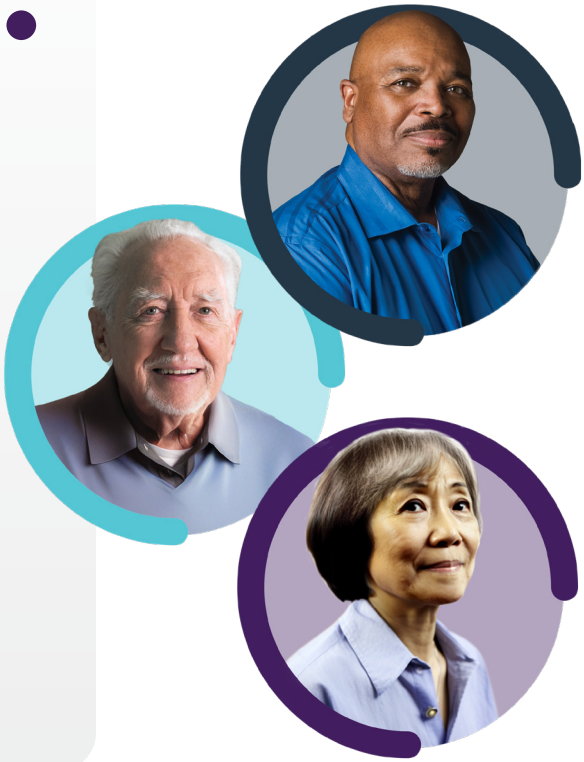
XPOVIO® (selinexor)

After a relapse on an anti-CD38 mAb-based regimen in RRMM...

TARGET PROGRESSION. DIFFERENTLY.[1]

XPOVIO provides the opportunity to:

- Introduce a **different treatment class**[1]
- Deliver **proven efficacy*** in combination with Vd, with **efficacy observed across a variety of patient subgroups**[1,2]
- Offer **oral, once-weekly tablets** that can be taken at home[1†]
- Administer treatment and monitor patients **without required hospitalization**[1]



†XPOVIO® (selinexor) is a prescription medicine approved in combination with subcutaneous bortezomib injection and oral dexamethasone.

XVd is a preferred NCCN Category 1 regimen in early RRMM[3]

Oral, once-weekly selinexor (XPOVIO®) in combination with bortezomib and dexamethasone (XVd) is recommended by the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) as a preferred NCCN Category 1‡ therapeutic option in previously treated (1–3 prior lines), lenalidomide-refractory MM.

***XVd vs Vd trial:** Phase 3, global, open-label study of adult patients with MM who received 1–3 prior therapies that compared XVd with Vd in 402 patients randomized into two study arms. 195 patients were treated with once-weekly XVd and twice-weekly dexamethasone. 207 patients were treated with twice-weekly bortezomib and four-times-weekly dexamethasone. The primary endpoint was PFS and select secondary endpoints included ORR and DOR. The XVd mPFS of the ITT population was 13.9 months vs. a Vd mPFS of 9.5 months [HR: 0.70 (95% CI: 0.53, 0.9), *P*=0.0075].[1]

‡Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

INDICATION

XPOVIO® (selinexor) is a prescription medicine approved in combination with bortezomib and dexamethasone (XVd) to treat adult patients with multiple myeloma who have received at least one prior therapy.

IMPORTANT SAFETY INFORMATION

Thrombocytopenia: XPOVIO can cause life-threatening thrombocytopenia, potentially leading to hemorrhage. Thrombocytopenia was reported in patients with multiple myeloma.

Thrombocytopenia is the leading cause of dosage modifications. Monitor platelet counts at baseline and throughout treatment. Monitor more frequently during the first 3 months of treatment. Monitor patients for signs and symptoms of bleeding. Interrupt, reduce dose, or permanently discontinue based on severity of adverse reaction.

Please see Important Safety Information throughout and accompanying full Prescribing Information.

Patients are in need of novel treatment options once refractory to an anti-CD38 mAb[4,5]

>70% exposed to an anti-CD38 mAb by 2L

According to Komodo claims data from 2022,
Over 30% of patients were exposed to an anti-CD38 mAb-based regimen in 1L, and over 70% of patients were exposed after receiving their 2L treatment[6]

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Poor outcomes once refractory

In MAMMOTH*, a retrospective analysis of 275 patients refractory to an anti-CD38 mAb,
31% of patients refractory to an anti-CD38 mAb responded to their next therapy, with mPFS of 3.4 months and mOS of 9.3 months[5]

The NCCN recommends against recycling anti-CD38 mAbs once refractory†

The National Comprehensive Cancer Network® (NCCN®) suggests regimens without anti-CD38 be considered for those refractory to anti-CD38 antibody as long as they have not received or are refractory to other agents in the regimen[3]

