Multiple Myeloma Satellite Symposium
at the 31st European Hematology Association Congress

Optimizing outcomes in multiple myeloma: Navigating resistance with innovative approaches

Saturday, 13th June | 08:00–09:30

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Introduction

Joshua Richter, MD, FACP

Associate Professor of Medicine,Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai

Director of Myeloma, Blavatnik Family Chelsea Medical Center at Mount Sinai

New York, NY, US

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During this symposium, you will learn about…

- The key areas of **unmet medical needs** for patients with MM, with a focus on the **role of XPO1 inhibition** in addressing these challenges
- The **combination and sequencing** of MM treatments through **real-world experiences**, including **practical approaches to managing toxicities** associated with novel therapies
- The **optimal use** and **positioning of selinexor** in the **evolving MM treatment landscape**

MM, multiple myeloma; XPO1, exportin 1.

Faculty

Joshua Richter (Chair)

Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, and Blavatnik Family Chelsea Medical Center at Mount Sinai, New York, NY, US

Paula Rodríguez-Otero

Clinica Universidad de Navarra, IdiSNA, Pamplona, Spain

Gabriele Buda

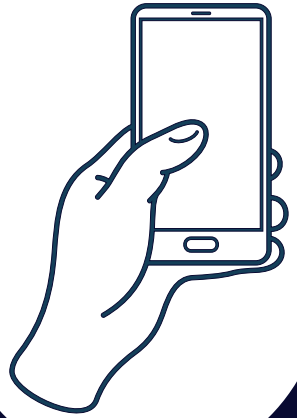
University of Pisa, Pisa, Italy

Agenda

Time (CEST)	Title	Presenter
08:00–08:05	**Introduction**	**Joshua Richter (Chair)**
08:05–08:30	**Current unmet medical needs and the role of XPO1 inhibition in the treatment of relapsed/refractory multiple myeloma**	**Paula Rodríguez-Otero**
08:30–08:55	**Maximizing efficacy with optimal sequencing: A case-based discussion**	**Joshua Richter**
08:55–09:20	**Translating evidence into practice: A case-led discussion of real-world practice challenges**	**Gabriele Buda**
09:20–09:30	**Q&A and closing remarks**	**Joshua Richter**

XPO1, exportin 1.

Submit your questions!



Scan the QR code to submit your questions for the Q&A session at the end of this symposium

Current unmet medical needs and the role of XPO1 inhibition in the treatment of relapsed/refractory multiple myeloma

Paula Rodríguez-Otero

Clinica Universidad de Navarra, IdiSNA, Pamplona, Spain

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Disclosures

- **Honoraria from lectures:** BMS-Celgene, J&J Innovative Medicine, Sanofi, GSK, Pfizer, Menarini Stemline, and AbbVie
- **Participation in advisory board meetings:** BMS, J&J Innovative Medicine, Sanofi, Roche, AstraZeneca, AbbVie, Menarini Stemline, Pfizer, Regeneron, H3 Biomedicine, and GSK
- **Consultant:** BMS-Celgene, AbbVie, AstraZeneca, Regeneron, Roche, J&J Innovative Medicine, and Pfizer
- **Research funding:** Pfizer (institution)
- **Travel support**: Pfizer

Several unmet needs remain in the early R/R setting

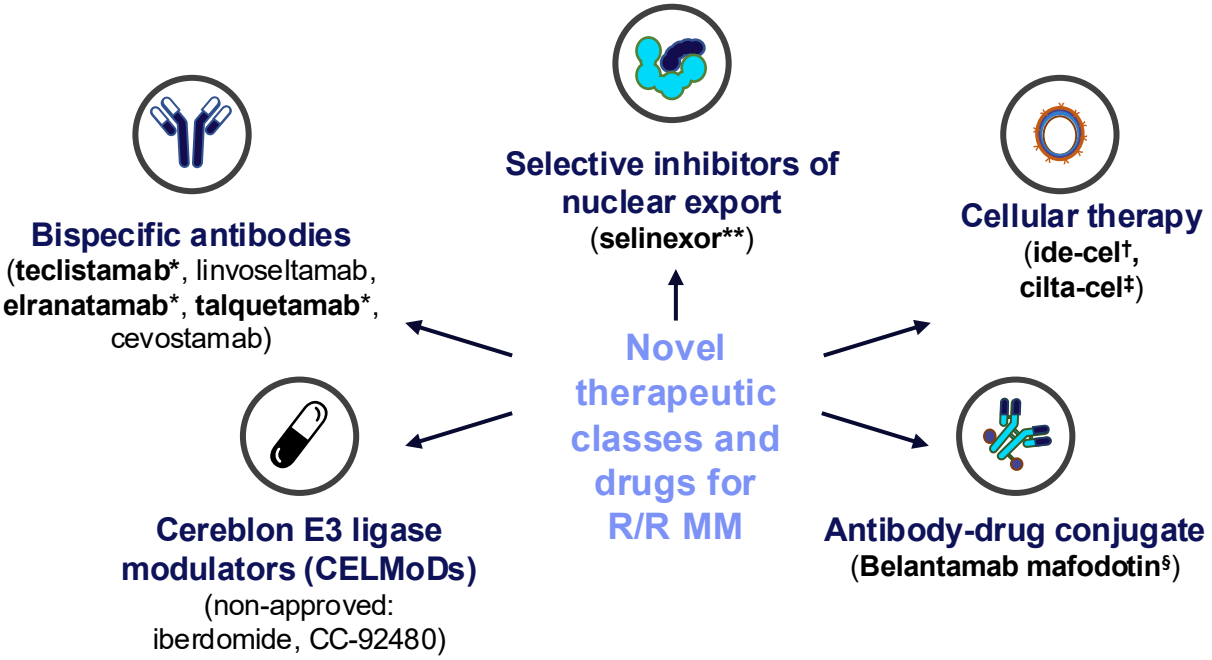
- Limited effective treatment options for **early relapsed double-** and **triple-refractory patients**[1]
- Many patients do not progress to third-line treatment due to **patient attrition** at each LOT[2]
- Limited effective treatment options currently available for **transplant-ineligible patients relapsing during** or **after Dara-Rd**, including disappointing results with daratumumab retreatment[3,4]
- **Lack of clear SoC** on the **use**, **combination,** and **sequencing** of the growing number of **MM treatment options**, complicated by the heterogeneity of this population[5,6]
- Issues with **access** (approval and cost) to **novel immunotherapies** in many countries[7]

Populations with greatest unmet need include those **refractory to lenalidomide and/or daratumumab** at **early relapse**[8,9]

Dara, daratumumab; LOT, line of therapy; MM, multiple myeloma; Rd, lenalidomide and dexamethasone; R/R, relapsed/refractory; SoC, standard of care.

1. Kastritis E, et al. *Blood*. 2022;139:2904–2917; 2. Fonseca R, et al. *BMC Cancer*. 2020;20:1087; 3. Dimopoulos MA, et al. *Ann Oncol*. 2021;32:309–322; 4. Kastritis E, et al. Presented at ASH 2022; abstract 3256; 5. Mateos MV, et al. *Leukemia*. 2022;36:1371–1376; 6. Ntanasis-Stathopoulos I, et al. *Clin Lymphoma Myeloma Leuk*. 2021;21:379–385; 7. Bhatt P, et al. *Curr Oncol*. 2023;30:2322–2347; 8. Mateos MV, et al. *Blood*. 2020;136:22–23; 9. Zamanillo I, et al. *Blood*. 2024;143:2029–2036.

Innovative therapeutic approaches with novel mechanisms of action are expanding treatment options in R/R MM

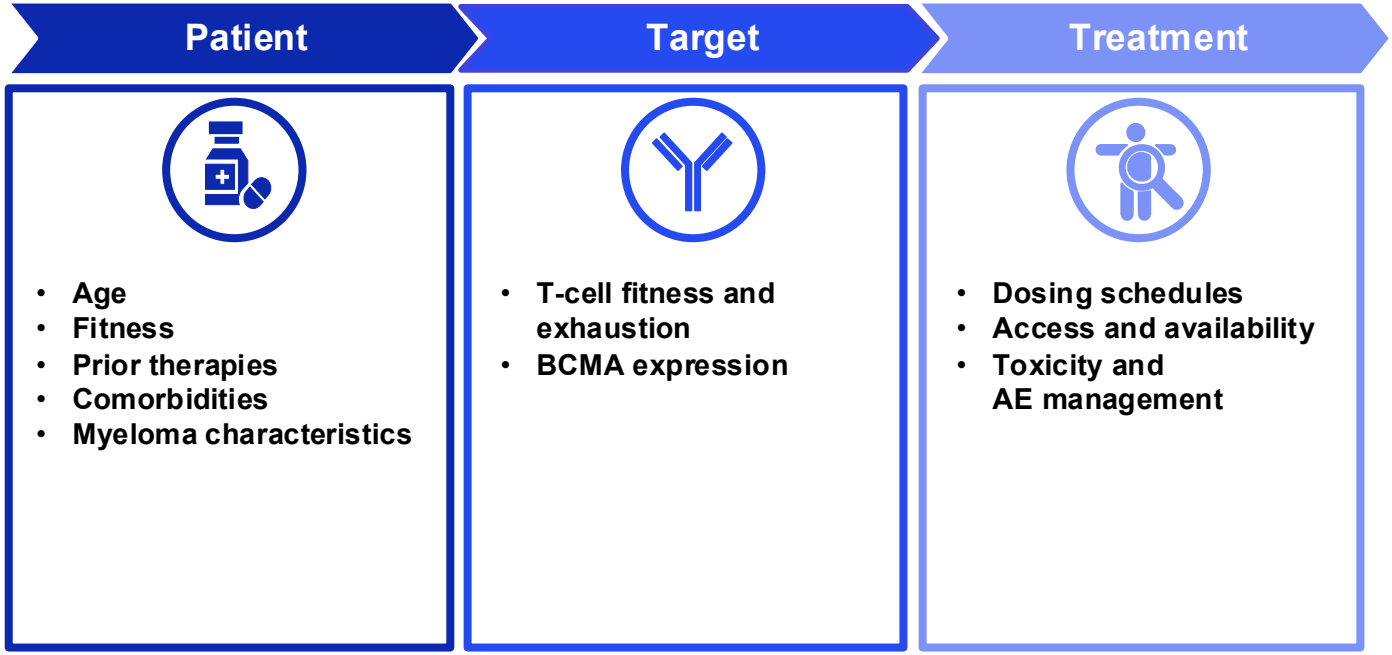


Many new therapies are emerging for MM, but challenges still remain…

- Patients relapse or become refractory to PIs, IMiDs, and anti-CD38 mAbs
- Many patients may not be eligible for ASCT
- Considering patient-related factors will support treatment sequencing decisions and impact survival outcomes

*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, EMA approved 1L+ in combination Vd or Pd.
ASCT, autologous stem cell transplant; CAR-T, chimeric antigen receptor T; cilta-cel, ciltacabtagene autoleucel; EMA, European Medicines Agency; ide-cel, idecabtagene vicleucel; IMiD, immunomodulatory drug; L, line; mAb, monoclonal antibody; MM, multiple myeloma; Pd, pomalidomide/dexamethasone; PI, proteasome inhibitor; R/R, relapsed/refractory; Vd, bortezomib/dexamethasone.
Davis LN, et al. *Cancers*. 2021;13:1686; Fazio F, et al. *Medterr J Hematol Infect Dis*. 2025;17(1):e2025025.

When selecting treatment at relapse, patient-, target-, and treatment-related factors should be considered alongside guideline recommendations

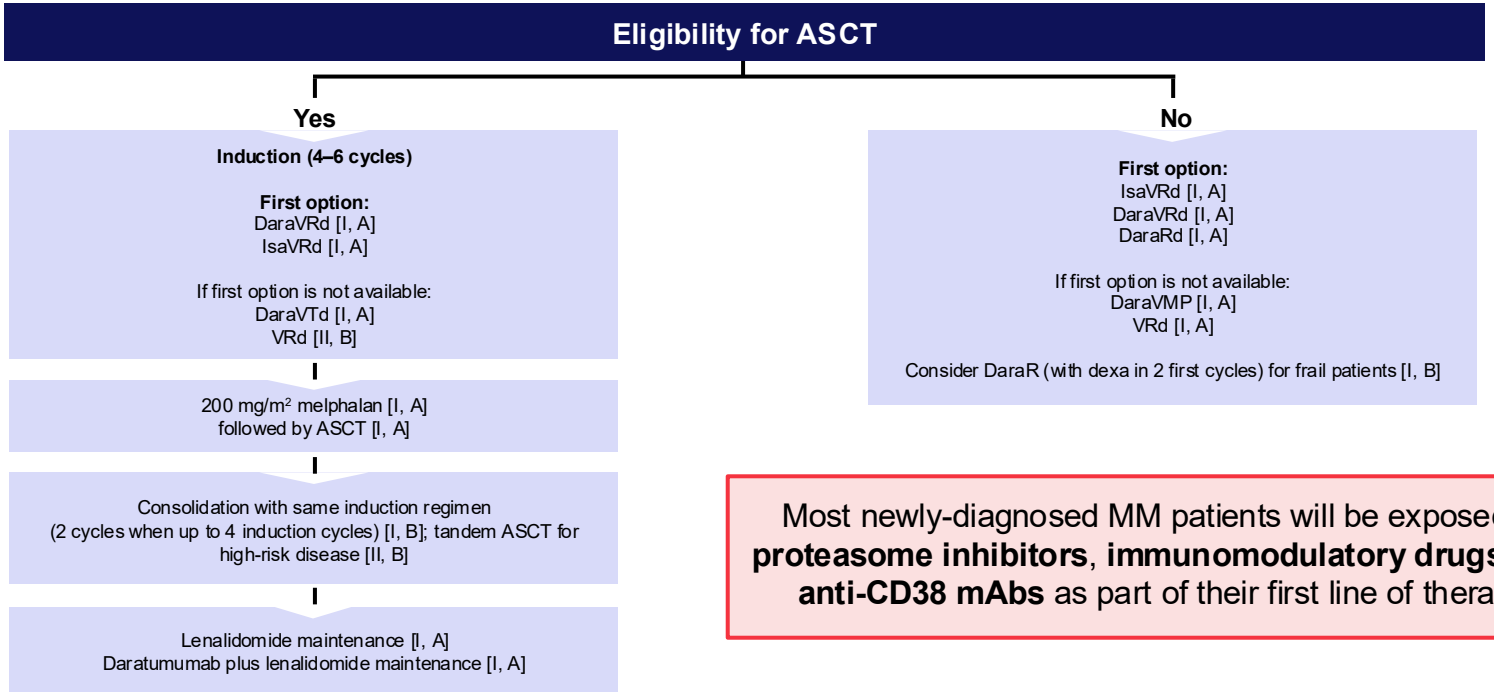


AE, adverse event; BCMA, B-cell maturation antigen.

Devarakonda S, et al. *Hematology Am Soc Hematol Educ Program*. 2022;2022:560–568; 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; Jaggers JL, et al. *J Geriatr Oncol*. 2021;12:235–238.

EHA-EMN 2025 guidelines

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

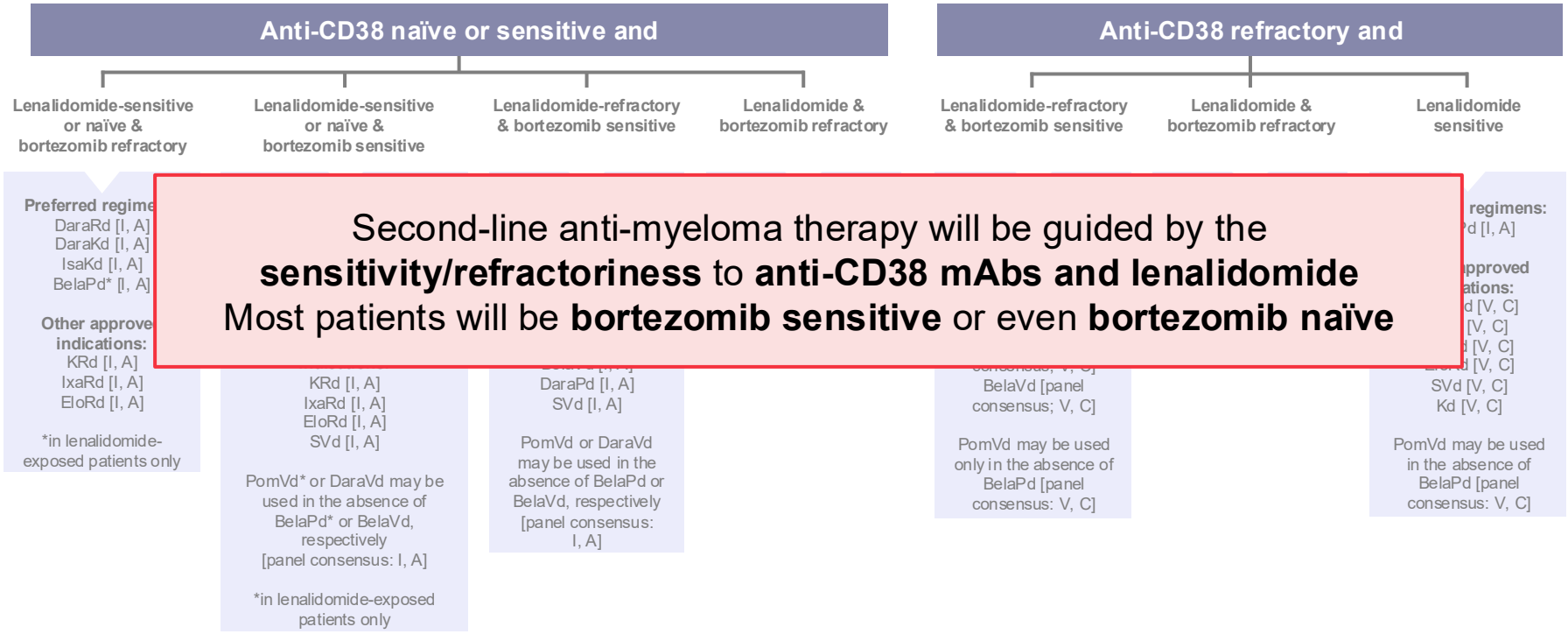


Most newly-diagnosed MM patients will be exposed to **proteasome inhibitors**, **immunomodulatory drugs,** and **anti-CD38 mAbs** as part of their first line of therapy

Figure from Dimopoulos MA, et al. EHA-EMN Evidence-Based Guidelines for diagnosis, treatment and follow-up of patients with multiple myeloma. *Nat Rev Clin Oncol*. 2025;22(9):680–700. Spinger Nature.
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, et al. *Nat Rev Clin Oncol*. 2025;22:680–700.

EHA-EMN 2025 guidelines

Most patients coming to second line will be bortezomib-sensitive



Second-line anti-myeloma therapy will be guided by the **sensitivity/refractoriness** to **anti-CD38 mAbs and lenalidomide**
Most patients will be **bortezomib sensitive** or even **bortezomib naïve**

Figure from Dimopoulos MA, et al. EHA-EMN Evidence-Based Guidelines for diagnosis, treatment and follow-up of patients with multiple myeloma. *Nat Rev Clin Oncol*. 2025;22(9):680–700. Spinger Nature.
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.
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Choice of MM treatment may be guided by ASCT eligibility and treatment history

First line

ASCT eligible

- Anti-CD38 + PI + IMiD + dex
- ASCT
- Len / DaraR

ASCT ineligible

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

Second line

Based on sensitivity/refractoriness to daratumumab and lenalidomide

- Anti-CD38 + Kd
- Anti-CD38 + Pd

- PVd
- SVd
- Kd

- Cilta-cel
- Belantamab-Vd
- Belantamab-Pd

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New combinations:

- Teclistamab-Dara / elranatamab
- Talquetamab-Dara +/- Pom
- Teclistamab-talquetamab
- Linvoseltamab
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ASCT, autologous stem cell transplant; cilta-cel, ciltacabtagene autoleucel; Dara, daratumumab; dex, dexamethasone; IMiD, immunomodulatory drug; Kd, carfilzomib/dexamethasone; len, lenalidomide; MM, multiple myeloma; Pd, pomalidomide/dexamethasone; PI, proteasome inhibitor; Pom, pomalidomide; PVd, pomalidomide/bortezomib/dexamethasone; RVd, lenalidomide/bortezomib/dexamethasone; SVd, selinexor/bortezomib/dexamethasone; Vd, bortezomib/dexamethasone; VMP, bortezomib/melphalan/prednisolone.

Speaker personal communication. Dimopoulos MA, et al. *Ann Oncol*. 2022;32:309–322.

For daratumumab-sensitive patients, CD38 mAb-based triplet regimens remain a valid option

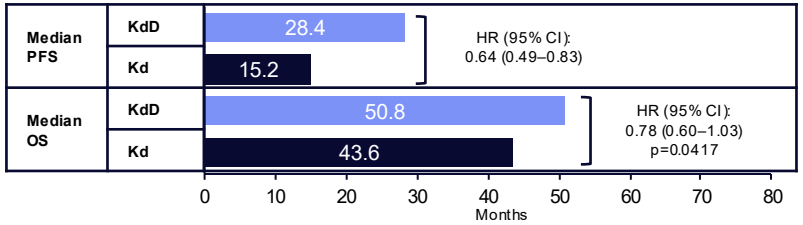
CANDOR[1]

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

2:1
- KdD (n=312)
- Kd (n=154)

Primary endpoint
- PFS

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



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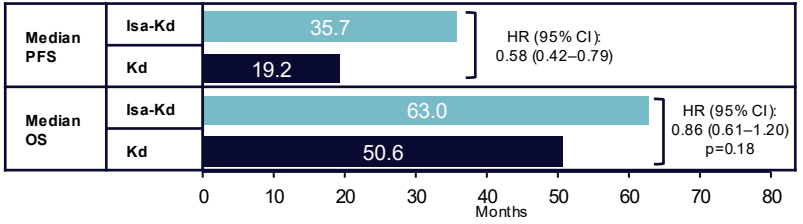
Secondary endpoints
- ORR, ≥VGPR with MRD-, CR rate, OS



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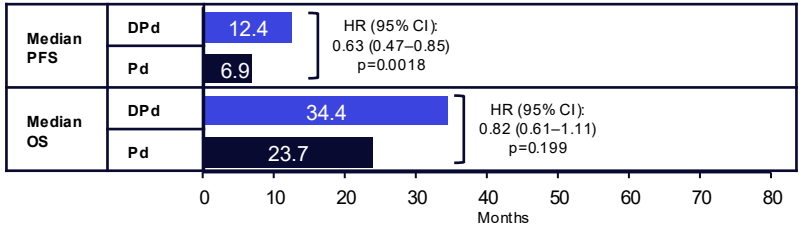
Secondary endpoints
- ORR, ≥VGPR, ≥CR, MRD, OS, time to response, DoR, TTNT, safety, HRQoL



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; mAb, monoclonal antibody; MM, multiple myeloma; 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.

