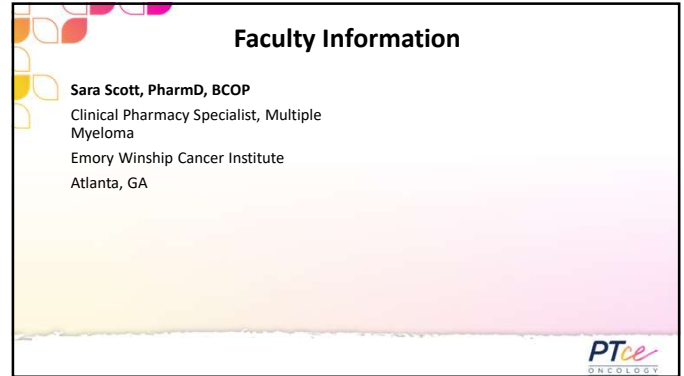
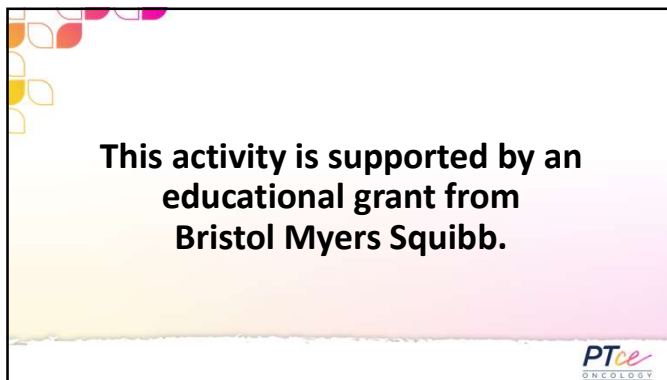


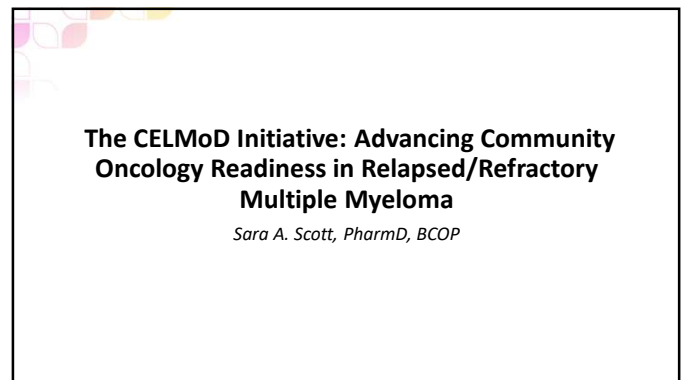
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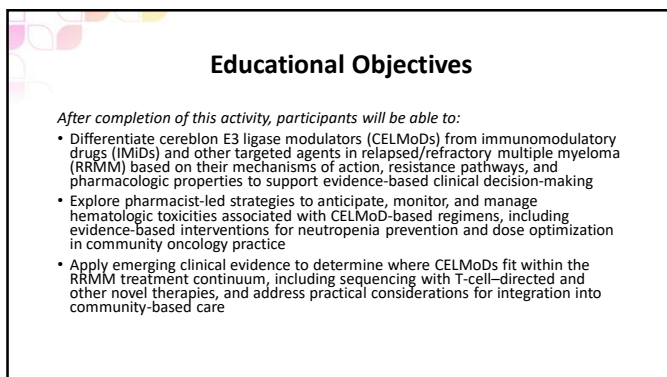
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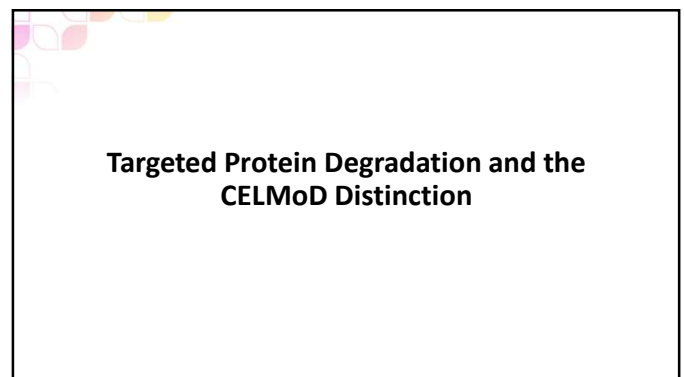
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6

