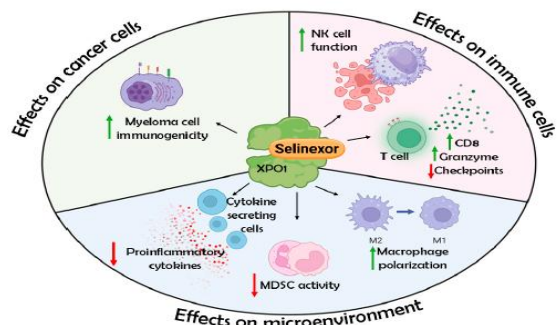
CD8, cluster of differentiation 8; M1, M1 macrophage (classically activated macrophage phenotype); M2, M2 macrophage (alternatively activated macrophage phenotype); MDSC, myeloid-derived suppressor cell; NK, natural killer (cell); XPO1, exportin 1

1. Khouri J, et al. J Clin Med. 2025 Jun 9;14(12):4071. 2. Costa LJ, et al. Leukemia. 2025;39:543–554.

# Selinexor, an XPO1 inhibitor, has potential to promote T-cell fitness and reduce T-cell exhaustion

## XPO1 inhibitors:<sup>1</sup>

- Have direct cytotoxic effects on tumour cells
- can reduce proinflammatory cytokine signaling
- May facilitate a favourable immune microenvironment for effector T cells to combat T-cell exhaustion
- Is associated with increased antibody-directed cytotoxicity of NK cells against cancer target cells



*The XPO1 inhibitors selinexor and eltanexor have been shown to reduce T-cell exhaustion in cell lines and animal models, suggesting their potential role in revitalising these key effector cells<sup>1</sup>*

NK, natural killer (cell); XPO1, exportin 1.

1. Binder AF, et al. Front Immunol. 2023;14:1275329; 2. Costa LJ, et al. Leukemia. 2025;39:543–554. 3. Khouri J, et al. J Clin Med. 2025 Jun 9;14(12):4071

*“In addition to direct cytotoxicity against malignant cells, XPO1 inhibitors may modulate the immune microenvironment to promote T-cell fitness and reduce markers of T-cell exhaustion”<sup>2</sup>*

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MULTIPLE MYELOMA, GAMMOPATHIES

International myeloma working group immunotherapy committee recommendation on sequencing immunotherapy for treatment of multiple myeloma

Luciano J. Costa<sup>1,2</sup>, Rahul Banerjee<sup>3</sup>, Hira Mian<sup>4</sup>, Katja Weisel<sup>4</sup>, Susan Bal<sup>1</sup>, Benjamin A. Derman<sup>5</sup>, Maung M. Htut<sup>6</sup>, Chandramouli Nagarajan<sup>7</sup>, Cesar Rodriguez<sup>8</sup>, Joshua Richter<sup>8</sup>, Matthew J. Frigault<sup>9</sup>, Jing C. Ye<sup>10</sup>, Niels W. C. J. van de Donk<sup>11</sup>, Peter M. Voorhees<sup>12</sup>, Benjamin Puliafito<sup>9</sup>, Nizar Bahlis<sup>13</sup>, Rakesh Popat<sup>14</sup>, Wee Joo Chng<sup>15</sup>, P. Joy Ho<sup>16</sup>, Gurbakhash Kaur<sup>8</sup>, Prashant Kapoor<sup>17</sup>, Juan Du<sup>18</sup>, Fredrik Schjesvold<sup>19</sup>, Jesus Berdeja<sup>20</sup>, Hermann Einsele<sup>21</sup>, Adam D. Cohen<sup>22</sup>, Joseph Mikhael<sup>23,24</sup>, Yelak Biru<sup>24</sup>, S. Vincent Rajkumar<sup>17</sup>, Yi Lin<sup>17</sup>, Thomas G. Martin<sup>25</sup> and Ajai Chari<sup>25</sup>

