Opening Remarks

Mary DeRome, MS

MMRF
iPads

• To view the materials for this Summit, please log on to the iPad with your e-mail address
  – View slides
  – Answer questions
  – Take notes
  – Submit questions to panel
  – Program evaluation

Throughout the Summit, use the same e-mail address to log on to any iPad.

Program Faculty

Program Host

David H. Vesole, MD, PhD
MedStar Georgetown University Hospital
Georgetown University School of Medicine
Washington, District of Columbia
John Theurer Cancer Center, Hackensack Meridian School of Medicine
Hackensack, New Jersey

Faculty

Noa Biran, MD
John Theurer Cancer Center
Hackensack University Medical Center
Hackensack, New Jersey

Kimberley Doucette, MD
MedStar Georgetown University Hospital
Georgetown Lombardi Comprehensive Cancer Center
Washington, District of Columbia

Susan M. Kumka, RN, MSN, APN
John Theurer Cancer Center
Hackensack University Medical Center
Hackensack, New Jersey

Ann McNeill, RN, MSN, APN
John Theurer Cancer Center
Hackensack University Medical Center
Hackensack, New Jersey
# Summit Agenda

<table>
<thead>
<tr>
<th>Time (ET)</th>
<th>Topic</th>
<th>Speakers</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:00 – 9:10 AM</td>
<td>Introduction to the MMRF</td>
<td>Mary DeRome, MS</td>
</tr>
<tr>
<td>9:10 – 9:20 AM</td>
<td>Welcome</td>
<td>David H. Vesole, MD, PhD, FACP</td>
</tr>
<tr>
<td>9:20 – 10:00 AM</td>
<td>Myeloma 101 and Health Care Disparities in Multiple Myeloma</td>
<td>Kimberley Doucette, MD</td>
</tr>
<tr>
<td>10:00 – 10:30 AM</td>
<td>Treating Relapsed/Refractory Multiple Myeloma</td>
<td>Noa Biran, MD</td>
</tr>
<tr>
<td>10:30 – 11:00 AM</td>
<td>Town Hall Q&amp;A</td>
<td>Panel</td>
</tr>
<tr>
<td>11:00 AM – 11:30 AM</td>
<td>CAR T-Cell Therapy and Bispecific Antibodies</td>
<td>David H. Vesole, MD, PhD, FACP</td>
</tr>
<tr>
<td>11:30 AM – 12:00 PM</td>
<td>Supportive Care</td>
<td>Susan M. Kumka, RN, MSN, APN</td>
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<td></td>
<td></td>
<td>Ann McNeil, RN, MSN, APN</td>
</tr>
<tr>
<td>12:00 – 1:00 PM</td>
<td>Lunch, Patient Journey</td>
<td>Lucretia Agee</td>
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<tr>
<td>1:00 – 1:30 PM</td>
<td>Town Hall Q&amp;A</td>
<td>Panel</td>
</tr>
<tr>
<td>1:30 PM</td>
<td>Closing Remarks</td>
<td>Mary DeRome, MS</td>
</tr>
</tbody>
</table>
The Work of the MMRF

The MMRF does three things in relentless pursuit of its mission to accelerate a cure for each and every myeloma patient.

1. **We accelerate new treatments**
   - Bringing next-generation therapies to patients faster

2. **We drive precision medicine**
   - Using data to deliver better answers and more precise treatments for patients

3. **We empower patients**
   - Putting them on The Right Track and guiding them to the right team, tests, and treatments to extend their lives

---

**MMRF CoMMpass Study: Advancing Personalized Medicine Research**

- Landmark study focusing on the genomics of myeloma

- **Goals**
  - Learn which patients respond best to which therapies
  - Identify new targets and new hypotheses

- Newly diagnosed patients are followed for at least 8 years

All participants undergo a type of detailed DNA testing called *genomic sequencing* at diagnosis and each relapse.
CoMMpass Is a Trial of Discovery

- CoMMpass data has
  - Provided the myeloma community with information on
    - Frequency of genetic abnormalities
    - How genetic abnormalities play a role in myeloma
      - Drive multiple myeloma cell growth and survival
      - Contribute to drug resistance
      - May predict which patients respond to which therapy
    - Genetic abnormalities that help refine risk assessment
  - Led to conception of the MyDRUG trial and CureCloud Research Study

MyDRUG Trial

Functional High Risk Patients

Profiling for alterations (NCT02884102)

- No detectable "actionable" alterations
- RAF/BAS mutations
- CDK pathway activating alterations
- FGFR3 activating alterations
- t(11;14)
  - 2 cycles

- abemaciclib + Dex
- cobimetinib + IPd
- erdafitinib + IPd
- venetoclax + IPd
- daratumumab + IPd

*Assess single agent activity after 2 cycles: After cycle 2, add backbone to single agent
MMRF CureCloud – Recent Changes

- A new and better assay is being developed to look at patient DNA data from myeloma cells in their blood sample – while this assay is being developed, patients who join will no longer be able to receive their DNA test results, but their DNA will still be analyzed, and the results placed in the CureCloud along with their clinical information.

- Patients can still sign up for the CureCloud research study from home, but soon will be able to enroll at select clinical sites with help from site research staff – sites in preparation include UTSW, WashU, Hackensack, Emory, Ochsner, Karmanos, and the VA – by the end of 2023 we anticipate 15 sites will be approved for on-site enrollment.

- For now, all patients will still provide their blood sample using an at-home blood draw.

- Patients who live in New York may now enroll in CureCloud.

- We anticipate that patients will be able to receive their DNA results from samples collected sometime in 2024.
MMRF CureCloud

How Does the MMRF CureCloud® Work?

1. Convenient at-home blood test. A medical professional will come to you.
2. Sign up on the MMRF CureCloud website or in person at a CureCloud participating clinic and see if you are eligible.
3. Medical record collection. Provide your myeloma doctors and we'll contact them.
4. Personalized insights. Learn more about your myeloma.
5. Discuss with your doctor.

CureCloud Enrollment Tracker

This is the total number of patients who have enrolled in the CureCloud study. Monitor enrollment progress as we work toward our goal of 5,000 patient participants over 5 years. Explore anonymous CureCloud patient data below and find more information about each section in the (i) icon.

PROGRESS TOWARDS GOAL

- 19% complete
- 941 patients enrolled

- 685 patient samples sequenced
- 247 patient health records pulled
MMRF CureCloud Demographics

- Demographics by sex:
  - Male: 40%
  - Female: 60%
- Demographics by age:
  - Ages:
    - 0-20: 10%
    - 21-40: 30%
    - 41-60: 40%
    - 61+: 20%
- Demographics by race:
  - Caucasian: 90%
  - African American: 5%
  - Other: 5%
- Demographics by ethnicity:
  - Hispanic: 2.4%
  - Non-Hispanic: 96.7%
  - Other: 0.9%
  - Not Recorded:
Question

Are you a...
A. Patient
B. Caregiver (family member or friend who helps patient manage his or her disease)
C. Other

Question

At what stage is your myeloma? (If you are a caregiver, what is the stage of the patient’s myeloma?)
A. Newly diagnosed
B. Relapsed/refractory
C. Remission: still on therapy
D. Remission: not on therapy
E. MGUS or smoldering myeloma not currently requiring treatment
F. Other
G. I don’t know.
Have you had a stem cell transplant?
A. No, but I will soon!
B. No, but I am considering one (or my doctor is discussing with me).
C. No, my doctor tells me I am not a candidate.
D. Yes
E. Not applicable

Do you know if you had any molecular characterization performed on your tumor, such as FISH, cytogenetics, or sequencing?
A. No
B. Yes, I had FISH.
C. Yes, I had cytogenetics.
D. Yes, I had sequencing.
E. Yes, I had more than one of these tests performed.
F. I don’t know.
Question

Have you and your care team ever discussed the possibility of you joining a clinical trial that you are eligible for? (If you are a caregiver, do you know if joining a clinical trial has ever been discussed?)

A. Yes
B. No
C. I don’t know.

Myeloma 101 and Health Care Disparities in Multiple Myeloma

Kimberley Doucette, MD
MedStar Georgetown University Hospital
Georgetown Lombardi Comprehensive Cancer Center
Washington, District of Columbia
What is multiple myeloma?

- Multiple myeloma is a **blood cancer** that starts in the **bone marrow**, the place where all **blood cells** are produced.
- Multiple myeloma is caused when a type of **white blood cell** called a **plasma cell** becomes cancerous and grows out of control.
Multiple Myeloma Affects Your Bones, Blood, and Kidneys

**BLOOD**
- MM is a cancer of the blood
- MM crowds out normal blood cells

**BONES**
- Surrounding bone where MM cells grow is affected
- MM cells activate bone destruction

**KIDNEYS**
- Large amounts of M protein can overwork or cause damage to the kidneys

The clinical features that are characteristic of multiple myeloma:

- **C**: High levels of calcium in the blood
- **R**: Decreased kidney (renal) function
- **A**: Low amount of red blood cells (anemia)
- **B**: Presence of bone damage
Effects of Myeloma and Common Symptoms

Disease presentation and myeloma-related complications after myeloma diagnosis are different in patients by race

- More common in Black patients
  - Hypercalcemia
  - Kidney dysfunction
    - Hemodialysis
  - Anemia

- Less common in Black patients
  - Bone fractures

About 10% to 20% of patients with newly diagnosed myeloma do not have any symptoms.

- Low blood counts
- Weakness
- Fatigue
- Infection

- Decreased kidney function
- Weakness

- Bone damage
- Bone pain

Effects of Myeloma and Common Symptoms

Infections and Vaccinations in Multiple Myeloma

- Risk of infection higher for myeloma patients than for general population

- Types of infections include
  - Bacterial: pneumonia (an infection of the lungs), bacteremia
  - Viral: varicella zoster (shingles), influenza, COVID

- Preventive strategies (prophylaxis) are recommended
  - Hand-washing, avoiding sick contacts
  - Vaccines/pre-exposure antibodies
  - Other precautions (antibiotics, growth factors)

- Risk of infection higher for myeloma patients than for general population

- Types of infections include
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- Preventive strategies (prophylaxis) are recommended
  - Hand-washing, avoiding sick contacts
  - Vaccines/pre-exposure antibodies
  - Other precautions (antibiotics, growth factors)
**Demographic Risk Factors: Multiple Myeloma**

- Older age
- Male sex
- Obesity
- Race
  - ↑ Blacks (2× Whites)
  - Ashkenazi Jews
  - Europe: Ireland
  - ↓ Asian

**Family history risks**

- One first-degree relative with multiple myeloma
- Relatives of multiple myeloma patients have more monoclonal gammopathy of undetermined significance (MGUS)


**Following the Proper Path Will Help Patients Get the Best Treatment and Results for Their Specific Type of Myeloma**

- **Right Team**
  Access experts and centers that have extensive experience treating multiple myeloma

- **Right Tests**
  Get the information, tests and precise diagnoses to make the right treatment decisions

- **Right Treatment**
  Work with your team to decide on the best treatment plan and identify clinical trials that are right for you
The Right Team

Connect with a myeloma specialist—a doctor who diagnoses and treats a high number of myeloma patients

Available resources

MMRF’s online myeloma treatment locator: themmrf.org/resources/find-a-treatment-center

Seek a second opinion at any point in your journey

Contact the MMRF Patient Navigation Center: themmrf.org/resources/patient-navigation-center
1-888-841-MMRF (6673)

The Right Tests

Common laboratory tests conducted

Blood tests
- Complete blood count (CBC)
- Complete metabolic panel (CMP)
- Chemistries
  - Calcium
  - Creatinine
  - Lactate dehydrogenase (LDH)
  - Beta-2 microglobulin
- Serum protein electrophoresis (SPEP) with immunofixation electrophoresis (IFE)
- Serum free light chain assay (SFLC)

Urine tests
- Urine protein electrophoresis (UPEP) with IFE
- 24-hour urine

Bone marrow biopsy
- Conventional
  - Fluorescence in situ hybridization (FISH)
- New
  - Genomic sequencing

Imaging tests
- X-ray
- MRI
- Whole-body, low-dose CT scan
- PET scan
- Metastatic bone survey

Assess changes in the bone structure and determine the number and size of tumors in the bone

Confirms the type of myeloma

Determines how advanced the myeloma is and identifies the myeloma subtype

Detects the extent of bone disease and the presence of myeloma outside of the bone marrow
Learn Your Labs!

