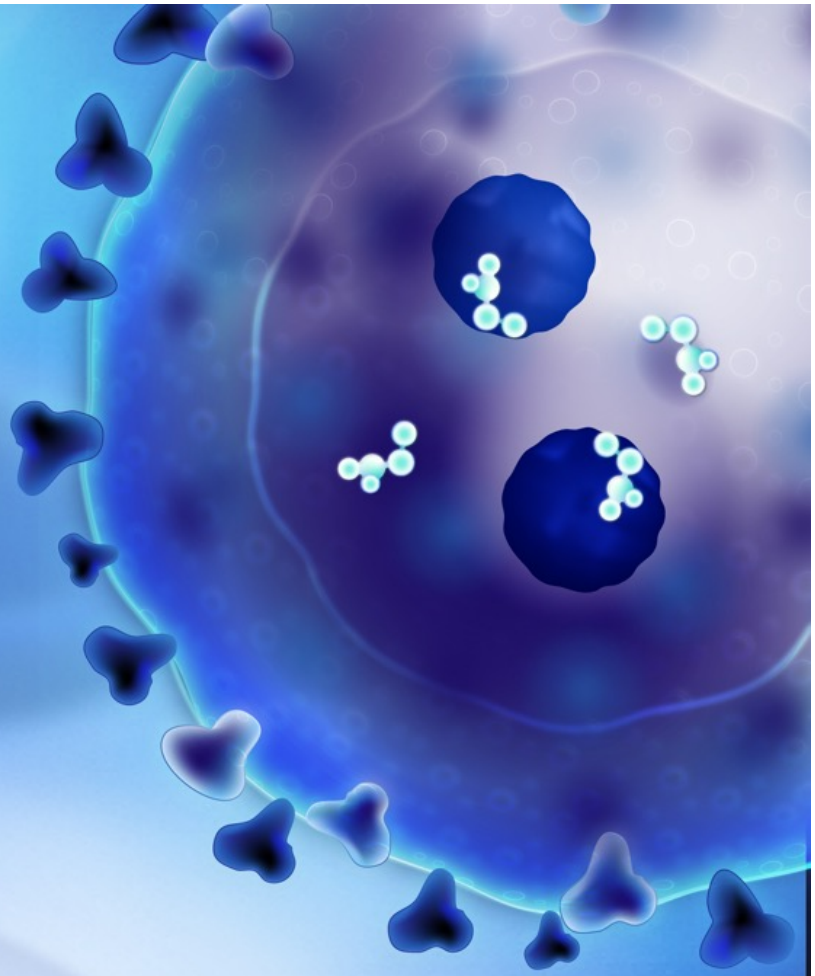
Multiple Myeloma Satellite Symposium at the
30th European Hematology Association Congress

Innovating relapsed refractory multiple myeloma care: Unmet needs, therapy management, and real-world experience

Saturday, 14th June | 10:00–11:30



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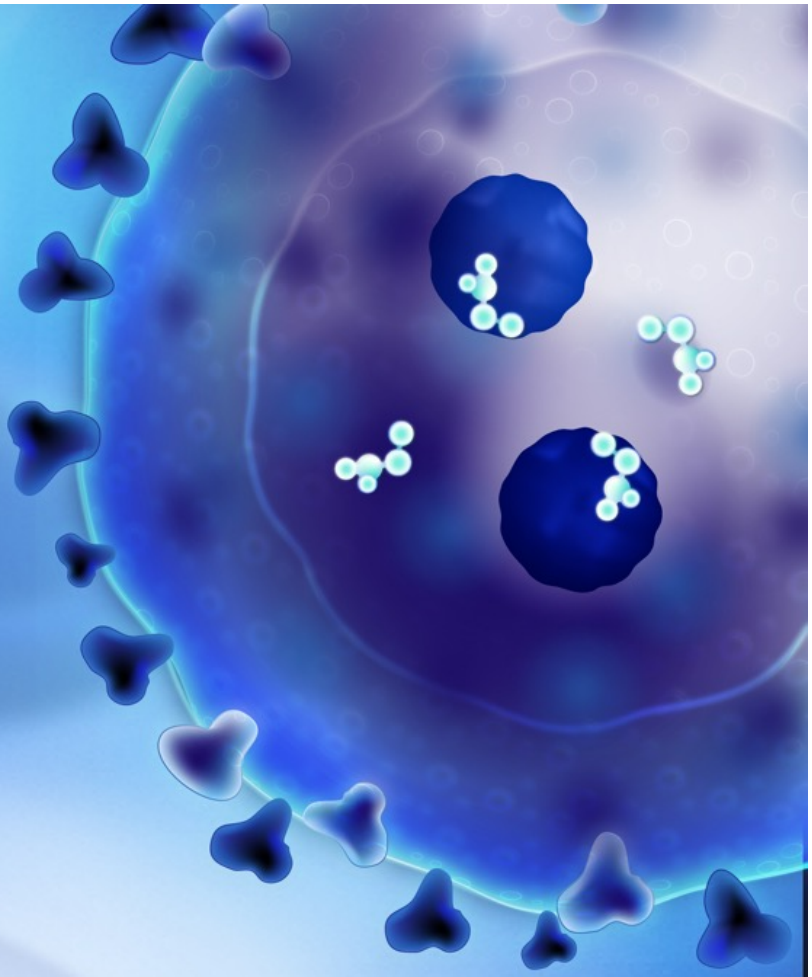
Introduction

María Victoria Mateos
University of Salamanca, Salamanca, Spain



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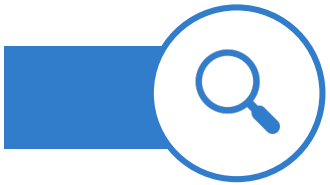
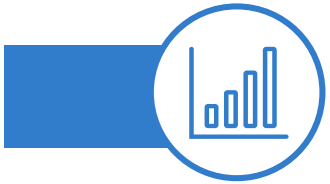
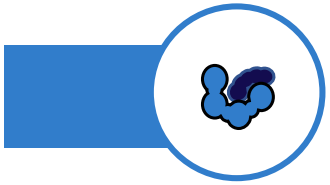
During this symposium you will learn about…



The continued **unmet needs of patients** with early relapsed refractory MM, with a focus on **the role of XPO1 inhibition** in addressing these challenges



The **latest clinical data and strategies for the therapeutic management** of relapsed refractory MM



Real-world experiences with selinexor-based combination regimens and their positioning in the evolving MM treatment landscape

Innovative treatment approaches for enhancing care in patients with relapsed refractory MM

MM, multiple myeloma; XPO1, exportin 1.

Faculty

María Victoria Mateos (Chair)

University of Salamanca, Salamanca, Spain

Karthik Ramasamy

Oxford University Hospitals NHS Foundation Trust, Oxford, UK

Elena Zamagni

University of Bologna, Bologna, Italy

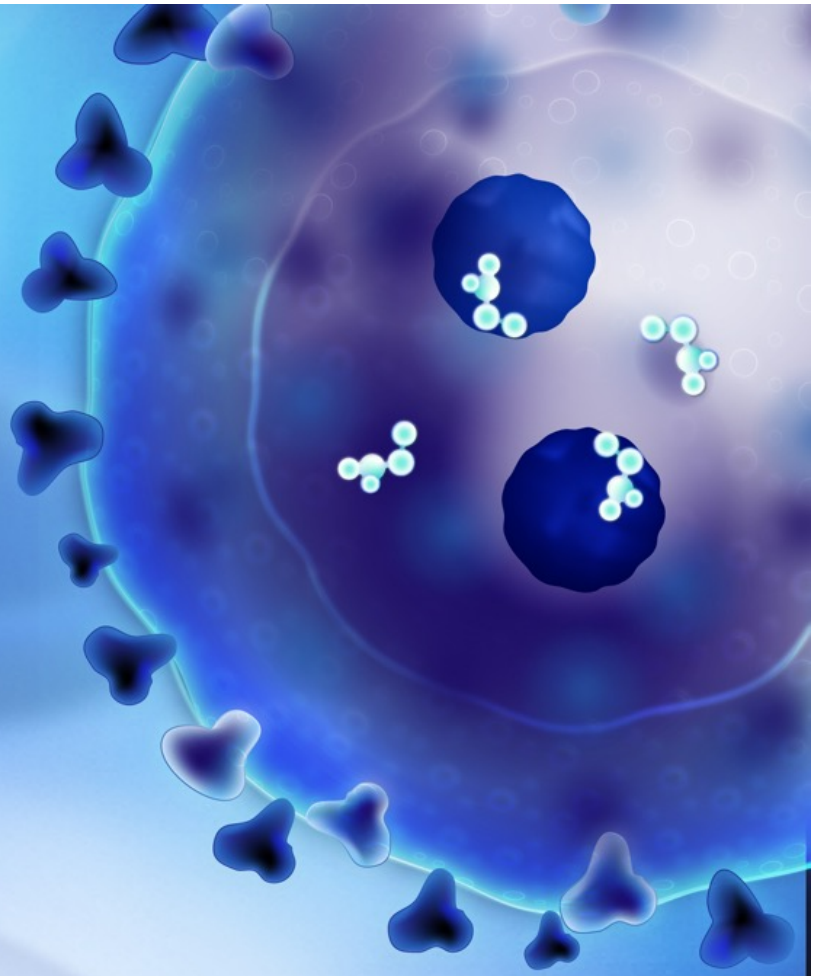
Agenda

Time (CEST)	Title	Presenter
10:00–10:05	**Introduction**	**María Victoria Mateos (Chair)** *University of Salamanca, Salamanca, Spain*
10:05–10:40	**Addressing unmet needs with a new mechanism of action: Role and place of XPO1 inhibition**	**María Victoria Mateos**
10:40–11:00	**Streamlining therapy management: Practical strategies for enhanced treatment outcomes**	**Karthik Ramasamy** *Oxford University Hospitals NHS Foundation Trust, Oxford, UK*
11:00–11:20	**Bridging evidence and practice: Real-world insights and clinical case discussions**	**Elena Zamagni** *University of Bologna, Bologna, Italy*
11:20–11:30	**Q&A and closing remarks**	**María Victoria Mateos**

XPO1, exportin 1.

Addressing unmet needs with a new mechanism of action: Role and place of XPO1 inhibition

María Victoria Mateos
University of Salamanca, Salamanca, Spain



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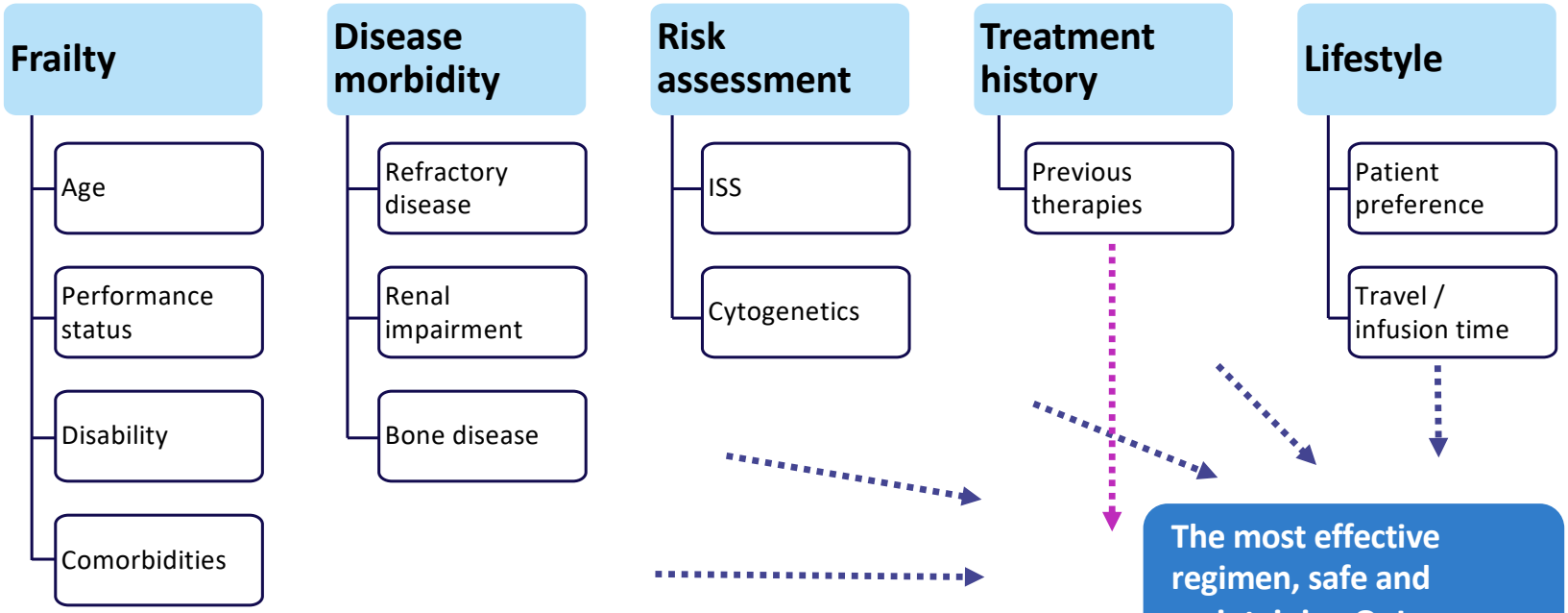
Disclosures

- Honoraria derived from lectures and participation in advisory boards from Janssen, BMS, Amgen, GSK, AbbVie, Pfizer, Regeneron, Roche, Sanofi, Menarini Stemline, and Kite

Disease and patient-based factors influencing treatment decision-making at the relapse setting



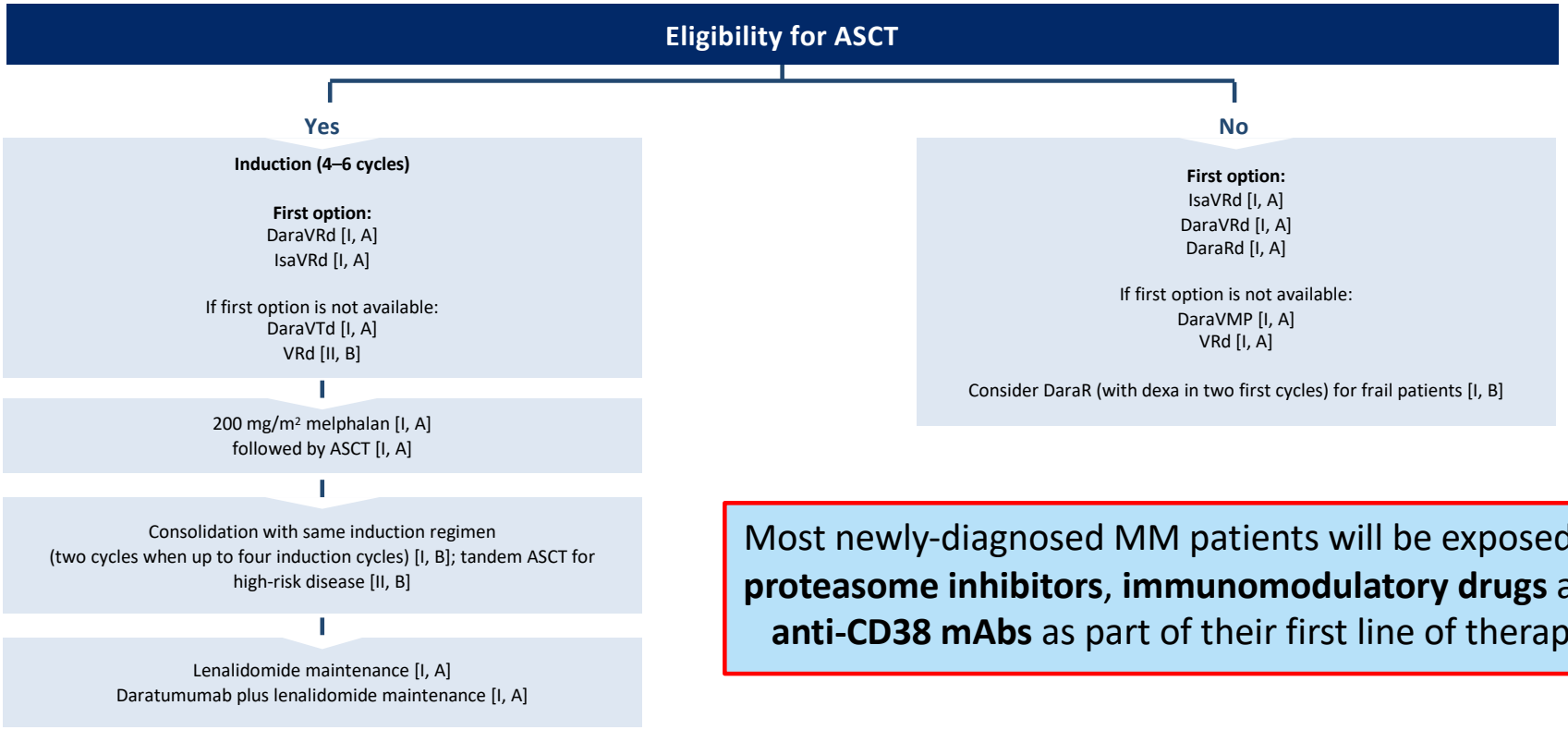
Treatment history is a crucial factor

ISS, International Staging System; QoL, quality of life.

Information based on speaker's expert opinion.

EHA-EMN 2025 guidelines

Newly-diagnosed MM: Exposure to proteasome inhibitors, immunomodulatory drugs, and anti-CD38 mAbs



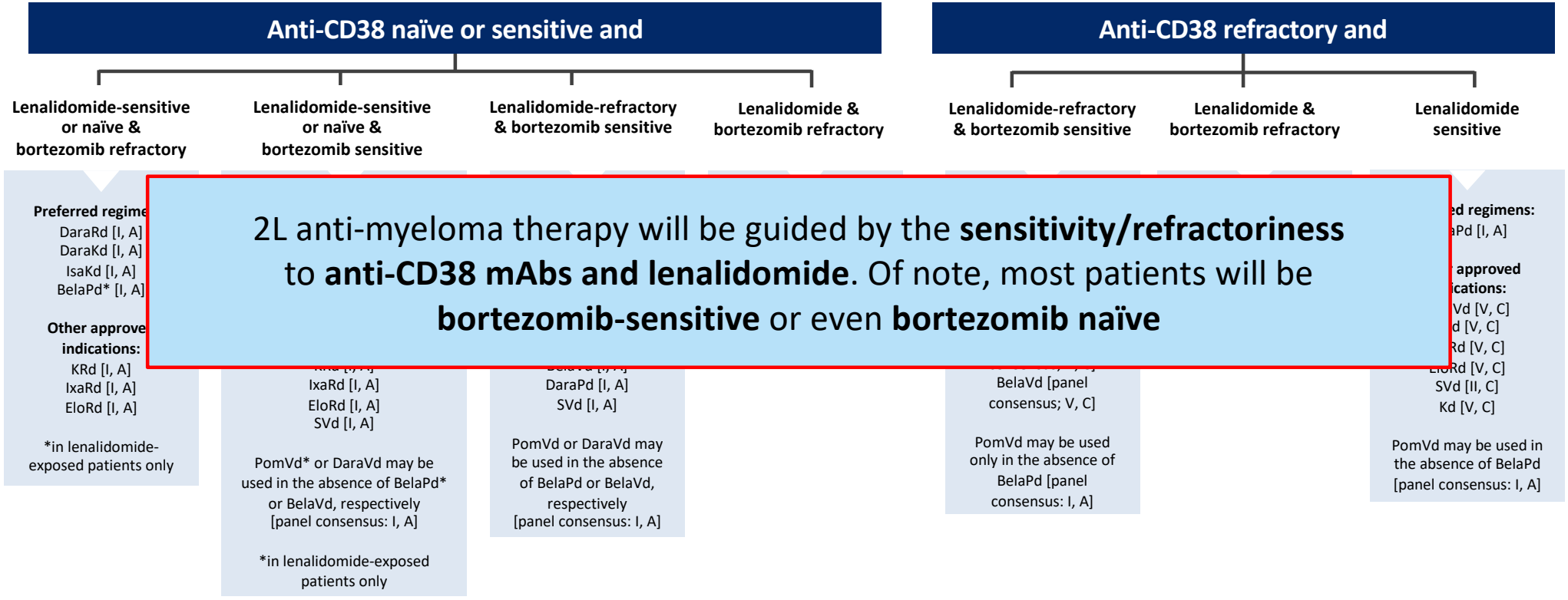
Most newly-diagnosed MM patients will be exposed to **proteasome inhibitors**, **immunomodulatory drugs** and **anti-CD38 mAbs** as part of their first line of therapy

ASCT, autologous stem cell transplantation; Dara, daratumumab; dexa, dexamethasone; EHA, European Hematology Association; EMN, European Myeloma Network; Isa, isatuximab; mAb, monoclonal antibody; MM, multiple myeloma; R, lenalidomide; Rd, lenalidomide/dexamethasone; VMP, bortezomib/melphalan/prednisone; VRd, bortezomib/lenalidomide/dexamethasone; VTd, bortezomib/thalidomide/dexamethasone.

Dimopoulos MA, Terpos E, et al. *Nat Rev Clin Oncol.* 2025 (under minor revision).

EHA-EMN 2025 guidelines

Most patients coming to 2L will be bortezomib-sensitive



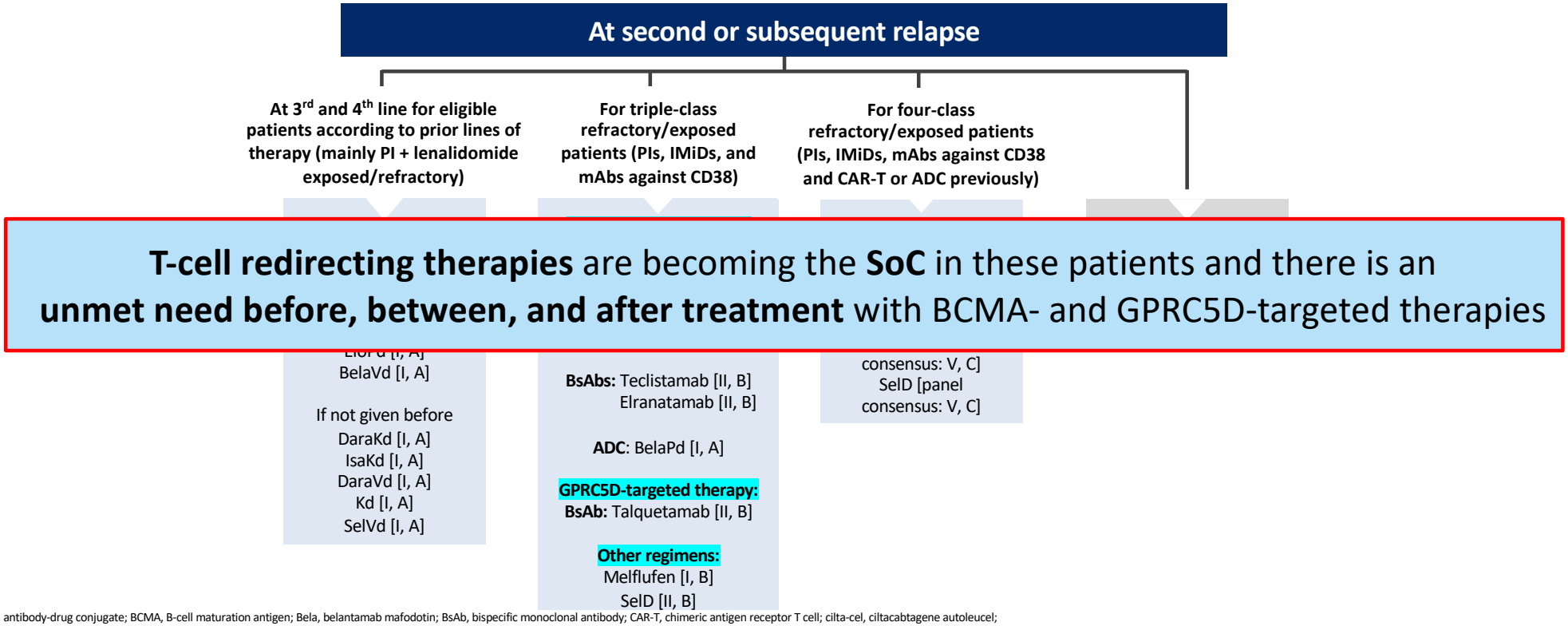
2L anti-myeloma therapy will be guided by the **sensitivity/refractoriness** to **anti-CD38 mAbs and lenalidomide**. Of note, most patients will be **bortezomib-sensitive** or even **bortezomib naïve**

Bela, belantamab mafodotin; cilta-cel, ciltacabtagene autoleucel; d, dexamethasone; Dara, daratumumab; EHA, European Hematology Association; Elo, elotuzumab; EMN, European Myeloma Network; Isa, isatuximab; Ixa, ixazomib; K, carfilzomib; Kd, carfilzomib/dexamethasone; KRd, carfilzomib/lenalidomide/dexamethasone; L, line; mAb, monoclonal antobody; Pd, pomalidomide/dexamethasone; PomVd, pomalidomide/bortezomib/dexamethasone; R, lenalidomide; Rd, lenalidomide/dexamethasone; S, selinexor; Vd, bortezomib/dexamethasone.

Dimopoulos MA, Terpos E, et al. *Nat Rev Clin Oncol.* 2025 (under minor revision).

EHA-EMN 2025 guidelines

If anti-BCMA–directed therapy is used in 2L, subsequent use of another anti-BCMA or GPRC5D-targeted agent will likely require an intervening line of therapy to mitigate resistance and restore target antigen expression



T-cell redirecting therapies are becoming the **SoC** in these patients and there is an **unmet need before, between, and after treatment** with BCMA- and GPRC5D-targeted therapies

ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; Bela, belantamab mafodotin; BsAb, bispecific monoclonal antibody; CAR-T, chimeric antigen receptor T cell; cilta-cel, ciltacabtagene autoleucel; D, dexamethasone; Dara, daratumumab; EHA, European Hematology Association; Elo, elotuzumab; EMN, European Myeloma Network; GPRC5D, G-protein-coupled receptor class C group 5 member D; ide-cel, idecabtagene vicleucel; IMiD, immunomodulatory drug; Isa, isatuximab; Ixa, ixazomib; K, carfilzomib; Kd, carfilzomib/dexamethasone; L, line; Pd, pomalidomide/dexamethasone; PI, proteasome inhibitor; PomVd, pomalidomide/bortezomib/dexamethasone; R, lenalidomide; Rd, lenalidomide/dexamethasone; S, selinexor; SoC, standard of care; Vd, bortezomib/dexamethasone.

Dimopoulos MA, Terpos E, et al. *Nat Rev Clin Oncol.* 2025 (under minor revision).

Treatment landscape in multiple myeloma

1st line

ASCT eligible

- Anti-CD38 + PI + IMiD + dex
- ASCT
- Len / dara-len

ASCT ineligible

- Dara-len-dex
- Dara-VMP / RVd
- Anti-CD38 + PI + IMiD + dex

2nd line

Based on sensitivity/refractoriness to daratumumab and lenalidomide

- Anti-CD38 + carfilzomib-dex
- Anti-CD38 + pom-dex

- Pom-bortezomib-dex
- Selinexor-bortezomib-dex
- Carfilzomib-dex

Cilta-cel

New combinations:

- Belantamab-Vd (DREAMM-7)
- Belantamab-Pd (DREAMM-8)
- Teclistamab-dara / elranatamab
- Talquetamab-pom or teclistamab-talquetamab
- Linvoseltamab
- Etentamig

ASCT, autologous stem cell transplant; cilta-cel, ciltacabtagene autoleucel; dara, daratumumab; dex, dexamethasone; IMiD, immunomodulatory drug; len, lenalidomide; Pd, pomalidomide/dexamethasone; PI, proteasome inhibitor; pom, pomalidomide; RVd, lenalidomide/bortezomib/dexamethasone; Vd, bortezomib/dexamethasone; VMP, bortezomib/melphalan/prednisolone.

Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2022;32(3):309–322.

Options for daratumumab sensitive patients

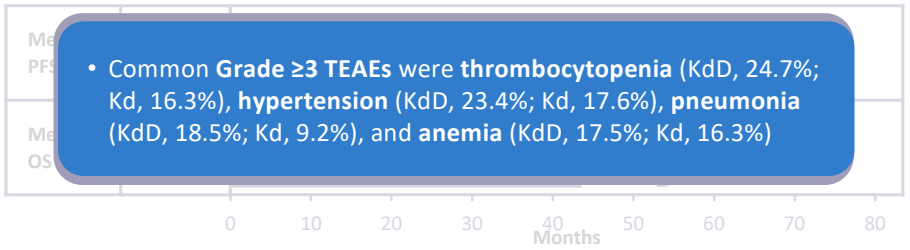
CANDOR[1]

Patients (N=466)
- ≥18 years old
- R/R MM
- 1–3 prior LOT

2:1
- KdD (n=313)
- Kd (n=154)

Primary endpoint
- PFS

Secondary endpoints
- ORR, MRD-CR at 12 mo, OS, safety



- Common **Grade ≥3 TEAEs** were **thrombocytopenia** (KdD, 24.7%; Kd, 16.3%), **hypertension** (KdD, 23.4%; Kd, 17.6%), **pneumonia** (KdD, 18.5%; Kd, 9.2%), and **anemia** (KdD, 17.5%; Kd, 16.3%)

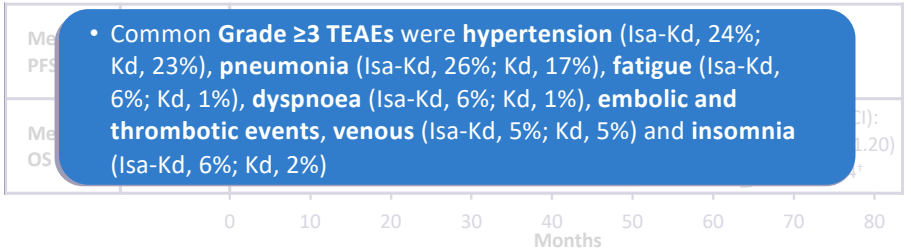
IKEMA[2,3]

R/R MM (N=302)
- 1–3 prior LOT
- No prior carfilzomib
- Not refractory to prior anti-CD38

3:2
- Isa-Kd (n=179)
- Kd (n=123)

Primary endpoint
- PFS

Secondary endpoints
- ORR, ≥VGPR with MRD-, CR rate, OS



- Common **Grade ≥3 TEAEs** were **hypertension** (Isa-Kd, 24%; Kd, 23%), **pneumonia** (Isa-Kd, 26%; Kd, 17%), **fatigue** (Isa-Kd, 6%; Kd, 1%), **dyspnoea** (Isa-Kd, 6%; Kd, 1%), **embolic and thrombotic events, venous** (Isa-Kd, 5%; Kd, 5%) and **insomnia** (Isa-Kd, 6%; Kd, 2%)

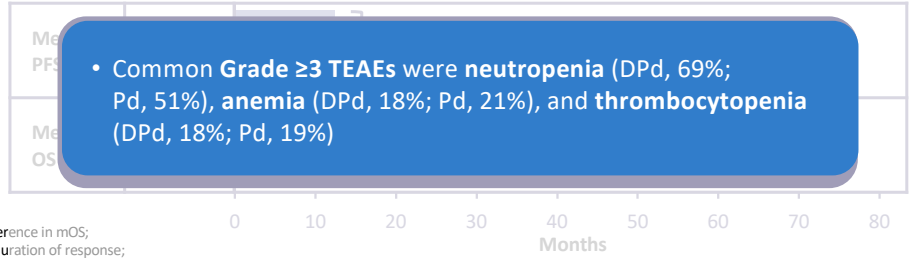
APOLLO[4]

Patients (N=304)
- R/R MM
- ≥1 prior line with both LEN and a PI
- ECOG PS ≤2
- CrCl ≥30 mL/min^2

1:1
- DPd (n=151)
- Pd (n=153)

Primary endpoint
- PFS

Secondary endpoints
- ORR, ≥VGPR, ≥CR, MRD, OS, time to response, DOR, TTNT, safety, HRQoL

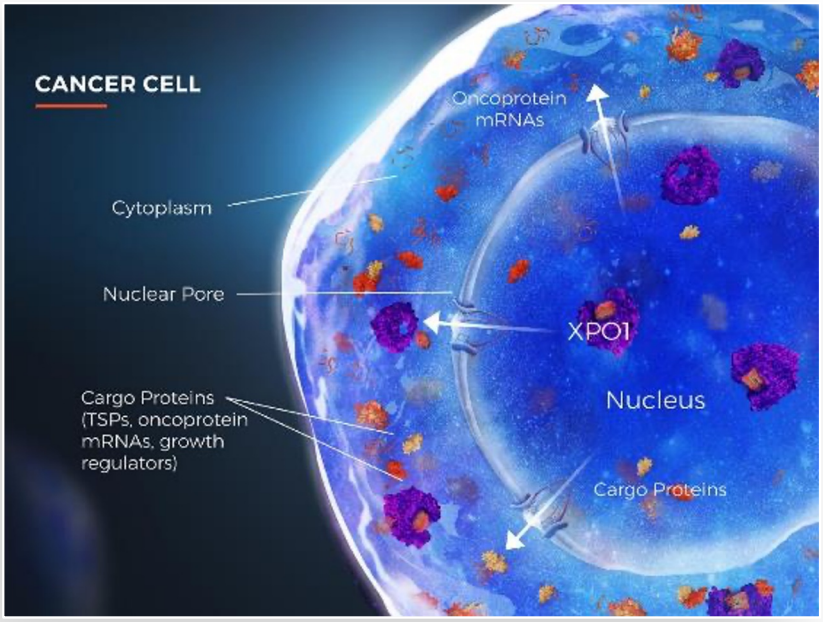


- Common **Grade ≥3 TEAEs** were **neutropenia** (DPd, 69%; Pd, 51%), **anemia** (DPd, 18%; Pd, 21%), and **thrombocytopenia** (DPd, 18%; Pd, 19%)

*mOS was calculated by extrapolating the observed trend (NR [95% CI: 52.17–NR) for an additional 12 months of follow-up; this corresponds to an estimated 1-year difference in mOS;
†HR correlates with difference in median OS prior to extrapolating the observed trend. CI, confidence interval; CR, complete response; CrCl, creatinine clearance; DOR, duration of response; DPd, daratumumab/pomalidomide/dexamethasone; ECOG PS, Eastern Cooperative Oncology Group Performance Status; HR, hazard ratio; HRQoL, health-related quality of life; Isa-Kd, isatuximab/carfilzomib/dexamethasone; Kd, carfilzomib/dexamethasone; KdD, carfilzomib/ daratumumab/dexamethasone; LEN, lenalidomide; LOT, line of therapy; MM, multiple myeloma; mo, months; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; Pd, pomalidomide/dexamethasone; PFS, progression-free survival; PI, proteasome inhibitor; R/R, relapsed refractory; TTNT, time to next treatment; VGPR, very good partial response.

1. Usmani S, et al. *Blood Adv*. 2023;7(14):3739–3748; 2. Yong K, et al. *Lancet Haematol*. 2024;11(10):e741–e750;
3. Martin T, et al. *Blood Cancer J*. 2023; 13: 72; 4. Dimopoulos MA, et al. *Lancet Haematol*. 2023;10(10):e813–e824.

Selinexor: A first-in-class oral exportin 1 (XPO-1) inhibitor[1]



XPO1 overexpression:

Inactivates tumor suppressor proteins[2]

- TSPs need to be localized in the nucleus to initiate apoptosis thereby suppressing tumor growth[3,4]
- Overexpression of XPO1 results in their functional inactivation of TSPs[2]

Enhances proto-oncogene translation[5]

- XPO1 overexpression increases nuclear export, and subsequent translation and protein synthesis of multiple eIF4E-bound oncogenic mRNAs

Disrupts growth regulation[2,3]

- Increased XPO1 expression promotes sustained cellular proliferation through increased cytoplasmic localization and expression of master growth regulators

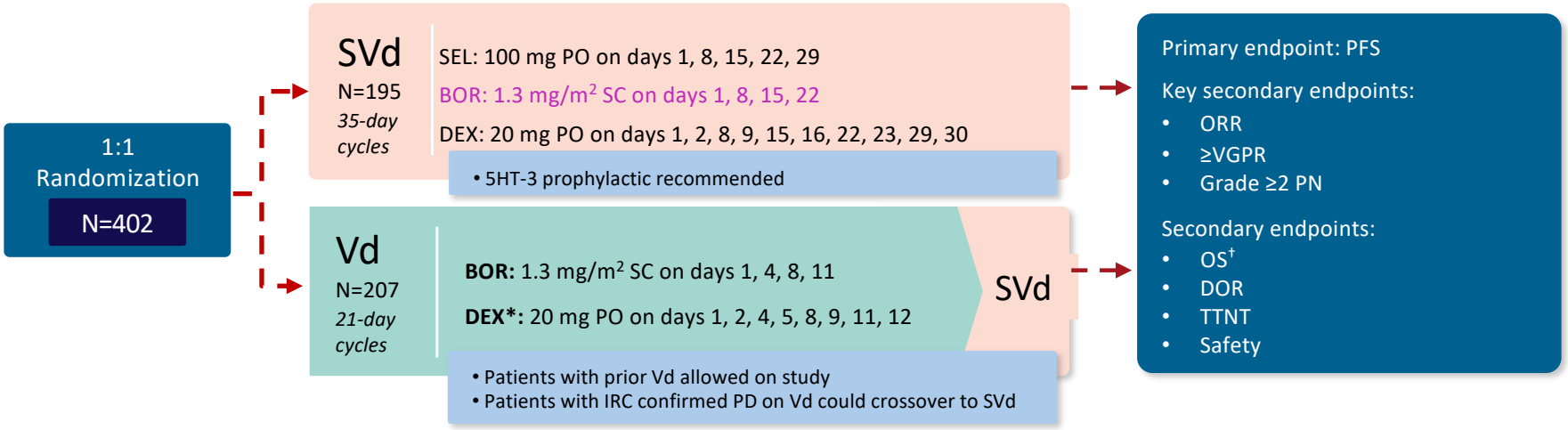
Selinexor is indicated i) in combination with bortezomib and dexamethasone for the treatment of adult patients with MM who have received ≥1 prior therapy ii) in combination with dexamethasone for the treatment of MM in adult patients who have received ≥4 prior therapies and whose disease is refractory to ≥2 proteasome inhibitors, two immunomodulatory agents and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.
eIF4E, eukaryotic translation initiation factor 4E; TSP, tumor suppressor protein; XPO1, exportin-1.

1. Peterson TJ, et al. *Ann Pharmacother*. 2020;54(6):577–582; 2. Sun Q, et al. *Signal Transduct Target Ther*. 2016;1:16010; 3. Tai Y-T, et al. *Leukemia*. 2014;28(1):155–165; 4. O'Hagan HM, et al. *Oncogene*. 2004;23(32):5505–5512; 5. Culjkovic-Kraljacic B, et al. *Cell Rep*. 2012;2(2):207–215.

BOSTON: A Phase 3, global, randomized, open-label, controlled study in patients with multiple myeloma who had received 1–3 prior therapies

Study design

Phase 3, multicenter, randomized, open-label study (NCT03110562)



- Median age was 67 years (IQR 59–73) and 81 (20%) patients were aged ≥75 years or older
- Median number of previous regimens was two (1–2), 75 (19%) patients had received three previous lines of therapy, and 139 (35%) patients had undergone SCT

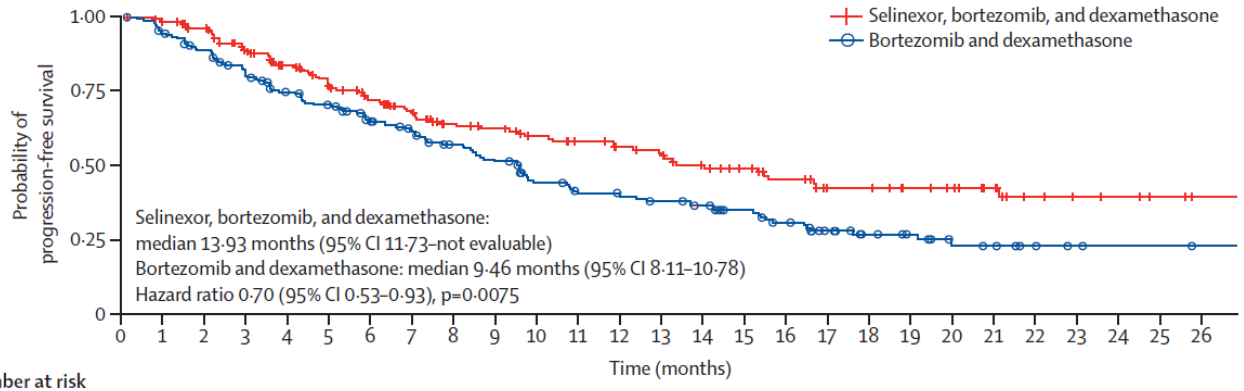
*DEX dosing presented is for cycles 1–8; for cycles ≥9 DEX was given as 20 mg on days 1, 2, 8, 9, 15, 16, 22, 23, 29, and 30 of each 35-day cycle; †OS is not yet reached.
BOR, bortezomib; DEX, dexamethasone; DOR, duration of response; IQR, interquartile range; IRC, independent review committee; OS, overall survival; PD, progressive disease; PFS, progression free survival; PN, peripheral neuropathy; PO, taken orally; SC, subcutaneous; SCT, stem cell transplant; SEL, selinexor; SVd, selinexor/bortezomib/dexamethasone; TTNT, time to next treatment; Vd, bortezomib/dexamethasone; VGPR, very good partial response.

Grosicki S, et al. *Lancet*. 2020;396(10262):1563–1573.

Significant increase in mPFS with SVd vs. Vd in BOSTON

	SVd arm (n=195)	Vd arm (n=207)
Median PFS, months (95% CI)*	13.93 (11.73–NE)	9.46 (8.11–10.78)
HR 0.70 (95% CI: 0.53–0.93); one-sided p=0.0075		

Kaplan-Meier estimates of progression-free survival among patients in the ITT population



Number at risk (number censored)																									
Selinexor, bortezomib, and dexamethasone	195 (0)	187 (5)	175 (12)	152 (21)	135 (31)	117 (37)	106 (42)	89 (50)	79 (57)	76 (59)	69 (63)	64 (66)	57 (71)	51 (73)	45 (76)	41 (80)	35 (83)	27 (89)	26 (90)	22 (94)	19 (97)	14 (102)	9 (106)	7 (108)	6 (109)	4 (111)	2 (113)
Bortezomib and dexamethasone	207 (0)	187 (8)	175 (10)	152 (15)	138 (20)	127 (22)	111 (29)	100 (32)	90 (37)	81 (37)	66 (41)	59 (43)	56 (44)	53 (45)	49 (47)	42 (52)	35 (55)	26 (60)	20 (65)	16 (69)	10 (73)	8 (75)	5 (78)	4 (79)	3 (80)	3 (80)	2 (81)

These data represent:

1. An increase of 4.47 months in median PFS
2. A 30% reduction in the risk of disease progression

*The study was ongoing at the time of publication; the analysis was performed after a median follow-up period of 13.2 months for the SVd arm and 16.5 months for the Vd arm (data cutoff: 18 February 2020).
CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; NE, not evaluable; PFS, progression free survival; SVd, Selinexor/bortezomib/dexamethasone; Vd, bortezomib/dexamethasone.

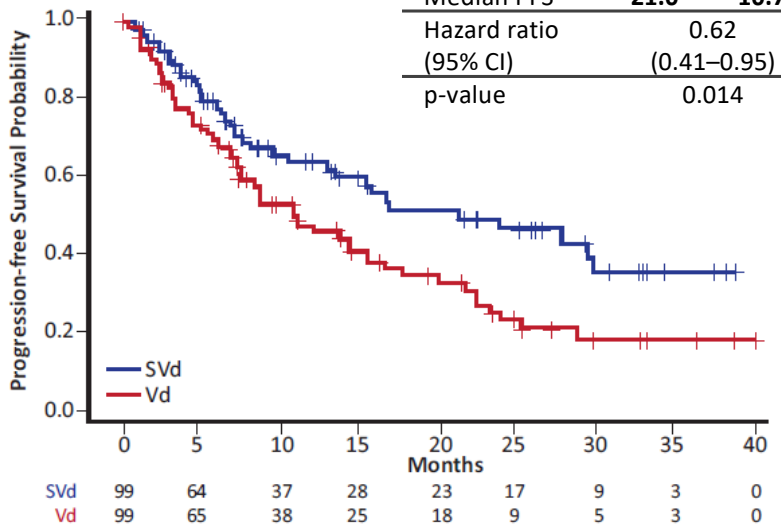
Grosicki S, et al. *Lancet*. 2020;396(10262):1563–1573.

SVd vs. Vd in R/R MM: Updated results by prior therapies and bortezomib naïve

- **51% (SVd)** and **48% (Vd)** of patients received **one prior line of therapy**[1]
- Among patients who received one prior line of therapy (SVd vs. Vd)[2]
  - *Median age:* 67 vs. 69 years
  - *Male:* 56% vs. 54%
  - *ECOG PS 0–1*: 92% vs. 94%
  - *High-risk cytogenetic abnormalities*: 51% vs. 48%
  - *R-ISS stage I–II*: 86% vs. 86%
  - *Median time since diagnosis*: 2.9 vs. 2.8 years
  - *Prior SCT*: 39% vs. 23%
  - *Creatine clearance at baseline >60 mL/min*: 71% vs. 65%

PFS in patients with one prior line of therapy[2]

	SVd	Vd
Median PFS	**21.0**	**10.7**
Hazard ratio (95% CI)	0.62 (0.41–0.95)	
p-value	0.014	



- **ORR: 80.8% in SVd arm vs. 66.7% in Vd arm**

Median follow-up: 29.0 months for SVd and 28.7 months for Vd.
CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group Performance Status; ISS, International Staging System; MM, multiple myeloma; ORR, overall response; PFS, progression-free survival; R/R, relapsed/refractory; SCT, stem cell transplant; SVd, selinexor/bortezomib/dexamethasone; Vd, bortezomib/dexamethasone.

1. Dimopoulos MA, et al. Abstract 8501; presented at ASCO 2020; 2. Mateos MV, et al. *Eur J Haematol* 2024;113(2):242–252.

SVd vs. Vd in R/R MM: Updated results by prior therapies and bortezomib naïve

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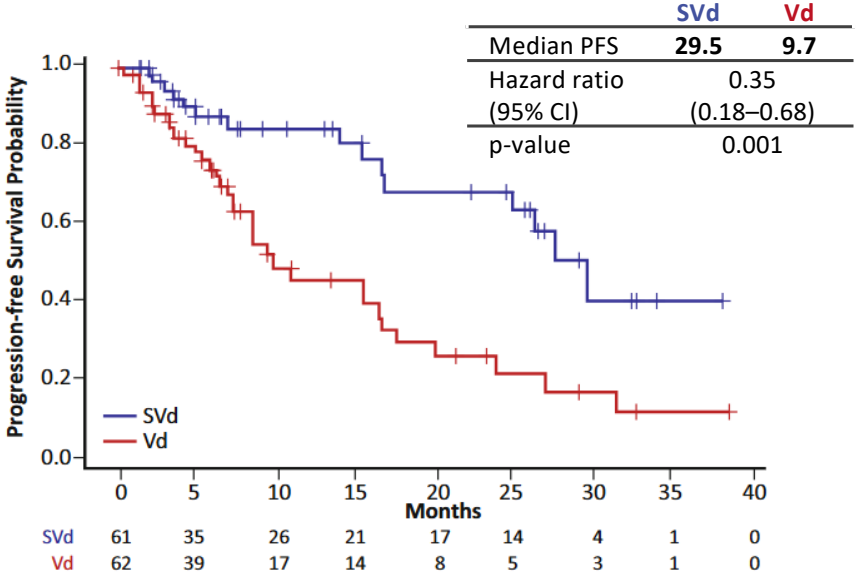
  - *Creatine clearance at baseline >60 mL/min*: 71% vs. 65%

PFS in bortezomib-naïve patients[2]



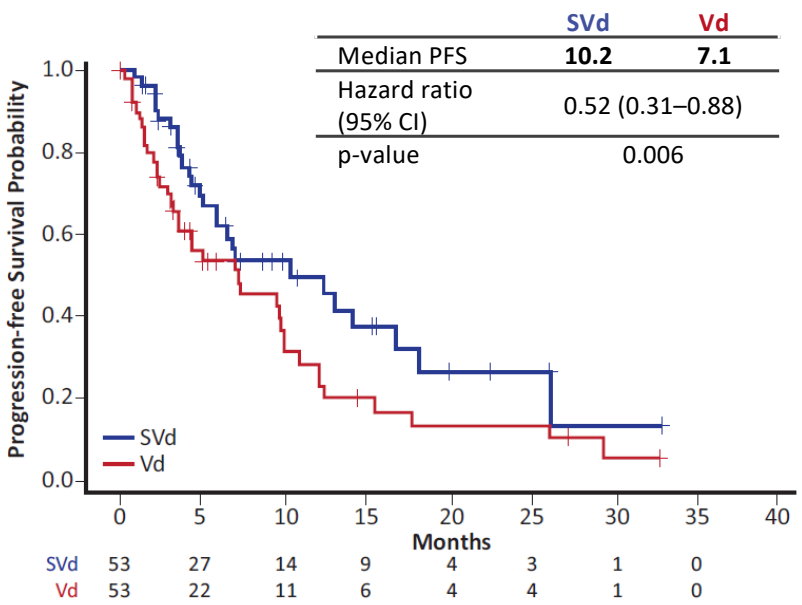
- **ORR: 75.4% in SVd arm vs. 69.4% in Vd arm**

Median follow-up: 29.0 months for SVd and 28.7 months for Vd.
CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group Performance Status; ISS, International Staging System; MM, multiple myeloma; ORR, overall response; PFS, progression-free survival; R/R, relapsed/refractory; SCT, stem cell transplant; SVd, selinexor/bortezomib/dexamethasone; Vd, bortezomib/dexamethasone.

1. Dimopoulos MA, et al. Abstract 8501; presented at ASCO 2020; 2. Mateos MV, et al. *Eur J Haematol* 2024;113(2):242–252.

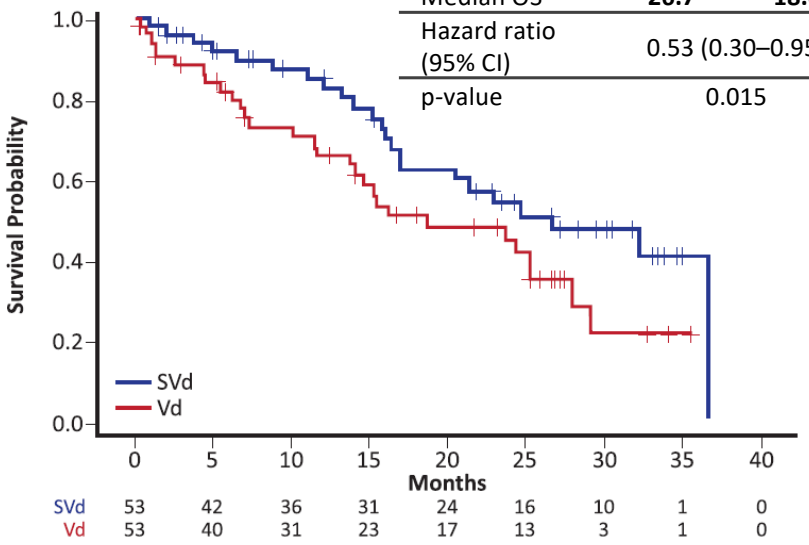
BOSTON subgroup analysis of patients with lenalidomide-refractory MM: Significant improvement in PFS and OS with SVd vs. Vd

PFS



	SVd	Vd
Median PFS	**10.2**	**7.1**
Hazard ratio (95% CI)	0.52 (0.31–0.88)	
p-value	0.006	

OS



	SVd	Vd
Median OS	**26.7**	**18.6**
Hazard ratio (95% CI)	0.53 (0.30–0.95)	
p-value	0.015	

- Higher ORR with SVd vs. Vd (67.9% vs. 47.2%; OR 2.59 [95% CI: 1.17–5.77]; p=0.009)
- Higher ≥VGPR with SVd vs. Vd (35.8% vs. 24.5%; OR 1.74 [95% CI: 0.72–4.21]; p=0.109)

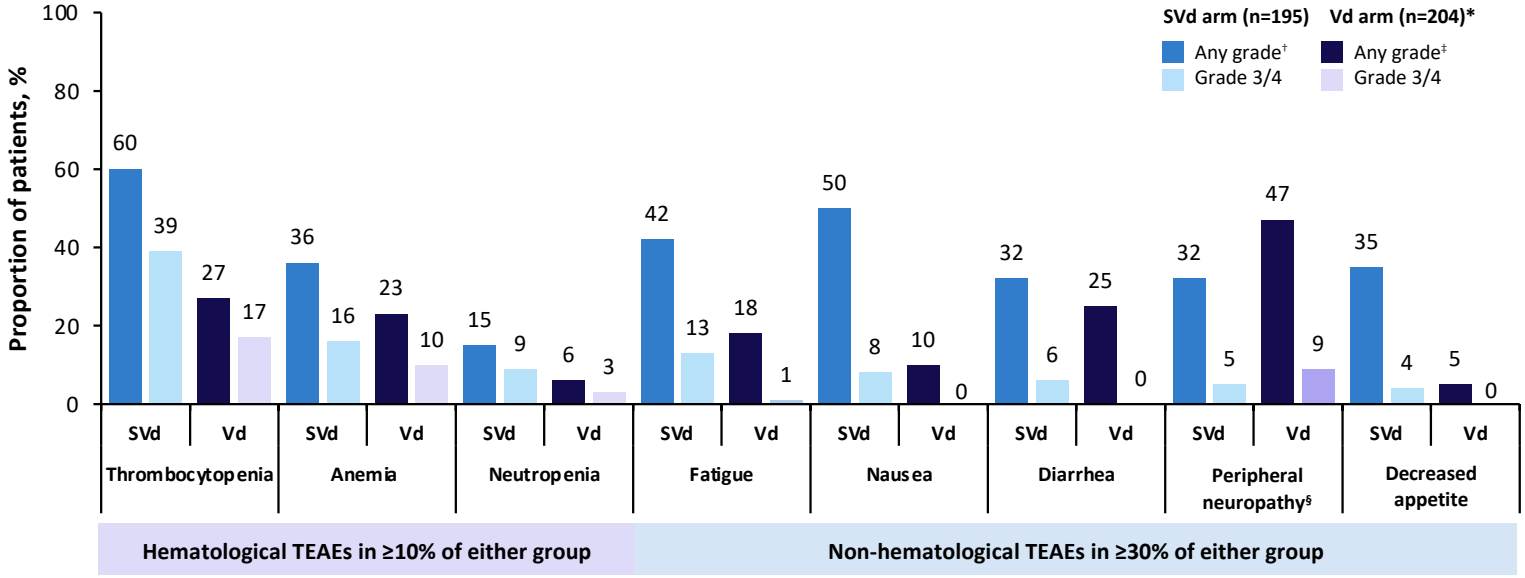
CI, confidence intervals; MM, multiple myeloma; OR, odds ratio; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; SVd, selinexor/bortezomib/dexamethasone; Vd, bortezomib/dexamethasone; VGPR, very good partial response.

