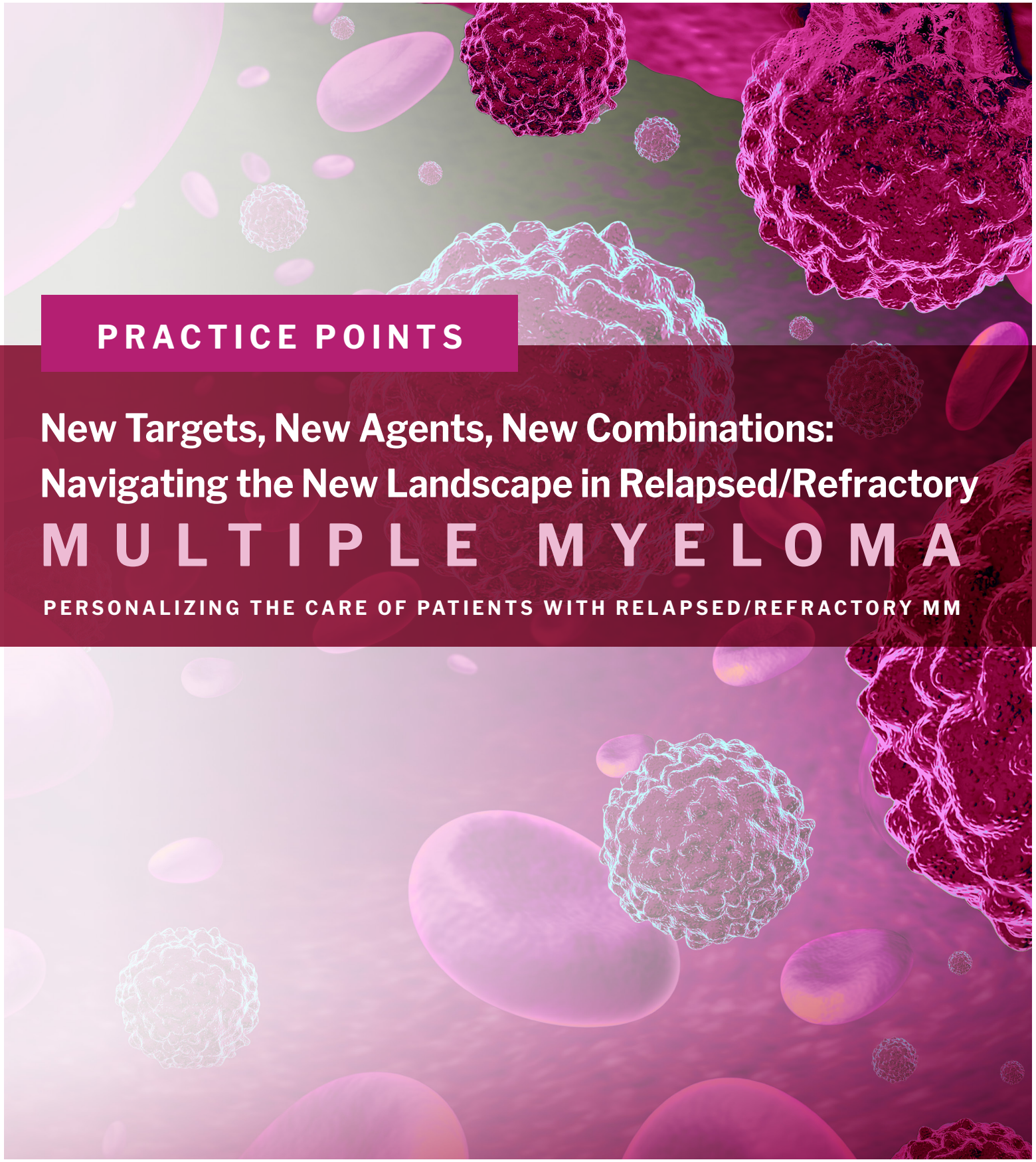


PRACTICE POINTS

New Targets, New Agents, New Combinations: Navigating the New Landscape in Relapsed/Refractory MULTIPLE MYELOMA