The NCCN recommends introducing different drugs/drug classes

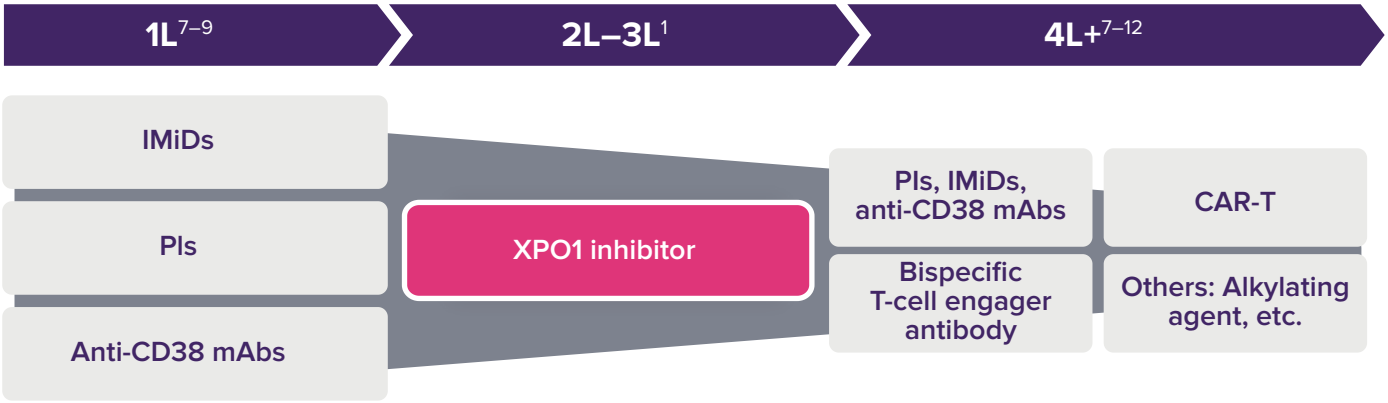
For early relapse (1–3 prior therapies) in MM, the NCCN recommends that an attempt should be made to use drugs/drug classes the patients have not been exposed to or exposed to >1 line prior[3]

*Data collected between January 2017 and June 2018. Among the subgroup of 249 patients who received >1 subsequent treatment beyond T_0 were analyzed using comparisons of PFS and OS estimates. T_0 was the time point when patients met the criteria of progression as defined by the IMWG Response Criteria.

†NCCN makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

Consider introducing a different treatment class with XPOVIO + Vd after patients relapse on an anti-CD38 mAb-based regimen in early lines of therapy[1]

Lines of therapy in MM



Select presentation - not intended to be comprehensive.

Patients who could benefit from a different treatment class after relapsing on an anti-CD38 mAb-based regimen include[1]:

Jon, 75

1L DRd

- Standard-risk cytogenetics
- ASCT-ineligible
- Prior anti-CD38 mAb
- Len-refractory

Joseph, 64

1L DRVd

- High-risk cytogenetics
- Prior ASCT
- Prior anti-CD38 mAb
- Len-refractory

Emily, 70

2L Anti-CD38 mAb-based triplet

- High-risk cytogenetics
- ≥65 years of age
- Renal impairment
- Prior anti-CD38 mAb

Jon, Joseph, and Emily are not actual patients. These patient characteristics do not represent all patient types for whom XPOVIO may be appropriate.

IMPORTANT SAFETY INFORMATION (continued)

Neutropenia: XPOVIO can cause life-threatening neutropenia, potentially increasing the risk of infection.

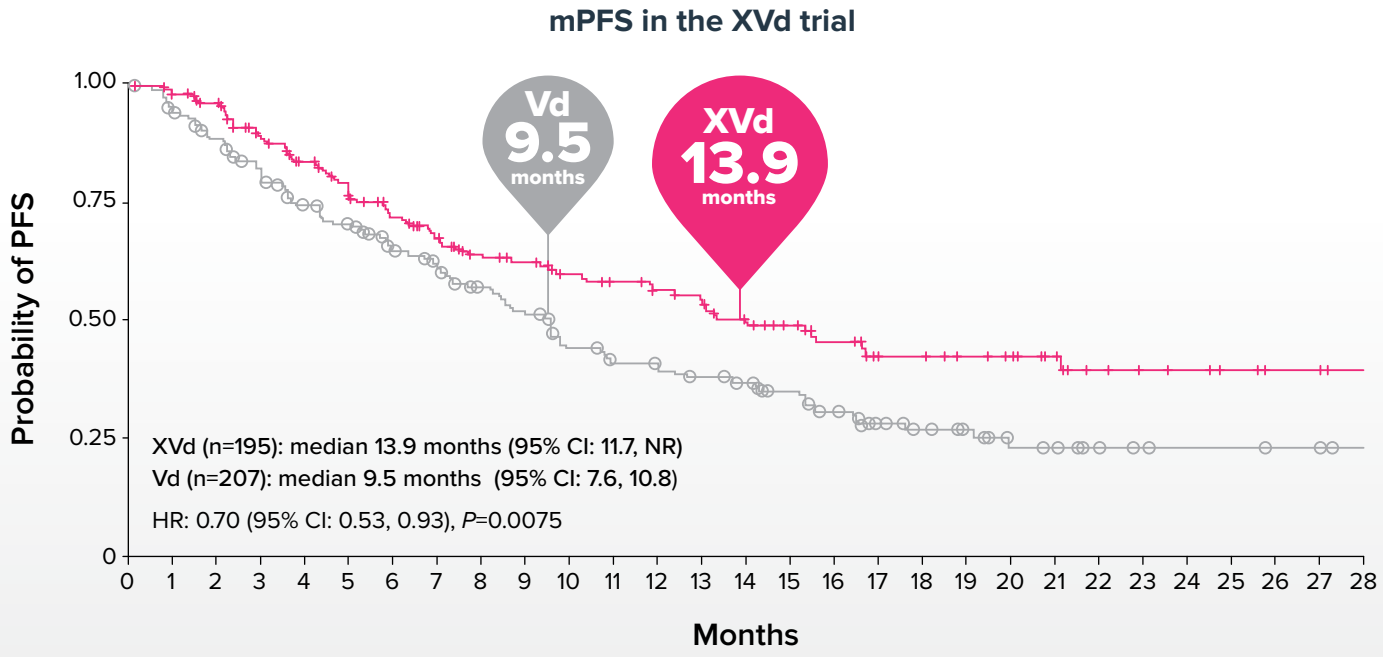
Monitor more frequently during the first 3 months of treatment. Consider supportive measures, including antimicrobials and growth factors (e.g., G-CSF). Interrupt, reduce dose, or permanently discontinue based on severity of adverse reaction.