Mateos MV, et al. *Eur J Haematol* 2024;113(2):242–252.

SVd safety: BOSTON

Safety profile was manageable; the most common any grade AEs were GI AEs, thrombocytopenia and anemia, the most common Grade 3/4 AEs were thrombocytopenia, fatigue, anemia and pneumonia

- AEs may be managed by dose modification and supportive therapeutic measures



*Three patients from this group who did not receive any doses of study drug were excluded from the safety population; †Includes four Grade 5 events: three (2%) cases of pneumonia and one (1%) case of bronchitis; ‡Includes four Grade 5 events: three (1%) cases of pneumonia and one (<1%) case of anemia; §Includes high-level MedDRA term "peripheral neuropathies NEC".
AE, adverse event; GI, gastrointestinal; MedDRA, medical dictionary for regulatory activities; SVd, selinexor/bortezomib/dexamethasone; TEAE, treatment-emergent adverse event; Vd, bortezomib/dexamethasone.

Grosicki S, et al. *Lancet*. 2020;396(10262):1563–1573.

Treatment landscape in multiple myeloma

1st line

ASCT eligible

- Anti-CD38 + PI + IMiD + dex
- ASCT
- Len / dara-len

ASCT ineligible

- Dara-len-dex
- Dara-VMP / RVd
- Anti-CD38 + PI + IMiD + dex

2nd line

Based on sensitivity/refractoriness to daratumumab and lenalidomide

- Anti-CD38 + carfilzomib-dex
- Anti-CD38 + pom-dex

- Pom-bortezomib-dex
- Selinexor-bortezomib-dex
- Carfilzomib-dex

Cilta-cel

New combinations:

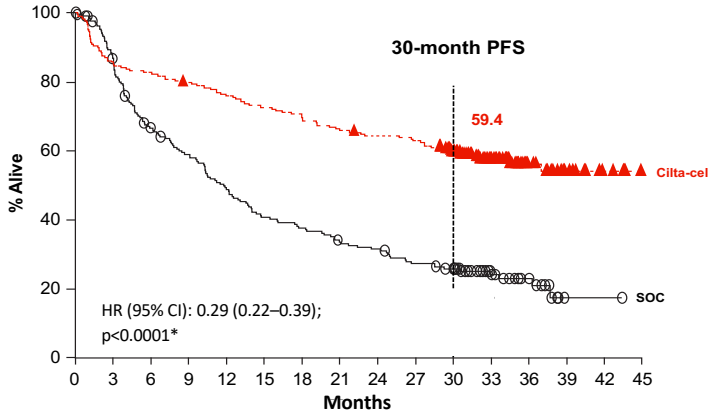
- **Belantamab-Vd (DREAMM-7)**
- **Belantamab-Pd (DREAMM-8)**
- Teclistamab-dara / elranatamab
- Talquetamab-pom or teclistamab-talquetamab
- Linvoseltamab
- Etentamig

ASCT, autologous stem cell transplant; cilta-cel, ciltacabtagene autoleucel; dara, daratumumab; dex, dexamethasone; IMiD, immunomodulatory drug; len, lenalidomide; Pd, pomalidomide/dexamethasone; PI, proteasome inhibitor; pom, pomalidomide; RVd, lenalidomide/bortezomib/dexamethasone; Vd, bortezomib/dexamethasone; VMP, bortezomib/melphalan/prednisolone.

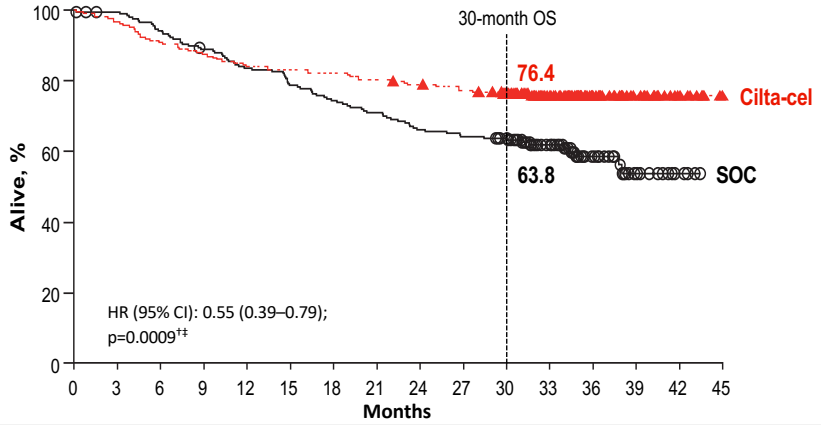
Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2022;32(3):309–322.

CARTITUDE-4: Phase 3 trial of cilta-cel vs. PVd/DPd in lenalidomide-refractory MM after 1–3 prior lines[1]

PFS (ITT; 33.6 months median follow-up)[1]



OS (ITT; 33.6 months median follow-up)[1]



- Cilta-cel provided **high ORR and sCR/CR rate** with **sustained DOR**[1]
- At 33.6 months follow-up, **ORR was 84.6%** (sCR/CR: 76.9%) in the **cilta-cel arm** vs. **67.3%** (sCR/CR: 24.2%) in the **SoC arm**[1]
- **Median DOR** (95% CI) was **NR** (NE–NE) in the **cilta-cel arm** and **18.7 months** (12.9–23.7) in the **SoC arm**[1]

- Safety profile consistent with previous analysis[2]
  - All grade and **Grade ≥3 treatment-emergent infections** occurred in **63.5%** and **28.4%** of patients in the **cilta-cel arm** vs. **76.4%** and **29.8%** in the **SoC arm**[3]
  - **SPMs** occurred in **13.0%** of patients in the **cilta-cel arm** vs. **11.5%** in the **SoC arm**; of these **7.2%** were cutaneous/non-invasive in each arm[3§]
  - **No new cases of cranial nerve palsy or MNT** in the cilta-cel arm[3]

*Nominal p-value; †Log-rank test. p-value, 0.0009, crossed the prespecified boundary of 0.0108 as implemented by the Kim-DeMets spending function with parameter=2; ‡HR and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory; §Multiple SPMs could occur in the same patient.
CI, confidence interval; cilta-cel, ciltacabtagene autoleucel; CR, complete response; DOR, duration of response; DPd, daratumumab/pomalidomide/dexamethasone; HR, hazard ratio; ITT, intention-to-treat; MNT, movement and neurocognitive treatment-emergent adverse event; NE, not estimable; NR, not reached; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PVd, pomalidomide/bortezomib/dexamethasone; sCR, stringent CR; SoC, standard of care; SPM, secondary primary malignancy.

1. Popat R, et al. Abstract 1032; oral presentation at ASH 2024;
2. San-Miguel J, et al. *N Engl J Med.* 2023;389(4):335–347;
3. Mateos MV, et al. Abstract #1437; oral presentation at IMS 2024.

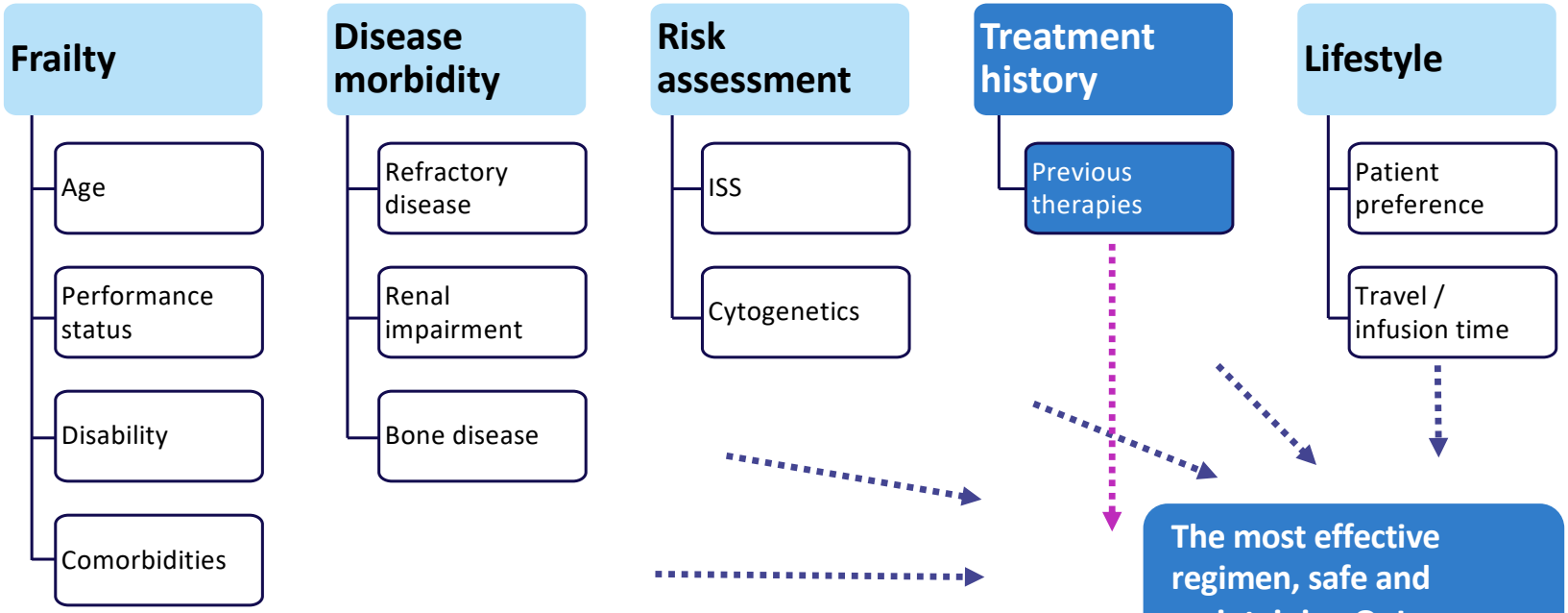
Phase 3 DREAMM-7/8 studies: Summary

	Study design	Baseline characteristics	Median PFS, mos*	Median OS, mos*	ORR, % (95% CI)†	Safety profile‡	Belantamab-associated AEs
DREAMM-7[1]	1:1 **BVd (n=243)** **DVd (n=251)** **Primary endpoint:** PFS **Secondary endpoints:** OS, DOR, MRD-negative status	• **1 prior LOT**: BVd, 51%; DVd, 50% • **High-risk cytogenetics**: BVd, 28%; DVd, 27% • **LEN-refractory:** BVd, 33%; DVd, 35%	**BVd, 36.6 vs. DVd, 13.4** *HR 0.41 (95% CI: 0.31–0.53); p<0.001*	**NR vs. NR** At 18 months: **BVd, 84% vs. DVd, 73%** *HR 0.57 (95% CI: 0.40–0.80)*	**BVd, 83%** (77–87%) **vs. DVd, 71%** (65–77%)	**AEs** Any grade: 100%; Grade 3–4: 95% **Serious AEs** 50% **Discontinuation due to AEs** 26%	**Ocular events** Any grade: 79%; Grade 3–4: 34% **Blurred vision** Any grade: 66%; Grade 3–4: 22% **Worsening vision from normal to:** 20/50, 34%; 20/200, 2% **Infections** Any grade: 70%; Grade 3–4: 31%
DREAMM-8[2]	1:1 **BPd (n=155)** **PVd (n=147)** **Primary endpoint:** PFS **Secondary endpoints:** ORR, MRD negativity, DOR	• **1 prior LOT**: BPd, 53%; PVd, 52% • **High-risk cytogenetics**: BPd, 34%; PVd, 32% • **LEN-refractory:** BPd, 81%; PVd, 76% • **Anti-CD38 mAb-refractory:** BPd, 23%; PVd, 24%	**BPd, NR vs. PVd, 12.7** *HR 0.52 (95% CI: 0.37–0.73); p<0.001*	**NR vs. NR** 12-month estimate: **BPd, 83% vs. PVd, 76%** *HR 0.77 (95% CI: 0.53–1.14)*	**BPd, 77%** (70–84%) **vs. PVd, 72%** (64–79%)	**AEs** Any grade: 99%; Grade 3–4: 94% **Serious AEs** 63% **Discontinuation due to AEs** 15%	**Ocular events** Any grade: 89%; Grade 3–4: 43% **Blurred vision** Any grade: 79%; Grade 3–4: 17% **Worsening vision from normal to:** 20/50 34%; 20/200: 1% **Infections** Any grade: 82%; Grade 3–4: 49%

Median follow-up for DREAMM-7 was 28.2 months, and for DREAMM-8 was 21.8 months. *HRs estimated using the stratified Cox proportional hazards model and p-value was produced based on the 1-sided stratified log-rank test; †PR or better; ‡BVd arm in DREAMM-7.
AE, adverse event; BPd, belantamab mafodotin/pomalidomide/dexamethasone; BVd, belantamab mafodotin/bortezomib/dexamethasone; CI, confidence interval; DOR, duration of response; DVd, daratumumab/bortezomib/dexamethasone; HR, hazard ratio; LEN, lenalidomide; LOT, line of therapy; mAb, monoclonal antibody; MRD, minimal residual disease; NR, not reached; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; PVd, pomalidomide/bortezomib/dexamethasone.

1. Hungria V, et al. *N Engl J Med.* 2024;391(5):393–407; 2. Dimopoulos MA, et al. *N Engl J Med.* 2024;391:408–421.

Disease and patient-based factors influencing treatment decision-making at the relapse setting



Open questions:

- Who will be eligible for BCMA-targeted therapies after 1 prior line based on PI/IMiDs/anti-CD38 mAb?
- Who will be eligible for carfilzomib, pomalidomide, SVd…. after 1 prior line based on PI/IMiDs/anti-CD38 mAb?

We need to wait to see more efficacy/safety data to make the right choice

BCMA, B-cell maturation antigen; IMiD, immunomodulatory drug; ISS, International Staging System; mAb, monoclonal antibody; PI, proteasome inhibitor; QoL, quality of life; SVd, selinexor/bortezomib/dexamethasone.

Information based on speaker's expert opinion.

Treatment landscape in multiple myeloma in the future

1st line

ASCT eligible

- Anti-CD38 + PI + IMiD + dex
- ASCT
- Len / dara-len x 2 yrs or len s/a

ASCT ineligible

- Dara-len-dex
- Dara-VMP / RVd
- Anti-CD38 + PI + IMiD + dex

2nd line

Early relapses

- **Cilta-cel**
- Elranatamab s/a
- BCMA-BsAb + dara
- GPRC5D-BsAb + dara
- Belamaf-Vd / Belamaf-Pd
- **Selinexor-Vd**

Intermediate/ late relapses

- **Cilta-cel**
- Elranatamab s/a
- Belamaf-Vd / Belamaf-Pd
- BCMA-BsAb + dara
- GPRC5D-BsAb + dara
- **Kd Anti-CD38 / Pd Anti-CD38**
- **Selinexor-Vd**

Patients relapsing after Dara-Rd

- **Cilta-cel**
- Elranatamab s/a
- Belamaf-Vd / Belamaf-Pd
- **PVd**
- **Selinexor-Vd**

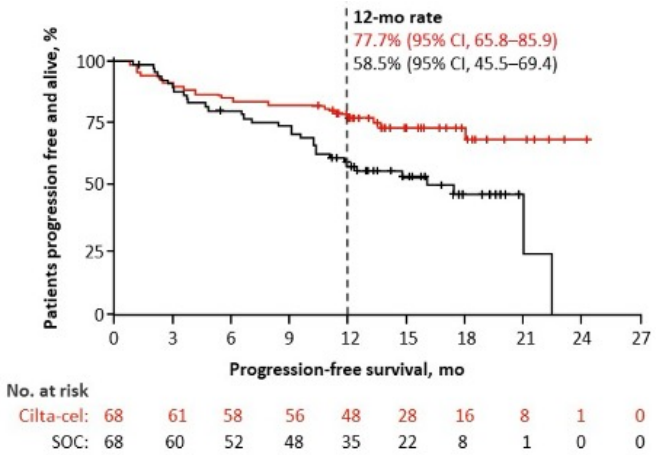
ASCT, autologous stem cell transplant; BCMA, B cell maturation antigen; BsAb, bispecific antibody; cilta-cel, ciltacabtagene autoleucel; dara, daratumumab; dex, dexamethasone; GPRC5D, G-protein-coupled receptor class C group 5 member D; IMiD, immunomodulatory drug; Kd, carfilzomib/dexamethasone; len, lenalidomide; PI, proteasome inhibitor; Pd, pomalidomide/dexamethasone; PVd, pomalidomide/bortezomib/dexamethasone; Rd, lenalidomide/dexamethasone; RVd, lenalidomide/bortezomib/dexamethasone; Vd, bortezomib/dexamethasone; VMP, bortezomib/melphalan/prednisolone; yrs, years.

Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2022;32(3):309–322.

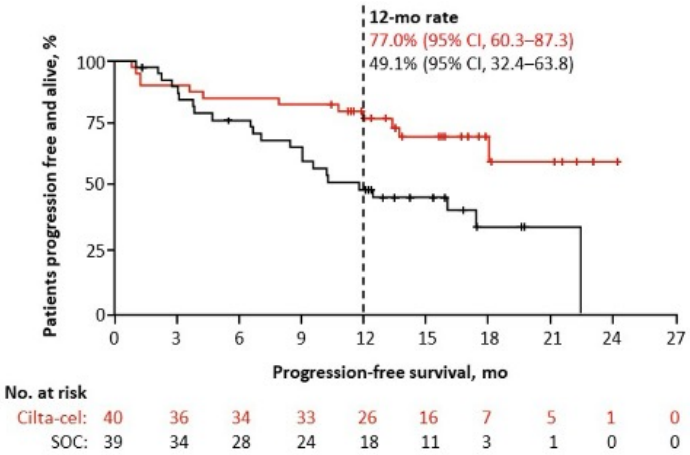
CARTITUDE-4 subgroup analysis: PFS in functional high-risk R/R MM

Functionally high risk (FHR): PD ≤18 months after ASCT or the start of initial 1L therapy in patients with no ASCT

PFS in patients with 1 prior LOT



PFS in patients with 1 prior LOT + FHR



PFS	1 Prior LOT		1 Prior LOT + FHR	
	Cilta-cel (n=68)	SoC (n=68)	Cilta-cel (n=40)	SoC (n=39)
Median (95% CI), months	NR (NE–NE)	17.41 (11.10–NE)	NR (18.00–NE)	11.79 (8.44–NE)
HR (95% CI); p-value	0.35 (0.19–0.66); 0.0007		0.27 (0.12–0.60); 0.0006	

- **CAR-T associated AEs of special interest** (All grade: *1 prior LOT vs. 1 prior LOT and FHR, below*) were generally **low grade in severity**; **no Grade 4 events** occurred
  - CRS (64.7% vs. 62.5%)
  - ICANS (2.9% vs. 5.0%)
  - Cranial nerve palsy (8.8% vs. 7.5%)
  - Movement and neurocognitive TEAEs (1.5% vs. 0%)
  - Peripheral neuropathy (2.9% vs. 5.0%)

AE, adverse event; ASCT, autologous stem cell transplant; CAR-T, chimeric antigen receptor T cell; CI, confidence interval; CRS, cytokine release syndrome; FHR, functionally high risk; HR, hazard ratio; ICANS, immune cell associated neurotoxicity syndrome; LOT, line of therapy; MM, multiple myeloma; NE, not estimable; NR, not reached; PD, progressive disease; PFS, progression-free survival; R/R, relapsed/refractory; SoC, standard of care; TEAE, treatment-emergent adverse event.

Costa L, et al. Abstract 7504; presented at ASCO 2024 ; Weisel K, et al. Abstract P959; presented at EHA 2024.

Treatment landscape in multiple myeloma in the future

1st line

ASCT eligible

- Anti-CD38 + PI + IMiD + dex
- ASCT
- Len / dara-len x 2 yrs or len s/a

ASCT ineligible

- Dara-len-dex
- Dara-VMP / RVd
- Anti-CD38 + PI + IMiD + dex

2nd line

Early relapses

- **Cilta-cel**
- Elranatamab s/a
- BCMA-BsAb + dara
- GPRC5D-BsAb + dara
- Belamaf-Vd / Belamaf-Pd
- **Selinexor-Vd**

Intermediate/ late relapses

- **Cilta-cel**
- Elranatamab s/a
- Belamaf-Vd / Belamaf-Pd
- BCMA-BsAb + dara
- GPRC5D-BsAb + dara
- **Kd anti-CD38 / Pd anti-CD38**
- **Selinexor-Vd**

Patients relapsing after Dara-Rd

- **Cilta-cel**
- Elranatamab s/a
- Belamaf-Vd / Belamaf-Pd
- **PVd**
- **Selinexor-Vd**

ASCT, autologous stem cell transplant; BCMA, B cell maturation antigen; BsAb, bispecific antibody; cilta-cel, ciltacabtagene autoleucel; dara, daratumumab; dex, dexamethasone; GPRC5D, G-protein-coupled receptor class C group 5 member D; IMiD, immunomodulatory drug; Kd, carfilzomib/dexamethasone; len, lenalidomide; PI, proteasome inhibitor; Pd, pomalidomide/dexamethasone; PVd, pomalidomide/bortezomib/dexamethasone; Rd, lenalidomide/dexamethasone; RVd, lenalidomide/bortezomib/dexamethasone; Vd, bortezomib/dexamethasone; VMP, bortezomib/melphalan/prednisolone; yrs, years.

Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2022;32(3):309–322.

Treatment landscape in multiple myeloma in the future

1st line

ASCT eligible

- Anti-CD38 + PI + IMiD + dex
- ASCT
- Len / dara-len x 2 yrs or len s/a

ASCT ineligible

- Dara-len-dex
- Dara-VMP / RVd
- Anti-CD38 + PI + IMiD + dex

2nd line

Relapse during Dara-R or early after Dara stopping

- Cilta-cel
- Elranatamab s/a
- Belamaf-Vd / Belamaf-Pd
- **Selinexor-Vd**

Late relapse after Dara stopped and continued with R/R s/a

- Cilta-cel
- Elranatamab s/a
- Belamaf-Vd / Belamaf-Pd
- BCMA-BsAb + dara
- GPRC5D-BsAb + dara
- **Kd anti-CD38 / Pd anti-CD38**
- **Selinexor-Vd**

Patients relapsing after Dara-Rd

- Cilta-cel
- Elranatamab s/a
- Belamaf-Vd / Belamaf-Pd
- **PVd**
- **Selinexor-Vd**

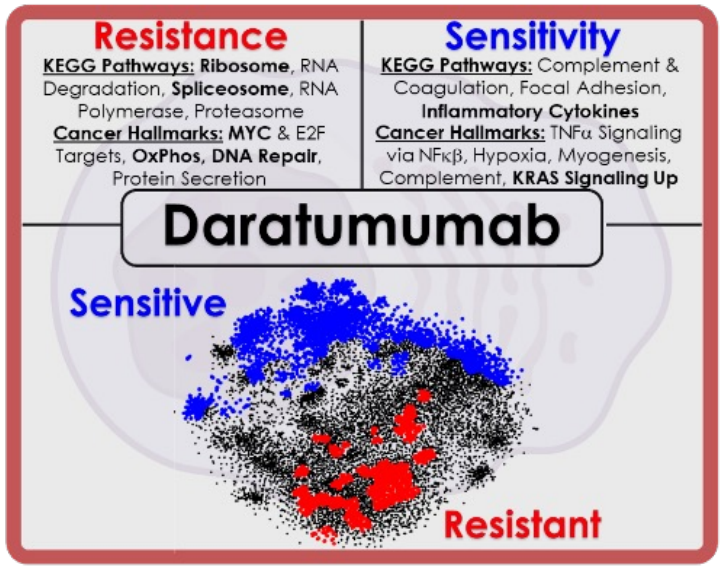
Patients relapsing after Dara-Rd present a challenge when considering subsequent therapies

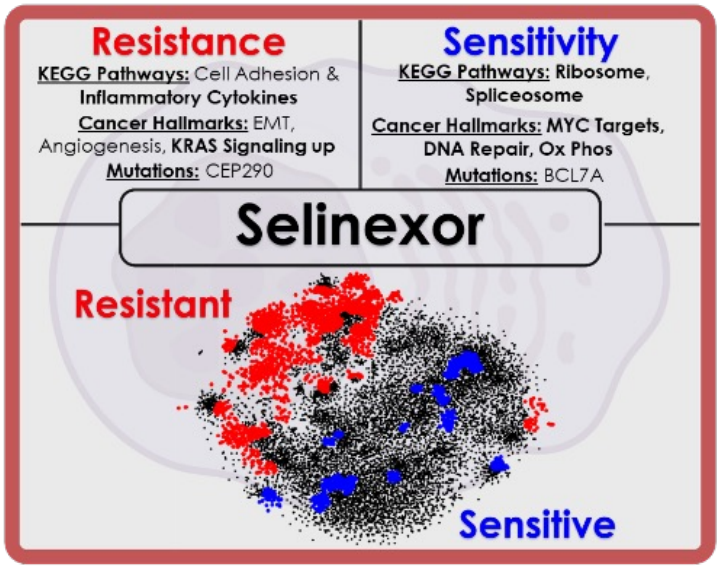
ASCT, autologous stem cell transplant; BCMA, B cell maturation antigen; BsAb, bispecific antibody; cilta-cel, ciltacabtagene autoleucel; dara, daratumumab; dex, dexamethasone; GPRC5D, G-protein-coupled receptor class C group 5 member D; IMiD, immunomodulatory drug; Kd, carfilzomib/dexamethasone; len, lenalidomide; PI, proteasome inhibitor; Pd, pomalidomide/dexamethasone; PVd, pomalidomide/bortezomib/dexamethasone; Rd, lenalidomide/dexamethasone; RVd, lenalidomide/bortezomib/dexamethasone; Vd, bortezomib/dexamethasone; VMP, bortezomib/melphalan/prednisolone; yrs, years.

Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2022;32(3):309–322.

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

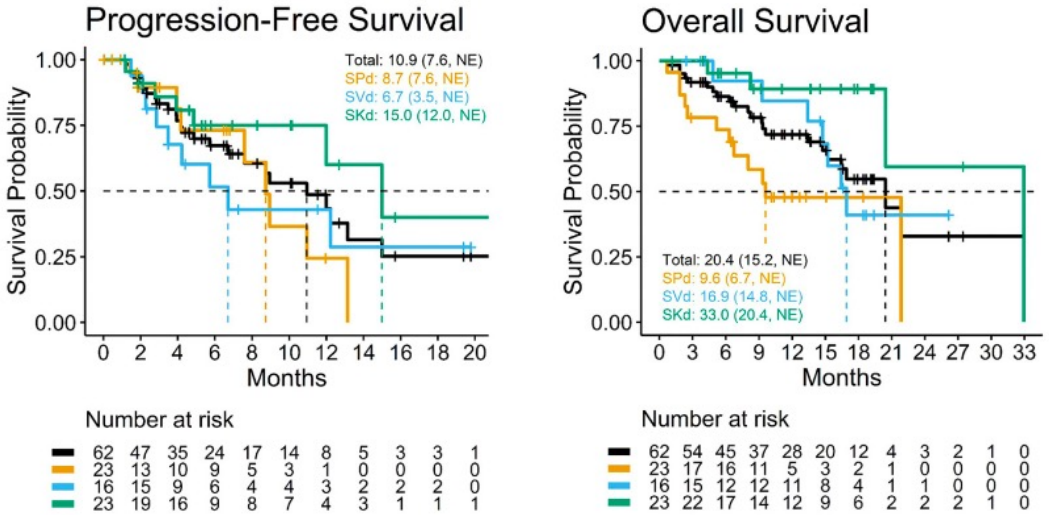
BCL7A, BAF chromatin remodeling complex subunit BCL7A; CEP290, centrosomal protein 290; KEGG, kyoto encyclopedia of genes and genomes; NFκβ, nuclear factor kappa B; MM, multiple myeloma; MYC, MYC proto-oncogene; TNFα, tumor necrosis factor alpha.

