

# New Strategies for Multiple Myeloma Care: Case Studies for Nurses

## Part 2: Relapsed Multiple Myeloma



International Myeloma Foundation  
800-452-CURE (2873)  
<http://myeloma.org>

### Relapsed Multiple Myeloma

CASE #3: Steve\*

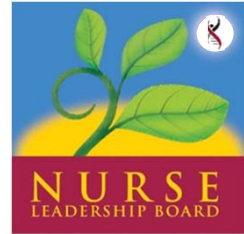
CASE #4: Michelle\*

\*HIPAA-compliant; not actual patient names

**Amy Pierre, RN, MSN, ANP-BC**

**Beth Faiman, PhD, RN, MSN, APRN-BC, AOCN®, FAAN**

HIPAA = Health Insurance Portability and Accountability Act.



**INTERNATIONAL  
MYELOMA  
FOUNDATION**

### Objectives

- Identify common treatment regimens in early relapsed multiple myeloma
- Apply knowledge of nursing management of patients with multiple myeloma, including effective symptom management




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## Part 2: Relapsed Multiple Myeloma

**CASE #3**

**Steve\***

- 50-year-old man diagnosed with IgA lambda MM, standard risk in 2013
- Treated with VRd then ASCT
  - No maintenance
  - Complete response




\*HIPAA-compliant, stock photo (not actual patient).

**Decided against clinical trial participation due to job and family responsibilities**

ASCT = autologous stem cell transplantation; HIPAA = Health Insurance Portability and Accountability Act; Ig = immunoglobulin; MM = multiple myeloma; VRd = bortezomib lenalidomide dexamethasone.


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**CASE #3**

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\*HIPAA-compliant, stock photo (not actual patient).

**Decided against clinical trial participation due to job and family responsibilities**

**Now:**  
Slow biochemical progression

ASCT = autologous stem cell transplantation; HIPAA = Health Insurance Portability and Accountability Act; Ig = immunoglobulin; MM = multiple myeloma; VRd = bortezomib lenalidomide dexamethasone.

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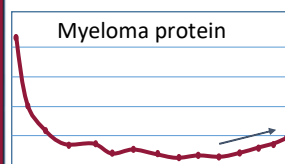
## Part 2: Relapsed Multiple Myeloma

### How Patients With Myeloma Relapse



#### Symptomatic

- New, worsening bone pain
- Increasing fatigue, anemia
- Next steps: relapse workup, many therapy choices



#### Asymptomatic Biochemical Relapse

Steve

- Sequentially rising myeloma protein, free light chain
- No other symptoms
- Decisions: if, when, how to treat

Falman B, et al. *J Adv Pract Oncol*. 2016;7(suppl 1):17-29. Kurtin S, et al. *J Adv Pract Oncol*. 2016;7(suppl 1):59-70.

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### Relapse Workup

#### Lab tests

- Serum protein electrophoresis (SPEP)
- Urine protein electrophoresis (UPEP)
- CBC + differential + chemistry (metabolic panel)
- FLC ratio of free kappa/lambda light chains (plasma)
- Monoclonal protein analysis (MPA)

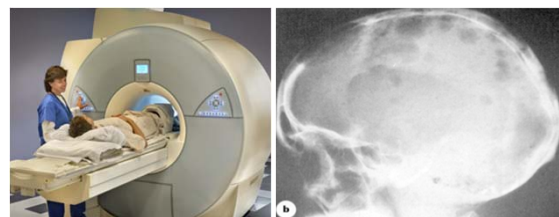
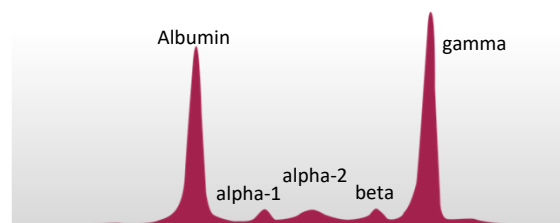
#### Consider bone marrow biopsy

- Cytogenetics and FISH

#### Imaging

- PET/CT
- Skeletal survey
- Whole-body low-dose CT
- MRI

Which imaging depends on individual's symptoms and available testing options



CBC = complete blood count; CT = computed tomography; FISH = fluorescence in situ hybridization; FLC = free light chain; MRI = magnetic resonance imaging; PET = positron emission tomography.