**Blood Tests**

- **CBC**: Number of red blood cells, white blood cells, and platelets
- **CMP**: Measure levels of albumin, calcium, lactate dehydrogenase (LDH), blood urea nitrogen (BUN), and creatinine. Assess function of kidney, liver, and bone status and the extent of disease
- **B2M**: Determine the level of a protein that indicates the presence/extent of MM and kidney function
- **SPEP**: Detect the presence and level of M protein
- **IFE**: Identify the type of abnormal antibody proteins
- **SFLC**: Freelite test measures light chains (kappa or lambda)

CBC, complete blood count; CMP, complete metabolic panel; B2M, beta-2 microglobulin; SPEP, serum protein electrophoresis; IFE, immunofixation electrophoresis; SFLC, serum free light chain assay

Learn Your Labs!

**Urine Tests**

- **UPEP**: Detect Bence Jones proteins (otherwise known as myeloma light chains)
- **24-hr urine analysis**: Determine the presence and levels of M protein and Bence Jones protein

UPEP, urine protein electrophoresis
Types of Multiple Myeloma Based on Blood or Urine Tests

- **Intact M protein**
  - Named for the type of immunoglobulin and light chain pair; for example, IgG kappa (κ) or IgG lambda (λ)
  - 80%

- **Light chain only**
  - Also known as Bence Jones protein
  - Renal failure more common in light chain multiple myeloma
  - 20%

- **Non-secretory**
  - No M protein present
  - 3%

Know Your Imaging Tests!

Assess changes in the bone structure and determine the number and size of tumors in the bone

- **X-ray**
  - Conventional x-rays reveal lytic lesions, osteoporosis, or fractures in 75% of patients.

- **MRI**
  - MRI and PET/CT appear to be more sensitive (85%) than skeletal x-rays for the detection of small lytic bone lesions.

- **CT scan**

- **PET scan**
Know Your Bone Marrow Tests!

Bone marrow aspiration and biopsy
- Jamshidi needle

Chromosome
Bone marrow
Hip bone
Skin

Myeloma cell
DNA

Putting the Results Together

Staging, prognosis, and risk assessment
Multiple Myeloma Prognosis and Risk

Revised International Staging System (R-ISS)

<table>
<thead>
<tr>
<th>R-ISS stage</th>
<th>Laboratory measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>• Serum β2M level &lt;3.5 mg/L</td>
</tr>
<tr>
<td></td>
<td>• Serum albumin level ≥3.5 g/dL</td>
</tr>
<tr>
<td></td>
<td>• No high-risk CA*</td>
</tr>
<tr>
<td></td>
<td>• Normal LDH level</td>
</tr>
<tr>
<td>II</td>
<td>All other possible combinations</td>
</tr>
<tr>
<td>III</td>
<td>• Serum β2M level ≥5.5 mg/L</td>
</tr>
<tr>
<td></td>
<td>• High-risk CA* or high LDH level</td>
</tr>
</tbody>
</table>

*Risk-ISS stage I
• Serum β2M level <3.5 mg/L
• Serum albumin level ≥3.5 g/dL
• No high-risk CA*
• Normal LDH level

*Risk-ISS stage II
All other possible combinations of the test results means that a patient is R-ISS stage I

*Risk-ISS stage III
• Serum β2M level ≥5.5 mg/L
• High-risk chromosomal abnormality* or high LDH level

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

<table>
<thead>
<tr>
<th>High risk</th>
<th>Standard risk</th>
</tr>
</thead>
</table>
| • High-risk genetic abnormalities
  - t(4;14)  
  - t(14;20)
  - del 17p
  - ps3 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) |

β2M: beta-2 microglobulin; LDH, lactate dehydrogenase

*High-risk chromosomal abnormality by FISH: del(17p) and/or t(4;14) and/or t(14;16)

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

Multiple Myeloma Prognosis and Risk

Many blood test and bone marrow biopsy test results can determine a patient’s risk for myeloma that is aggressive (high risk) or not (standard risk) based on the Revised International Staging System (R-ISS)

Standard risk
• Serum β2M level <3.5 mg/L
• Serum albumin level ≥3.5 g/dL
• No high-risk chromosomal abnormality*
• Normal LDH level

High risk
• Serum β2M level ≥5.5 mg/L
• High-risk chromosomal abnormality* or high LDH level

*Risk-ISS stage II
All other possible combinations of the test results means that a patient is R-ISS stage II

*High-risk chromosomal abnormality by FISH: del(17p) and/or t(4;14) and/or t(14;16)
β2M: beta-2 microglobulin; LDH, lactate dehydrogenase; FISH, fluorescent in situ hybridization
The Right Treatment

- Know the treatment options available to you based on your myeloma subtype at each stage of your disease.
- Be aware of the pros and cons of each option.
- Clearly communicate your treatment goals and concerns to the care team.
- Find clinical trials that are right for you.

Getting the Right Treatment: Goals of Multiple Myeloma Therapy

- Reduce the amount of M protein (as measured by serum protein electrophoresis) or light chains (as measured via the free light chain test) to the lowest level possible.
- Eliminate myeloma cells from the bone marrow (as measured via minimal residual disease [MRD] testing).
- Improve quality of life with as few treatment side effects as possible.
- Provide the longest possible period of response before first relapse.
- Prolong overall survival.
Myeloma Survival Has Improved Over Time Mainly Due to Current Drugs

The percentage of people expected to survive 5 years or more after being diagnosed with myeloma

- 1975: 26.5%
- 1985: 27.4%
- 1995: 33.5%
- 2005: 47.2%
- 2013: 56.9%
- 2014 and beyond

Available treatments:

- Chemotherapy + dexamethasone + stem cell transplantation
- Velcade (bortezomib)
- Revlimid (lenalidomide)
- Kyprolis (carfilzomib)
- Pomalyset (pomalidomide)
- Ninlaro (ixazomib)
- Empliciti (elotuzumab)
- Darzalex (daratumumab)
- Xpovio (selinexor)
- Sarclisa (isatuximab)
- Blenrep (belantamab mafodotin)
- Abecma (idecabtagene vicleucel)
- Carvykti (ciltaacabtagene autoleucel)

Current Treatment Paradigm for Newly Diagnosed Multiple Myeloma

- Induction therapy
- ± Consolidation therapy
- Maintenance therapy

Transplant candidate:
- Induction therapy
- ± Consolidation therapy
- Maintenance therapy

Non-transplant candidate:
- Induction therapy
- Maintenance therapy
Overview of Treatment Approach for Active Multiple Myeloma

Is the patient a candidate for autologous stem cell transplantation?

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
*2-drug regimen may be considered for frail patients

*In certain circumstances, consideration for a tandem transplant

Induction Therapy Regimens

<table>
<thead>
<tr>
<th>Preferred</th>
<th>Recommended</th>
<th>Certain circumstances</th>
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</thead>
<tbody>
<tr>
<td>Transplant eligible</td>
<td></td>
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</tr>
<tr>
<td>• Revlimid-Velcade-dex (RVd)*</td>
<td>• Darzalex-Revlimid-Velcade-dex (D-RVd)</td>
<td>• Velcade-Thalomid-dex (VTd)*</td>
</tr>
<tr>
<td>• Kyprolis-Revlimid-dex (KRd)</td>
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<td>• Velcade-Cytotoxan-dex (VCd)</td>
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<td></td>
<td></td>
<td>• Velcade-Doxil-dex (VDb)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Kyprolis-Cytotoxan-dex (KCd)</td>
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<tr>
<td></td>
<td></td>
<td>• Revlimid-Cytotoxan-dex (RCd)</td>
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<tr>
<td></td>
<td></td>
<td>• Darzalex-Velcade-Thalomid-dex (D-VTd)</td>
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<td>• Darzalex-Kyprolis-Revlimid-dex (D-KRd)</td>
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<td>• Darzalex-Cytotoxan-Velcade-dex (D-VCd)</td>
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<tr>
<td></td>
<td></td>
<td>• Ninlaro-Revlimid-dex (IRd)</td>
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<tr>
<td></td>
<td></td>
<td>• Ninlaro-Cytotoxan-dex (ICd)</td>
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<tr>
<td></td>
<td></td>
<td>• VTD-PACE</td>
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<tr>
<td>Transplant ineligible</td>
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<tr>
<td>• Revlimid-Velcade-dex (RVd)*</td>
<td>• Kyprolis-Revlimid-dex (Krd)</td>
<td>• Velcade-dex (Vd)</td>
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<tr>
<td>• Darzalex-Revlimid-dex (DRd)*</td>
<td>• Ninlaro-Revlimid-dex (IRd)</td>
<td>• Revlimid-dex (Rd)*</td>
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<tr>
<td></td>
<td>• Darzalex-Velcade-melphalan-prednisone (D-VMP)*</td>
<td>• Velcade-Cytotoxan-dex (VCd)</td>
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<td></td>
<td>• Darzalex-Cytotoxan-Velcade-dex (D-VCd)</td>
<td>• Revlimid-Cytotoxan-dex (RCd)</td>
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<tr>
<td></td>
<td></td>
<td>• Kyprolis-Cytotoxan-dex (KCd)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Revlimid-Velcade-dex (RVd)-lite</td>
</tr>
</tbody>
</table>

*Category 1 recommendation. Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Autologous Stem Cell Transplantation

1. Induction therapy
2. Collection of stem cells from the bloodstream
3. Freezing of stem cells
4. High-dose chemotherapy
5. Thawing and infusion of stem cells
6. Recovery

≥2 cycles
-2 to -3 weeks*
Stem cell mobilization
• Neupogen, Neulasta, Leukine, Cytoxan, Mozobil
Melphalan
• Alkeran, Evomela
Day 0
Days +1 to +100†

*The weeks leading up to the transplant; †The days after the transplant.