Multiple Myeloma

- Incurable hematologic malignancy defined by clonal proliferation of immunoglobulin (Ig)-secreting malignant plasma cells
 - Secretion of M-protein into serum or urine
 - Results in end-organ damage
- US prevalence in 2025
 - 14th most common malignancy
 - Estimated 36,110 new cases and 12,030 deaths
- Median age at diagnosis: 69 years

Siegel RL, CA Cancer J Clin. 2025;75(1):10-45; NIH. Accessed March 16, 2026. <https://www.cancer.gov/statfacts/html/mulmy.html>; American Cancer Society. Accessed March 16, 2026. <https://www.cancer.org/cancer/types/multiple-myeloma.html>

7

Multiple Myeloma Drug Development Timeline

SEER 8 5-Year Relative Survival Percent from 1975-2017, All Races, Both Sexes.

ADC, antibody drug conjugate; Auto/Allo-SCT, autologous/allogeneic stem cell transplantation; BsAb, bispecific antibody; CAR, chimeric antigen receptor; mAb, monoclonal antibody; SINE, selective inhibitor of nuclear export.

Figure adapted from NIH. Accessed March 16, 2026. <https://seer.cancer.gov/statfacts/html/mulmy.html>; International Myeloma Foundation. Updated November 7, 2025. Accessed March 16, 2026. <https://www.myeloma.org/multiple-myeloma-drugs>

Approvals since 2015
Oral SINE: selinexor
mAb: isatuximab
CAR T cell: idecabtagene vicleucei, ciltacabtagene autoleucei
BsAb: tedditamab, ebranatamab, talquetamab, linvoseltamab
ADC: belantamab mafodotin

8

General Principles for Selecting Treatment in RRMM

Patient	Disease	Treatment	Regimen
<ul style="list-style-type: none"> Age/frailty Performance status Lifestyle Patient preference Caregiver support Comorbidities <ul style="list-style-type: none"> Renal status Neuropathy Cardiac Diabetes Cytopenias 	<ul style="list-style-type: none"> Disease burden: ISS <ul style="list-style-type: none"> Rate of progression Marrow burden CRAB symptoms Extramedullary disease Biology <ul style="list-style-type: none"> LDH Cytogenetics: <ul style="list-style-type: none"> del(17p) or TP53 mutation t(4,14) t(14,16) t(14,20) amp(14) Del(1p32) t(11,14) 	<ul style="list-style-type: none"> AEs <ul style="list-style-type: none"> Myelosuppression Infections Neuropathy Secondary cancers Access and cost Administration route Relapsed vs refractory Depth/duration of response to prior treatment 	<ul style="list-style-type: none"> Triplet is preferred over doublet Include ≥1 agent from a new or nonrefractory class Previously used agents may be effective in different combinations Treat to maximum response Depth/duration of response to prior treatment Maintain on ≥1 agent until progression or intolerance

AE, adverse effect; CRAB, calcium elevation, renal failure, anemia, bone disease; ISS, international staging system; LDH, lactate dehydrogenase; RRMM, relapsed/refractory multiple myeloma.
 NCCN. Clinical Practice Guidelines in Oncology. Multiple Myeloma, version 5.2026. Accessed March 16, 2026. https://www.nccn.org/professionals/physician_glg/pdf/multiplemyeloma.pdf; Sanchez L et al. Expert Rev Hematol. 2020;13(9):943-958; Sonnabend P, Brin J. A. Haematologica. 2016;101(4):396-406; Mapiex KT et al. Clin Adv Hematol Oncol. 2023;21(5):247-256; Avel Lohrhou H et al. J Clin Oncol. 2025;43(26):2789-2795.