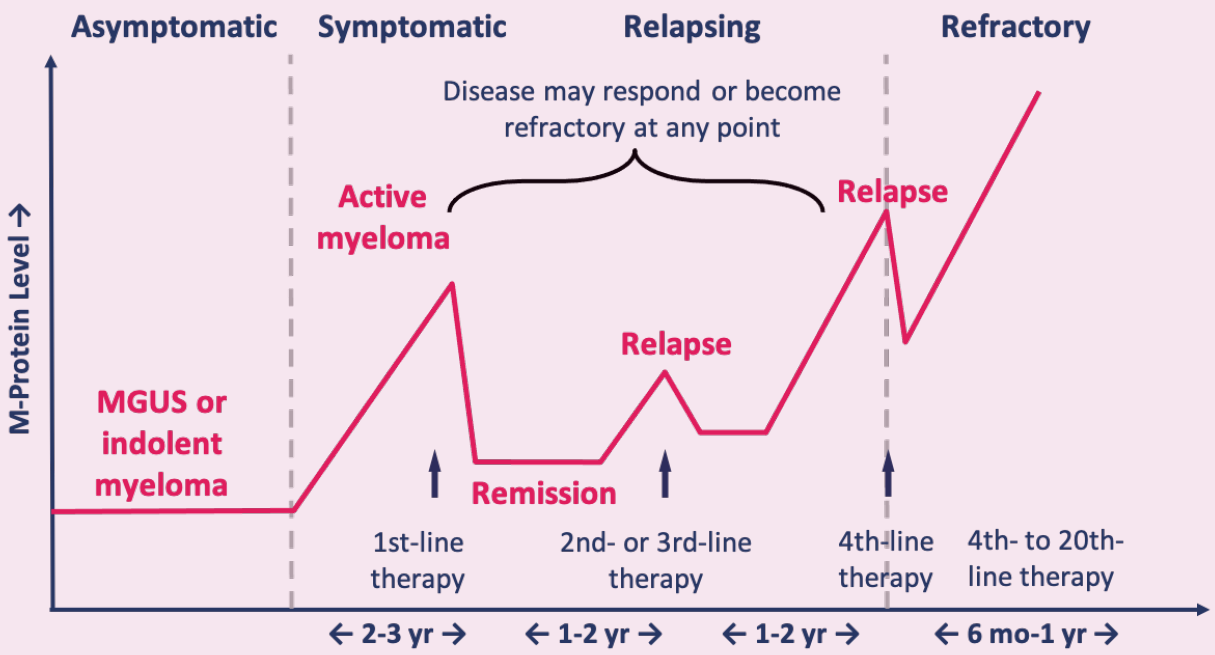
PERSONALIZING THE CARE OF PATIENTS WITH RELAPSED/REFRACTORY MM

This activity is jointly provided by PIM Postgraduate Institute for Medicine Bio Ascend™

Table of Contents

This activity is jointly provided by PIM Postgraduate Institute for Medicine Bio Ascend™

The Course of Myeloma Therapy – Lack of Cure



Relapsed/refractory MM
Progression after achieving at least minor response or progression within 60 days of most recent therapy

Primary refractory MM
Progression without achieving at least minor response

Relapsed MM
Progressive disease but does not fit definition of relapsed/refractory or primary refractory

Durie BGM. IMF Concise Review. 2018 Edition. https://imf-d8-prod.s3.us-west-1.wasabisys.com/resource/ConciseReview.pdf. Accessed July 1, 2021.

Factors in Selecting Treatment for R/R MM

Disease-related factors

- Duration of response to initial therapy
- High-risk vs low-risk status
- Molecular disease progression vs symptomatic progression
- Other comorbid conditions, patient frailty
- Treatment-related factors

Previous therapy exposure (relapsed or refractory)

- Toxicity/tolerability of previous regimen (combination vs single agent)
- Mode of administration (PO or IV or SC)
- Cost and convenience (out-of-pocket co-pays for IV vs PO)
- Patient preference: control may be more desirable than cure at relapse

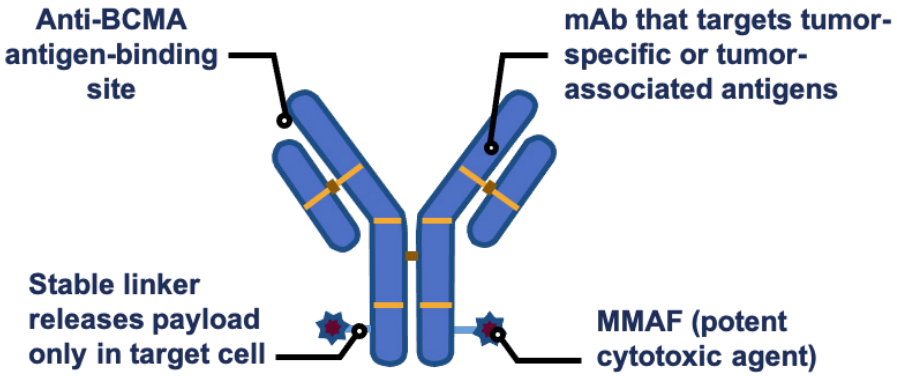
Recently Approved Agents/Regimens for Relapsed/Refractory MM*