Continuous or Maintenance Therapy Options

<table>
<thead>
<tr>
<th>Transplant eligible</th>
<th>Preferred</th>
<th>Recommended</th>
<th>Certain circumstances</th>
</tr>
</thead>
</table>
| Transplant ineligible | • Revlimid* | • Ninlaro  
• Velcade  
• Darzalex | • Velcade-Revlimid ± dex  
• Kyprolis-Revlimid |
| Transplant ineligible | • Revlimid* | • Ninlaro  
• Velcade | • Velcade-Revlimid |

*Category 1 recommendation. Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate. National Comprehensive Cancer Network Guidelines Version 3.2023. Multiple Myeloma.
Measuring Response to Therapy

Degree (or depth) of response is usually associated with better prognosis. Some patients do well despite never achieving a CR.

Myeloma cell burden

Stable disease
Minor response
Partial response
Very good partial response
Complete response (CR)
Stringent CR
Minimal residual disease negative

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

Where is the myeloma field going?

- Staging with genomics and advanced imaging
- Higher efficacy using four-drug regimens
- Precision medicine and targeted therapies in subsets of patients—for example, t(11;14)
- MRD-driven therapy
- Minimize long-term toxicities since myeloma patients living (much) longer
- New drug classes and immunotherapies
Summary

- Multiple myeloma is a rare blood cancer that can negatively affect the bones, kidneys, and the bone marrow, leading to lowered blood counts.
- The prognosis of multiple myeloma depends on the genetic makeup of myeloma cell chromosomes; R-ISS is used for staging in multiple myeloma.
- Survival rates are improving because of new drugs and new combinations of drugs.
- The treatment paradigm will continue to change with the approval of additional novel agents.
- Knowledge is power: right team, right test, right treatment.

Be an informed and empowered part of your health care team!
How common is multiple myeloma?


Incidence rates, 2014–2018
Myeloma, by state

Average annual rate per 100,000, age adjusted to the 2000 US standard population.
Data sources: North American Association of Central Cancer Registries (NAACCR), 2021

Death rates, 2015–2019
Myeloma, by state

Average annual rate per 100,000, age adjusted to the 2000 US standard population.
Data sources: National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention, 2021
Multiple Myeloma Is Twice as Common in Black Patients

Rate of new cases per 100,000 persons by race/ethnicity and sex

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Races</td>
<td>8.8</td>
<td>5.7</td>
</tr>
<tr>
<td>White</td>
<td>8.2</td>
<td>5.0</td>
</tr>
<tr>
<td>Black</td>
<td>16.3</td>
<td>12.1</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>4.8</td>
<td>3.1</td>
</tr>
<tr>
<td>American Indian/Alaska Native</td>
<td>6.8</td>
<td>4.9</td>
</tr>
<tr>
<td>Hispanic</td>
<td>8.2</td>
<td>6.0</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>8.9</td>
<td>5.7</td>
</tr>
</tbody>
</table>

Death rate per 100,000 persons by race/ethnicity and sex

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Races</td>
<td>4.0</td>
<td>4.1</td>
</tr>
<tr>
<td>White</td>
<td>3.8</td>
<td>3.3</td>
</tr>
<tr>
<td>Black</td>
<td>7.2</td>
<td>4.1</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>1.9</td>
<td>1.3</td>
</tr>
<tr>
<td>American Indian/Alaska Native</td>
<td>3.9</td>
<td>2.5</td>
</tr>
<tr>
<td>Hispanic</td>
<td>3.3</td>
<td>2.2</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>4.1</td>
<td>2.5</td>
</tr>
</tbody>
</table>

Multiple Myeloma Incidence and Mortality by Race/Ethnicity

Risk of Myeloma Diagnosis by Age

Black patients are diagnosed at an earlier age and have a twofold risk of being diagnosed with multiple myeloma.

Data from National Cancer Institute Surveillance, Epidemiology, and End Results Program (SEER)

Multiple Myeloma in Black Patients

Demographics
- Myeloma prevalence (2x White patients)
- Older adults have prevalence of the myeloma precursor condition MGUS
- Younger

Clinical factors
- Comorbidities
- Incidence of all myeloma-defining events (for example, hypercalcemia, renal dysfunction, anemia, dialysis) except bone fractures

Molecular (genetic) factors
- Significant differences in the frequency of certain chromosomal abnormalities:
  - High risk cytogenetics including del17p are seen less frequently
  - Some other mutations seen more frequently but significance not known

Treatment
- Significantly lower stem cell transplant utilization

References:
Disparities in Care in Black Patients

- Several studies have shown that the use of standard therapies tends to be significantly lower in Black patients.
- However, with equal access to standard therapy, the outcome in Black patients is equal or superior to that of White patients.

<table>
<thead>
<tr>
<th>Treatment type</th>
<th>Use in Black patients</th>
<th>Use in White patients</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triplet therapy</td>
<td>47%</td>
<td>61%</td>
<td>0.004</td>
</tr>
<tr>
<td>Stem cell transplantation</td>
<td>30%</td>
<td>40%</td>
<td>0.034</td>
</tr>
</tbody>
</table>

Reasons for Disparities in Outcomes for Black Americans With Multiple Myeloma and Other Cancers

- Less access to cancer screening services
- Structural racism
- Social determinants of health
- Shortage of African American physicians and lack of familiarity with Black economic and social conditions
- Comorbid conditions
- Delayed onset of diagnosis and severity of disease at the time of diagnosis
- Lack of access to the same level of treatment as White patients
- Low enrollment in clinical trials
Key Points

Despite disparities in incidence and outcomes of multiple myeloma among Black patients, evidence suggests that these disparities can be overcome:

- Ensure equal access to appropriate therapeutic options for Black patients
- Increase awareness of these disparities and their solutions to patients, physicians, and the communities

Please take a moment to answer two questions about this presentation.
Treating Relapsed/Refractory Multiple Myeloma

Noa Biran, MD
John Theurer Cancer Center
Hackensack University Medical Center
Hackensack, New Jersey

MGUS or smoldering myeloma
Asymptomatic Symptomatic
Induction ± SCT
1st RELAPSE
Plateau remission
Second line
2nd RELAPSE
Third line

Multiple Myeloma Is a Marathon, Not a Sprint

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 many factors requires 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>Monoclonal antibodies</th>
<th>Cellular therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thalomid (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 vicleucel)</td>
</tr>
<tr>
<td>Revlimid (lenalidomide)</td>
<td>Kyprolis (carfilzomib)</td>
<td>Doxil (liposomal doxorubicin)</td>
<td>Bendamustine</td>
<td>Prednisone</td>
<td>Venclexta (venetoclax)*</td>
<td>Darzalex (daratumumab)</td>
<td>Carvykti (cilta-cabtagene autoleucel)</td>
</tr>
<tr>
<td>Pomalyst (pomalidomide)</td>
<td>Ninlaro (ixazomib)</td>
<td>Melphalan</td>
<td></td>
<td></td>
<td>Epoxydak (Panobinostat)*</td>
<td>Sarcidisa (isatuximab)</td>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

*Not yet FDA-approved for patients with multiple myeloma; †Withdrawn from the US market in 2021; ‡Antibody-drug conjugate, withdrawn from the US market in 2022; §Bispecific antibody

**New formulations, new dosing, and new combinations, too!**

67

68
Three Drugs Withdrawn From US Market

What happened?

All drugs were granted accelerated approval by the FDA which requires further clinical studies to verify a drug’s clinical benefit.

<table>
<thead>
<tr>
<th>Withdrawn 2021</th>
<th>Withdrawn 2022*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Farydak (panobinostat)</strong>&lt;br&gt;• The required clinical studies were not completed within the FDA-specified timeframe</td>
<td><strong>Blenrep (belantamab mafodotin)</strong>&lt;br&gt;• Results from the confirmatory phase 3 DREAMM-3 study that compared Blenrep with Pomalyst-dex in patients with relapsed/refractory myeloma after at least two prior lines of therapy showed that progression-free survival with Blenrep was not improved versus Pomalyst-dex&lt;br&gt;• The DREAMM clinical study program is continuing as a path forward for approval with two ongoing phase 3 studies (DREAMM-7 and DREAMM-8) testing Blenrep in combinations in an earlier treatment setting for patients who have tried at least one prior line of therapy&lt;br&gt;• Results are anticipated in the first half of 2023</td>
</tr>
<tr>
<td><strong>Pepaxto (melflufen)</strong>&lt;br&gt;• The phase 3 OCEAN study compared Pepaxto-dex with Pomalyst-dex in patients with relapsed/refractory myeloma&lt;br&gt;  – Overall survival with Pepaxto-dex was not improved versus Pomalyst-dex which didn’t pass the regulatory hurdles to confirm the accelerated approval in the US</td>
<td></td>
</tr>
</tbody>
</table>

*Marketing of Blenrep continues in other countries where it has been approved.

Treatment Approach

First relapse

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

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
  - DVd, SVd, Ven-Vd (for t[11;14])*

>1 Relapse

- Approved therapies
  - Sd, belamaf, ide-cel, cilt-cel, Tecvayli
- Clinical trials
  - Bispecific/trispecific antibodies, cellular therapies (CAR T-cells, NK cells), CELMoDs

D, daratumumab (Darzalex); K, carfilzomib (Kyprolis); d, dexamethasone; Isa, isatuximab (Sarcilisa); P, pomalidomide (Pomalyst); Elo, elotuzumab (Empliciti); V, bortezomib (Velcade); S, selinexor (Xpovio); Ven, venetoclax (Venclexta); belamaf, belantamab mafodotin (Blenrep); ide-cel, idecabtagene vicleucel (Abecma); cilt-cel, ciltacabtagene autoleucel (Carvykti);*Not yet approved for use in myeloma patients.
### Currently Available Naked Monoclonal Antibodies for One to Three Prior Lines of Therapy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulation</th>
<th>Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Darzalex (daratumumab)</td>
<td>SC once a week for first 8 weeks, then every 2 weeks for 4 months, then monthly</td>
<td>• For relapsed/refractory myeloma as a single agent and as a triplet with Revlimid or Velcade or Kyprolis or Pomalyst plus dexamethasone</td>
</tr>
<tr>
<td>Empliciti (elotuzumab)</td>
<td>IV once a week for first 8 weeks, then every 2 weeks (or every 4 weeks with pom)</td>
<td>• For relapsed/refractory myeloma as a triplet with Revlimid or Pomalyst and dexamethasone</td>
</tr>
<tr>
<td>Sarclisa (isatuximab)</td>
<td>IV once a week for first 4 weeks, then every 2 weeks</td>
<td>• For relapsed/refractory myeloma as a triplet with Pomalyst or Kyprolis and dexamethasone</td>
</tr>
</tbody>
</table>