Hillengass J, et al. *Lancet Oncol*. 2019;20(6):e302-e312. Ghobrial IM, et al. *Blood*. 2014;124:3380-3388. Rajkumar SV, et al. *Lancet Oncol*. 2014;15:e538-548. Falman B. *Clin Lymphoma Myeloma Leuk*. 2014;14:436-440.

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## Part 2: Relapsed Multiple Myeloma

CASE #3

Steve\*
}

- February 2020: biochemical relapse
  - M-protein from undetectable g/dL to 0.96 g/dL over 2.5 year
  - No other symptoms
  - Lab values normal
  - Low-dose whole-body CT, no new lesions

LABORATORY RESULTS

Flowsheet Data

x M-protein Concentration

The graph shows the data in chronological order (5/20/2013 – 2/14/2020)

\*HIPAA-compliant, stock photo (not actual patient).

CT = computed tomography; HIPAA = Health Insurance Portability and Accountability Act; M-protein = monoclonal protein.

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## Many Treatment Options at Early Relapse (1-3 Prior Therapies)

FDA-approved myeloma therapies	Common Combinations
Bortezomib (SC admin)	VRd, Vd
Lenalidomide	VRd, Rd
Carfilzomib	KRd, Kd, Kd-Dara
Pomalidomide <sup>a</sup>	Pd, DPd, EPd, PCd
Ixazomib	IRd
Daratumumab	Dara-Rd, Dara-Vd, Dara-Pd, Dara-VMP, Dara-Kd
Elotuzumab	ERd, EPd
Isatuximab <sup>a</sup>	Isa-Pd
<b>New agents or regimens in clinical trials are always an option</b>	

C = cyclophosphamide; D or Dara = daratumumab; d = dexamethasone; E = elotuzumab; FDA = US Food and Drug Administration; Isa = isatuximab; I = ixazomib; K = carfilzomib; M = melphalan; P = pomalidomide; PACE = cisplatin doxorubicin cyclophosphamide etoposide; R = lenalidomide; SC = subcutaneous; T = thalidomide; V = bortezomib.

<sup>a</sup>2 prior therapies.

Falman B, et al. *J Adv Pract Oncol*. 2016;2016:7(suppl 1):17-29. Mikhael J. <https://www.medscape.com/viewarticle/882042>. Accessed May1, 2020. Rajkumar SV. How I treat. 2020. <https://twitter.com/vincentr/status/1203058085776035840>. Accessed May 1, 2020. Prescribing Information.

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## Part 2: Relapsed Multiple Myeloma

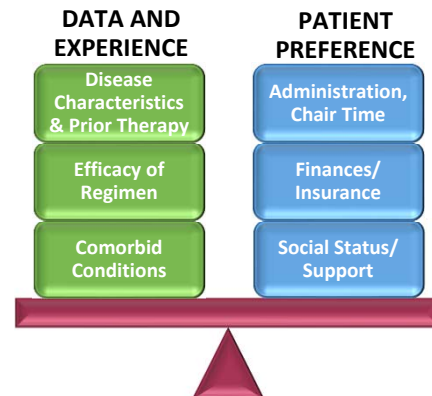
### Practical Approach to Treatment of Patients With Relapsed Myeloma

#### Disease-related factors

- Duration of response to initial therapy
- High-risk vs low-risk status
- Molecular relapse vs symptomatic relapse
- Other comorbid conditions, patient frailty

#### Treatment-related factors

- Previous/current therapy exposure (relapsed or refractory)
- Toxicity/tolerability of previous regimen
- Mode of administration (ie, PO or IV)
- Cost and convenience (out-of-pocket copays for IV vs po)
- Patient preference



IV = intravenous; PO = by mouth.  
 Falman B, et al. *J Adv Pract Oncol*. 2016;2016:7(suppl 1):17-29.

