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

Submit your questions throughout the program!

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

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Santiago Thibaud, MD
Icahn School of Medicine at Mount Sinai
New York, New York
## Summit Agenda

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<td>Mary DeRome, MS</td>
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<td>Welcome</td>
<td>Hearn Jay Cho, MD, PhD Sundar Jagannath, MD</td>
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<td>9:30 – 9:45 AM</td>
<td>Multiple Myeloma Biology</td>
<td>Cesar Rodriguez, MD</td>
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<td>9:45 – 10:00 AM</td>
<td>Treatment for Newly Diagnosed Multiple Myeloma</td>
<td>Joshua Richter, MD</td>
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<td>Autologous Stem Cell Transplant</td>
<td>Shambavi Richard, MD</td>
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<td>Town Hall Q&amp;A</td>
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<td>Break</td>
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<td>10:45 – 11:00 AM</td>
<td>Treatment for Relapsed/Refractory Multiple Myeloma</td>
<td>Santiago Thibaud, MD</td>
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<td>11:00 – 11:15 AM</td>
<td>Personalized Medicine</td>
<td>Samir S. Parekh, MD</td>
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<td>Supportive Care</td>
<td>Leora A. Giacolia, MS, FNP-BC, ACHPN</td>
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<tr>
<td>11:30 – 11:45 AM</td>
<td>Town Hall Q&amp;A</td>
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<tr>
<td>11:45 AM – 12:15 PM</td>
<td>Lunch and Patient Speaker</td>
<td>Roger Rawlings</td>
</tr>
<tr>
<td>12:15 – 12:30 PM</td>
<td>Closing Remarks</td>
<td>Mary DeRome, MS, and Sundar Jagannath, MD</td>
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**MMRF Introduction**

Mary DeRome, MS and Hearn Jay Cho, MD, PhD

**MMRF**
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

MyDRUG Trial

- Functional high-risk patients
- Profiling for alterations (NCT02884102)
  - No detectable actionable alterations
  - RAF/RAS mutations
  - CDK pathway–activating alterations
  - FGFR3-activating alterations
  - t(11;14)

  - Daratumumab + IPd
  - Cobimetinib + dex
  - Abemaciclib + IPd
  - Erdafitinib + IPd
  - Venetoclax + IPd

  *Assess single-agent activity after 2 cycles: after cycle 2, add backbone to single agent
MMRF Research Initiatives

1. MMRF Myeloma Accelerator Challenge (MAC) Grants
   - Broad, multi-institutional research grants designed to advance clinical trial concepts in the areas of
     • High-risk newly diagnosed multiple myeloma (NDMM)
     • High-risk smoldering myeloma (SMM)
   - Each research network will be funded up to $7M over 3 years

2. MMRF Horizon Adaptive Platform Trials
   - Paired with MAC grants
   - Done in collaboration with 13 MMRC sites
   - Trials in relapsed/refractory myeloma, high-risk NDMM, high-risk SMM

For more information, visit themmrf.org

2023 Myeloma Accelerator Challenge Program Grant Recipients

- **Transforming Treatment of High-Risk Myeloma**
  - **Network includes**: Tisch Cancer Center at Mt Sinai, Albert Einstein Medical College, Hackensack University Medical Center, Stanford University Medical Center, UCSF, Washington University of Saint Louis
  - **Samir Parekh, MD**

- **A Systems Biology Approach to High-Risk Myeloma**
  - **Network includes**: Erasmus Medical Center, Rotterdam; Amsterdam University Medical Centers; Julius Maximilian University of Wurzburg; University of Turin; University of Salamanca
  - **Pieter Sonneveld, MD, PhD**

- **Clinical and Multi-Omics Platforms to Define High-Risk Smoldering Myeloma**
  - **Network includes**: Emory University, Atrium Health Levine Cancer Institute, Icahn School of Medicine at Mt. Sinai, Mass General Hospital, Mayo Clinic, MSKCC Institute, Dana-Farber Cancer Institute
  - **Sagar Lonial, MD**

