Management of Patients Who Have Relapsed After One to Three Prior Lines of Therapy

March 8, 2023

Tech Support

1-719-234-7952
Resources

- Resource tab includes
  - Speaker bios
  - Copy of the slide presentation
  - Exhibit Hall

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MMRF Research Initiatives

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Speakers

Larry D. Anderson, Jr., MD, PhD  
UT Southwestern Medical Center  
Simmons Comprehensive Cancer Center  
Dallas, Texas

Faith E. Davies, MBBCh, MD  
Perlmutter Cancer Center  
New York University/Langone Health  
New York, New York
Treatment Options and Considerations for Multiple Myeloma Patients at Relapse

Faith E. Davies, MBBCh, MD
Perlmutter Cancer Center
New York University/Langone Health
New York, New York

Multiple Myeloma Is a Marathon, Not a Sprint

Asymptomatic | Symptomatic | Relapsing | Refractory

MGUS or smoldering myeloma

Induction remission ± SCT

1st RELAPSE

Plateau remission

2nd RELAPSE

REFRACTORY RELAPSE

First-line therapy | Second line | Third line

Adapted from Borrello I. Leuk Res. 2012;36 Suppl. 1:S3.
Definitions: What is relapsed/refractory disease and a line of therapy?

- **Relapsed**: recurrence (reappearance of disease) after a response to therapy
- **Refractory**: progression despite ongoing therapy
- **Progression**: change in M protein/light chain values
- **Line of therapy**: change in treatment due to either progression of disease or unmanageable side effects
  - **Note**: initial (or induction) therapy + stem cell transplant + consolidation/maintenance therapy = 1 line of therapy

Biochemical Relapse or Clinical Relapse

**Biochemical**
- Patients with asymptomatic rise in blood or urine M protein, free light chains, or plasma cells

**Clinical**
- Based on direct indicators of increasing disease and/or end-organ dysfunction

Timing of therapy initiation/escalation dependent on numerous factors

Mandates immediate initiation/escalation of therapy
### Choosing Therapy for First or Second Relapse

**Choices are broadest and guided by**
- Disease biology
- Nature of relapse
- Patient preference

**Factors to consider**
- Prior autologous stem cell transplant
- Prior therapies
- Aggressiveness of relapse
- Comorbidities
- Psychosocial issues
- Access to care

### Options for Relapsed/Refractory Disease Continue to Increase

<table>
<thead>
<tr>
<th>IMiDs</th>
<th>Proteasome inhibitors</th>
<th>Chemotherapy anthracyclines</th>
<th>Chemotherapy alkylators</th>
<th>Steroids</th>
<th>Novel mechanisms of action</th>
<th>mAbs</th>
<th>Cellular therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thalidomide (thalidomide)</td>
<td>Velcade (bortezomib)</td>
<td>Adriamycin</td>
<td>Cytoxan (cyclophosphamide)</td>
<td>Dexamethasone</td>
<td>XPOVIO (selinexor)</td>
<td>Empliciti (elotuzumab)</td>
<td>Abecma (idecabtagene viciecul)</td>
</tr>
<tr>
<td>Revlimid (lenalidomide)</td>
<td>Kyprolis (carfilzomib)</td>
<td>Doxil (liposomal doxorubicin)</td>
<td>Bendamustine</td>
<td>Prednisone</td>
<td>Venclexa (venetoclax)*</td>
<td>Darzalex (daratumumab)</td>
<td>Canvykti (ciltaclabtagene autoleucel)</td>
</tr>
<tr>
<td>Pomalyst (pomalidomide)</td>
<td>Ninlaro (ixazomib)</td>
<td>Melphalan</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

*Not yet FDA-approved for patients with multiple myeloma; †Withdrawn from the US market in 2021; ‡Antibody-drug conjugate

**New formulations, new dosing, and new combinations, too!**
Management of Patients Who Have Relapsed After One to Three Prior Lines of Therapy
Webinar March 8, 2023