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### Carfilzomib (K): IV Proteasome Inhibitor

#### • IV proteasome inhibitor, indications:

- In combination with dex or len-dex in patients with relapsed or refractory MM who have received 1-3 lines of therapy
- As a single agent in patients with relapsed or refractory multiple myeloma who have received 1 or more lines of therapy

#### • Clinical pearls

- Escalate dose
- Dose-dependent 10- or 30-min infusion
- Hydration but not overhydration
- Premedication (dex)
- Aspirin vs full anticoagulation
- Monitor blood counts, response
- Monitor for infection
- Herpesvirus prophylaxis
- Know cardiac and pulmonary status and optimize heart failure and blood pressure management
- Diuretic (furosemide or torsemide) or inhalers if needed
- Avoid dyspnea over the weekend; start new patients first dose early in the week

**Kd**  
 20/70 mg/m<sup>2</sup>  
 Once weekly  
 30-min infusion

**Kd or K**  
 20/56 mg/m<sup>2</sup>  
 Twice weekly  
 30-min infusion

**KRd or K**  
 20/27 mg/m<sup>2</sup>  
 Twice weekly  
 10-min infusion

d or dex = dexamethasone; IV = intravenous; K = carfilzomib; Kd = carfilzomib dexamethasone; KRd = carfilzomib lenalidomide dexamethasone; len = lenalidomide;  
 MM = multiple myeloma.  
 Stewart K, et al. *N Engl J Med*. 2015;372:142-152. Kyprolis® (carfilzomib) Prescribing Information.

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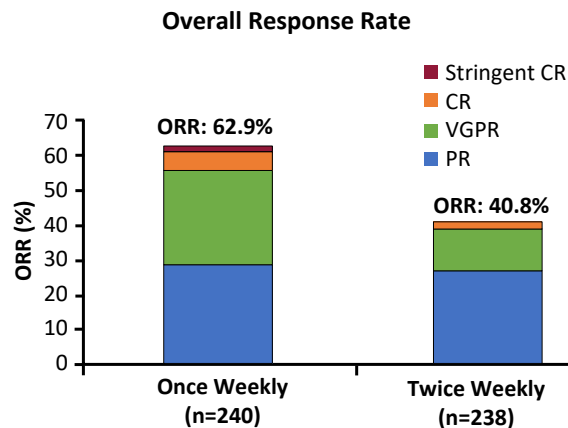
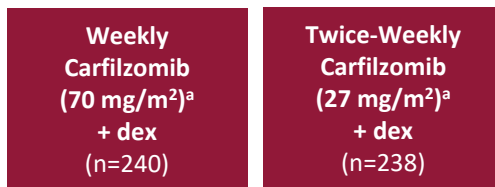


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## Part 2: Relapsed Multiple Myeloma

### Once-Weekly Carfilzomib Dosing in ARROW Clinical Trial

Patients with R/R MM  
2 or 3 previous lines of therapy with IMiD and PI  
exposure (no carfilzomib or oprozomib)  
ECOG PS 0/1, and CrCl  $\geq 30$  mL/min  
(N=478)



CrCl = creatinine clearance; CR = complete response; Dex = dexamethasone; IMiD = immunomodulatory drug; MM = multiple myeloma; ORR = overall response rate; PI = proteasome inhibitor; PR = partial response; PS = performance status; R/R = relapsed/refractory; VGPR = very good partial response.  
<sup>a</sup>After 20 mg/m<sup>2</sup> ramp-up dose(s).  
Mateos MV, et al. ASCO 2018. Abstr #8000.