Each network will receive $7M over 3 years for a total $21M investment by the MMRF, meant to foster collaboration and advance compelling hypotheses that are ready for rapid testing in clinical trials.
MMRC Horizon Adaptive Platform Trial Structure

Master Protocol Adaptive Platform
Patients Meet Uniform Inclusion/Exclusion
Consent to Master Protocol and Randomization

Randomized to an Available Sub-study/Arm

Sub-study/Arm
One

Sub-study/Arm
Two

Sub-study/Arm
Three

Sub-study/Arm
Four

Control
Arm

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MMRF 2023 Scholars Grant Awardees

Eden Biltibo
Vanderbilt University Medical Center

Grant Proposal:
Identifying Effective and Cost-Conscious Maintenance Daratumumab Dosing
Frequent hospital visits cost money and increases exposure to bad bugs. If we prove every 8-week daratumumab works as good, patients won’t have to come to the hospital on a monthly basis.

Eden Biltibo, MD, MS is a Hematology/Oncology clinical fellow at Vanderbilt University Medical Center, who is passionate about developing strategies to bridge health care disparities in Multiple Myeloma care. She particularly focuses on the equitable utilization of immunotherapeutics in multiple myeloma and improving racial diversity of clinical trial participants in those trials.

Joselle Cook, MBBS
Mayo Clinic, Rochester

Grant Proposal:
Prevalence Of MGUS Among Unique Populations Of Black People
For people who test positive for MGUS, we will perform DNA testing which will inform us about ancestral origins and will give information on genetic variations that we know are associated with MGUS and MM.

Joselle Cook, MBBS is an assistant professor and Hematology/Oncology Fellow at Mayo Rochester. Dr. Cook received her medical degree from University of the West Indies Faculty of Medical Sciences. She completed her residency and fellowship training in 2022.
Welcome!

Question

Are you a...
1. Patient
2. Caregiver (family member or friend who helps patient manage his or her disease)
3. Other
Question

At what stage is your myeloma? (If you are a caregiver, what is the stage of the patient’s myeloma?)
1. Newly diagnosed
2. Relapsed/refractory
3. Remission: still on therapy
4. Remission: not on therapy
5. MGUS or smoldering myeloma not currently requiring treatment
6. Other
7. I don’t know.

Question

Have you had a stem cell transplant?
1. No, but I will soon!
2. No, but I am considering one (or my doctor is discussing with me).
3. No, my doctor tells me I am not a candidate.
4. Yes
5. Not applicable
Question

Do you know if you had any molecular characterization performed on your tumor, such as FISH, cytogenetics, or sequencing?
1. No
2. Yes, I had FISH.
3. Yes, I had cytogenetics.
4. Yes, I had sequencing.
5. Yes, I had more than one of these tests performed.
6. 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?)
1. Yes
2. No
3. I don’t know.
Multiple Myeloma Biology

Cesar Rodriguez, MD
Icahn School of Medicine at Mount Sinai
New York, New York

Disclosures

- Research Support/PI: Amgen, Celgene, ORIC, Janssen, BMS, Teneobio
- Employee: N/A
- Consultant: Amgen, Bristol Myers Squibb, Janssen, Karyopharm, Sanofi, Abbvie, Artiva
- Major Stockholder: N/A
- Speakers Bureau: BMS, Takeda
- Honoraria: N/A
- Scientific Advisory Board: BMS, Janssen, Sanofi, Abbvie, Artiva
How common is multiple myeloma?

Multiple myeloma is the 2nd most common cancer of the blood, with an estimated 35,730 new cases in 2023. Myeloma represents 1.8% of all new cancer cases in the U.S., and the median age at diagnosis is 69 years.