### Treatment Approach

#### First relapse
- Proteasome inhibitor (PI)/immunomodulatory drug (IMiD)/antibody-based therapy

#### >1 Relapse
- Any options for first relapse not tried
  - Refractory to Velcade and Revlimid
    - DKd, Isa-Kd, DPd, Elo-Pd, Isa-Pd, or KPd
  - Refractory to an IMiD but sensitive to a PI or
    - DVd, SVd, Ven-Vd (for t[11;14])

#### Triple-class refractory
- Approved therapies
  - Sd, belamaf, ide-cel, ciltacabtagene autoleucel
  - Bispecific antibodies, CAR T cells, CELMoDs

**Approved therapies**
- Clinical trials

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*Not yet approved for use in myeloma patients

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### Second ASCT an Option for Early Relapse

- **Time to progression**

  ![Graph showing progression-free (%) vs. time from randomization (months)](image)

  - **P < 0.0001**
  - **Second ASCT**
  - **Cyclophosphamide**

Proteasome Inhibitor–Based Regimens for Early Relapse

<table>
<thead>
<tr>
<th>OPTIMISMM</th>
<th>ASPIRE</th>
<th>TOURMALINE-MM1</th>
<th>BOSTON</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regimens Compared</td>
<td>VPd: 11 vs 7 months</td>
<td>KRd: 26 vs 17 months</td>
<td>XPO-Vd: 14 vs 9 months</td>
</tr>
<tr>
<td>Median progression-free survival favored:</td>
<td>Vp: 11 vs 7 months</td>
<td>KRd: 26 vs 17 months</td>
<td>IRd: 21 vs 15 months</td>
</tr>
</tbody>
</table>

Important Considerations for Use of Proteasome Inhibitors

**Velcade**
- Risk of peripheral neuropathy (PN; numbness, tingling, burning sensations and/or pain due to nerve damage)
  - Avoid in patients with severe existing PN
  - Reduced with subcutaneous once-weekly dosing
- High risk of shingles
  - Use appropriate vaccination
- No dose adjustment for kidney issues; but adjust for liver issues

**Kyplosis**
- Less PN than Velcade
- High risk of shingles
  - Use appropriate vaccination
- Monitor for heart, lung, and kidney side effects
  - Use with caution in older patients with cardiovascular risk factors
- High blood pressure
- No dose adjustment for kidney issues; but adjust for liver issues

**Ninlaro**
- Less PN than Velcade
- High risk of shingles
  - Use appropriate vaccination
- Monitor for rash and gastrointestinal (GI) side effects
  - GI effects occur early
- Needs to be taken at least 1 hour before or 2 hours after a meal

*Do not take any supplements without consulting with your doctor.*
Important Considerations for Use of Immunomodulatory Drugs

**Revlimid***
- Rash
  - Consider antihistamines
- Diarrhea
  - Consider bile acid sequestrants
- Risk of blood clots
- Risk of second primary malignancies
- Dose adjustment based on kidney function

**Pomalyst***
- Low blood counts
- Less rash than Revlimid
- Risk of second primary malignancies
- Risk of blood clots

*Black box warning.

Important Considerations for Use of XPOVIO

- **Gastrointestinal**
  - Begin prophylactic anti-nausea medications. Consult with your doctor if nausea, vomiting, or diarrhea occur or persist.

- **Low sodium** (hyponatremia)
  - Maintain fluid intake. Salt tabs

- **Fatigue**
  - Stay hydrated and active.

- **Low blood counts** (cytopenias)
  - Report signs of bleeding right away. Report signs of fatigue or shortness of breath.