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- HR for **PFS is sustained across all subgroups** of pts including those refractory to LEN (~30%) after ≥1 prior LOT

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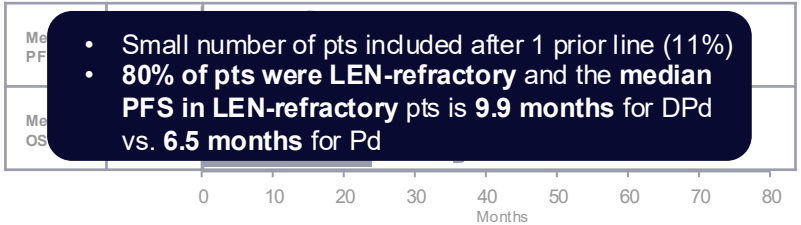

- Small number of pts included after 1 prior line (11%)
- **80% of pts were LEN-refractory** and the **median PFS in LEN-refractory** pts is **9.9 months** for DPd vs. **6.5 months** for Pd

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; mAb, monoclonal antibody; MM, multiple myeloma; 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.

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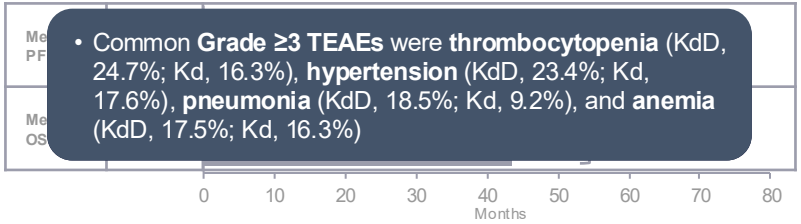

- Common **Grade ≥3 TEAEs** were **thrombocytopenia** (KdD, 24.7%; Kd, 16.3%), **hypertension** (KdD, 23.4%; Kd, 17.6%), **pneumonia** (KdD, 18.5%; Kd, 9.2%), and **anemia** (KdD, 17.5%; Kd, 16.3%)

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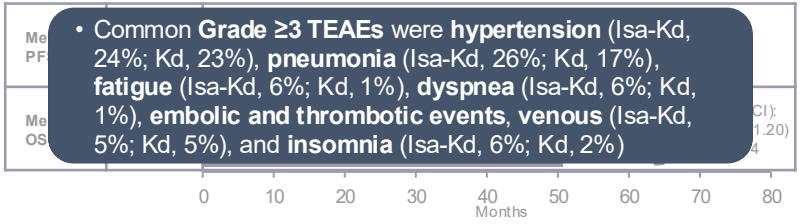

- Common **Grade ≥3 TEAEs** were **hypertension** (Isa-Kd, 24%; Kd, 23%), **pneumonia** (Isa-Kd, 26%; Kd, 17%), **fatigue** (Isa-Kd, 6%; Kd, 1%), **dyspnea** (Isa-Kd, 6%; Kd, 1%), **embolic and thrombotic events**, **venous** (Isa-Kd, 5%; Kd, 5%), and **insomnia** (Isa-Kd, 6%; Kd, 2%)

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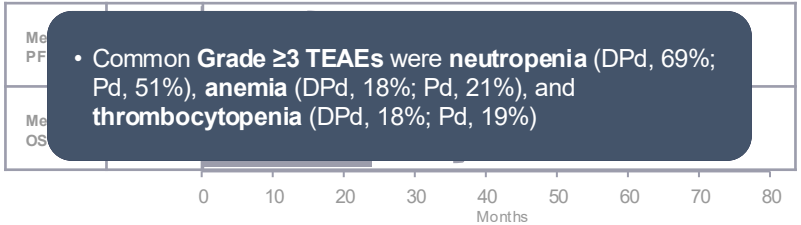

- Common **Grade ≥3 TEAEs** were **neutropenia** (DPd, 69%; Pd, 51%), **anemia** (DPd, 18%; Pd, 21%), and **thrombocytopenia** (DPd, 18%; Pd, 19%)

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; mAb, monoclonal antibody; MM, multiple myeloma; 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; TEAE, treatment-emergent adverse event; TTNT, time to next treatment; VGPR, very good partial response.

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- Anti-CD38 + Pd

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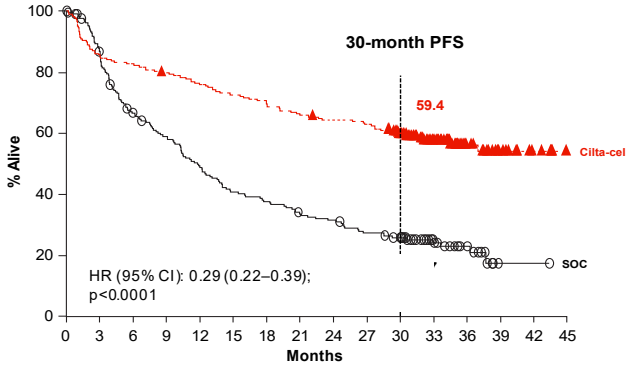
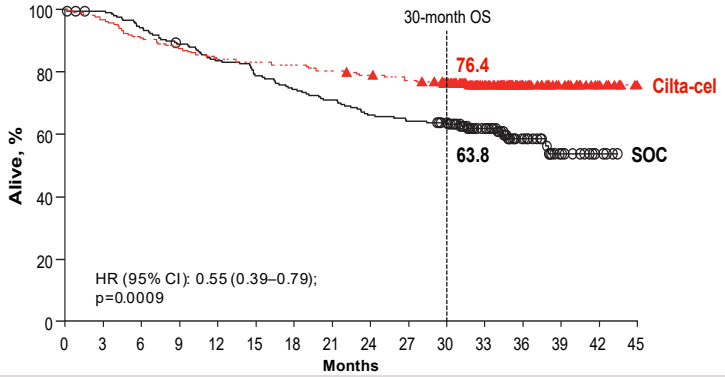
Speaker personal communication. Dimopoulos MA, et al. *Ann Oncol*. 2022;32:309–322.

CARTITUDE-4: A 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**[2]
- 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**[2]
- **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**[2]

- Safety profile consistent with previous analysis[3]
  - 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**, respectively[2]
  - **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[2*]
  - **No new cases of cranial nerve palsy or MNT** in the cilta-cel arm[2]

*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; MM, multiple myeloma; 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. Presented at ASH 2024; oral presentation 1032; 2. Mateos MV, et al. Presented at IMS 2024; oral presentation 1437; 3. San-Miguel J, et al. *N Engl J Med.* 2023;389:335–347.

DREAMM-7/8: Phase 3 trials of belantamab-based combination therapies in R/R MM

	Study design	Baseline characteristics	Median PFS, mos*	Median OS, mos*	ORR, % (95% CI)†	Safety profile	Belantamab-associated AEs
DREAMM-7[1,2]	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%[1] • **High-risk cytogenetics**: BVd, 28%; DVd, 27%[1] • **LEN-refractory:** BVd, 33%; DVd, 35%[1]	**BVd, 36.6 vs. DVd, 13.4** *HR 0.41 (95% CI: 0.31–0.53); p<0.001*[1]	**NR vs. NR** At 36 months: **BVd, 74% vs. DVd, 60%** *HR 0.58 (95% CI: 0.43–0.79)*[2]	**BVd, 83%** (78–88%) **vs. DVd, 71%** (65–77%)[2]	**AEs‡** Any grade: 100%; Grade 3–4: 95%[2] **Serious AEs** 53%[2] **Discontinuation due to AEs** 32%[2]	**Ocular events** Any grade: 79%; Grade 3–4: 34%[1] **Blurred vision** Any grade: 68%; Grade 3–4: 24%[2] **Worsening vision from normal to:** 20/50, 34%; 20/200, 2%[1] **Infections** Any grade: 70%; Grade 3–4: 31%[1]
DREAMM-8[3,4]	1:1 BPd (n=155) / PVd (n=147) **Primary endpoint:** PFS **Secondary endpoints:** ORR, MRD negativity, DoR	• **1 prior LOT**: BPd, 53%; PVd, 52%[3] • **High-risk cytogenetics**: BPd, 34%; PVd, 32%[3] • **LEN-refractory:** BPd, 81%; PVd, 76%[3] • **Anti-CD38 mAb-refractory:** BPd, 23%; PVd, 24%[3]	**BPd, 32.6 vs. PVd, 12.5** *HR 0.49 (95% CI: 0.36–0.67)*[4]	**NR vs. NR** 12-month estimate: **BPd, 83% vs. PVd, 76%** *HR 0.77 (95% CI: 0.53–1.14)*[3]	**BPd, 77%** (70–84%) **vs. PVd, 72%** (64–79%)[3]	**AEs** Any grade: 99%; Grade ≥3: 94%[3] **Serious AEs** 63%[3] **Discontinuation due to AEs** 15%[3]	**Ocular events** Any grade: 89%; Grade 3–4: 43%[3] **Blurred vision** Any grade: 79%; Grade ≥3: 17%[3] **Worsening vision from normal to:** 20/50, 34%; 20/200, 1%[3] **Infections** Any grade: 82%; Grade ≥3: 49%[3]

Median follow-up for DREAMM-7 was 28.2 months for PFS and safety, and 39.4 months for OS, ORR, and safety, and for DREAMM-8 was 28.0 months for OS, ORR and safety, and 35.8 months for PFS.
*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; PFS, progression-free survival; PR, partial response; PVd, pomalidomide/bortezomib/dexamethasone.
1. Hungria V, et al. *N Engl J Med.* 2024;391:393–407. 2. Hungria V, et al. *Lancet Oncol* 2025;26(8):1067–1080; 3. Dimopoulos MA, et al. *N Engl J Med.* 2024;391:408–421; 4. Trudel S, et al. Presented at ASH 2025; Abstract 2264.

Several bispecific antibodies are under investigation in Phase 3 clinical trials for use in earlier lines of therapy

Clinical trial	Investigational arm	Control arm	N	Key patient characteristics	Status
MajesTEC-3[1]	**Teclistamab-Dara**	Dara-Pd or Dara-Vd	587	✓ Exposure to **PI and IMiD** after **1–3 prior lines** × **Anti-CD38 refractory** patients	Active, not recruiting
MajesTEC-9[2]	**Teclistamab**	Kd or PVd	614	✓ Exposure to **anti-CD38 and Len** after **1–3 prior lines**	Active, not recruiting
MonumenTAL-3[3]	**Talquetamab-Dara** **Talquetamab-Pom-Dara**	Dara-Pd	864	✓ Exposure to **PI and IMiD** after **≥1 prior line** ✓ If **only 1 prior line**, must be **Len-refractory**	Active, not recruiting
MonumenTAL-6[4,5]	**Teclistamab-Talquetamab** **Talquetamab-Pom**	EloPd or PVd	795	✓ Exposure to **anti-CD38 and Len** after **1–4 prior lines**	Recruiting
MagnetisMM-5[6,7]	**Elranatamab**	Dara-Pd	944	✓ Exposure to **PI and IMiD** after **≥1 prior line** ✓ Exposure to anti-CD38 and anti-BCMA allowed after a washout period of ≥6 months	Recruiting
MagnetisMM-32[8]	**Elranatamab**	Kd, PVd, or EloPd	492	✓ Exposure to **anti-CD38 and Len** after **1–4 prior lines**	Recruiting
LinkerMM-3[9]	**Linvoseltamab**	EloPd	410	✓ Exposure to **PI and IMiD** after **1–4 prior lines**	Recruiting
CERVINO[10]	**Etentamig**	EloPd, SVd, or Kd	380	✓ **Triple class-exposed** after **≥2 prior lines**	Recruiting

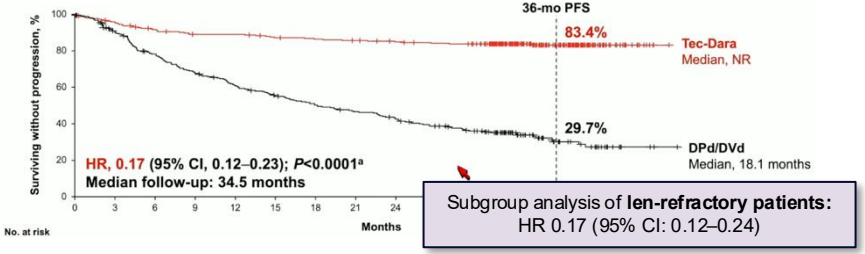
BCMA, B-cell maturation antigen; Dara, daratumumab; Dara-Pd, daratumumab/pomalidomide/dexamethasone; Dara-Vd, daratumumab/bortezomib/dexamethasone; EloPd, elotuzumab/pomalidomide/dexamethasone; IMiD, immunomodulatory drug; Kd, carfilzomib/dexamethasone; Len, lenalidomide; PI, proteasome inhibitor; Pom, pomalidomide; PVd, pomalidomide/bortezomib/dexamethasone; SVd, selinexor/bortezomib/dexamethasone.

1. https://clinicaltrials.gov/study/NCT05083169 (Accessed June 2026); 2. https://clinicaltrials.gov/study/NCT05572515 (Accessed June 2026); 3. https://clinicaltrials.gov/study/NCT05455320 (Accessed June 2026);
4. https://clinicaltrials.gov/study/NCT06208150 (Accessed June 2026); 5. Nooka AK, et al. *Blood*. 2024;144(Suppl_1):47571; 6. https://clinicaltrials.gov/study/NCT05020236 (Accessed June 2026);
7. Leleu X, et al. *Hemasphere*. 2023;7(Suppl):e052316a; 8. https://clinicaltrials.gov/study/NCT06152575 (Accessed June 2026); 9. https://clinicaltrials.gov/study/NCT05730036 (Accessed June 2026);
10. https://clinicaltrials.gov/study/NCT06158841 (Accessed June 2026).

MajesTEC-3: A Phase 3 trial of Tec-Dara vs. Dara-based SoC in R/R MM after 1–3 prior lines

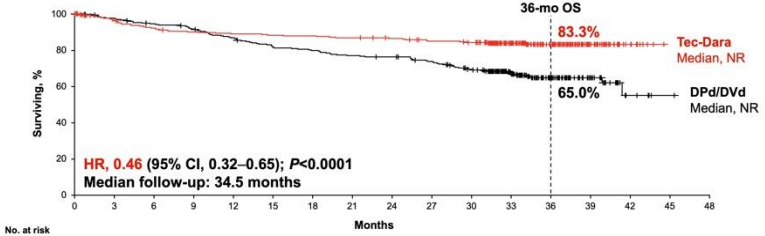
At baseline, **~5% of participants** had been **previously exposed to Dara** and **~80% of participants** were **len-refractory**

PFS (primary endpoint; 34.5 months median follow-up)



Subgroup analysis of **len-refractory patients:**
HR 0.17 (95% CI: 0.12–0.24)

OS (34.5 months median follow-up)



Key secondary endpoints	Tec-Dara	DPd/DVd	OR; p-value
ORR, %	89.0	75.3	2.65; p<0.0001
≥CR, %	81.8	32.1	9.56; p<0.0001
Median DoR (95% CI), months	NE (NE–NE)	23.5 (19.8–29.9)	NR
MRD negativity (10^{-5}; NGS), %	58.4	17.1	6.78; p<0.001

Safety summary

The **TEAE safety profile** was **generally comparable** between Tec-Dara and Dara-based SoC

- In the **Tec-Dara arm**, most **CRS events** were **Grade 1** (44.2%), with 15.9% Grade 2
- In the **Tec-Dara arm**, **13 (4.6%) of deaths were due to infection**; 12 occurred within 6 months of treatment and 9/12 patients did not receive IgRT*†

*In Feb 2023, the protocol was amended to reinforce IgRT supplementation and antimicrobial prophylaxis (protocol amendment #6); †In the Dara-based SoC group, 4 patients had a fatal infection, 2 of which occurred after the implementation of protocol amendment #6.
CI, confidence interval; CR, complete response; CRS, cytokine release syndrome; DoR, duration of response; DPd, daratumumab/pomalidomide/dexamethasone; DVd, daratumumab/bortezomib/dexamethasone; HR, hazard ratio; IgRT, immunoglobulin replacement therapy; MRD, minimal residual disease; NE, not estimable; NGS, next generation sequencing; NR, not reported; OR, odds ratio; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; R/R MM, relapsed/refractory multiple myeloma; SoC, standard of care; TEAE, treatment-emergent adverse event; Tec-Dara, teclistamab/daratumumab.
Mateos MV, et al. Presented at ASH 2025; oral presentation LBA-6; Costa LJ, et al. *N Engl J Med.* 2026;394:739–752.

MajesTEC-9: A Phase 3 study of Tec monotherapy vs. PVd/Kd in patients with R/R MM

Patients with R/R MM and 1–3 prior LOTs, including anti-CD38 and Len, were randomized 1:1 to receive 28-day cycles of Tec or investigator's choice of PVd/Kd

1. **Primary endpoint:** PFS by IRC
2. **Secondary endpoints:** OS, ≥CR, and safety

Efficacy

Key efficacy	Tec (n=296)	PVd/Kd (n=297)	HR or OR (95% CI); p-value
Median follow-up, months	17.3	17.3	—
Median PFS, months	NR	8.2	HR, 0.29 (0.23–0.38); p<0.0001
18-month PFS rate, %	69.8	26.9	—
Median OS, months	—	—	HR, 0.60 (0.43–0.83); p=0.0020
≥CR rate, %	65.9	16.8	OR, 10.42 (6.89–15.76); p<0.0001

- Of 174 PVd/Kd pts who received subsequent treatment, **68.4% received BsAb or CAR-T**
- PFS favored Tec **across all prespecified subgroups**, including **anti-CD38-refractory and len-refractory patients**

Safety

Key safety	Tec (n=296)	PVd/Kd (n=297)
Median treatment duration, months	13.1	7.0
Any grade TEAEs, %	99.7	97.9
Grade 3/4 TEAEs, %	84.9	76.3
Grade 5 TEAEs, %	6.5	3.5
Treatment discontinuations due to TEAEs, %	10.7	13.1

- **Grade 3/4 infections** were **higher with Tec** vs. PVd/Kd (41.6% vs. 29.0%)
- **CRS** occurred in **66.0%** of patients with Tec (Grade 1/2: 48.8%/16.5%) and **ICANS** occurred in **4.1%** (Grade 1/2: 2.4%/1.4%)

Tec monotherapy **significantly improved PFS/OS vs. SoC** in this high unmet need population
CRS and infections were managed with established protocols

BsAb, bispecific antibody; CAR-T, chimeric antigen receptor T; CI, confidence interval; CR, complete response; CRS, cytokine release syndrome; HR, hazard ratio; ICANS, immune effector cell-associated neurotoxicity syndrome; IRC, independent review committee; Kd, carfilzomib/dexamethasone; len, lenalidomide; LOT, line of therapy; OR, odds ratio; OS, overall survival; PFS, progression-free survival; PVd, pomalidomide/bortezomib/dexamethasone; R/R MM, relapsed/refractory multiple myeloma; Tec, teclistamab; TEAE, treatment-emergent adverse event.

Mateos MV, et al. Presented at ASCO 2026; Abstract 7507.

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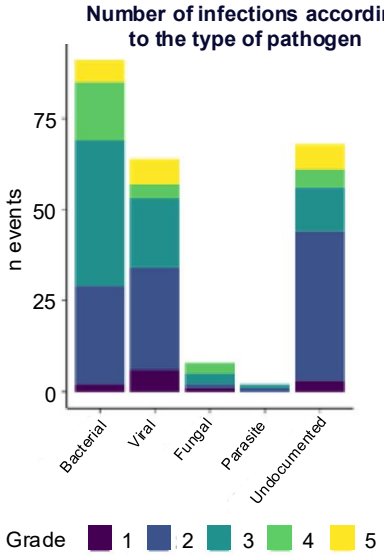
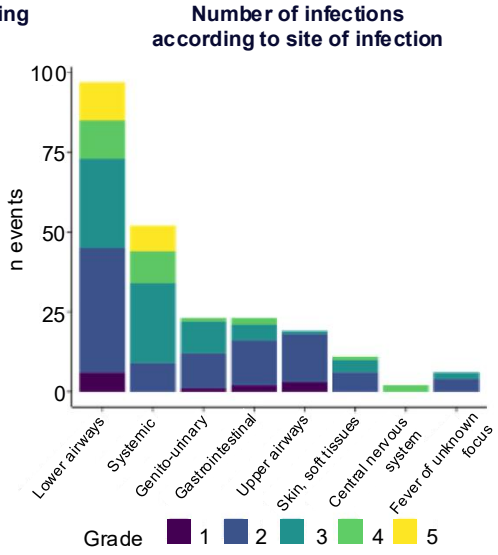
In the real-world setting, bispecific antibodies are associated with frequent infections

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 1 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 antibodies** (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)

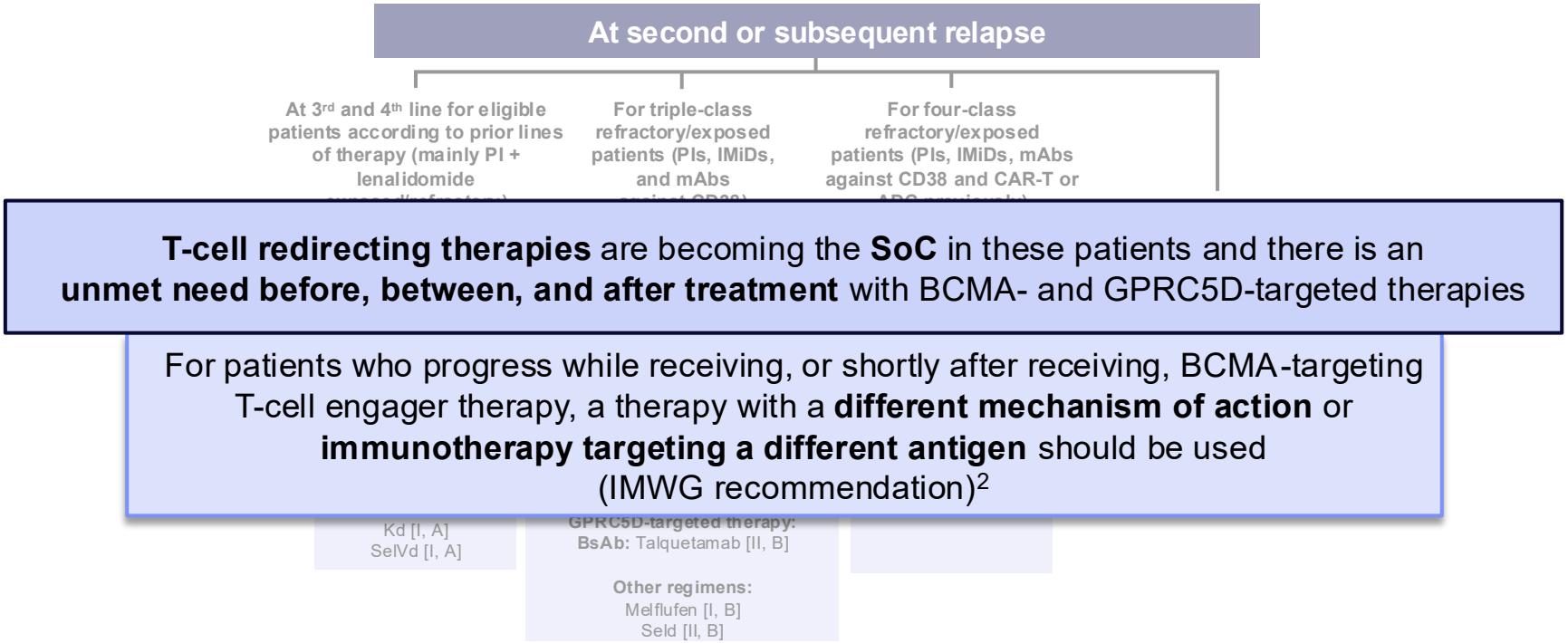




BCMA, B-cell maturation antigen; CI, confidence interval; CRS, cytokine release syndrome; GPRC5D, G protein-coupled receptor class C group 5 member D; HR, hazard ratio; ICANS, immune effector cell-associated neurotoxicity syndrome; IFM, Intergroupe Francophone du Myelome; MM, multiple myeloma.
Jourdes A, et al. *Clin Microbiol Infect.* 2024;30:764–771.