Multiple Myeloma Affects Your Bones, Blood, and Kidneys

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

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

**KIDNEYS**
- Large amounts of M protein can overwork or cause damage to the kidneys
Effects of Myeloma and Common Symptoms

- Low blood counts: Weakness, Fatigue, Infection
- Decreased kidney function: Weakness
- Bone damage: Bone pain

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

Demographic Risk Factors: Multiple Myeloma

- Older age
- Male sex
- Obesity
- Race: 2× incidence in African Americans

Family history:

- One first-degree relative with multiple myeloma
- Relatives of multiple myeloma patients have more monoclonal gammopathy of undetermined significance (MGUS)
- Current recommendation is to not screen families

The Right Tests: Common Tests Conducted in Myeloma Patients

Blood tests
Urine tests

- Confirms the type of myeloma or precursor condition

Bone marrow biopsy

- Confirms diagnosis of myeloma
- Determines how advanced the myeloma or precursor condition is

Imaging tests

- Detects the presence and extent of bone disease and the presence of myeloma outside of the bone marrow

Not All M Spikes Are Myeloma!

MONOCLONAL GAMMOPATHIES
MAYO CLINIC

n=34,633

MGUS 59% (20,580)

Multiple myeloma 18% (6,112)

Lymphoproliferative 3% (1,089)

Amyloidosis (AL) 9% (3,185)

Solitary or extramedullary 2% (705)

Macro 2% (785)

Other 3% (877)

Medical oncology best practices. 2012.
**Type of Disorder Has the Potential to Evolve**

- **Normal plasma cell**
- **Plasmablast**
- **MGUS**
- **Smoldering myeloma**
- **Intramedullary myeloma**
- **Extramedullary myeloma**

**MGUS**
- M protein <3 g/dL
- Clonal plasma cells in bone marrow <10%
- No myeloma-defining events

**Smoldering myeloma**
- M protein ≥3 g/dL (serum) or ≥500 mg/24 hrs (urine)
- Clonal plasma cells in bone marrow ≥10% to 60%
- No myeloma-defining events

**Multiple myeloma**
- Underlying plasma cell proliferative disorder AND
  - ≥1 myeloma-defining event
  - ≥1 CRAB feature
  - Clonal plasma cells in bone marrow ≥60%
  - Serum free light chain ratio ≥100
  - >1 MRI focal lesion


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**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 Bone Marrow Tests!

Types of chromosomal abnormalities

- Translocation
- Deletion
- Gain or amplification

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>

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

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

High risk
- 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

Standard risk
- 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.

β2M: beta-2 microglobulin; LDH: lactate dehydrogenase; GEP: gene-expression profiling
Know Your Imaging Tests!

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

- **X-ray**
- **MRI**
- **CT scan**
- **PET scan**

Natural History of MM After Treatment

- **Clonal expansion**
- **MGUS**
- **Early myeloma**
- **Late myeloma**
- **Plasma cell leukaemia**

- **Asymptomatic**
- **Symptomatic**
- **ACTIVE MYELOMA**
- **REFRACTORY RELAPSE**

- **MGUS or smouldering myeloma**
- **First-line therapy**
- **Second line**
- **Third line**

- **Plateau remission**
- **1. RELAPSE**
- **2. RELAPSE**

M Protein (g/L)

1. RELAPSE
Summary

- Multiple myeloma is a rare blood cancer that can negatively affect the bones, kidneys, and bone marrow, leading to lowered blood counts.
- The prognosis of multiple myeloma depends on the genetic makeup of the myeloma cell and its chromosomes; R-ISS is used for staging in multiple myeloma.
- Knowledge is power: right team, right test, right treatment.

*Be an informed and empowered part of your health care team!*

Please take a moment to answer two questions about this presentation.
Treatment for Newly Diagnosed Multiple Myeloma

Joshua Richter, MD, FACP
Icahn School of Medicine at Mount Sinai
New York, New York

Disclosures

- Consultant/advisor: Janssen, BMS, Pfizer, Karyopharm, Sanofi, Takeda, Genentech, AbbVie, Regeneron, Forus, Menarini/Stemline, Antengene
- Speakers Bureau: Janssen, BMS, Sanofi, Adaptive Biotechnologies
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 Novel Agents and Immune Therapies (including mAbs)

- The percentage of people expected to survive 5 years or more after being diagnosed with myeloma has dramatically improved in the last 20 years.
  - 26.5% in 1975
  - 27.4% in 1985
  - 33.5% in 1995
  - 47.2% in 2005
  - 56.9% in 2013
  - ~ 65% in 2014 and beyond