Journal of Clinical Medicine MDPI

Communication

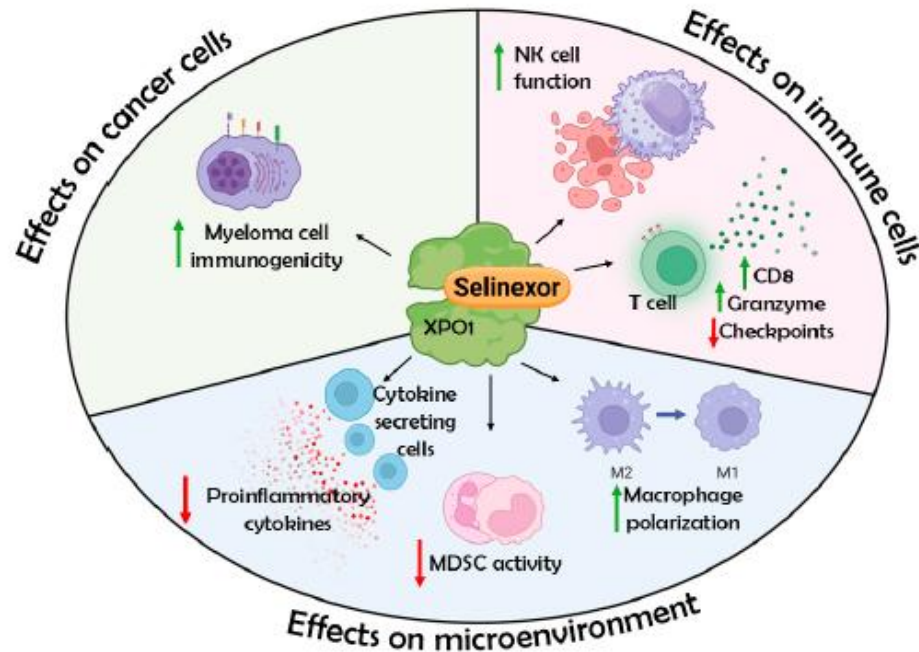
Focusing on Selinexor for Holding and Bridging Prior to CAR-T in Relapsed/Refractory Multiple Myeloma

Jack Khouri<sup>1</sup>, Douglas Sborov<sup>2</sup>, Adriana Rossi<sup>3</sup>, Thomas Martin<sup>4</sup>, Trinayan Kashyap<sup>5</sup>, Tomer Mark<sup>5</sup> and Muhamed Baljevic<sup>6,\*</sup>





# Selinexor, an XPO1 inhibitor, has potential to promote T-cell fitness and reduce T-cell exhaustion



## Effects of selinexor on:<sup>2,3</sup>

- **Cancer cells**
  - Induce **cell cycle arrest** and **apoptosis** of cancer cells
  - **Enhance immunogenicity** of surviving myeloma cells
  - **Selinexor may upregulate BCMA expression** and increase myeloma cell immunogenicity
- **Immune cells**
  - **Enhance CD8+ T-lymphocyte**
  - XPO1 activity is associated with **increased antibody-directed cytotoxicity of NK cells** against cancer and disrupts NK cell inhibition
  - BM samples from patients in clinical studies show that **selinexor increases CD8 and granzyme B expression** in T-cells without induction of immune checkpoints
- **Microenvironment**
  - **Polarize macrophages towards M1** and away from a tumour-promoting M2 state
  - **Inhibit of myeloid-derived suppressor cells** and neutrophil extracellular traps which provide potent immunosuppressive effects
  - **Enhance anti-tumour activity**
  - **Reduce pro-inflammatory cytokine signalling** (often through the NF- $\kappa$ B pathway)

*The **XPO1 inhibitors** selinexor and eltanexor have been shown to **reduce T-cell exhaustion** in cell lines and animal models, suggesting their potential role in revitalising these key effector cells<sup>1</sup>*