EHA-EMN 2025 guidelines[1]

If anti-BCMA–directed therapy is used in second line, 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

For patients who progress while receiving, or shortly after receiving, BCMA-targeting T-cell engager therapy, a therapy with a **different mechanism of action** or **immunotherapy targeting a different antigen** should be used (IMWG recommendation)[2]

Figure from Dimopoulos MA, et al. EHA-EMN Evidence-Based Guidelines for diagnosis, treatment and follow-up of patients with multiple myeloma. *Nat Rev Clin Oncol*. 2025;22(9):680–700. Spinger Nature.
ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; Bela, belantamab mafodotin; BsAb, bispecific monoclonal antibody; CAR-T, chimeric antigen receptor T; cilta-cel, ciltacabtagene autdeucel; 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; IMWG, International Myeloma Working Group; Isa, isatuximab; Ixa, ixazomib; K, carfilzomib; Kd, carfilzomib/dexamethasone; mAb, monoclonal antibody; Pd, pomalidomide/dexamethasone; PI, proteasome inhibitor; PomVd, pomalidomide/bortezomib/dexamethasone; Sel, selinexor; SoC, standard of care; Vd, bortezomib/dexamethasone.
1. Dimopoulous MA, et al. *Nat Rev Clin Oncol*. 2025;22:680–700; 2. Costa LJ, et al. *Leukemia*. 2025;39:543–554.

In patients double-exposed or double-refractory to daratumumab and lenalidomide, there remains a need for effective second-line treatments

Second line

Based on sensitivity/refractoriness to daratumumab and lenalidomide[1]

- Anti-CD38 + Kd
- Anti-CD38 + Pd

- PVd
- SVd
- Kd

- Cilta-cel
- Belantamab-Vd
- Belantamab-Pd

- Cilta-cel
- Belantamab-Vd
- Belantamab-Pd

New combinations:

- Teclistamab-Dara / elranatamab
- Talquetamab-Dara +/- Pom
- Teclistamab-talquetamab
- Linvoseltamab
- Etentamig

Owing to frequent use of daratumumab- and lenalidomide-based regimens in the first line, an increasing proportion of patients are **double-exposed or double-refractory in later treatment lines**[2]

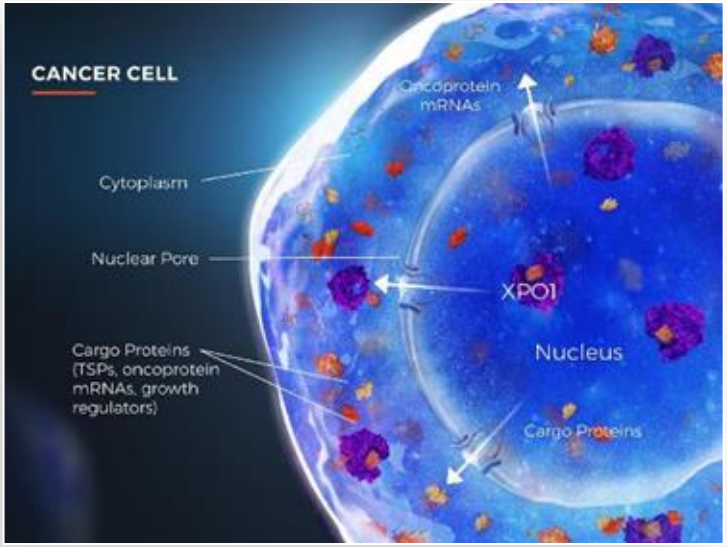
Despite FDA and EMA approval for use in earlier treatment lines, several factors **limit the availability of CAR-T therapy** across different regions and countries[3–6]

Therefore, there is **a need for alternative high-efficacy treatment options** for patients double-exposed or double-refractory to daratumumab and lenalidomide

CAR-T, chimeric antigen receptor T; cilta-cel, ciltacabtagene autoleucel; Dara, daratumumab; EMA, European Medicines Agency; FDA, Food and Drug Administration; Kd, carfilzomib/dexamethasone; len, lenalidomide; Pd, pomalidomide/dexamethasone; PVd, pomalidomide/bortezomib.dexamethasone; Pom, pomalidomide; SVd, selinexor/bortezmob/dexamethasone; Vd, bortezomib/dexamethasone.

Speaker personal communication; 1. Dimopoulos MA, et al. *Ann Oncol*. 2022;32:309–322; 2. Martino E, et al. *ESMO Open* . 2025;10(8); 3. FDA. Carvykti Prescribing Information. Available at https://www.fda.gov/media/156560/download?attachment (Accessed June 2026); 4. EMA. Carvykti Summary of Product Characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/carvykti-epar-product-information_en.pdf (Accessed June 2026); 5. Medina-Olivares FJ, et al. *Front Oncol*. 2024;14:1397613; 6. Litvinova Y, et al. *Health Policy*. 2024;149:105153.

Selinexor: A first-in-class oral exportin 1 (XPO1) inhibitor[1]



XPO1 overexpression:

- Inactivates tumor suppressor proteins[2]
- Enhances proto-oncogene translation[2,3]
- Disrupts growth regulation[2,4]

There is growing evidence that selinexor may promote **T-cell fitness**[5] and influence the **tumor microenvironment,**[6] potentially **improving outcomes with subsequent therapies**[7,8]

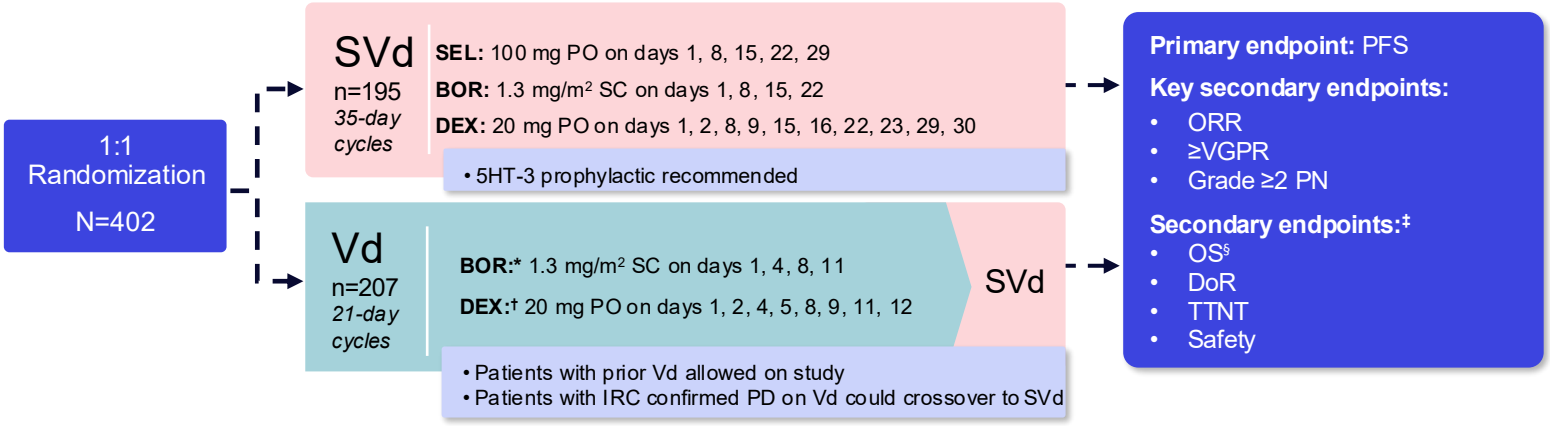
Selinexor is indicated i) in combination with bortezomib and dexamethasone for the treatment of adult patients with MM who have received ≥1 prior therapy; ii) in combination with dexamethasone for the treatment of MM in adult patients who have received ≥4 prior therapies and whose disease is refractory to ≥2 proteasome inhibitors, 2 immunomodulatory agents, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.[9]
MM, multiple myeloma; mRNA, messenger ribonucleic acid; TSP, tumor suppressor protein; XPO1, exportin-1.

Image from Karyopharm Therapeutics. Company Overview. Available at: https://www.karyopharm.com/wp-content/uploads/2021/04/KPTI-About-Press-Kit-Document (Accessed June 2026). 1. Peterson TJ, et al. *Ann Pharmacother*. 2020;54:577–582. 2. Sun Q, et al. *Signal Transduct Target Ther*. 2016;1:16010; 3. Culjkovic-Kraljacic B, et al. *Cell Rep*. 2012;2:207–215; 4. Tai Y-T, et al. *Leukemia*. 2014;28:155–165; 5. Binder AF, et al. *Front Immunol*. 2023;14:1275329; 6. Tasbihi K, et al. *Cells*. 2025;14:430; 7. Verbruggen C, et al. Presented at ASH 2025; poster presentation 6102; 8. Costa BA, et al. *J Clin Med*. 2025;14:1316; 9. EMA. Selinexor: SmPC. Available at: https://www.ema.europa.eu/en/documents/product-information/nexpovio-epar-product-information_en.pdf (Accessed JUne 2026).

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

Study design

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



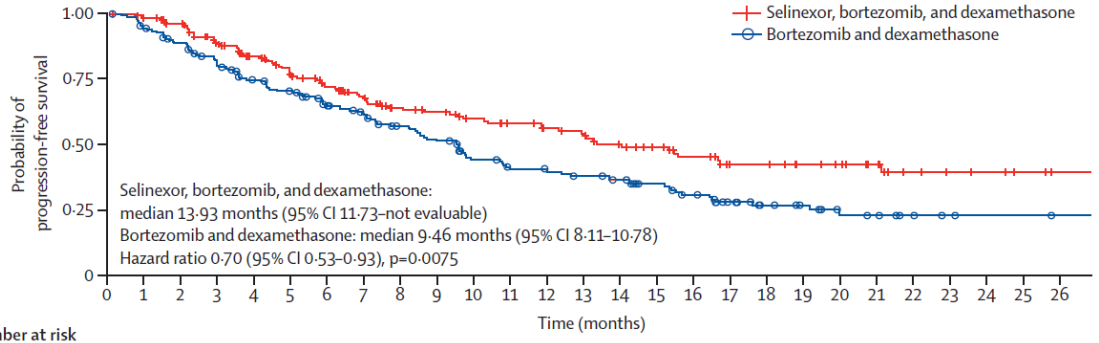
- Median age was 67 years (IQR 59–73) and 81 (20%) patients were aged ≥75 years or older
- Median number of previous regimens was 2 (1–2), 75 (19%) patients had received 3 previous lines of therapy, and 139 (35%) patients had undergone SCT

*BOR dosing presented is for cycles 1–8; for cycles ≥9 BOR was given as 1.3 mg/m² SC on days 1, 8, 15 and 22. †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; ‡Not all secondary endpoints are listed here; §OS is not yet reached for the SVd group.
BOR, bortezomib; DEX, dexamethasone; DoR, duration of response; IQR, interquartile range; IRC, independent review committee; MM, multiple myeloma; ORR, overall response rate; 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;396:1563–1573; CT.gov. NCT03110562. Available at: https://clinicaltrials.gov/study/NCT03110562 (Accessed June 2026).

BOSTON: A significant increase in mPFS with SVd vs. Vd was demonstrated

	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:

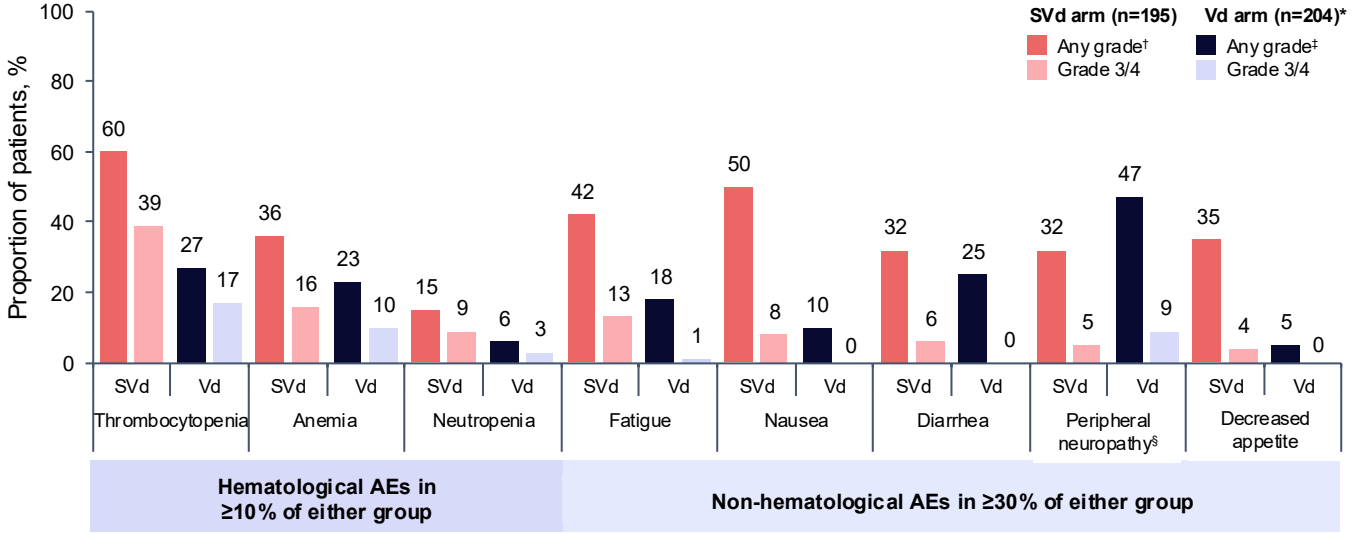
1. An increase of 4.47 months in median PFS
2. A 30% reduction in the risk of disease progression

*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).
Figure reprinted from *The Lancet*, 396(10262). Grosicki S, et al. Once-per-week selinexor, bortezomib, and dexamethasone versus twice-per-week bortezomib and dexamethasone in patients with multiple myeloma (BOSTON): a randomised, open-label, phase 3 trial. 1563–1573, Copyright (2026), with permission from Elsevier.
CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; (m)PFS, (median) progression-free survival; NE, not evaluable; SVd, selinexor/bortezomib/dexamethasone; Vd, bortezomib/dexamethasone.
Grosicki S, et al. *Lancet*. 2020;396:1563–1573.

BOSTON: The safety profile of SVd was manageable

The most common any Grade AEs were GI AEs, thrombocytopenia, fatigue, and anemia, and the most common Grade 3/4 AEs were thrombocytopenia, anemia, fatigue, 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: 3 (2%) cases of pneumonia and 1 (1%) case of bronchitis; ‡Includes four Grade 5 events: 3 (1%) cases of pneumonia and 1 (<1%) case of anemia; §Includes high-level MedDRA term "peripheral neuropathies NEC".
AE, adverse event; GI, gastrointestinal; MedDRA, medical dictionary for regulatory activities; NEC, not elsewhere classified; SVd, selinexor/bortezomib/dexamethasone; TEAE, treatment-emergent adverse event; Vd, bortezomib/dexamethasone.
Grosicki S, et al. *Lancet*. 2020;396:1563–1573.

Efficacy outcomes varied across treatment options in patients refractory to lenalidomide

Study	Regimen	Arm	mPFS in lenalidomide-refractory patients
ENDEAVOR[1,2]* 1–3 prior lines of therapy	**Kd**[1,2]: Doublet, PI, 1 new MoA	Kd	8.6
		Vd	6.6
			HR 0.80 (95% CI: 0.57–1.11)
OPTIMISMM[3]† 1–3 prior lines of therapy, received prior treatment with a lenalidomide-containing regimen for ≥2 consecutive cycles, not bortezomib refractory	**PVd**[3]: Triplet, PI, 1 new MoA	PVd	9.5
		Vd	5.6
			HR 0.65 (95% CI: 0.50–0.84)
BOSTON[4]‡ 1–3 prior lines of therapy	**SVd**[4]: Triplet, PI, 2 new MoAs	SVd	10.2
		Vd	7.1
			HR 0.52 (95% CI: 0.31–0.88)

These data are derived from separate clinical trials utilizing distinct methodologies and patient populations. Direct cross-trial comparisons should not be used to infer comparative clinical efficacy or safety.

Data presented side by side for illustration purposes only – this is not a head-to-head comparison of these studies.
*Median follow-up was not reported; †After median follow-up of 15.9 months; ‡Median follow-up was 28.2 months (SVd) and 27.1 months (Vd).
CI, confidence interval; HR, hazard ratio; Kd, carfilzomib/dexamethasone; MoA, mechanism of action; mPFS, median progression-free survival; PI, proteasome inhibitor; PVd, pomalidomide/bortezomib/dexamethasone; SVd, selinexor/bortezomib/dexamethasone; Vd, bortezomib/dexamethasone.
1. Moreau P, et al. *Leukemia*. 2017;31:115–122; 2. Dimopoulos MA, et al. *Lancet Oncol*. 2016;17(1):27–38; 3. Richardson PG, et al. *Lancet Oncol*. 2019;20:781–94; 4. Mateos MV, et al. *Eur J Haematol*. 2024;113:242–252.

Efficacy outcomes varied across treatment options in patients refractory to lenalidomide

Study	Regimen	Arm	mPFS in lenalidomide-refractory patients
ENDEAVOR[1]* 1–3 prior lines of therapy	**Kd**[1]: Doublet, PI, 1 new MoA	Kd Vd	**No significant difference in mOS** with Kd vs. Vd in lenalidomide-refractory patients[4§]: Kd, 29.2 months vs. Vd, 21.4 months; HR 0.86 (95% CI: 0.62–1.18)
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, 1 new MoA	PVd Vd	**No significant difference in mOS** with PVd vs. Vd in lenalidomide-refractory patients[5‖]: Kd, 29.8 months vs. Vd, 24.2 months; HR 0.89 (95% CI: 0.71–1.12)
BOSTON[3]‡ 1–3 prior lines of therapy	**SVd**[3]: Triplet, PI, 2 new MoAs	SVd Vd	**mOS was significantly longer** with SVd vs. Vd in lenalidomide-refractory patients[3‡]: SVd, 26.7 months vs. Vd, 18.6 months; HR 0.53 (95% CI: 0.30–0.95); P=0.015

These data are derived from separate clinical trials utilizing distinct methodologies and patient populations. Direct cross-trial comparisons should not be used to infer comparative clinical efficacy or safety.

Data presented side by side for illustration purposes only – this is not a head-to-head comparison of these studies.
*Median follow-up was not reported; †After median follow-up of 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.
CI, confidence interval; HR, hazard ratio; Kd, carfilzomib/dexamethasone; MoA, mechanism of action; mOS, median overall survival; mPFS, median progression-free survival; PI, proteasome inhibitor; PVd, pomalidomide/bortezomib/dexamethasone; SVd, selinexor/bortezomib/dexamethasone; 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;113:242–252; 4. Orlowski RZ, et al. *Clin Lymphoma Myeloma Leuk*. 2019;19(8):522–30.e1; 5. Richardson P, et al. *Eur J Haematol*. 2025;114(5):822–831.

Efficacy outcomes varied across treatment options in proteasome inhibitor-naïve patients

Study	Regimen	Arm	mPFS in bortezomib-naïve patients
ENDEAVOR[1]* 1–3 prior lines of therapy	**Kd[1]**: Doublet, PI, 1 new MoA	Kd	17.7
		Vd	9.4
			HR 0.47 (95% CI: 0.25–0.88) p=0.0084
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, 1 new MoA	PVd	20.7
		Vd	9.5
			HR 0.62 (95% CI: 0.35–1.11) p=0.1055
BOSTON[3]‡ 1–3 prior lines of therapy	**SVd[3]**: Triplet, PI, 2 new MoAs	SVd	29.5
		Vd	9.7
			HR 0.35 (95% CI: 0.18–0.68) p=0.001

These data are derived from separate clinical trials utilizing distinct methodologies and patient populations. Direct cross-trial comparisons should not be used to infer comparative clinical efficacy or safety.

