Applying the Latest Clinical Data in Multiple Myeloma Patient Care in the Community Setting

Joshua Richter, MD
Associate Professor of Medicine
Tisch Cancer Institute/
Icahn School of Medicine at Mount Sinai
Director of Myeloma: Blavatnik Family –
Chelsea Medical Center at Mount Sinai
New York, New York
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### Multiple Myeloma Care Among Black Patients

#### Initial therapy
- Median time to first-line therapy initiation significantly longer in Black patients
- Black patients less likely to initiate first-line triplet therapy for multiple myeloma

#### Utilization of stem cell transplant
- Significantly lower stem cell transplant utilization in Black patients

#### Treatment outcomes
- With equal access, Black patients have superior survival compared to White patients with multiple myeloma
- Outcomes of Black patients same as White patients in cooperative-group clinical trials

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### IMWG Criteria for Diagnosis of Multiple Myeloma

<table>
<thead>
<tr>
<th>Monoclonal gammopathy of undetermined significance (MGUS)</th>
<th>Smoldering multiple myeloma (SMM)</th>
<th>Ultra–high-risk SMM = active myeloma</th>
<th>Multiple myeloma</th>
</tr>
</thead>
<tbody>
<tr>
<td>M protein &lt;3 g/dL</td>
<td>M protein ≥3 g/dL (serum) or ≥500 mg/24 hrs (urine)</td>
<td>Not CRAB but SLiM CRAB</td>
<td>Underlying plasma cell proliferative disorder</td>
</tr>
<tr>
<td>Clonal plasma cells in BM &lt;10%</td>
<td>Clonal plasma cells in bone marrow ≥10%–60%</td>
<td>M (MRI ≥1 focal lesion)</td>
<td>AND ≥1 myeloma-defining events</td>
</tr>
<tr>
<td>No myeloma-defining events</td>
<td>No myeloma-defining events</td>
<td>C (calcium elevation)</td>
<td>≥1 CRAB* feature</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R (renal insufficiency)</td>
<td>Clonal plasma cells in bone marrow ≥60%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>A (anemia)</td>
<td>Serum free light chain ratio ≥100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B (bone disease)</td>
<td>&gt;1 MRI focal lesion</td>
</tr>
</tbody>
</table>

*C: Calcium elevation (>11 mg/dL or >1 mg/dL higher than ULN)
R: Renal insufficiency (creatinine clearance <40 mL/min or serum creatinine >2 mg/dL)
A: Anemia (Hb <10 g/dL or 2 g/dL < normal)
B: Bone disease (≥1 lytic lesions on skeletal radiography, CT, or PET-CT)

Multiple Myeloma Prognosis and Risk Assessment

Revised-International Staging System (R-ISS)¹

<table>
<thead>
<tr>
<th>R-ISS stage</th>
<th>Laboratory measurements</th>
<th>5-year OS (%)</th>
<th>5-year PFS (%)</th>
</tr>
</thead>
</table>
| I           | • Serum β2M level <3.5 mg/L  
• Serum albumin level ≥3.5 g/dL  
• No high-risk CA*  
• Normal LDH level | 82 | 55 |
| II          | All other possible combinations | 62 | 36 |
| III         | • Serum β2M level ≥5.5 mg/L  
• High-risk CA* or high LDH level | 40 | 24 |

OS, overall survival; PFS, progression-free survival; β2M, beta-2 microglobulin; LDH, lactate dehydrogenase; GEP, gene expression profiling.


Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSMART) Consensus Guidelines²

<table>
<thead>
<tr>
<th>High risk</th>
<th>Standard risk</th>
</tr>
</thead>
</table>
| • High-risk genetic abnormalities  
  – t(4;14)  
  – t(14;16)  
  – t(14;20)  
  – del 17p  
  – p53 mutation  
  – gain 1q  
  • R-ISS Stage 3  
  • High plasma cell S phase  
  • GEP: high-risk signature | • All others including:  
  – Trisomies  
  – t(11;14)  
  – t(6;14)  

• Double-hit myeloma: any two high-risk genetic abnormalities  
• Triple-hit myeloma: three or more high-risk genetic abnormalities

Currently cannot identify with great certainty all high-risk patients.