*IV, intravenous; SC, subcutaneous*
### Currently Available Agents for One to Three Prior Lines of Therapy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulation</th>
<th>Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Velcade (bortezomib)</td>
<td>• IV infusion  • SC injection  • For relapsed/refractory myeloma</td>
<td></td>
</tr>
<tr>
<td>Kyprolis (carfilzomib)</td>
<td>• IV infusion  • Weekly dosing  • For relapsed/refractory myeloma as a single agent, as a doublet with dexamethasone, and as a triplet with Revlimid or Darzalex plus dexamethasone</td>
<td></td>
</tr>
<tr>
<td>Ninlaro (ixazomib)</td>
<td>Once-weekly pill  • For relapsed/refractory myeloma as a triplet with Revlimid and dexamethasone</td>
<td></td>
</tr>
<tr>
<td>Revlimid (lenalidomide)*</td>
<td>Once-daily pill  • For relapsed/refractory myeloma in combination with dexamethasone</td>
<td></td>
</tr>
<tr>
<td>Pomalyst (pomalidomide)*</td>
<td>Once-daily pill  • For relapsed/refractory myeloma in combination with dexamethasone</td>
<td></td>
</tr>
<tr>
<td>XPOVIO (selinexor)</td>
<td>Once-weekly pill  • For relapsed/refractory myeloma as a triplet with Velcade and dexamethasone</td>
<td></td>
</tr>
</tbody>
</table>

*Black box warnings: embryo-fetal toxicity; hematologic toxicity (Revlimid); venous and arterial thromboembolism

IV, intravenous; SC, subcutaneous

### Monoclonal Antibody–Based Regimens for Early Relapse: Darzalex

#### POLLUX
- Darzalex-Revlimid-dex (DRd) vs Rd
  - Median progression-free survival favored: DRd: 45 vs 18 months
  - Clinical considerations: Consider for relapses from Revlimid or Velcade maintenance; DRd associated with more upper respiratory infections, low blood white blood cell counts, and diarrhea

#### CASTOR
- Darzalex-Velcade-dex (DVd) vs Vd
  - Median progression-free survival favored: DVd: 17 vs 7 months
  - Clinical considerations: Consider for patients who are Revlimid-refractory without significant neuropathy; DVd associated with more low blood cell counts

#### CANDOR
- Darzalex-Kyprolis-dex (DKd) vs Kd
  - Median progression-free survival favored: DKd: 29 vs 15 months
  - Clinical considerations: Consider for younger, fit patients who are double-refractory to Revlimid and Velcade; DKd associated with more respiratory infections; Severe side effects (possibly fatal) in intermediate fit patients 65 and older

#### APOLLO
- Darzalex-Pomalyst-dex (DPd) vs Pd
  - Median progression-free survival favored: DPd: 12 vs 7 months
  - Clinical considerations: Consider in patients who are double-refractory to Revlimid and a proteasome inhibitor (Velcade, Kyprolis, Ninlaro); Severe low white blood cell counts
### 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><strong>Regimens compared</strong></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><strong>Median progression-free survival favored</strong></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>
<tr>
<td><strong>Clinical considerations</strong></td>
<td>Consider for non-Revlimid refractory, frailer patients</td>
<td>Overall survival benefit with Empliciti-Rd</td>
<td>Consider for patients refractory to Revlimid and a proteasome inhibitor (Velcade, Kyprolis, Ninlaro)</td>
</tr>
</tbody>
</table>

### Proteasome Inhibitor– and Immunomodulatory Drug–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><strong>Regimens compared</strong></td>
<td>Velcade-Pomalyst-dex (VPd) vs Vd</td>
<td>Kyprolis-Revlimid-dex (KRd) vs Rd</td>
<td>Ninlaro-Rd (IRd) vs Rd</td>
</tr>
<tr>
<td><strong>Median progression-free survival favored</strong></td>
<td>VPd: 11 vs 7 months</td>
<td>KRd: 26 vs 17 months</td>
<td>IRd: 21 vs 15 months</td>
</tr>
<tr>
<td><strong>Clinical considerations</strong></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>
</tr>
</tbody>
</table>

- **Optimism**
  - KRd: 26 vs 17 months
  - KRd associated with more upper respiratory infections and high blood pressure than Rd

- **Aspire**
  - IRd: 21 vs 15 months
  - IRd an oral regimen

- **Tourmaline-MM1**
  - XPO-Vd: 14 vs 9 months
  - XPO-Vd associated with low platelet counts and fatigue with triplet, but less neuropathy than the Vd
### Important Considerations for Use of Monoclonal Antibodies

<table>
<thead>
<tr>
<th><strong>Darzalex</strong></th>
<th><strong>Empliciti</strong></th>
<th><strong>Sarclisa</strong></th>
</tr>
</thead>
</table>
| - Infusion reactions  
  - Less with SC use  
- Risk of shingles  
  - Use appropriate vaccination  
- Increased risk of hypogamma-globulinemia and upper respiratory infections  
  - Bactrim prophylaxis  
  - IVIG support | - Infusion reactions  
  
- Risk of shingles  
  - Use appropriate vaccination | - Infusion reactions  
  
- Risk of shingles  
  - Use appropriate vaccination |

### Important Considerations for Use of Proteasome Inhibitors

<table>
<thead>
<tr>
<th><strong>Velcade</strong></th>
<th><strong>Kyprolis</strong></th>
<th><strong>Ninlaro</strong></th>
</tr>
</thead>
</table>
| - 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; adjust for liver issues | - 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; adjust for liver issues | - Less PN than Velcade  
- High risk of shingles  
  - Use appropriate vaccination  
- Monitor for rashes and gastrointestinal (GI) side effects  
  - GI effects occur early  
- Needs to be taken at least 1 hour before or 2 hours after a meal |
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

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

Maintain fluid intake. Salt tabs

Stay hydrated and active.

Report signs of bleeding right away. Report signs of fatigue or shortness of breath.

**Update From the 2022 American Society of Hematology (ASH) Meeting**

**Sarclisa After Early or Late Relapse**

**IKEMA Study**

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

- 179 patients
- 123 patients

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Early Relapse</th>
<th>Late Relapse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sarclisa-Kd</td>
<td>24.7</td>
<td>42.7</td>
</tr>
<tr>
<td>Kd</td>
<td>17.2</td>
<td>21.9</td>
</tr>
<tr>
<td>Sarclisa-Kd</td>
<td>90.4</td>
<td>15.2</td>
</tr>
<tr>
<td>Kd</td>
<td>86.1</td>
<td>37.5</td>
</tr>
</tbody>
</table>

- Median progression-free survival (months)
- Overall response rate (%)
- ≥VGPR rate (%)
- MRD negativity rate (%)
- MRD-negative CR rate (%)

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)


---

**Treatment Approach**

**First relapse**

- Proteasome inhibitor/immunomodulatory drug/antibody-based therapy

**>1 Relapse**

- Any options for first relapse not tried

- Refractory to Velcade and Revlimid
- Refractory to an IMiD, but sensitive to a PI
- Refractory to Velcade and Revlimid

- Triple-class refractory

- Approved therapies
- Clinical trials

D, daratumumab (Darzalex); K, carfilzomib (Kyprolis); d, dexamethasone; Isa, isatuximab (Sarclisa); P, pomalidomide (Pomalyst); Elo, elotuzumab (Empliciti); V, bortezomib (Velcade); S, selinexor (Xpovio); Ven, venetoclax (Venclexta); belanaf, belantamab mafodotin (Blenrep); ide-cel, idecabtagene vicalucel (Abecma); cilta-cel, ciltacabtagene autoleucel (Carvykti)

*Not yet approved for use in myeloma patients.
### Triple-Class Refractory

- For patients with relapsed or refractory multiple myeloma who have received treatment with—and did not respond satisfactorily to, or progressed while on treatment with—the three main classes of drugs currently used to treat myeloma are...

<table>
<thead>
<tr>
<th>Proteasome inhibitors</th>
<th>Immunomodulatory drugs</th>
<th>Anti-CD38 monoclonal antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Velcade (bortezomib)</td>
<td>• Revlimid (lenalidomide)</td>
<td>• Darzalex (daratumumab)</td>
</tr>
<tr>
<td>• Kyprolis (carfilzomib)</td>
<td>• Pomalyst (pomalidomide)</td>
<td>• Sarclisa (isatuximab)</td>
</tr>
<tr>
<td>• Ninlaro (ixazomib)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Currently Available Drugs for Triple-Class Refractory Myeloma

<table>
<thead>
<tr>
<th>Class</th>
<th>Drug</th>
<th>Formulation</th>
<th>Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nuclear export inhibitor</td>
<td>XPOVIO (selinexor)</td>
<td>Twice-weekly pill</td>
<td>• For relapsed/refractory myeloma in combination with dexamethasone (after at least 4 prior therapies and whose disease is refractory to at least 2 PIs, at least 2 IMiDs, and an anti-CD38 mAb)</td>
</tr>
<tr>
<td>Chimeric antigen receptor (CAR) T cell</td>
<td>Abecma (idecabtagene vicleucel)*</td>
<td>300 to 460 × 10⁶ genetically modified autologous CAR T cells in one or more infusion bags</td>
<td>• For relapsed/refractory myeloma (after 4 or more prior lines of therapy, including an IMiD, a PI, and an anti-CD38 mAb)</td>
</tr>
<tr>
<td>CAR T cell</td>
<td>Carvykti (ciltaclabtagene autoleucel)†</td>
<td>0.5 to 1.0 × 10⁶ genetically modified autologous CAR T cells/kg of body weight</td>
<td>• For relapsed/refractory myeloma (after 4 or more prior lines of therapy, including a PI, an IMiD, and an anti-CD38 mAb)</td>
</tr>
<tr>
<td>Bispecific antibody</td>
<td>Tecvayli (teclistamab)‡</td>
<td>Step-up dosing† the first week then once weekly thereafter by subcutaneous injection</td>
<td>• For relapsed/refractory myeloma (after 4 or more prior lines of therapy, including an IMiD, an IM, and an anti-CD38 mAb)</td>
</tr>
</tbody>
</table>

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

*Black box warning: cytokine release syndrome; neurologic toxicities; hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS); prolonged cytopenia
†Black box warning: cytokine release syndrome; neurologic toxicities; Parkinsonism and Guillain-Barré syndrome; hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS); prolonged cytopenia
‡Black box warning: cytokine release syndrome; neurologic toxicities
§Patients are hospitalized for 48 hours after administration of all step-up doses.