Please see additional Important Safety Information throughout.

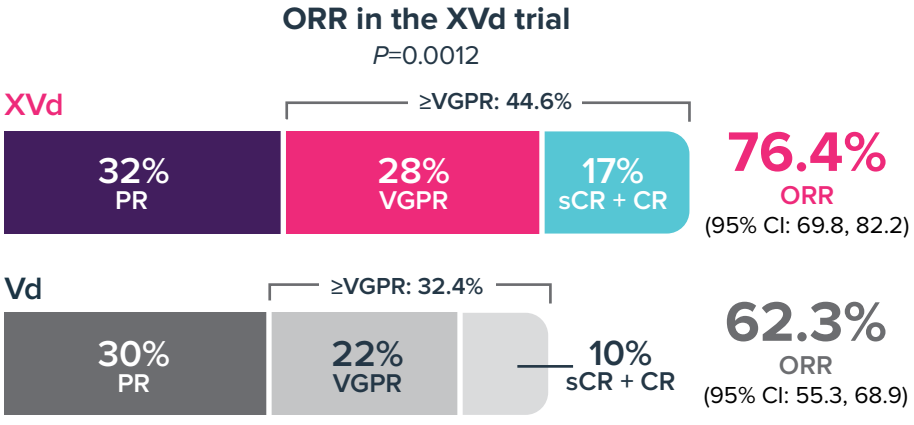
XPOVIO® (selinexor)

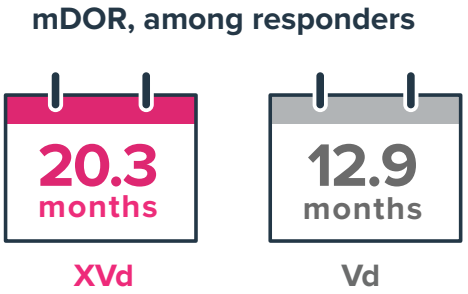
XPOVIO + Vd was proven to improve outcomes for patients with RRMM in early lines of therapy[1]

XVd provided an early and sustained PFS benefit over Vd



XVd offered deep and durable responses





Among patients who received XPOVIO, the **median duration of XPOVIO treatment was 29 weeks**

IMPORTANT SAFETY INFORMATION (continued)

Gastrointestinal Toxicity: XPOVIO can cause severe gastrointestinal toxicities in patients.

Nausea/Vomiting/Diarrhea: Provide prophylactic antiemetics or treatment as needed.

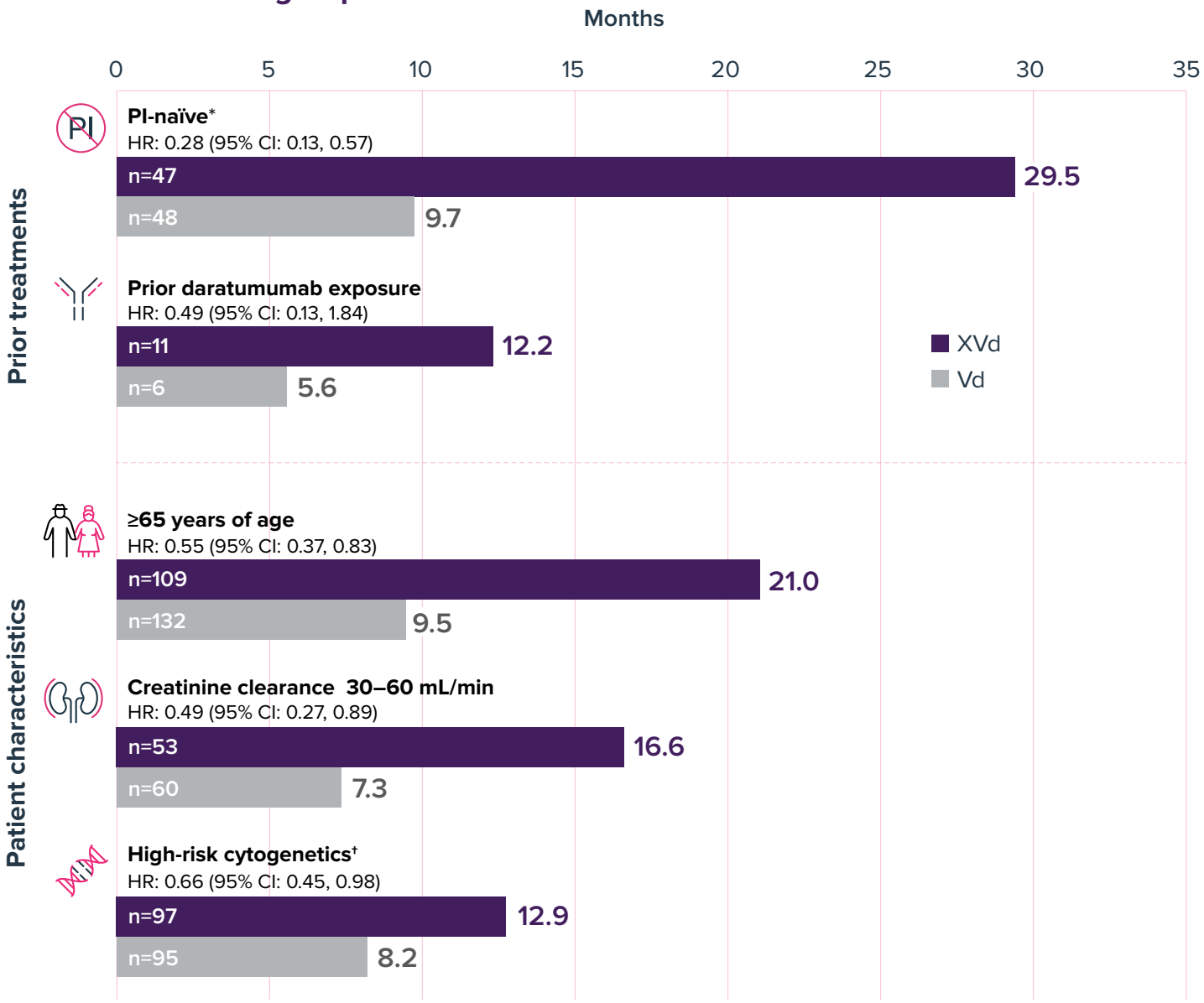
Anorexia/Weight Loss: Monitor weight, nutritional status, and volume status at baseline and throughout treatment and provide nutritional support, fluids, and electrolyte repletion as clinically indicated.