Recent Advances in the Treatment of Newly Diagnosed Multiple Myeloma (NDMM)
Applying the Latest Clinical Data in Multiple Myeloma Patient Care in the Community Setting

Overview of Treatment Approach for Active NDMM

Is the patient a candidate for autologous stem cell transplantation (ASCT)?

- **Yes**
  - 3–4 cycles of induction therapy
  - 3- to 4-drug regimen generally preferred
  - Clinical trial
  - Stem cell collection and storage
  - High-dose melphalan + stem cell transplant
  - Consolidation and or continuous/maintenance therapy
  - Supportive care

- **No**
  - Any of the regimens used for transplant candidates*
  - Clinical trial
  - *Two-drug regimen may be considered for frail patients

Can ASCT be delayed?

NCCN Guidelines for Transplant-Eligible NDMM

- **Bortezomib-lenalidomide-dex (RVd)**†‡
- **Carfilzomib-lenalidomide-dex (KRd)**
- **Daratumumab-lenalidomide-bortezomib-dex (D-RVd)**†‡

*Preferred regimen.
†Category 1 recommendation.
‡Recommended regimen.

Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate. Other regimens may be appropriate based on the clinical scenario, such as in cases of renal failure, frailty, etc.

Phase 3 Study of Early vs Late ASCT in Patients With NDMM

**Determination Trial**

- Newly diagnosed myeloma patients
- EARLY TRANSPLANT ARM: 365 patients
- LATE TRANSPLANT ARM: 357 patients
- Induction
- Stem cell collection
- Transplant
- RVd
- ASCT
- RVd
- R
- Consolidation
- Maintenance
- R

The study enrolled 19% Black myeloma patients.

### Progression-free survival (PFS)

- PFS for early transplant was 22 months longer than for late transplant (68 mos vs 46 mos). However, Black patients did not seem to have the same PFS advantage with early transplant as other patients.

### Overall survival (OS)

- No difference was seen in OS between treatment groups (5-yr OS rate: 81% vs 79%)

- 5-year PFS in MRD-negative patients was similar regardless of ASCT timing (53.5% for early transplant vs 59.2% for late transplant)

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MRD-Negativity Results From Phase 2 Study of Dara-RVd vs RVd in Transplant-Eligible NDMM

**GRIFFIN Trial**

<table>
<thead>
<tr>
<th>Newly diagnosed myeloma patients</th>
<th>104 patients</th>
<th>103 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dara-RVd</td>
<td>Induction</td>
<td>R</td>
</tr>
<tr>
<td>ASCT</td>
<td>Transplant</td>
<td>ASCT</td>
</tr>
<tr>
<td>Dara-RVd</td>
<td>Consolidation</td>
<td>RVd</td>
</tr>
<tr>
<td>Dara-R</td>
<td>Maintenance</td>
<td>R</td>
</tr>
</tbody>
</table>

Sustained MRD-negativity rates at $10^{-5}$ lasting ≥6 and ≥12 months were higher for D-RVd vs RVd among all high-risk subgroups.*

Dara-RVd was superior to RVd for rates of sustained MRD negativity lasting >12 months for patients with greater than or equal to a CR (53.7% vs 20.3%) and sCR (59.1% vs 17.4%).

MRD negativity rates in patients treated with Dara-RVd were consistent across all subgroups of patients, including those with high-risk features.

*ISS stage III or high-risk cytogenetics del(17p), t(4;14); t(14;16), t(14;20), or gain 1q

The findings support the role of D-RVd as the new standard of care for this patient population.