Abecma, Carvykti, and Tecvayli are available only through a restricted distribution program.
XPOVIO + Dexamethasone in Relapsed/Refractory Myeloma

<table>
<thead>
<tr>
<th>Previous therapies to which the disease was refractory, n (%)</th>
<th>No. patients with ( \geq PR ) (%)$^1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>32 (26)</td>
</tr>
<tr>
<td>Velcade, Kyprolis, Revlimid, Pomalyst, and Darzalex</td>
<td>21 (25)</td>
</tr>
<tr>
<td>Kyprolis, Revlimid, Pomalyst, and Darzalex</td>
<td>26 (26)</td>
</tr>
<tr>
<td>Velcade, Kyprolis, Pomalyst, and Darzalex</td>
<td>25 (27)</td>
</tr>
<tr>
<td>Kyprolis, Pomalyst, and Darzalex</td>
<td>31 (26)</td>
</tr>
</tbody>
</table>

Additional analyses showed clinical benefit with XPOVIO regardless of patient age and kidney function.$^{2,3}$


Now Approved: Tecvayli, the First Bispecific Antibody!

Median duration of response 18.4 months

Emerging Treatment Options

Cereblon E3 ligase modulators (CELMoDs)

Immunocytokines

More bispecific antibodies (BCMA, GCPR5D, Fc5H targets)

More chimeric antigen receptor (CAR) T-cell therapies

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 and 100% were triple-class refractory (one third were previously exposed to anti-BCMA therapy)—received treatment with mezigdomide-dex

Phase 3 trials of iberdomide and mezigdomide are under way.

Modakafusp Alfa: An Immunocytokine

Modakafusp alfa is an antibody that is fused to the cytokine interferon-alpha and that can bind to CD38 on myeloma cells.

Immunocytokines are engineered to deliver cytokines (a protein produced by immune cells) that can prevent myeloma cells from dividing and help boost myeloma-fighting immune cells.

100 patients who had a median of 7 prior lines of therapy were treated with different doses of modakafusp (19% had prior CAR T-cell therapy and 14% prior T-cell engagers).

Overall response rate was 43% in patients receiving 1.5 mg/kg dose every 4 weeks (n=30); 27% of anti-BCMA exposed patients responded.

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, patient, and caregivers and are based on many 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.
Please take a moment to answer two questions about this presentation.

Town Hall Questions & Answers
CAR T-Cell Therapy and Bispecific Antibodies

David H. Vesole, MD, PhD
MedStar Georgetown University Hospital
Georgetown University School of Medicine
Washington, District of Columbia
John Theurer Cancer Center, Hackensack Meridian School of Medicine
Hackensack, New Jersey

CAR T-Cell Therapy

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

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

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

Examples:

- Abecma (ide-cel)
- Canvykti (cilta-cel)
- CT103A
- Gamma secretase inhibitor followed by CAR T-cells

CAR, chimeric antigen receptor; MM, multiple myeloma

B-cell maturation antigen (BCMA)
Autologous CAR T-Cell Therapy: Underlying Principles

<table>
<thead>
<tr>
<th>Leukapheresis</th>
<th>Manufacturing</th>
<th>Infusion</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collect patient's white blood cells</td>
<td>Isolate and activate T cells</td>
<td>Expand CAR T cells</td>
<td>Infuse patient with CAR T cells</td>
</tr>
<tr>
<td></td>
<td>Engineer T cells with CAR gene</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Viral vector with CAR DNA</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CAR-engineered T cell</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median manufacturing time: 17–28 days</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Patients undergo lymphodepleting (and possibly salvage/bridging) therapy


BCMA in Multiple Myeloma

- Expressed on late memory B cells committed to plasma cell (PC) differentiation and PCs.
- BCMA plays a role in survival of long-lived PCs.
- γ-secretase cleaves BCMA from the cell surface, yielding soluble BCMA.

Two CAR T-Cell Therapies Approved!

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulation</th>
<th>Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abecma (idecabtagene vicleucel)*</td>
<td>300 to 460 × 10^6 genetically modified autologous CAR T cells in one or more infusion bags</td>
<td>• For relapsed/refractory myeloma (after 4 or more prior lines of therapy, including an IMiD, a PI, and an anti-CD38 mAb)</td>
</tr>
<tr>
<td>Carvykti (cilta-cabtagene autoleucel)†</td>
<td>0.5 to 1.0 × 10^6 genetically modified autologous CAR T cells/kg of body weight</td>
<td>• For relapsed/refractory myeloma (after 4 or more prior lines of therapy, including a PI, an IMiD, and an anti-CD38 mAb)</td>
</tr>
</tbody>
</table>

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

*Black box warning: cytokine release syndrome; neurologic toxicities; hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS); prolonged cytopenia

†Black box warning: cytokine release syndrome; neurologic toxicities; Parkinsonism and Guillain-Barré syndrome; HLH/MAS; prolonged cytopenia

Abecma and Carvykti are available only through a restricted distribution program.

### Abecma and Carvykti in Relapsed and Refractory Multiple Myeloma

**Abecma**

- ORR 73%
- Average PFS 9 months
- Patients (%)

**Carvykti**

- ORR 97.9%
- 27-month PFS 55%
- Patients (%)

ORR, overall response rate; PR, partial response; VGPR, very good partial response; CR, complete response; sCR, stringent complete response; MRD, minimal residual disease; PFS, progression-free survival.


Future Directions for Abecma and Carvykti in Myeloma

### Studies in Earlier Stage of Disease

<table>
<thead>
<tr>
<th>Study</th>
<th>Agent</th>
<th>Phase</th>
<th>Patient Populations/Study Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>KarMMa-2</td>
<td>Abecma</td>
<td>2</td>
<td>Multiple cohorts, including early relapse</td>
</tr>
<tr>
<td>CARTITUDE-2</td>
<td>Carvykti</td>
<td>2</td>
<td>Multiple cohorts, including early relapse</td>
</tr>
<tr>
<td>KarMMa-3</td>
<td>Abecma</td>
<td>3</td>
<td>Abecma vs SoC in patients with 2-4 prior lines</td>
</tr>
<tr>
<td>CARTITUDE-4</td>
<td>Carvykti</td>
<td>3</td>
<td>Carvykti vs SoC in patients with 1-3 prior lines</td>
</tr>
</tbody>
</table>

### Studies in Frontline Setting

<table>
<thead>
<tr>
<th>Study</th>
<th>Agent</th>
<th>Phase</th>
<th>Patient Populations/Study Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>KarMMa-4</td>
<td>Abecma</td>
<td>1</td>
<td>High-risk, newly diagnosed MM</td>
</tr>
<tr>
<td>CARTITUDE-5</td>
<td>Carvykti</td>
<td>3</td>
<td>VRd → Carvykti vs VRd → Rd in newly diagnosed, transplant-ineligible patients</td>
</tr>
<tr>
<td>CARTITUDE-6</td>
<td>Carvykti</td>
<td>3</td>
<td>Trial of DVRd → Carvykti vs DVRd → ASCT in newly diagnosed MM</td>
</tr>
</tbody>
</table>

*Carvykti met PFS end point in relapsed/lenalidomide-refractory multiple myeloma: January 27, 2023.

Abecma or Standard Regimens in Relapsed and Refractory Multiple Myeloma

### Progression-Free Survival

- Median PFS: 13.3 months
- Median duration of response (mos): 14.8

### Treatment Response

<table>
<thead>
<tr>
<th></th>
<th>Abecma (n=254)</th>
<th>Standard regimen (n=132)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall response (%)*</td>
<td>71</td>
<td>42</td>
</tr>
<tr>
<td>Complete response (%)</td>
<td>39</td>
<td>5</td>
</tr>
<tr>
<td>Best overall response (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stringent complete</td>
<td>35</td>
<td>5</td>
</tr>
<tr>
<td>Complete response</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Very good partial response</td>
<td>22</td>
<td>10</td>
</tr>
<tr>
<td>Partial response</td>
<td>11</td>
<td>27</td>
</tr>
<tr>
<td>Minimal response</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Stable disease</td>
<td>12</td>
<td>36</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>9</td>
<td>8</td>
</tr>
</tbody>
</table>

*P<0.001

CAR T: Expected Toxicities

<table>
<thead>
<tr>
<th>CRS</th>
<th>ICANS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset</strong></td>
<td>1–9 days after CAR T-cell infusion</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>5–11 days</td>
</tr>
</tbody>
</table>
| **Symptoms** | • Fever  
• Difficulty breathing  
• Dizziness  
• Nausea  
• Headache  
• Rapid heartbeat  
• Low blood pressure | • Headache  
• Confusion  
• Language disturbance  
• Seizures  
• Delirium  
• Cerebral edema |
| **Management** | • Actemra (tocilizumab)  
• Corticosteroids  
• Supportive care | • Antiseizure medications  
• Corticosteroids |

ICANS, immune effector cell-associated neurotoxicity syndrome


*Based on the ASTCT consensus; †Based on vasopressor; ‡For adults and children >12 years; §For children ≤12 years; ‖Only when concurrent with CRS

Transplant vs CAR T Cells

<table>
<thead>
<tr>
<th>Cellular therapies</th>
<th>CAR T-cell therapy</th>
<th>Autologous stem cell transplantation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient’s cells collected</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Types of cells collected</td>
<td>T cells*</td>
<td>Stem cells†</td>
</tr>
<tr>
<td>Collected cells are genetically engineered in a lab</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Patient given chemotherapy before cells are infused back into patient</td>
<td>Yes, lymphodepleting therapy</td>
<td>Yes, melphalan</td>
</tr>
<tr>
<td>When in the course of myeloma is this usually done?</td>
<td>After multiple relapses</td>
<td>As part of initial treatment</td>
</tr>
<tr>
<td>Side effects of treatment</td>
<td>Cytokine release syndrome; confusion</td>
<td>Fatigue, nausea, diarrhea</td>
</tr>
</tbody>
</table>

*An immune cell that is the “business end” of the system, in charge of maintaining order and removing cells.  
†Precursor cells that give rise to many types of blood cells. We actually collect CD34+ve cells.
## BCMA CAR T-Cell Therapies: Summary