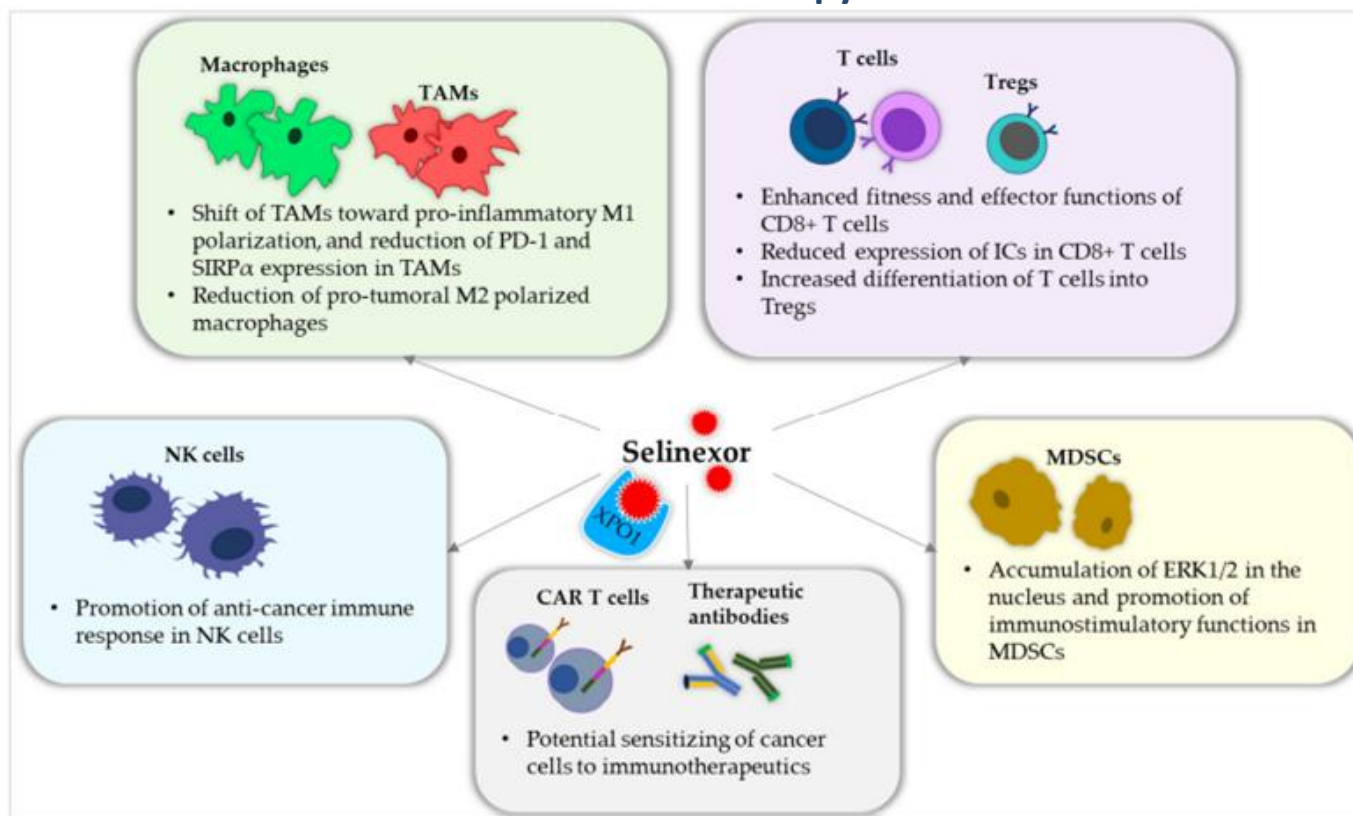
BCMA, B cell maturation antigen; BM, bone marrow; CAR-T, chimeric antigen receptor T; MDSC, myeloid-derived suppressor cells; NK, natural killer.

1. Binder AF, et al. Front Immunol. 2023;14:1275329; 2. Khouri J, et al. J Clin Med. 2025 Jun 9;14(12):4071; 3. Tasbihi K, Bruns H. Cells. 2025;14(6):430.