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**Lenalidomide as Maintenance Therapy**

- Reduction in myeloma progression (3 large studies)¹⁻³

- Improved survival (1 of 3 studies; meta-analysis)³,⁴

- Increased risk of second cancers when used after melphalan*³

- Approved for use as maintenance treatment after ASCT⁴

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¹Low risk when used in the context of ASCT

Lenalidomide Maintenance Therapy: Improves Depth of Response

<table>
<thead>
<tr>
<th>Disease response</th>
<th>Before len maintenance (n)</th>
<th>During/after len maintenance (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRD negative</td>
<td>37</td>
<td>72</td>
</tr>
<tr>
<td>CR</td>
<td>57</td>
<td>49</td>
</tr>
<tr>
<td>VGPR</td>
<td>34</td>
<td>14</td>
</tr>
<tr>
<td>≤PR</td>
<td>11</td>
<td>4</td>
</tr>
</tbody>
</table>

Achievement of MRD-negative status at any time (before or during maintenance) was associated with improved PFS (median PFS 83 mos for MRD negative vs 48 mos for MRD positive, \( P<0.01 \))


Lenalidomide Maintenance Duration

STaMINA Trial (BMT-CTN0702)

- **Consolidation**
  - MEL 200 mg/m²
  - RVd × 4
  - No consolidation

- **Maintenance**
  - R × 3 yrs
  - Auto/Auto group
  - Auto/RVD group
  - Auto/Rev group

247 pts

254 pts

257 pts

ASCT melphalan 200 mg/m²

There was no difference in PFS or OS between the 3 groups.

Discontinuation of lenalidomide @ 3 years did not affect overall second primary malignancies (SPM) rates @ 6 years

Phase 3 Trial of KRd vs R as Maintenance After ASCT

**ATLAS trial**

<table>
<thead>
<tr>
<th>Newly diagnosed myeloma patients</th>
<th>KRd</th>
<th>R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Induction therapy (any)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autologous stem cell transplant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>92 patients</td>
<td>86 patients</td>
<td></td>
</tr>
<tr>
<td><strong>KRd</strong></td>
<td><strong>R</strong></td>
<td></td>
</tr>
<tr>
<td>Risk-adapted maintenance</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Response assessed after first six cycles and patients who are standard risk and achieve MRD negativity proceeded on R maintenance. High risk considered to have t(4;14), t(14;16), or del(17p).
†MRD negativity ≥10⁻⁵ or higher by NGS.


<table>
<thead>
<tr>
<th>Period</th>
<th>KRd</th>
<th>R</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 cycles (%)†</td>
<td>47</td>
<td>29</td>
</tr>
<tr>
<td>Median PFS (mos)</td>
<td>59</td>
<td>41.4</td>
</tr>
<tr>
<td>≥G3 side effects (%)</td>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>Low white blood cell counts (neutropenia)</td>
<td>47</td>
<td>59</td>
</tr>
<tr>
<td>Low platelet counts (thrombocytopenia)</td>
<td>13</td>
<td>7</td>
</tr>
<tr>
<td>Infections</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Secondary malignancies</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

The first randomized phase 3 trial demonstrating superior PFS with extended post-transplant KRd therapy compared to R maintenance

NCCN Guidelines for Transplant-Ineligible NDMM

- **Bortezomib-lenalidomide-dex (RVd)**††
- **Daratumumab-lenalidomide-dex (DRd)**††
- **Daratumumab-bortezomib-melphalan-prednisone (D-VMP)**††
- **Carfilzomib-lenalidomide-dex (KRd)**‡
- **Ixazomib-lenalidomide-dex (IRd)**‡
- **Daratumumab-cyclophosphamide-bortezomib-dex (D-VCd)**‡

*Preferred regimen.
†Category 1 recommendation.
‡Recommended regimen.
Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate. Other regimens may be appropriate based on the clinical scenario, such as in cases of renal failure, frailty, etc.