Data presented side by side for illustration purposes only – this is not a head-to-head comparison of these studies.
*Median follow-up was not reported; †After median follow-up of 16.4 months; ‡Median follow-up was 27.8 months (SVd) and 29.7 months (Vd).
CI, confidence interval; HR, hazard ratio; Kd, carfilzomib/dexamethasone; MoA, mechanism of action; mPFS, median progression-free survival; PI, proteasome inhibitor; PVd, pomalidomide/bortezomib/dexamethasone; SVd, selinexor/bortezomib/dexamethasone; Vd, bortezomib/dexamethasone.
1. Goldschmidt H, et al. *Leuk Lymphoma*. 2018;59:1364–1374; 2. Dimopoulos M, et al. *Leukemia*. 2021;35:1722–1731; 3. Mateos MV, et al. *Eur J Haematol*. 2024;113:242–252.

Safety outcomes varied across treatment options in R/R MM patients

Study	Regimen	Arm	Safety summary
ENDEAVOR[1] 1–3 prior lines of therapy	**Kd**[1]: Doublet, PI, 1 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)[1]
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, 1 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% [PVd arm])[2]
BOSTON[3] 1–3 prior lines of therapy	**SVd**[3]: Triplet, PI, 2 new MoAs	SVd Vd	**Common Grade 3/4 AEs** included **thrombocytopenia** (SVd, 39% vs. Vd, 17%), **fatigue** (SVd, 13% vs. Vd, 1%), **anemia** (SVd, 16% vs. Vd, 10%) and **pneumonia** (SVd, 11% vs. Vd, 11%)[3]

These data are derived from separate clinical trials utilizing distinct methodologies and patient populations. Direct cross-trial comparisons should not be used to infer comparative clinical efficacy or safety.

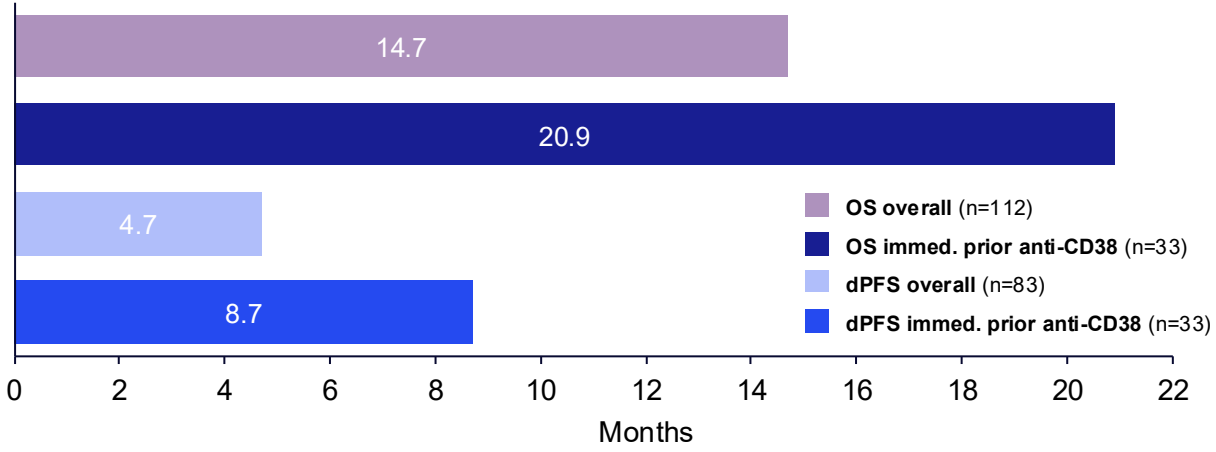
Data presented side by side for illustration purposes only – this is not a head-to-head comparison of these studies.
AE, adverse event; Kd, carfilzomib/dexamethasone; MoA, mechanism of action; PI, proteasome inhibitor; PVd, pomalidomide/bortezomib/dexamethasone; R/R MM, relapsed/refractory multiple myeloma; SVd, selinexor/bortezomib/dexamethasone; TEAE, treatment-emergent adverse event; Vd, bortezomib/dexamethasone.

1. Orlowski RZ, et al. *Clin Lymphoma Myeloma Leuk*. 2019;19:522–530.e1; 2. Richardson P, et al. *Eur J Haematol*. 2025;114:822–831; 3. Grosicki S, et al. *Lancet*. 2020;396:1563–1573.

Outcomes with selinexor triplet regimens in patients with R/R MM with prior exposure to an anti-CD38 mAb in the immediate prior LOT have been assessed

A **real-world analysis** of treatment patterns and survival outcomes using an EHR-derived, de-identified database of patients with R/R MM treated with a **selinexor-containing triplet-based regimen***

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



Patients were **heavily pretreated**, with **95% triple-class exposed**, and **94% receiving the selinexor triplet at ≥4 lines of therapy**

Patients with **prior exposure to anti-CD38 mAbs** in the regimen prior to the selinexor treatment had **numerically higher survival outcomes**

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.
*Regimens included combinations with dexamethasone and pomalidomide, bortezomib, carfilzomib, or daratumumab.
dPFS, derived progression-free survival; EHR, electronic health record; immed, immediate; LOT, line of therapy; mAb, monoclonal antibody; R/R MM, relapsed/refractory multiple myeloma; OS, overall survival.
Whiteley A, et al. *Curr Oncol.* 2025;32:268.

Despite the availability of high-efficacy treatment options in the second line, questions regarding the optimal sequencing of therapies remain

Second line

Based on sensitivity/refractoriness to daratumumab and lenalidomide[1]

- Anti-CD38 + Kd
- Anti-CD38 + Pd

- PVd
- SVd
- Kd

- Cilta-cel
- Belantamab-Vd
- Belantamab-Pd

- Cilta-cel
- Belantamab-Vd
- Belantamab-Pd

New combinations:

- Teclistamab-Dara / elranatamab
- Talquetamab-Dara +/- Pom
- Teclistamab-talquetamab
- Linvoseltamab
- Etentamig

With evidence suggesting that **the effectiveness of immunotherapies at later treatment lines can be influenced by earlier treatment lines**, the sequencing of treatments should be carefully considered[2,3]

Cilta-cel, ciltacabtagene autdeucel; Dara, daratumumab;; Kd, carfilzomib/dexamethasone; Pd, pomalidomide/dexamethasone; PVd, pomalidomide/bortezomib/dexamethasone; Pom, pomalidomide; SVd, selinexor/bortezomib/dexamethasone; Vd, bortezomib/dexamethasone.

Speaker personal communication; 1. Dimopoulos MA, et al. *Ann Oncol*. 2022;32:309–322. 2. van de Donk NWC, et al. *Hemasphere*. 2025;9:e70260; 3. FDA. Carvykti Prescribing Information. Available at https://www.fda.gov/media/156560/download?attachment (Accessed June 2026).

Summary

Many **novel immunotherapies** are moving into earlier lines of treatment, expanding options for patients with MM. While this presents more options for patients, there is **no SoC on optimal sequencing** and **unmet medical needs persist**

Despite the emergence of CAR-T cell therapies and novel bispecific antibodies, there remains a need for an **alternative high-efficacy treatment option** with a **different MoA** in the second line

Selinexor introduces a **novel MoA** to the MM treatment landscape, with the **BOSTON trial** validating its combination with bortezomib and dexamethasone (SVd) in a **broad R/R MM patient population**, as well as in **len-refractory patients**

In the expanding and evolving R/R MM treatment landscape, there is a need to understand how to **optimally sequence** high-efficacy treatment options for **improved patient outcomes** at each relapse

CAR-T, chimeric antigen receptor T; len, lenalidomide; MM, multiple myeloma; MoA, mechanism of action; R/R MM, relapsed/refractory multiple myeloma; SoC, standard of care; SVd, selinexor/bortezomib/dexamethasone.

Maximizing efficacy with optimal sequencing: A case-based discussion

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Disclosures

- **Consultant/advisory board:** Janssen, BMS, Pfizer, Karyopharm, Sanofi, Takeda, Genentech, Abbvie, Regeneron, Forus, Menarini, Kite/Arcellx, UB Therapeutics, Legend
- **Speakers Bureau:** Janssen, BMS, Sanofi, Pfizer

EHA/EMN recommendations for the treatment of relapsed/refractory multiple myeloma at second or subsequent relapse

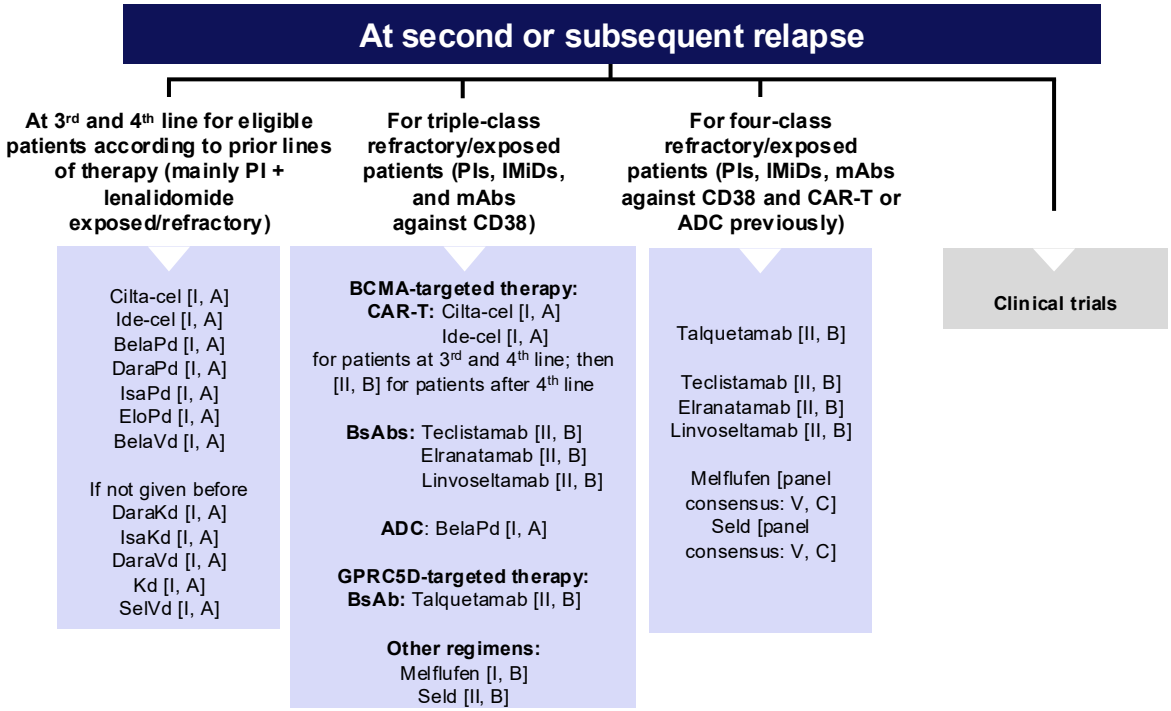


Figure from Dimopoulos MA, et al. EHA-EMN Evidence-Based Guidelines for diagnosis, treatment and follow-up of patients with multiple myeloma. *Nat Rev Clin Oncol*. 2025;22(9):680–700. Springer Nature.
ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; Bela, belantamab mafodotin; BsAb, bispecific monoclonal antibody; CAR-T, chimeric antigen receptor T; cilta-cel, ciltacabtagene autdeucel; 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; K, carfilzomib; Kd, carfilzomib/dexamethasone; L, line; mAb, monoclonal antibody; Pd, pomalidomide/dexamethasone; PI, proteasome inhibitor; Sel, selinexor; Vd, bortezomib/dexamethasone.
Dimopoulous MA, et al. *Nat Rev Clin Oncol*. 2025;22:680–700.

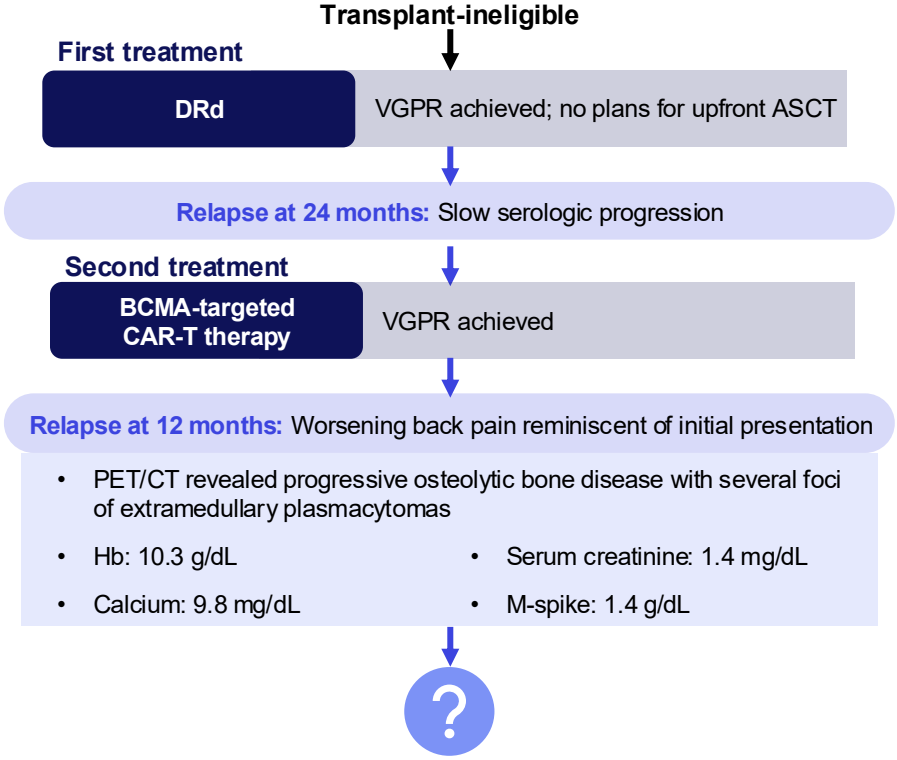
Age	76 years old
Sex	Male
MM diagnosis	• IgG Kappa multiple myeloma • Progressive bone aches and pains • Mild fatigue • PET/CT: Diffuse osteolytic bone disease in the axial and appendicular skeleton
Comorbidities	• Hypertension • Hyperlipidemia • Obstructive sleep apnea • Obesity
Additional notes	• Karyotype: 46, XY

MM diagnosis: Key findings		
Myeloma subtype	• IgG Kappa • M-spike: 4.1 • IgG: 4980 mg/dL, IgA: 30 mg/dL, IgM: 10 mg/dL	
SLiM CRAB	• S -	Clonal plasma cells: 70% kappa-restricted monotypic plasma cells
	• Li -	KLR: / LLC: Kappa: 200/ Lambda: 3
	• M -	MRI: N/A
	• C -	Calcium: 10.3 mg/dL
	• R -	Serum creatinine: 1.36 mg/dL
	• A -	Hb: 10.9 g/dL
	• B -	X-ray: Diffuse osteolytic lesions
Staging	• Durie-Salmon Stage IIIa • ISS Stage III (B2M, 6.1 mg/L; albumin, 3.0 g/dL) • R-ISS Stage III • LDH: 452 U/L • FISH: del 17p, 1q amplification, 13q-	

B2M, beta-2 microglobulin; CRAB, hypercalcemia, renal insufficiency, anemia and bone disease; FISH, fluorescence in situ hybridization; Hb, hemoglobin; IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M; ISS, International Staging System; KLR, kappa/lambda ratio; LDH, lactate dehydrogenase; LLC, involved free light chain level; MM, multiple myeloma; MRI, magnetic resonance imaging; PET/CT, positron emission tomography/computed tomography; R-ISS, Revised International Staging System; SLiM, ≥60% clonal plasma cells, light chain ratio ≥100, and >1 focal lesion on MRI.

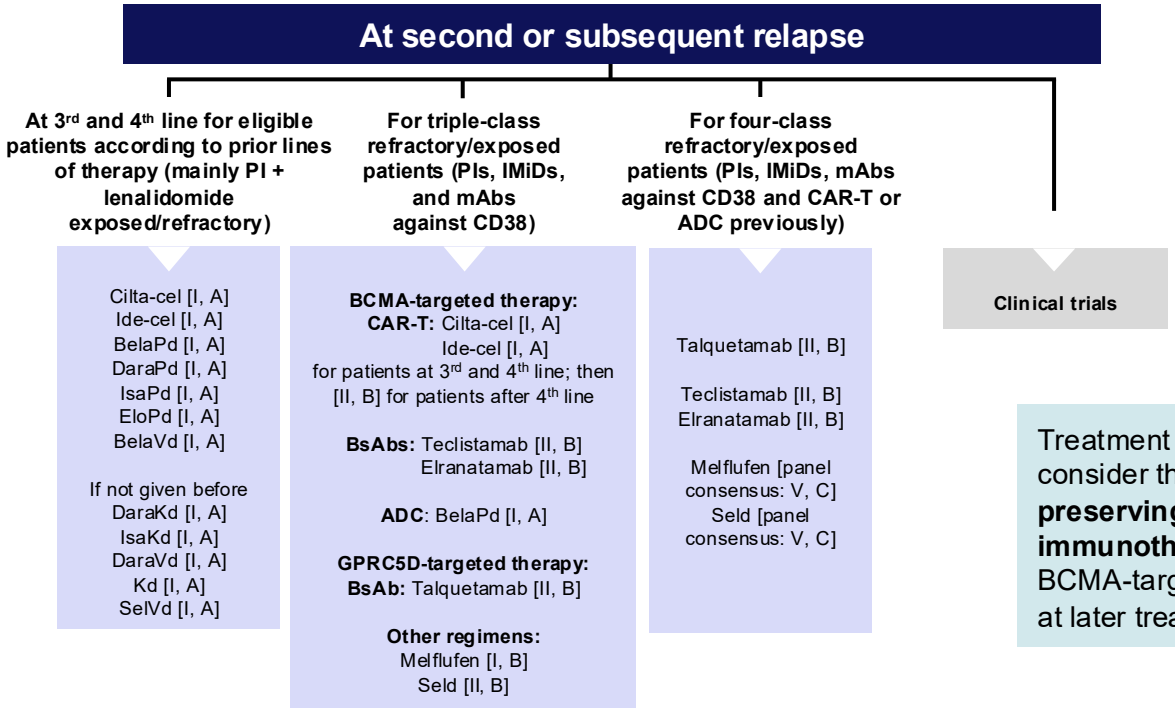
Representative patient case provided by Dr Richter.

Age	76 years old
Sex	Male
MM diagnosis	• IgG Kappa multiple myeloma • Progressive bone aches and pains • Mild fatigue • PET/CT: Diffuse osteolytic bone disease in the axial and appendicular skeleton
Comorbidities	• Hypertension • Hyperlipidemia • Obstructive sleep apnea • Obesity
Additional notes	• Karyotype: 46, XY



ASCT, autologous stem cell transplant; BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T; DRd, daratumumab/lenalidomide/dexamethasone; Hb, hemoglobin; IgG, immunoglobulin G; PET/CT, positron emission tomography/computed tomography; VGPR, very good partial response.
Representative patient case provided by Dr Richter.

EHA/EMN recommendations for the treatment of relapsed/refractory multiple myeloma at second or subsequent relapse[1]



Treatment sequencing should consider the **importance of preserving the effectiveness of immunotherapies**, such as BCMA-targeted therapies, at later treatment lines[2,3]

Figure from Dimopoulos MA, et al. EHA-EMN Evidence-Based Guidelines for diagnosis, treatment and follow-up of patients with multiple myeloma. *Nat Rev Clin Oncol*. 2025;22(9):680–700. Springer Nature.
ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; Bela, belantamab mafodotin; BsAb, bispecific monoclonal antibody; CAR-T, chimeric antigen receptor T; cilta-cel, ciltacabtagene autdeucel; 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; IMWG, international myeloma working group; Isa, isatuximab; K, carfilzomib; Kd, carfilzomib/dexamethasone; mAb, monoclonal antibody; Pd, pomalidomide/dexamethasone; PI, proteasome inhibitor; Sel, selinexor; SoC, standard of care; Vd, bortezomib/dexamethasone.
1. Dimopoulous MA, et al. *Nat Rev Clin Oncol*. 2025;22:680–700; 2. van de Donk NWC, et al. *Hemasphere*. 2025;9:e70260; 3. Costa LJ, et al. *Leukemia*. 2025;39:543–554.

Innovative therapeutic approaches with novel mechanisms of action are expanding treatment options in R/R MM

Bispecific antibodies

Selective inhibitors of nuclear export
(selinexor)**

Cellular therapy

We need to better understand the **optimal sequencing of these novel therapies** to **improve patient survival rates**

Cereblon E3 ligase modulators (CELMoDs)
(non-approved:
iberdomide, CC-92480)

therapeutic classes and drugs for R/R MM

Antibody-drug conjugate
(Belantamab mafodotin§)

*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, EMA approved 1L+ in combination Vd or Pd.
Cilta-cel, ciltacabtagene autoleucel; EMA, European Medicines Agency; ide-cel, idecabtagene vicleucel; IMiD, immunomodulatory drug; L, line; MM, multiple myeloma; Pd, pomalidomide/dexamethasone; PI, proteasome inhibitor; R/R, relapsed/refractory; Vd, bortezomib/dexamethasone.
Davis LN, et al. *Cancers*. 2021;13:1686.

When selecting treatment at relapse, it is important to consider the treatment target

BCMA, B-cell maturation antigen.

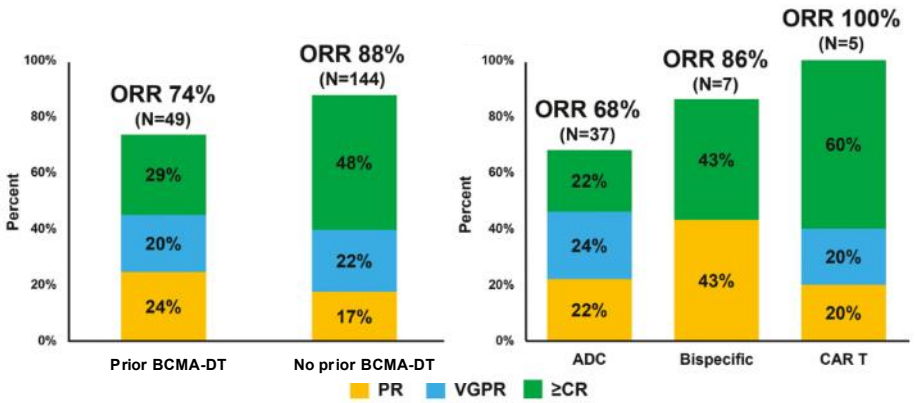
Devarakonda S, et al. *Hematology Am Soc Hematol Educ Program*. 2022;2022:560–568; Nathwani N, et al. *Am Soc Clin Oncol Educ Book*. 2021;41:358–375; Binder AF, et al. *Front Immunol*. 2023:14:1275329; Zhou X, et al. *Haematologica*. 2023;108:958–968; Jaggers JL, et al. *J Geriatr Oncol*. 2021;12:235–238.