Sudalagunta PR, et al. Abstract #893; presented at ASH 2021.

Efficacy of selinexor triplet among patients treated with an anti-CD38 mAb in prior lines of therapy PFS and OS

- The efficacy of selinexor-containing triplet regimens was analyzed in a subset of **STOMP* and BOSTON study patients** (n=62) with MM enrolled after a **median of 4 prior lines**[1]
- **At a median follow-up of 6.9 months**[1]:
  - mPFS was 10.9 months
  - Highest mPFS was observed with SKd (15.0 months)
- **At a median follow-up of 14.5 months**[1]:
  - mOS was 20.4 months
  - Highest OS was also observed with SKd (33.0 months)
- Among all patients, **ORR was 58.1%**[1]
  - ORR was highest in the SKd cohort (65.2%)[1]
  - Among patients treated with an anti-CD38 mAb in their most recent prior line of therapy, ORR was 56.1%[1]
- CBR was 72.6% among all patients, with similar percentages in each cohort[1]

Kaplan-Meier curves comparing PFS and OS of patients treated with SPd, SVd, SKd and all cohorts combined[1]



- **In the BOSTON study, 11 patients in the SVd arm had prior daratumumab with a mPFS of 12.2 months**[2]

*Selinexor combinations in the STOMP trial are not all approved.
CBR, clinical benefit rate; mAb, monoclonal antibody; (m)OS, (median) overall survival; (m)PFS, (median) progression-free survival; MM, multiple myeloma; NE, not estimable; ORR, overall response rate; SKd, selinexor/carfilzomib/dexamethasone; SPd, selinexor/dexamethasone/pomalidomide; SVd, selinexor/bortezomib/dexamethasone.

1. Schiller G, et al. *Clin Lymphoma Myeloma Leuk.* 2023;23(9):e286–e296.e4;
2. Mateos MV, et al. *Eur J Haematol.* 2024;113(2):242–252.

What about the other combinations in patients naïve to proteasome inhibitors, for example PVd?

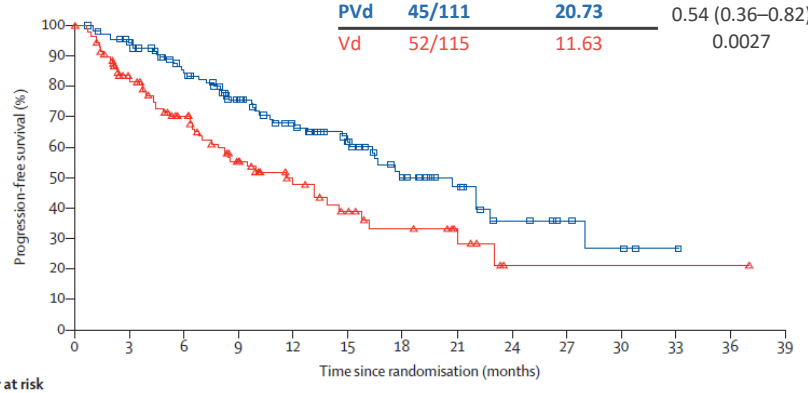
PVd, pomalidomide/bortezomib/dexamethasone.

PVd vs. Vd: PFS by prior lines and prior bortezomib exposure

- PVd significantly reduced the risk of progression or death by 53% in bortezomib-exposed patients (p=0.0068)

PFS after 1 prior line[1]

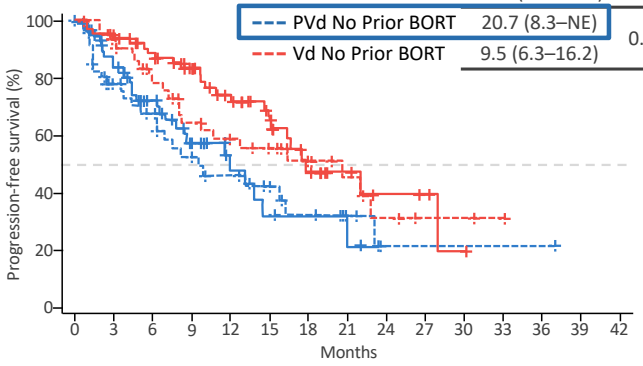
	Events/N	Median PFS, months	HR (95% CI) p-value
PVd	**45/111**	**20.73**	0.54 (0.36–0.82)
Vd	52/115	11.63	0.0027



Number at risk (number censored)														
Pomalidomide, bortezomib, and dexamethasone	111	100	81	63	49	37	24	15	8	5	3	1	0	0
	(0)	(5)	(14)	(24)	(32)	(40)	(47)	(55)	(59)	(62)	(63)	(65)	(66)	(66)
Bortezomib and dexamethasone	115	78	57	37	23	16	11	7	1	1	1	1	1	0
	(0)	(19)	(29)	(38)	(48)	(51)	(54)	(58)	(62)	(62)	(62)	(62)	(62)	(63)

Without prior bortezomib[2]

	Median PFS, months (95% CI)	HR (95% CI)	p-value
PVd Prior BORT	17.8 (15.2–28.0)	0.47 (0.26–0.82)	0.0068
Vd Prior BORT	12.0 (7.9–21.1)		
PVd No Prior BORT	20.7 (8.3–NE)	0.62 (0.35–1.11)	0.1055
Vd No Prior BORT	9.5 (6.3–16.2)		



Patients at risk														
PVd Prior BORT	67	61	51	40	30	21	12	7	4	3	1	0	0	0
Vd Prior BORT	67	47	33	20	10	6	5	3	0	0	0	0	0	0
PVd No Prior BORT	44	39	30	23	19	16	12	8	4	2	2	1	0	0
Vd No Prior BORT	48	31	24	17	13	10	6	4	1	1	1	1	0	0

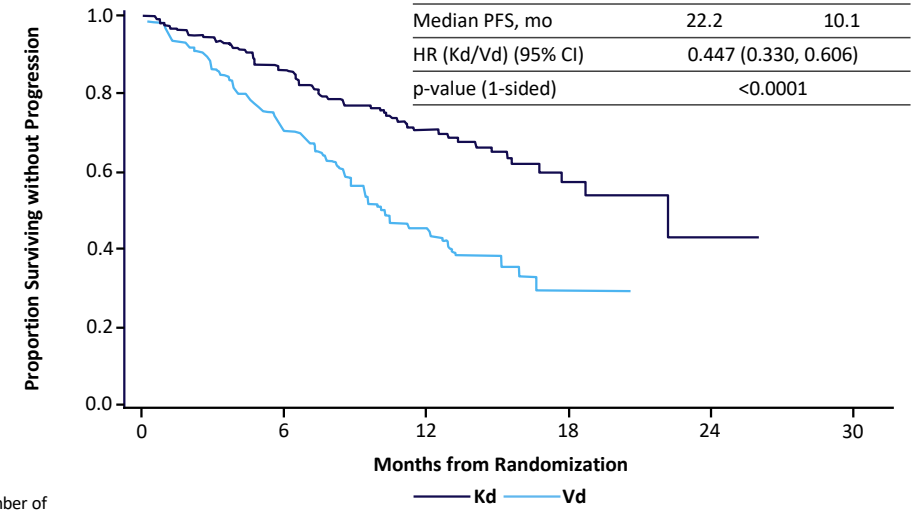
BORT, bortezomib; CI, confidence Interval; PFS, progression-free survival; HR, hazard ratio; NE, not evaluated; PVd, pomalidomide/bortezomib/dexamethasone; Vd, bortezomib/dexamethasone.

1. Richardson PG, et al. *Lancet Oncol* 2019;20(6):781–794; 2. Dimopoulos MA, et al. *Leukemia.* 2021;35(6):1722–1731(supplement).

Kd vs. Vd: PFS by prior lines of therapy and no prior bortezomib exposure

PFS after one prior line of therapy[1]

	Kd (N=232)	Vd (N=232)
Progression/death, n (%)	70 (30.2%)	109 (47.0%)
Median PFS, mo	22.2	10.1
HR (Kd/Vd) (95% CI)	0.447 (0.330, 0.606)	
p-value (1-sided)	<0.0001	

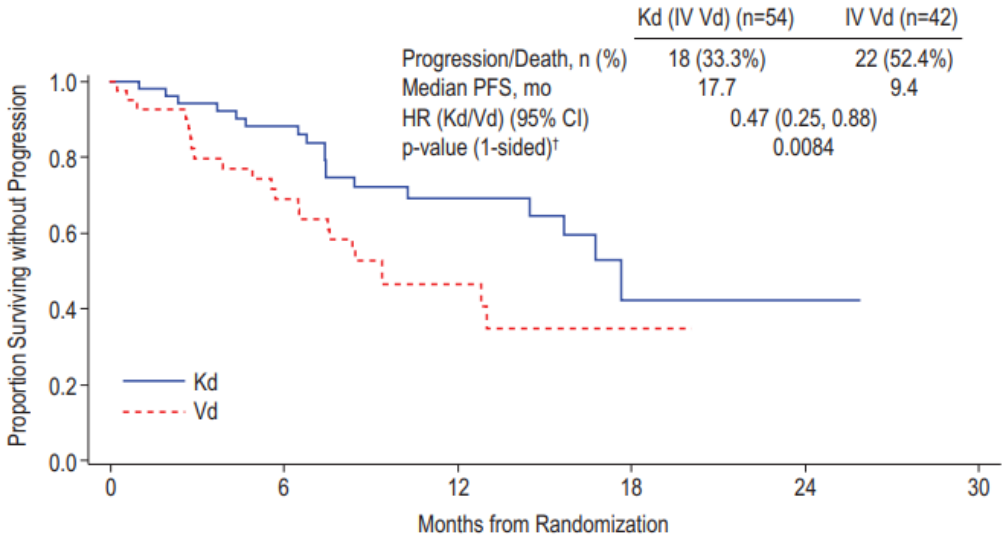


Number of subjects at risk:

Kd 232	182	84	21	3	0
Vd 232	133	42	8	0	

PFS in bortezomib naïve[2]

	Kd (IV Vd) (n=54)	IV Vd (n=42)
Progression/Death, n (%)	18 (33.3%)	22 (52.4%)
Median PFS, mo	17.7	9.4
HR (Kd/Vd) (95% CI)	0.47 (0.25, 0.88)	
p-value (1-sided)†	0.0084	



Number of Subjects at Risk:

Kd 54	41	20	4	1	0
Vd 42	26	10	1	0	

CI, confidence interval; HR, hazard ratio; IV, intravenous; Kd, carfilzomib/dexamethasone; (m)PFS, (median) progression-free survival; pt, patient; Vd, bortezomib/dexamethasone.

1. Moreau P, et al. *Leukemia* 2017;31(1):115–122; 2. Goldschmidt H, et al. *Leuk Lymphoma*. 2018;59(6):1364–1374.

Treatment landscape in multiple myeloma in the future

1st line

ASCT eligible

- Anti-CD38 + PI + IMiD + dex
- ASCT
- Len / dara-len x 2 yrs or len s/a

ASCT ineligible

- Dara-len-dex
- Dara-VMP / RVd
- Anti-CD38 + PI + IMiD + dex

2nd line

Early relapses

SVd: PFS of 29.5 months in PI naïve

- PVd: PFS of 20.7 months in PI naïve
- Kd: PFS was 17.7 in PI naïve*

Intermediate/ late relapses

Patients relapsing after dara-Rd

This information is relevant for the elderly patients coming from dara-Rd in first relapse and naïve for bortezomib

*Specifically in bortezomib naïve patients, with data presented for IV Kd.
ASCT, autologous stem cell transplant; dara, daratumumab; dex, dexamethasone; IV, intravenous; Kd, carfilzomib/dexamethasone; len, lenalidomide; PFS, progression-free survival; PI, proteasome inhibitor; PVd, pomalidomide/bortezomib/dexamethasone; Rd, lenalidomide/dexamethasone; RVd, lenalidomide/bortezomib/dexamethasone; SVd, selinexor/bortezomib/dexamethasone; VMP, bortezomib/melphalan/prednisolone; yrs, years.

Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2022;32(3):309–322; Goldschmidt H, et al. *Leuk Lymphoma*. 2018;59(6):1364–1374; Richardson PG, et al. *Eur J Haematol*. 2025;114(5):822–831; Mateos MV, et al. Eur J Haematol. 2024;113:242–252.

Treatment landscape in multiple myeloma in the future

1st line

ASCT eligible

- Anti-CD38 + PI + IMiD + dex
- ASCT
- Len / dara-len x 2 yrs or len s/a

ASCT ineligible

- Dara-len-dex
- Dara-VMP / RVd
- Anti-CD38 + PI + IMiD + dex

2nd line

Relapse during dara-R or early after dara stopping

Late relapse after dara stopped and continued with R/R s/a

Patients relapsing after dara-Rd

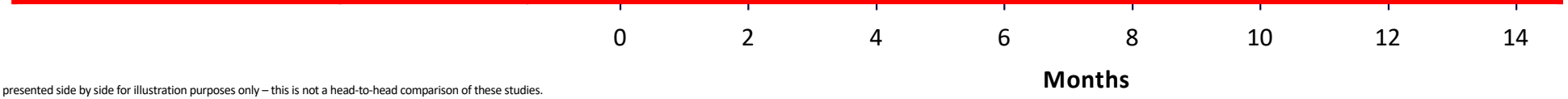
But… what about lenalidomide-refractory patients?

ASCT, autologous stem cell transplant; dara, daratumumab; dex, dexamethasone; len, lenalidomide; PI, proteasome inhibitor; Rd, lenalidomide/dexamethasone; RVd, lenalidomide/bortezomib/dexamethasone; VMP, bortezomib/melphalan/prednisolone; yrs, years.

Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2022;32(3):309–322.

PFS and OS in lenalidomide-refractory patients

Study	Regimen	Arm	mPFS in lenalidomide-refractory patients
ENDEAVOR[1*] 1–3 prior lines of therapy	**Kd**[1]: Doublet, PI, one new MoA	Kd Vd	**Common Grade ≥3 TEAEs** included **anemia** (Kd, 17.3% vs. Vd, 10.1%), **hematopoietic thrombocytopenia** (Kd, 12.5% vs. Vd, 14.7%), **hypertension** (Kd, 14.9% vs. Vd, 3.3%), and **fatigue** (Kd, 6.9% vs. Vd. 7.7)[4¶]
OPTIMISMM[2†] 1–3 prior lines of therapy, received prior treatment with a lenalidomide-containing regimen for ≥2 consecutive cycles, not bortezomib refractory	**PVd**[2]: Triplet, PI, one new MoA	PVd Vd	**Grade 3/4 TEAEs** occurred in **93.2% of patients** in the **PVd arm** and **71.9% of patients** in the Vd arm, most commonly **neutropenia** in the **PVd arm** (**47.1%,** vs. 8.9% [Vd arm]) and **thrombocytopenia** in the **Vd arm** (**29.3%,** vs. 28.1% [SVd arm])[5¶]
BOSTON[3‡] 1–3 prior lines of therapy	**SVd**[3]: Triplet, PI, two new MoAs	SVd Vd	**Common Grade 3/4 TRAEs** included **thrombocytopenia** (SVd, 45% vs. Vd, 31%), **cataract** (SVd, 13% vs. Vd, 2%), and **diarrhea** (SVd, 11% vs. Vd, 0%)[3]



Data presented side by side for illustration purposes only – this is not a head-to-head comparison of these studies.
*Median follow-up was 11.9 months (Kd arm) and 11.1 months (Vd arm); †Median follow-up was 15.9 months; ‡Median follow-up was 28.2 months (SVd) and 27.1 months (Vd); §Median follow-up approximately 44 months; ‖Median follow-up of 64.5 months; ¶AEs not specific to lenalidomide refractory patients.
CI, confidence interval; DRd, daratumumab/lenalidomide/dexamethasone; HR, hazard ratio; Kd, carfilzomib/dexamethasone; Len, lenalidomide; MoA, mechanism of action; (m)PFS, (median) progression-free survival; (m)OS, (median) overall survival; PI, proteasome inhibitor; PVd, pomalidomide/bortezomib/dexamethasone; SVd, selinexor/bortezomib/dexamethasone; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event; Vd, bortezomib/dexamethasone.

1. Moreau P, et al. *Leukemia.* 2017;31:115–122; 2. Richardson PG, et al. *Lancet Oncol.* 2019;20:781–94; 3. Mateos MV, et al. *Eur J Haematol.* 2024;113:242–25; 4. Orlowski RZ, et al. *Clin Lymphoma Myeloma Leuk.* 2019;19(8):522–530.e1; 5. Richardson P, et al. *Eur J Haematol.* 2025;114(5):822–831.

Treatment landscape in multiple myeloma in the future

1st line

ASCT eligible

- Anti-CD38 + PI + IMiD + dex
- ASCT
- Len / dara-len x 2 yrs or len s/a

ASCT ineligible

- Dara-len-dex
- Dara-VMP / RVd
- Anti-CD38 + PI + IMiD + dex

2nd line

Early relapses

Intermediate/ late relapses

Patients relapsing after dara-Rd

SVd: mPFS of 10.2 months in lenalidomide-refractory
- ***Significantly longer mOS for SVd vs. Vd***

- PVd: mPFS of 9.5 months in lenalidomide-refractory
  - *No significant difference in mOS for PVd vs. Vd*
- Kd: mPFS of 8.6 months in lenalidomide-refractory
  - *No significant difference in mOS for Kd vs. Vd*

- The lenalidomide-refractory population is a challenging population
- Cilta-cel has been especially conducted in lenalidomide-refractory patients and is more effective, but not available worldwide

ASCT, autologous stem cell transplant; cilta-cel, ciltacabtagene autoleucel; dara, daratumumab; dex, dexamethasone; IMiD, immunomodulatory drug; Kd, carfilzomib/dexamethasone; len, lenalidomide; mPFS, median progression-free survival; mOS, median overall survival; PI, proteasome inhibitor; PVd, pomalidomide/bortezomib/dexamethasone; Rd, lenalidomide/dexamethasone; RVd, lenalidomide/bortezomib/dexamethasone; SVd, selinixor/bortezomib/dexamethasone; Vd, bortezomib/dexamethasone; VMP, bortezomib/melphalan/prednisolone; yrs, years.

Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2022;32(3):309–322; Moreau P, et al. *Leukemia*. 2017;31:115–122; Richardson PG, et al. *Lancet Oncol*. 2019;20:781–94; Mateos MV, et al. *Eur J Haematol*. 2024;113:242–25;

Treatment landscape in multiple myeloma in the future

1st line

ASCT eligible

- Anti-CD38 + PI + IMiD + dex
- ASCT
- Len / dara-len x 2 yrs or len s/a

ASCT ineligible

- Dara-len-dex
- Dara-VMP / RVd
- Anti-CD38 + PI + IMiD + dex

2nd line

Early relapses

- Cilta-cel
- Elranatamab s/a
- Tec or tal-based combos
- Linvo / enentamig
- **Belamaf-Vd / belamaf-Pd**

Intermediate/ late relapses

- Cilta-cel
- Elranatamab s/a
- Tec or tal-based combos
- Linvo / enentamib
- **Belamaf-Vd / belamaf-Pd**
- Kd AntiCD38 / Pd AntiCD38

Patients relapsing after dara-Rd

- Cilta-cel
- **Belamaf-Vd / belamaf-Pd**
- Elranatamab s/a
- Tec or tal-based combos
- Linvo / enentamib
- PVd / selinexor-Vd

**Belantamab-based combinations can be a good option in this landscape…
but their use means targeting BCMA earlier and some physicians prefer to reserve BCMA for CAR-T or BsAbs when available**

ASCT, autologous stem cell transplant; BCMA, B cell maturation antigen; BsAb, bispecific antibody; CAR-T, chimeric antigen receptor T cell; cilta-cel, ciltacabtagene autoleucel; dara, daratumumab; dex, dexamethasone; IMiD, immunomodulatory drug; Kd, carfilzomib/dexamethasone; len, lenalidomide; PI, proteasome inhibitor; Pd, pomalidomide/dexamethasone; PVd, pomalidomide/bortezomib/dexamethasone; Rd, lenalidomide/dexamethasone; RVd, lenalidomide/bortezomib/dexamethasone; tal, talquetamab; tec, teclistamab; Vd, bortezomib/dexamethasone; VMP, bortezomib/melphalan/prednisolone; yrs, years.

Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2022;32(3):309–322.

Treatment landscape in multiple myeloma today: realistic situation

1st line

ASCT eligible

- Anti-CD38 + PI + IMiD + dex
- ASCT
- Len / dara-len

ASCT ineligible

- Dara-len-dex
- Dara-VMP / RVd
- Anti-CD38 + PI + IMiD + dex

2nd line

Based on sensitivity/refractoriness to daratumumab and lenalidomide

- Anti-CD38 + carfilzomib-dex
- Anti-CD38 + pom-dex

- Pom-bortezomib-dex
- Selinexor-bortezomib-dex
- Carfilzomib-dex

Cilta-cel

3rd line

- Anti-CD38 + pom-dex
- Elotuzumab-pom-dex
- Previous combos if pt is eligible
- Ide-cel based on KarMMa-3

4th line

Other drugs
- Melflufen
- Sel-dex

BCMA-targeted therapy
- Ide-cel (*CAR-T*)
- Cilta-cel (*CAR-T*)
- Teclistamab (*BsAb*)
- Elranatamab(*BsAb*)

GPRC5D-targeted therapy
- Talquetamab (*BsAb*)

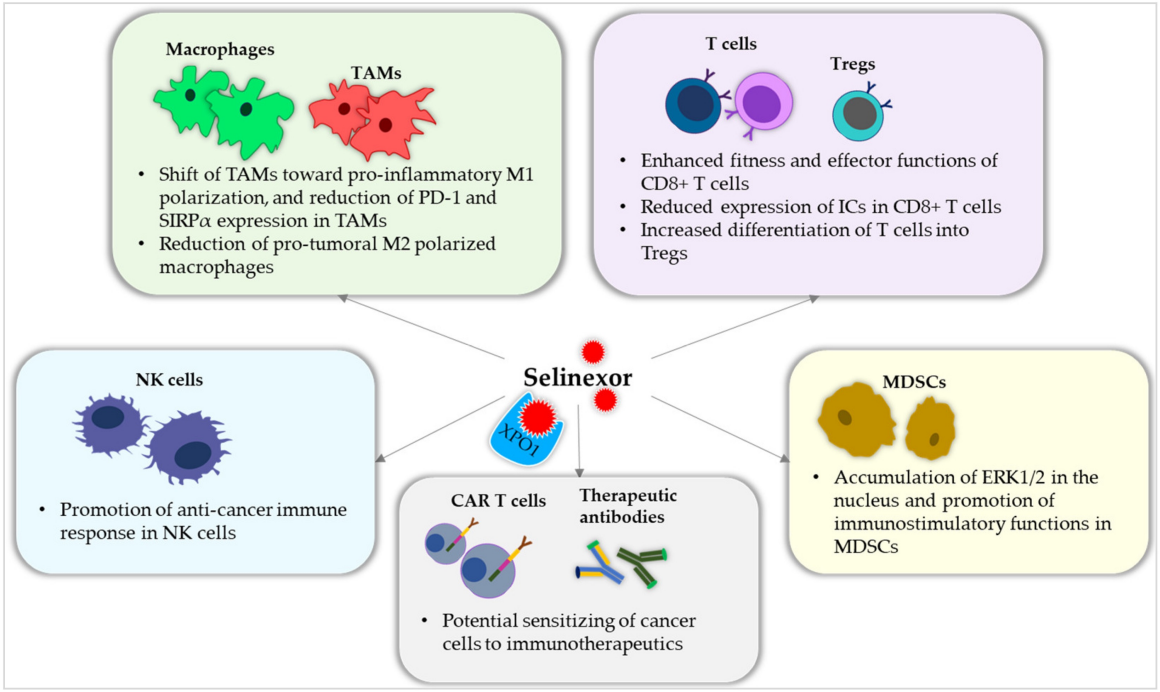
The label is for R/R MM after ≥3 PL of therapy including PI, IMiD and anti-CD38 and refractory to the last line of therapy

ASCT, autologous stem cell transplant; BCMA, B cell maturation antigen; BsAb, bispecific antibody; cilta-cel, ciltacabtagene autoleucel; dara, daratumumab; dex, dexamethasone; GPRC5D, G-protein-coupled receptor class C group 5 member D; ide-cel, idecabtagene vicleucel; IMiD, immunomodulatory drug; len, lenalidomide; PL, prior line; pom, pomalidomide; PI, proteasome inhibitor; pt, patient; R/R MM, relapsed/refractory multiple myeloma; RVd, lenalidomide/bortezomib/dexamethasone; sel, selinexor; VMP, bortezomib/melphalan/prednisolone.

Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2022;32(3):309–322.

Selinexor influences multiple immune cells pathways

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



Selinexor is suggested to **impact macrophages** and **tumor-associated macrophages** (TAMs), **myeloid-derived suppressor cells** (MDSCs), **natural killer** (NK) **cells**, and T cells in the **tumor microenvironment**

Selinexor potentially **sensitizes cancer cells** to **CAR-T cells** and therapeutic **antibodies***

*Selinexor SmPC does not specify guidance on its use in sequence with CAR-T cells.
CAR-T, chimeric antigen receptor T cell; 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, tumor-associated macrophage; Treg, regulatory T cell.

