Consider switching class with XPOVIO® for patients at relapse:

XPOVIO® (selinexor)

See how XPOVIO may be an option within four different patient journeys in multiple myeloma

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

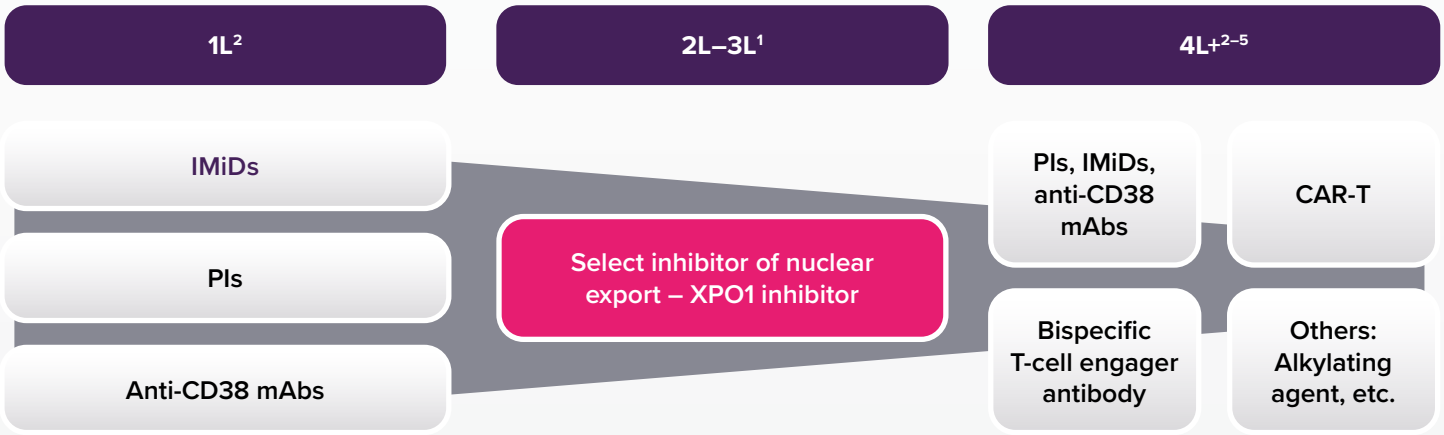
Thrombocytopenia: XPOVIO can cause life-threatening thrombocytopenia, potentially leading to hemorrhage. Thrombocytopenia was reported in patients with multiple myeloma. Thrombocytopenia is the leading cause of dosage modifications.

Please see additional Important Safety Information on the next page and throughout this brochure.

All patient cases throughout this brochure are hypothetical and are not actual patients.

Consider switching class with XPOVIO® for patients at relapse, including those who have been exposed to an anti-CD38 mAb-based regimen[1]

LINES OF THERAPY IN MM



Select presentation - not intended to be comprehensive.

XPOVIO is the first and only FDA-approved XPO1 inhibitor that helps restore the body's own tumor suppressor pathways to fight MM after at least one prior therapy[1,6,7]

NCCN Category 1 Recommendation

Oral, once-weekly selinexor (XPOVIO®) in combination with bortezomib and dexamethasone (XVd) is recommended by the National Comprehensive Cancer Network® (NCCN®) as a Category 1* therapeutic option in previously treated MM (1–3 prior therapies).†[2]

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

IMPORTANT SAFETY INFORMATION

Thrombocytopenia (cont'd): 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.

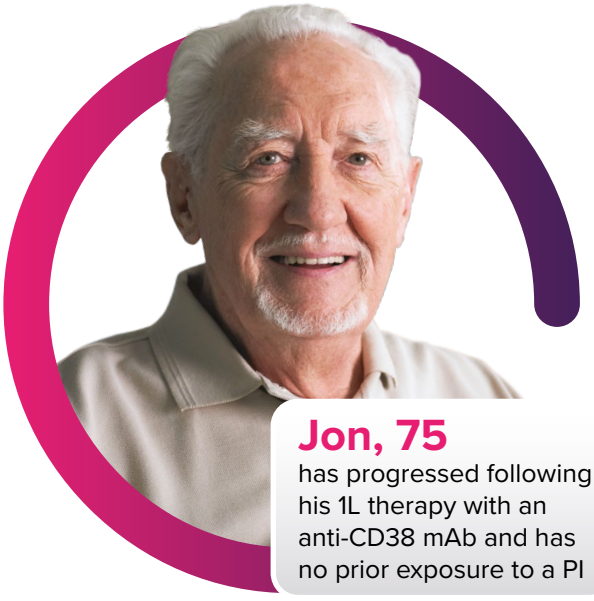
Please see additional Important Safety Information on the next page and throughout this brochure.

MEET OUR PATIENTS‡

XPOVIO® (selinexor)

Michelle, 66
has recently relapsed following her 2L therapy

Emily, 69
has chronic kidney disease and has progressed following her 2L therapy, which included an anti-CD38 mAb treatment



Jon, 75
has progressed following his 1L therapy with an anti-CD38 mAb and has no prior exposure to a PI

Joseph, 68
has high-risk cytogenetics and was treated with a quadruplet combination as 1L therapy with stem cell transplant; after 2 years, his disease has progressed

IMPORTANT SAFETY INFORMATION

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 on the next page and throughout this brochure.