Treatment outcomes with CAR-T cell therapy are negatively impacted by 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 with the cohort without prior BCMA-DT

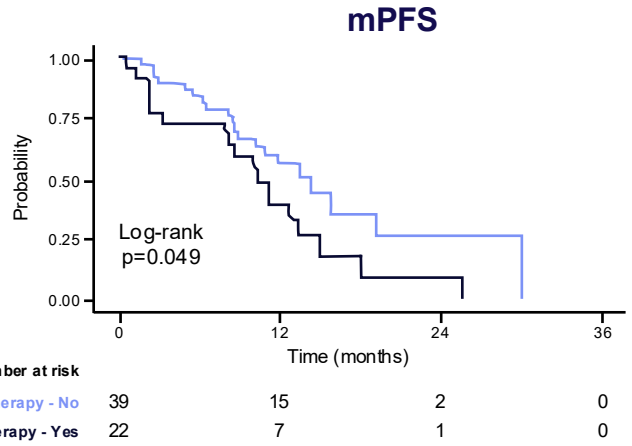
Treatment with ide-cel after prior BCMA-DT resulted in a relatively high ORR, **but significantly lower ORR, median DoR, and median PFS compared with patients not receiving a prior BCMA-DT**

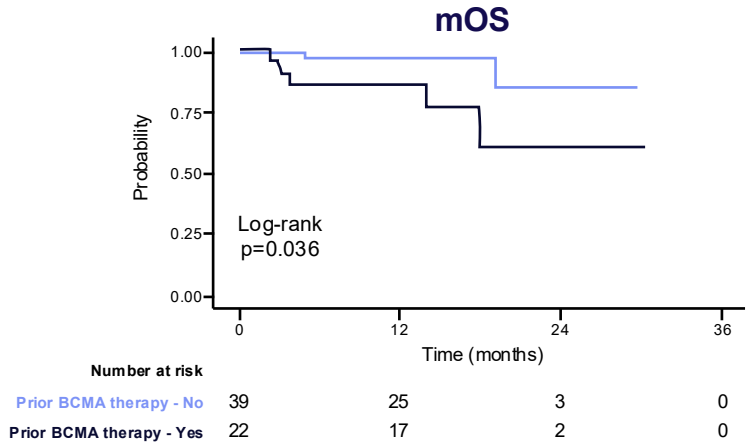


ADC, antibody drug conjugate; BCMA-DT, B-cell maturation antigen-directed therapy; CAR-T, chimeric antigen receptor T; CR, complete response; DoR, duration of response; ide-cel, idecabtagene vicleucel; MM, multiple myeloma; ORR, overall response rate; PFS, progression-free survival; PR, partial response;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

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

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

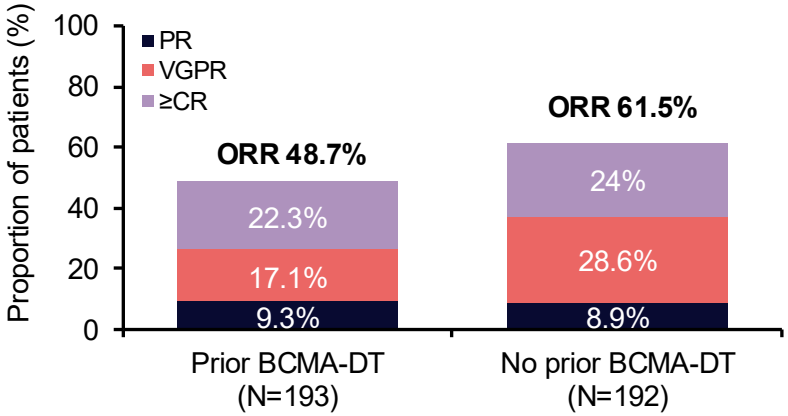


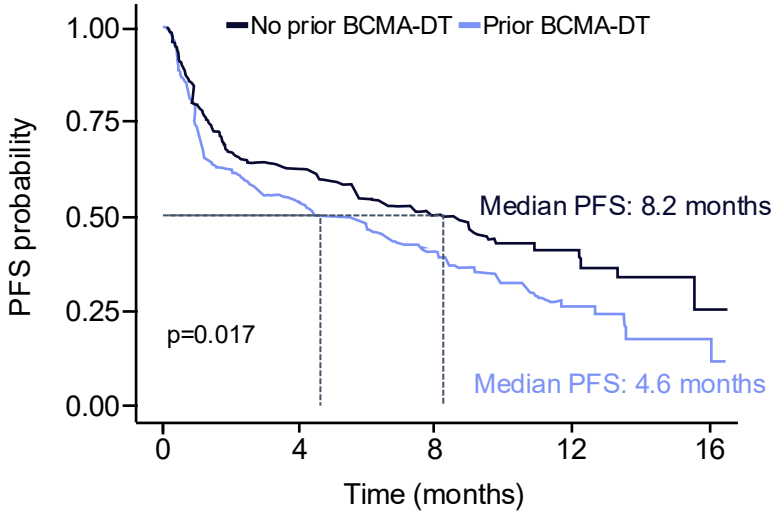


- Patients with **prior exposure to belantamab** had significantly **inferior median PFS** (p=0.049) and **median OS** (p=0.036) vs. those without prior exposure to belantamab
- Among patients who received belantamab, **median PFS was significantly lower in patients who had a partial response or better 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. Presented at ASH 2024; poster presentation 3789.

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

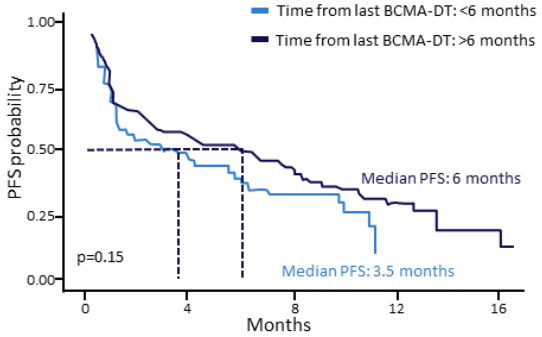


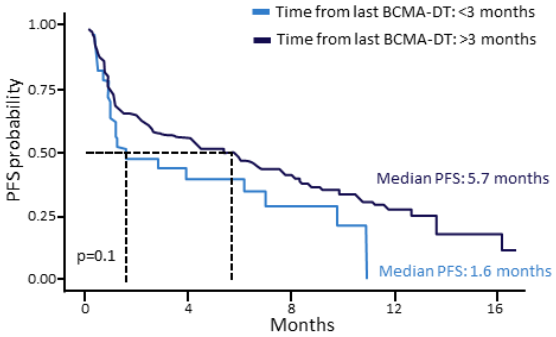


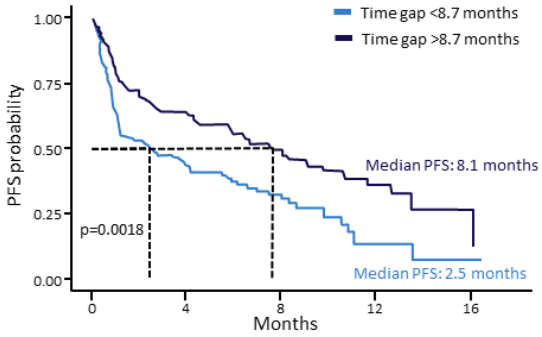
- The prior BCMA-DT cohort had **worse ORR** (p=0.012) **and ≥VGPR** (p=0.009), but **similar ≥CR rates** (p=0.78) compared with those without prior BCMA-DT
- In MVA, there was a strong signal for worse ORR in the prior BCMA-DT cohort; however, prior BCMA-DT was not independently associated with the 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; 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. Presented at ASH 2024; oral presentation 897.

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



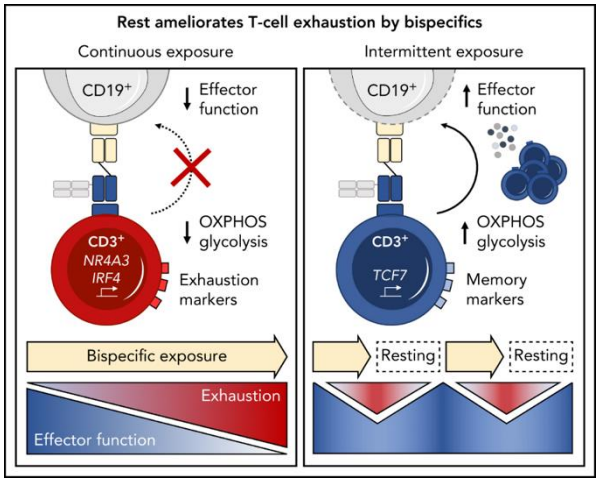




Patients with >8.7 months between last exposure to prior BCMA-DT and teclistamab initiation had a **superior median PFS with teclistamab** (8.1 months, 95% CI: 4.6–11.7) vs. <8.7 months (2.5 months, 95% CI: 1.1–5.7; p=0.001)

BCMA-DT, B-cell maturation antigen-directed therapy; CI, confidence interval; PFS, progression-free survival.
Dima D, et al. Presented at ASH 2024; oral presentation 897.

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
- Accumulating data suggest that **treatment-free intervals** can be **beneficial** in functional and transcriptional T-cell rejuvenation

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

Figure reprinted from *Blood*, 140(10), Philipp N, et al. T-cell exhaustion induced by continuous bispecific molecule exposure is ameliorated by treatment-free intervals. 1104–1118, Copyright (2026), with permission from Elsevier.
BCMA, B-cell maturation antigen.
Binder AF, et al. *Front Immunol*. 2023:14:1275329; Philipp N, et al. *Blood*. 2022:140:1104–1118.

The IMWG recommend using different mechanisms of action 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 combinations 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 who relapsed post-BCMA-targeted CAR-T cell therapies[3]

IMWG 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 T-cell engager

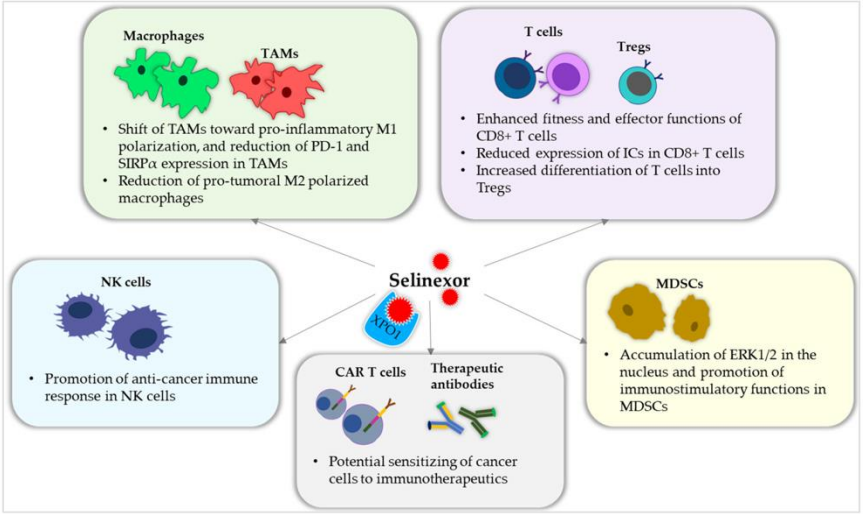
*Selinexor and selinexor-based combinations were 1 of 5 therapeutic options described by the authors. Post-TCRT salvage with non-TCRT therapies has not been systematically investigated; †Selinexor combinations in the STOMP trial are not all approved.

BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T; IMWG, International Myeloma Working Group; TCRT, T-cell redirecting therapy; XPO1, exportin 1.

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

Selinexor influences multiple immune cell pathways, with the potential to influence the immunological tumor microenvironment in MM

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



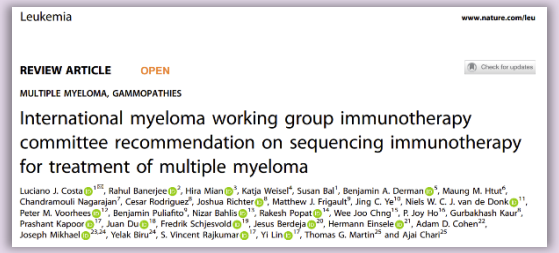
Selinexor is suggested to **impact macrophages** and **tumor-associated macrophages** (TAMs), **myeloid-derived suppressor cells** (MDSCs), **natural killer** (NK) **cells**, and T cells in the **tumor microenvironment**

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; ERK1/2, extracellular-signal regulated kinase 1/2; IC, immune checkpoint; MDSC, myeloid-derived suppressor cell; MM, multiple myeloma; NK, natural killer; PD-1, programmed death 1; SIRPα, signal regulatory protein alpha; TAM, tumor-associated macrophage; Treg, regulatory T cell; XPO1, exportin 1.
Tasbihi K, Bruns H. *Cells*. 2025;14:430.

XPO1 inhibitors have the potential to promote T-cell fitness, reduce T-cell exhaustion, and decrease T-cell activation

Promote T-cell fitness[1]


Leukemia

www.nature.com/leu

REVIEW ARTICLE OPEN

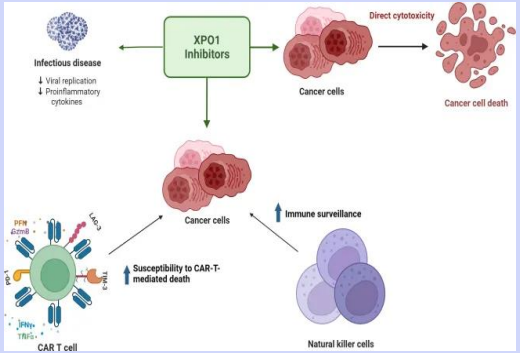
MULTIPLE MYELOMA, GAMMOPATHIES

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[9], Matthew J. Frigault[9], Jing C. Ye[10], Niels W. C. J. van de Donk[11], Peter M. Voorhees[12], Benjamin Puliafito[13], Nizar Bahlis[14], Rakesh Popat[15], Wee Joo Chng[16], P. Joy Ho[17], Gurbakhush Kaur[6], 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]

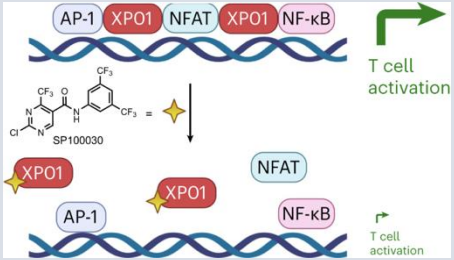
*"In addition to direct cytotoxicity against malignant cells, XPO1 inhibitors may **modulate the immune microenvironment to promote T-cell fitness**"*

Reduce T-cell exhaustion[2]



*"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"*

Decrease T-cell activation[3*]



XPO1 is essential for the chromatin occupancy of NFAT transcription factors, a key component of appropriate T-cell activation

XPO1 inhibitors may **disrupt the binding of XPO1 to chromatin**, **decreasing T-cell activation** without inducing cytotoxicity

*Figure reprinted from *Nat Chem Biol*, 20(10), Chen YF, et al. Targeting the chromatin binding of exportin-1 disrupts NFAT and T cell activation. 1260–1271, Copyright (2026), with permission from Elsevier.
AP-1, activator protein-1; NF-kB, nuclear factor kappa B; NFAT, nuclear factor of activated T-cells; XPO1, exportin 1.

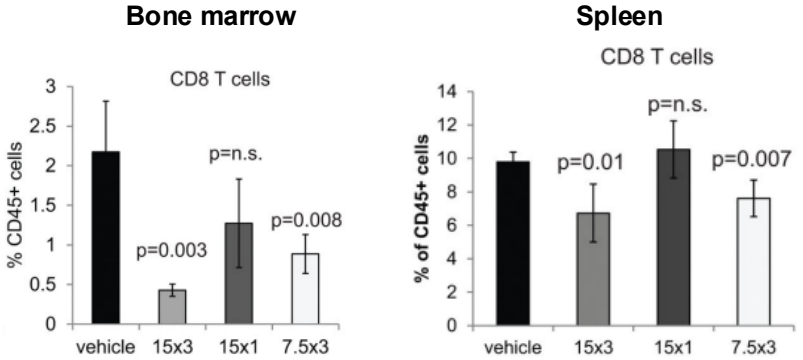
1. Costa LJ, et al. *Leukemia*. 2025;39:543–554; 2. Binder AF, et al. *Front Immunol*. 2023;14:1275329; 3. Chen YF, et al. *Nat Chem Biol*. 2024;20:1260–1271.

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)

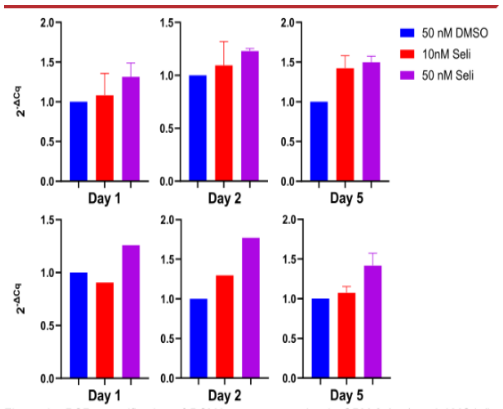
Group	Treatment	Schedule
Vehicle	Vehicle	3x week
15x3	Selinexor 15 mg/kg	3x week
15x1	Selinexor 15 mg/kg	1x week
7.5x3	Selinexor 7.5 mg/kg	3x week



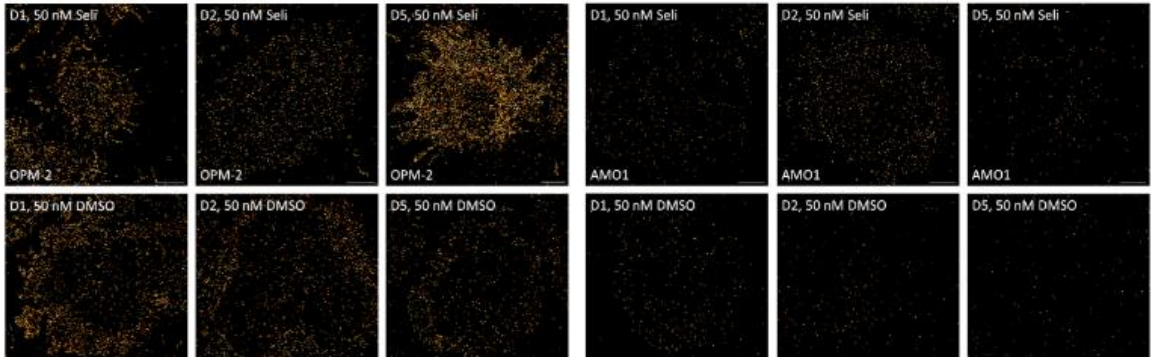
Figures reprinted from *Mol Cancer Ther*, 2017;16(3):428–439, Tyler P, et al. Clinical Dosing Regimen of Selinexor Maintains Normal Immune Homeostasis and T-cell Effector Function in Mice: Implications for Combination with Immunotherapy, with permission from AACR
n.s., not significant.
Tyler P, et al. *Mol Cancer Ther*. 2017;16:428–439.

Selinexor treatment leads to a time- and dose-dependent upregulation of BCMA expression in MM cell lines

Selinexor increased BCMA gene expression*



Selinexor increased BCMA receptor expression†



In **OPM-2 cells**, after 5 days, selinexor-treated cells exhibited a **4.2-fold elevation in BCMA receptor density** compared with controls

- In **AMO1 cells**, despite lower baseline BCMA expression, a **comparable trend** was observed

The significant increase in BCMA receptor density in a time- and dose-dependent fashion suggests that selinexor may **enhance target antigen availability on the cell surface**, potentially **improving the efficacy of BCMA-directed immunotherapies**

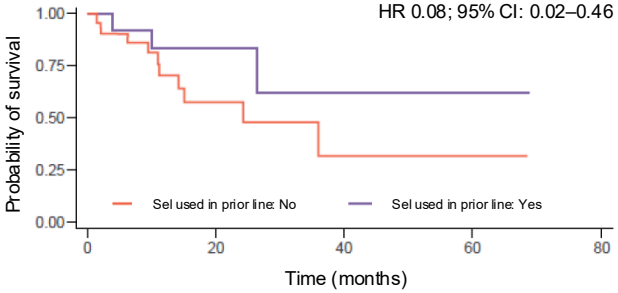
*qPCR was employed to measure gene expression levels; †dSTORM images of OPM-2 and AMO1 cells after 1, 2, and 5 days of treatment, respectively. Scale bars, 3 µm. Each yellow dot corresponds to 1 BCMA receptor.
BMCA, B-cell maturation antigen; DMSO, dimethyl sulfoxide; dSTORM, direct stochastic optical reconstruction microscopy; MM, multiple myeloma; qPCR, quantitative polymerase chain reaction; Seli, selinexor.
Verbruggen C, et al. Presented at ASH 2025; poster presentation 6102.