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### CANDOR Phase 3: Carfilzomib Dexamethasone ± Daratumumab in Patients With R/R MM

#### Design

- Multicenter, randomized phase 3
  - 466 patients with R/R MM 1-3 prior therapies
  - ECOG PS 0-2; CrCl  $\geq 20$  mL/min; LVEF  $\geq 40\%$

#### Results

- Median time to first response was 1 month in the KdD and Kd arms

Responses, %	KdD (n=312)	Kd (n=154)
ORR	84.3*	74.7*
VGPR or better	69.2	48.7
CR or better	28.5	10.4
MRD negative at 12 months ( $10^{-5}$ threshold)	17.6	3.9
MRD-negative CR at 12 months ( $10^{-5}$ threshold)	12.5 <sup>†</sup>	1.3 <sup>†</sup>
Best MRD-negative CR ( $10^{-5}$ threshold)	13.8	3.2

\*P = .0040. <sup>†</sup>P < .0001.

#### CANDOR Conclusions

- 37% reduction in risk of progression or death with KdD compared with Kd
- 10x higher MRD-negative CR rate with KdD compared with Kd
- PFS benefit maintained for len-refractory patients

CR = complete response; CrCl = creatinine clearance; ECOG = Eastern Cooperative Oncology Group; Kd = carfilzomib dexamethasone; KdD = carfilzomib dexamethasone daratumumab; len = lenalidomide; LVEF = left ventricular ejection fraction; MM = multiple myeloma; MRD = minimal residual disease; ORR = overall response rate; PS = performance status; R/R = relapsed/refractory; VGPR = very good partial response.  
Usmani SZ, et al. ASH 2019. Abstr #LBA-6.

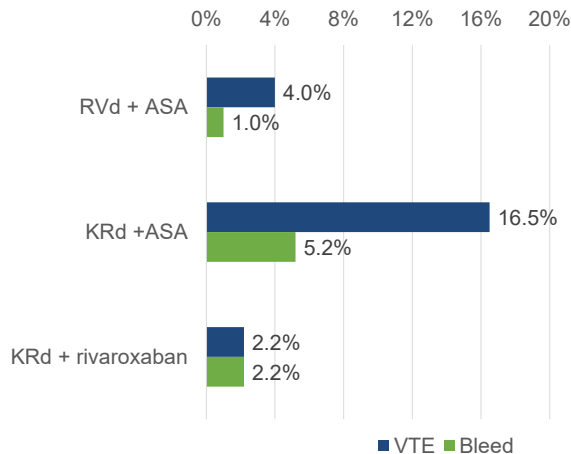
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## Part 2: Relapsed Multiple Myeloma

### Consider Full Anticoagulation for Patients on Carfilzomib Regimens



NEW

New data suggest rivaroxaban may be a more-effective antithrombotic agent for patients on KRd

ASA = aspirin; KRd = carfilzomib lenalidomide dexamethasone; RVd = bortezomib lenalidomide dexamethasone; VTE = venous thrombotic embolism. Piedra KM, et al. ASH 2019. Abstr #1835.

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### Ixazomib: Oral Proteasome Inhibitor

- Oral proteasome inhibitor
  - Indication: patients with multiple myeloma who have received at least 1 prior therapy
  - In combination with Rd
- Administration
  - Oral capsule 1x per week; do not crush, chew capsules or open capsule
  - Empty stomach: 1 hour before or 2 hours after food
- Clinical pearls
  - Adherence, schedule, viral prophylaxis
  - Rapid response (1.1 months); fast absorption (if vomit, do NOT repeat dose)
  - Monitor blood counts: cyclic thrombocytopenia
  - Peripheral neuropathy, peripheral edema
  - Herpes prophylaxis
  - In combination with Rd, so DVT prophylaxis

Ixazomib + Rd  
FDA approved  
November 2015

DVT = deep vein thrombosis; FDA = US Food and Drug Administration; Rd = lenalidomide dexamethasone. NINLARO® (ixazomib) Prescribing Information. Falman B, et al. J Adv Pract Oncol. 2016;7:45-52.