Please see additional Important Safety Information throughout.

XPOVIO® (selinexor)

XPOVIO + Vd efficacy observed across a variety of patient subgroups[2,13]

mPFS in select subgroups



Limitations of subgroup analyses:

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

*These subgroup data are derived from an updated efficacy analysis from the XVd trial.
†Includes any of del(17p)/p53, t(14;16), t(4;14), 1q21.

IMPORTANT SAFETY INFORMATION (continued)

Hyponatremia: XPOVIO can cause severe or life-threatening hyponatremia. Monitor sodium level at baseline and throughout treatment.

Serious Infection: XPOVIO can cause serious and fatal infections. Atypical infections reported after taking XPOVIO include, but are not limited to, fungal pneumonia and herpesvirus infection.

Please see additional Important Safety Information throughout.

XPOVIO® (selinexor)

XPOVIO + Vd offers a well-established safety profile[1,14]

Most common ARs in the XVd trial (≥20% in the XPOVIO + Vd arm)

	XVd arm (n=195)		Vd arm (n=204)*	
	Any grade	Grade 3–4	Any grade	Grade 3–4
Hematological ARs (%)[14]				
Thrombocytopenia	60	39	27	17
Anemia	36	16	23	10
Non-hematological ARs (%)[1]				
Fatigue†	59	21	28	5
Nausea	50	8	10	0
Diarrhea	32	6	25	<1
Decreased appetite	35	4	5	0
Peripheral neuropathy‡	32	5	47	9
Upper respiratory tract infection§	29	4	22	2
Weight decrease	26	2	12	1
Cataract	22	9	6	2
Vomiting	21	4	4	0

- Fatal ARs occurred in 6% of patients within 30 days of last treatment, including pneumonia (n=3) and sepsis (n=3)[1]
- Serious ARs occurred in 52% of patients. Treatment discontinuation rate due to ARs was 19%. The most frequent ARs requiring permanent discontinuation in >2% of patients included fatigue, nausea, thrombocytopenia, decreased appetite, peripheral neuropathy and vomiting[1]

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

†Fatigue includes fatigue and asthenia.

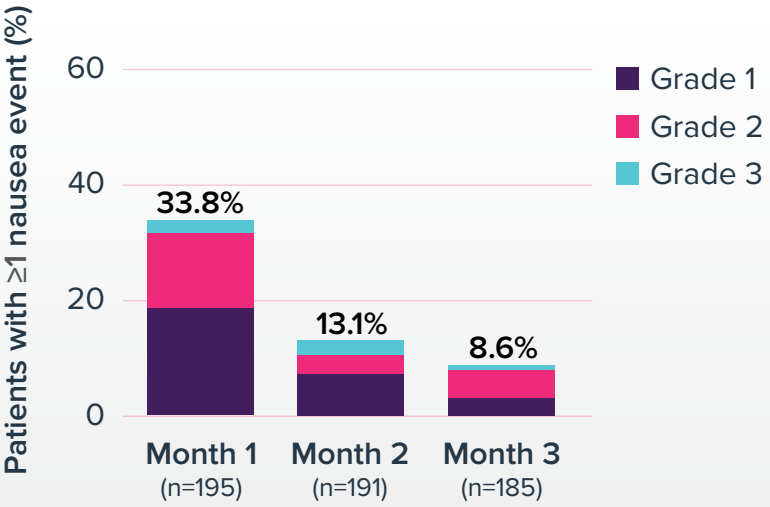
‡Peripheral neuropathy includes neuropathy peripheral, peripheral sensory neuropathy, polyneuropathy, peripheral sensorimotor neuropathy, toxic neuropathy, and peripheral motor neuropathy.

§Upper respiratory tract infection includes upper respiratory infection, nasopharyngitis, pharyngitis, respiratory syncytial virus infection, respiratory tract infection, rhinitis, and viral upper respiratory tract infection.