# Selinexor influences multiple-immune cell pathways

## Schematic illustration of selinexor's influences on immune cells and immunotherapy



- Selinexor is suggested to impact **macrophages** and **tumour-associated macrophages** (TAMs), **myeloid-derived suppressor cells** (MDSCs), **natural killer** (NK) cells, and **T cells** in the tumour microenvironment
- Selinexor potentially **sensitises cancer cells** to **CAR-T cells** and therapeutic antibodies
- Further in vitro and in vivo **experimental studies** with primary human cells and **randomised controlled clinical trials** on selinexor **sequencing regimens** are needed to **expand knowledge** in this area

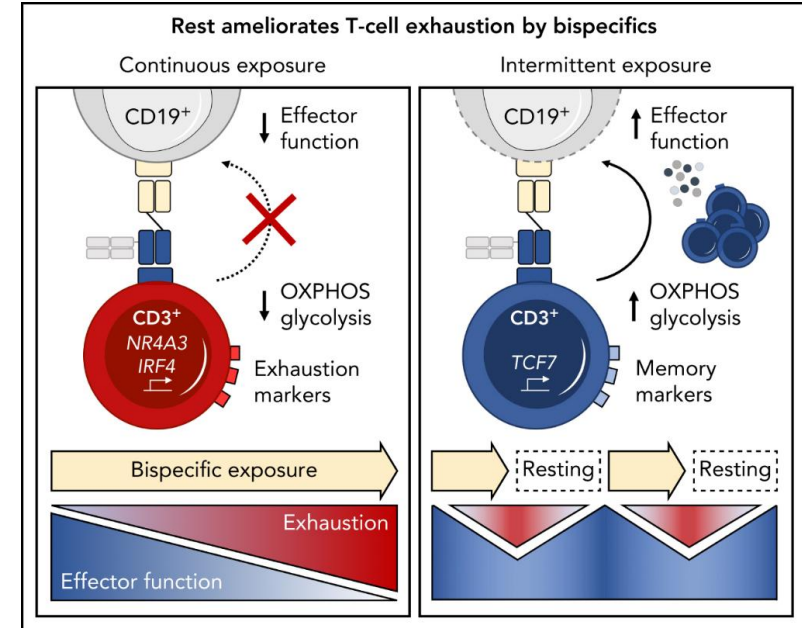
CAR, chimeric antigen receptor; CD8, cluster of differentiation 8; ERK1/2, extracellular-signal regulated kinases 1/2; IC, immune checkpoint; MDSC, myeloid-derived suppressor cell; NK, natural killer; PD-1, programmed death 1; SIRPα, signal regulatory protein alpha; TAM, tumour-associated macrophage; Treg, regulatory T cell.

1. Tasbihi K, Bruns H. Cells. 2025;14(6):430.

# XPO1 inhibition as a mechanism for enhancing BCMA-directed therapy outcomes<sup>1,2</sup>

- To **improve outcomes with BCMA targeted therapies**, without risk to efficacy, it is important that the treatment sequence **does not include two consecutive BCMA targeted therapies**
- Most bispecific antibody therapies have been developed with **continuous therapy schedules**, which can be detrimental to T-cell fitness
- Accumulating data suggest that **treatment-free intervals** can be **beneficial** in functional and transcriptional T-cell rejuvenation

Incorporating selinexor combinations as BCMA-free regimens can enhance benefits following prior BCMA-directed therapy by optimising treatment sequencing



- Continuous exposure to a CD19xCD3 bispecific molecule induces T-cell exhaustion
- Treatment-free intervals transcriptionally reprogramme and functionally reinvigorate T cells

BCMA, B-cell maturation antigen.

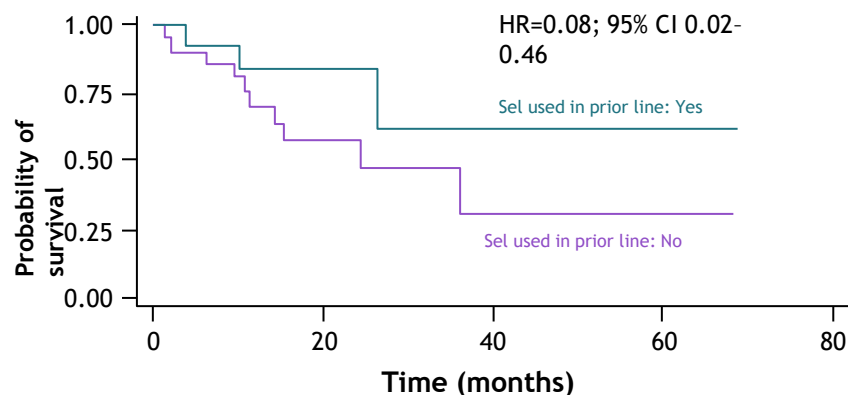
1. Binder AF, et al. Front Immunol. 2023;14:1275329; 2. Philipp N, et al. Blood. 2022;140:1104–1118.