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# New Strategies for Multiple Myeloma Care: Case Studies for Nurses

## Part 2: Relapsed Multiple Myeloma

### IRd: All-Oral Regimen Dosing Calendar

#### Ixazomib dosing 28-day cycle

Recommended  
starting doses:










Ixazomib 4 mg



Lenalidomide 25 mg



Dexamethasone 40 mg

1   	2 	3 	4 	5 	6 	7 
8   	9 	10 	11 	12 	13 	14 
15   	16 	17 	18 	19 	20 	21 
22 	23	24	25	26	27	28

IRd = ixazomib lenalidomide dexamethasone.

NINLARDO® (ixazomib) Prescribing Information. Fauman B, et al. J Adv Pract Oncol. 2016;7:45-52.

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### CASE #3

#### Steve\*

- Deciding among many excellent options
  - Not refractory to bortezomib, lenalidomide
  - Has not received monoclonal antibodies
- Given COVID-19 situation and uncertainty, considering an all-oral regimen: IRd
- Opportunity to use risk-adapted approach



\*HIPAA-compliant, stock photo (not actual patient).

COVID-19 = coronavirus 2019; HIPAA = Health Insurance Portability and Accountability Act; IRd = ixazomib lenalidomide dexamethasone.

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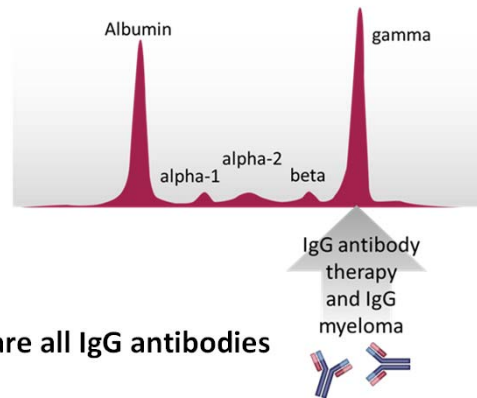
## Part 2: Relapsed Multiple Myeloma

### Special Considerations With Antibody Therapy

- Potential interference with laboratory tests
  - Co-migration of therapeutic antibody with M-protein: overestimation of M-protein and reduced CR rates
- Solutions
  - Awareness
  - Laboratory assays to minimize effects (eg, high-resolution mass spectrometry)



**Daratumumab, elotuzumab, and isatuximab are all IgG antibodies**

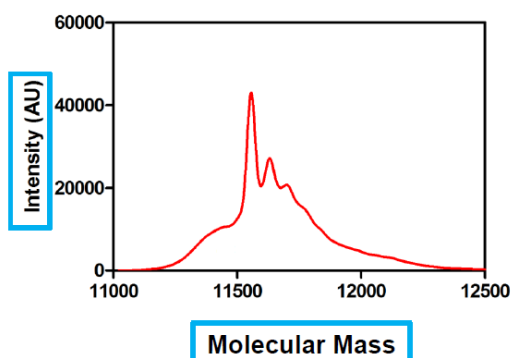


CR = complete response; Ig = immunoglobulin; M-protein = monoclonal protein.  
Mills JR, Murray DL. J Appl Lab Med. 2017;1(4):421-431.

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### Mass Spectrometry Can Resolve Antibody Interference



- Molecular mass can identify amount of monoclonal protein specifically
- Has the potential to resolve antibody interference

**WATCH FOR**

**New testing options for mass spectrometry to resolve antibody interference**

**The result is a highly sensitive and specific approach to monitor M-proteins**

M-protein = monoclonal protein.  
Pulig N, et al. ASH 2019. Abstr #581.