Serious organ toxicities of the cardiac, pulmonary, renal, or liver systems were not observed with XVd[15]

Nausea associated with XVd was transient and resolved over time¶[16]

Percentage of patients who experienced nausea events in the XVd arm of the XVd trial



92% (61/66) of nausea cases were resolved/resolving within **the first month**

100% (16/16) of nausea cases were resolved/resolving within **the third month**

¶The XVd trial protocol required a prophylactic 5-HT3 antagonist and other anti-nausea treatment agents prior to and during treatment with XPOVIO to address nausea and allowed for other interventions as required.

Please see additional Important Safety Information throughout.

XPOVIO® (selinexor)

Oral, once-weekly XPOVIO tablets are readily accessible and can be taken at home[1]

Oral, once-weekly tablets can be taken at home

The majority of patients receive treatment in <1 week of prescription[17]

Hospitalization is not required for administration or monitoring

Dose reductions are available to help mitigate ARs and may help keep patients on therapy

Recommended dosing schedule[1]

DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
XPOVIO 100 mg **+ bortezomib 1.3 mg/m²** for first 4 weeks, followed by 1 week off **+ dexamethasone 20 mg**	**Dexamethasone 20 mg**	No dose	No dose	No dose	No dose	No dose
Recommended prophylactic antiemetics*[18,19]						
Ondansetron 8 mg 30 minutes prior to XPOVIO then Q8 hours + **Olanzapine** 2.5–5 mg QHS	**Ondansetron** 8 mg Q8 hours + **Olanzapine** 2.5–5 mg QHS	**Ondansetron** 8 mg Q8 hours + **Olanzapine** 2.5–5 mg QHS	**Olanzapine** 2.5–5 mg QHS	**Olanzapine** 2.5–5 mg QHS	**Olanzapine** 2.5–5 mg QHS	**Olanzapine** 2.5–5 mg QHS

*An NK-1 antagonist (e.g., aprepitant or rolapitant) could also be used as an antiemetic. Antiemetics such as olanzapine and NK-1 inhibitors can be reduced or stopped after 8 weeks if patients are tolerating XPOVIO.

Specific antiemetics listed above are for reference purposes only. All treatment decisions must be individualized and made solely at the discretion of the healthcare professional.

For additional information regarding the dosing and administration of bortezomib or dexamethasone, refer to the prescribing information for each.

Four dosage strengths are available for dose modifications to help mitigate ARs[1]

100 mg
RECOMMENDED STARTING DOSE

80 mg
FIRST REDUCTION

60 mg
SECOND REDUCTION

40 mg
THIRD REDUCTION

PERMANENTLY DISCONTINUE

IMPORTANT SAFETY INFORMATION (continued)

Neurological Toxicity: XPOVIO can cause life-threatening neurological toxicities. Coadministration of XPOVIO with other products that cause dizziness or mental status changes may increase the risk of neurological toxicity.

Advise patients to refrain from driving and engaging in hazardous occupations or activities until the neurological toxicity fully resolves. Institute fall precautions as appropriate.

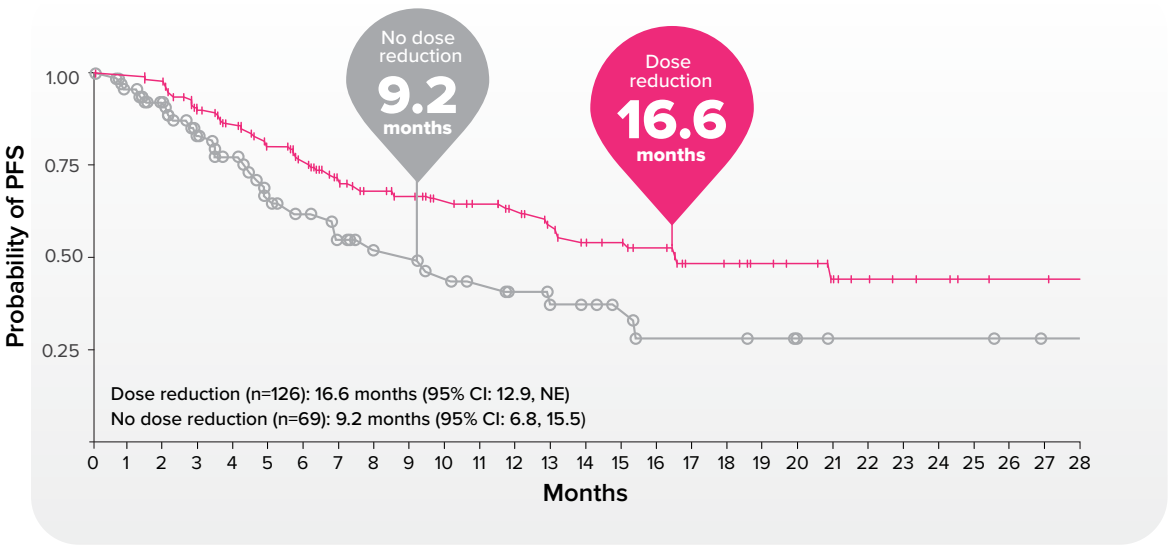
Please see additional Important Safety Information throughout.

XPOVIO® (selinexor)

Consider reducing the dose of XPOVIO to help mitigate ARs[1,20,21]

Efficacy maintained with XPOVIO dose reductions[20,21]

mPFS in the XVd trial



Limitations of post-hoc analyses:

- This post hoc analysis was exploratory in nature and was not a study objective.
- This post hoc analysis was underpowered to detect clinically meaningful differences in treatment effect.
- This post hoc analysis was intended to provide information about dose modifications and not to compare efficacy across treatment groups.