9

Unmet Need in Patients With MM

ADDITIONAL ACTIVE TREATMENTS IN RELAPSED SETTING

- Patients receive triplet or quadruplet regimens within their first and second-line treatments—this may result in fewer existing treatment options for later lines of therapy.
- As CAR T-cell therapies and BsAbs are used earlier in the treatment algorithm, there is an emerging need for treatment options with activity in the post-T-cell redirection therapy setting.

SUBOPTIMAL OUTCOMES IN SPECIFIC POPULATIONS

- Elderly/frail patients: poor tolerance to intensive regimens
- High-risk cytogenetics: poor response across treatment settings
 - Current therapies insufficient to overcome high-risk biology
- Penta-exposed/refractory patients
- Post-T-cell redirecting therapy setting in the context of immune exhaustion

PATIENT-CENTERED CARE GAPS

- Oncology patients prefer oral chemotherapy over IV
- Oral therapies improve convenience, reduce clinic visits
- Adherence is still a challenge: 38% reported nonadherence
- Access/availability of CAR T-cell therapy

TV, intravenous.
 Ramasamy K et al. Clin Lymphoma Myeloma Leuk. 2025;25(5):337-348.e2; Rajkumar SV. Am J Hematol. 2022;97(8):1086-1107; Salkar ME, Mark TM. Curr Oncol. 2022;29(7):4464-4477; Erik D et al. Patient Prefer Adherence. 2016;10:359-362; Khan H et al. Clin Lymphoma Myeloma Leuk. 2023;23(1):38-45.

10

CELMoD: Mechanism of Action

- Highly selective molecular degraders that reprogram the cereblin ubiquitin ligase complex
- Leads to degradation of Ikaros and Aiolos and suppression of c-Myc and IRF4 signaling, induction of apoptosis, and immunostimulatory effect to enhance NK and T-cell activity

CELMoDs, cereblin E3 ligase modulators; IMiDs, immunomodulatory drugs.

Patel TH et al. Clin Lymphoma Myeloma Leuk. 2024;24(11):762-769; Ioannou N et al. Int J Mol Sci. 2021;22(16):8572; Costacurra M et al. J Pers Med. 2021;11(11):1185; Republished from D'Souza C et al. Front Immunol. 2021;12:682399, under the terms of the under the terms of the Creative Commons Attribution License (CC BY).

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CELMoDs vs IMiDs

Compound	Molecular structure	CRBN binding affinity (IC ₅₀)	CRBN closed confirmation	Half-life (hours)	Renal dosing	Liver metabolism
Lenalidomide		≈1.5 μM	—	3-5	Adjustments for CrCl <60 mL/min	Minimal
Pomalidomide		≈1.2 μM	20%	7.5-9.5	Adjustments for severe renal impairment requiring dialysis	Partially metabolized by CYP1A2, CYP3A4, substrate for p-glycoprotein CYP2C19, CYP2D6, CYP3A4
Iberdomide		≈0.05 μM	50%	9-13	NA	Primarily metabolized by CYP3A
Mexidomide		≈0.03 μM	100%	16-19	NA	Primarily liver metabolized

CRCl, creatinine clearance.

Patel TH et al. Clin Lymphoma Myeloma Leuk. 2024;24(11):762-769; Costacurra M et al. J Pers Med. 2021;11(11):1185; Hartley-Brown MA et al. Cancers (Basel). 2024;16(6):1166; van de Donk NMGJ et al. Oncol Targets Ther. 2023;16:921-931; Lee H et al. Hematol Oncol Clin North Am. 2024;38(2):305-319; Watson ER et al. Science. 2022;378(6619):549-553.