*Chari A et al. Manuscript under preparation.*
### Proteasome Inhibitor–Based Regimens for Early Relapse

<table>
<thead>
<tr>
<th>Regimens compared</th>
<th>OPTIMISMM</th>
<th>ASPIRE</th>
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<th>BOSTON</th>
</tr>
</thead>
<tbody>
<tr>
<td>Velcade-Pomalyst-dex (VPd) vs Vd</td>
<td>Velcade-Revlimid-dex (KRd) vs Rd</td>
<td>Ninlaro-Rd (IRd) vs Rd</td>
<td>XPOVIO-Velcade-dex (XPO-Vd) vs Vd</td>
<td></td>
</tr>
<tr>
<td>Median progression-free survival favored</td>
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<td>XPO-Vd: 14 vs 9 months</td>
</tr>
<tr>
<td>Clinical considerations</td>
<td>Consider for relapse on Revlimid</td>
<td>KRd associated with more upper respiratory infections and high blood pressure than Rd</td>
<td>IRd an oral regimen</td>
<td>XPO-Vd associated with low platelet counts and fatigue with triplet, but less neuropathy than the Vd</td>
</tr>
</tbody>
</table>

### Monoclonal Antibody–Based Regimens at Relapse

**Larry D. Anderson, Jr., MD, PhD**  
UT Southwestern Medical Center  
Simmons Comprehensive Cancer Center  
Dallas, Texas
### Monoclonal Antibody–Based Regimens for Early Relapse: Darzalex

<table>
<thead>
<tr>
<th>POLLUX</th>
<th>CASTOR</th>
<th>CANDOR</th>
<th>APOLLO</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Regimens compared</strong></td>
<td><strong>DRd: Not reached vs 17 months</strong></td>
<td><strong>DVd: 17 vs 7 months</strong></td>
<td><strong>DKd: Not reached vs 16 months</strong></td>
</tr>
<tr>
<td><strong>Median progression-free survival favored</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Darzalex-Revlimid-dex (DRd) vs Rd</strong></td>
<td><strong>Darzalex-Velcade-dex (DVd) vs Vd</strong></td>
<td><strong>Darzalex-Kyprolis-dex (DKd) vs Kd</strong></td>
<td><strong>Darzalex-Pomalyst-dex (DPd) vs Pd</strong></td>
</tr>
</tbody>
</table>

### Important Considerations for Use of Darzalex

- **Darzalex**
  - Infusion reactions
    - Less with SC use
  - Risk of shingles
    - Use appropriate vaccination

  IV infusion or SC injection
Monoclonal Antibody–Based Regimens for Early Relapse: Darzalex

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<td>Regimens compared</td>
<td>Darzalex-Revlimid-dex (DRd) vs Rd</td>
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<td>DKd: Not reached vs 16 months</td>
</tr>
<tr>
<td>Clinical considerations</td>
<td>Consider for relapses from Revlimid or Velcade maintenance</td>
<td>Consider for patients who are Revlimid-refractory without significant neuropathy</td>
<td>Consider for younger, fit patients who are double-refractory to Revlimid and Velcade</td>
</tr>
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Monoclonal Antibody–Based Regimens for Early Relapse: Sarclisa and Empliciti

<table>
<thead>
<tr>
<th>ELOQUENT-2</th>
<th>ELOQUENT-3</th>
<th>ICARIA-MM</th>
<th>IKEMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regimens compared</td>
<td>Empliciti-Revlimid-dex vs Rd</td>
<td>Empliciti-Pomalyst-dex vs Pd</td>
<td>Sarclisa-Pomalyst-dex vs Pd</td>
</tr>
<tr>
<td>Median progression-free survival favored:</td>
<td>Empliciti-Rd: 19 vs 15 months</td>
<td>Empliciti-Pd: 10 vs 5 mos</td>
<td>Sarclisa-Pd: 12 vs 7 mos</td>
</tr>
</tbody>
</table>
### Important Considerations for Use of Monoclonal Antibodies