‡Michelle, Jon, Emily, and Joseph are not actual patients.

Michelle, 66, has relapsed following 2L therapy

XPOVIO® (selinexor)

Diagnosis: R-ISS stage II MM

- 5-month history of fatigue
- New onset hip pain
- Tenderness upon palpation at the hips and lower back

1st Line

RVd: (8 cycles) lenalidomide + bortezomib + dexamethasone

Stem cell transplant

Maintenance lenalidomide (8 months)

2nd Line

DPd: daratumumab + pomalidomide + dexamethasone

Continuous therapy DPd (13 months)*

Consider XPOVIO + Vd for patients who may benefit from a class switch at second relapse, including those like Michelle

*Daratumumab dosing frequency is weekly for Weeks 1–8, biweekly for Weeks 9–24, every four weeks for Weeks 25 onwards.[8]

The XVd trial was a Phase 3, global, randomized, open-label, study in adult patients with MM who had received 1–3 prior therapies that compared XVd vs Vd[1,9†]

402 Patients

- **XVd (n=195)** Once-weekly XPOVIO + bortezomib with twice-weekly dexamethasone
- **Vd (n=207)** Twice-weekly bortezomib + four-times-weekly dexamethasone

Primary endpoint:
Progression-free survival (PFS)

Select secondary endpoints:
Overall response rate (ORR)
Very good partial response (VGPR)
Duration of response (DOR)
Safety and tolerability

†Efficacy results are from topline data analysis unless otherwise noted.

IMPORTANT SAFETY INFORMATION

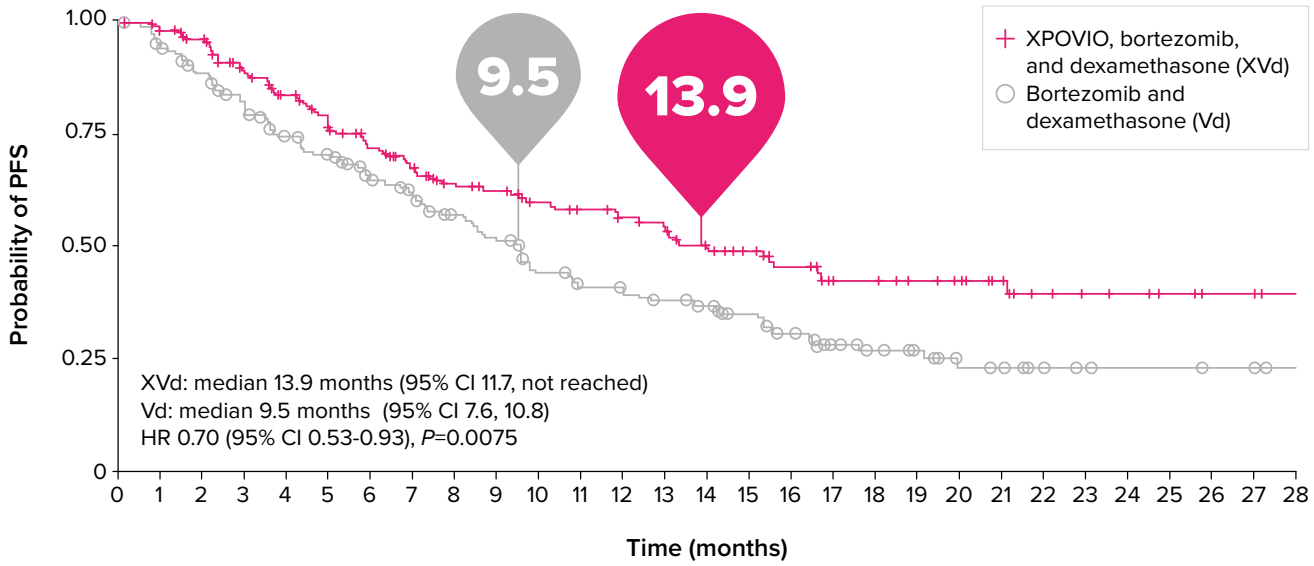
Gastrointestinal Toxicity: XPOVIO can cause severe gastrointestinal toxicities in patients.

Please see additional Important Safety Information on the next page and throughout this brochure.

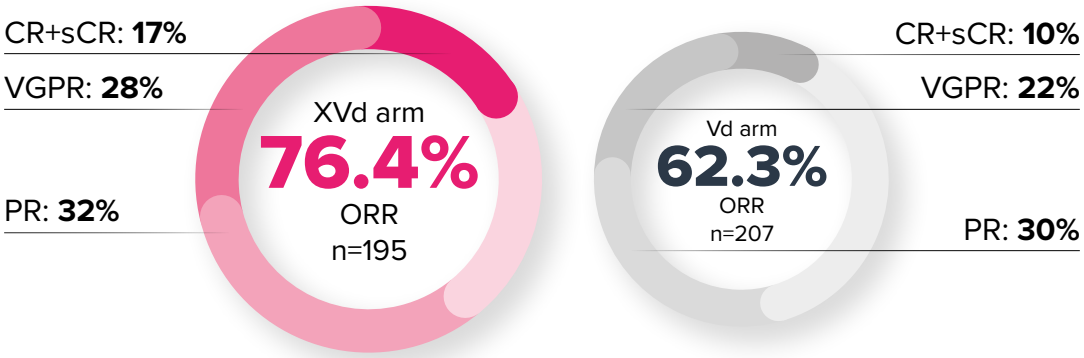
In the XVd trial, XVd demonstrated an early and sustained PFS benefit over Vd, with deep and durable responses[1]