65% (126/195) of patients **had an XPOVIO dose reduction**[20]

80 mg was the median **once-weekly dose** of XPOVIO[1]

34.5 weeks was the median treatment duration with an XPOVIO dose reduction **vs. 20 weeks without**[20]

Incidence of duration-adjusted ARs observed with XPOVIO dose reductions*[20]

	On or before first XPOVIO reduction (n=195)		After first XPOVIO reduction (n=126)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Hematological ARs (%)				
Thrombocytopenia	62.5	29.6	47.6	19.2
Anemia	17.9	4.7	10.3	3.2
Non-hematological ARs (%)				
Nausea	31.6	3.9	7.3	2.7
Fatigue	28.1	4.1	9.9	2.7
Decreased appetite	21.5	1.6	6.4	0.4
Vomiting	14.4	2.4	3.8	0.7
Diarrhea	12.9	2.0	5.2	0.7
Weight decrease	9.0	0.6	5.9	0.7
Peripheral neuropathy	7.9	0.3	5.2	1.3

*Duration-adjusted incidence of ARs is defined as the average number of events per 100 patients during a 4-week cycle.

IMPORTANT SAFETY INFORMATION (continued)

Embryo-Fetal Toxicity: XPOVIO can cause fetal harm when administered to a pregnant woman.

Please see additional Important Safety Information throughout.

XPOVIO® (selinexor)

Consider introducing XPOVIO + Vd to patients like Jon, who have relapsed on DRd in 1L

Jon, 75

Key patient characteristics

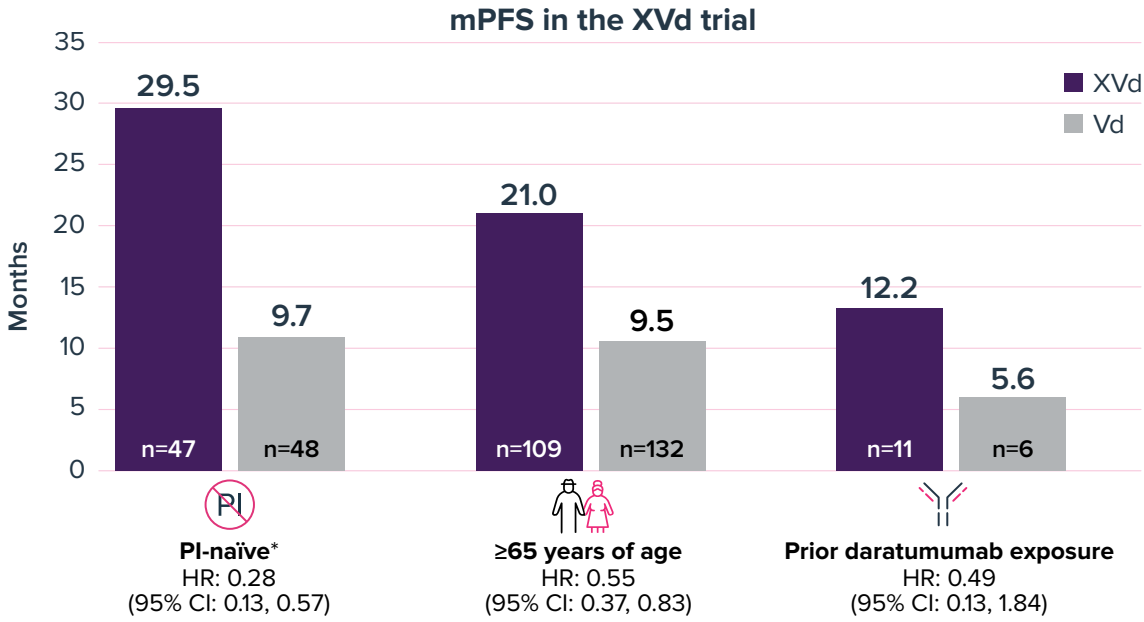
- **Standard-risk cytogenetics**
- **ASCT-ineligible**
- **Anti-CD38 mAb exposure in prior line**
- **Refractory to an IMiD**

1L therapy

- **DRd:** (38 cycles) daratumumab + lenalidomide + dexamethasone

Relapse

Efficacy observed in multiple subgroups[2,13]



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*These subgroup data are derived from an updated efficacy analysis from the XVd trial.

XVd is a preferred NCCN Category 1 regimen for lenalidomide-refractory patients[3]

Oral, once-weekly selinexor (XPOVIO®) in combination with bortezomib and dexamethasone (XVd) is recommended by the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) as a preferred NCCN Category 1† therapeutic option in previously treated (1–3 prior lines), lenalidomide-refractory MM.

†Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

IMPORTANT SAFETY INFORMATION (continued)

Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential and males with a female partner of reproductive potential to use effective contraception during treatment with XPOVIO and for 1 week after the last dose.

Please see additional Important Safety Information throughout.