<table>
<thead>
<tr>
<th>Sarclisa</th>
<th>Empliciti</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Infusion reactions&lt;br&gt;• Risk of shingles&lt;br&gt;– Use appropriate vaccination</td>
<td>• Lower rate of infusion reactions than Darzalex or Sarclisa&lt;br&gt;• Risk of shingles&lt;br&gt;– Use appropriate vaccination</td>
</tr>
</tbody>
</table>

![IV infusion icon](image)

### Monoclonal Antibody–Based Regimens for Early Relapse: Sarclisa and Empliciti

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<td><strong>Sarclisa-Pd: 12 vs 7 mos</strong></td>
</tr>
<tr>
<td><strong>Clinical considerations</strong></td>
<td><strong>Consider for non-Revlimid refractory, frailer patients</strong>&lt;br&gt;<strong>Overall survival benefit with Empliciti-Rd</strong>&lt;br&gt;<strong>Empliciti-Rd associated with more infections</strong></td>
<td><strong>Consider for patients refractory to Revlimid and a proteasome inhibitor (Velcade, Kyprolis, Ninlaro)</strong>&lt;br&gt;<strong>Sarclisa-Pd associated with severe low white blood cell counts, more dose reductions, upper respiratory infections, and diarrhea</strong></td>
<td><strong>Consider for patients refractory to Revlimid and Velcade</strong>&lt;br&gt;<strong>Sarclisa-Kd associated with higher MRD negativity rates</strong>&lt;br&gt;<strong>Sarclisa-Kd associated with severe respiratory infections</strong></td>
</tr>
</tbody>
</table>
Current and Emerging Therapies for Relapsed/Refractory Multiple Myeloma

Current therapies

**Antibody-drug conjugates**
- Blenrep
- Targets BCMA
- A monoclonal antibody conjugated by a protease-resistant linked to a microtubule-disrupting agent

**Chimeric antigen receptor (CAR) T cells**
- Abecma and Carvykti
- Targets BCMA
- Genetically modified autologous T cells that attack myeloma cells

Emerging therapies

**Bispecific antibodies**
- Teclistamab, elranatamab, and others
- Targets BCMA on myeloma cells and CD3 on T cells
- Redirects T cells to myeloma cells

**Cereblon E3 ligase modulators (CELMoDs)**
- Iberdomide
- Targets cereblon
- Enhances tumoricidal and immune-stimulatory effects compared with immunomodulatory agents

**Small molecule inhibitors**
- Venetoclax
- Targets Bcl-2
- Induces multiple myeloma cell apoptosis

Summary

- We now have many different options for relapsed myeloma depending on patient and myeloma factors at relapse.
- Therapy choices will depend on teamwork between physician and patient and caregivers and are based on multiple decision points.
- Combinations of proteasome inhibitors with either immunomodulatory drugs or selinexor improve progression-free survival.
- We have three different monoclonal antibodies that improve progression-free survival when added to other standard therapies without significantly increasing side effects.
- In general, three-drug combinations are going to work better than two drugs.
- Many other exciting immunotherapy options are in trials and look very promising.
Recent Updates

Sarclisa After Early or Late Relapse

IKEMA Study

Patients with relapsed/refractory myeloma who received 1–3 prior therapies, had no prior therapy with Kyprolis, and were not refractory to prior anti-CD38 antibody

<table>
<thead>
<tr>
<th>Early relapse</th>
<th>Late relapse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sarclisa-Kd</td>
<td>Kd</td>
</tr>
<tr>
<td>Kd</td>
<td>Sarclisa-Kd</td>
</tr>
</tbody>
</table>

- **Median PFS (months)**
  - Early: 24.7
  - Late: 21.9
- **Overall response rate (%)**
  - Early: 82
  - Late: 90.4
- **≥VGPR rate (%)**
  - Early: 67.2
  - Late: 76
- **MRD negativity rate (%)**
  - Early: 24.6
  - Late: 37.5
- **MRD-negative CR rate (%)**
  - Early: 18
  - Late: 30.8

Data evaluated according to patients who experienced an early* versus late† relapse.