July 9, 2021:	Daratumumab + pomalidomide and dexamethasone for patients with MM who have received at least one prior line of therapy including lenalidomide and a proteasome inhibitor
March 31, 2021:	Isatuximab + carfilzomib and dexamethasone for R/R MM who have received 1-3 prior lines of therapy
March 26, 2021:	Idecabtagene vicleucel for R/R MM after 4 or more lines of therapy
February 26, 2021:	Melphalan flufenamide + dexamethasone for R/R MM who have received at least 4 prior lines of therapy and are refractory to at least one PI, IMiD, and CD38-directed mAb
December 18, 2020:	Selinexor + bortezomib and dexamethasone for R/R MM who have received at least 1 prior therapy
August 5, 2020:	Belantamab mafodotin for R/R MM who have received at least 4 prior therapies, including an anti-CD38 mAb, a PI, and an IMiD
March 2, 2020:	Isatuximab + pomalidomide and dexamethasone for R/R MM who have received at least 2 prior therapies including lenalidomide and a PI

IMiD=immunomodulatory agent; mAb=monoclonal antibody; PI=proteasome inhibitor
*As of July 1, 2021.
FDA website. https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications?t=493234. Accessed July 1, 2021

Belantamab Mafodotin Summary

Belantamab mafodotin: humanized, afucosylated, IgG1 BCMA-targeted ADC that neutralizes soluble BCMA



Cytotoxic agent	MMAF (highly potent auristatin)
Afucosylation	Enhanced ADCC
Linker	Stable in circulation

FDA approved: For patients with R/R MM after ≥4 previous therapies including an anti-CD38 mAb, a PI, and an IMiD

DOSING **2.5 mg/kg IV once every 3 wk as infusion over 30 min**

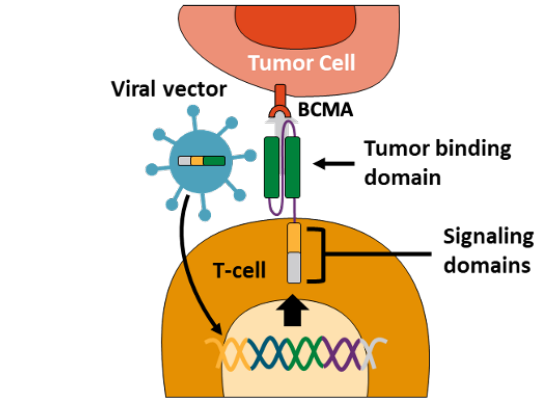
- Systemic steroids not required prior to initial infusion or in combination with belantamab, but patients should be monitored for infusion-related reactions
- Belantamab is only available through REMS program due to potential for ocular toxicity
- Counsel patients on what to expect when receiving belantamab, including about the risk of ocular toxicity and the need for ophthalmic examinations prior to each dose

IMiD=immunomodulatory agent; mAb=monoclonal antibody; PI=proteasome inhibitor

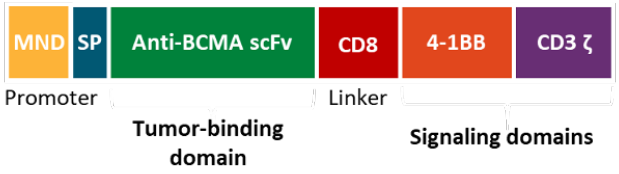
Tai YT, et al. *Blood*. 2014;123:3128-3138. Trudel S, et al. *Lancet Oncol*. 2018;19:1641-1653. Trudel S, et al. *Blood Cancer J*. 2019;9:37. BLENREP [package insert]. Research Triangle Park: GlaxoSmithKline; 2020.