XPOVIO® (selinexor)

Consider introducing XPOVIO + Vd to patients like Joseph, who relapsed after receiving DRVd in 1L

Joseph, 64

Key patient characteristics

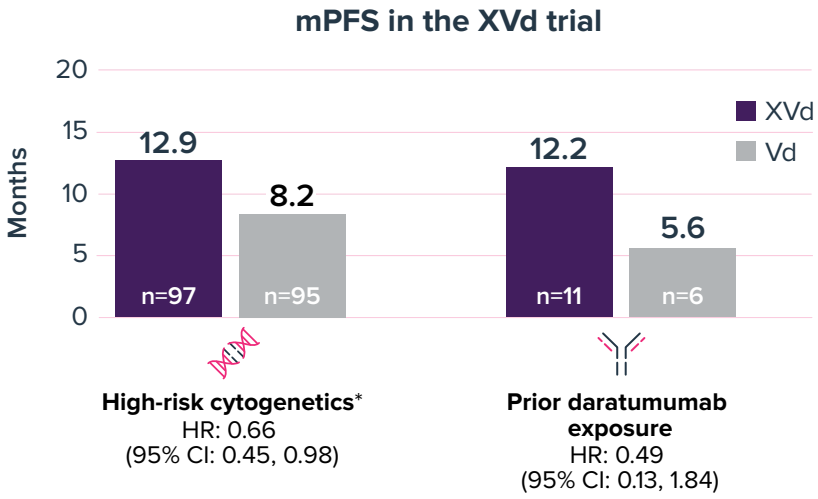
- **High-risk cytogenetics**
- **Prior ASCT**
- **Anti-CD38 mAb exposure in prior line**
- **Refractory to an IMiD**

1L therapy

- **DRVd:** 4 cycles
- **ASCT**
- **DRVd (consolidation):** 2 cycles
- **Maintenance therapy:** DR 36 cycles

Relapse

Efficacy observed in multiple subgroups[2]



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ADVERSE REACTIONS (continued)

Cataracts: New onset or exacerbation of cataract has occurred during treatment with XPOVIO. The incidence of new onset or worsening cataract requiring clinical intervention was reported.

Please see additional Important Safety Information throughout.

XPOVIO® (selinexor)

Consider introducing XPOVIO + Vd to patients like Emily, who relapsed on an anti-CD38 mAb-based regimen in 2L

Emily, 70

Key patient characteristics

- **High-risk cytogenetics**
- **≥65 years of age**
- **Renal impairment**
- **Anti-CD38 mAb exposure in prior line**

1L therapy

- **RVd:** 8 cycles
- **ASCT**
- **Maintenance therapy:** lenalidomide 36 cycles

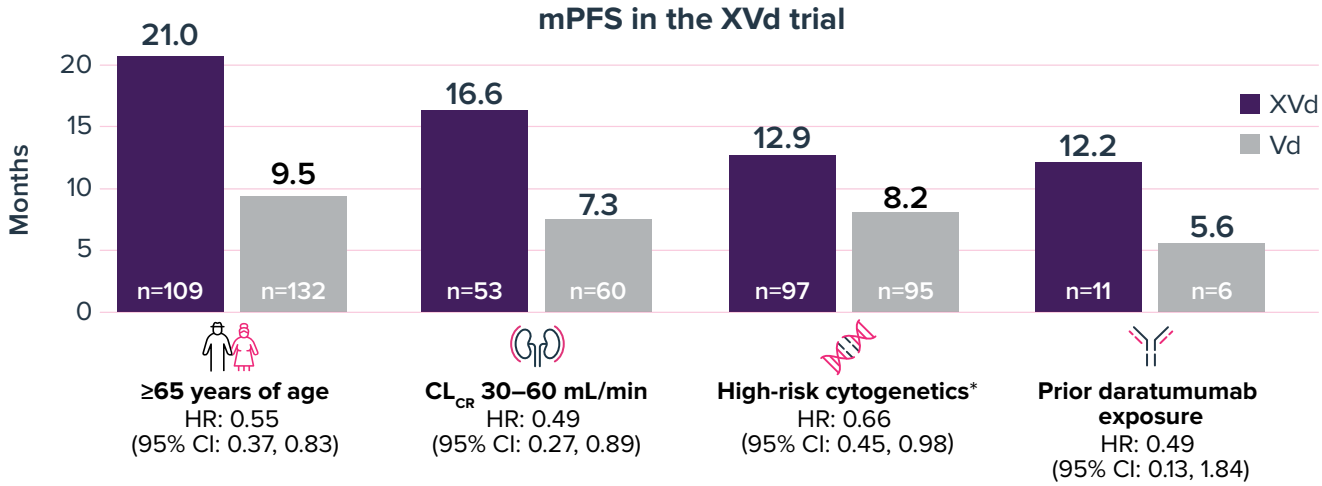
Relapse

2L therapy

- **DPd:** 14 cycles

Relapse

Efficacy observed in multiple subgroups[2]



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- These subgroup analyses were not powered or adjusted for multiplicity to assess PFS across these subgroups.

*Includes any of del(17p)/p53, t(14;16), t(4;14), 1q21.

ADVERSE REACTIONS (continued)

The most common adverse reactions (ARs) (≥20%) in patients with multiple myeloma who received XVd were fatigue, nausea, decreased appetite, diarrhea, peripheral neuropathy, upper respiratory tract infection, decreased weight, cataract, and vomiting.

Grade 3–4 laboratory abnormalities (≥10%) were thrombocytopenia, lymphopenia, hypophosphatemia, anemia, hyponatremia and neutropenia. Fatal ARs occurred in 6% of patients within 30 days of last treatment. Serious ARs occurred in 52% of patients. Treatment discontinuation rate due to ARs was 19%. The most frequent ARs requiring permanent discontinuation in >2% of patients included fatigue, nausea, thrombocytopenia, decreased appetite, peripheral neuropathy and vomiting. Adverse reactions led to XPOVIO dose interruption in 83% of patients and dose reduction in 64% of patients.