*<12 months from initiation of most recent line of therapy (for patients who had ≥2 lines of therapy); <18 months (for patients who had 1 prior line of therapy) and <12 months from ASCT
†≥12 months from initiation of most recent line of therapy (for patients who had ≥2 lines of therapy; ≥18 months for patients who had 1 prior line of therapy)

Regardless of early or late relapse, RRMM patients benefit from the use of isa-Kd with respect to depth of response and prolonged PFS.

CAR T-Cell Therapy

Genetically modified T cells designed to recognize specific proteins on myeloma cells

CAR T cells are activated once in contact with the myeloma cell and can destroy it

CAR T cells can persist for long periods of time in the body

CAR T cells are created from a patient’s own blood cells, but the technology is evolving to develop “off-the-shelf” varieties

CAR, chimeric antigen receptor; MM, multiple myeloma; BCMA, B-cell maturation antigen


B-cell maturation antigen (BCMA)

Two CAR T-cell therapies approved!
• Abecma (ide-cel)
• Carvykti (cilta-cel)

Prognostic value of depth of response following CAR T-cell therapy

• Achieving sustained, undetectable MRD after Abecma is associated with prolonged PFS
• Only MRD status—not complete response (CR) status—predicted early relapse 1 month after Abecma
• Both MRD and CR status at 12 months were required to identify patients with longer PFS

Real-world outcome with Abecma after BCMA-targeted therapy

• 11 US academic centers conducted a retrospective analysis on the real-world outcome for patients treated with Abecma after previously receiving BCMA-targeted therapy
• Prior BCMA-targeted treatment is associated with inferior PFS and a trend toward inferior outcomes for patients receiving Abecma within 6 months of having received prior BCMA-targeted therapy
• WARRANTS further investigation into the optimal timing of Abecma infusion

Outcomes and options following relapse from CAR T

• A retrospective analysis of 78 patients with RRMM who received BCMA-targeted CAR T-cell therapy
• Patients who had previously been refractory to a specific drug class re-responded after CAR-T relapse
• Median OS after progressing on CAR T was 14.8 months and 18 months for patients who received subsequent BCMA CAR T or BCMA bispecific antibodies within 6 months of progressing on CAR T

Assessment of cytopenias from CAR T

• Retrospective review of data from 90 patients 4 months after CAR T-cell infusion
• Patients with poor hematologic recovery (28%) compared with adequate recovery (72%) were older, more heavily pretreated, and more likely to have received ≥1 ASCT

Abecma in earlier lines of treatment

• KarMMa-2 phase 2 multicenter study of Abecma in 37 patients with RRMM with high-risk disease
• Results show a benefit to Abecma in earlier line of treatment

*Early relapse after frontline therapy or inadequate response after frontline ASCT

What’s next for CAR T-cell therapy?

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Features</strong></td>
<td>• Targets BCMA with a shortened manufacturing time through the NEXT-T process</td>
<td>• Targets BCMA and CD19 • Manufacturing process that takes as little as 24 hours</td>
<td>• Targets GPRC5D</td>
</tr>
<tr>
<td><strong>Trial details</strong></td>
<td>• Phase 1 trial of 55 patients with RRMM with a median of 5 prior lines of therapy</td>
<td>• Phase 1 trial of 13 newly diagnosed high-risk myeloma patients ineligible for stem cell transplant</td>
<td>• Phase 1 trial of 17 heavily pretreated patients with RRMM, including those who relapsed from BCMA CAR-T therapy</td>
</tr>
<tr>
<td><strong>Results</strong></td>
<td>• CRS occurred in 80% of patients with only 1 patient experiencing ≥G3 • Neurotoxicity occurred in 10.9% of patients (one grade 4) • Overall response rate was 98.1% with 57.4% achieving ≥VGPR (29.6% ≥CR)</td>
<td>• 100% of patients achieved ≥VGPR (69% sCR) • All patients achieved MRD negativity (by EuroFlow) • CRS observed in 23% of patients (all low grade)</td>
<td>• Neutropenia and thrombocytopenia most frequent grade 3/4 adverse events • Additional adverse events include skin- and nail-related; CRS; ICANS; dysgeusia/dysphagia • 88% evaluable patients responded, including 7 of 11 patients treated with prior BMCA-targeted treatment</td>
</tr>
</tbody>
</table>


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Bispecific Antibodies

Bispecific antibodies are also referred to as dual specific antibodies, bifunctional antibodies, or T-cell engaging antibodies.