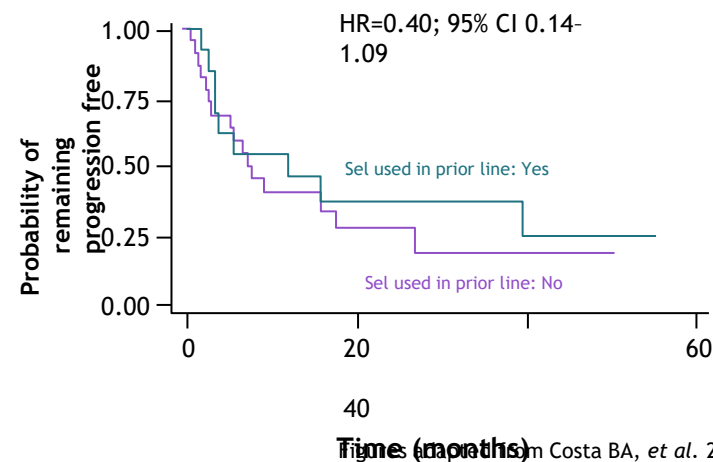
# Sequencing selinexor and BCMA-directed therapy

- In a retrospective cohort study, the impact of prior treatment with a selinexor-containing regimen on CAR-T outcomes was evaluated in patients (n = 45) with RRMM
- The BCMA-directed CAR-T products administered included ide-cel (60%), cilta-cel (35.6%) and CC-98633/BMS-986354 (4.4%)
- At a median follow-up of 68 months, **median DoR was 8.1 months** (IQR: 2.6-39), **median PFS was 8.1 months** (IQR: 3.1-39.5), and **median OS was 35.9 months** (IQR: 14.2-NR)

OS if selinexor was used in the immediate prior LOT before CAR-T therapy



PFS if selinexor was used in the immediate prior LOT before CAR-T therapy



Patients who received selinexor in the therapy line immediately preceding CAR-T demonstrated longer PFS and OS compared with those exposed in earlier lines

Prior selinexor exposure did not compromise the efficacy or safety of anti-BCMA CAR-T in RRMM, with encouraging PFS and OS observed post-CAR-T in patients previously treated with selinexor

BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T cell; CI, confidence interval; cilta-cel, ciltacabtagene autoleucel; DoR, duration of response; ide-cel, idecabtagene vicleucel; HR, hazard ratio; IQR, interquartile range; LOT, line of therapy; MM, multiple myeloma; NR, not reached; OS, overall survival; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma; BCMA, B-cell maturation antigen. Costa BA, et al. *J Clin Med*. 2025;14:1316.



# Selinexor-based regimens after prior BCMA-directed therapy

- This retrospective analysis evaluated the responses to therapy with selinexor of 11 patients who received anti-BCMA therapy in the prior line in STOMP study.
- Median age was 71 years (range 46–85); patients received a median of **6 prior lines of therapy** (range 4–10).

	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5	Pt 6	Pt 7	Pt 8	Pt 9	Pt 10	Pt 11
<b>STOMP arm</b>	SVd	SVd	SVd	SPd	SPd	SPd	SKd	SPVd	SPEd	SPd	SKd
<b>Most recent anti-BCMA therapy*</b>	blmf	blmf	blmf	blmf	MEDI2228	Ide-cel + Dara	blmf + pembro	SEA-BCMA + dex	BCMA BiTE	blmf	Ide-cel
Duration (mos)	1.5	0.8	1.1	4.3	1.7	2.7	1.4	1.4	1.7	24.9	5.8
Best response	PR	SD	SD	VGPR	PD	PR	SD	SD	Unk	VGPR	PR
<b>Time from end of anti-BCMA to 1<sup>st</sup> STOMP dose (mos)</b>	0.8	1.0	7.4	35.2	0.2	1.3	1.1	1.0	14.2	1.0	2.6
<b>Best response on STOMP</b>	PR	SD	MR	SD	PR	VGPR	PR	PR	MR	PR	VGPR
<b>Duration of STOMP treatment (mos)</b>	7.9	6.0	8.1	1.4	2.9	15.1	15.8 <sup>a</sup>	12.9	1.4	12.2 <sup>a</sup>	13.1 <sup>a</sup>