Sequencing selinexor and BCMA-directed CAR-T therapy may positively impact treatment outcomes

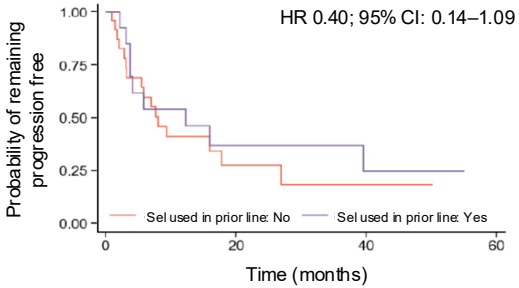
- In a retrospective cohort study, the impact of prior treatment with a selinexor-containing regimen on CAR-T outcomes was evaluated in patients with R/R MM
- The BCMA-directed CAR-T products administered included ide-cel (60%), cilta-cel (35.6%), and CC-98633/BMS-986354 (4.4%)

- At a median follow-up of 68 months, **median DoR was 8.1 months** (IQR 2.6–39), **median PFS was 8.1 months** (IQR 3.1–39.5), and **median OS was 35.9 months** (IQR 14.2–NR)

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



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



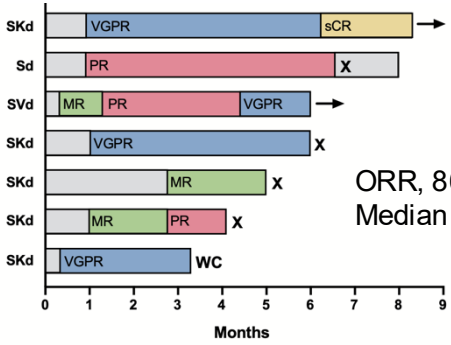
Patients who received selinexor in the **therapy line immediately preceding CAR-T** demonstrated **longer PFS and OS** compared with those exposed in earlier lines

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

Selinexor combinations after BCMA therapy

Retrospective analysis of 7 heavily pretreated patients with MM progressing after BCMA CAR-T therapy who received selinexor-containing regimens[1]

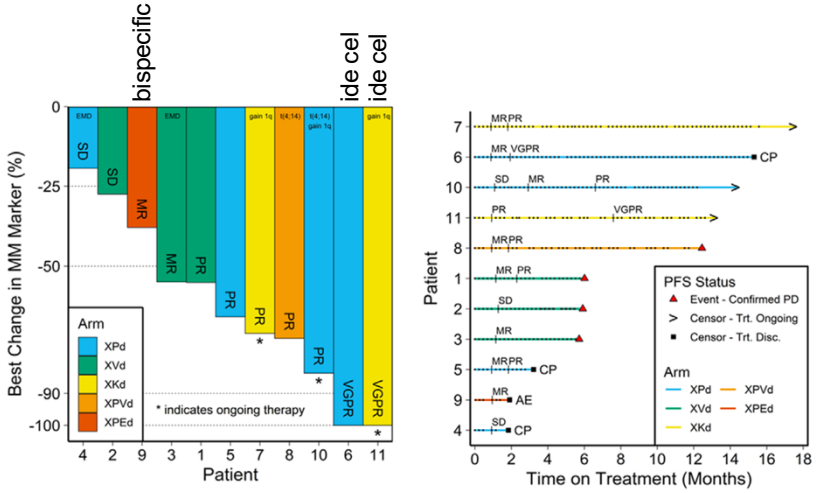
Pt	Treatment	Best response on selinexor regimen	Time to response ≥PR (months)	Time on study (months)	Duration of response ≥PR (months)	Off study Reason	Therapy after selinexor regimen
1	Sd	PR	0.9	8.0	5.6	PD	TAK573
2	SKd	PR	2.7	4.1	1.4	PD	Not Started
3	SKd	sCR	0.9	8.3+	7.4+	Ongoing	–
4	SKd	VGPR	1.0	6.0	5.0	PD	CC220 + Carfilzomib
5	SKd	MR	–	5.0	–	PD	DCEP
6	SKd	VGPR	0.3	3.7	3.4	WC	BET inhibitor
7	SVd	VGPR	1.4	6.0+	4.6+	Ongoing	–



ORR, 86%
Median PFS, ~6 months

STOMP (NCT02343042): Open-label, Phase 1b/2 clinical study[2]

Data from 11 heavily pretreated patients who received anti-BCMA agents and were treated with five different selinexor-containing regimens



- 7/11 had prior anti-BCMA ADC (mainly belantamab mafodotin, 1 had MEDI2228)
- 2/11 had prior CAR-T (ide-cel ± Dara)
- 1/11 had prior anti-BCMA bispecific antibody (BCMA BiTE)
- 8/11 had anti-BCMA therapy as last prior LOT

ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; BET, bromodomain and extra-terminal; BiTE, bispecific T-cell engager; CAR-T, chimeric antigen receptor T; dara, daratumumab; DCEP, dexamethasone, cyclophosphamide, etoposide and cisplatin; ide-cel, idecabtagene vicleucel; LOT, line of therapy; MM, multiple myeloma; MR, minimal response; ORR, overall response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; sCR, stringent complete response; Sd, selinexor/dexamethasone; SKd, selinexor/carfilzomib/dexamethasone; SVd, selinexor/bortezomib/dexamethasone; VGPR, very good partial response; WC, withdrawal of consent; X, selinexor.

1. Chari A, et al. *Br J Haematol*. 2020;189(4):e126-e130. 2. Baljevic M, et al. *EJHaem*. 2022;3(4):1270-1276.

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Age	76 years old
Sex	Male
MM diagnosis	• IgG Kappa multiple myeloma • Progressive bone aches and pains • Mild fatigue • PET/CT: Diffuse osteolytic bone disease in the axial and appendicular skeleton
Comorbidities	• Hypertension • Hyperlipidemia • Obstructive sleep apnea • Obesity
Additional notes	• Karyotype: 46, XY

First treatment

DRd — VGPR achieved; no plans for upfront ASCT

Second treatment

BCMA-targeted CAR-T therapy — VGPR achieved

Relapse at 12 months: Worsening back pain reminiscent of initial presentation

Considerations for third-line treatment:

- Concern for downregulation of the BCMA target
- CD38 refractory
- IMiD-refractory
- PI-naïve
- Concern for T-cell compromise given lymphodepletion chemotherapy and CAR-T relapse

ASCT, autologous stem cell transplant; BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T-cell; DRd, daratumumab/lenalidomide/dexamethasone; IgG, immunoglobulin G; IMiD, immunomodulatory imide drug; PET/CT, positron emission tomography/computed tomography; PI, proteasome inhibitor; VGPR, very good partial response.
Representative patient case provided by Dr Richter.

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Third treatment

SVd
S: 100 mg QW
V: 1.3 mg/m^2 QW
d: 20 mg BIW

- At Cycle 3 Day 1, platelet count was 40 ×10^9/L
- Treatment held; selinexor dose reduced to 80 mg
- Platelet count recovered and patient continued SVd
- **Deepest remission was VGPR**

Relapse at 11 months: Serologic progression

Fourth treatment

Clinical trial with a BCMAxGPRC5dxCD3 trispecific antibody

- Currently in CR/MRD- state at Cycle 6
- Tolerating therapy well

ASCT, autologous stem cell transplant; BCMA, B-cell maturation antigen; BIW, twice weekly; CAR-T, chimeric antigen receptor T; CR, complete response; DRd, daratumumab/lenalidomide/dexamethasone; IgG, immunoglobulin G; MRD, minimal residual disease; PET/CT, positron emission tomography/computed tomography; QW, once weekly; SVd, selinexor/bortezomib/dexamethasone; VGPR, very good partial response.
Representative patient case provided by Dr Richter.

Summary
Maximizing efficacy with optimal sequencing: A case-based discussion

- With the **emergence of novel therapies** for R/R MM, there is a need to better understand the **optimal sequencing of therapeutics** to improve patient survival outcomes
- Treatment outcomes with BCMA-directed therapies at later lines can be **negatively impacted by prior exposure** to other **BCMA-directed therapies**
- **Treatment-free intervals** can be beneficial in **counteracting T-cell exhaustion** and **improving T-cell rejuvenation**
- Incorporating **selinexor combinations** as **BCMA-free regimens** can optimize sequencing and improve outcomes **prior to or between BCMA-targeted therapies**

BCMA, B-cell maturation antigen; R/R MM, relapsed refractory multiple myeloma.

Translating evidence into practice: A case-led discussion of real-world practice challenges

Gabriele Buda

University of Pisa, Pisa, Italy

MENARINI group

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Disclosures

- **Participation in advisory board meetings:** GSK, J&J, BMS, Takeda, Sanofi, Pfizer, Amgen, Menarini Stemline, and Oncopeptides
- **Other:** GSK, J&J, BMS, Takeda, Sanofi, Pfizer, Amgen, Menarini Stemline, and Oncopeptides

Age	72 years old
Sex	Male
MM diagnosis	• Anemia – Hb: 9.2 g/dL • Bone disease – Whole body CT: Multiple osteolytic lesions
Comorbidities	Hypertension and dyslipidemia
Performance status	• ECOG PS: 1 • ADL: 6 / IADL: 7 • CCI: 3 • LVEF: 60% • IMWG frailty: Intermediate-fit • No baseline neuropathy

MM diagnosis: Key findings

Myeloma subtype	• IgG kappa • M-protein: 3.8 g/dL	
SLiM CRAB	• S -	Clonal plasma cells: 45%
	• Li -	Kappa FLC: 420 mg/L | Ratio 18
	• M -	Spine MRI: Focal lesions L2–L4
	• C -	Calcium: 10.1 mg/dL
	• R -	Creatinine: 1.3 mg/dL
	• A -	Hb: 9.2 g/dL
	• B -	Whole-body CT: Multiple osteolytic lesions
Staging	• ISS Stage II / R-ISS Stage II • CD38+, CD138+, and CD56+ • FISH: Isolated del(13q) • β2-macroglobulin: 4.8 mg/L	

ADL, activities of daily living; CCI, Charleson Comorbidity Index; CT, computed tomography; del(13q), deletion of 13q14; ECOG PS, Eastern Cooperative Oncology Group Performance Status; FISH, fluorescence in situ hybridization; FLC, free light chain; Hb, hemoglobin; IADL, instrumental activities of daily living; IgG, immunoglobulin G; IMWG, International Myeloma Working Group; ISS, International Staging System; LVEF, left ventricular ejection fraction; MM, multiple myeloma; MRI, magnetic resonance imaging; R-ISS, Revised International Staging System.
Representative patient case provided by Dr Buda.

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Transplant-ineligible

First treatment

Dara-Rd (continuous) → VGPR achieved after 6 cycles

Relapse at 36 months: Rapid biochemical progression (0.7 to 3.5 g/dL)

- Hb: Decline from 9.2 g/dL to 8.7 g/dL
- FLC doubling time: <3 months
- PET-CT: New hypermetabolic lesions (~T7; iliac bone)
- Clonal plasma cells: 60%
- Lenalidomide-refractory disease

Considerations for second line treatment

- Novel mechanism needed
- Avoid cumulative neuropathy
- Prior anti-CD38 exposure
- Route of administration
- Lenalidomide-refractory disease

ADL, activities of daily living; CCI, Charleson Comorbidity Index; CT, computed tomography; Dara-Rd, daratumumab/lenalidomide/dexamethasone; ECOG PS, Eastern Cooperative Oncology Group Performance Status; FLC, free light chain; Hb, hemoglobin; IADL, instrumental activities of daily living; IMWG, International Myeloma Working Group; LVEF, left ventricular ejection fraction; PET-CT, positron emission tomography-computed tomography; VGPR, very good partial response.

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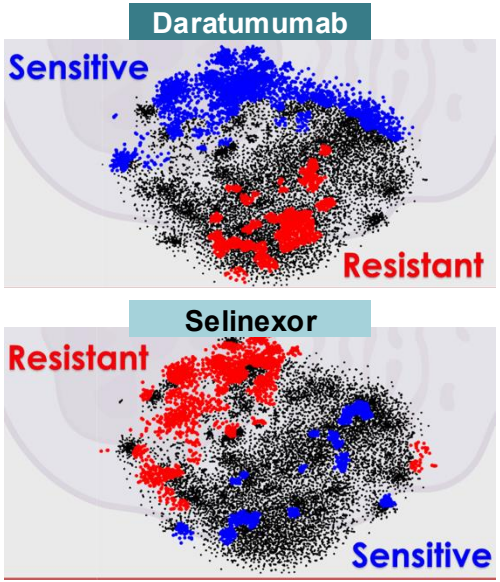
- Route of administration
- Lenalidomide-refractory disease

ADL, activities of daily living; CCI, Charleson Comorbidity Index; CT, computed tomography; Dara-Rd, daratumumab/lenalidomide/dexamethasone; ECOG PS, Eastern Cooperative Oncology Group Performance Status; FLC, free light chain; Hb, hemoglobin; IADL, instrumental activities of daily living; IMWG, International Myeloma Working Group; LVEF, left ventricular ejection fraction; PET-CT, positron emission tomography-computed tomography; VGPR, very good partial response.

Representative patient case provided by Dr Buda.

Gene clusters associated with daratumumab resistance have been shown to be linked to selinexor sensitivity *ex vivo*

Daratumumab	
Sensitivity	Resistant
KEGG pathways	
• Inflammatory cytokines • Complement and coagulation • Focal adhesion	• Ribosome • Spliceosome • RNA degradation • RNA polymerase • Proteasome
Cancer hallmarks	
• KRAS up-signaling • TNFα signaling via NFκβ • Hypoxia • Myogenesis • Complement	• MYC and E2F targets • OxPhos • DNA repair • Protein secretion
Mutations	



Selinexor	
Sensitivity	Resistant
KEGG pathways	
• Ribosome • Spliceosome	• Inflammatory cytokines • Cell adhesion
Cancer hallmarks	
• MYC targets • OxPhos • DNA repair	• KRAS up-signaling • EMT • Angiogenesis
Mutations	
• *BCL7A*	• *CEP290*

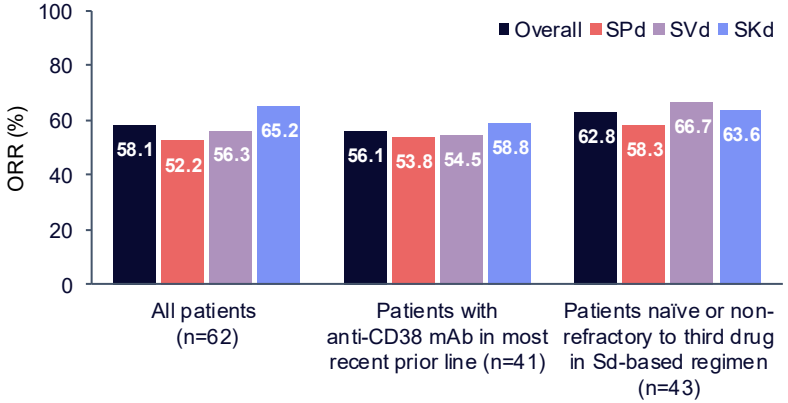
BCL7A, BAF chromatin remodeling complex subunit BCL7A; *CEP290*, centrosomal protein 290; DNA, deoxyribonucleic acid; EMT, epithelial-mesenchymal transition; KEGG, Kyoto Encyclopedia of Genes and Genomes; KRAS, KRAS proto-oncogene; MYC, MYC proto-oncogene; NFκβ, nuclear factor kappa-light-chain-enhancer of activated B cells; OxPhos, oxidative phosphorylation; RNA, ribonucleic acid; TNFα, tumor necrosis factor-α.
Sudalagunta PR, et al. Presented at ASH 2021; Oral presentation #898.

Selinexor-based regimens may serve as efficacious treatment options for patients who have received prior anti-CD38 mAb therapies

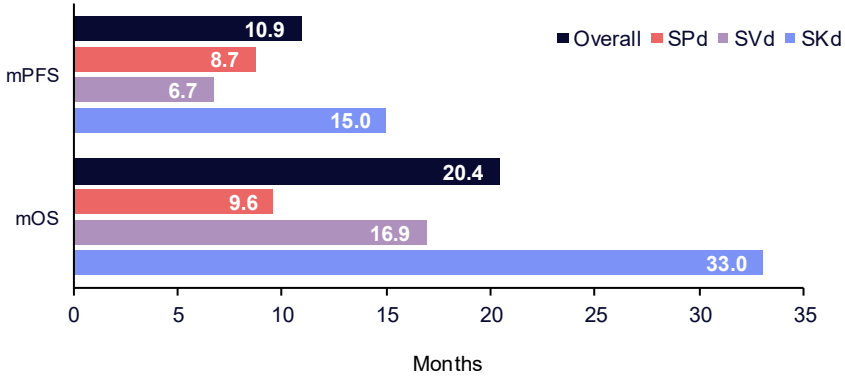
A subset analysis of selinexor-based triplet regimens in STOMP and BOSTON study patients who were previously treated with an anti-CD38 mAb[1]

Patients had received a median of **4.0 prior lines of therapy**, **90.3%** were **anti-CD38 mAb-refractory**, and **59.7%** were **triple-class refractory**

Overall response rate[1]



PFS and OS*[1]



CBR was 72.6% among all patients, with similar percentages in each cohort

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

Only SVd is indicated in the SmPC; SPd and SKd are not approved regimens within the SmPC[2].
*Median follow-up in the overall population was 6.9 months for PFS and 14.5 months for OS.
CBR, clinical benefit rate; mAb, monoclonal antibody; m, median; ORR, overall response rate; mOS, median overall survival; mPFS, median progression-free survival; SKd, selinexor/carfilzomib/dexamethasone; SPd, selinexor/pomalidomide/dexamethasone; SVd, selinexor/bortezomib/dexamethasone.

1. Schiller GJ, et al. *Clin Lymphoma Myeloma Leuk*. 2023;23:e286–e296. 2. EMA. Selinexor: SmPC. Available at: https://www.ema.europa.eu/en/documents/product-information/nexpovio-epar-product-information_en.pdf (Accessed June 2026).

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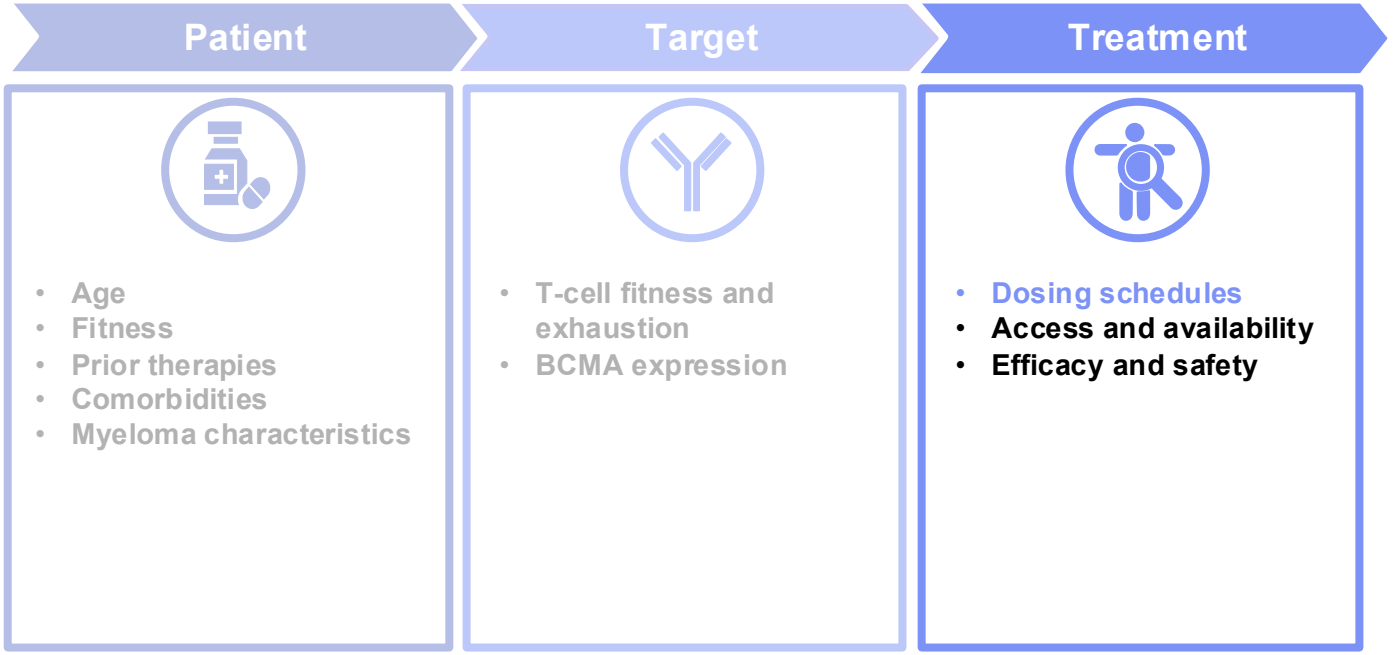
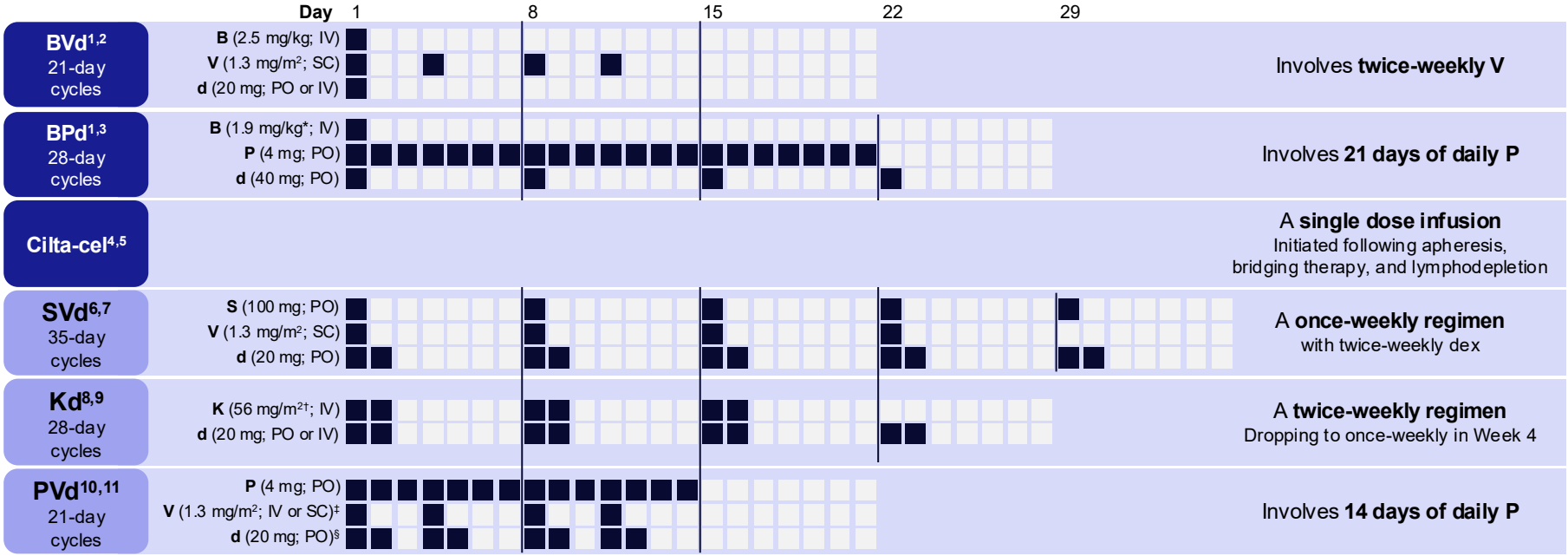
Treatment-related factors should be evaluated when selecting treatment options at relapse



BCMA, B-cell maturation antigen.