XPOVIO® (selinexor)

mPFS in the XVd trial



ORR in the XVd trial (*P*=0.0012)



95% CI: 69.8, 82.2

95% CI: 55.3, 68.9

Median DOR in the XVd trial

20.3 months — **Once-weekly XVd**
95% CI: 12.5, NE

12.9 months — **Twice-weekly Vd**
95% CI: 9.3, 15.8

IMPORTANT SAFETY INFORMATION

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 this brochure.

Safety profile of XPOVIO + Vd[1]

XPOVIO® (selinexor)

ARs (≥10%) in patients with MM who received XVd with a difference between arms of >5% compared to Vd

	Weekly XVd		Twice-weekly Vd	
	All grades (%)	Grade 3 or 4 (%)	All grades (%)	Grade 3 or 4 (%)
GASTROINTESTINAL				
Nausea	50.0	8.0	10.0	0
Diarrhea	32.0	6.0	25.0	<1
Vomiting	21.0	4.1	4.4	0
GENERAL CONDITIONS				
Fatigue*	59.0	21	28.0	5
Pyrexia	15.0	1.5	11.0	1
METABOLISM AND NUTRITION				
Appetite decrease	35.0	3.6	5.0	0
Weight decrease	26.0	2.1	12.0	1
NERVOUS SYSTEM				
Peripheral neuropathy†	32.0	4.6	47.0	9
Dizziness	12.0	<1	3.9	0
INFECTIONS				
Upper respiratory tract infection‡	29.0	3.6	22.0	1.5
EYE DISORDERS				
Cataract	22.0	9.0	6.0	1.5
Vision blurred§	13.0	<1.0	6.0	0

*Fatigue includes fatigue and asthenia. †Peripheral neuropathy includes peripheral neuropathy, 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. §Vision blurred includes blurred vision, visual acuity reduced, and visual impairment.

Considerations for optimizing treatment for Michelle[1]:

- In the XVd trial, **nausea events were observed in 50% of patients** (8% Grade 3 or 4) who received the XVd regimen
  - Before starting therapy with XPOVIO, provide two prophylactic antiemetics such as a 5-HT3 receptor antagonist and other anti-nausea agents

Please see additional Important Safety Information throughout this brochure.

Select laboratory abnormalities associated with XPOVIO + Vd[1]

XPOVIO® (selinexor)

The following laboratory abnormalities (≥15%) worsened from baseline in patients with MM who received XVd[1]

	Weekly XVd		Twice-weekly Vd	
	All grades (%)	Grade 3 or 4 (%)	All grades (%)	Grade 3 or 4 (%)
HEMATOLOGIC				
Platelet count decrease	92.0	43.0	51.0	19.0
Lymphocyte count decrease	77.0	38.0	70.0	27.0
Hemoglobin decrease	71.0	17.0	51.0*	12.0
Neutrophil count decrease	48.0	12.0	19.0	7.0
CHEMISTRY				
Glucose increase	62.0	3.8	47.0	4.1
Phosphate decrease	61.0	23.0	42.0	11.0
Sodium decrease	58.0	14.0	25.0	3.0
Calcium decrease	55.0	2.1	47.0	1.0
Blood urea nitrogen increase	41.0	5.0	40.0	5.0
Creatinine increase	28.0	3.6	24.0	1.5
Potassium decrease	27.0	6.0	22.0	3.5
Magnesium decrease	27.0	<1.0	23.0	1.5
Potassium increase	18.0	4.1	21.0	2.5
HEPATIC				
ALT increase	33.0	3.1	30.0	<1.0
Albumin decrease	27.0	<1.0	35.0	<1.0
AST increase	24.0	1.5	19.0	<1.0
Bilirubin increase	16.0	1.0	13.0	2.0
ALP increase	12.0	0.0	16.0	<1.0

The denominator used to calculate the rate varied from 91 to 201 based on the number of patients with at least one post-treatment value.
*Includes one fatal anemia.

- The median treatment duration was 30 weeks (range: 1–120 weeks) in patients who received once-weekly XVd as compared to 32 weeks (range: 1–122 weeks) in patients who received twice-weekly Vd
- Permanent discontinuation of XPOVIO due to an AR occurred in 19% of patients
- ARs that resulted in permanent discontinuation of XPOVIO in >2% of patients included fatigue (3.6%), nausea (3.1%), thrombocytopenia, decreased appetite, peripheral neuropathy, and vomiting (2.1% each)

XVd was not associated with serious organ toxicities of the cardiac, pulmonary, renal, or liver systems[10]

Please see additional Important Safety Information on the next page and throughout this brochure.