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# New Strategies for Multiple Myeloma Care: Case Studies for Nurses

## Part 2: Relapsed Multiple Myeloma

### Daratumumab (DARA, D): Monoclonal Antibody

#### Summary

- Monoclonal antibody targeting CD38
  - New SC dosing and original IV
- Multiple indications for MM—prescribing information for details

#### Clinical pearls

- SC dose form for SC only; IV for IV only
- Antibody interference—type and cross BEFORE starting
- Premeds: corticosteroids, antipyretics, and antihistamine, montelukast
- Post-med: oral corticosteroid for 2 days after
- Educate patients/caregivers about expectations
- Herpes prophylaxis
- Remember appropriate prophylaxis for combination partner drugs

NEW

**Subcutaneous injection dose form**

**Dara-VTd**  
(First-line transplant eligible)

**DRd, VMP + Dara**  
(First-line non-transplant)

**DRd, DVd**  
(1 prior therapy)

**DPd**  
(2 prior therapies)

**Dara monotherapy**  
(3 prior therapies)

D or Dara = daratumumab; DRd = daratumumab lenalidomide dexamethasone; DVd = daratumumab bortezomib dexamethasone; DPd = daratumumab prednisone dexamethasone; IMiD = immunomodulatory drug; IV = intravenous; MM = multiple myeloma; Rd = lenalidomide dexamethasone; SC = subcutaneous; VMP = bortezomib melphalan prednisone; VTd = bortezomib thalidomide dexamethasone.  
DARZALEX® (daratumumab) Prescribing Information. DARZALEX FASPRO™ (daratumumab and hyaluronidase-fihj) Prescribing Information. Gleason C, et al. J Adv Pract Oncol. 2016;7(suppl 1):53-57.

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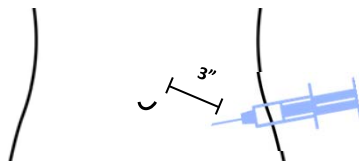


### Daratumumab (DARA, D) Cont'd

#### SC Clinical Pearls:

INJECTION INTO ABDOMEN

NEW



- Inject **15 mL** into subcutaneous tissue **over 3-5 minutes**
- 3" from navel on **right or left side**
- Pause or slow if patient experiences pain

#### IV Clinical Pearls:

SLOW FIRST INFUSION



ALTERNATIVE: DIVIDED FIRST INFUSION



Example: 4-week cycle with Rd

SC or IV: SCHEDULES DEPEND on REGIMEN: CHECK PRESCRIBING INFORMATION

WEEKS 1-8  
**WEEKLY**  
(9 doses)

WEEKS 9-24  
**EVERY 2 WEEKS**  
(5 doses)

WEEK 25  
**EVERY 4 WEEKS**  
Until progression

- Schedule becomes less frequent
- If no injection/infusion reaction after 3 doses, consider discontinuing corticosteroid pre/post medications

D or Dara = daratumumab; IV = intravenous; Rd = lenalidomide dexamethasone; SC = subcutaneous.  
DARZALEX® (daratumumab) Prescribing Information. DARZALEX FASPRO™ (daratumumab and hyaluronidase-fihj) Prescribing Information.

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# New Strategies for Multiple Myeloma Care: Case Studies for Nurses

## Part 2: Relapsed Multiple Myeloma

### Elotuzumab (E): Monoclonal Antibody

- IV monoclonal antibody targeting *SLAMF-7*
- Prescribed with len-dex or pom-dex
  - DVT prophylaxis (for len or pom)
  - Steroid side effects and schedule (AM vs PM)
- Clinical pearls
  - Risk of infusion reaction: 10%
    - 3-24 hours before = dex 28 mg; 45-90 minutes before = dex 8 mg IV, H1, H2, and acetaminophen
  - Infuse at rate of 0.5 mL/min and escalate to 5 mL/min over time
  - Give weekly for 8 weeks then twice monthly until progressive disease
- Monitoring
  - Blood counts (hold/adjust dose if needed)
  - Response assessment (monthly); interference
  - Glucose (dex can affect)
  - Renal, hepatic function