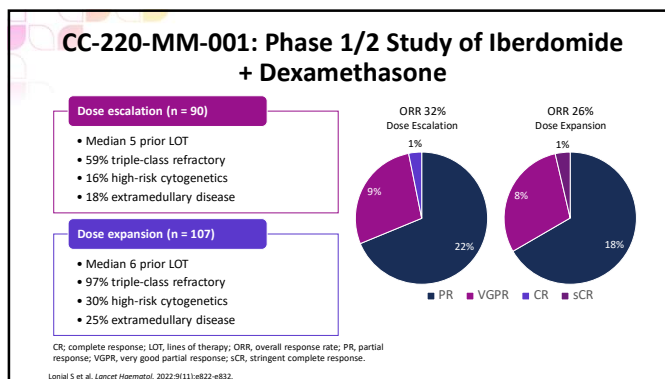
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CELMoDs vs IMiDs

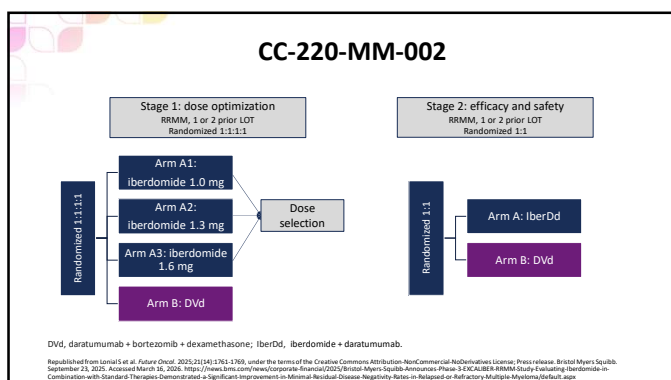
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Iberdomide		≈0.06 μM	50%	9-13	NA	Primarily metabolized by CYP3A
Mezigdomide		≈0.03 μM	100%	16-19	NA	Primarily liver metabolized

Patel TH et al. Clin Lymphoma Myeloma Leuk. 2024;24(11):762-769; Costacura M et al. J Pers Med. 2021;11(11):1183; Hartley-Brown MA et al. Cancers (Basel). 2024;16(6):1166; van de Donk RWJG et al. Onco Targets Ther. 2025;18:921-933; Lee H et al. Hematol Oncol Clin North Am. 2024;38(2):305-319; Watson ER et al. Science. 2022;378(6630):549-553.

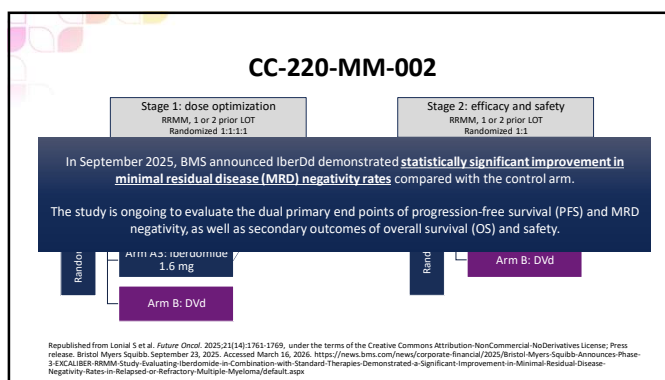
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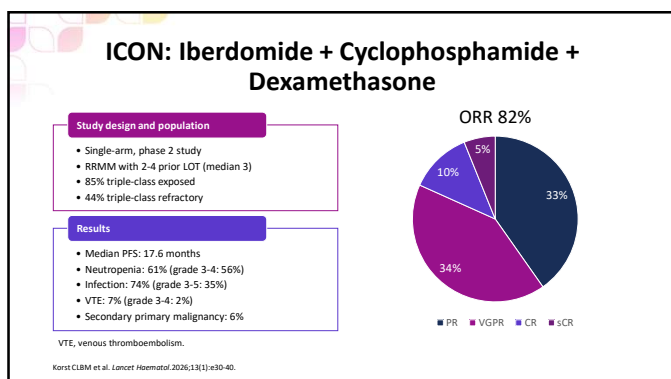
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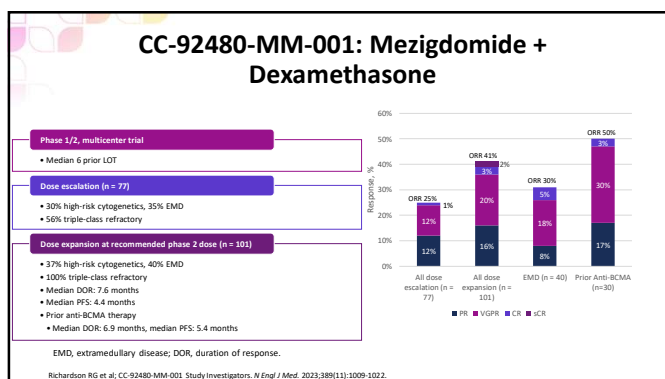
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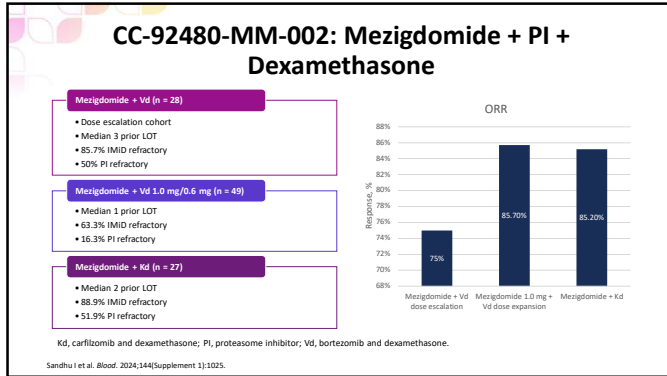
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SUCCESSOR Trials: Phase 3 Mezidomide Combinations