Bispecific antibodies can target two cell surface molecules at the same time (one on the myeloma cell and one on a T cell).

Many different bispecific antibodies are in clinical development; none are approved for use in myeloma.

Availability is off-the-shelf, allowing for immediate treatment.

Bispecifics Discussed at ASH in 2022

**BCMA**
- Highly expressed only on the surface of plasma cells
- Myeloma patients have significantly higher serum BCMA levels than healthy individuals

**GPRC5D**
- Highly expressed on myeloma cells in the bone marrow
- Lowly expressed on hair follicles, but not on other healthy cells
- Expression on myeloma cells is independent of BCMA

**FcRH5**
- Selectively expressed on B cells and plasma cells

**CD3:** a T-cell receptor

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Elranatamab in Patients With Relapsed/Refractory Multiple Myeloma

**Updated efficacy and safety results with elranatamab (MagnetisMM-1 Study)¹**

Phase 1 study in RRMM (91% triple-class refractory)

- **Patients Responding (%)**
  - PR: 27.3
  - VGPR: 10.9
  - CR: 18.2
  - sCR: 7.3

Median duration of response 17.1 months.

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**MagnetisMM-3 study of elranatamab²**

Phase 2 study in RRMM refractory to at least 1 PI, 1 IMiD, and 1 anti-CD38 antibody—no prior BMCA-targeted treatment

- **Patients Responding (%)**
  - PR: 13
  - VGPR: 14.6
  - CR: 27.6
  - sCR: 5.7

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IMiD, immunomodulatory drug; PI, proteasome inhibitor

Phase 1 Study of Alnuctamab in Patients With Relapsed/Refractory Multiple Myeloma

**Intravenous Formulation Results**

<table>
<thead>
<tr>
<th></th>
<th>IV alnuctamab (n=55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median follow up (months)</td>
<td>8.0</td>
</tr>
<tr>
<td>Overall response rate (%)</td>
<td>39</td>
</tr>
<tr>
<td>Median duration of response (months)</td>
<td>33.6</td>
</tr>
<tr>
<td>Responses ongoing (%)</td>
<td>48</td>
</tr>
<tr>
<td><strong>Median PFS (months)</strong></td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>3.1</td>
</tr>
<tr>
<td>Responders</td>
<td>36.4</td>
</tr>
<tr>
<td>Nonresponders</td>
<td>1.7</td>
</tr>
</tbody>
</table>

**Subcutaneous Formulation Results**

<table>
<thead>
<tr>
<th></th>
<th>PR</th>
<th>VGPR</th>
<th>CR</th>
<th>sCR</th>
</tr>
</thead>
<tbody>
<tr>
<td>All doses (n=55)</td>
<td>16</td>
<td>14</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>&lt;30 mg (n=29) Target Dose</td>
<td>16</td>
<td>14</td>
<td>19</td>
<td>1</td>
</tr>
<tr>
<td>30 mg (n=26)</td>
<td>11</td>
<td>14</td>
<td>27</td>
<td>19</td>
</tr>
</tbody>
</table>

**Most frequent adverse events, %**

<table>
<thead>
<tr>
<th></th>
<th>Any grade</th>
<th>Grade 3/4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematologic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>32</td>
<td>37</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>24</td>
<td>9</td>
</tr>
<tr>
<td>Non-hematologic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRS</td>
<td>53</td>
<td>0</td>
</tr>
<tr>
<td>Infections</td>
<td>34</td>
<td>9</td>
</tr>
<tr>
<td>ICANS</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>ALT increase</td>
<td>12</td>
<td>6</td>
</tr>
</tbody>
</table>