Devarakonda S, et al. *Hematology Am Soc Hematol Educ Program*. 2022;2022:560–568; 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; Jaggers JL, et al. *J Geriatr Oncol*. 2021;12:235–238.

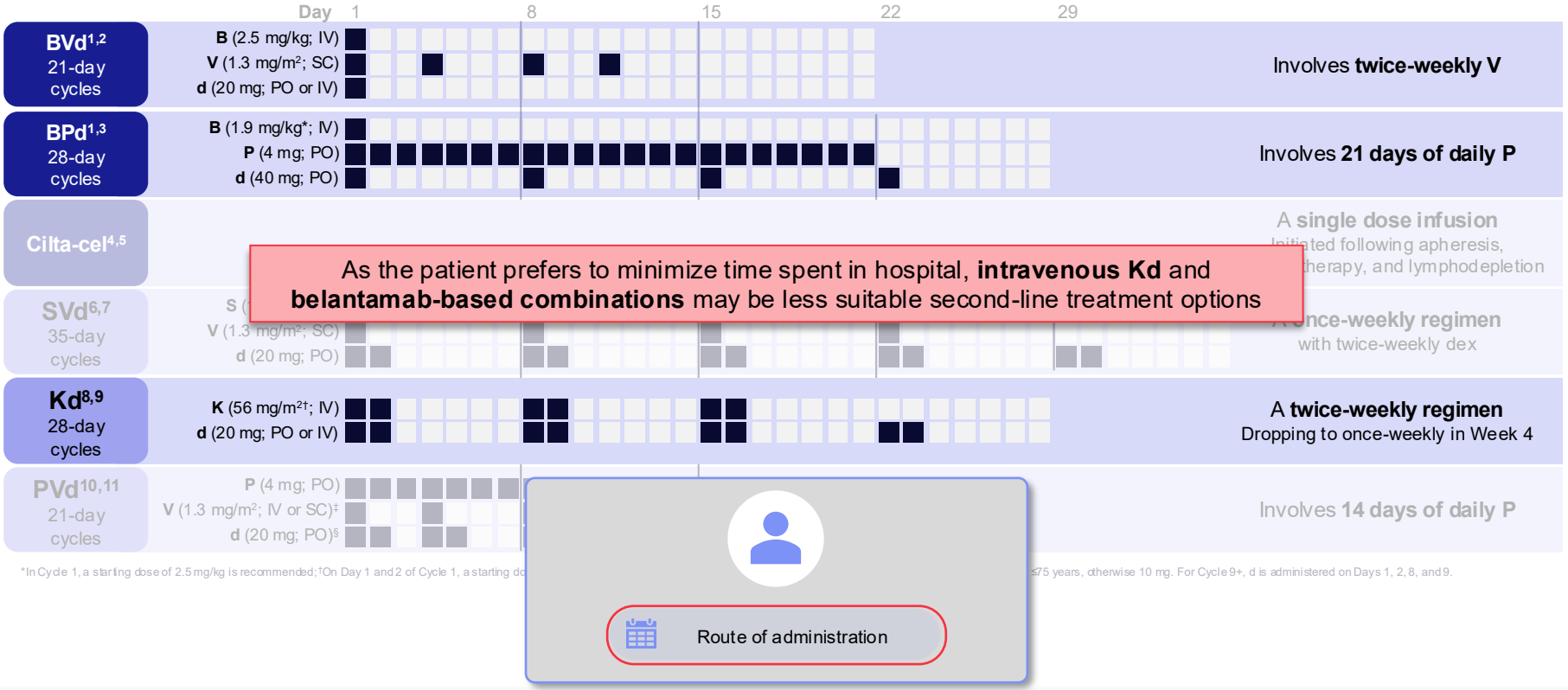
Differences in dosing schedules between second-line treatment options may influence treatment selection



*In Cycle 1, a starting dose of 2.5 mg/kg is recommended; †On Day 1 and 2 of Cycle 1, a starting dose of 20 mg/m² is recommended; ‡For Cycle 9+, V is administered on Days 1 and 8; §20 mg if aged ≤75 years, otherwise 10 mg. For Cycle 9+, d is administered on Days 1, 2, 8, and 9.

BPd, belantamab mafodotin/pomalidomide/dexamethasone; BVd, belantamab mafodotin/bortezomib/dexamethasone; cilta-cel, ciltacabtagene autoleucel; dex, dexamethasone; IV, intravenous; Kd, carfilzomib/dexamethasone; P, pomalidomide; PO, oral; PVd, pomalidomide/bortezomib/dexamethasone; SC, subcutaneous; SVd, selinexor/bortezomib/dexamethasone; V, bortezomib.
1. EMA. Belantamab mafodotin: SmPC. Available at: https://www.ema.europa.eu/en/documents/product-information/blenrep-epar-product-information_en.pdf (Accessed June 2026). 2. Hungria V, et al. *N Eng J Med*. 2024;391:393–407; 3. Dimopoulos MA, et al. *N Engl J Med*. 2024;391:408–421; 4. EMA. Cilta-cel: SmPC. Available at: https://www.ema.europa.eu/en/documents/product-information/carvykti-epar-product-information_en.pdf (Accessed June 2026). 5. San-Miguel J, et al. *N Engl J Med*. 2023;389:335–347; 6. EMA. Selinexor: SmPC. Available at: https://www.ema.europa.eu/en/documents/product-information/nexpovio-epar-product-information_en.pdf (Accessed June 2026). 7. Grosicki S, et al. *Lancet*. 2020;396:1563–1573; 8. EMA. Carfilzomib: SmPC. Available at: https://www.ema.europa.eu/en/documents/product-information/kyprolis-epar-product-information_en.pdf (Accessed June 2026). 9. Dimopoulos MA, et al. *Lancet Oncol*. 2016;17:27–38; 10. EMA. Pomalidomide: SmPC. Available at: https://www.ema.europa.eu/en/documents/product-information/imnovid-epar-product-information_en.pdf (Accessed June 2026). 11. Richardson PG, et al. *Lancet Oncol*. 2019;20:781–794.

Differences in dosing schedules between second-line treatment options may influence treatment selection



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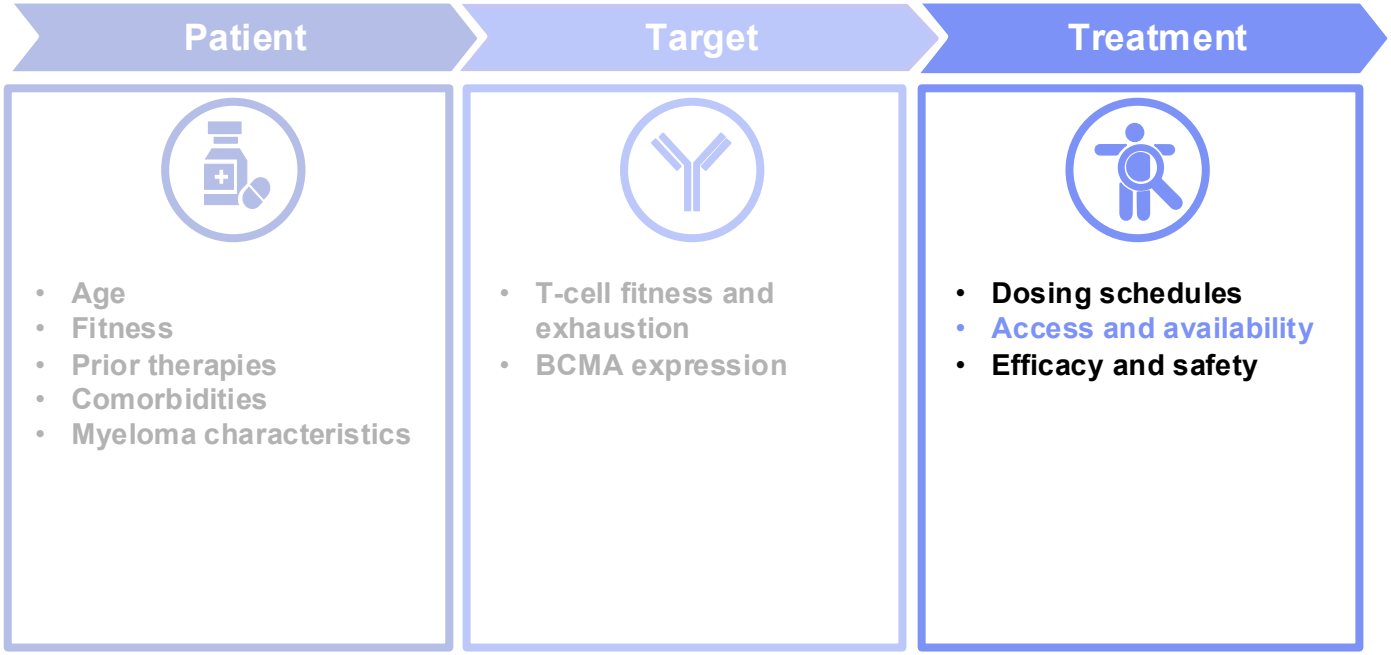
1. EMA. Belantamab mafodotin: SmPC. Available at: https://www.ema.europa.eu/en/documents/product-information/belrinep-epar-product-information_en.pdf (Accessed June 2026); 2. Hungria V, et al. *N Eng J Med*. 2024;391:393–407; 3. Dimopoulos MA, et al. *N Engl J Med*. 2024;391:408–421; 4. EMA. Cilta-cel: SmPC. Available at: https://www.ema.europa.eu/en/documents/product-information/carvykti-epar-product-information_en.pdf (Accessed June 2026); 5. San-Miguel J, et al. *N Engl J Med*. 2023;389:335–347; 6. EMA. Selinexor: SmPC. Available at: https://www.ema.europa.eu/en/documents/productinformation/nexpovio-epar-product-information_en.pdf (Accessed June 2026); 7. Grosicki S, et al. *Lancet*. 2020;396:1563–1573; 8. EMA. Carfilzomib: SmPC. Available at: https://www.ema.europa.eu/en/documents/product-information/kyprolis-epar-product-information_en.pdf (Accessed June 2026); 9. Dimopoulos MA, et al. *Lancet Oncol*. 2016;17:27–38; 10. EMA Pomalidomide: SmPC. Available at: https://www.ema.europa.eu/en/documents/product-information/imnovid-epar-product-information_en.pdf (Accessed June 2026); 11. Richardson PG, et al. *Lancet Oncol*. 2019;20:781–794.

Treatment-related factors should be evaluated when selecting treatment options at relapse



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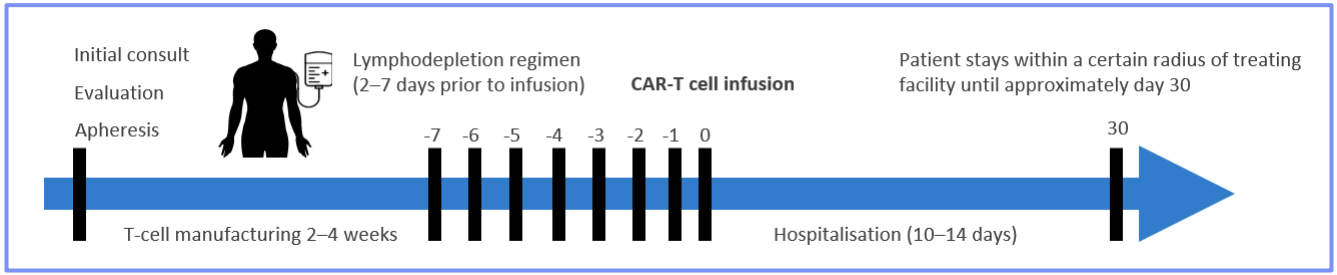
The accessibility and availability of CAR-T cell therapies is limited by manufacturing and administration complexities



Manufacturing-related challenges[1]

- Adherence to **strict regulatory standards**
- Requirement for **rigorous quality control** measures
- Autologous nature requires a **personalized therapy** for each patient
- Need for close collaboration between manufacturer and treatment teams to coordinate complex logistics and **minimize 'vein-to-vein' duration**
- **Disease progression** can occur during the manufacturing and coordination period, leading to **ineligibility**

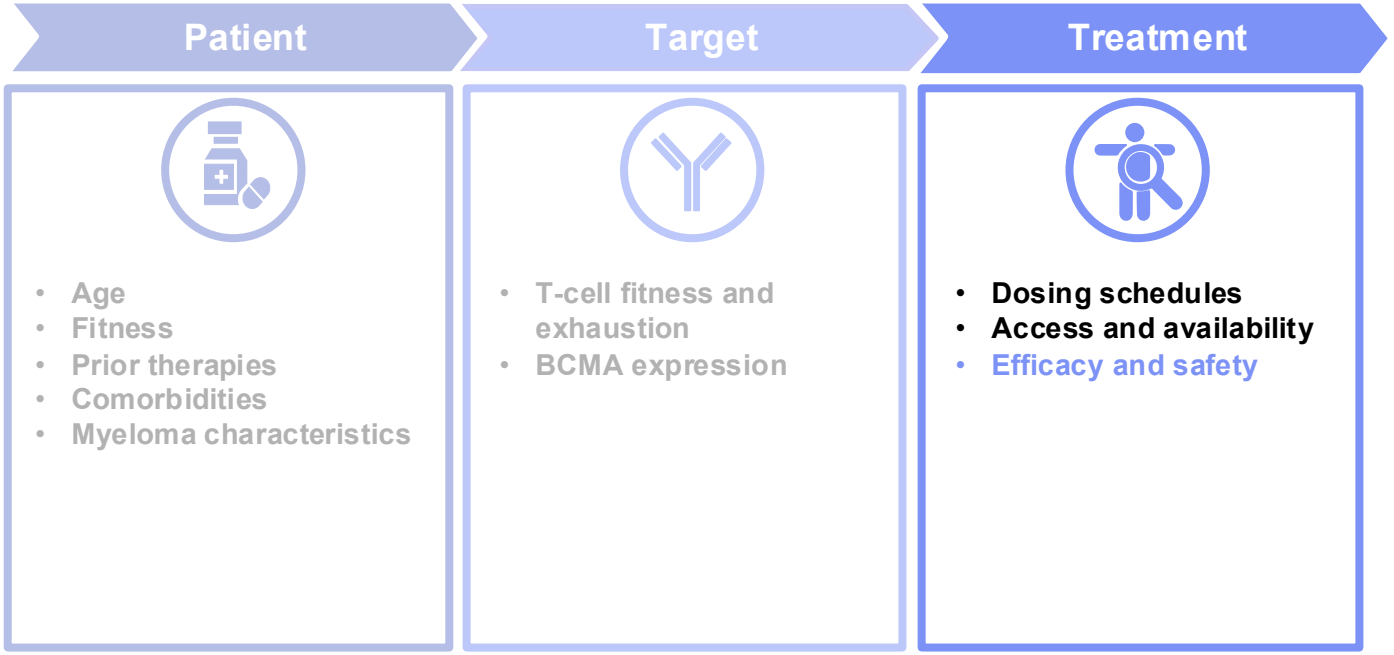
Administration-related challenges[2,3]

- Requirement for **specialist trained personnel**[2]
- Requirement for **specialized treatment centers**[2]
- Availability of **hospital beds** for inpatient treatment[3]
- Time required to assess patient safety and **feasibility of outpatient management**[3]

These factors contribute to the **high cost** of CAR-T cell therapies, which **poses a challenge to healthcare systems**

CAR-T, chimeric antigen receptor T.
1. Bailey S, et al. *Eur J Immunol*. 2023;53:2250039. 2. Ravindranath A, et al. *Cytotherapy*. 2022;24(2):101-109. 3. Lipe DN, et al. *Front Oncol*. 2023;13:1122329.

Treatment-related factors should be evaluated when selecting treatment options at relapse



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Efficacy and safety considerations across emerging and existing second-line treatment options

Treatment	Efficacy considerations (primary endpoint: mPFS)	Safety considerations
BVd or BPd	**BVd vs DVd (DREAMM-7): 36.6 months vs. 13.4 months**[1] • mFU: 28.2 months • HR (95% CI): 0.41 (0.31–0.53); P<0.001 **BPd vs PVd (DREAMM-8): 32.6 months vs. 12.5 months**[2] • mFU: 35.8 months • HR (95% CI): 0.49 (0.36–0.67)	Belantamab mafodotin is commonly associated with **ocular events**[1,3]
Cilta-cel	**Cilta-cel vs SoC (CARTITUDE-4): NR vs. 11.8 months**[4] • mFU: 33.6 months • HR (95% CI): 0.29 (0.22–0.39)	Cilta-cel is commonly associated with **CRS** and **ICANS**;[5,6] therefore, the frailty and fitness of the patient should be considered when evaluating this treatment option[6]
SVd	**SVd vs Vd (BOSTON): 13.93 months vs. 9.46 months**[7] • mFU: SVd, 13.2 months; Vd, 16.5 months • HR (95% CI): 0.70 (0.53–0.93); P=0.0075	Selinexor is commonly associated with **gastrointestinal**, **constitutional** (fatigue and reduced appetite), **hematologic** (thrombocytopenia and neutropenia), and **biochemical** (hyponatremia) adverse events[8]
Kd	**Kd vs Vd (ENDEAVOR): 18.7 months vs. 9.4 months**[9] • mFU: Kd,11.9 months; Vd, 11.1 months • HR (95% CI): 0.53 (0.44–0.65); P<0.0001	Carfilzomib is commonly associated with **cardiovascular toxicities** (e.g., hypertension, heart failure, ischemic heart disease arrhythmias), particularly among patients ≥75 years old and in those of Asian ethnicity[10,11]
PVd	**PVd vs Vd (OPTIMISMM): 11.2 months vs. 7.1 months**[12] • mFU: 15.9 months • HR (95% CI): 0.61 (0.49–0.77); P<0.0001	Pomalidomide is associated with an increased risk of **VTE, MI, and stroke**, which is further heightened when used in combination with dexamethasone[13]

BPd, belantamab mafodotin/pomalidomide/dexamethasone; BVd, belantamab mafodotin/bortezomib/dexamethasone; CI, confidence interval; cilta-cel, ciltacabtagene autoleucel; CRS, cytokine release syndrome; DVd, daratumumab/bortezomib/dexamethasone; HR, hazard ratio; ICANS, immune effector cell-associated neurotoxicity syndrome; Kd, carfilzomib/dexamethasone; mFU, median follow-up; MI, myocardial infarction; mPFS, median progression-free survival; NR, not reached; PVd, pomalidomide/bortezomib/dexamethasone; SoC, standard of care; SVd, selinexor/bortezomib/dexamethasone; VTE, venous thromboembolism.

1. Hungria V, et al. *N Engl J Med*. 2024;391:393–407; 2. Trudel S, et al. Presented at ASH 2025; Abstract #2264; 3. Dimopoulos MA, et al. *N Engl J Med*. 2024;391:408–421; 4. Einsele H, et al. *Lancet Oncol*. 2026;27(2):254–268; 5. San-Miguel J, et al. *N Engl J Med*. 2023;389:335–347; 6. Goel U, et al. *Cancer Manag Res*. 2025;17:357–372; 7. Grosicki S, et al. *Lancet*. 2020;396:1563–1573; 8. Gavriatopoulou M, et al. *Leukemia*. 2020;34:2430–2440; 9. Dimopoulos MA, et al. *Lancet Oncol*. 2016;17(1):27–38; 10. EMA. Carfilzomib: SmPC. Available at: https://www.ema.europa.eu/en/documents/product-information/kyprolis-epar-product-information_en.pdf (Accessed June 2026); 11. Gao Y, et al. *Front Pharmacol*. 2025;16:1570017; 12. Richardson P, et al. *Lancet Oncol*. 2019;20:781–794; 13. Nadeem O, et al. *Cancers (Basel)*. 2024;16:1023.

Efficacy and safety considerations across emerging a second-line treatment options

Treatment	Efficacy considerations (primary endpoint: mPFS)	Safety considerations
BVd or BPd	**BVd vs DVd (DREAMM-7): 36.6 months vs 13.4 months**[1] • mFU: 28.2 months • HR (95% CI): 0.42 (0.31–0.53); P<0.001 **BPd vs PVd (DREAMM-8): 32.6 months vs 12.5 months**[2] • mFU: 35.8 months • HR (95% CI): 0.49 (0.36–0.67)	Belantamab mafodotin **events**[1–3]
Cilta-cel	**Cilta-cel vs SoC (CARTITUDE-4): NR vs 11.8 months**[4] • mFU: 33.6 months • HR (95% CI): 0.29 (0.22–0.39); P<0.0001	Cilta-cel is commonly therefore, the frailty ar considered when eval
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PVd	**PVd vs Vd (OPTIMISMM): 11.20 months vs 7.10 months**[12]	Pomalidomide is associated with an increased risk of **VTE, MI,** d in combination with dexamethasone

Age	72 years old
Sex	Male
MM diagnosis	• Anemia – Hb: 9.2 g/dL • Bone disease – Whole body CT: Multiple osteolytic lesions
Comorbidities	Hypertension and dyslipidemia
Performance status	• ECOG PS: 1 • ADL: 6 / IADL: 7 • CCI: 3 • LVEF: 60% • IMWG frailty: Intermediate-fit • No baseline neuropathy

As the patient has hypertension, **Kd may not be suitable** as a second line treatment option

ADL, activities of daily living; CCI, Charlson Comorbidity Index; CI, confidence interval; CT, computed tomography; ECOG PS, European Cooperative Oncology Group performance status; HR, hazard ratio; IADL, instrumental activities of daily living; IMWG, International Myeloma Working Group; Kd, carfilzomib/dexamethasone; LVEF, left ventricular ejection fraction; mFU, median follow-up; Vd, bortezomib/dexamethasone.