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

Summary

Addressing unmet needs with a new mechanism of action: Role and place of XPO1 inhibition

Despite many novel therapeutics in R/R MM, **unmet needs** continue to exist and we need to understand **optimal sequencing** to **improve patient outcomes**

Available options in **anti-CD38-** and **lenalidomide-refractory** patients are limited and **Kd and PVd** have their own **safety challenges**

Selinexor introduces a **novel MoA**; the **BOSTON** trial validates its **combination with bortezomib (SVd)**, and has an effective utility with **double antiemetic prophylaxis** and **dose modifications**

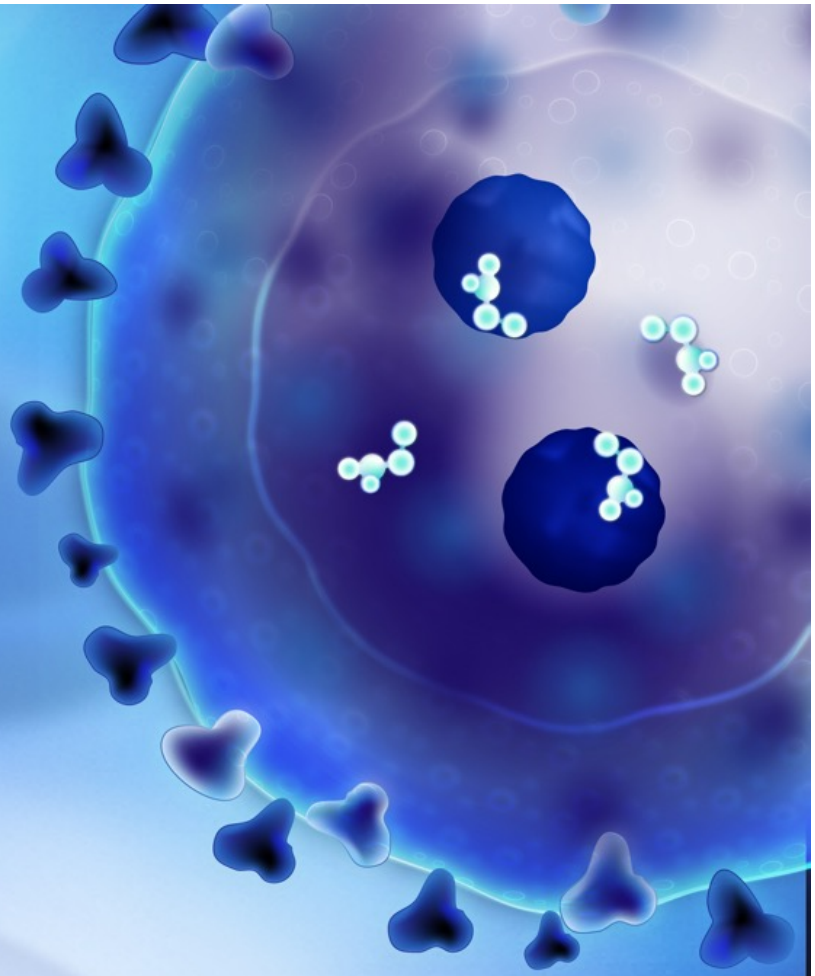
Selinexor is included in **worldwide guidelines** for the management of patients with myeloma after at least **1 prior line** in this competitive landscape:

- SVd showed benefit in the **lenalidomide-refractory population**, including survival benefit
- SVd is a viable treatment option that allows for the **preservation of BCMA-TT for later lines***
- SVd can also be used **after BCMA-TT** in early lines, without compromising and potentially having a positive effect on subsequent lines of T-cell redirecting therapies*

*Statements not explicitly supported by or mentioned in selinexor SmPC.
BCMA, B-cell maturation antigen; Kd, carfilzomib/dexamethasone; MM, multiple myeloma; MoA, mechanism of action; SVd, selinexor/bortezomib/dexamethasone; PVd, pomalidomide/ bortezomib/dexamethasone; R/R, relapsed/refractory; TT, targeted therapy; XPO1, exportin 1.

Streamlining therapy management: Practical strategies for enhanced treatment outcomes

Karthik Ramasamy
Oxford University Hospitals NHS Foundation Trust, Oxford, UK



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Disclosures

- **Advisory board**: AbbVie, Amgen, Adaptive Biotechnologies, Celgene, EUSA Pharma, GSK, Janssen, Karyopharm Therapeutics, Menarini Stemline, Pfizer, Sanofi, Takeda, and Recordati

- **Honoraria**: Adaptive Biotechnologies, Celgene (BMS), GSK, Janssen, Menarini Stemline, Sanofi, Takeda, Recordati, and Pfizer

- **Research support**: Amgen, Celgene, GSK, J&J, Sanofi, and Takeda

Key considerations for choice of relapse treatment

Patient & treatment related

- **Prior regimen** used
- Patient **age** and **frailness**
- **Comorbidities**

Therapy-management related

- Therapy **waiting time**
- **ICANS/CRS** management for CAR-T and bispecific antibodies
- **GI** side effects
- **Infection rates** and other specific toxicities

Target related

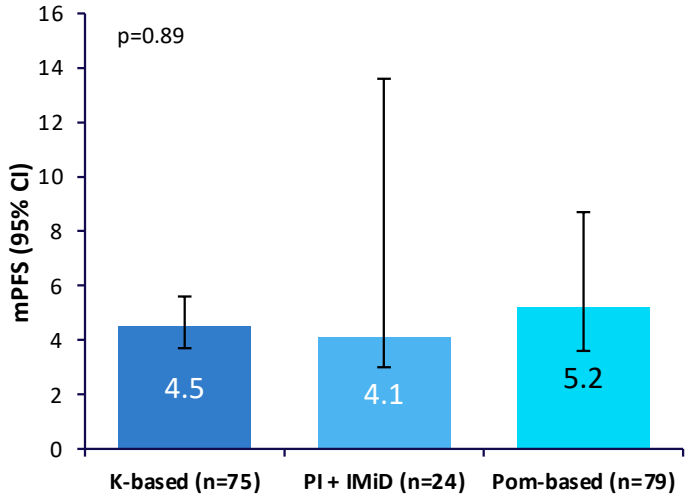
- **T-cell fitness & T-cell exhaustion**

CAR-T, chimeric antigen receptor T cell; CRS, cytokine release syndrome; GI, gastrointestinal; ICANS, immune effector cell-associated neurotoxicity syndrome.

Devarakonda S, et al. *Hematology Am Soc Hematol Educ Program.* 2022;2022(1):560–568; Nathwani N, et al. *Am Soc Clin Oncol Educ Book.* 2021;41:358–375; Binder AF, et al. *Front Immunol.* 2023:14:1275329; Zhou X, et al. *Haematologica.* 2023;108:958–968.

Dismal outcomes for patients relapsing after daratumumab regimens

PFS of patients in subsequent therapy following dara-containing regimens, based on regimen types



Previous treatment with DVd

Median prior lines of treatment: 2–3

	n	Median PFS	95% CI
Carfilzomib-based therapy	12	4.3	1.8–6.2
Pomalidomide-based therapy	47	7.3	4.1–9.7
IMiD + PI based on carfilzomib and/or pomalidomide	4	4.5	0–NRY

Previous treatment with DRd

Median prior lines of treatment: 2–3

	n	Median PFS	95% CI
Carfilzomib-based therapy	41	2.8	1.9–4.6
Pomalidomide-based therapy	24	3.4	1.3–5.2
IMiD + PI based on carfilzomib and/or pomalidomide	9	3.6	0.9–NRY

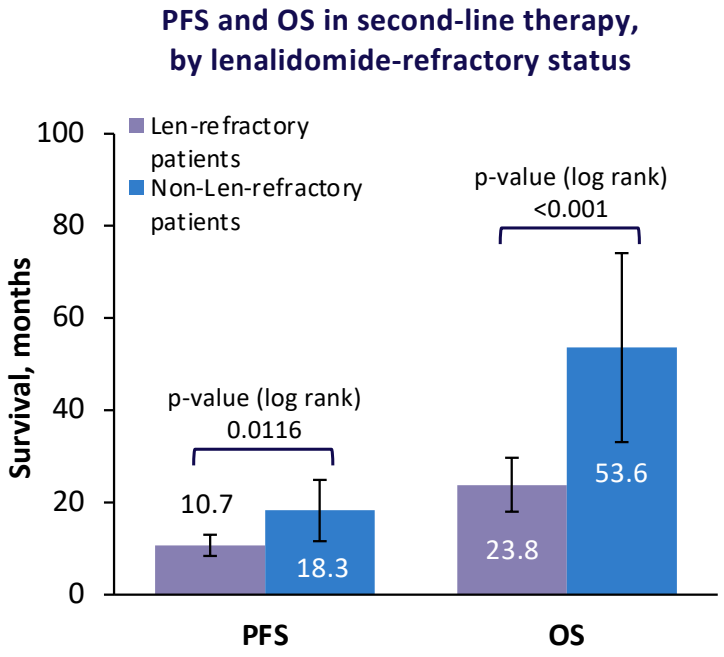
The poor outcome of MM patients when standard regimens based on carfilzomib and/or pomalidomide are utilized directly after daratumumab-based therapy given in the relapsed setting. Novel therapies, including immune therapies, are urgently needed to improve the outcomes of these daratumumab-exposed patients.

CI, confidence interval; DRd, daratumumab/lenalidomide/dexamethasone; DVd, daratumumab/bortezomib/dexamethasone; IMiD, immunomodulatory drug; K, carfilzomib; MM, multiple myeloma; (m)PFS, (median) progression-free survival; NRY, not reached yet; PI, proteasome inhibitor; pom, pomalidomide.

LeBlanc R, et al. *Eur J Haematol*. 2023;111(5):815–823.

Dismal outcomes for patients relapsing after first line lenalidomide regimens

Greek experience[1]



German MYRIAM registry[2]

Response (from start of 2L, non SCT)	Relapsed (n=89)	Refractory (n=155)
ORR, n (%)	27 (30.3)	44 (28.4)
CR, n (%)	4 (4.5)	3 (1.9)
VGPR, n (%)	12 (13.5)	10 (6.5)

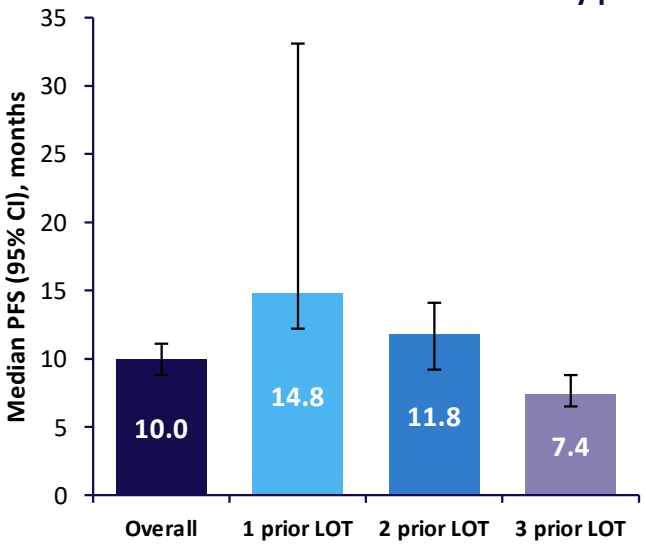
Survival (from start of 2L, non SCT)	Relapsed (n=89)	Refractory (n=155)
mPFS (95% CI), mos	11.9 (6.0–25.1)	8.6 (4.8–10.4)
mOS (95% CI), mos	NR	20.9 (15.1–37.9)
2-yr OS (95% CI), %	63 (47–74)	–

CI, confidence interval; CR, complete response; L, line; (m)PFS, (median) progression-free survival; (m)OS, (median) overall survival; mos, months; NR, not reached; ORR, overall response rate; SCT, stem cell transplant; VGPR, very good partial response.

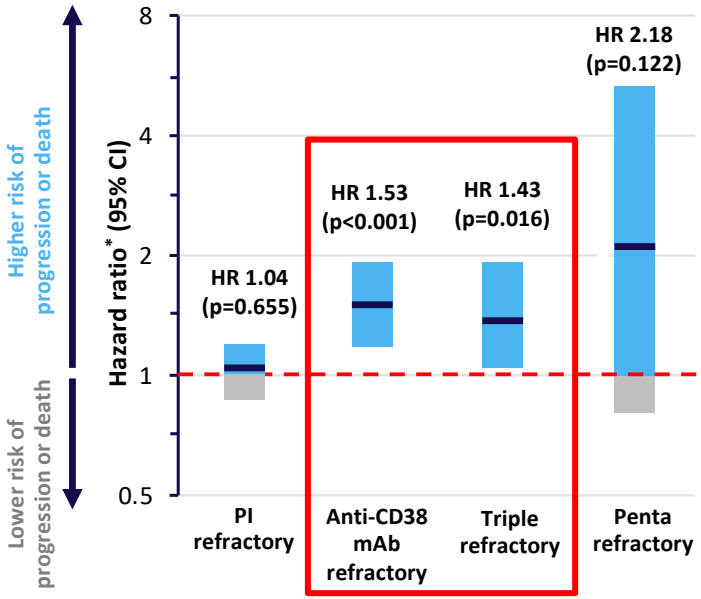
1. Kastritis E, et al. *Clin Lymphoma Myeloma Leuk.* 2024;24(7):468–477; 2. Reiser M, et al. Poster 909; presented at EHA 2024.

Poor PFS in lenalidomide-refractory and triple-class refractory patients

PFS by number of prior LOT after first index treatment in lenalidomide-refractory patients



Prognostic factors for PFS: Refractory status



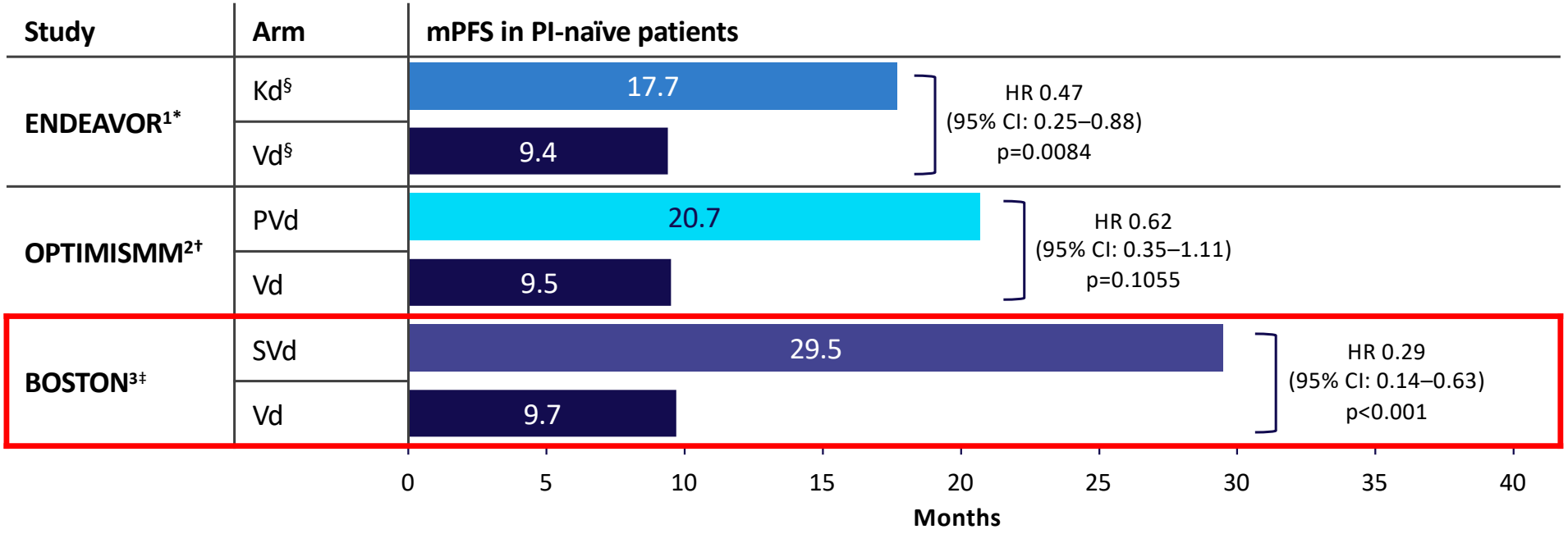
- Patients with **lenalidomide-refractory** MM have **poor outcomes**
- PFS for **anti-CD38-mAb-refractory** MM is at least as **poor** as with **triple-refractory** MM
- **Same outcomes** were observed for **OS**

There is a need for novel and effective treatment options for use as early as 2L therapy for lenalidomide-refractory MM

Analysis of individual patient-level data from daratumumab clinical trials: APOLLO, CASTOR, CANDOR, EQUULEUS, ALCYONE, MAIA, GRIFFIN, POLLUX, and CASSIOPEIA. *Reference for each factor was the absences of the refractory state.
2L, second-line; CI, confidence interval; HR, hazard ratio; L, line; LOT, line-of-therapy; mAb, monoclonal antibody; MM, multiple myeloma; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor.

Yong K, et al. *Eur J Cancer*. 2025;215:115157.

PFS in proteasome inhibitor-naïve patients



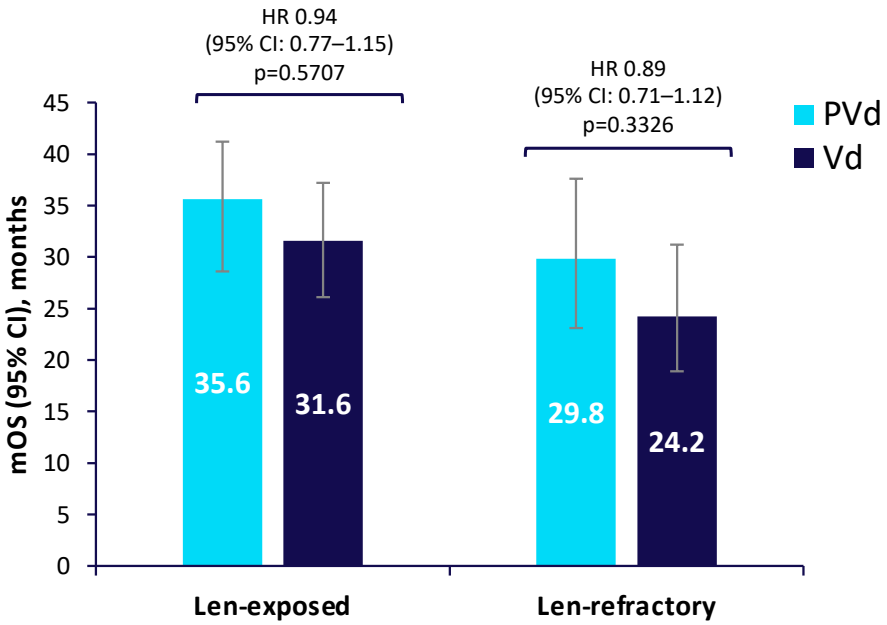
The **combination** of **selinexor** and **proteasome inhibitors** has been shown to exert **synergistic cytotoxicity** *in vitro* and *in vivo*[4]

Data presented side by side for illustration purposes only – this is not a head-to-head comparison of these studies.
*Data presented are for patients without previous bortezomib treatment. Median follow-up was 11.9 months (Kd arm) and 11.1 months (Vd arm);
†After median follow-up of 15.9 months; ‡Median follow-up was 28.2 months (SVd) and 27.1 months (Vd); §intravenous administration.
CI, confidence interval; DRd, daratumumab/lenalidomide/dexamethasone; HR, hazard ratio; Kd, carfilzomib/dexamethasone; len, lenalidomide;
(m)PFS, (median) progression-free survival; (m)OS, (median) overall survival; NE, not estimable; PI, proteasome inhibitor;
PVd, pomalidomide/bortezomib/dexamethasone; SVd, selinexor/bortezomib/dexamethasone; Vd, bortezomib/dexamethasone.

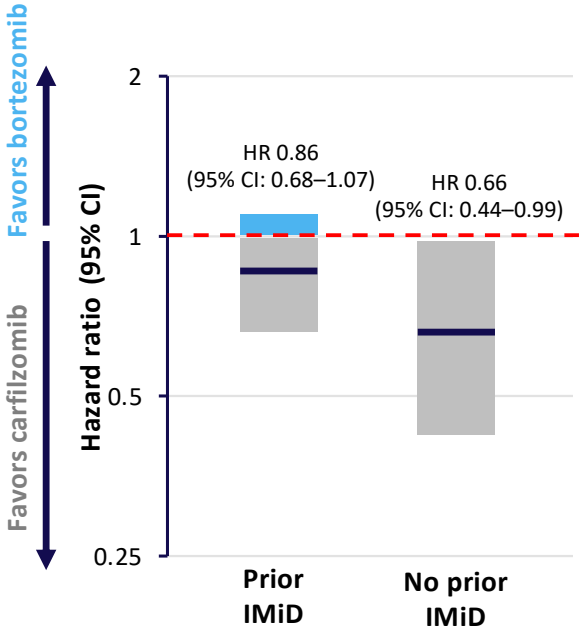
1. Goldschmidt H, et al. *Leuk Lymphoma*. 2018;59(6):1364–1374; 2. Dimopoulos M, et al. *Leukemia*. 2021;35(6):1722–1731;
3. Mateos MV, et al. *Eur J Haematol*. 2024;113:242–252; 4. Kashyap T, et al. *Oncotarget*. 2016;7(48):78883–78895.

OPTIMISMM and ENDEAVOR: No benefit in survival

OPTIMISMM: OS in patients with LEN-exposed or LEN-refractory disease[1]



ENDEAVOR: OS by prior IMiD[2]

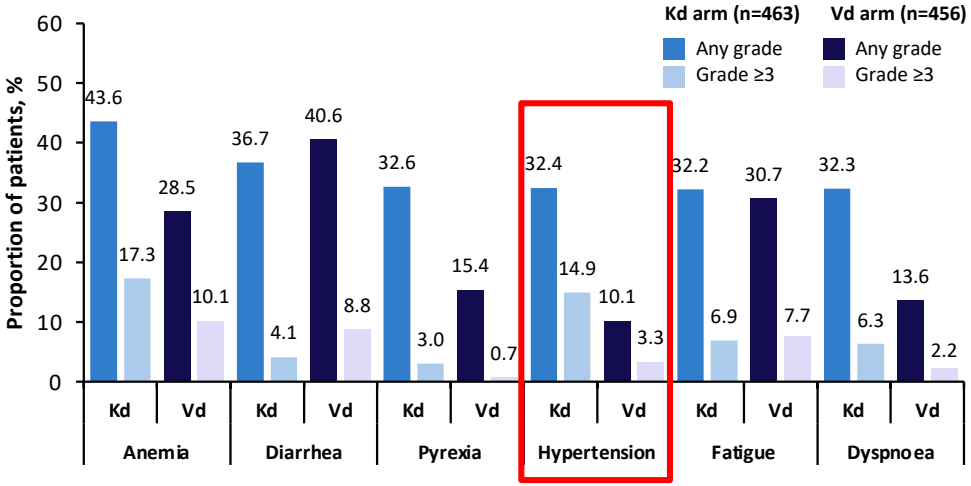


CI, confidence interval; HR, hazard ratio; IMiD, immunomodulatory drug; LEN, lenalidomide; (m)OS, (median) overall survival; PVd, pomalidomide/bortezomib/dexamethasone; Vd, bortezomib/dexamethasone.

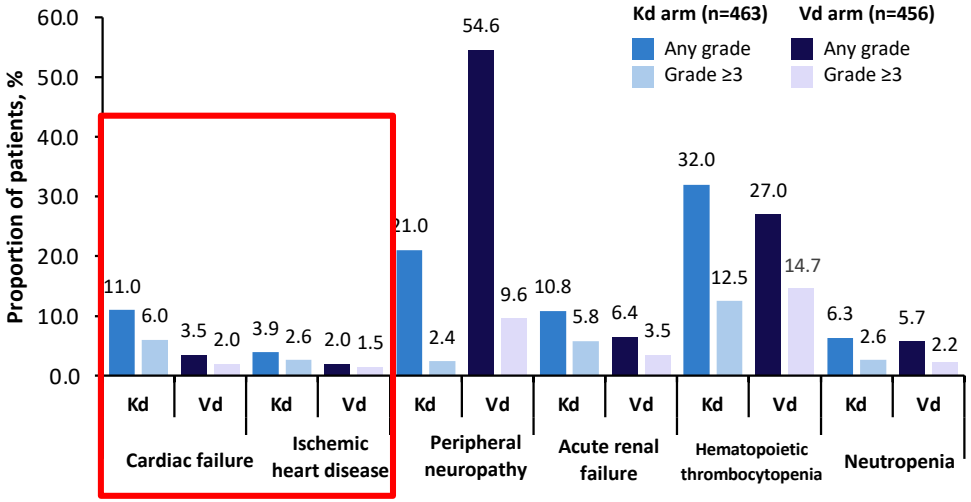
1. Richardson P, et al. *Eur J Haematol.* 2025;114(5):822–831;
2. Dimopoulos MA, et al. *Lancet Oncol.* 2017;18(10):1327–1337.

ENDEAVOR: Kd safety

Most common TEAEs



Events of interest



The most common all grade AEs were anemia, diarrhea, pyrexia, hypertension, fatigue and dyspnoea

The most common Grade 3/4 AEs were anemia, thrombocytopenia, hypertension and cardiotoxicity (cardiac failure and IHD)

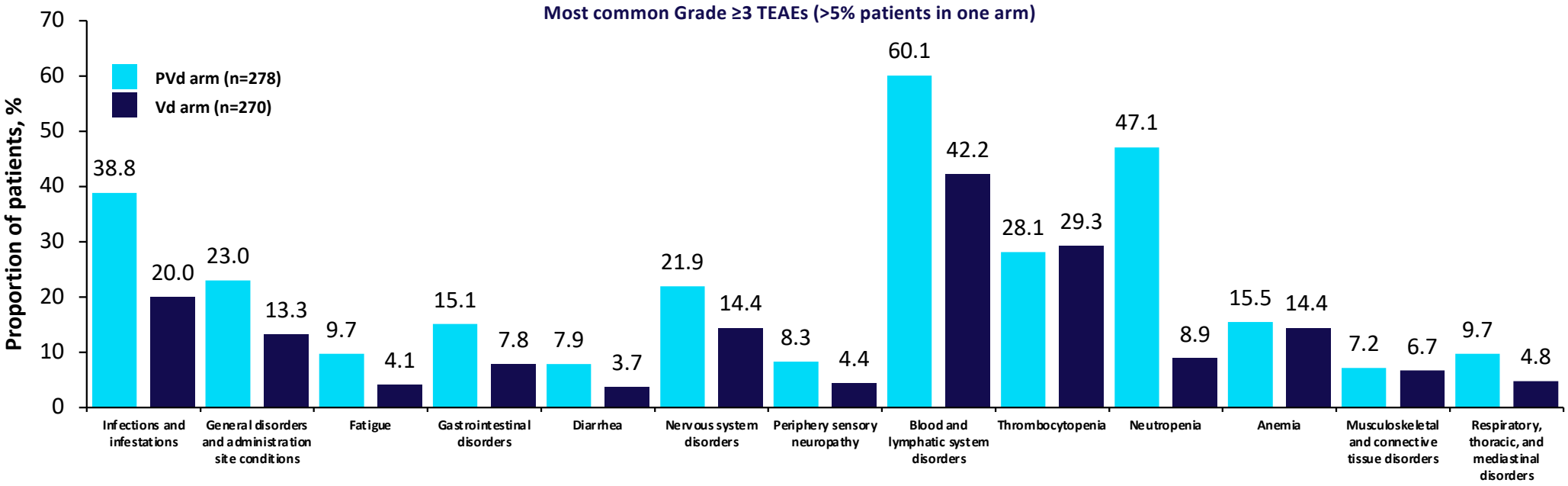
AE, adverse event; IHD, ischemic heart disease; Kd, carfilzomib/dexamethasone; TEAE, treatment-emergent adverse event; Vd, bortezomib/dexamethasone.

Orlowski R, et al. *Clin Lymphoma*. 2019;2152–2650.

OPTIMISMM: PVd safety

The most common **all Grade AEs** were **infections, GI toxicities, peripheral neuropathy, cytopenia** and **fatigue**

The most common **Grade ≥3 AEs in the PVd arm** were **cytopenia and infections**



AE, adverse event; GI, gastrointestinal; PVd, pomalidomide/bortezomib/dexamethasone; Vd, bortezomib/dexamethasone.

Richardson P, et al. *Eur J Haematol.* 2025;114(5):822–831.

Key considerations for choice of relapse treatment

Patient & treatment related

- **Prior regimen** used
- Patient **age** and **frailness**
- **Comorbidities**

Therapy-management related

- Therapy **waiting time**
- **ICANS/CRS** management for CAR-T and bispecific antibodies
- **GI** side effects
- **Infection rates** and other specific toxicities

Target related

- **T-cell fitness & T-cell exhaustion**

CAR-T, chimeric antigen receptor T cell; CRS, cytokine release syndrome; GI, gastrointestinal; ICANS, Immune Effector Cell-Associated Neurotoxicity Syndrome.

Devarakonda S, et al. *Hematology Am Soc Hematol Educ Program.* 2022;2022(1):560–568; Nathwani N, et al. *Am Soc Clin Oncol Educ Book.* 2021;41:358–375; Binder AF, et al. *Front Immunol.* 2023:14:1275329; Zhou X, et al. *Haematologica.* 2023;108:958–968.