Tecvayli in Combination With Darzalex and Revlimid

**Phase 1b study (MajesTEC-2) in RRMM with 1–3 prior lines of therapy (including an IMiD and a PI)**

32 patients—who had received at least 2 prior lines of therapy—received treatment with the triplet and Tecvayli at 2 different doses (0.72 mg/kg and 1.5 mg/kg) subcutaneously

**Most frequent non-hematologic adverse events, %**

<table>
<thead>
<tr>
<th></th>
<th>Any grade</th>
<th>Grade 3/4</th>
</tr>
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<tbody>
<tr>
<td>CRS</td>
<td>25.8</td>
<td>0</td>
</tr>
<tr>
<td>Fatigue</td>
<td>46.9</td>
<td>6.3</td>
</tr>
<tr>
<td>Infections (≥1)</td>
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<td>37.5</td>
</tr>
<tr>
<td>COVID-19</td>
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<td>12.5</td>
</tr>
<tr>
<td>Upper respiratory</td>
<td>31.3</td>
<td>0</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>25</td>
<td>15.6</td>
</tr>
<tr>
<td>COVID pneumonia</td>
<td>12.5</td>
<td>3.1</td>
</tr>
<tr>
<td>Sepsis</td>
<td>9.4</td>
<td>9.4</td>
</tr>
<tr>
<td>Pneumonia pseudomonal</td>
<td>6.3</td>
<td>6.3</td>
</tr>
<tr>
<td>CMV</td>
<td>6.3</td>
<td>6.3</td>
</tr>
</tbody>
</table>

IMiD, immunomodulatory drug; PI, proteasome inhibitor
Talquetamab in Patients With Relapsed/Refractory Multiple Myeloma

Phase 1/2 study (MonumenTAL-1) in RRMM

288 patients—with no prior T cell-redirecting therapies—received treatment with talquetamab at 2 different doses (0.4 mg/kg every week and 0.8 mg/kg every other week) subcutaneously.

Data from this trial was recently used to submit a Biologics License Application to the US Food and Drug Administration for the treatment of patients with relapsed or refractory multiple myeloma.

IMID, immunomodulatory drug; PI, proteasome inhibitor

Forimtamig (RG6234) in Patients With Relapsed/Refractory Multiple Myeloma

Phase 1 study in RRMM

105 patients received treatment with RG6234 in 2 different formulations (intravenous and subcutaneous).

Expected Toxicities With T-Cell Activating Therapies (CAR T and Bispecific Antibodies)

- **Cytokine release syndrome (CRS)**
  - Usually occurs within first 1–2 weeks
  - Frequency (all grade and grade 3–5) higher with CAR T

- **Infections**
  - Viruses: CMV, EBV
  - PCP/PJP
  - Ongoing discussions regarding prophylactic measures
    - IVIG
    - Anti-infectives

- **Cytopenias**
  - Dysgeusia

- **Neurotoxicity (ICANS)**
  - Usually occurs within first 1–2 weeks
  - Frequency (all grade and grade 3–5) higher with CAR T

- **Off-target effects (with GPRC5D-targeted agents)**
  - Cytokine release syndrome (CRS)
  - Neurotoxicity (ICANS)
  - Cytopenias
  - Infections

ICANS, immune effector cell-associated neurotoxicity syndrome; CMV, cytomegalovirus; EBV, Epstein-Barr virus; PCP/PJP, pneumocystis pneumonia/pneumocystis jiroveci pneumonia

Pretreatment With Tocilizumab Reduces Incidence and Severity of CRS

- **Cevostamab** is an FcRH5-targeted bispecific antibody under investigation in patients with RRMM

- An ongoing phase 1 study evaluating the use of tocilizumab (an IL-6 antibody) prior to the first dose of cevostamab. A single 8 mg/kg dose of tocilizumab was administered to 28 patients 2 hours prior to cevostamab

- 35.7% of patients receiving tocilizumab experienced CRS compared to 90.9% of patients who didn’t receive tocilizumab.