MAIA: Adding Daratumumab to Rd in Non-ASCT Candidates Substantially Improved PFS and OS

After ~5 years of follow-up, a significant and clinically meaningful OS improvement was demonstrated with DRd versus Rd, representing a 32% reduction in the risk of death¹


Response Evaluation in Myeloma Therapy

ClonoSEQ is an FDA-approved next-generation sequencing (NGS) test to measure MRD in MM patients.

ClonoSEQ is an FDA-approved next-generation sequencing (NGS) test to measure MRD in MM patients.
Guiding Principles for NDMM Management

- Use at least three drugs for induction therapy
  - Consider four-drug induction regimen for high-risk disease
- Aim for the deepest response (includes MRD)
- Prolonged maintenance therapy with lenalidomide improved depth of response
- Consider stem cell transplant either now or later
- Approach, regimens, and goals must be individualized based on age, organ function, risk assessment, and personal factors

The Expanding Treatment Armamentarium for RRMM
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NCCN Guidelines for Early RRMM Category 1 Recommendations (1–3 Prior Therapies)

- Carfilzomib/lenalidomide/dex*
- Daratumumab + Vd, Kd, Pd, or Rd*
- Isatuximab + pom/dex or Kd*
- Ixazomib/lenalidomide/dex*
- Pom/bortezomib/dex*
- Bortezomib/liposomal doxorubicin/dex†
- Carfilzomib (twice weekly)/dex†
- Elotuzumab/lenalidomide/dex†
- Selinexor/bortezomib/dex†

Note: Triplet combinations, including antibody-based options, are among the recommended strategies.

*Preferred regimen.
†Other recommended regimen.
Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate. Other regimens may be appropriate based on the clinical scenario, such as in cases of renal failure, frailty, etc.

Current Guidelines and Evidence for Use of Triplet Combinations Anchored by Anti-CD38 Antibodies in RRMM

<table>
<thead>
<tr>
<th>Preferred antibody-based regimens (Category 1)¹</th>
<th>Daratumumab + Vd, Kd, Pd, or Rd</th>
<th>Isatuximab + Pd or Kd</th>
</tr>
</thead>
<tbody>
<tr>
<td>CANDOR²</td>
<td>KdD (n=312)</td>
<td>Kd (n=154)</td>
</tr>
<tr>
<td>Median PFS, mo</td>
<td>28.6</td>
<td>15.2</td>
</tr>
<tr>
<td>HR for KdD vs Kd (95% CI)</td>
<td>0.59 (0.45–0.78), P&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>APOLLO¹</td>
<td>DPd (n=151)</td>
<td>Pd (n=153)</td>
</tr>
<tr>
<td>Median PFS, mo</td>
<td>12.4</td>
<td>6.9</td>
</tr>
<tr>
<td>HR for DPd vs Pd (95% CI)</td>
<td>0.63 (0.47–0.85), P=0.0018</td>
<td></td>
</tr>
<tr>
<td>ICARIA-MM²</td>
<td>IsaPd (n=154)</td>
<td>Pd (n=153)</td>
</tr>
<tr>
<td>Median PFS, mo</td>
<td>11.5</td>
<td>6.4</td>
</tr>
<tr>
<td>HR for IsaPd vs Pd (95% CI)</td>
<td>0.536 (0.4360–0.814), P=0.001</td>
<td></td>
</tr>
<tr>
<td>IKEMA³</td>
<td>IsaKd (n=179)</td>
<td>Kd (n=123)</td>
</tr>
<tr>
<td>Median PFS, mo</td>
<td>NR</td>
<td>19.15</td>
</tr>
<tr>
<td>HR for IsaKd vs Kd (95% CI)</td>
<td>0.53 (0.4360–0.814), P=0.0007</td>
<td></td>
</tr>
</tbody>
</table>


This is for educational purposes only.
NCCN Guidelines for Late Relapses (>3 Prior Therapies)