## Patients receiving selinexor-based combinations

- ORR** was **63.6%** in patients receiving selinexor-based combinations
- CBR** was **81.8%** in patients receiving selinexor-based combinations
- mPFS** was **NR** (95% CI 6.0–NR) in patients receiving selinexor-based comb with median follow-up of 14.3 months
- 6-month PFS** probability was **75.0%** (95% CI: 50.3–100.0)

## Efficacy prior anti-BCMA regimen

- ORR** was **50%** \*for the prior anti BCM containing regimen
- CBR** was **50%** with prior anti-BCMA therapy
- mPFS** was **2 months** (95% CI: 1.5–NR) with prior anti-BCMA therapy and **6-month PFS** probability was **12.0%** (95% CI: 1.9–74.4)

\*One patient had an unknown response.

BCMA, B-cell maturation antigen; BiTE, bi-specific T-cell engager; blmf, belantamab mafodotin; Dara, daratumumab; DoR, duration of response; Ide-cel, idecabtagene vicleucel; IMiD, immunomodulatory drug; MM, multiple myeloma; mos, months; MR, minimal response; PD, progressive disease; pembro, pembrolizumab; PR, partial response; SD, stable disease; unk, unknown; VGPR, very good partial response; SKd, selinexor, carfilzomib, dexamethasone; SPd, selinexor, pomalidomide, dexamethasone; SVd, selinexor, bortezomib, dexamethasone; SPEd, selinexor, pomalidomide, elotuzumab, dexamethasone; SPVd, selinexor, pomalidomide, bortezomib, dexamethasone. \*Patients number 1–5 and 10 were treated with ADC anti-BCMA therapies.

1. Baljevic M, et al. eJHaem. 2022;3:1270–1276.

# Selinexor-based regimens after prior BCMA-directed therapy

This retrospective analysis evaluated responses to SvD therapy among 18 penta-drug refractory patients (aged 40–76 years; median of 7 prior lines of therapy) who were also refractory to both BCMA- and GPRC5D-directed therapies

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
<b>PFS under anti-BCMA therapy (months)</b>	5.5	6.3	8.8	5.9	9.9	PREF	14.5	10.0	7.1	10.1	23	13.1	9	12.5	3.3*	9.9	7.9	6.3
<b>PFS under anti-GPRC5D therapy (months)</b>	2.0	PREF	6.2	13.0	6.5	3.8	4.4	PREF	3.2	12.0	16	6.4	15.4	8.6	9.9	4.9	3.2	6.3
<b>PFS under SvD (months)</b>	8.6	6.9	10.0	NR	N/A	4.3	N/A	NR	3.7	1.6	NR	N/A	NE	7.9	3.6	7.2	N/A	NR

## Patient Characteristics

- **Median age was 61.7** years (range 40-76);
- patients received a **median of 7 prior** lines of therapy (range 5-9) and
- **58%** of the patients had **extramedullary disease (EMD)**
- **58%** of the patients present **High-Risk cytogenetics** at the start of SvD.
- Penta-drug refractoriness defined as disease refractory to two different proteasome inhibitors (bortezomib, ixazomib, carfilzomib), two immunomodulatory agents (lenalidomide, thalidomide, pomalidomide), and antiCD38 monoclonal antibodies (daratumumab or isatuximab)

## Key efficacy findings:

- **ORR was 61%**; first responses occurred after a median of 0.9 months
- **mPFS was 4.3 months** (mFU: NR)
- **EMD** (including paraosseous lesions) was present in nine patients at the start of SvD treatment; four patients **achieved complete or near-complete radiographic resolution**
- Following SvD treatment, two patients were **successfully bridged to subsequent CAR-T cell therapy, and two patients were successfully bridged to CAR-T apheresis and await CAR-T infusion**

\*On teclistamab. AE, adverse event; BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor-T cell; EMD, extramedullary disease; GPRC5D, ; mFU, median follow-up; mPFS, median progression-free survival; N/A, not applicable; NR, not reported; ORR, overall response rate; PFS, progression-free survival; PREF, primary refractory; SvD, selinexor-bortezomib-dexamethasone; TRAE, treatment-related adverse event.