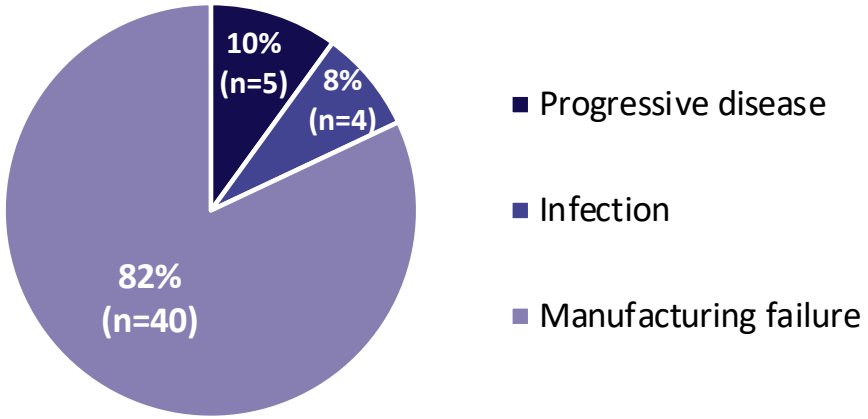
Patients who do not reach CAR-T administration have poorer disease control and outcomes

Single-center analysis of all patients assessed by MM specialist and waitlisted for ide-cel or cilta-cel

- Attrition rate (defined as death prior to infusion)
- N=185; March 2021 to March 2024
  - Of 138 patients who either received CAR-T or died, the **overall attrition rate was 36%,** declining from 44% in 2021–2022 to **15% in 2023–2024**
  - **OS** was **significantly longer** for **those receiving CAR-T** vs. non-recipients (NR vs 9.4 months; p<0.001; median follow-up 17.2 months)

Primary reasons for attrition

(among evaluable patients who experienced CAR-T attrition, n=49)



CAR-T, chimeric antigen receptor T cell; MM, multiple myeloma; NR, not reached; OS, overall survival.

Portuguese AJ, et al. Abstract #3772; presented at ASH 2024.

CAR-T therapy: Toxicities that require specific management

Acute Toxicities

- Cytokine-release syndrome
- Cytopenias
- Immune effector cell–associated neurotoxicity syndrome
- Immune effector cell associated HLH-like syndrome

Generally managed by treatment center

Delayed Toxicities

- B-cell aplasia/hypogammaglobulinemia
- Prolonged cytopenias
- Late infections
- Long-term neurologic events/movement and neurocognitive treatment-emergent AEs
- Transient cardiac toxicities
- Secondary malignancies

Generally managed by primary oncologist (treatment center or community setting)

Therapy management

Grade	Neurotoxicity (ICANS)	CRS + Neurotoxicity (ICANS)
1	Supportive care (± steroids)	Supportive care (± tocilizumab)*
2	Steroids (dexamethasone or methylprednisolone)	Tocilizumab + steroids (dexamethasone)
3	Steroids (dexamethasone)	Tocilizumab + steroids (dexamethasone)
4	High-dose steroids (methylprednisolone) ICU/critical care	Tocilizumab + high-dose steroids (methylprednisolone) ICU/critical care

Add anticonvulsants (levetiracetam, benzodiazepines)
Low threshold for inpatient management
(if outpatient at time of onset)
Multidisciplinary team approach

Infection prophylaxis and vaccinations

- Recommended that **outstanding vaccinations are completed** ≥2 weeks prior to therapy start
- **Consider G-CSF in patients with severe neutropenia**
- **Antibacterial and antifungal prophylaxis** recommended for **patients at high risk of infection**; HSV/VZV and PJP prophylaxis recommended for all patients

*High-burden, high-risk products; older; comorbidities, etc.
AE, adverse event; CRS, cytokine release syndrome; G-CSF, granulocyte colony stimulating factor; HLH, hemophagocytic lymphohistiocytosis; HSV, herpes simplex virus; ICANS, immune effector cell-associated neurotoxicity syndrome; ICU, intensive care unit; IEC-HS, immune effector cell-associated HLH-like syndrome; PJP, pneumocystis jirovecii pneumonia; VZV, varicella-zoster virus.

Cohen AD, et al. *Blood*. 2023;141(3):219–230; Maus MV, *J Immunother Cancer*. 2020;8(2):e001511; Chakraborty R, et al. *Transplant Cell Ther*. 2021;27(3):222–229.

Bispecific antibodies: Toxicities that need careful mitigation

Acute Toxicities

- Cytokine-release syndrome
- Immune effector cell–associated neurotoxicity syndrome
- Neurologic toxicity
- Infections
- Neutropenia
- Hypersensitivity or injection-site reactions

Generally managed by treatment center

Delayed Toxicities

- Hepatotoxicity
- Cytopenias
- Infections
- Neurologic toxicity

Generally managed by primary oncologist (treatment center or community setting)

Therapy management

Grade	Neurologic toxicity*	ICANS
1	Withhold until symptoms resolve or stabilize	Withhold until resolution
2	Withhold until symptoms improve to Grade ≤1	Withhold until resolution + steroids + 48-hr hospitalization with next dose
3	*First occurrence*: Grade 2 actions + supportive therapy *Recurrence*: Grade 4 actions	*First occurrence*: Grade 2 actions + supportive therapy + steroids *Recurrence*: Grade 4 actions + steroids
4	Permanently discontinue + steroids (dexamethasone or methylprednisolone); ICU/critical care	

Add anticonvulsants (levetiracetam, benzodiazepines)
Low threshold for inpatient management
(if outpatient at time of onset)
Multidisciplinary team approach

Infection prophylaxis and vaccinations

- Recommended that **outstanding vaccinations are completed** ≥2 weeks prior to therapy start
- **Consider G-CSF in patients with severe neutropenia**
- **Antibacterial and antifungal prophylaxis** recommended for **patients at high risk of infection**; HSV/VZV and PJP prophylaxis recommended for all patients

*Excluding ICANS.
CRS, cytokine release syndrome; G-CSF, granulocyte colony stimulating factor; HSV, herpes simplex virus;
ICANS, immune effector cell–associated neurotoxicity syndrome, ICU, intensive care unit; PJP, pneumocystis jirovecii pneumonia; VZV, varicella-zoster virus.

ELREXFIO. European Medicines Agency. SmPC; Tecvayli. European Medicines Agency. SmPC; Talvey . European Medicines Agency. SmPC; Martin TG, et al. *Cancer*. 2023;129(13):2035–2046.

Bispecific antibodies may require management of CRS, infections and hematologic-related events

AE N (%)	Teclistamab[1] Phase 1/2 MajesTEC-1 trial N=165		Elranatamab[2] Phase 2 MagnetisMM-3 trial N=123		Talquetamab[3] Phase 1/2 MonumenTAL-1 trial			
					405 µg/kg, N=30		800 µg/kg, N=44	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4	Any Grade	Grade 3/4	Any Grade	Grade 3/4
CRS	119 (72.1)	1 (0.6)	71 (57.7)	0	23 (77)	1 (3)	35 (80)	0
Infections	126 (76.4)	74 (44.8)	86 (69.9)	49 (39.8)	14 (47)	2 (7)	15 (34)	3 (7)
Hematological AEs								
Neutropenia	117 (70.9)	106 (64.2)	60 (48.8)	60 (48.8)	20 (67)	18 (60)	16 (36)	14 (32)
Anemia	86 (52.1)	61 (37.0)	60 (48.8)	46 (37.4)	18 (60)	9 (30)	19 (43)	10 (23)
Thrombocytopenia	66 (40.0)	35 (21.2)	38 (30.9)	29 (23.6)	11 (37)	7 (23)	10 (23)	5 (11)
Decreased weight	–	–	–	–	9 (30)	0	14 (32)	1 (2)
Decreased appetite	–	–	41 (33.3)	1 (0.8)	6 (20)	1 (3)	9 (20)	0

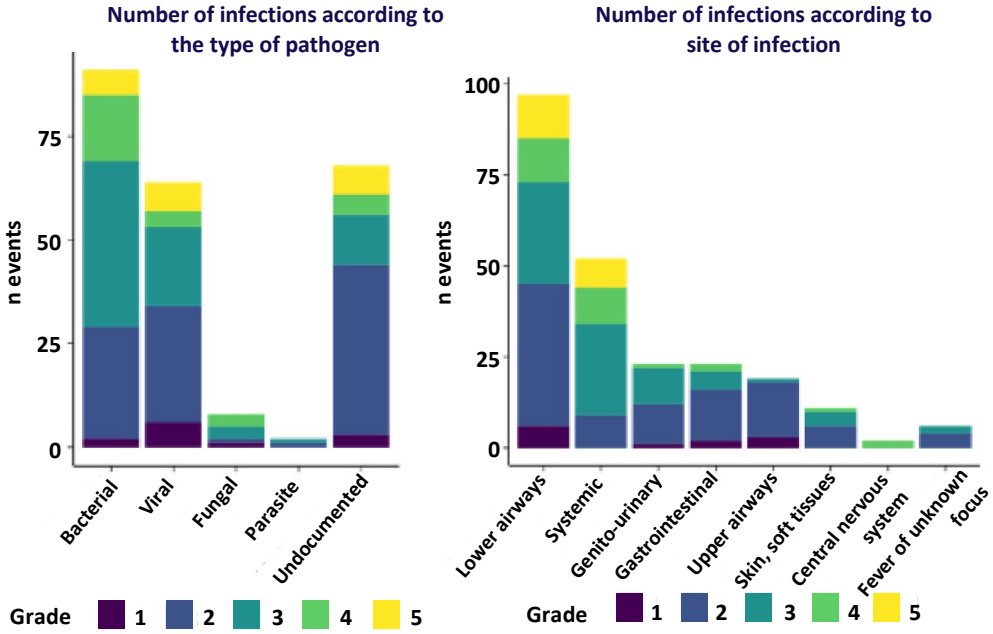
Head-to-head studies have not been conducted. Cross-trial comparisons are not appropriate.
AE, adverse event; CRS, cytokine release syndrome.

1. Moreau P, et al. *N Engl J Med.* 2022;387:495–505; 2. Lesokhin A, et al. *Nat Med.* 2023;29:2259–2267;
3. Chari A, et al. *N Engl J Med.* 2022;387:2232–2244.

Bispecific antibodies in the real world: Infection risk

- A **retrospective, multicenter study** in bispecific antibody-treated patients with MM in 14 IFM centers
- **N=229** (153 [67%] teclistamab; 47 [20%] elranatamab; 29 [13%] talquetamab)

- **142/229 (62%) patients** presented at least one infection affecting patient management with a median number of infections per patient of 1.0 (range 1–7)
- Of the **234 infectious events** recorded:
  - 123 (53%) were Grade ≥3
  - 103 (44%) had an effect on the course of MM treatment, with discontinuation in 31 cases (13%)
  - 9% resulted in death
- The infection rate was **lower with GPRC5D-targeted bispecific antibody** (51%) when compared with anti-BCMA agents (73%)
- **Use of corticosteroids for CRS/ICANS** correlated with a higher risk of first infection (HR 2.01; 95% CI: 1.27–3.19)



CI, confidence interval; CRS, cytokine release syndrome; HR, hazard ratio; ICANS, immune effector cell-associated neurotoxicity; IFM, Intergroupe Francophone du Myelome; IVIG, intravenous immunoglobulin; LOT, line of therapy; MM, multiple myeloma.

Jourdes A, et al. *Clin Microbiol Infect*. 2024;30(6):764–771.

Toxicities and management: Belantamab mafodotin

Most frequent toxicities[1,2]
▪ Ocular events
▪ Neutropenia
▪ Thrombocytopenia
▪ Infections

- To minimize the risk of ocular toxicity, patients should see an **eye specialist for baseline assessment** prior to starting treatment and **prior to each subsequent dose** to monitor for worsening eye symptoms[3]
- To help reduce ocular events, the **provider should educate** the patient on the **use of preservative-free ophthalmic lubricants** at least four times daily starting prior to the first treatment and continuing to the end of treatment[3]

Grade*	Recommendations[4]
1 (mild superficial keratopathy, BCVA decline up to 1 line)	Continue belantamab without changes
2 (moderate superficial keratopathy, BCVA decline of 2–3 lines)	• Hold belantamab until Gr 2 becomes Gr 1 • When Gr 1, resume belantamab at same dose
3 (severe superficial keratopathy, BCVA decline of >3 lines)	• Hold belantamab until Gr 3 becomes Gr 1 • When Gr 1, resume belantamab at same dose
4 (corneal defects such as ulcer, BCVA worse than 20/200)	• Consider belantamab discontinuation • Hold belantamab until Gr 4 becomes Gr 1 • When Gr 1, may resume belantamab at reduced dose weighing risks vs. benefits

Management of toxicity includes **dosage modifications**, treatment **interruption or discontinuations** and preservative-free **artificial tears** along with close **ophthalmology and hematology-oncology** follow-ups[3]

*KVA scale (slit lamp, Snellen visual acuity); recommendations are derived from DREAMM-2 protocol.
BCVA, best corrected visual acuity; Gr, grade; KVA, keratopathy and visual acuity.

1. Hungria V, et al. *N Engl J Med*. 2024;391(5):393–407; 2. Dimopoulos MA, et al. *N Engl J Med*. 2024;391(5):408–421;
3. Lu R, et al. *J Adv Pract Oncol*. 2023;1;14(4):300–306; 4. Wahab A, et al. *Front Oncol*. 2021;11:678634.

DREAMM-7: Ophthalmological assessment

Blurred vision was the **most frequent ocular adverse reaction in the BVd arm**, with 68% and 24% of patients experiencing all grades and Grade 3/4 events, respectively

Discontinuation due to any ocular events was 10%

BVd	Bilateral worsening of BCVA in patients with normal baseline 20/25 or better	
	20/50 or worse	**20/200 or worse**
Patients, n/N (%)	84/242 (35)	5/242 (2)
Time to onset of first event, median (range), days	79 (16–1320)	105 (47–304)
Time to resolution of first event to baseline, median (range), days	64 (8–908)	87 (22–194)
Time to improvement of first event, median (range), days	22 (6–257)	19 (8–26)
First event resolved, n/N (%)	78/84 (93)	4/5 (80)
First event improved, n/N (%)	81/84 (96)	5/5 (100)
Follow-up ended with event ongoing, n/N (%)	2/84 (2)	0

BCVA, best corrected visual acuity; BVd, belantamab mafodotin/bortezomib/dexamethasone; DVd, daratumumab/bortezomib/dexamethasone.

DREAMM-7; clinicaltrials.gov. Available at: https://clinicaltrials.gov/study/NCT04246047?term=NCT04246047&rank=1&tab=results; Hungria V, et al. Abstract #772; oral presentation at ASH 2024; image from Shi Cet al. *J Vis*. 202;20(8):29.

Phase 3 DREAMM-7/8 studies: Summary

	Study design	Baseline characteristics	Median PFS, mos*	Median OS, mos*	ORR, % (95% CI)†	Safety profile‡	Belantamab-associated AEs
DREAMM-7[1]	1:1 BVd (n=243) DVd (n=251) **Primary endpoint:** PFS **Secondary endpoints:** OS, DOR, MRD-negative status	• **1 prior LOT**: BVd, 51%; DVd, 50% • **High-risk cytogenetics**: BVd, 28%; DVd, 27% • **LEN-refractory:** BVd, 33%; DVd, 35%	**BVd, 36.6 vs. DVd, 13.4** *HR 0.41 (95% CI: 0.31–0.53); p<0.001*	**NR vs. NR** At 18 months: **BVd, 84% vs. DVd, 73%** *HR 0.57 (95% CI: 0.40–0.80)*	**BVd, 83%** (77–87%) **vs. DVd, 71%** (65–77%)	**AEs** Any grade: 100%; Grade 3–4: 95% **Serious AEs** 50% **Discontinuation due to AEs** 26%	**Ocular events** Any grade: 79%; Grade 3–4: 34% **Blurred vision** Any grade: 66%; Grade 3–4: 22% **Worsening vision from normal to:** 20/50, 34%; 20/200, 2% **Infections** Any grade: 70%; Grade 3–4: 31%
DREAMM-8[2]	1:1 BPd (n=155) PVd (n=147) **Primary endpoint:** PFS **Secondary endpoints:** ORR, MRD negativity, DOR	• **1 prior LOT**: BPd, 53%; PVd, 52% • **High-risk cytogenetics**: BPd, 34%; PVd, 32% • **LEN-refractory:** BPd, 81%; PVd, 76% • **Anti-CD38 mAb-refractory:** BPd, 23%; PVd, 24%	**BPd, NR vs. PVd, 12.7** *HR 0.52 (95% CI: 0.37–0.73); p<0.001*	**NR vs. NR** 12-month estimate: **BPd, 83% vs. PVd, 76%** *HR 0.77 (95% CI: 0.53–1.14)*	**BPd, 77%** (70–84%) **vs. PVd, 72%** (64–79%)	**AEs** Any grade: 99%; Grade 3–4: 94% **Serious AEs** 63% **Discontinuation due to AEs** 15%	**Ocular events** Any grade: 89%; Grade 3–4: 43% **Blurred vision** Any grade: 79%; Grade 3–4: 17% **Worsening vision from normal to:** 20/50 34%; 20/200: 1% **Infections** Any grade: 82%; Grade 3–4: 49%

Median follow-up for DREAMM-7 was 28.2 months, and for DREAMM-8 was 21.8 months. *HRs estimated using the stratified Cox proportional hazards model and p-value was produced based on the 1-sided stratified log-rank test; †PR or better; ‡BVd arm in DREAMM-7.
AE, adverse event; BPd, belantamab mafodotin/pomalidomide/dexamethasone; BVd, belantamab mafodotin/bortezomib/dexamethasone; CI, confidence interval; DOR, duration of response; DVd, daratumumab/bortezomib/dexamethasone; HR, hazard ratio; LEN, lenalidomide; LOT, line of therapy; mAb, monoclonal antibody; MRD, minimal residual disease; NR, not reached; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; PVd, pomalidomide/bortezomib/dexamethasone.

1. Hungria V, et al. *N Engl J Med.* 2024;391(5):393–407; 2. Dimopoulos MA, et al. *N Engl J Med.* 2024;391:408–421.

Side effects related to selinexor are largely dosage and schedule dependent

Prophylactic use of antiemetics

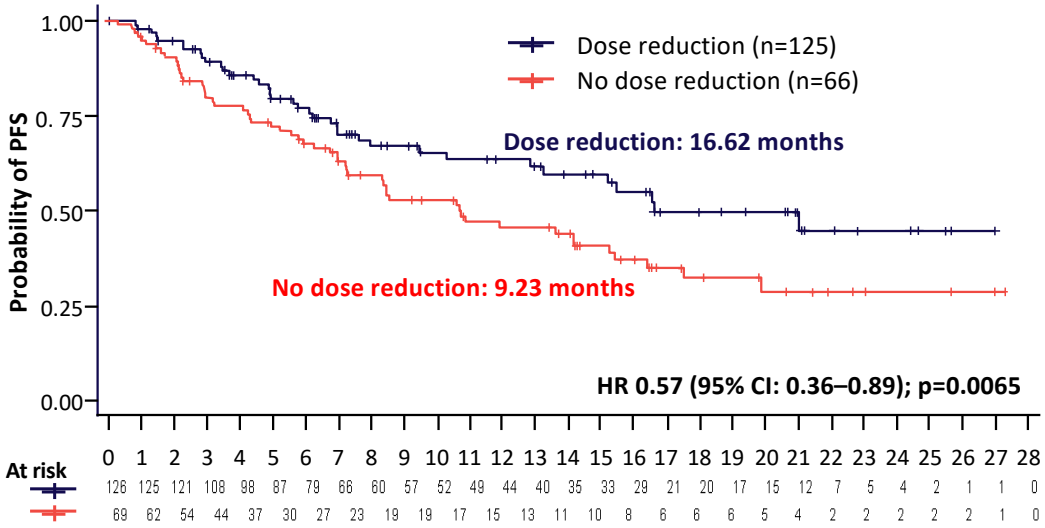
Dose reductions

The supportive care guidance provided herein are prepared by FORUS Therapeutics Inc. and should not be relied upon as being complete or mandating any particular course of medical care. All treatment decisions are solely at the discretion of the treating physician or healthcare professional. Prophylactic antithrombotic, antimicrobial, or antiemetic agents are not required for treatment with selinexor but may be indicated in specific patients and/or when other anticancer drugs are administered. *Using dexamethasone together with aprepitant and/or netupitant + palonosetron may increase the effects of dexamethasone; if using either of these agents, the dose of dexamethasone may need to be reduced[5]; †Side effects related to selinexor are largely dosage and schedule dependent and may be mitigated with prophylactic antiemetics and standard monitoring with dose adjustments as needed.
AE, adverse event; PO, by mouth; qam, every morning; qhs, every night; SVd, selinexor/bortezomib/dexamethasone; Vd, bortezomib/dexamethasone..

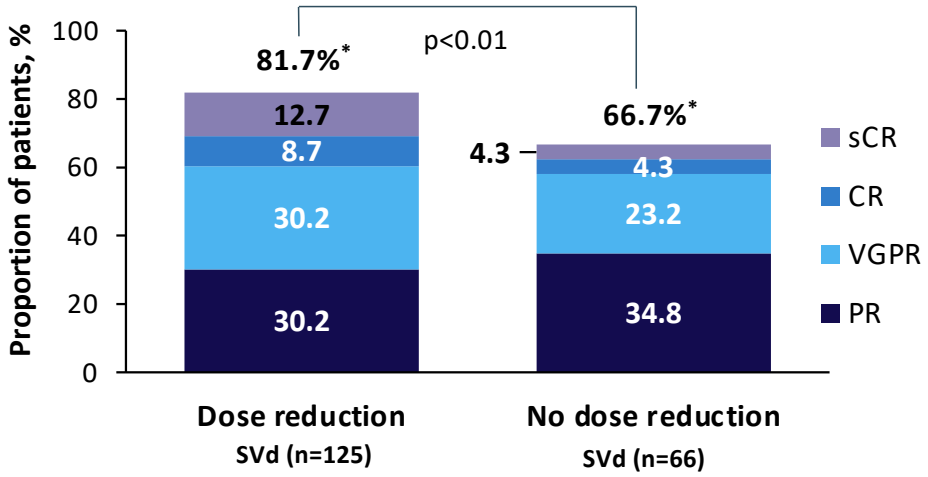
1. Selinexor. Product monograph. FORUS Therapeutics Inc. May 2022; 2. Gavriatopoulou M, et al. *Leukemia*. 2020;34:2430–2440;
3. Olanzapine. Product monograph. Mylan Pharmaceuticals. February 2017; 4. Mikhael J, et al. *Clin Lymphoma Myeloma Leuk*. 2020;20:351–357;
5. Aprepitant. Product monograph. Merck Canada Inc. January 2014; 6. Netupitant and palonosetron. Product monograph. Knight Therapeutics Inc. November 2022; 7. Magen H, et al. *Clin Lymphoma Myeloma Leuk*. 2020;20:e947–e955; 8. Lacey J, et al. *Can Hematol Today*. 2022;1(suppl 11);
9. Grosicki S, et al. *Lancet*. 2020;396:1563–1573; 10. Nexpovio (selinexor) Summary of Product Characteristics.
Available at: https://www.ema.europa.eu/en/documents/product-information/nexpovioepar-product-information_en.pdf.

BOSTON: Selinexor dose reduction was associated with improved efficacy

PFS by dose reduction in patients in the SVd arm



ORR by dose reduction of selinexor in the SVd arm



- These subgroup analyses were exploratory in nature, not included in the study objectives, and do not control for type 1 error
- The analyses were not powered or adjusted for multiplicity to assess efficacy outcomes across these subgroups

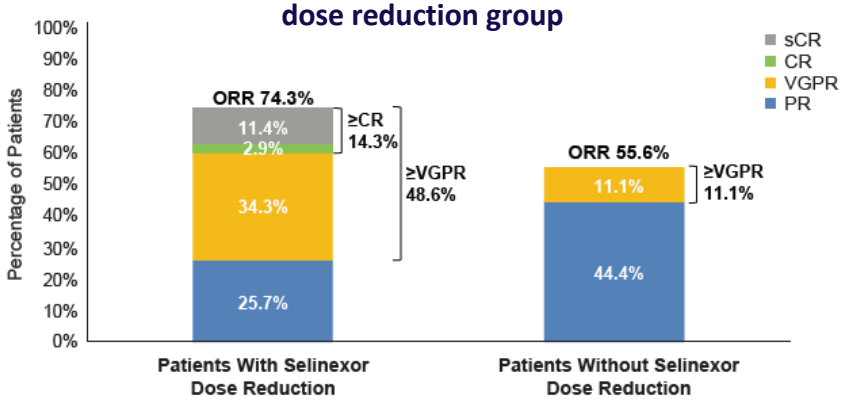
*ORR is the proportion of patients who have a PR or better, before IRC-confirmed PD or initiating a new multiple myeloma treatment or crossover.
CR, complete response; HR, hazard ratio; IRC, independent review committee; mPFS, median progression-free survival; ORR, overall response rate; PD, progressive disease; PFS, progression-free survival; sCR, stringent complete response; SVd, selinexor/bortezomib/dexamethasone; VGPR, very good partial response.

Jagannath S, et al. Abstract #3793; poster presented at ASH 2021.

BOSTON: Positive impact of selinexor dose reductions in LEN-refractory MM

BOSTON SVd arm: 53 LEN-refractory patients (35 had selinexor dose reductions and 18 did not)

Response to SVd in LEN-refractory patients by dose reduction group



Parameter	Patients with Sel dose reductions (n=35)	Patients without Sel dose reductions (n=18)
Median time to best response (PR or better), mo (range)	2.7 (0.7–11.7)	1.4 (0.7–2.1)
Median DOR, mo (95% CI)	15.3 (12.2–NE)	4.2 (4.2–NE)
Median TTNT, mo (95% CI)	14.8 (13.4–26.7)	4.8 (4.2–NE)
Median PFS, mo (95% CI)	13.9 (6.9–NE)	5.1 (3.5–NE)
Median OS, mo	26.7	24.6
HR (95% CI)	0.91 (0.37–2.28)	

- **Global health status QoL** scores showed greater **improvement** in patients with dose reductions vs. patients without
- In patients with dose reductions, a **lower proportion** experienced **any-grade TRAEs** after the first dose reduction (except thrombocytopenia)

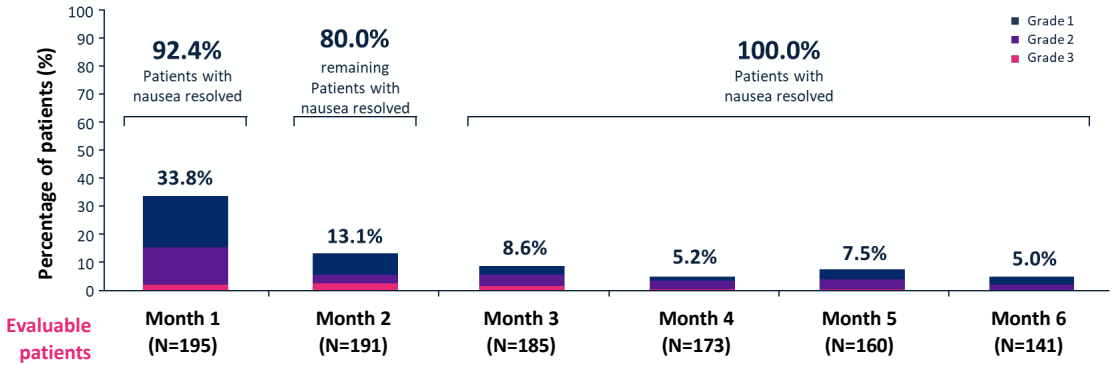
In **LEN-refractory patients**, **selinexor dose reductions** were associated with **improvements** in **safety**, **efficacy**, and **quality of life** and were consistent with the analysis of selinexor dose reductions for the ITT population

CI, confidence interval; CR, complete response; DOR, duration of response; HR, hazard ratio; ITT, intention-to-treat; LEN, lenalidomide; MM, multiple myeloma; mo, months; NE, not estimable; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; sCR, stringent complete response; SVd, selinexor/bortezomib/dexamethasone; TRAE, treatment-related adverse events; TTNT, time to next treatment; VGPR, very good partial response

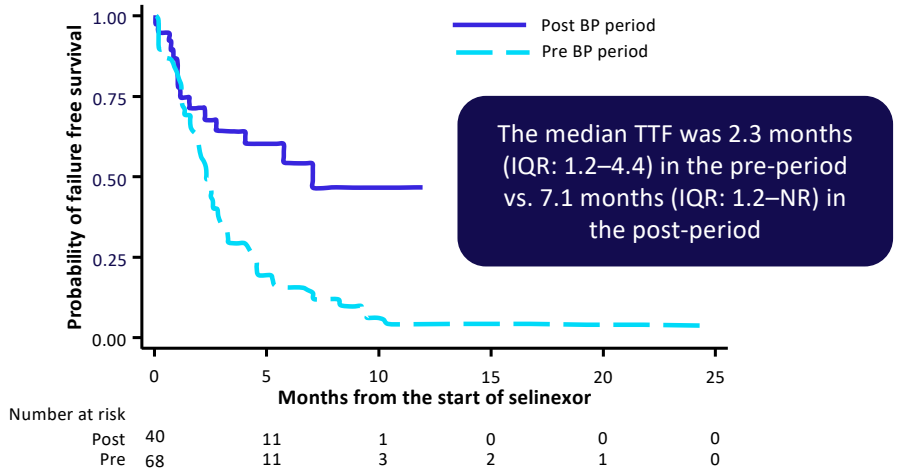
Delimpasi S, et al. Abstract #PF743; poster presentation at EHA 2025.