After ≥4 prior therapies, including an anti-CD38 mAb, a PI, and an IMiD
• Idecabtagene vicleucel
• Ciltacabtagene autoleucel
• Teclistamab-cqyv

After ≥4 prior therapies and in patients whose disease is refractory to ≥2 PIs, ≥2 IMiDs, and an anti-CD38 mAb
• Selinexor/dexamethasone

BOSTON: Adding Selinexor to Bortezomib/Dex Improved PFS in RRMM

<table>
<thead>
<tr>
<th></th>
<th>SVd (n=195)</th>
<th>Vd (n=207)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median PFS (mos) Hazard ratio (P value)</td>
<td>13.93 0.70 (0.0075)</td>
<td>9.46 1.96 (0.0012)</td>
</tr>
<tr>
<td>ORR (%) Hazard ratio (P value)</td>
<td>76.4 1.96 (0.0012)</td>
<td>62.3 1.96 (0.0012)</td>
</tr>
<tr>
<td>≥VGPR (%)</td>
<td>44.6</td>
<td>32.4</td>
</tr>
<tr>
<td>DOR (months)</td>
<td>20.3</td>
<td>12.9</td>
</tr>
</tbody>
</table>

BCMA-Targeted Therapies for MM

Figure 3 from Yu B et al. BCMA-targeted immunotherapy for multiple myeloma. J Hematol Oncol. 2020;13:125. Available under a Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by/4.0/).

Figure 1B of Shah N et al. B-cell maturation antigen (BCMA) in multiple myeloma: rationale for targeting and current therapeutic approaches. Leukemia. 2020;34(4):985-1005. http://creativecommons.org/licenses/by/4.0/.

CAR T-cell therapies
Idecabtagene vicleucel
Ciltacabtagene autoleucel

Bispecific T-cell engagers
Tecristamab
Erlotinatamab
Talquetamab

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 the myeloma cell
CAR T cells can persist for long periods 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

Approved:
Idecabtagene vicleucel (ide-cel)
Ciltacabtagene autoleucel (cilta-cel)
**KarMMa: Ide-Cel in Triple-Class–Refractory MM**

- **Primary (ORR >50%) and key secondary (CRR >10%) end points were met in the ide-cel–treated population**
  - ORR: 73% (95% CI, 65.8–81.1; P<0.0001)
  - CRR (CR/sCR): 33% (95% CI, 24.7–40.9; P<0.0001)

- **Median PFS**
  - 8.8 months (95% CI, 5.6 to 11.6) in Total
  - 12.1 months (95% CI, 8.8 to 12.3) at the 450 × 10⁶ dose
  - 20.2 months in patients with CRR (CR/sCR)


**CARTITUDE-1: 2-Year Follow-Up With Cilta-Cel in RRMM**

2 years post-last patient in (LPI) results

- ORRª remained 97.9%
- 83% of patients achieved a sCR with longer follow-up
- Cilta-cel is being assessed in earlier lines of therapy
  - CARTITUDE-3, CARTITUDE-4, CARTITUDE-5, CARTITUDE-6

ªORR assessed by independent review committee; ªNo patient had CR or stable disease
CARTITUDE-1: PFS Follow-Up 2 Years With Post-LPI With Cilta-Cel in RRMM


CRS and ICANS With CAR T Therapy

<table>
<thead>
<tr>
<th>Safety</th>
<th>Cilta-cel, % (n)¹</th>
<th>Ide-cel, % (n)²</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRS (all, grade 3 or 4)</td>
<td>95 (5)</td>
<td>84 (5)</td>
</tr>
<tr>
<td>Median onset CRS</td>
<td>7 days</td>
<td>1 day</td>
</tr>
<tr>
<td>ICANS (all, grade 3 or 4)</td>
<td>17 (2)</td>
<td>18 (3)</td>
</tr>
<tr>
<td>Infections (all, grade 3 or 4)</td>
<td>58 (20)</td>
<td>69 (22)</td>
</tr>
<tr>
<td>Grade 3 or 4 neutropenia &gt;1 mo, n</td>
<td>10</td>
<td>41</td>
</tr>
<tr>
<td>Grade 3 or 4 thrombocytopenia &gt;1 mo, n</td>
<td>25</td>
<td>48</td>
</tr>
<tr>
<td>Delayed neurotoxicity (all, grade 3 or 4)</td>
<td>12 (9)</td>
<td>None</td>
</tr>
</tbody>
</table>