Available treatments:
- Chemotherapy + dexamethasone + stem cell transplantation (ASCT), bisphosphonates
- Thalomid (thalidomide)
- Velcade (bortezomib)
- Revlimid (lenalidomide)
- Kyprolis (carfilzomib)
- Pomalyst (pomalidomide)

mAbs, monoclonal antibodies

- Ninlaro (ixazomib)
- Empliciti (elotuzumab)
- Darzalex (daratumumab)
- Xpovio (selinexor)
- Sarcisia (isatuximab)
- Abecma (idecabtagene vicleucel)
- Carvykti (ciltaclabtagene autoleucel)
- Tecvayli (teclistamab)
- Talveey (talquetamab)
- Elexrefio (elranatamab)
# Overview of Treatment Approach for Active Multiple Myeloma

## Induction Therapy Regimens

**Preferred**
- Revlimid-Velcade-dex (RVd)*
- Kyprolis-Revlimid-dex (KRd)

**Recommended**
- Darzalex-Revlimid-Velcade-dex (D-RVd)
- Kyprolis-Revlimid-dex (KRd)
- Darzalex-Velcade-Thalomid-dex (D-VTd)
- Darzalex-Kyprolis-Revlimid-dex (D-KRd)
- Darzalex-Cytoxan-Velcade-dex (D-VCd)
- Sarclisa-Revlimid-Velcade-dex
- VTD-PACE

**Certain circumstances**
- Velcade-Cytoxan-dex (VCd)
- Velcade-Doxil-dex (VDd)
- Kyprolis-Cytoxan-dex (KCd)
- Velcade-Revlimid-dex (Vd)
- Revlimid-dex (Rd)*
- Velcade-Cytoxan-dex (VCd)
- Revlimid-Cytoxan-dex (RCd)
- Kyprolis-Cytoxan-dex (KCd)
- Revlimid-Velcade-dex (RVd)-lite

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

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*Supportive care* is given throughout treatment.
Phase 3 SWOG S0777 Trial
*Bortezomib + Lenalidomide + dex (VRd) vs Lenalidomide + dex (Rd) and Rd Maintenance*

Newly diagnosed myeloma (transplant eligible and non-eligible patients)

<table>
<thead>
<tr>
<th>Patients With Confirmed Response (%)</th>
<th>VRd (n=216)</th>
<th>Rd (n=214)</th>
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</thead>
<tbody>
<tr>
<td>ORR: <strong>81.5%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CR:</strong> 15.7%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>VGPR:</strong> 27.8%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PR:</strong> 36.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PD or death:</strong> 2.8%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SD: 15.7%</td>
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*Assessable VRd (n=216)*

<table>
<thead>
<tr>
<th>Hazard ratio (95% CI)</th>
<th>RdVRD</th>
</tr>
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<tbody>
<tr>
<td>0.712 (0.560 - 0.906)</td>
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</table>

<table>
<thead>
<tr>
<th>Median PFS, months</th>
<th>VRD</th>
<th>Rd</th>
<th>Hazard ratio (95% CI)</th>
</tr>
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<tbody>
<tr>
<td>6.04</td>
<td>30</td>
<td>43</td>
<td>1.21 (0.95 - 1.54)</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Median OS, months</th>
<th>VRD</th>
<th>Rd</th>
<th>Hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>54.96</td>
<td>75</td>
<td>64</td>
<td>1.21 (0.95 - 1.54)</td>
</tr>
</tbody>
</table>

ORR, overall response rate; CR, complete response; VGPR, very good partial response; PR, partial response; SD, stable disease; PD, progressive disease; CI, confidence interval; PFS, progression-free survival; OS, overall survival


MAIA: Updated Efficacy Results

- Phase 3 Study of lenalidomide and dex ± daratumumab
- Median duration of follow-up: 56.2 mos