XPOVIO® (selinexor)

Emily, 69, has chronic kidney disease, and progressed following her 2L therapy with an anti-CD38 mAb

Diagnosis: R-ISS stage I MM

- Chronic fatigue
- New onset back pain
- Tenderness upon palpation at the hips and lower back

1st Line

RVd: (8 cycles) lenalidomide + bortezomib + dexamethasone

Stem cell transplant

Maintenance lenalidomide (14 months)

2nd Line

DKd: daratumumab + carfilzomib + dexamethasone

Continuous therapy DKd (28 months)*

Emily's Key Patient Characteristics

- CL_{CR}: 45 mL/min
- Previous anti-CD38 mAb exposure

A class switch to XPOVIO + Vd may be an option for patients, like Emily, who have renal insufficiency

*Daratumumab dosing frequency is twice the first week, weekly for Weeks 2–8, every two weeks for Weeks 9–24, every four weeks for Weeks 25 onwards[8]

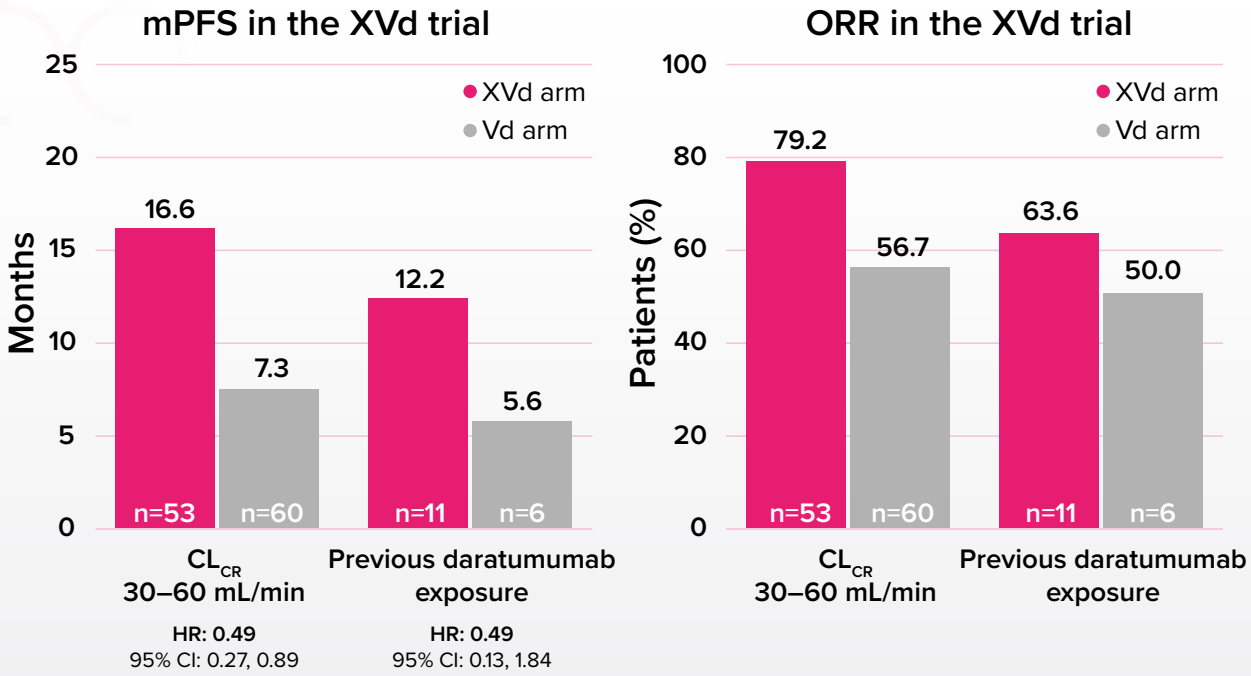
IMPORTANT SAFETY INFORMATION

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

Please see additional Important Safety Information on the next page and throughout this brochure.

Efficacy observed in multiple subgroups[10]

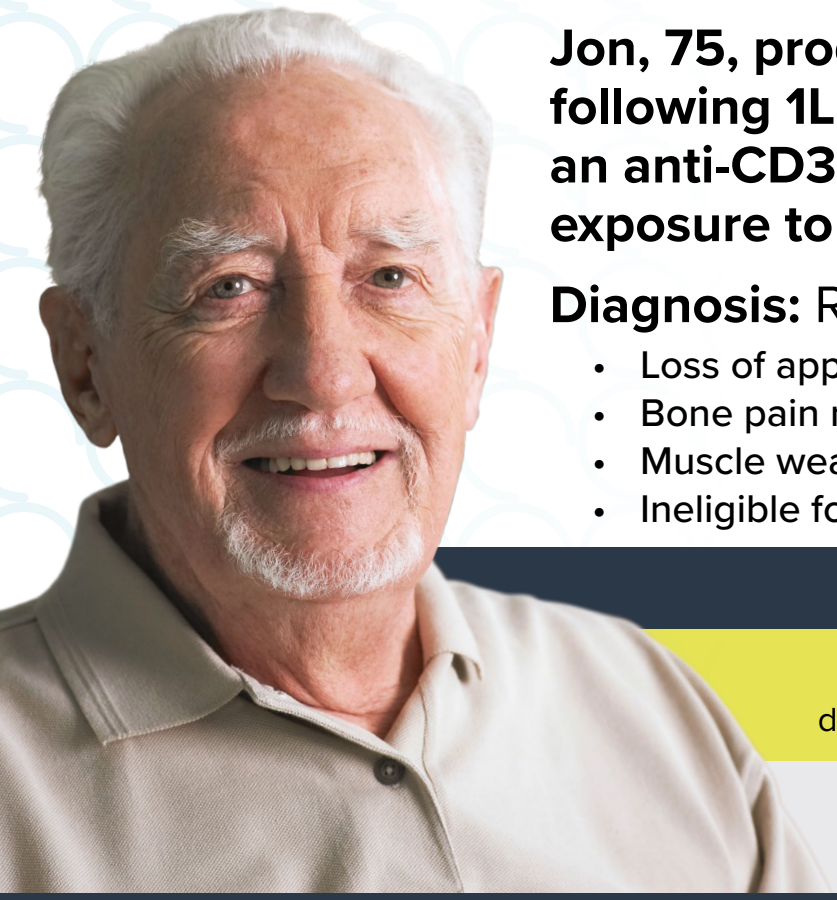
XPOVIO® (selinexor)