Idecabtagene Vicleucel Summary

Idecabtagene vicleucel: BCMA-directed genetically modified autologous CAR T-cell therapy



Idecabtagene CAR design



FDA approved: For patients with R/R MM after ≥4 previous lines of therapy including a PI, an IMiD, and an anti-CD38 mAb

DOSING

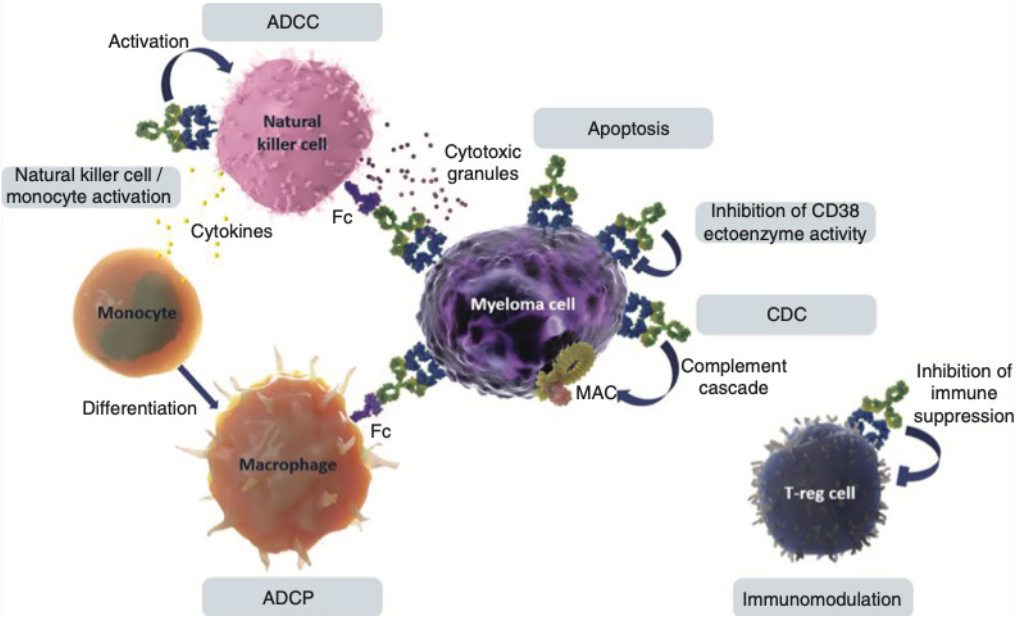
Recommended dose range: 300 to 460 × 10^6 CAR-positive T-cells

- Must be administered at certified healthcare facility under REMS; lymphodepleting chemotherapy regimen (cyclophosphamide and fludarabine) must be administered before infusion
- Premedicate with acetaminophen and H1-antihistamine, but avoid prophylactic use of systemic corticosteroids (eg, dexamethasone)
- Counsel patients on what to expect when receiving idecabtagene vicleucel, including the risk of CRS and neurotoxicity

ABECMA [package insert]. Summit, NJ: Celgene Corporation, a Bristol-Myers Squibb Company; 2021.

Isatuximab Summary

Isatuximab: a CD38-directed cytolytic antibody



FDA approved: In combination with pomalidomide and dexamethasone for patients who have received at least 2 prior therapies including lenalidomide and a PI

In combination with carfilzomib and dexamethasone for patients who have received 1-3 prior lines of therapy

DOSING

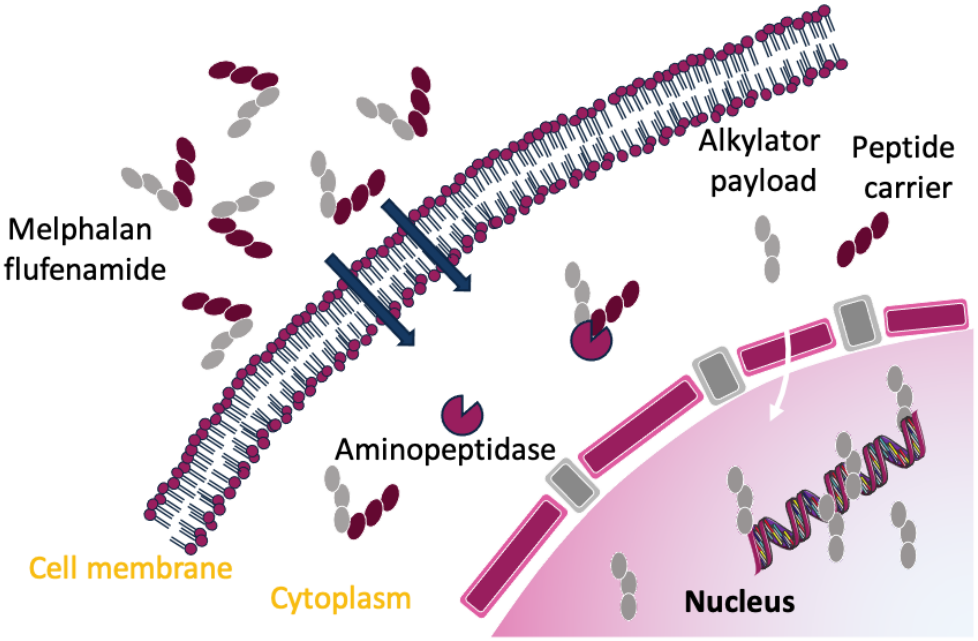
10 mg/kg IV every week for 4 weeks, followed by every 2 weeks until PD or toxicity