SUCCESSOR-1: MeziVd vs Pvd

- RRMM with 1-3 prior LOT, including lenalidomide
- Stage 1 dose optimization followed by stage 2 efficacy and safety analysis
- Primary end point: PFS
- Key secondary end points: ORR, CRR, OS, safety, MRD negativity, HRQOL

SUCCESSOR-2: MeziKd vs Kd

- RRMM with ≥1 prior LOT, including lenalidomide and an anti-CD38 mAb
- Stage 1 dose optimization followed by stage 2 efficacy and safety analysis
- Primary end point: PFS
- Key secondary end points: ORR, CRR, OS, safety, MRD negativity, HRQOL

ORR, complete response rate; HRQOL, health-related quality of life; Pvd, pomalidomide, bortezomib, and dexamethasone. Dimopoulos M et al. 21st International Myeloma Society Annual Meeting. Abstract P-389.

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SUCCESSOR Trials: Phase 3 Mezidomide Combinations

SUCCESSOR-1: MeziVd vs Pvd

- RRMM with 1-3 prior LOT, including lenalidomide
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SUCCESSOR-2: MeziKd vs Kd

- RRMM with ≥1 prior LOT, including lenalidomide and an anti-CD38 mAb
- Stage 1 dose optimization followed by stage 2 efficacy and safety analysis
- Primary end point: PFS
- Key secondary end points: ORR, CRR, OS, safety, MRD negativity, HRQOL

March 9, 2026: BMS announced MeziKd demonstrated statistically significant and clinically meaningful improvement in PFS compared with Kd at the interim analysis of SUCCESSOR-2.

The study is ongoing to evaluate survival and safety.

Dimopoulos M et al. 21st International Myeloma Society Annual Meeting. Abstract P-389. Press release. Bristol Myers Squibb. March 9, 2026. Accessed March 16, 2025. <https://www.bms.com/news/corporate-financial/2026/bristol-myers-squibb-announces-phase-3-results-from-the-succ2026-2-sub-of-our-mezigdomide-in-relapsed-and-refractory-multiple-myeloma-clinical-trial>