GI AEs: Manageable, non-cumulative with high resolution rate

Percentage of patients experiencing nausea events in the first 6 months in the selinexor + Vd arm of BOSTON[1]



TTF during the pre- and post-best practice implementation period[2]



The median TTF was 2.3 months (IQR: 1.2–4.4) in the pre-period vs. 7.1 months (IQR: 1.2–NR) in the post-period

Features of the BP program included[2]:

- Upfront use of antiemetics
- Suggested initiation of selinexor at a lower dose
- Active follow up with the patient

The BOSTON protocol required a prophylactic 5-HT3 antagonist to manage nausea but allowed for other interventions as required.
AE, adverse event; BP, best practice; GI, gastrointestinal; IQR, interquartile range; MM, multiple myeloma; NR, not reached; R/R, relapsed refractory; TTF, time to treatment failure; Vd, bortezomib/dexamethasone.

1. Nooka AK, et al. *Clin Lymphoma Myeloma Leuk*. 2022;22(7):e526–e531; 2. Gordan LN, et al. *Curr Oncol*. 2024;31(1):501–510.

Key considerations for choice of relapse treatment

Patient & treatment related

- **Prior regimen** used
- Patient **age** and **frailness**
- **Comorbidities**

Therapy-management related

- Therapy **waiting time**
- **ICANS/CRS** management for CAR-T and bispecific antibodies
- **GI** side effects
- **Infection rates** and other specific toxicities

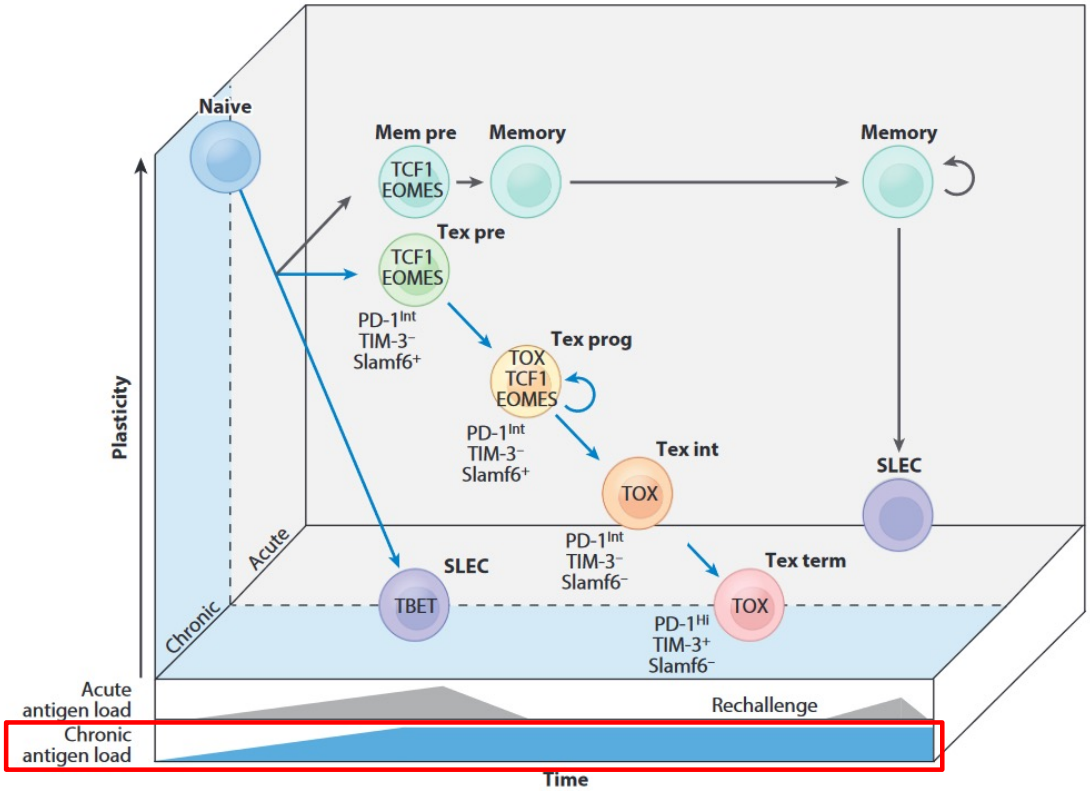
Target related

- **T-cell fitness & T-cell exhaustion**

CAR-T, chimeric antigen receptor T cell; CRS, cytokine release syndrome; GI, gastrointestinal; ICANS, immune effector cell-associated neurotoxicity syndrome.

Devarakonda S, et al. *Hematology Am Soc Hematol Educ Program.* 2022;2022(1):560–568; Nathwani N, et al. *Am Soc Clin Oncol Educ Book.* 2021;41:358–375; Binder AF, et al. *Front Immunol.* 2023:14:1275329; Zhou X, et al. *Haematologica.* 2023;108:958–968.

T-cell differentiation / exhaustion in response to acute and chronic stimuli

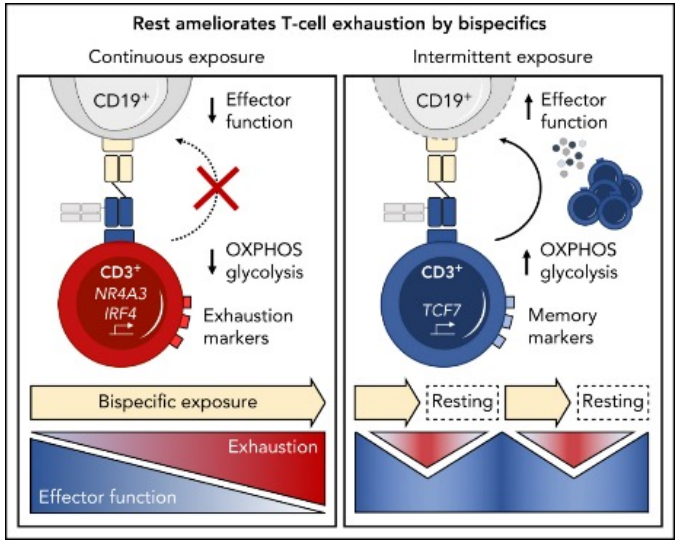


Int, intermediate; mem pre, memory precursor; pre, precursor; prog, progenitor; SLECs, short-lived effector cells; TCF1, T cell factor 1; Term, terminally; Tex, exhausted T cell; TOX, thymocyte selection–associated HMG box protein.

Baessler A, Vignali DAA. *Annu Rev Immunol*. 2024;42:179–206.

Treatment-free intervals may counteract T-cell exhaustion

- Most bispecific antibody therapies have been developed with **continuous therapy schedules**, which can be detrimental to T-cell fitness[1]
- Accumulating data suggest that **treatment-free intervals** can be beneficial in functional and transcriptional T-cell rejuvenation[1]



- Continuous exposure to a CD19xCD3 bispecific molecule induces T-cell exhaustion[2]
- Treatment-free intervals transcriptionally reprogram and functionally reinvigorate T cells[2]

1. Binder AF, et al. *Front Immunol*. 2023:14:1275329; 2. Philipp N, et al. *Blood*. 2022:140(10):1104–1118.

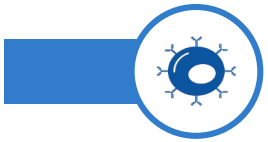
Summary

Streamlining therapy management: Practical strategies for enhanced treatment outcomes

Considering **factors related to the patient, treatment targets and AE profiles** will help individual treatment decisions

Novel therapeutic options have specific toxicities such as CRS, ICANS, infections or ocular events that require careful management and follow up

Selinexor's clinical utility is maximized with double antiemetic prophylaxis and dose modifications

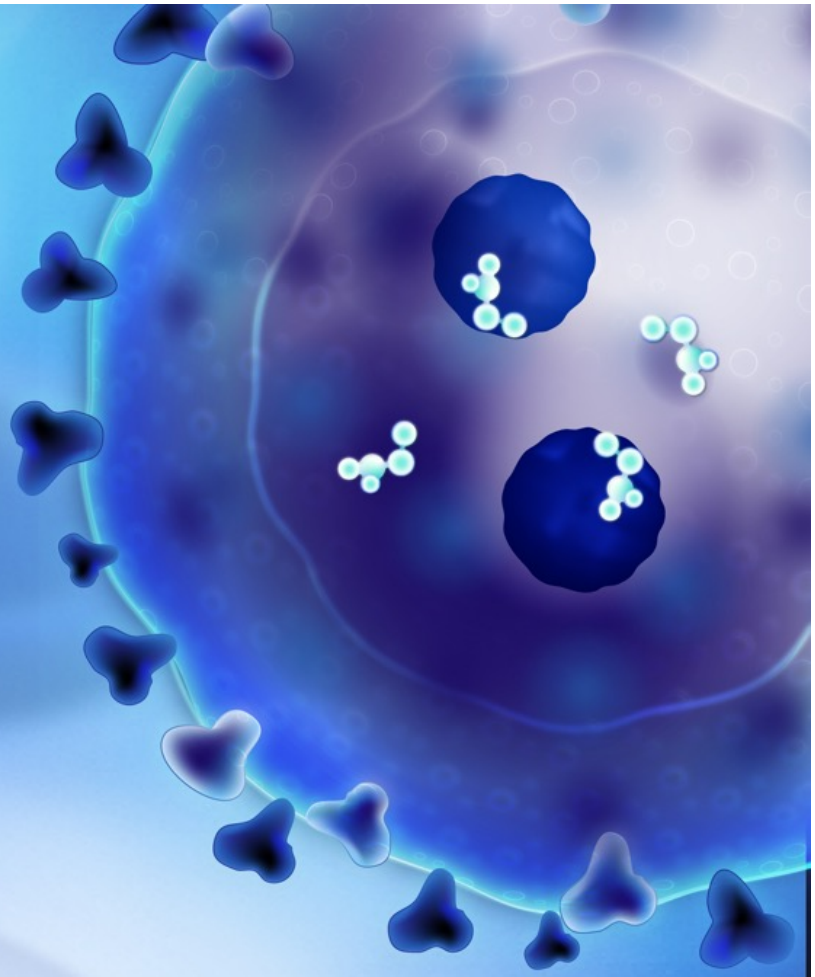


The **effectiveness of T-cell therapies may depend on the status of a patient's immune system**, including T-cell fitness or exhaustion

AE, adverse event; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity.

Bridging evidence and practice: Real-world insights and clinical case discussions

Elena Zamagni
University of Bologna, Bologna, Italy



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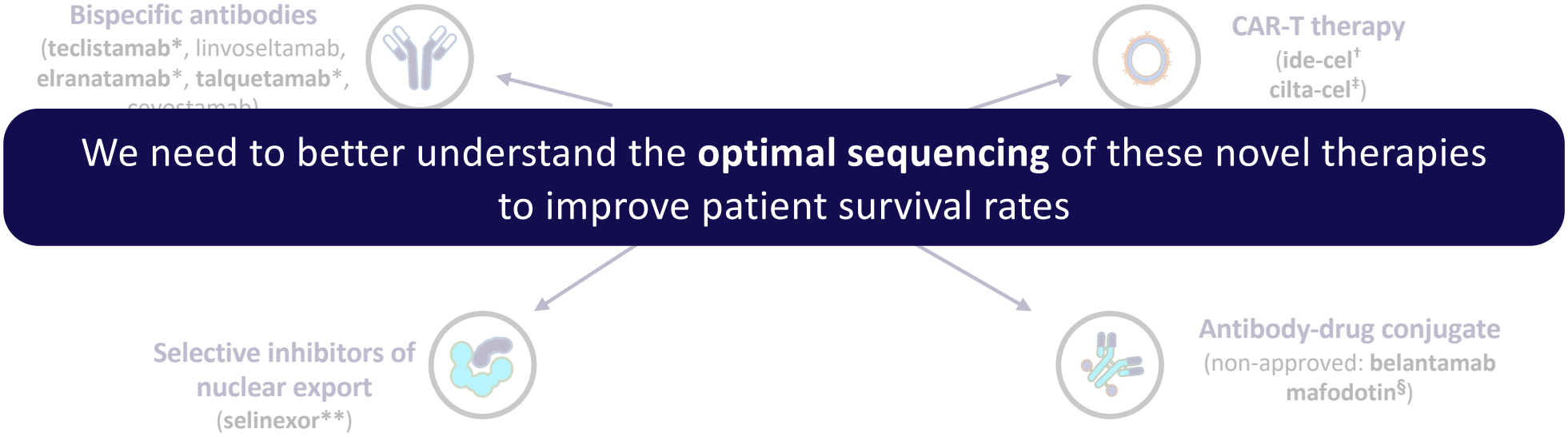
Disclosures

- **Advisory board participation and consultancy**: Janssen, BMS, Pfizer, Sanofi, Amgen, Oncopeptide, Menarini Stemline, and GSK

Novel strategies for R/R MM



*EMA approved 4L+ with previous exposure to a PI, IMiD and an anti-CD38 antibody; **EMA approved 2L+; †EMA approved 3L+ with previous exposure to a PI, IMiD and an anti-CD38 antibody; ‡EMA approved 2L+ with previous exposure to a PI and IMiD; §Monotherapy withdrawn from market, combination therapies not yet EMA approved.
CAR-T, chimeric antigen receptor T cell; EMA, European Medicines Agency; IMiD, immunomodulatory drug; L, line; MM, multiple myeloma; R/R, relapsed/refractory.

Davis LN, et al. *Cancers.* 2021;13:1686.

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[1]:

- 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[2]
- Selinexor or selinexor-based combinations induced objective responses in 6 of 7 patients with relapse post BCMA-targeted CAR-T cells[3]

RECOMMENDATION[1]

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; †Selinexor combinations in the STOMP trial are not all approved.
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.

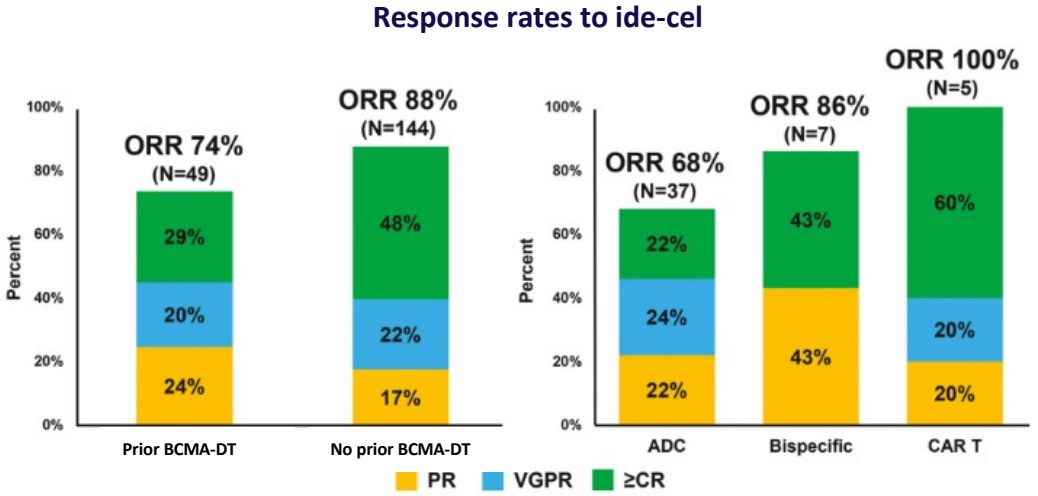
1. Costa LJ, et al. *Leukemia*. 2025;39(3):543–554; 2. Baljevic M, et al. *EJHaem*. 2022;3(4):1270–1276; 3. Chari A, et al. *Br J Haematol*. 2020;189(4):e126–e130.

Outcomes of CAR-T cell therapy after prior BCMA-DT

- In a retrospective, multicenter observational study, the impact of prior BCMA-DT was evaluated in patients with R/R MM receiving ide-cel
- A total of **50 patients** with **prior BCMA-DT exposure** (**38 ADC, 7 bispecific antibodies, 5 CAR-T**) and 153 patients with no prior BCMA-DT were infused with ide-cel

- The **prior BCMA-DT cohort** had a **lower ORR**, **median DoR** (**7.4 vs. 9.6 months**; p=0.03), and **median PFS** (**3.2 months vs. 9.0 months**; p=0.0002) compared to the cohort without prior BCMA-DT

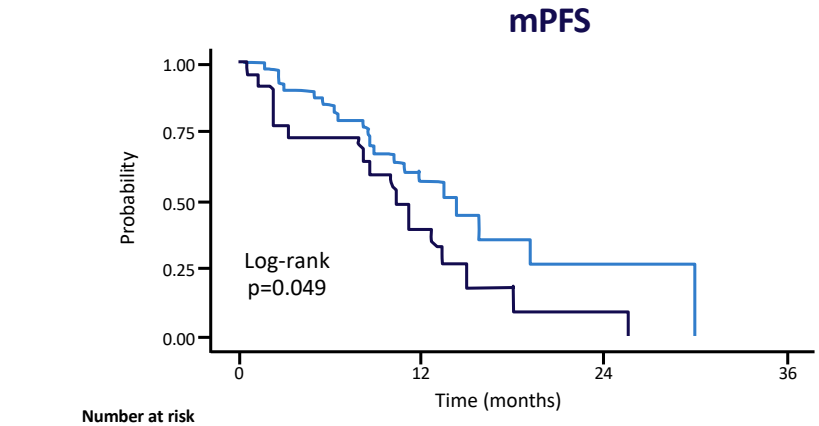
Treatment with ide-cel after prior BCMA-DT resulted in a relatively high ORR, **but significantly lower ORR, median DOR, and median PFS compared to patients not receiving a prior BCMA-DT**



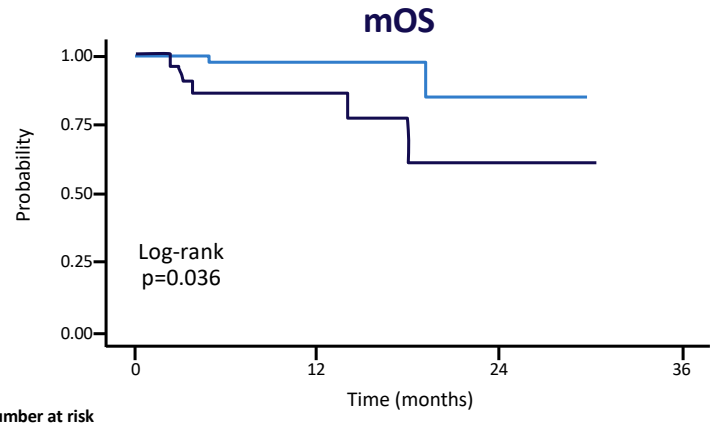
ADC, antibody drug conjugate; BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T cell; CR, complete response; DoR, duration of response; DT, directed therapy; ide-cel, idecabtagene vicleucel; MM, multiple myeloma; ORR, overall response rate; PFS, progression-free survival; PR, partial response; R/R, relapsed/refractory; VGPR, very good partial response.

Ferreri CJ, et al. *Blood Cancer J.* 2023;13(1):117.

Prior exposure to belantamab adversely impacted efficacy outcomes with ide-cel therapy in late-line settings



Number at risk				
Prior BCMA therapy - No	39	15	2	0
Prior BCMA therapy - Yes	22	7	1	0



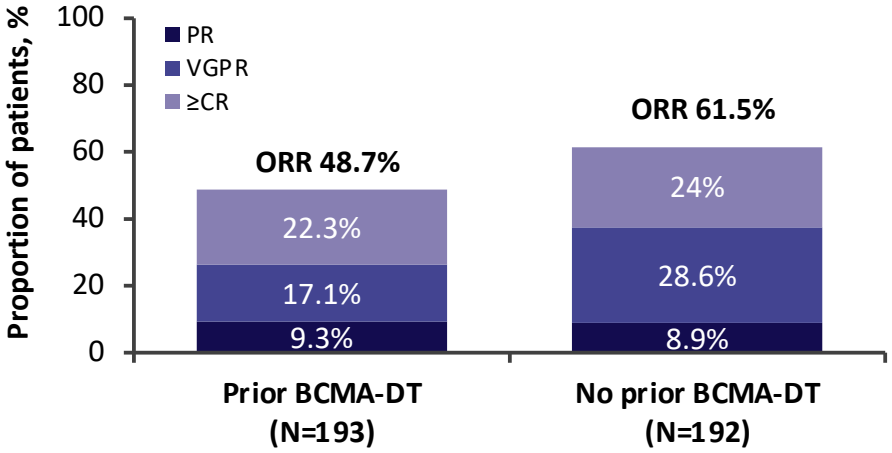
Number at risk				
Prior BCMA therapy - No	39	25	3	0
Prior BCMA therapy - Yes	22	17	2	0

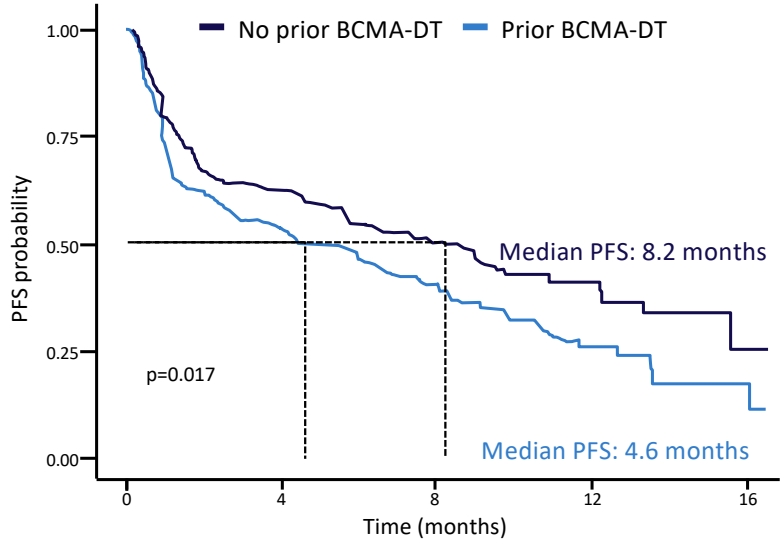
- Patients with **prior exposure to belantamab** had significantly **inferior median PFS** (p=0.049) and **median OS** (p=0.036) vs. those without prior exposure to belantamab
- Among patients who received belantamab, **median PFS was significantly lower in patients who had a partial response or better with belantamab** vs. patients with no response (p=0.014)
- **PFS and OS did not differ significantly** based on the **time from the last dose of belantamab to the ide-cel infusion**

BCMA, B-cell maturation antigen; ide-cel, idecabtagene vicleucel; m, median; OS, overall survival; PFS, progression-free survival.

Lal BM, et al. Abstract #3789; poster presented at ASH 2024.

Teclistamab efficacy is strongly affected by prior exposure to BCMA-DT



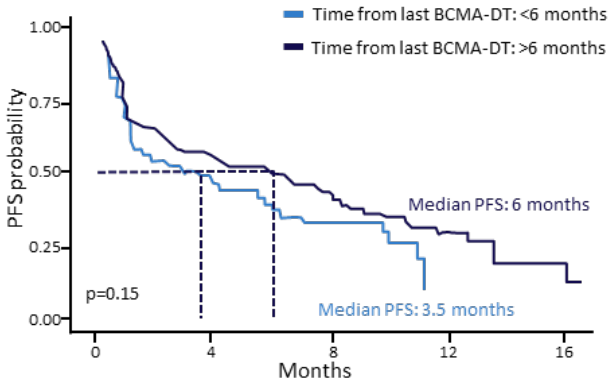


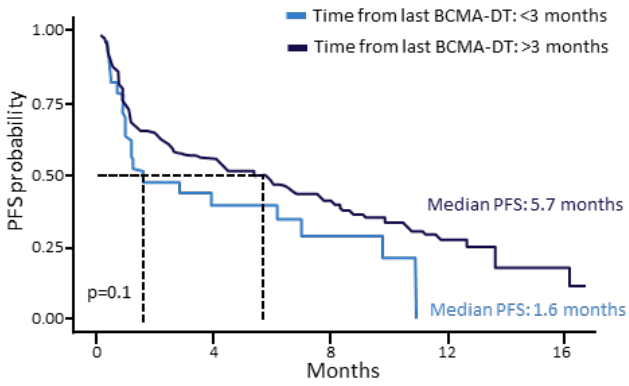
- The prior BCMA-DT cohort had **worse ORR** (p=0.012) **and ≥VGPR** (p=0.009), but **similar ≥CR rates** (p=0.78) compared with those without prior BCMA-DT
- In MVA there was a strong signal for worse ORR in the prior BCMA-DT cohort; however, prior BCMA-DT was not independently associated with the likelihood of achieving response (HR 0.64, 95% CI: 0.41–1.01; p=0.057)

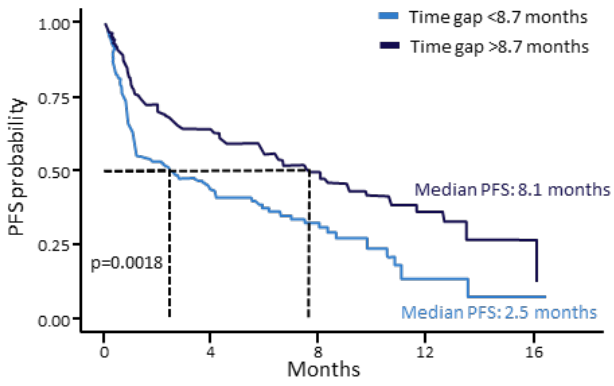
BCMA-DT, B-cell maturation antigen directed therapy; CI, confidence Interval; CR, complete response; DoR, duration of response; DT: directed therapy; HR, hazard ratio; MVA, multivariate analysis; ORR, overall response rate; PFS, progression-free survival; PR, partial response; VGPR, very good partial response.