**EPd**  
(2+ prior therapies)

**ERd**  
(1-3 prior therapies)

d or dex = dexamethasone; DVT = deep vein thrombosis; H = histamine; IV = intravenous; len or R = lenalidomide; PD = progressive disease; P or pom = pomalidomide; *SLAMF-7* = signaling lymphocytic activation molecule 7 (also CD319, CS1).  
EMPLICIT<sup>™</sup> (elotuzumab) Prescribing Information. Gleason C, et al. *J Adv Pract Oncol*. 2016;7(suppl 1):53-57.

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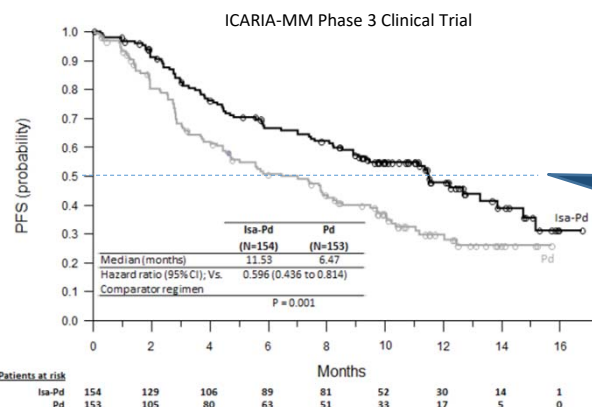


### Isatuximab New Anti-CD38 Monoclonal Antibody: Approved in Combination with Pd

- Monoclonal antibody targeting CD38; IV administration
  - Indication: at least 2 prior therapies, including lenalidomide and a proteasome inhibitor
- Improved ORR: 60.4% Isa-Pd vs 35.3% Pd

**NEW**

**Isatuximab Pd**  
At least 2 prior treatments  
FDA approved March 2020



**Significant increase in median PFS demonstrated with isatuximab + Pd vs Pd alone**

40% reduction in the risk of disease progression or death in patients treated with isatuximab + Pd vs Pd

FDA = US Food and Drug Administration; Isa = isatuximab; IV = intravenous; ORR = overall response rate; Pd = pomalidomide dexamethasone; PFS = progression-free survival.  
SARCLISA<sup>®</sup> (isatuximab) Prescribing Information.

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# New Strategies for Multiple Myeloma Care: Case Studies for Nurses

## Part 2: Relapsed Multiple Myeloma

### Isatuximab: Safety and Clinical Pearls

#### Safety

- IRR (38%): the most-common AR specific to isatuximab
- Isa-Pd common ARs: cytopenias, IRR, infections, dyspnea, GI ARs

#### Dosing

- Slower first and second infusions
- Weekly for 4 weeks then every 2 weeks



- Discontinue if IRR Grade  $\geq 3$

AR = adverse reaction; ASCO = American Society of Clinical Oncologists; dex = dexamethasone; DVT = deep vein thrombosis; GI = gastrointestinal; H = histamine; Isa = isatuximab; IRR = infusion rate reaction; IV = intravenous; KRd = carfilzomib lenalidomide dexamethasone; ORR = overall response rate; Pd = pomalidomide dexamethasone; PFS = progression-free survival.  
SARCLISA® (isatuximab) Prescribing Information. Weisel K, et al. ASCO 2020. Abstr #8508.