<table>
<thead>
<tr>
<th>Response</th>
<th>DRd</th>
<th>Rd</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>92.9%</td>
<td>81.3%</td>
</tr>
<tr>
<td>PR</td>
<td>13.6%</td>
<td>28.2%</td>
</tr>
<tr>
<td>VGPR</td>
<td>31.8%</td>
<td>28.2%</td>
</tr>
<tr>
<td>CR</td>
<td>17.1%</td>
<td>12.5%</td>
</tr>
<tr>
<td>sCR</td>
<td>30.4%</td>
<td>12.5%</td>
</tr>
<tr>
<td>≥VGPR</td>
<td>79.3%</td>
<td>53.1%</td>
</tr>
<tr>
<td>MRD- (10⁻⁶)</td>
<td>31%</td>
<td>10%</td>
</tr>
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Drop the Dex


What is the role of ASCT in the current age of modern induction regimens?

Phase 3 Study of Darzalex + Velcade + Revlimid + Dex vs Velcade + Revlimid + Dex in NDMM

NDMM, newly diagnosed multiple myeloma


Investigational Phase 3 With RVd Backbone

GMMG-HD7 Study

Transplant-eligible newly diagnosed multiple myeloma

331 patients

Isa-RVd (x 3)

RVD (x 3)

HDT + ASCT

Induction

Maintenance

Isa-R

R

329 patients

HDT, high-dose therapy; HRCA, high-risk chromosomal abnormalities; R-ISS, Revised International Staging System; OR, odds ratio

KRd vs VRd Superior >VGPR But Comparable PFS and OS


Post-consolidation MRD negativity by NGS
Subgroup analysis by cytogenetic risk

NGS, 10^-5

NGS, 10^-6

1 HRCA was defined as the presence of one of the following high-risk cytogenetic abnormalities: del(17p13.1), t(4;14) (p16.3;q32.3), t(14;16) (q32.3;q23), gain(1q21), or amp(1q21); 2+ HRCA was defined as the presence of at least two high-risk cytogenetic abnormalities.

NGS, next-generation sequencing
MASTER: MRD Response-Adapted Therapy Using a Dara-KRd Platform

- MRD assessment after completion of each cassette of therapy
- Transition to observation with 2 consecutive MRD-negative readouts at $10^{-5}$

<table>
<thead>
<tr>
<th>Treatment phase</th>
<th>0 HRCA abnormalities</th>
<th>1 HRCA abnormality</th>
<th>$\geq$ 2 HRCA abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MRD-10^5</td>
<td>MRD-10^6</td>
<td>MRD-10^5</td>
</tr>
<tr>
<td>Post induction</td>
<td>38%</td>
<td>26%</td>
<td>40%</td>
</tr>
<tr>
<td>Post SCT</td>
<td>65%</td>
<td>43%</td>
<td>60%</td>
</tr>
<tr>
<td>Post MRD-directed consolidation</td>
<td>80%</td>
<td>66%</td>
<td>78%</td>
</tr>
</tbody>
</table>

*HRCA: gain or amp 1q21, del(17p), t(4;14), t(14;16), t(14;20)


Continuous or Maintenance Therapy

**Successful maintenance therapy must...**

- Be convenient
- Be safe and well tolerated long term
- Not interfere with the use of other future treatments

**Preferred**

- Revlimid*

**Recommended**

- Velcade

**Certain circumstances**

- Velcade-Revlimid
- Kyprolis-Revlimid
- Darzalex ± Revlimid
- Ninlaro

- Velcade-Revlimid
- Ninlaro

*N: Category 1 recommendation. Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate. National Comprehensive Cancer Network Guidelines Version 4.2023. Multiple Myeloma.
Revlimid Maintenance Duration

**STAMINA Trial (BMT-CTN0702)**

- **Auto/Auto group**
  - 247 pts
  - MEL 200 mg/m²
  - REV × 3 yrs

- **Auto/RVD group**
  - 254 pts
  - RVd × 4
  - REV × 3 yrs

- **Auto/Rev group**
  - 257 pts
  - No consolidation
  - REV × 3 yrs

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

Discontinuation of Revlimid maintenance at 3 years is not recommended because of the increased risk of disease progression.