<table>
<thead>
<tr>
<th>CAR T-cell therapy</th>
<th>CARTITUDE-1&lt;sup&gt;1&lt;/sup&gt; Carvykti Phase 1</th>
<th>KarMMa&lt;sup&gt;2&lt;/sup&gt; Abecma Phase 2</th>
<th>CRB-402&lt;sup&gt;3&lt;/sup&gt; bb21217 Phase 1</th>
<th>LUMMICAR-2&lt;sup&gt;4&lt;/sup&gt; CT053 Phase 1b</th>
<th>PRIME&lt;sup&gt;5&lt;/sup&gt; BCMA-101 Phase 1/2</th>
<th>GC012F&lt;sup&gt;6&lt;/sup&gt; Dual CAR T-Cell BCMA + CD19</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n</td>
<td>97</td>
<td>128</td>
<td>72</td>
<td>20</td>
<td>98</td>
<td>19</td>
</tr>
<tr>
<td>Median prior regimens, n</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>5</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Triple refractory, %</td>
<td>87.6</td>
<td>84</td>
<td>64</td>
<td>85</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>CAR T-cell therapy dose</td>
<td>0.75 x 10&lt;sup&gt;6&lt;/sup&gt; (0.5–1.0 x 10&lt;sup&gt;6&lt;/sup&gt;)</td>
<td>450 x 10&lt;sup&gt;6&lt;/sup&gt; (150–450 x 10&lt;sup&gt;6&lt;/sup&gt;)</td>
<td>150, 300, 450 x 10&lt;sup&gt;6&lt;/sup&gt;</td>
<td>1.5–1.8/2.5–3.0 x 10&lt;sup&gt;6&lt;/sup&gt;</td>
<td>0.75–15 x 10&lt;sup&gt;5&lt;/sup&gt;</td>
<td>1.0–3.0 x 10&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td>ORR, %</td>
<td>97.9</td>
<td>73</td>
<td>69/81&lt;sup&gt;*&lt;/sup&gt;</td>
<td>94</td>
<td>57.1&lt;sup&gt;1&lt;/sup&gt;</td>
<td>94.7</td>
</tr>
<tr>
<td>CR/sCR, %</td>
<td>82.5</td>
<td>33</td>
<td>36/41&lt;sup&gt;*&lt;/sup&gt;</td>
<td>25</td>
<td>21.4&lt;sup&gt;1&lt;/sup&gt;</td>
<td>84.2</td>
</tr>
<tr>
<td>CRS (all grades), %</td>
<td>94.8</td>
<td>84</td>
<td>75</td>
<td>77/83&lt;sup&gt;1&lt;/sup&gt;</td>
<td>28</td>
<td>95</td>
</tr>
<tr>
<td>CRS (grade ≥3), %</td>
<td>5.4</td>
<td>4</td>
<td>4&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0/0&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0</td>
<td>11</td>
</tr>
<tr>
<td>Neurotoxicity (all grades), %</td>
<td>20.6</td>
<td>18</td>
<td>15</td>
<td>15/17&lt;sup&gt;1&lt;/sup&gt;</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Neurotoxicity (grade ≥3), %</td>
<td>10.3</td>
<td>4</td>
<td>4&lt;sup&gt;1&lt;/sup&gt;</td>
<td>8/0&lt;sup&gt;1&lt;/sup&gt;</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

1. After manufacturing change. 2. Two grade 5 events: 1 on Day 15 with grade 3 NT and 1 on Day 6 with afib and cardiac arrest. 3. Data for each dosing cohort.

### References

---

## GPRC5D-Targeted CAR T Cells for Myeloma

### Clinical Responses in All Patients With or Without Previous BCMA-Directed Therapies

<table>
<thead>
<tr>
<th>Response</th>
<th>All Patients</th>
<th>Previous BCMA Therapies</th>
<th>No Previous BCMA Therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Dose Levels (n=17)</td>
<td>25–150 x 10&lt;sup&gt;6&lt;/sup&gt; CAR T Cells (n=12)</td>
<td>All Dose Levels (n=10)</td>
</tr>
<tr>
<td>Partial response or better (%)</td>
<td>71</td>
<td>58</td>
<td>70</td>
</tr>
<tr>
<td>Very good partial response or better (%)</td>
<td>59</td>
<td>42</td>
<td>60</td>
</tr>
<tr>
<td>Complete response or better (%)</td>
<td>35</td>
<td>25</td>
<td>40</td>
</tr>
<tr>
<td>Negativity for MRD in bone marrow* (%)</td>
<td>47</td>
<td>50</td>
<td>30</td>
</tr>
</tbody>
</table>

*By flow cytometry (×10<sup>5</sup>)

ALLO-715, An Allogeneic Anti-BCMA CAR T-Cell Product

- Gene editing specifically designed to:
  - Reduce risk of graft-vs-host disease
  - Allow the use of ALLO-647 (a humanized anti-CD52 mAb) to selectively deplete host T cells while simultaneously protecting donor cells

Rituximab recognition domains

Human anti-BCMA scFv

Knockout of CD52 for selective lymphodepletion with ALLO-647

CD52

TCR

Signaling domains

Knockout of TRAC to minimize risk of GVHD

Phase 1 UNIVERSAL trial interim results


What’s next for CAR T-cell therapy?

**BMS-986354[^1]**

- Targets BCMA with a shortened manufacturing time through the NEXT-T process
- Phase 1 trial of 55 patients with RRMM with a median of 5 prior lines of therapy
- 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).

**FasT CAR-T GC012F[^2]**

- Targets BCMA and CD19
- Manufacturing process that takes as little as 24 hours
- Phase 1 trial of 13 newly diagnosed high-risk MM patients ineligible for stem cell transplant
- 100% of patients achieved ≥VGPR (69% sCR)
- All patients achieved MRD negativity (by EuroFlow).
- CRS observed in 23% of patients (all low grade).

**BMS-986393[^3]**

- Targets GPRC5D
- Phase 1 trial of 17 heavily pretreated patients with RRMM, including those who relapsed from BCMA CAR-T therapy
- Neutropenia and thrombocytopenia most frequent grade 3/4 adverse events
- Additional adverse events include skin- and nail-related; dysgeusia/dysphagia; CRS; ICANS
- 86% evaluable patients responded including 7 of 11 patients treated with prior BMCA-targeted treatment

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.

Examples:
- Elranatamab
- Teclistamab
- TNB-303B (ABBV-383)
- Linvoseltamab
- Alnuctamab
- Cevostamab
- Talquetamab

Bispecific Antibody Agents

<table>
<thead>
<tr>
<th>Bispecific Antibody</th>
<th>Target (on MM cell × T cell)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tecvayli (teclistamab)</td>
<td>BCMA × CD3</td>
</tr>
<tr>
<td>Elranatamab</td>
<td>BCMA × CD3</td>
</tr>
<tr>
<td>Linvoseltamab</td>
<td>BCMA × CD3</td>
</tr>
<tr>
<td>Alnuctamab</td>
<td>BCMA × CD3</td>
</tr>
<tr>
<td>ABBV-383</td>
<td>BCMA × CD3</td>
</tr>
<tr>
<td>Talquetamab</td>
<td>GPRC5D × CD3</td>
</tr>
<tr>
<td>Forintamig (RG6234)</td>
<td>GPRC5D × CD3</td>
</tr>
<tr>
<td>Cevostamab</td>
<td>FcRH5 × CD3</td>
</tr>
</tbody>
</table>

GPRC5D, G protein-coupled receptor family C group 5 member D
Now Approved: Tecvayli, the First Bispecific Antibody

**Drug** | **Formulation** | **Approval**
--- | --- | ---
Tecvayli (teclistamab)* | Step-up dosing† the first week then once weekly thereafter by subcutaneous injection | For relapsed refractory myeloma (after 4 or more prior lines of therapy, including an IMiD, a PI, and an anti-CD38 mAb)

IMiD, immunomodulatory agent; PI, proteasome inhibitor; mAb, monoclonal antibody
*Black box warning: cytokine release syndrome; neurologic toxicities
†Patients are hospitalized for 48 hours after administration of all step-up doses.
Tecvayli is available only through a restricted distribution program.

<table>
<thead>
<tr>
<th>MRD negative (10-5), %</th>
<th>All patients (n=165)</th>
<th>Median time to first response (mos)</th>
<th>All patients (n=165)</th>
<th>Median time to best response (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRD negative</td>
<td>26.7</td>
<td>1.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRD evaluate</td>
<td>81.5</td>
<td>3.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRD negativity with ≥CR (%)</td>
<td>46.2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

63.0% (104/165) ≥CR: 39.4% ≥VGPR: 58.8% 19.4% 6.7%

63.0% (104/165)

Median duration of response 18.4 months


Tecvayli Side Effects

- Cytokine release syndrome
- Injection-related reactions
- Injection-site reaction
- Infections
- Neutropenia
- Anemia
- Thrombocytopenia
- Neurotoxicity

**Side Effect Management**

- Available only through a Risk Evaluation and Mitigation Strategies (REMS) due to the risk of cytokine release syndrome
- Patients will receive step-up dosing and will be monitored in an inpatient setting
- Cytokine release syndrome is managed in the same fashion as CAR T
- Injection reactions are managed with oral antihistamines and topical steroids
- Infection prevention!
- COVID precautions
### Similarities and Differences Between CAR T-Cell Therapy and Bispecific Antibodies

<table>
<thead>
<tr>
<th></th>
<th>CAR T-cell therapy</th>
<th>Bispecific antibody</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Approved product</strong></td>
<td>Abecma, Carvykti</td>
<td>Tecvayl</td>
</tr>
<tr>
<td><strong>Efficacy</strong></td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td><strong>How given</strong></td>
<td>One-and-done</td>
<td>IV or SC, weekly to every 3 weeks until progression</td>
</tr>
<tr>
<td><strong>Where given</strong></td>
<td>Academic medical centers</td>
<td>Academic medical centers</td>
</tr>
<tr>
<td><strong>Notable adverse events</strong></td>
<td>CRS and neurotoxicity</td>
<td>CRS and neurotoxicity</td>
</tr>
<tr>
<td><strong>Cytokine release syndrome</strong></td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td><strong>Neurotoxicity</strong></td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td><strong>Availability</strong></td>
<td>Wait time for manufacturing</td>
<td>Off-the-shelf, close monitoring for CRS and neurotoxicity</td>
</tr>
<tr>
<td><strong>Advantages</strong></td>
<td>Personalized</td>
<td>Off the shelf</td>
</tr>
<tr>
<td></td>
<td>Targeted immunocytotoxicity</td>
<td>Targeted immunocytotoxicity</td>
</tr>
<tr>
<td></td>
<td>Single infusion (“one and done”)</td>
<td>No lymphodepletion</td>
</tr>
<tr>
<td></td>
<td>Potentially persistent</td>
<td>Minimal steroids</td>
</tr>
<tr>
<td><strong>Disadvantages</strong></td>
<td>FACT-accredited center required (hospitalization likely required)</td>
<td>Initial hospitalization required</td>
</tr>
<tr>
<td></td>
<td>CRS and neurotoxicity; requires ICU and neurology services</td>
<td>CRS and neurotoxicity possible</td>
</tr>
<tr>
<td></td>
<td>Dependent on T-cell health (manufacturing failures)</td>
<td>Dependent on T-cell health (T-cell exhaustion)</td>
</tr>
<tr>
<td></td>
<td>Requires significant social support; caregiver required</td>
<td>Requires continuous administration</td>
</tr>
<tr>
<td></td>
<td>$$$$</td>
<td>$$$$</td>
</tr>
</tbody>
</table>

### Updates from the 2022 American Society of Hematology Meeting
TRIMM-2: Response With Teclistamab + Daratumumab in Relapsed/Refractory MM

**Clinical Response**

<table>
<thead>
<tr>
<th>Dose level (mg/kg)</th>
<th>ORR 74.1%</th>
<th>ORR 75%</th>
<th>ORR 100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 mg/kg (n = 27)</td>
<td>11.1</td>
<td>7.4</td>
<td>7.4</td>
</tr>
<tr>
<td>1.5 mg/kg (n = 20)</td>
<td>55.6</td>
<td>18.5</td>
<td>18.5</td>
</tr>
<tr>
<td>3 mg/kg (n = 4)</td>
<td>30.0</td>
<td>15.0</td>
<td>15.0</td>
</tr>
</tbody>
</table>

+ SC Dara 1800 mg

<table>
<thead>
<tr>
<th>PD</th>
<th>SD</th>
<th>PR</th>
<th>VGPR</th>
<th>CR</th>
</tr>
</thead>
</table>

*Response evaluable patients.
Rodriguez-Otero. EHA 2022. Abstract S188.