Al-Bazaz M, et al. Pre-print. Available at: <https://doi.org/10.21203/rs.3.rs-8124153/v1> (Accessed March 2026)



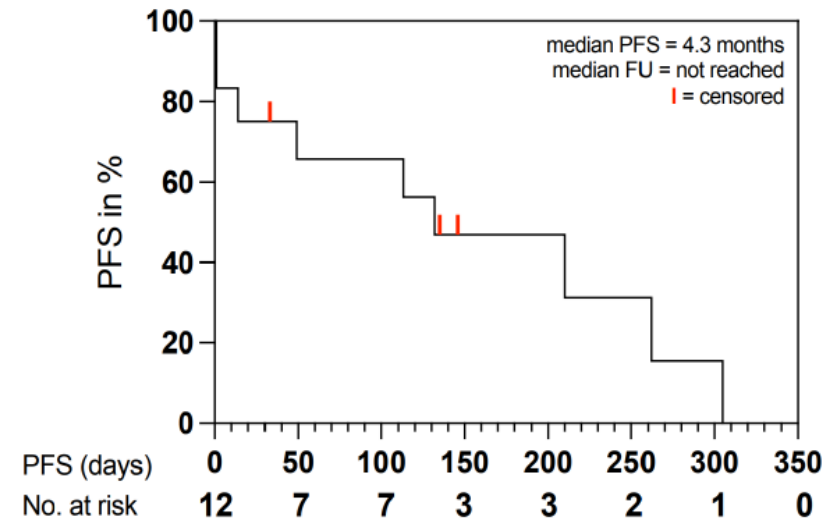
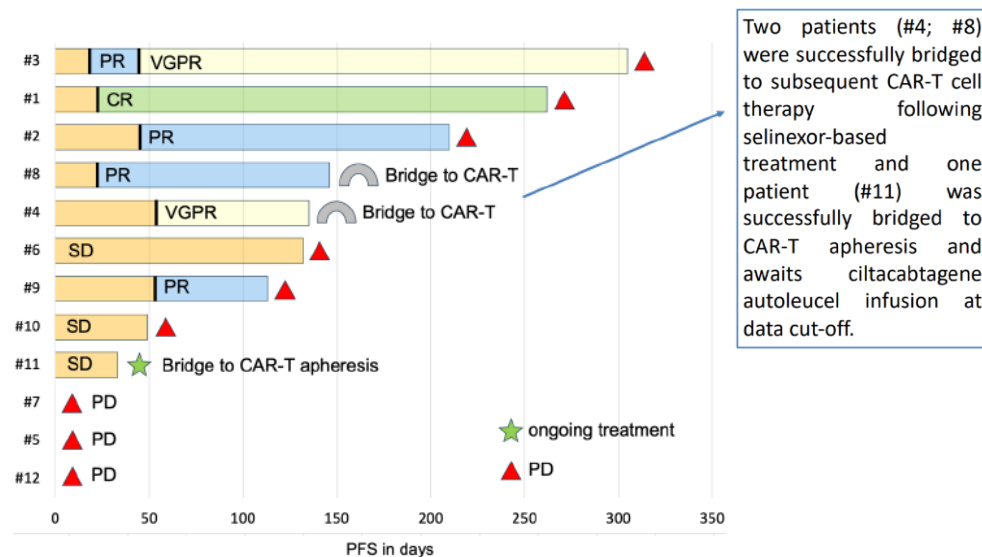


# Selinexor-based regimens after prior BCMA-directed therapy

This retrospective analysis evaluated the responses to therapy with Selinexor combined with bortezomib, and dexamethasone (SVd) of 12 penta-drug refractory patients (aged 40 to 76 years) who were also refractory to both BCMA-and GPRC5D directed therapies.