Principles for CAR T Therapy

Ide-cel recommended dose range$^1$
300–460 × 10^6
CAR-positive viable T cells

Cilta-cel recommended dose range$^2$
0.5–1.0 × 10^6
CAR-positive viable T cells
(Maximum dose of 1 × 10^8 CAR-positive viable T cells per single-dose infusion)

Do not use a leukodepleting filter when administering

Administer a lymphodepleting chemotherapy regimen of cyclophosphamide and fludarabine before CAR T infusion

Premedicate with acetaminophen and an H1 antihistamine

Avoid prophylactic use of dexamethasone or other systemic corticosteroids

Monitor for CRS and ICANS and confirm tocilizumab availability before infusion

Other adverse events (AEs) to monitor for:
- neurologic events, lymphohistocytic/macrophage activation syndrome, cytopenias

Ide-cel and cilta-cel are available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS)

**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; teclistamab is the only one approved for use in myeloma.

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

Modified from Figure 3 of Shah N et al. B-cell maturation antigen (BCMA) in multiple myeloma: rationale for targeting and current therapeutic approaches. Leukemia. 2020;34(4):985-1005. http://creativecommons.org/licenses/by/4.0/.

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**Examples:**
- Teclistamab
- Elranatamab
- Talquetamab
- Cevostamab
- TNB-303B (ABBV-383)
- REGN5458

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**Teclistamab (BCMA × CD3 Bispecific Antibody) in Patients With RRMM**

**Updated efficacy and safety results with teclistamab (MajesTEC-1 study)**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Patients Responding (%)</th>
<th>n=165</th>
</tr>
</thead>
<tbody>
<tr>
<td>sCR</td>
<td>32.7</td>
<td></td>
</tr>
<tr>
<td>CR</td>
<td>6.7</td>
<td></td>
</tr>
<tr>
<td>VGPR</td>
<td>19.4</td>
<td></td>
</tr>
<tr>
<td>PR</td>
<td>4.2</td>
<td></td>
</tr>
</tbody>
</table>

Deep and durable responses in heavily pretreated RRMM patients. Phase 3 studies under way.

**Teclistamab in patients with prior BCMA-targeted treatment (MajesTEC-1 study)**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Patients Responding (%)</th>
<th>n=165</th>
</tr>
</thead>
<tbody>
<tr>
<td>sCR</td>
<td>32.7</td>
<td></td>
</tr>
<tr>
<td>VGPR</td>
<td>26.7</td>
<td></td>
</tr>
<tr>
<td>PR</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>CR</td>
<td>27.5</td>
<td></td>
</tr>
</tbody>
</table>

A potential off-the-shelf T-cell–redirecting therapy for patients with RRMM and prior exposure to other BCMA-targeted agents.

**Teclistamab experience vs real-world clinical practice (LocoMMotion study)**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Patients Responding (%)</th>
<th>n=165</th>
</tr>
</thead>
<tbody>
<tr>
<td>sCR</td>
<td>62.7</td>
<td></td>
</tr>
<tr>
<td>CR</td>
<td>26.8</td>
<td></td>
</tr>
<tr>
<td>PR</td>
<td>16.3</td>
<td></td>
</tr>
</tbody>
</table>

A potential treatment option for patients with RRMM who have been exposed to three or more lines of therapy.