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/ORR across these subgroups.

Considerations for optimizing treatment for Emily[1]:

- In the XVd trial, **59% (21% Grade 3 or 4) of patients who received the XVd regimen experienced fatigue.**
- For Grade 2 lasting greater than 7 days OR Grade 3:
  - Interrupt, monitor until fatigue resolves to Grade 1 or baseline, then restart XPOVIO at 1 dose lower
  - Consider providing nutritional support



XPOVIO® (selinexor)

Jon, 75, progressed following 1L therapy with an anti-CD38 mAb and has no prior exposure to a proteasome inhibitor

Diagnosis: R-ISS stage I MM

- Loss of appetite for 8 weeks
- Bone pain near chest
- Muscle weakness upon examination
- Ineligible for stem cell transplant

1st Line

DRd: (8 cycles)
daratumumab + lenalidomide + dexamethasone

Continuous therapy DRd (30 months)*

Jon's Key Patient Characteristics

PI-naïve

≥65 years

Consider a class switch to XPOVIO + Vd at first relapse for patients like Jon, who are at least 65 years of age and have not had prior PI exposure

*Daratumumab dosing frequency is weekly for Weeks 1–8, every two weeks for Weeks 9–24, every four weeks for Weeks 25 onwards.[8]

IMPORTANT SAFETY INFORMATION

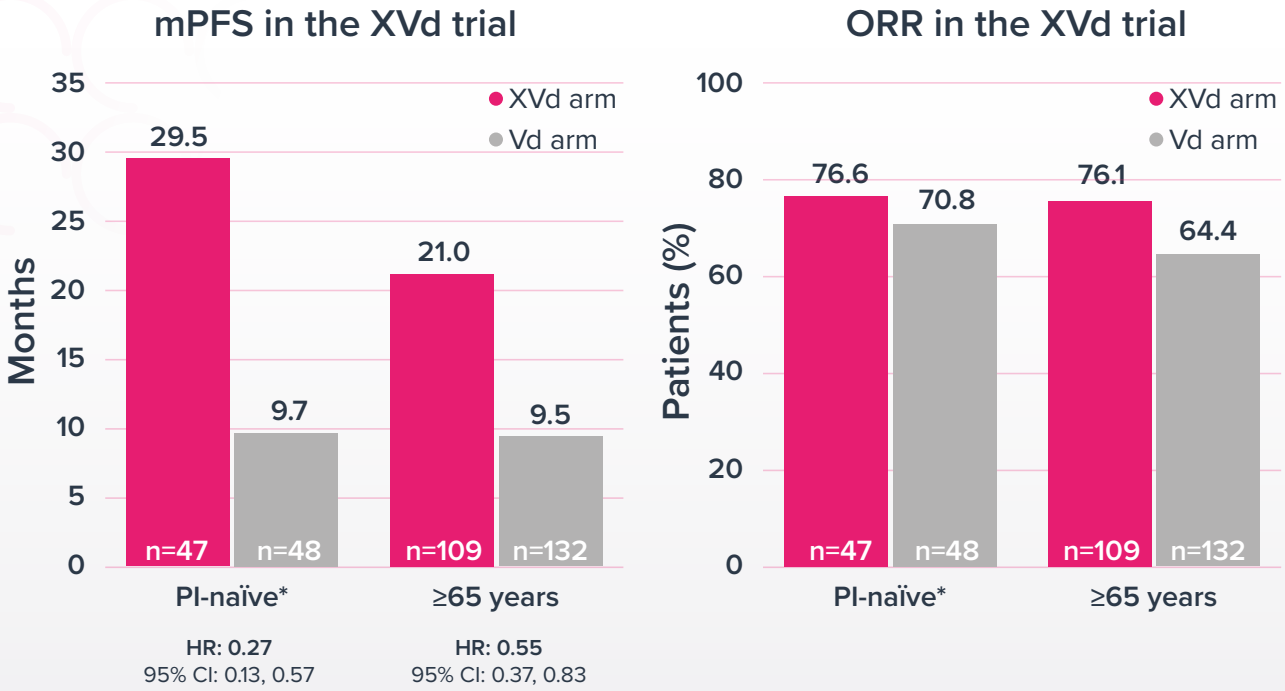
Neurological Toxicity: XPOVIO can cause life-threatening neurological toxicities.