**Duration of Response (n=39)**

- Responses were durable and deepened over time
- At median follow-up of 8.6 mo (range: 0.3-19.6), 66.7% of responders were alive and continuing on treatment

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 with Tecvayli at 2 different doses (0.72 mg/kg and 1.5 mg/kg) subcutaneously

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

**Updated Efficacy and Safety Results with Elranatamab (MagnetisMM-1 Study)**

<table>
<thead>
<tr>
<th>Patients Responding (%)</th>
<th>All patients (n=55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PR</td>
<td>27.3</td>
</tr>
<tr>
<td>VGPR</td>
<td>10.9</td>
</tr>
<tr>
<td>CR</td>
<td>18.2</td>
</tr>
<tr>
<td>sCR</td>
<td>17.3</td>
</tr>
</tbody>
</table>

Median duration of response 17.1 months.

**MagnetisMM-3 Study of Elranatamab**

<table>
<thead>
<tr>
<th>Patients Responding (%)</th>
<th>Patients with no prior BCMA-targeted treatment (n=123)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PR</td>
<td>61%</td>
</tr>
<tr>
<td>VGPR</td>
<td>14.6</td>
</tr>
<tr>
<td>CR</td>
<td>27.6</td>
</tr>
<tr>
<td>sCR</td>
<td>6.7</td>
</tr>
</tbody>
</table>

Elranatamab to be investigated alone and in combination with other drugs in phase 3 studies.

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

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

**Intravenous Formulation Results**

<table>
<thead>
<tr>
<th>IV Alnuctamab (n=70)</th>
<th>Median follow up (months)</th>
<th>Overall response rate (%)</th>
<th>Median duration of response (months)</th>
<th>Responses ongoing (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>8.0</td>
<td>39</td>
<td>33.6</td>
<td>48</td>
</tr>
</tbody>
</table>

**Subcutaneous Formulation Results**

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>30 mg (n=26)</th>
<th>30 mg (n=29)</th>
<th>Overall response rate (%)</th>
<th>Median duration of response (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PR</td>
<td>19</td>
<td>14</td>
<td>41%</td>
<td>65%</td>
</tr>
<tr>
<td>VGPR</td>
<td>14</td>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CR</td>
<td>14</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>sCR</td>
<td>19</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Most frequent adverse events, %**

<table>
<thead>
<tr>
<th>Event</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>38</td>
<td>25</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>37</td>
<td>32</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>


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)

Cevostamab (Targets FcRH5)

- Fc receptor-homolog 5 (FcRH5)
  - Expressed exclusively in B-cell lineage (myeloma cells > normal B cells)
  - Near ubiquitous expression on myeloma cells
- Cevostamab bispecific antibody
  - Targets membrane-proximal domain of FcRH5 on myeloma cells and epsilon domain of CD3 on T cells
  - Dual binding results in T-cell directed killing of myeloma cells

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

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

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 Cytokine Release Syndrome

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.


BCMA-Targeted Bispecific Agents: Summary

<table>
<thead>
<tr>
<th></th>
<th>MajesTEC-1†</th>
<th>MagnetisMM-1</th>
<th>REGN-5458</th>
<th>AMG-7014 (Pavurutamab)</th>
<th>ABBV-383 (TNB-383B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n</td>
<td>165</td>
<td>55</td>
<td>73</td>
<td>85</td>
<td>118</td>
</tr>
<tr>
<td>Median prior regimens, n</td>
<td>5</td>
<td>6</td>
<td>5</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Dosing</td>
<td>SC weekly (RP2D)</td>
<td>SC weekly</td>
<td>Q2 wk after W16</td>
<td>IV weekly</td>
<td>IV Q3 wk</td>
</tr>
<tr>
<td>ORR, %</td>
<td>62.0</td>
<td>70</td>
<td>51 (75 at high dose)</td>
<td>26</td>
<td>53–81 in cohorts</td>
</tr>
<tr>
<td>CR/sCR, %</td>
<td>28.7</td>
<td>30</td>
<td>43 (16 at high dose)</td>
<td>9.7</td>
<td>13–39 in cohorts</td>
</tr>
<tr>
<td>CRS (all grades), %</td>
<td>71.5</td>
<td>87.3 (1 with priming and pre-meds)</td>
<td>38</td>
<td>65</td>
<td>54</td>
</tr>
<tr>
<td>CRS (grade ≥3), %</td>
<td>0.6</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>Neurotoxicity (all grades), %</td>
<td>12.7</td>
<td>—</td>
<td>4</td>
<td>—</td>
<td>5.1</td>
</tr>
<tr>
<td>Neurotoxicity (grade ≥3), %</td>
<td>0</td>
<td>—</td>
<td>0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Notes</td>
<td>9-mo PFS: 58.5%</td>
<td>22% received prior BCMA-targeted tx</td>
<td>Allowed for CrCl 30</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Key Points**

- CAR T and bispecific antibodies are very active even in heavily pretreated patients.

- Side effects of CAR T cells and bispecific antibodies include cytokine release syndrome, confusion, and low blood counts, all of which are treatable.

- Abecma and Carvykti are only the first-generation CAR T cells and target the same protein. Different CAR Ts and different targets are on the way.

- Bispecific antibodies represent an “off-the-shelf” immunotherapy; Tecvayli was approved in October 2022.

- Several additional bispecific antibodies are under clinical evaluation.

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Please take a moment to answer two questions about this presentation.
Supportive Care

Susan M. Kumka, RN, MSN, APN
John Theurer Cancer Center
Hackensack University Medical Center
Hackensack, New Jersey

Ann McNeill, RN, MSN, APN
John Theurer Cancer Center
Hackensack University Medical Center
Hackensack, New Jersey

Effects of Myeloma

Low blood counts
Bone damage
Decreased kidney function
**Effects of Myeloma: Bone Disease**

- Occurs in 85% of patients
- Weakened bone due to lesions or “holes”
- Increased levels of calcium in the blood (hypercalcemia)
- Leads to
  - Pathologic fractures
  - Spinal cord compression/collapse
  - Bone pain

**Bone Strengthening Agents for Myeloma Bone Disease**

- Prevent bone disease from getting worse
- Decrease pain and reduce skeletal-related fractures
  - Zometa (zoledronic acid): 15-minute infusion
  - Aredia (pamidronate): 2-hour infusion
  - Xgeva (denosumab): injection
- Zometa/Aredia: IV infusion in doctor’s office every 3–4 weeks
- Xgeva: injection once every 4 weeks
- Fracture of the femur
- Osteonecrosis of the jaw (ONJ)

OC, osteoclast (inhibited, halting bone breakdown); BP, bisphosphonate
Recommendations for Reducing the Risk of ONJ

- Complete major dental work before beginning treatment for bone disease
- Practice good oral hygiene
- Schedule regular dental visits
- Let your dentist know that you are receiving treatment for bone disease
- Keep your doctor informed of dental issues/need for dental work
- Be attentive! ONJ seems to be related to the length of time patients are on treatment for bone disease

ONJ, osteonecrosis of the jaw

Orthopedic Procedures to Stabilize the Spine

- Minimally invasive procedures
- Can be performed without hospitalization
- Small incision
- Cement filler stabilizes bone
- Potential for relatively rapid symptom relief (approximately 1 month with kyphoplasty)
Radiation Therapy for Pain Management

Acetaminophen (Tylenol)
Will not hurt your kidneys; high dosage can hurt your liver

NSAIDs (nonsteroidal anti-inflammatory drugs)
Prefer to avoid with MM due to increased risk of kidney injury

Opioids
Will not hurt kidneys, liver, stomach; potential for constipation, sedation, confusion, dependence, addiction

Corticosteroids (dexamethasone, prednisone)
Will not hurt kidneys; can raise blood sugar; short- and long-term effects

Gabapentin

Pain Management Medications
Effects of Myeloma: Low Blood Counts

**Low red blood cells (anemia)**
- **Symptoms**
  - Fatigue; depression/mood changes; difficulty breathing; rapid heartbeat; dizziness
- **Other causes**
  - Low levels of iron, folate, and vitamin B12

**Treatment:** Identify and treat causes other than myeloma; supplements; medications to increase number of red blood cells; blood transfusions

**Low white blood cells (leukopenia)**
- **Symptoms**
  - Fatigue; frequent infections
- **Other causes**
  - Radiotherapy
  - Infection

**Treatment:** Medications to stimulate production of white blood cells; antibiotics; antifungal medications; infection prevention

**Low platelets (thrombocytopenia)**
- **Symptoms**
  - Easy or excessive bruising; superficial bleeding into the skin; prolonged bleeding from cuts; bleeding from the gums or nose; blood in urine or stool
- **Other causes**
  - Viral infection (hep B or C); immune thrombocytopenia; medications

**Treatment:** Identify and treat causes other than myeloma; platelet transfusion; hold anticoagulation

Effects of Myeloma: Decreased Kidney Function

**Detection**
- Decreased amount of urine
- Increase in creatinine and other proteins

**Other causes beside myeloma**
- Hypertension
- Diabetes
- Some medications

**Treatment**
- Fluids
- Avoid nonsteroidal anti-inflammatory drugs such as Aleve, Advil/Motrin
- Plasmapheresis
- Treat other causes
- Dialysis (severe)
Main Body Systems Affected by Myeloma Treatment

- MM patients are at increased risk of developing blood clots
- Several MM drugs are associated with an increased risk of deep vein thrombosis (DVT)
- Peripheral neuropathy is a condition that affects the nerves, resulting in pain, tingling, burning sensations, and numbness in the hands and feet
- Peripheral neuropathy may be caused by MM or its treatments
- Cardiovascular side effects (including high blood pressure or congestive heart failure) can occur with some MM drugs
- Commonly used MM drugs may cause a variety of gastrointestinal problems, such as constipation, diarrhea, and nausea/vomiting

Blood

Central Nervous System

Cardiovascular

Gastrointestinal

Class: Immunomodulatory Drugs Side Effects and Management

**Revlimid***
- Potential for blood clots
- Reduced blood counts
- Rash
- Fatigue
- Muscle pain or muscle cramping
- Diarrhea
- Small chance of second new cancers when given with melphalan

**Pomalyst***
- Fatigue and weakness
- Reduced blood counts
- GI effects
- Shortness of breath
- Upper respiratory infection
- Back pain
- Fever
- Blood clots
- Mental fogginess

**Management**
- Blood thinners
- Tonic water/increased fluid intake for cramps
- GI toxicity: avoid dairy; fibers (Metamucil); Imodium; colestipol; cholestyramine; dose reduction
- Sleep hygiene, regular exercise, dose reduction for fatigue