- Grade 3 CRS was observed in only one patient in each group and no G4/5.

- The frequency of neutropenia was higher for patients receiving tocilizumab compared with those who didn’t (64.3% vs 38.6% G3/4).

- No impact on response was observed with tocilizumab pretreatment.

Fixed-Duration Therapy With Bispecifics Cevostamab

At the time of this presentation, no patients who achieved an sCR have relapsed!


Mezigdomide: A Cereblon E3 Ligase Modulator (CELMoD)

CELMoDs are related to the immunomodulatory drugs (IMiDs) but are more potent and may overcome resistance to IMiDs

A phase 1/2 study of mezigdomide combined with dex in relapsed/refractory patients

101 patients who had received at least 6 prior lines of therapy (all were triple-class refractory; one third were previously exposed to anti-BCMA therapy) received treatment with mezigdomide-dex

Questions & Answers
Myeloma Mentors® allows patients and caregivers the opportunity to connect with trained mentors. This is a phone-based program offering an opportunity for a patient and/or caregiver to connect one-on-one with a trained patient and/or caregiver mentor to share his or her patient journeys and experiences.

No matter what your disease state—smoldering, newly diagnosed, or relapsed/refractory—our mentors have insights and information that can be beneficial to both patients and their caregivers.

Contact the Patient Navigation Center at 888-841-6673 to be connected to a Myeloma Mentor or to learn more.
MMRF Events

Our events are returning live and in-person, and there are so many ways to get involved. Most have a virtual option, too. Join us today!

Endurance Events

5K Walk/Run Events

Independent Events

**FIND AN EVENT AND JOIN US**: themmrf.org/get-involved/mmrf-events/

### Upcoming Patient Education Events

**Save the Date**

<table>
<thead>
<tr>
<th>Topic</th>
<th>Date and Time (ET)</th>
<th>Speakers</th>
</tr>
</thead>
</table>
| Patient Summit                                       | Saturday, March 11 9:00 AM to 1:40 PM ET | David Vesole, MD, PhD  
Noa Biran, MD  
Kimberley Doucette, MD  
Ann McNeill, RN, MSN, APN  
Susan Kumka, APN       |
| Patient Summit                                       | Saturday, March 11 9:00 AM to 1:40 PM ET | David Vesole, MD, PhD  
Noa Biran, MD  
Kimberley Doucette, MD  
Ann McNeill, RN, MSN, APN  
Susan Kumka, APN       |
| Facebook Live FAQs                                   | Tuesday, March 14 3:00 to 4:00 PM ET  | Gurbakhash Kaur, MD  
Sonia Patel, MPH, MSN, AGACNP-BC, APRN, AOCNP                           |
| Webinar: BCMA-Targeted Bispecific Antibodies in Multiple Myeloma | Tuesday, March 21 4:00 to 5:00 PM ET  | Jesus Berdeja, MD  
Amrita Krishnan, MD                                                   |
| Patient Summit                                       | Saturday, March 25 9:00 AM to 3:45 PM MT | Leif Bergsagel, MD  
Clarence Adoo, MD  
Jonathan Keats, PhD  
Sumit Madan, MD  
Suzanne Hyde, MSW, LCSW  
Barbara Kavanagh, MSW, LCSW  
Joan Kuerber-Walker  
William Brown                                                  |
| Webinar (rebroadcast): Multiple Myeloma Precursor Conditions | Wednesday, April 5 2:30 to 3:30 PM ET  | Sagar Lonial, MD  
Omar Nadeem, MD                                                   |

For more information or to register, visit themmrf.org/resources/education-program
Thank you!