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 on the next page and throughout this brochure.

Efficacy observed in multiple subgroups[10]

XPOVIO® (selinexor)



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/ORR across these subgroups.

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

Considerations for optimizing treatment for Jon[1]:

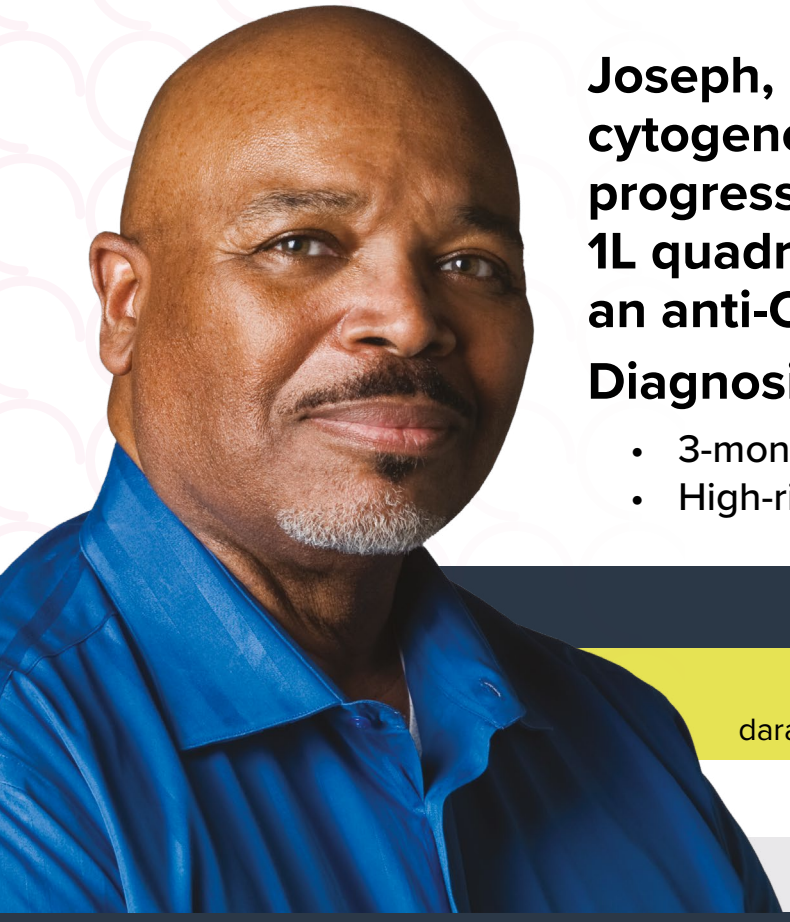
- **In the XVd trial, thrombocytopenia was reported in 92% (43% Grade 3 or 4) of patients who received the XVd regimen**
  - Monitor platelet counts at baseline and throughout treatment and administer platelet transfusion and/or other treatments as clinically indicated

IMPORTANT SAFETY INFORMATION

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

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 on the next page and throughout this brochure.



XPOVIO® (selinexor)

Joseph, 68, has high-risk cytogenetics, and progressed following his 1L quadruplet therapy with an anti-CD38 mAb

Diagnosis: R-ISS stage I MM

- 3-month history of fatigue
- High-risk cytogenetics: del[17p]

1st Line

DVTd: (8 cycles)
daratumumab + bortezomib + thalidomide + dexamethasone

Stem cell transplant

Maintenance daratumumab (24 months)*

Joseph's Key Patient Characteristics

- High-risk cytogenics: del[17p]
- Previous anti-CD38 mAb exposure

XPOVIO + Vd may be an option for patients who have high-risk cytogenetics, including those like Joseph, who may benefit from a class switch

*Daratumamab dosing frequency is every two weeks for Weeks 1–8.[8]

IMPORTANT SAFETY INFORMATION

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

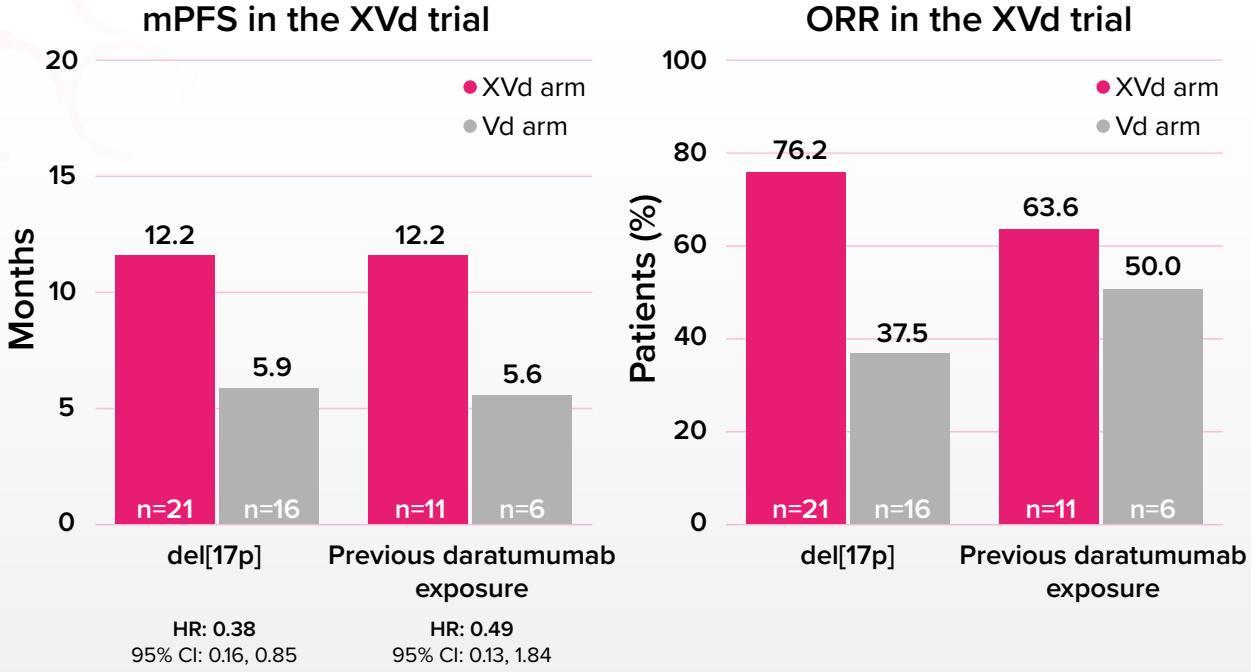
Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential and males with a female partner of reproductive potential to use effective contraception during treatment with XPOVIO and for 1 week after the last dose.