21

CELMod Toxicity

ADE, % (grade 3-4)	Iberdomide	Mezigdomide	
	CC-220-MM-001: iberdomide + dexamethasone (N = 107)	CC-92480-MM-001: mezigdomide + dexamethasone (N = 101)	CC-92480-MM-002: MeziKd (N = 27) / CC-92480-MM-002: MeziVd (N = 49)
Neutropenia	60 (45)	77 (76)	Grade 3-4: 44.4 / Grade 3-4: 63.3
Anemia	41 (28)	52 (36)	Grade 3-4: 14.8 / Grade 3-4: 7.9
Thrombocytopenia	36 (22)	43 (28)	Grade 3-4: 14.8 / Grade 3-4: 26.5
Infection	58 (27)	65 (35)	70.4 (33.3) / 79.6 (32.7)
Fatigue	24 (3)	36 (5)	NR / NR
Diarrhea	23 (1)	31 (3)	0 (0) / NR
Rash	20 (3)	NR	0 (0) / NR
VTE	0 (0)	3 (1)	NR / NR

ADE, adverse drug effect.

Lonial S et al. Lancet Haematol. 2022;9(11):e822-e832; Richardson RG et al. CC-92480-MM-001 Study Investigators. N Engl J Med. 2023;389(11):1009-1022; Sandhu I et al. Blood. 2024;144(Supplement 1):1025.

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Fatigue	24 (3)	36 (5)	NR / NR
Diarrhea	23 (1)	31 (3)	0 (0) / NR
Rash	20 (3)	NR	0 (0) / NR
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Lonial S et al. Lancet Haematol. 2022;9(11):e822-e832; Richardson RG et al. CC-92480-MM-001 Study Investigators. N Engl J Med. 2023;389(11):1009-1022; Sandhu I et al. Blood. 2024;144(Supplement 1):1025.

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Role in RRMM Therapy

IMiD-refractory patients

- Iberdomide for early relapse
 - PDUFA date 8/17/2026 for iberdomide + daratumumab + dexamethasone in RRMM
- Mezigdomide for later relapse and post-BCMA therapy

Combination with T-cell-redirecting agents

- Enhanced T-cell activation with increased tumor infiltration
- Potential cytokine release mitigation with CELMod pretreatment
- Rejuvenate CAR T-cell function and reverse T-cell exhaustion

PDUFA, Prescription Drug User Fee Act.

Hartley-Brown MA et al. Concurr (Basel). 2024;16(6):1166; Liu Y et al. Expert Rev Hematol. 2024;17(8):445-465; Aleman A et al. EHA 2025. Abstract PF685.

24

Future Directions

- Iberdomide in earlier lines
 - Smoldering myeloma
 - Post-transplant maintenance
 - Newly diagnosed myeloma for both transplant-eligible and ineligible patients
- Mezigdomide combinations
- Combinations with T-cell–redirecting therapies
 - MagnetisMM-30: iberdomide + elranatamab
- Therapy sequencing

Joseph NS et al. *Blood*. 2024;144(Supplement 1):1983. Puig N et al. *EHA 2025, Abstract P51784*; Amantangelo M et al. *Blood*. 2024;144(Supplement 1):1973; White et al. *ASCO, Abstract 7532*; Dimopoulos M et al. 23rd International Myeloma Society Annual Meeting, Abstract P-389; Tuchman S et al. *Blood*. 2025;146(Supplement 1):2289; Suvannasankha A et al. *Blood*. 2025;146(Supplement 1):100; Byun JM et al. *Blood*. 2025;146(Supplement 1):583; Bar N et al. *Blood*. 2025;146(Supplement 1):8246.

25

The Role of the Pharmacist

EHR integration

Specialty pharmacy collaboration

Formulary decision-making

Interprofessional education

Patient education


Toxicity management

EHR, electronic health record.
Segal EM et al. *J Oncol Pharm Pract*. 2019;25(8):1945-1967.

26

Case 1: Management of Treatment-Related Neutropenia

CG is a 68-year-old woman with a history of IgG lambda MM diagnosed in 2013. She recently started iberdomide + dexamethasone and presents to the clinic for initiation of cycle 2.