## Results

- **SVd achieved a 50% overall response rate and a median progression-free survival of 4.3 months.**
- **All responses occurred within the first month of treatment.**
- **EMD including paraosseous lesions was present in four patients at start of SVd treatment (Patient #1, #2, #4, #5). Three achieved complete radiographic resolution**



1. Al-BazazM et al.. DGHO Kongress2025, Abstract Nr. P12585..



# Selinexor-based regimens after prior BCMA-directed therapy

This retrospective analysis evaluated the responses to therapy with Selinexor combined with bortezomib, and dexamethasone (SVd) of 12 penta-drug refractory patients (aged 40 to 76 years) who were also refractory to both BCMA-and GPRC5D directed therapies.

**Key safety findings:**

- **TRAEs** resulted in selinexor **dose modifications** in five patients and discontinuation in one patient
- **No Grade ≥3 infections** or **treatment-related deaths** occurred

Most common TRAEs					
Haematological AEs, n (%)	Grade 1/2	Grade 3/4	Non-haematological AEs, n (%)	Grade 1/2	Grade 3/4
Anaemia	5 (33)	8 (53)	Fatigue	13 (72)	1 (6)
Thrombocytopenia	3 (19)	10 (63)	Nausea	9 (53)	0 (0)
Neutropenia	6 (38)	4 (25)	Loss of appetite	12 (71)	0 (0)

Selinexor’s activity is **antigen-independent** and **not dependent on T-cell function**, so it remains effective despite antigen escape or T-cell exhaustion resulting from immunotherapy treatments.

Data support the rationale for using selinexor to stabilize disease while preparing for subsequent interventions, further reinforced by findings indicating that selinexor does not impair T-cell viability or collection capacity.<sup>2</sup>

Selinexor offers the advantage of oral administration, enabling outpatient treatment.

1. Al-BazazM et al.. DGHO Kongress2025, Abstract Nr. P12585..

# Conclusions



**Selinexor is a first-in-class, oral XPO1 inhibitor with a unique MoA<sup>1,2</sup>**

**SVd is indicated in adults with RRMM who have received at least one prior therapy<sup>3</sup>**

**Recent subgroup analyses from the BOSTON study support the use of SVd in several RRMM populations:<sup>2,4</sup>**

- Lenalidomide-refractory RRMM
- PI-naïve relapsed or refractory RRMM
- Bortezomib-naïve relapsed or refractory RRMM

**SVd is the only approved triplet therapy allowing double class switch in DRd-exposed patients<sup>1</sup>**

**The use of bortezomib prior to carfilzomib or pomalidomide in later lines of therapy is a sequence allowed by the ESMO guidelines<sup>1</sup>**

**SVd has demonstrated a generally manageable safety profile with AEs that can be lessened using dose reductions, without compromising efficacy<sup>5–8</sup>**

2L, second line; AE, adverse event; MM, multiple myeloma; MoA, mechanism of action; PI, proteasome inhibitor; RRMM, relapsed/refractory multiple myeloma; SVd, selinexor + bortezomib + dexamethasone.

1. Dimopoulos MA, et al. *Ann Oncol*. 2021;32(3):309–322. 2. Mateos MV, et al. Poster P917. Presented at EHA2023 Hybrid Congress, 8–11 June 2023, Frankfurt, Germany. 3. NEXPOVIO® (selinexor) Summary of Product Characteristics. May 2022. 4. Mateos MV, et al. Poster P886. Presented at EHA2023 Hybrid Congress, 8–11 June 2023, Frankfurt, Germany. 5. Chari A, et al. *New Engl J Med*. 2019;381:727–738. 6. Grosicki S, et al. *Lancet*. 2020;396(10262):1563–1573. 7. Jagannath S, et al. *Blood*. 2021;138(Suppl. 1):3793. 8. Jagannath S, et al. Poster presented at: 63rd ASH Annual Meeting and Exposition; December 13, 2021; Atlanta, GA.



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