*Black box warning.
GI, gastrointestinal
Class: Proteasome Inhibitors
Side Effects and Management

<table>
<thead>
<tr>
<th>Velcade</th>
<th>Kryprolis</th>
<th>Ninlaro</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>• PN (numbness, tingling, burning sensations and/or pain due to nerve damage)</td>
<td>• Fatigue</td>
<td>• Diarrhea</td>
<td>• PN occurs less often when subcutaneous or once weekly dosing is used for Velcade</td>
</tr>
<tr>
<td>• Low platelets</td>
<td>• Nausea</td>
<td>• Constipation</td>
<td>• Other PN prevention:</td>
</tr>
<tr>
<td>• GI problems: nausea, diarrhea, vomiting, loss of appetite</td>
<td>• Low platelets</td>
<td>• Low platelets</td>
<td>– Vitamins and other supplements*</td>
</tr>
<tr>
<td>• Fatigue</td>
<td>• Shortness of breath</td>
<td>• PN</td>
<td>– Certain medications such as gabapentin, pregabalin, duloxetine, opioids</td>
</tr>
<tr>
<td>• Rash</td>
<td>• Diarrhea</td>
<td>• Nausea</td>
<td>– Acupuncture</td>
</tr>
<tr>
<td></td>
<td>• Fever</td>
<td>• Peripheral edema</td>
<td>– Physical therapy</td>
</tr>
<tr>
<td></td>
<td>• Hypertension</td>
<td>• Vomiting</td>
<td>• Shingles-prevention pills</td>
</tr>
<tr>
<td></td>
<td>• Cardiac toxicity</td>
<td>• Back pain</td>
<td>• Blood thinners</td>
</tr>
</tbody>
</table>

*Do not take any supplements without consulting with your doctor.
PN, peripheral neuropathy; GI, gastrointestinal

Class: Monoclonal Antibodies
Side Effects and Management

<table>
<thead>
<tr>
<th>Emplichiti</th>
<th>Darzalex*/Sarclisa</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Low blood counts</td>
<td>• Infusion reactions</td>
<td>• Premedication in anticipation of infusion reactions</td>
</tr>
<tr>
<td>• Infusion reactions</td>
<td>• Fatigue</td>
<td>• Post-infusion medications (Darzalex)</td>
</tr>
<tr>
<td></td>
<td>• Upper respiratory tract infection</td>
<td></td>
</tr>
</tbody>
</table>

*Now approved as subcutaneous injection with fewer side effects.
XPOVIO: Selective Inhibitor of Nuclear Export Side Effects and Management

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

Low sodium (hyponatremia)
Maintain fluid intake

Fatigue
Stay hydrated and active

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


Bispecific Antibodies

Tecvayli
- Cytokine release syndrome
- Injection-related reactions
- Injection-site reaction
- Infections
- Neutropenia
- Anemia
- Thrombocytopenia

Management
- Available only through a Risk Evaluation and Mitigation Strategies (REMS) due to the risk of cytokine release syndrome
- Patients will receive step-up dosing and will be monitored in an inpatient setting
- Cytokine release syndrome is managed in the same fashion as CAR T
- Injection reactions are managed with oral antihistamines and topical steroids
- Infection prevention!
- COVID precautions
**Infection Can be Serious for Patients With Myeloma**

**Multiple myeloma**

**Immune dysfunction**

- 7–10–fold increased risk of bacterial and viral infections for people with myeloma
- Report fever of more than 100.4°F, shaking chills even without fever, dizziness, shortness of breath, low blood pressure to HCP as directed.

**General infection-prevention tips**
- Good personal hygiene (skin, oral)
- Environmental control (wash hands, avoid crowds and sick people, etc)
- Growth factor (Neupogen [filgrastim])
- Immunizations (NO live vaccines)
- Medications (antibacterial, antiviral)

---

**Mitigation and monitoring for cytokine release syndrome (CRS)**
- Step-up dosing with hospitalization for monitoring
- Frequent vital signs
- Rule out infection
- Laboratory monitoring
- Early intervention with tocilizumab

---

**RESPIRATORY**
- Difficultly breathing
- Shortness of breath

**NEUROLOGIC**
- Tremors
- Altered wakefulness
- Difficulty speaking

**CARDIOVASCULAR**
- Rapid heart rate
- Low blood pressure
- Arrhythmias

**GASTROINTESTINAL**
- Nausea
- Vomiting
- Diarrhea

**MUSCULOSKELETAL**
- Weakness

**HEPATIC**
- Altered liver function tests in the blood

**RENAL**
- ↑ Serum creatinine
- Renal insufficiency

**HEMATOLOGIC**
- Anemia
- Thrombocytopenia
- Neutropenia

**CONSTITUTIONAL**
- Fever
- Fatigue
- Headache

---

ALP, alkaline phosphatase; CPK, creatine phosphokinase; CRP, C-reactive protein; CRS, cytokine release syndrome; LDH, lactate dehydrogenase; O2, oxygen; TLS, tumor lysis syndrome.

BCMA-Targeted Therapies Are Associated With an Increased Risk of Infections

• Both viral and bacterial
  – Up to 1/3 of patients in clinical trials have serious infections (requiring IV antibodies or hospitalization)
• Increased risk of serious COVID complications despite history of vaccination
  – Antibody levels
  – Immediate treatment once diagnosed nirmatrelvir with ritonavir (Paxlovid)
    • Start as soon as possible; must begin within 5 days of when symptoms start
  – Oral prophylactic antimicrobials

Infection Prevention

• Avoid crowds
• Ensure handwashing, hygiene
• Growth factor (for example, filgrastim)
• IVIG for hypogammaglobulinemia
  – Know your healthy IgG level
• Immunizations (No live vaccines)
  – COVID-19 vaccination + booster(s)
  – Pneumococcal 20-valent conjugate vaccine
  – Seasonal inactivated influenza vaccine (×2 or high-dose)
  – Shingles vaccine: zoster vaccine recombinant, adjuvanted
• COVID-19 prevention
  – Antibody levels
  – Tixagevimab co-packaged with cilgavimab
Side Effects of Steroids (Dexamethasone)

- **Insomnia**
  - Healthy sleep habits
  - Timing
  - Medication to assist with sleeping as needed

- **Fluid retention**
  - Monitor for swelling of extremities and “puffy” face
  - Monitor weight changes/gain
  - Reduce dose

- **Mood changes**
  - Irritable, anxiety, difficulty concentrating
  - Severe cases → depression, euphoria

- **Dyspepsia—heartburn**
  - Dietary modifications (spicy, acidic foods)
  - Avoid NSAIDs
  - Acid-blocking medications
  - Take steroid with food; use enteric-coated aspirin with food

- **Elevation in glucose**
  - Monitor glucose and refer/treat as needed

Symptom Management

**Constipation**

- **Stimulant laxatives**
  - Mild: senna/sennoside (Senokot)
    - 1–2 pills twice a day
  - More potent: bisacodyl (Dulcolax)

- **Osmotic laxatives**
  - Gentle, pulls water into the intestine
    - Lactulose
    - Miralax

- **Bulking agents**
  - Soluble fiber: psyllium (Metamucil)
Symptom Management
Acid Reflux/Heartburn

- Our stomachs make a powerful acid to digest food, hydrochloric acid
- Hydrochloric acid can also digest our stomach lining → leads to gastritis and ulcers

A few ways to treat
1. Decrease the amount of acid the stomach is making
   - a. Zantac, Pepcid
   - b. Prilosec, Prevacid, Protonix, Nexium
2. Absorb excess acid: Tums, Maalox, Mylanta
3. Coat stomach: Carafate
4. Avoid late night eating

Symptom Management
Insomnia

- Causes: anxiety, stress, meds—dexamethasone
- Sleep hygiene
  - Routine: go to bed, wake up at routine times
  - Exercise
  - No TV or screens when trying to sleep
  - Relaxation training; meditation/yoga/Reiki
  - Counseling support
- Medications: useful but all have drawbacks
  - Lorazepam (Ativan)
  - Zolpidem (Ambien)
  - Diphenhydramine (Benadryl)
Marijuana

- Claims and hype: advocates and detractors
  - Promoted as relieving pain and muscle spasm, improving appetite, decreasing nausea, helping anxiety and insomnia, *and even curing cancer*
- Laws vary by state
- Marijuana contains 100 *cannabinoids*, most notably *THC* and *CBD*
- Sativex contains equal parts THC and CBD
  - Available in Great Britain and Canada
  - Double-blind trial in 2015: effective but no more effective than placebo for cancer pain; not available in U.S.
- Bottom line: Marijuana *has* been shown to have modest benefits in symptom management; claims of dramatic results are anecdotal and have not been proven

Daily Living

- Proper nutrition
- Exercise
- Rest
- Social contacts
Taking Care of Yourself

- Talk to your provider about side effects… there is usually a way to make treatment tolerable.
- Pay attention to your own needs and don’t be afraid to ask for help.
- Learn more about multiple myeloma.
- Look for the positive.

Please take a moment to answer two questions about this presentation.
Patient Experience

Town Hall Questions & Answers
Thank you!
Don’t Forget!

Complete your evaluation
Leave the iPad at your seat

Upcoming Patient Education Events
Save the Date

<table>
<thead>
<tr>
<th>Topic</th>
<th>Date and Time</th>
<th>Speakers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facebook Live: FAQs on Newly Diagnosed Multiple Myeloma</td>
<td>Tuesday, March 14 3:00 PM – 4:00 PM (ET)</td>
<td>Gurbakhash Kaur, MD Sonia Patel, MSN, AGACNP-BC, APRN, AOCNP</td>
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<td>Webinar: BCMA-Targeted Bispecific Antibody Therapy</td>
<td>Tuesday, March 21 4:00 PM – 5:00 PM (ET)</td>
<td>Jesus G. Berdeja, MD Amrita Y. Krishnan, MD</td>
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<td>Patient Summit Scottsdale, AZ In collaboration with Arizona Myeloma Network</td>
<td>Saturday, March 25 9:00 AM to 3:45 PM MT</td>
<td>Leif Bergsagel, MD Clarence Adoo, MD Jonathan Keats, PhD Sumit Madan, MD Suzanne Hyde, MSW, LCSW Barbara Kavanagh, MSW, LCSW Joan Koerber-Walker William Brown</td>
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<tr>
<td>Facebook Live: FAQs on Relapsed/Refractory Multiple Myeloma</td>
<td>Tuesday, March 28 2:00 PM – 3:00 PM (ET)</td>
<td>Brandon Blue, MD Dana Spiak, RN</td>
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<td>Webinar: Multiple Myeloma Precursor Conditions</td>
<td>Wednesday, April 5 2:30 PM – 3:30 PM (ET)</td>
<td>Sagar Lonial, MD Omar Nadeem, MD</td>
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For more information or to register, please visit themmrf.org/resources/education-program
MMRF Patient Resources

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!

Find an event and join us: https://themmrf.org/get-involved/mmrf-events/