#### Clinical pearls

- IRR protection: premedicate with
  - Dexamethasone: 40 mg oral or IV (or 20 mg for patients  $\geq 75$  years)
  - Acetaminophen: 650 mg to 1000 mg
  - H2 antagonists
  - Diphenhydramine: 25 mg to 50 mg oral or IV; IV preferred for at least the first 4 infusions
- Antibody interference—type and cross BEFORE starting
- In combo with pomalidomide + dex: DVT prophylaxis
- Herpes prophylaxis

No dose adjustments for isatuximab

NEW DATA  
at ASCO 2020

**New regimens: Isa-KRd regimen in newly diagnosed high-risk MM at ASCO 2020**

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### Pomalidomide

- Oral immunomodulatory drug active in R-refractory patients
- Indication: at least 2 prior therapies, including R and a PI, and have demonstrated disease progression on or within 60 days of completion of the last therapy
- Monitor
  - Blood counts—neutropenia most-frequent Grade 3/4 AE
  - Liver function
  - Response
- Proactive AE management
- Clinical pearls
  - Adherence and REMS
  - DVT prophylaxis
  - Monitor blood counts (neutropenia), liver enzymes
  - Refrain from smoking (reduces pom exposure)
  - Protect renal health (renal excretion of pom)
    - Hydration
    - Avoid NSAIDs, IV contrast, other drugs with renal interactions

NEW

**Isatuximab Pd**

FDA approved March 2020

**EPd**

**Dara-Pd**

**Pd**

AE = adverse event; Dara = daratumumab; DVT = deep vein thrombosis; EPd = elotuzumab pomalidomide dexamethasone; FDA = US Food and Drug Administration; IV = intravenous; NSAID = nonsteroidal anti-inflammatory drug; Pd = pomalidomide dexamethasone; PI = proteasome inhibitor; R = lenalidomide; REMS = Risk Evaluation and Mitigation Strategies.  
POMALYST® (pomalidomide) Prescribing Information. Falman B, et al. J Adv Pract Oncol. 2016;7:45-52.

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# New Strategies for Multiple Myeloma Care: Case Studies for Nurses

## Part 2: Relapsed Multiple Myeloma

### CASE #4

#### Michelle\*

- 72-year-old woman diagnosed with IgG lambda MM, standard risk in June 2014
- Treated with RVd lite continuous x2 years
- Declined ASCT due to caregiver issues
- Biochemical disease progression
- Started ixazomib lenalidomide dex January 2018
- Symptomatic relapse (pain, new bone lesions on PET-CT)
- Started isatuximab pomalidomide dex May 2020



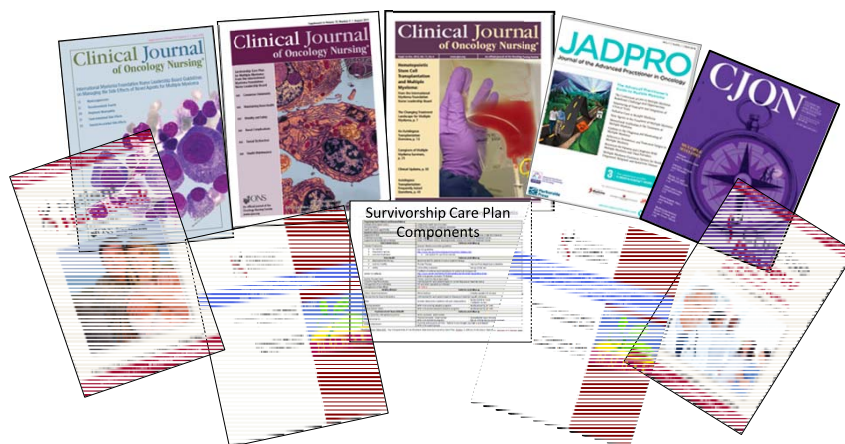
\*HIPAA-compliant, stock photo (not actual patient).

ASCT = autologous stem cell transplantation; CT = computed tomography; dex = dexamethasone; HIPAA = Health Insurance Portability and Accountability Act; Ig = immunoglobulin; MM = multiple myeloma; PET = positron emission tomography; RVd = lenalidomide bortezomib dexamethasone.

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## Resources to Enhance Your Ability to Care for Your Patients With MM: Download or Receive a USB Drive by Mail



...and Much, Much More

Instructions for accessing these resources are provided in the post-course evaluation

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