1. Hungria V, et al. *N Engl J Med*. 2024;391:393–407; 2. Trudel S, et al. Presented at ASH 2025; Abstract #2264; 3. Dimopoulos MA, et al. *N Engl J Med*. 2024;391:408–421; 4. Einsele H, et al. *Lancet Oncol*. 2026;27(2):254–268; 5. San-Miguel J, et al. *N Engl J Med*. 2023;389:335–347; 6. Goel U, et al. *Cancer Manag Res*. 2025;17:357–372; 7. Grosicki S, et al. *Lancet*. 2020;396:1563–1573; 8. Gavriatopoulou M, et al. *Leukemia*. 2020;34:2430–2440; 9. Dimopoulos MA, et al. *Lancet Oncol*. 2017;17(1):27–38; 10. EMA. Carfilzomib: Summary of Product Characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/kyprolis-epar-product-information_en.pdf (Accessed February 2026); 11. Gao Y, et al. *Front Pharmacol*. 2025;16:1570017; 12. Richardson P, et al. *Lancet Oncol*. 2019;20:781–794; 13. Nadeem O, et al. *Cancers (Basel)*. 2024;16:1023.

Efficacy and safety considerations across emerging and existing second-line treatment options

Treatment	Efficacy considerations (primary endpoint: mPFS)	Safety considerations
BVd or BPd	Treatment sequencing consideration: Use may **limit the efficacy** of **subsequent BCMA-directed** therapies[1]	
Cilta-cel		
SVd	Treatment sequencing consideration: Use could **potentially improve outcomes** with **subsequent BCMA-directed** therapies[2,3]	
Kd		
PVd		

BCMA, B-cel maturation antigen; BPd, belantamab mafodotin/pomalidomide/dexamethasone; BVd, belantamab mafodotin/bortezomib/dexamethasone; CI, confidence interval; cilta-cel, ciltacabtagene autoleucel; CRS, cytokine release syndrome; DVd, daratumumab/bortezomib/dexamethasone; HR, hazard ratio; ICANS, immune effector cell-associated neurotoxicity syndrome; Kd, carfilzomib-dexamethasone; mFU, median follow-up; MI, myocardial infarction; mPFS, median progression-free survival; NR, not reached; PVd, pomalidomide-bortezomib-dexamethasone; SoC, standard of care; SVd, selinexor/bortezomib/dexamethasone; VTE, venous thromboembolism.

1. Lal BM, et al. Presented at ASH 2024; Abstract #3789; 2. Verbruggen C, et al. Presented at ASH 2025; Poster #6102; 3. Costa BA, et al. *J Clin Med.* 2025;14:1316.

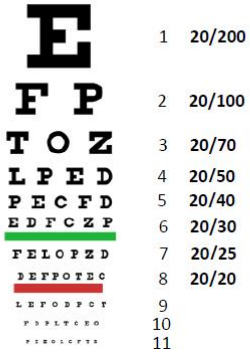
DREAMM-7/8: Ocular events were common amongst patients receiving belantamab combination therapy

	Study design	Baseline characteristics	Median PFS, mos*	Median OS, mos*	ORR, % (95% CI)†	Safety profile	Belantamab-associated AEs
DREAMM-7[1,2]	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%[1] • **High-risk cytogenetics**: BVd, 28%; DVd, 27%[1] • **LEN-refractory:** BVd, 33%; DVd, 35%[1]	**BVd, 36.6 vs. DVd, 13.4** *HR 0.41 (95% CI: 0.31–0.53); p<0.001*[1]	**NR vs. NR** At 36 months: **BVd, 74% vs. DVd, 60%** *HR 0.58 (95% CI: 0.43–0.79)*[2]	**BVd, 83%** (78–88%) **vs. DVd, 71%** (65–77%)[2]	**AEs‡** Any grade: 100%; Grade 3–4: 95%[2] **Serious AEs** 53%[2] **Discontinuation due to AEs** 32%[2]	**Ocular events** Any grade: 79%; Grade 3–4: 34%[1] **Blurred vision** Any grade: 68%; Grade 3–4: 24%[2] **Worsening vision from normal to:** 20/50, 34%; 20/200, 2%[1] **Infections** Any grade: 70%; Grade 3–4: 31%[1]
DREAMM-8[3,4]	1:1 BPd (n=155) / PVd (n=147) **Primary endpoint:** PFS **Secondary endpoints:** ORR, MRD negativity, DoR	• **1 prior LOT**: BPd, 53%; PVd, 52%[3] • **High-risk cytogenetics**: BPd, 34%; PVd, 32%[3] • **LEN-refractory:** BPd, 81%; PVd, 76%[3] • **Anti-CD38 mAb-refractory:** BPd, 23%; PVd, 24%[3]	**BPd, 32.6 vs. PVd, 12.5** *HR 0.49 (95% CI: 0.36–0.67)*[4]	**NR vs. NR** 12-month estimate: **BPd, 83% vs. PVd, 76%** *HR 0.77 (95% CI: 0.53–1.14)*[3]	**BPd, 77%** (70–84%) **vs. PVd, 72%** (64–79%)[3]	**AEs** Any grade: 99%; Grade ≥3: 94%[3] **Serious AEs** 63%[3] **Discontinuation due to AEs** 15%[3]	**Ocular events** Any grade: 89%; Grade 3–4: 43%[3] **Blurred vision** Any grade: 79%; Grade ≥3: 17%[3] **Worsening vision from normal to:** 20/50, 34%; 20/200, 1%[3] **Infections** Any grade: 82%; Grade ≥3: 49%[3]

Median follow-up for DREAMM-7 was 28.2 months for PFS and safety, and 39.4 months for OS, ORR, and safety, and for DREAMM-8 was 28.0 months for OS, ORR and safety, and 35.8 months for PFS.
*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; PFS, progression-free survival; PR, partial response; PVd, pomalidomide/bortezomib/dexamethasone.
1. Hungria V, et al. *N Engl J Med.* 2024;391:393–407. 2. Hungria V, et al. *Lancet Oncol* 2025;26(8):1067–1080; 3. Dimopoulos MA, et al. *N Engl J Med.* 2024;391:408–421; 4. Trudel S, et al. Presented at ASH 2025; Abstract 2264.

Ocular events observed with belantamab combination therapy

Snellen eye chart for visual acuity[1]



Simulations of visual acuity changes[1]

BCVA is the best possible visual acuity that an individual can achieve when wearing corrective lenses (such as glasses or contact lenses)[1]

- A clinically significant change in BCVA is 20/20 → 20/50
- Driving restrictions may be required at 20/70 or worse

Across DREAMM-7 and DREAMM-8, **a high proportion of patients experienced clinically significant visual acuity changes**:[1]

>60% experienced unilateral worsening of BCVA to **20/50 or worse**

>25% experienced unilateral worsening of BCVA to **20/100 or worse**

>10% experienced unilateral worsening of BCVA to **20/200 or worse**

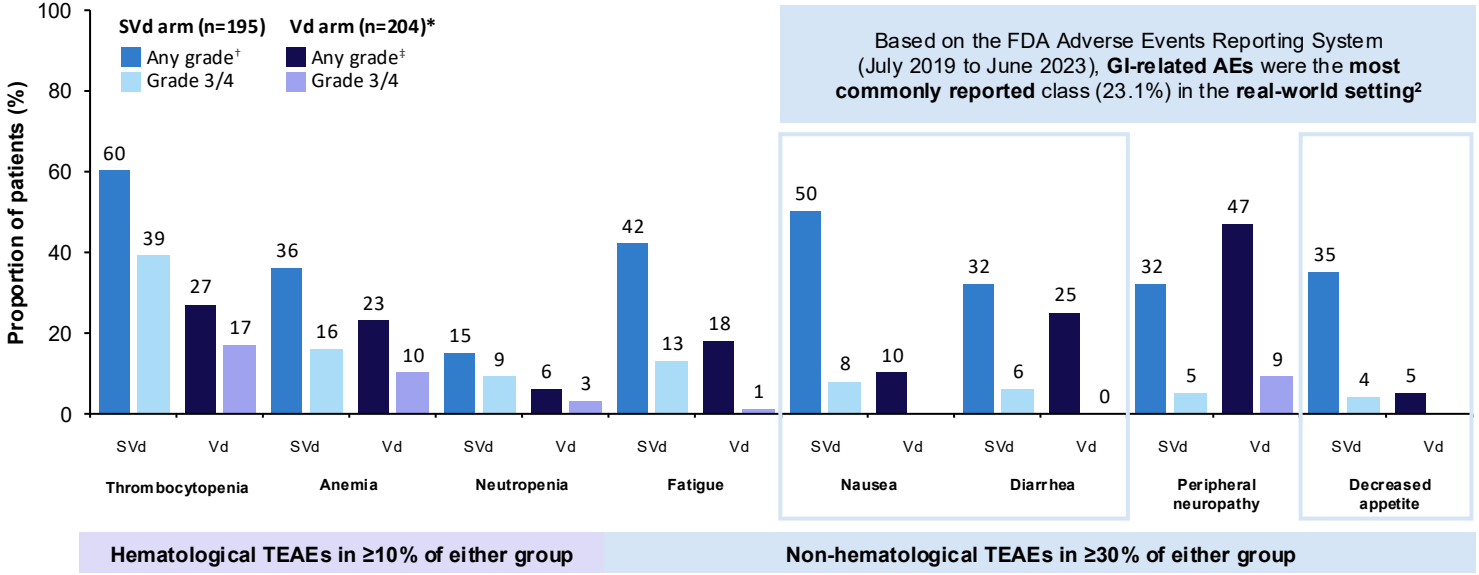
Ocular events were **effectively managed with dose modifications** and **generally reversible** with adequate follow-up, allowing patients to remain on treatment[2–4]

BCVA, best corrected visual acuity.

1. FDA. Belantamab Mafodotin BLA 761440: Oncologic Drugs Advisory Committee Meeting. Available at: https://www.fda.gov/media/187657/download (Accessed June 2026). 2. Hungria V, et al. *N Engl J Med.* 2024;391:393–407. 3. Hungria V, et al. *Lancet Oncol.* 2025;26(8):1067–1080; 4. Dimopoulos MA, et al. *N Engl J Med.* 2024;391:408–421.

BOSTON: GI AEs amongst the most commonly reported non-hematological TEAEs in patients receiving selinexor[1]

n (%)	SVd (n=195)	Vd (n=204)*
Serious AEs	101 (52)	77 (38)
Discontinuation due to AEs	41 (21)	32 (16)



*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".
AEs, adverse events; FDA, Food & Drug Administration; GI, gastrointestinal; NEC, not elsewhere classified; SVd, selinexor/bortezomib/dexamethasone; TEAE, treatment-emergent adverse event; Vd, bortezomib/dexamethasone.

1. Grosicki S, et al. *Lancet*. 2020;396(10262):1563–1573; 2. Liu Y, et al. *Sci Rep*. 2024;14:12231.

Dose modification and supportive care strategies for selinexor-related adverse events

A 5-HT_3 receptor antagonist and other antinausea agents should be provided prior to and during treatment with selinexor[1]

Ondansetron
8 mg PO 30 minutes prior to first dose; subsequent dose after 8 hours, then twice daily (every 12 hours for 12 hours after the last Selinexor dose)[2]

+

Olanzapine
2.5 mg–5.0 mg PO qhs[2,3]

AND/OR

Aprepitant*
125 mg PO qam day 1 and 80 mg for 2 days each week[2,4,5]

Alternatively, once-weekly oral dose of netupitant 300 mg + palonosetron 0.5 mg[6–8]

One or both antiemetics may be tapered after Cycle 2; maintain hydration and caloric intake[4]

Selinexor-related AEs may be managed by dose reductions: BOSTON study[9]

Dose reductions were experienced by 65% in the SVd arm[9]

The **following selinexor dose reduction** recommendations are suggested for patients who experience an adverse reaction† while taking **SVd**[10]

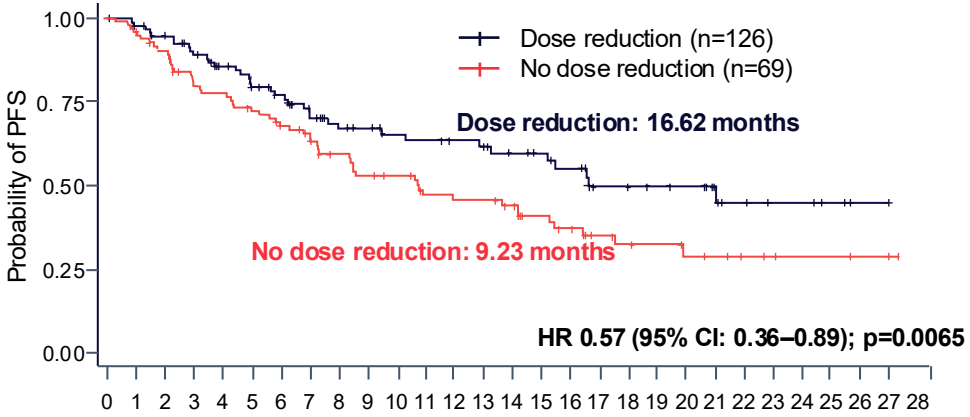
Dose reduction	SVd dose
Recommended starting dose	100 mg once weekly
First dose reduction	80 mg once weekly
Second dose reduction	60 mg once weekly
Third dose reduction	40 mg once weekly
Discontinue if symptoms do not resolve	

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 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.

5-HT_3, 5-hydroxytryptamine 3 receptor antagonist; 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) SmPC. Available at: https://www.ema.europa.eu/en/documents/product-information/nexpovioepar-product-information_en.pdf (Accessed June 2026).

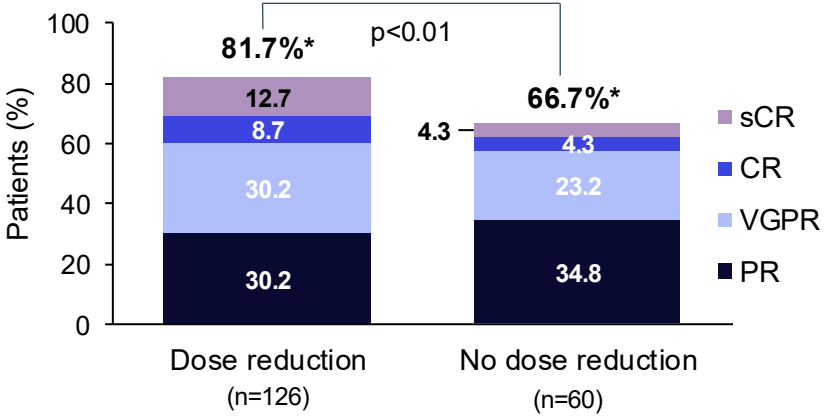
BOSTON: Selinexor dose reduction was associated with improved efficacy

PFS by dose reduction in patients in the SVd arm[1]



mPFS (95% CI) in a subgroup analysis of len-refractory patients (n=53):[2]
13.9 (6.9–NE) **months with dose reductions** vs.
5.1 (3.5–NE) **months without dose reductions**

ORR by dose reduction of selinexor in the SVd arm[1]



- These subgroup analyses were exploratory in nature, not included in the study objectives, and do not control for type 1 error[2]
- The analyses were not powered or adjusted for multiplicity to assess efficacy outcomes across these subgroups[2]

*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.
CI, confidence interval; CR, complete response; HR, hazard ratio; IRC, independent review committee; len, lenalidomide; mPFS, median progression-free survival; NE, not evaluable; ORR, overall response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; sCR, stringent complete response; SVd, selinexor/bortezomib/dexamethasone; VGPR, very good partial response.

1. Jagannath S, et al. Presented at ASH 2021; Poster #3793; 2. Delimpasi S, et al. *Br J Haematol.* 2026; doi: 10.1111/bjh.70479 [Online ahead of print].

Age	72 years old
Sex	Male
MM diagnosis	• Anemia – Hb: 9.2 g/dL • Bone disease – Whole body CT: Multiple osteolytic lesions
Comorbidities	Hypertension and dyslipidemia
Performance status	• ECOG PS: 1 • ADL: 6 / IADL: 7 • CCI: 3 • LVEF: 60% • IMWG frailty: Intermediate-fit • No baseline neuropathy

Transplant-ineligible

First treatment

Dara-Rd (continuous) → VGPR achieved after 6 cycles

Relapse at 36 months: Rapid biochemical progression (0.7 to 3.5 g/dL)

Second treatment

SVd
S: 80 mg QW
V (SC): 1.3 mg/m² QW
d: 20 mg QW
+ Antiemetic prophylaxis
+ Close monitoring in first cycles

PR achieved after 4 cycles
VGPR achieved after 8 cycles

Safety and management

- Grade 2 **nausea** → optimized **antiemetics**
- Grade 2 **thrombocytopenia** → **monitoring**
- No ≥Grade 3 neuropathy

Dose intensity maintained with **good adherence**

ADL, activities of daily living; CCI, Charleson Comorbidity Index; CT, computed tomography; Dara-Rd, daratumumab/lenalidomide/dexamethasone; ECOG PS, Eastern Cooperative Oncology Group Performance Status; Hb, hemoglobin; IADL, instrumental activities of daily living; IMWG, International Myeloma Working Group; LVEF, left ventricular ejection fraction; PR, partial response; QW, once weekly; SC, subcutaneous; SVd, selinexor/bortezomib/dexamethasone; VGPR, very good partial response.
Representative patient case provided by Dr Buda.

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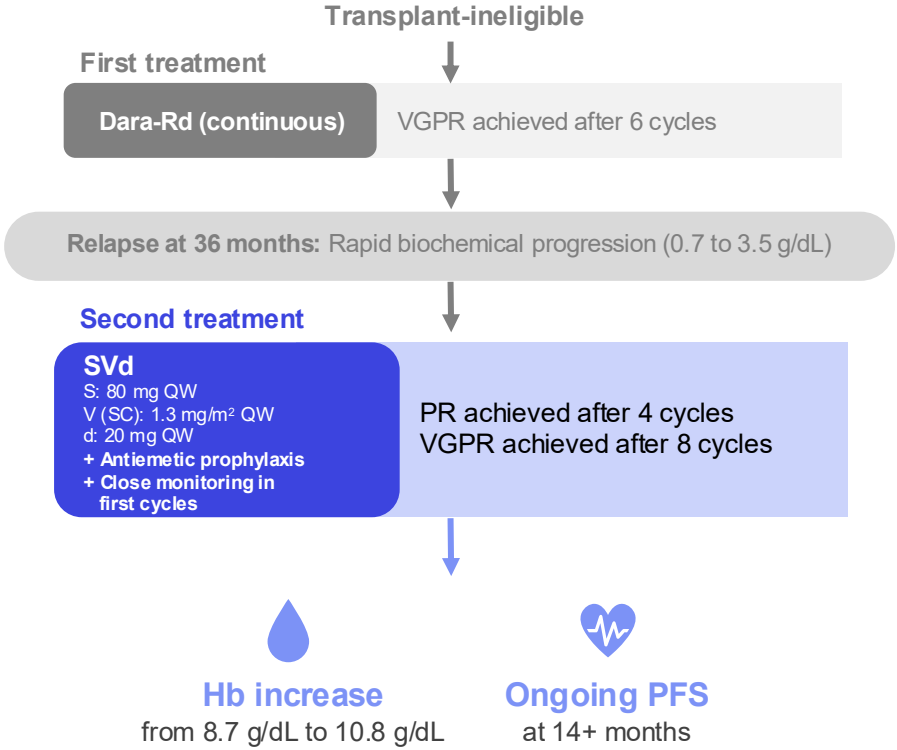

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SVd was an effective second-line treatment for this lenalidomide-refractory patient, and the weekly regimen and AE management enhanced tolerability

Transplant-ineligible

First treatment

Dara-Rd (continuous) → VGPR achieved after 6 cycles

Relapse at 36 months: Rapid biochemical progression (0.7 to 3.5 g/dL)

+ Close monitoring in first cycles

Hb increase
from 8.7 g/dL to 10.8 g/dL

Ongoing PFS
at 14+ months

AE, adverse event; ADL, activities of daily living; CCI, Charleson Comorbidity Index; CT, computed tomography; Dara-Rd, daratumumab/lenalidomide/dexamethasone; ECOG PS, Eastern Cooperative Oncology Group Performance Status; Hb, hemoglobin; IADL, instrumental activities of daily living; IMWG, International Myeloma Working Group; LVEF, left ventricular ejection fraction; PFS, progression-free survival; PR, partial response; QW, once weekly; SC, subcutaneous; SVd, selinexor/bortezomib/dexamethasone; VGPR, very good partial response.
Representative patient case provided by Dr Buda.

Summary

Translating evidence into practice: A case-led discussion of real-world practice challenges

The effective management of R/R MM relies on **personalized treatment selection,** considering factors related to the **patient, treatment targets, and toxicity profiles** to meet the needs of the **highly heterogenous patient population**

Careful consideration should be given to the **specific toxicities** associated with novel therapeutic options, as well as the associated **management and follow-up**, when evaluating treatment options at relapse

The **clinical utility** of selinexor may be **supported with double antiemetic prophylaxis** and **dose modifications**

R/R MM, relapsed/refractory multiple myeloma.

Q&A and closing remarks

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Director of Myeloma, Blavatnik Family Chelsea Medical Center at Mount Sinai

New York, US

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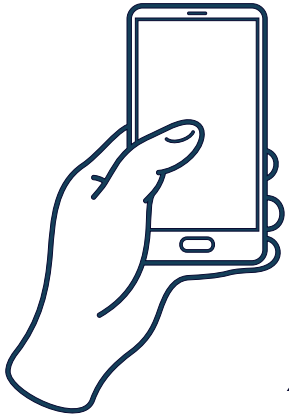
Q&A



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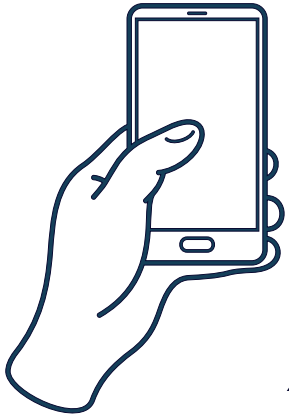
We value your feedback…



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