Dima D, et al. Abstract #897; oral presentation at ASH 2024.

The optimal cut-off for time from last BCMA-DT exposure to teclistamab initiation is 8.7 months







Patients with >8.7 months between last exposure to prior BCMA-DT and teclistamab initiation had a **superior median PFS with teclistamab** (8.1 months, 95% CI: 4.6–11.7) vs. <8.7 months (2.5 months, 95% CI: 1.1–5.7; p=0.001)

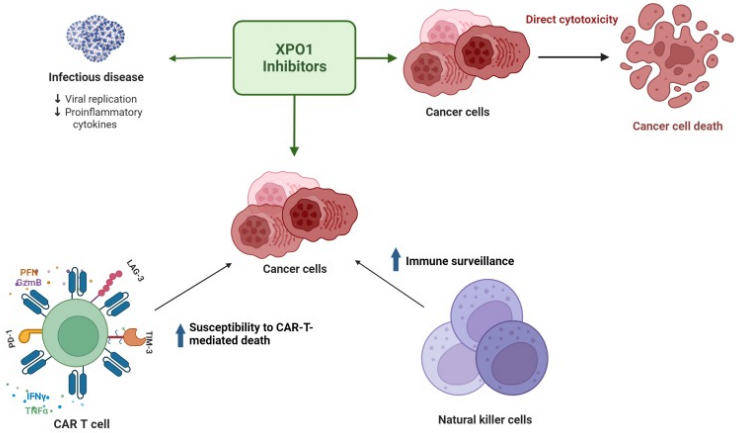
BCMA-DT, B-cell maturation antigen directed therapy; CI, confidence interval; PFS, progression-free survival.

Dima D, et al. Abstract #897; oral presentation at ASH 2024.

XPO1 inhibitors have potential to promote T-cell fitness and reduce T-cell exhaustion

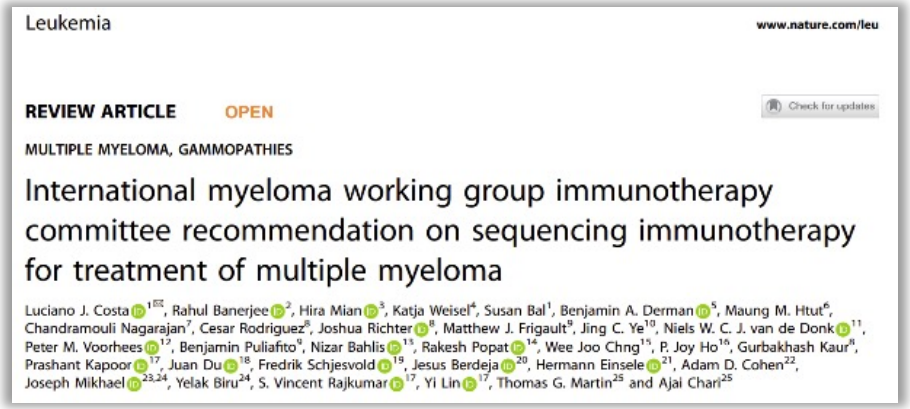
XPO1 inhibitors:[1]

- Have direct cytotoxic effects on tumor cells
- Decrease inflammation in infectious disease
- May facilitate a favorable immune microenvironment for effector T cells to combat T-cell exhaustion



*"The **XPO1 inhibitors** selinexor and eltanexor **reduced T-cell exhaustion** in cell lines and animal models, suggesting their potential role in revitalizing these key effector cells[1]"*

*"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[2]**"*



Leukemia www.nature.com/leu

REVIEW ARTICLE OPEN

MULTIPLE MYELOMA, GAMMOPATHIES

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

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

XPO1, exportin 1.

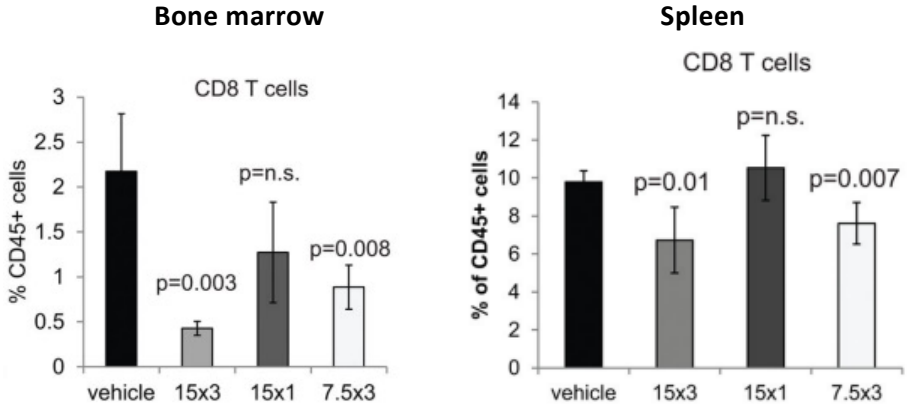
1. Binder AF, et al. *Front Immunol*. 2023:14:1275329; 2. Costa, LJ, et al. *Leukemia*. 2025;39(3):543–554.

Selinexor once or twice weekly dosing schedules allow for normal CD8+ T-cell functioning and development of anti-tumor immunity

- Many chemotherapeutics kill rapidly dividing cells, which includes cells of the immune system; effector CD8 T cells could easily be collateral damage in many combination regimens
- A preclinical study was conducted to examine the effects of selinexor on normal immune homeostasis in mice

In a model of implantable melanoma, decreased frequency of selinexor treatment restored immune homeostasis better than decreased dose (CD8 T cells comparable to vehicle treated mice)

Group	Treatment	Schedule
Vehicle	Vehicle	3x week
15x3	Selinexor 15 mg/kg	3x week
15x1	Selinexor 15 mg/kg	1x week
7.5x3	Selinexor 7.5 mg/kg	3x week



n.s., not significant.

Tyler P, et al. *Mol Cancer Ther*. 2017;16(3):428–439.

Clinical case study #1

Patient history

Age: ~71 years

- **IgGK MM** (diagnosed in Oct 2018) with anemia, acute kidney injury and bone lesions, ISS 3, R-ISS 3 (t[14;16] and ampl1q in FISH)
- *Comorbidities*: **skin melanoma** treated surgically in 2023

1–4L treatment

- *1L*: **4 cycles VTD** (+sFLC removal) obtaining a **VGPR** and metabolic CR, followed by **one ASCT** in Mar 2019. In Aug 2019, **biochemical relapse**.
  - *Adverse events*: restless legs syndrome
- *2L*: **DRd** (Sep 2019–Jan 2021); in Jan 2021, **biochemical relapse** and **PET progression** (skeletal lesion, possible EMD in liver but no biopsy undertaken due to bleeding risk)
  - *Adverse events*: Grade 3 **HBV infection**, Grade 3 **salmonella infection**
- *3L:* ***3*** **cycles Kd** (Feb 2021–Apr 2021); in Apr 2021, **biochemical relapse** and **MRI progression** with **paramedullary lesion** in D9, requiring orthopedic intervention
- *4L*: **2 cycles DPACE** in spring/summer 2021, obtaining a SD

Real-world clinical case provided by speaker.
Ampl1q, amplification of 1q; ASCT, autologous stem cell transplant; CR, complete response; DRd, daratumumab/lenalidomide/dexamethasone; DPACE,dexamethasone/cisplatin/doxorubicin/cyclophosphamide/etoposide; EMD, extramedullary MM; FISH, fluorescence in situ hybridization; HBV, Hepatitis B; IgGK, immunoglobulin G Kappa; Kd, carfilzomib/dexamethasone; L, line; (R-)ISS, (revised) international staging system; MM, multiple myeloma; MRI, magnetic resonance imaging; PET, positron emission tomography; SD, stable disease; sFLC, serum free light chains; VGPR, very good partial response; VTD, bortezomib/thalidomide/daratumumab.

Clinical case study #1

Patient history

Age: ~71 years

- **IgGK MM** (diagnosed in Oct 2018) with anemia, acute kidney injury and bone lesions, ISS 3, R-ISS 3 (t[14;16] and ampl1q in FISH)
- *Comorbidities*: **skin melanoma** treated surgically in 2023

5–7L treatment

- *5L*: **5 cycles EloPd** (Sep 2021–Jan 2022) obtaining a **VGPR**; **PET progression** in Jan 2022
- *6L*: **17 cycles belantamab mafodotin*** (Mar 2022–May 2023), obtaining a **metabolic and laboratory PR** (assessed in Mar 2022); **PET progression** in May 2023, in the absence of lab PD (non-secretory)
  - *Adverse events*: Grade 3 **H. influenzae pneumonia**
  - **Moderate KVA**, resolved after skipping and delaying doses
- *7L*: **15 cycles talquetamab**† (Jul 2023–Sep 2024), obtaining a **metabolic PR** (assessed in Oct 2023); **PET progression** in Sep 2024, yet **non-secretory**.
  - *Adverse events*: Grade 1 **CRS**, Grade 1 skin (painful **rash with desquamation**), oral (**dysgeusia**) and **nail toxicity**

Real-world clinical case provided by speaker.
*Belantamab was fully approved in Italy at time of this case study; †Talquetamab obtained via compassionate-use program in Italy.
Ampl1q, amplification of 1q; CRS, cytokine release syndrome; Elo, elotuzumab; FISH, fluorescence in situ hybridization; IgGK, immunoglobulin G Kappa; KVA, Keratopathy Visual Acuity; L, line; (R-)ISS, (revised) international staging system; MM, multiple myeloma; Pd, pomalidomide/dexamethasone; PET, positron emission tomography; PD, progressive disease; PR, partial response; VGPR, very good partial response.

Clinical case study #1

SVd therapy*: started in September 2024

- *Starting dose*: 60 mg† because of **multiple prior treatments and last line with talquetamab**, still with dysgeusia
- At the beginning of therapy, **no lab abnormalities**, **PD in PET** (left scapula, rib lesions, pelvic lesions, laterocervical lymph nodes and periscapular lymph nodes – the latter have been biopsied, but no diagnostic material was obtained)

SVd in 8L

- *Response*: **after 3 cycles**, **partial response in PET**: reduced uptake in the scapula and one of rib lesions, other rib and pelvic lesions no longer active along with lymph nodes; **PET repeated** after 6 months: **complete metabolic response**
- *Adverse events*: Grade 2 **diarrhea** starting from C1, requiring a **dose reduction of selinexor** from 60 mg to 40 mg from C5; **hypertensive crisis** (200/100 mmHg) in Apr 2025, requiring emergency care evaluation (brain CT scan, echocardiogram, troponin determinations normal)‡
- **Therapy still ongoing**
  - *Response*: **non secretory** pt, **PET still in CMR,** cycle 8 ongoing

Real-world clinical case provided by speaker.
*SVd obtained via Named Patient Program in Italy; †The recommended selinexor dose based on a 35-day cycle is 100 mg once weekly on Day 1 of each week. Dose modification should occur after adverse events in a prespecified stepwise manner (as outlined in selinexor SmPC); ‡Adverse events under control, 40 mg dose maintained.
C, cycle; CMR, complete metabolic response; CT, computed tomography; L, line; PD, progressive disease; PET, positron emission tomography; SVd, selinexor/bortezomib/dexamethasone.

Clinical case study #1: Key messages

SVd is effective in a **penta-refractory patient,** after multiple lines of therapy including TCR

SVd is effective at lower doses to **enhance compliance** and **tolerability** in a patient exposed to multiple lines of therapy

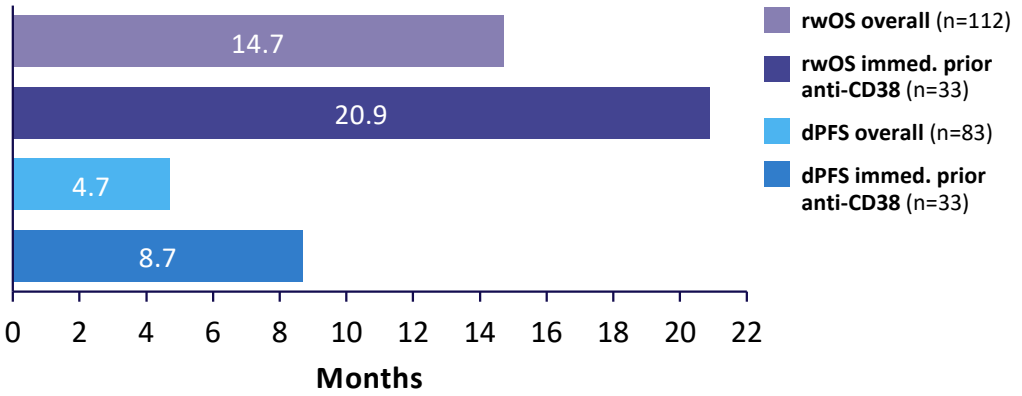
SVd, selinexor/bortezomib/dexamethasone; TCR, triple class refractory.

Selinexor triplet regimens are effective in patients with R/R MM, especially those with prior exposure to an anti-CD38 mAb in the immediate prior LOT

- This study analyzed real-world treatment patterns and survival outcomes using a nationwide electronic health record-derived, deidentified database of patients with R/R MM treated with an eligible **selinexor-containing**, **triplet-based regimen**, including combinations with dexamethasone and pomalidomide, bortezomib, carfilzomib, or daratumumab

- Patients had a **rwOS** of **14.7 months** (95% CI: 10.6–20.9) and a **dPFS** of **4.7 months** (95% CI: 3.4–6.7)
- Patients with **previous exposure to anti-CD38 mAbs** in the most recent regimen prior to the selinexor treatment had **numerically higher survival outcomes** (rwOS, 20.9 [95% CI: 13.4–NR] months; dPFS, 8.7 [95% CI: 5.8–11.7] months)

rwOS and dPFS in the overall study cohort and subgroup of patients who received immediate prior anti-CD38 mAb therapy



The median duration of follow-up for the study cohort was 9.4 months. Derived PFS is a calculated measure of time during which a patient does not have disease progression based on data collected in a clinical trial or real-world setting.
CI, confidence interval; dPFS, derived progression-free survival; LOT, line of therapy; mAb, monoclonal antibody; MM, multiple myeloma; NR, not reached; OS, overall survival; R/R, relapsed/refractory; rwOS, real-world OS.

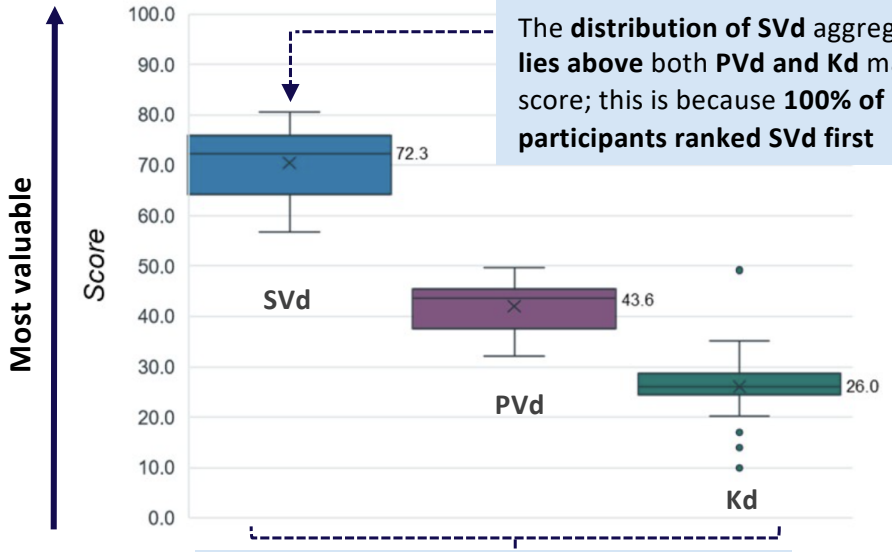
Whiteley A, et al. *Current Oncology* 2025; 32(5):268.

Assessment of post-DRd treatment options for MM in Italy: SVd as a preferred therapy from a multi-stakeholder perspective

- This study identified **key decision criteria*** for **assessing 2L therapies** for **post-DRd** MM from an **Italian multi-stakeholder perspective** (n=20, hematologists; n=1, methodologist; n=2, decision-makers; n=1, patient representative)
- **Efficacy was the most critical criterion**, indicating its priority role in the context of post-DRd treatment, **followed by safety** (peripheral neuropathy was identified as the most significant safety sub-criterion)

Based on elicited preferences, SVd was ranked as the most valuable therapy

Distribution of aggregate scores of alternative treatments



The **distribution of SVd** aggregate scores **lies above** both **PVd and Kd** maximum score; this is because **100% of participants ranked SVd first**

100% of clinicians had **preferences** compatible with **SVd > PVd > Kd**

*Decision criteria were identified through a targeted literature review, discussed in a multi-stakeholder workshop, and finalized with a pragmatic literature review to assess data availability for each alternative. Stakeholders were asked to weigh the importance of each criterion and sub-criterion and to score performance levels through an online structured questionnaire.
DRd, daratumumab/lenalidomide/dexamethasone; Kd, carfilzomib/dexamethasone; L, line; MM, multiple myeloma;
PVd, pomalidomide/bortezomib,/dexamethasone; SVd, selinexor/ bortezomib/dexamethasone.

Boccadoro M, et al. Abstract #P56; poster presentation at EMN Research Italy 2025;
Boccadoro M, et al. Abstract #PB2976; poster presentation at EHA 2025.

Clinical case study #2

Patient history

Age: ~79 years

- **IgG lambda MM** (diagnosed in May 2022)
- Treated based on slim-CRAB (2 MRI bone lesions, sFLC ratio >100, with evolving pattern); ISS 1, R-ISS 2 (t[4;14], amp1q21 in FISH)
- *Comorbidities*: **Ischemic cardiomyopathy**, treated with stent, positioned in 2016; **hypertension**; **dyslipidaemia**; **septic arthritis** in 2016 (need for a knee prothesis); **prostate adenoma** (treated with TURP)

1L treatment

23 cycles DRd, Jun 2022–May 2024

- **Daratumumab stopped in Apr 2024** for recurrent URIs and Grade 3 urinary tract infection
- *Best response*: **PR after 9 cycles**, but **biochemical relapse** from Mar 2024, **PET negative** in Mar 2024; **change of therapy** in May 2024 for **progressive increase of disease parameters**
  - *Adverse events*: **Recurrent infections**, **ataxic gait** (from the beginning of 2023), attributed to chronic cerebrovascular disease; **post-traumatic femur fracture** (Apr 2024)

Real-world clinical case provided by speaker.
Amp1q21, amplification of 1q21; DRd, daratumumab/lenalidomide/dexamethasone; FISH, fluorescence in situ hybridization; IgG, immunoglobulin G; (R-)ISS, (revised) international staging system; MM, multiple myeloma; MRI, magnetic resonance imaging; PET, positron emission tomography; PR, partial response; sFLC, serum free light chains; TURP, transurethral resection of the prostate; URI, upper respiratory infection.

Clinical case study #2

Patient history

Age: ~79 years

- **IgG lambda MM** (diagnosed in May 2022)
- Treated based on slim-CRAB (2 MRI bone lesions, sFLC ratio >100, with evolving pattern); ISS 1, R-ISS 2 (t[4;14], amp1q21 in FISH)
- *Comorbidities*: **Ischemic cardiomyopathy**, treated with stent, positioned in 2016; **hypertension**; **dyslipidaemia**; **septic arthritis** in 2016 (need for a knee prothesis); **prostate adenoma** (treated with TURP)

2L options

What to do in this elderly patient with double-refractory relapse and several comorbidities/ criteria for frailness?

- Not a lenalidomide-based triplet
- Not an anti-CD38 retreatment
- Not a clinical trial/immediate immunotherapy for recurrent infections/comorbidities
- Not PVd: Reserving pomalidomide for 3L

Selinexor-Vd in the Italian CNN access

Real-world clinical case provided by speaker.
Amp1q21, amplification of 1q21; FISH, fluorescence in situ hybridization; IgG, immunoglobulin G; (R-)ISS, (revised) international staging system; L, line; MM, multiple myeloma; MRI, magnetic resonance imaging; PVd, pomalidomide/bortezomib/dexamethasone; sFLC, serum free light chains; TURP, transurethral resection of the prostate; Vd, bortezomib/dexamethasone.

Clinical case study #2

SVd therapy: started in Jun 2024

- At the beginning of therapy, M protein 1985 mg/dl, sFLC lambda 593 mg/l, ratio 94, Hb 11.9 g/dl, normal kidney function, proteinuria 188 mg/day with positive immunofixation; PET/CT scan negative (June 2024)
- *Starting dose*: **Selinexor 80 mg*** (age, frailty); **bortezomib standard dose**; **dexamethasone 20 mg/week** (age, recurrent infections)

SVd in 2L

- *Response*: **PR after 1 cycle** (after 1 cycle: M protein 660 mg/dl, sFLC 110 mg/l); **VGPR** after 10 cycles: M protein 180 mg/dl, sFLC 85 mg/l, ratio k/l 9, Ifu negative
  - *Adverse events*: **Grade 3 pneumonia**† (Jan 2025) treated with **IV antibiotics** (amoxi/clav, then pip/tazo); for this reason, **C2 undergone without bortezomib**, **resumed in C3**. Introduced aprepitant and ondansetron since C1 with no nausea reported or no other Grade 1 side effects
- **Therapy still ongoing**, same dose
  - *Response*: **VGPR**, cycle 11 ongoing

Real-world clinical case provided by speaker.

*The recommended selinexor dose based on a 35-day cycle is 100 mg once weekly on Day 1 of each week. Dose modification should occur after adverse events in a prespecified stepwise manner (as outlined in selinexor SmPC); †Resolved after treatment.

Amoxi/clav, amoxicillin/clavulanate; C, cycle; CT, computed tomography; Hb, hemoglobin; IV, intravenous; L, line; PET, positron emission tomography; pip/tazo, piperacillin/tazobactam; PR, partial response; sFLC, serum free light chains; SmPC, summary of product characteristics; SVd, selinexor/bortezomib/dexamethasone; VGPR, very good partial response.

Clinical case study #2: Key messages

- SVd is **effective in second line** after double refractoriness
- SVd is feasible and **well tolerated** in **elderly/frail patients**
- SVd reserves the use of **subsequent anti BCMA/GPRC5D T-cell redirecting therapies**, in case patient fitness improves*

*Based on speaker opinion/not explicitly stated in selinexor SmPC.
BCMA, B-cell maturation antigen; GPRC5D, G-protein-coupled receptor class C group 5 member D; SVd, selinexor/bortezomib/dexamethasone.

GIMEMA: Observational study on the combination of selinexor with bortezomib and dexamethasone for the treatment of MM patients

Study design: Multicenter, observational, retrospective and prospective (approximately 30 centers involved and 159 patients to be enrolled)

Inclusion criteria: Adult patients with active MM, relapse after **1–3 lines of therapy**, treatment with SVd at the time the combination has entered clinical practice in Italy (AIFA authorization in Aug 2024), prior treatment with and refractoriness to lenalidomide

Primary objective and endpoint: Effectiveness of SVd, as measured by 12-month PFS

Secondary objectives and endpoints: Hematologic response rate; safety and tolerability profile; second PFS; duration of response; OS; time to progression and time to next therapy; minimal residual disease in a subgroup of patients with available data

GIMEMA trial is open for enrolment.
AIFA, Agenzia Italiana del Farmaco; MM, multiple myeloma; OS, overall survival; PFS, progression-free survival; SVd, selinexor/bortezomib/dexamethasone.

https://clinicaltrials.gov/study/NCT06933277. Accessed 09 June 2025.

Summary

Bridging evidence and practice: Real-world insights and clinical case discussions

Incorporating **selinexor combinations** as **T-cell sparing regimens** can optimize sequencing and improve outcomes **following prior BCMA-targeted therapies**

SVd demonstrated **efficacy** in a **penta-refractory patient** who had received multiple prior lines of therapy, including T-cell redirecting therapy (*Clinical case #1*)

SVd has shown **effectiveness** as a **second-line treatment** after double lenalidomide and daratumumab refractoriness, and may enable subsequent use of T-cell redirecting therapies (*Clinical case #2*)

The ongoing **GIMEMA** observational study aims to collect data on **SVd** in 159 patients **refractory to lenalidomide**, who have received **1–3 prior lines** of therapy

BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T cell; MM, multiple myeloma; SVd, selinexor/bortezomib/dexamethasone.

Q&A and closing remarks

María Victoria Mateos
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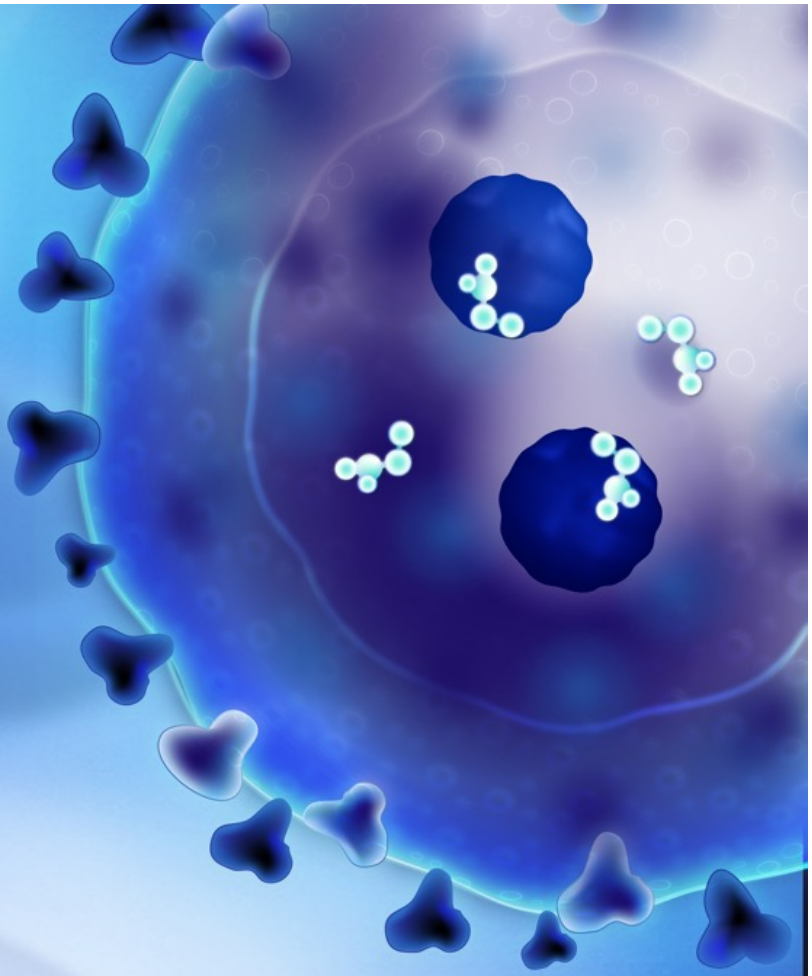

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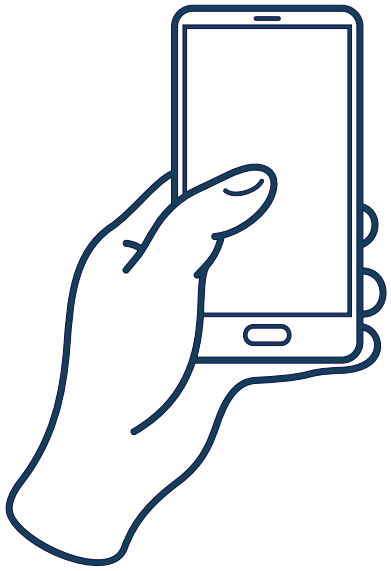

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