- **Myeloma markers**
 - Free lambda light chains: 35.6 mg/L
 - Free kappa light chains: 0.07 mg/L
 - Serum M-protein: 1.4 g/L
 - Bone marrow biopsy: 15% monoclonal plasma cells

- **Other pertinent lab results**
 - Serum creatinine: 0.8 mg/dL
 - Hemoglobin: 9.4 g/dL
 - White blood cells (WBCs): $0.6 \times 10^9/L$
 - Absolute neutrophil count (ANC): 425 cells/ μL
 - Platelet: 130,000 cells/ μL

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Audience Response Question

What interventions may be recommended for the management of CG's grade 4 neutropenia? (select all that apply)

- Hold iberdomide and dexamethasone until ANC ≥ 1000 cells/ μL and resume at the same dose.
- Continue therapy and assess complete blood count (CBC) in 1 week.
- Initiate filgrastim 5 mcg/kg subcutaneous injection 3x weekly to maintain ANC > 1000 cells/ μL .
- Initiate levofloxacin 500 mg daily until ANC ≥ 500 cells/ μL .

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Real-World Neutropenia Management

Emory Winship Cancer Institute	American Oncology Network	Fred Hutchinson Cancer Center
<ul style="list-style-type: none"> • Goal: Optimize efficacy by maintaining the patient on therapy. • Initiate filgrastim 2-3x weekly to maintain ANC ≥ 1000 cells/μL. • If neutropenia anticipated > 7 days: initiate levofloxacin 500 mg daily (or equivalent). • Consider a therapeutic hold based on disease status. • Consider dose reduction if ANC is not improved with G-CSF. 	<ul style="list-style-type: none"> • Hold therapy for ANC ≤ 1000 cells/μL, resume at the same dose when resolved, or lower dose if persistent (> 7 days), recurrent, or grade 4. • Consider G-CSF 2-3x weekly for ANC ≤ 1000 cells/μL without other significant toxicities. • Consider antibacterial and antifungal prophylaxis for ANC ≤ 100 cells/μL anticipated > 7 days. 	<ul style="list-style-type: none"> • Start filgrastim 2-3x weekly to maintain ANC $\geq 500-1000$ cells/μL. • If persistent neutropenia, consider temporarily holding treatment for 7 days. • If persistent neutropenia or recurrence after a temporary hold (with filgrastim), consider a dose reduction. • Start prophylaxis with levofloxacin if ANC < 500 cells/μL.

G-CSF, granulocyte colony-stimulating factor.

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Neutropenia and Management

NCCN hematopoietic growth factors
<ul style="list-style-type: none"> • Consider G-CSF based on patient-specific factors, but no direct guidance for intermittent G-CSF use • No direct guidance
ASCO recommendations for the use of WBC growth factors
<ul style="list-style-type: none"> • "Primary prophylaxis is recommended for the prevention of febrile neutropenia in patients who are at high risk on the basis of age, medical history, disease characteristics, and myelotoxicity of the chemotherapy regimen"
Clinical trial guidance
<ul style="list-style-type: none"> • Grade 4 neutropenia or febrile neutropenia: <ul style="list-style-type: none"> • Hold therapy for remainder of cycle and initiate G-CSF • Follow CBC at least weekly • Maintain CELMoD dose if neutropenia was the only therapy-related toxicity, or decrease by 1 dose level • Resume when ANC ≥ 1000 cells/μL • Initiate antibacterial prophylaxis during periods of susceptibility to infection

ASCO, American Society of Clinical Oncology; NCCN, National Comprehensive Cancer Network.
NCCN. Clinical Practice Guidelines in Oncology. Hematopoietic growth factors, version 3.2026. Accessed March 16, 2026. https://www.nccn.org/professional/physician_gf/pdf/growthfactors.pdf.
Smith T et al. *American Society of Clinical Oncology. Clin Oncol*. 2025;33(3):3199-3222. Lonial S et al. *Cancer Hematol*. 2022;3(1):482-492. Lonial S et al. *Future Oncol*. 2025;21(4):3743-3769. Richardson RG et al. *CC-92480-MM-001 Study Investigators. N Engl J Med*. 2021;385(11):1009-1022. Sandhu J et al. *Blood*. 2024;144(Supplement 1):1025.