Please see additional Important Safety Information throughout.

XPOVIO® (selinexor)

XPOVIO®
(selinexor)

For patients relapsing on an anti-CD38 mAb-based regimen, consider

XPOVIO – The fastest growing brand in 3L MM in 2023

Based on IntrinsiQ® claims analysis comparing U.S. XPOVIO market share in new patients vs. available brands approved in 3L MM in FY 2023[22]

XVd is a preferred NCCN Category 1 regimen in early RRMM[3]

Oral, once-weekly selinexor (XPOVIO®) in combination with bortezomib and dexamethasone (XVd) is recommended by the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) as a preferred NCCN Category 1* therapeutic option in previously treated (1–3 prior lines), lenalidomide-refractory MM.

*Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

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Monday through Friday, 8 AM to 8 PM ET or
VISIT **KaryForward.com/hcp**

KaryForward® is a patient support program for eligible XPOVIO patients and provides dedicated help with insurance information, financial assistance, and guidance from Nurse Case Managers.

USE IN SPECIFIC POPULATIONS

No overall difference in effectiveness of XPOVIO was observed in patients >65 years old when compared with younger patients. Patients ≥65 years old had a higher incidence of discontinuation due to an adverse reaction (AR) and a higher incidence of serious ARs than younger patients.

The effect of end-stage renal disease (CL_{CR} <15 mL/min) or hemodialysis on XPOVIO pharmacokinetics is unknown.

ADVERSE REACTIONS

The most common adverse reactions (ARs) (≥20%) in patients with multiple myeloma who received XVd were fatigue, nausea, decreased appetite, diarrhea, peripheral neuropathy, upper respiratory tract infection, decreased weight, cataract, and vomiting.

Please see Important Safety Information and accompanying full Prescribing Information.

Abbreviations: 1/2/3L, first-/second-/third-line; 5-HT3, serotonin; AR, adverse reaction; ASCT, autologous stem cell transplant; CAR-T, chimeric antigen receptor T cell; CD, cluster of differentiation; CI, confidence interval; CL_{CR}, creatinine clearance; CR, complete response; Dara, daratumumab; DOR, duration of response; DPd, daratumumab, pomalidomide, and dexamethasone; DR, daratumumab and lenalidomide; DRd, daratumumab, lenalidomide, and dexamethasone; DRVd, daratumumab, lenalidomide, bortezomib, and dexamethasone; FY, fiscal year; G-CSF, granulocyte-colony stimulating factor; HR, hazard ratio; IMiD, immunomodulatory drug; ITT, intention to treat; Len, lenalidomide; mAb, monoclonal antibody; MM, multiple myeloma; mOS, median overall survival; NCCN, National Comprehensive Cancer Network® (NCCN®); NE, not evaluable; NK-1, neurokinin 1; NR, not reached; ORR, overall response rate; (m)PFS, (median) progression-free survival; PI, proteasome inhibitor; PR, partial response; Q, every; QHS, at night; RRMM, relapsed and/or refractory multiple myeloma; RVd, lenalidomide, bortezomib, and dexamethasone; sCR, stringent complete response; T_0, time zero; Vd, bortezomib and dexamethasone; VGPR, very good partial response; XPO1, exportin 1; XVd, selinexor, bortezomib, and dexamethasone.

References: 1. XPOVIO® [prescribing information]. Newton, MA: Karyopharm Therapeutics Inc.; **2.** Data on File. Karyopharm Therapeutics Inc. 2021 [1]; **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) on Multiple Myeloma V2.2024. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed December 7, 2023. To view the most recent and complete version of the guideline, go online to www.NCCN.org; **4.** Dimopoulos MA, et al. *Clin Lymphoma Myeloma Leuk*. 2022;22(7):460–473; **5.** Ghandi UH, et al. *Leukemia*. 2019;33(9):2266–2275; **6.** Data on File. Karyopharm Therapeutics Inc. 2023 [1]; **7.** REVLIMID® [prescribing information]. Princeton, NJ: Bristol-Myers Squibb; **8.** VELCADE® [prescribing information]. Lexinton, MA: Takeda Pharmaceuticals America, Inc.; **9.** DARALEX® [prescribing information]. Beerse, Belgium: Janssen Pharmaceuticals, Inc.; **10.** TECVAYLI® [prescribing information]. Beerse, Berlin: Janssen Biotech, Inc.; **11.** EVOMELA® [prescribing information]. East Windsor, NJ: Acrotech Biopharma LLC; **12.** ABECMA® [prescribing information]. Summit, NJ: Bristol-Myers Squibb; **13.** Data on File. Karyopharm Therapeutics Inc. 2023 [2]; **14.** Grosicki S, et al. *Lancet*. 2020;396(10262):1563–1573; **15.** Data on File. Karyopharm Therapeutics Inc. 2024 [1]; **16.** Data on File. Karyopharm Therapeutics Inc. 2021 [2]; **17.** Data on File. Karyopharm Therapeutics Inc. 2023 [3]; **18.** Gavriatopoulou M, et al. *Leukemia*. 2020;34(9):2430–2440; **19.** Mikhael J, et al. *Clin Lymphoma Myeloma Leuk*. 2020;20(6):351–357; **20.** Jagannath S, et al. *Clin Lymphoma Myeloma Leuk*. 2023;23(12):917–923.e3; **21.** Jagannath S, et al. *Blood*. 2021;138 (Suppl.1):3793; **22.** Data on File. Karyopharm Therapeutics Inc. 2024 [2].

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