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Elranatamab (BCMA × CD3 Bispecific Antibody) in Patients With RRMM

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

- 64% of patients responded who received elranatamab at a dose greater than or equal to 215 µg/kg
- 35% of patients achieved a CR or better
- 54% of patients who received prior BCMA-directed therapy responded to elranatamab treatment (2 sCR, 1CR, 3 VGPR, and 1 PR)
- 100% of patients who achieved CR and sCR also achieved MRD negativity

Durable clinical and molecular responses, consistent with clinical findings from other investigational BCMA-targeted bispecific antibodies

Elranatamab in patients with no prior BCMA-directed treatment (MagnetisMM-3 study)2

- Patients had a median of five prior lines of therapy and were treated with a weekly dose of elranatamab
- 61% of patients responded

The trial is ongoing with results expected later this year.

Talquetamab (GPRC5D × CD3 Bispecific Antibody) in Patients With RRMM

Updated efficacy and safety results with talquetamab (MonumenTAL-1 study)

- 70% patients responding PR
- 37.7% patients responding VGPR
- 5.1% patients responding CR
- 1.1% patients responding sCR

Highly promising efficacy in heavily pretreated RRMM patients, including those who received three or more lines of prior therapy or were double refractory to a proteasome inhibitor and an immunomodulatory drug.

GPRC5D, G protein-coupled receptor family C group 5 member D
**Cevostamab in RRMM: Response**

- Responses occurred ≥20 mg target dose level (n=143)
- ORR increased with target dose
  - ORR in cycle 1 single step-up expansion (3.6 mg/90 mg): 29.0%
  - ORR in first cycle of double step-up expansion (0.3 mg/3.6 mg/160 mg): 54.8%

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Cevostamab (N=161)</th>
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<tbody>
<tr>
<td>Median time to response among responders, mo (range)</td>
<td>1.0 (0.7–5.9)</td>
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<tr>
<td>Median time to best response, mo (range)</td>
<td>2.1 (0.7–11.4)</td>
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<tr>
<td>MRD negativity at &lt;10^(-5) in patients with ≥VGPR, n/N (%)</td>
<td>7/10 (70)</td>
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</tbody>
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Best response in evaluable patients by dose level

- **ORR**: 36.1%
- **≥VGPR**: 20.5%
- **CR**: 15.7%
- **sCR**: 8.4%


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**Bispecific Antibodies: Expected Toxicities**

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

- **Cytokeratin change/rash**

- **Infections**
  - Incidence for bispecifics at RP2D not yet known
  - Viruses: CMV, EBV
  - PCP/PJP
  - Ongoing discussions regarding prophylactic measures
    - IVIG
    - Anti-infectives

ICANS, immune effector cell-associated neurotoxicity syndrome; RP2D, randomized phase 2 dose; CMV, cytomegalovirus; EBV, Epstein-Barr virus; PCP/PJP, pneumocystis pneumonia/Pneumocystis jiroveci pneumonia
### Key Takeaways for NDMM

- Black patients disproportionately affected by disparities in access to care
- Imperative to identify high-risk patients and to provide them with the most effective therapy
  - Attaining and maintaining a deep remission are key treatment goals
  - MRD negativity may emerge as a new goal of therapy
- RVd with or without ASCT followed by R maintenance is current standard of care for frontline therapy
- Quadruplet therapy is highly active as up-front therapy and may be the future of care
  - DETERMINATION: ASCT can be delayed in some cases
- Studies are evaluating new MRD-directed maintenance therapy

### Key Takeaways for RRMM

- Use of triplets containing an anti-CD38 antibody supported by current guidelines and evidence for use in early relapse
- BCMA-targeted CAR T-cell therapies are highly effective treatment options for triple-class refractory and beyond
  - CAR T-cell therapy: requires careful monitoring and management of CRS and ICANS
- Bispecific antibody are an "off-the-shelf" therapy that can target multiple cell surface proteins: BCMA, GPRC5D, FCRH5
- Small molecules with novel MOA such as selinexor are approved for RRMM
Thank you

Thank you for participating in this activity.

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