- Premedicate with dexamethasone, acetaminophen, H2 antagonists, and diphenhydramine
- Counsel patients on infusion-related reactions, neutropenia, SPMs, cardiac toxicities, interference with laboratory tests, and embryo-fetal toxicity

Moreau P, et al. *Future Oncol*. 2020;16:4347-4358. SARCLISA [package insert]. Bridgewater, NJ: sanofi-aventis US, LLC; 2021.

Melphalan Flufenamide Summary

Melphalan Flufenamide: first-in-class lipophilic peptide–drug conjugate hydrolyzed by peptidases to release hydrophilic alkylator payload



FDA approved: In combination with dexamethasone for patients with R/R MM after ≥4 previous lines of therapy and whose disease is refractory to ≥1 PI, 1 IMiD, and 1 anti-CD38 mAb

DOSING

40 mg IV once every mo as infusion via central venous access over 30 min

- Dexamethasone 40 mg orally or IV on Days 1, 8, 15, and 22

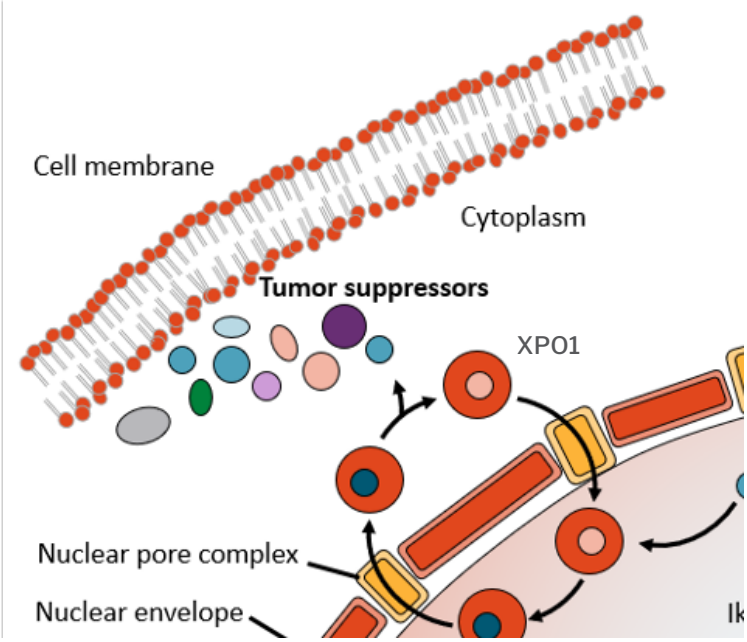
- Consider providing a 5-HT3 receptor antagonist or other antiemetics prior to and during treatment; patients should be monitored for infusion-related reactions
- Counsel patients on what to expect when receiving melphalan flufenamide, including nausea and need to monitor blood count and standard blood chemistry

XPOVIO [package insert]. Waltham, MA: Oncopeptides AB; 2021.

This activity is jointly provided by PIM Postgraduate Institute for Medicine Bio Ascend™

Selinexor Summary

Selinexor: an XPO1 inhibitor that induces nuclear retention and activation of TSPs and the GRPs in the presence of steroids and suppresses oncoprotein expression



FDA approved: In combination with bortezomib after ≥1 previous therapy. In combination with dexamethasone after ≥4 previous therapies and refractory to ≥2 PIs, ≥2 IMiDs, and an anti-CD38 mAb

Dosing With Vd **100 mg PO (five 20-mg tablets) once weekly**

Dosing With Dex **80 mg PO (four 20-mg tablets) on Days 1 and 3 of each wk**

- Patients should take 5-HT3 antagonists and/or other antinausea agents (eg, olanzapine) prior to and during treatment with selinexor
- Counsel patients on what to expect when receiving selinexor; advise patients to maintain adequate fluid and caloric intake; help patients with tools to ensure compliance with oral therapy

XPOVIO [package insert]. Newton, MA: Karyopharm Therapeutics Inc.; 2021. Gravina GL, et al. J *Hematol Oncol*. 2014;7:85. Culjkovic-Kraljacic B, et al. Cell Rep. 2012;2:207-215.