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 on the next page and throughout this brochure.

Efficacy observed in multiple subgroups[10]

XPOVIO® (selinexor)



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/ORR across these subgroups.

Considerations for optimizing treatment for Joseph[1]:

- **In the XVd trial, hyponatremia was reported in 58% (14% Grade 3 or 4) of patients who received the XVd regimen**
  - Monitor sodium level at baseline and throughout treatment and assess hydration status and manage hyponatremia per clinical guidelines

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.

Grade 3-4 laboratory abnormalities (≥10%) were thrombocytopenia, lymphopenia, hypophosphatemia, anemia, hyponatremia and neutropenia.

Please see additional Important Safety Information on the next page and throughout this brochure.

Getting started on XPOVIO

XPOVIO® (selinexor)

The recommended dosage of XPOVIO + Vd[1]

DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
 **XPOVIO 100 mg** + bortezomib 1.3 mg/m² + dexamethasone 20 mg	dexamethasone 20 mg	**No dose**	**No dose**	**No dose**	**No dose**	**No dose**

 = 50 mg

XPOVIO 100 mg taken orally once weekly on Day 1 of each week until disease progression or unacceptable toxicity in combination with

- **Bortezomib 1.3 mg/m² administered subcutaneously once weekly** on Day 1 of each week for 4 weeks, followed by 1 week off
- **Dexamethasone 20 mg taken orally twice weekly** on Days 1 and 2 each week

Oral once-weekly XPOVIO dose may be modified to help mitigate ARs[1]

Four dosage strengths are available for dose modifications[1]

100 mg | 80 mg | 60 mg | 40 mg

ADVERSE REACTIONS (cont'd)

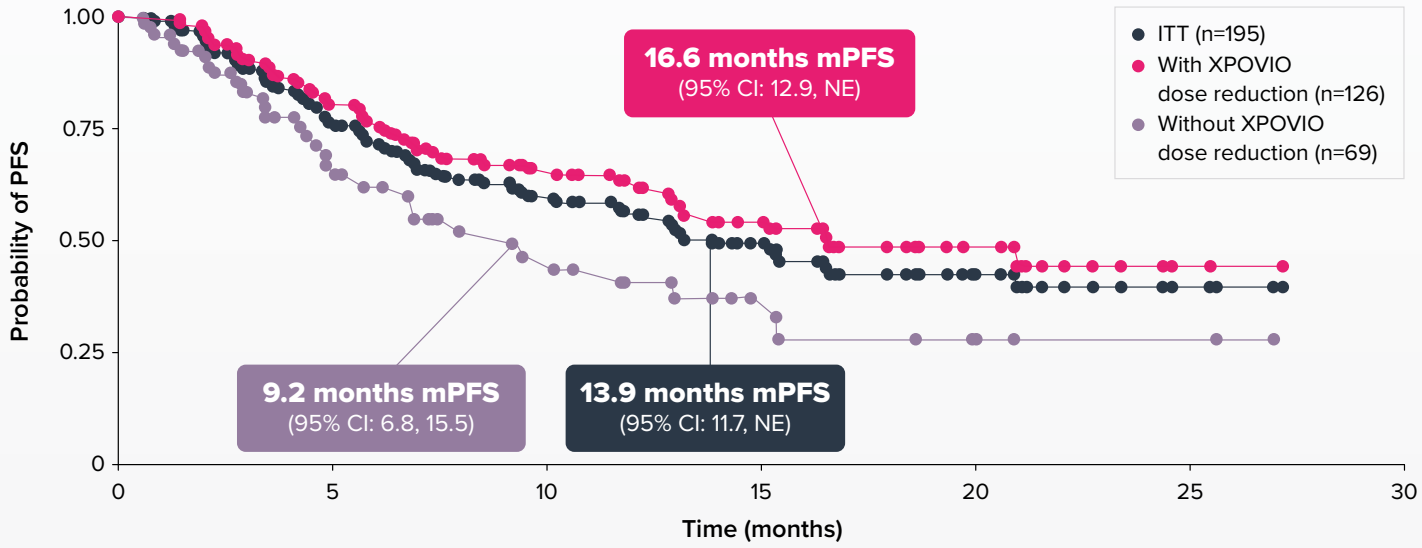
Fatal ARs occurred in 6% of patients within 30 days of last treatment. Serious ARs occurred in 52% of patients. Treatment discontinuation rate due to ARs was 19%. The most frequent ARs requiring permanent discontinuation in >2% of patients included fatigue, nausea, thrombocytopenia, decreased appetite, 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 on the next page and throughout this brochure.