30

The Role of the Pharmacist

Toxicity management protocols

Dose adjustment protocols

Infection prevention

Interprofessional education

Patient education

Segal EM et al. J Oncol Pharm Pract. 2019;25(8):1945-1967.

31

Case 2: Bringing CELMoDs Into the Real World

Picture this...the first CELMoD agent has just been FDA approved for RRMM.

Iberdomide in combination with daratumumab and dexamethasone

Approved for RRMM after 1 prior LOT

Not yet included in NCCN guidelines

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Case 2: Bringing CELMoDs Into the Real World

ESTABLISHING EMR ORDERS

Components of the treatment plan

- Iberdomide (dose, schedule, administration instructions)
- Concurrent therapy (daratumumab, dexamethasone)
- Supportive medications (aspirin, antiemetic, daratumumab premedications per institution protocol)
- Laboratory monitoring (CBC with differential, comprehensive metabolic panel, thyroid-stimulating hormone, myeloma markers)
- REMS reminders

REMS PREPAREDNESS

Providers

- Complete prescriber enrollment.
- Obtain monthly REMS authorization number.
- Include authorization number and patient risk category on each prescription.

Pharmacies

- Complete pharmacy enrollment and individual staff training/certification.
- Confirm provider steps completed, authorization number still valid, and prescription for 28-day supply or less.
- Obtain confirmation number and dispense within 24 hours.
- Certified counselor counsels and completes the checklist with the patient.

COMMUNICATION WORKFLOWS

Clinic and pharmacy

- Designate responsibilities
 - Initial REMS enrollment
 - Monthly authorization
 - Patient counseling/ checklist completion
 - Reporting ADEs
- Communicating ADEs, dose reductions, treatment holds

Clinic/pharmacy and patient

- Recognizing importance of responsiveness to phone calls
- Reporting ADEs
- Taking appropriate concomitant medications

EMR, electronic medical record; REMS, Risk Evaluation and Mitigation Strategy.

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Audience Response Question

When choosing between 2 treatment options with similar efficacy, what is the most important factor pharmacists should consider if all options are appropriate?

- A. AE profile and patient tolerability
- B. Cost and insurance coverage
- C. Patient preference and convenience
- D. Potential drug interactions and contraindications

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Case 2

The case continues...3 months following the approval of iberdomide, mezigdomide receives FDA approval in combination with carfilzomib and dexamethasone after ≥1 prior LOT.

Education and formulary

- Provider and staff education
- Patient education materials
- Considerations for formulary addition

Comparing iberdomide and mezigdomide

- Efficacy/relapse profiles
- Safety/toxicity profiles
- Selection based on patient/disease characteristics?

CELMoDs in the treatment continuum

- Sequencing with IMiDs, BCMA
- Sequencing with T-cell-directed therapy

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Conclusion

CELMoDs including iberdomide (CC-220) and mezigdomide (CC-92480) are high selective molecular degraders that reprogram the cereblon ubiquitin ligase complex.

CELMoDs have increased binding affinity for cereblon, enhanced degradation of Ikaros and Aiolos, and greater immunostimulatory effects than IMiDs.

These novel agents will help to address a therapeutic need for IMiD-refractory patients and may enhance the therapeutic activity of T-cell–redirecting therapies.

Pharmacists will play a key role in the therapeutic management of CELMoDs, including formulary decision-making, development of toxicity management protocols, and education for interdisciplinary teams and patients.

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Additional Resources

Resources	
International Myeloma Foundation	www.myeloma.org
mSMART Stratification for Myeloma & Risk-Adapted Therapy	www.msmaart.org/mm-treatment-guidelines
Multiple Myeloma Research Foundation	themmrf.org

Hicks LK et al. Treatment of multiple myeloma: ASCO-Ontario Health (Cancer Care Ontario) living guideline. *J Clin Oncol.* 2026;34(25):2587.