XPOVIO® (selinexor)

Efficacy maintained in patients with XPOVIO dose reduction to help mitigate ARs[11]

mPFS in dose-reduced patient population[1,11]



Limitations of subgroup analyses:

- This post hoc analysis was exploratory in nature and 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 in the XVd arm had an **XPOVIO dose reduction**[10]

80 mg (range 30–137 mg) taken once weekly was the **median dosage of XPOVIO** in the XVd arm[1]

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 (CLCR <15 mL/min) or hemodialysis on XPOVIO pharmacokinetics is unknown.

Please see Important Safety Information and full Prescribing Information.
To report SUSPECTED ADVERSE REACTIONS, contact Karyopharm Therapeutics Inc. at 1-888-209-9326 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see additional Important Safety Information on the next page and throughout this brochure.

XPOVIO® (selinexor)

Consider a **mechanistic switch** with XPOVIO for patients at relapse, including those who have been exposed to an anti-CD38 mAb-containing regimen

XPOVIO + Vd demonstrated an **early and sustained PFS benefit** over Vd, with deep and durable responses[1]

- The XVd mPFS was 13.9 months vs the Vd mPFS of 9.5 months (*P*=0.0075)
- The XVd ORR was 76.4% vs the Vd ORR of 62.3%

Oral, once-weekly XPOVIO **dosing may be adjusted** to help mitigate ARs[1]

NCCN Category 1 Recommendation

Oral, once-weekly selinexor (XPOVIO®) in combination with bortezomib and dexamethasone (XVd) is recommended by the National Comprehensive Cancer Network® (NCCN®) as a Category 1* therapeutic option in previously treated MM (1–3 prior therapies).†[2]

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

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VISIT KaryForward.com/hcp

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.

XVd vs Vd trial: Phase 3, global, randomized, open-label study of adult patients with MM who had received 1-3 prior therapies that compared XVd with Vd. In the trial, 402 patients were randomized into 2 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 endpoint included ORR.

Abbreviations: 1/2/3/4L, first-/second-/third-/fourth-line; 5-HT3, serotonin; ALP, alkaline phosphatase; ALT, alanine transaminase; AR, adverse reaction; AST, aspartate aminotransferase; CAR-T, chimeric antigen receptor T cell; CD, cluster of differentiation; 5-HT3, serotonin; CI, confidence interval; CL_{CR}, creatinine clearance; CR, complete response; D, daratumumab; DKd, daratumumab, carfilzomib, and dexamethasone; DOR, duration of response; DPd, daratumumab, pomalidomide, and dexamethasone; DRd, daratumumab, lenalidomide, and dexamethasone; DVTd, daratumumab, bortezomib, thalidomide, and dexamethasone; FDA, US Food and Drug Administration; G-CSF, granulocyte-colony stimulating factor; HR, hazard ratio; IMiD, immunomodulatory drug; ITT, intention to treat; mAb, monoclonal antibody; MM, multiple myeloma; NCCN, National Comprehensive Cancer Network® (NCCN®); NE, not evaluable; ORR, overall response rate; (m)PFS, (median) progression-free survival; PI, proteasome inhibitor; PR, partial response; R-ISS, Revised Multiple Myeloma International Staging System; RVd, lenalidomide, bortezomib, and dexamethasone; sCR, stringent complete response; 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.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) on Multiple Myeloma V.3.2023. ©National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed January 13, 2023. To view the most recent and complete version of the guideline, go online to www.NCCN.org; **3.** TECVAYLI® [prescribing information]. Beerse, Berlin: Janssen Biotech, Inc.; **4.** EVOMELA® [prescribing information]. East Windsor, NJ: Acrotech Biopharma LLC; **5.** ABECMA® [prescribing information]. Summit, NJ: Bristol-Myers Squibb; **6.** Azmi AS, et al. *Nat Rev Clin Oncol*. 2021;18(3):152–169; **7.** Benkova K, et al. *Blood Rev.* 2021;46:100758; **8.** DARALEX® [prescribing information]. Beerse, Belgium: Janssen Pharmaceuticals, Inc. **9.** Grosicki S, et al. *Lancet*. 2020;396(10262):1563–1573; **10.** Data on file. Karyopharm Therapeutics Inc. 2021. **11.** Jagannath S, et al. Clinical outcomes in patients (Pts) with dose reduction of selinexor in combination with bortezomib, and dexamethasone (XVd) in previously treated multiple myeloma from the BOSTON study. Poster presented at: 63rd ASH Annual Meeting and Exposition; December 13, 2021; Atlanta, GA.