Phase III Study of Daratumumab/rhuhp20 (nsc- 810307) + Lenalidomide or Lenalidomide as Post-Autologous Stem Cell Transplant Maintenance Therapy in Patients With Multiple Myeloma (mm) Using Minimal Residual Disease To Direct Therapy Duration (DRAMMATIC study): SWOG s1803

Continued maintenance

Stopped maintenance

P<0.001

79.5%

61%

Measuring Response to Therapy

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

Stable disease (no change in M protein of light chain)

Minor response (>30% decrease)

Partial response (>50% decrease)

Very good partial response (>90% decrease)

Complete response (100% decrease/<5% plasma cells in bone marrow biopsy)

Stringent complete response (no plasma cells in bone marrow biopsy)

Myeloma cell burden

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


MRD Is Important for Clinical Care and New Drug Registration

Currently assessed by BM-based technologies
- Flow cytometry
- Next-generation sequencing

Progress being made with blood-based technologies
- MS
- Cell-free DNA

A surrogate for patient outcome in clinical trials

Many clinical trials are using MRD-driven strategies

Accelerate innovative trials leading to regulatory approval

BM, bone marrow; MS, mass spectrometry

Summary

- Survival rates are improving because of new drugs and new combinations of drugs, including immune therapies and especially monoclonal antibodies.
- The body of evidence from phase 3 trials indicates that maintenance therapy improves PFS and likely OS.
- MRD is the deepest response after myeloma treatment, including bone marrow.
- MRD and imaging MRD. NGF and NGS are the two most commonly used marrow MRD tests. Blood-based MRD is in exploration.
- MRD is also useful as an end point in clinical trials helping to expedite new drug approval in myeloma.
- The treatment paradigm will continue to change with the approval of additional novel agents.

Please take a moment to answer two questions about this presentation.
Autologous Stem Cell Transplantation

Shambavi Richard, MD
Icahn School of Medicine at Mount Sinai
New York, New York

Disclosures

• Honoraria received – Janssen, BMS
• Steering Committee– Gracell Biotechnologies
• Research support – Janssen, BMS, C4 Therapeutics, Gracell Biotechnologies, Heidelberg Pharma
What does transplant mean?

Understanding the basics of autologous stem cell transplantation

Blood-forming stem cells are collected from the patient’s own blood. Stem cells are frozen and stored.

Patient gets high-dose chemotherapy (melphalan). Most myeloma cells are destroyed; some normal cells (hair follicles, taste buds, and blood cells) are also temporarily destroyed.

The previously collected stem cells are given back by IV infusion. Stem cells restore blood cells with fewer myeloma cells. Other cells (hair follicles and taste buds) recover.

Stem Cell Harvest
Autologous Stem Cell Transplantation (ASCT)

1. Induction therapy
   - ~3 to 6 cycles
   - Stem cell mobilization
     - Neupogen, Neulasta, Leukine, Cytoxan, Mozobil

2. Collection of stem cells from the bloodstream
   - Melphalan
     - Alkeran, Evomela

3. Freezing of stem cells

4. High-dose chemotherapy
   - Day 0

5. Thawing and infusion of stem cells
   - Days +1 to +100†

6. Bone marrow recovery
   - Days +1 to +100†

Side Effects of High-Dose Chemotherapy

Fatigue
- Expected
- May last 1–3 months

Nausea, vomiting, and diarrhea
- Symptoms much more manageable with newer anti-emetics
- Try to prevent nausea
- May include stomach cramping
- Encourage small amounts of food, more often
- Avoid milk, milk products, high-fiber foods

Mucositis
- Pain, sores in mouth; sore throat
- Pain meds, mouth swishes
- Avoid tart, acidic, salty, spicy foods
- Soft food better tolerated

Low blood counts
- Low white blood cell count (risk for infection)
- Hemoglobin drop (fatigue)
- Platelet count drop (bleeding risk)
- Blood transfusion
- Platelet transfusion
- Antibiotics

Hair loss
- White blood cells and platelets recover in 2 weeks

*The weeks leading up to the transplant; †The days after the transplant.
Current Treatment Paradigm for Newly Diagnosed Multiple Myeloma

High-Dose Chemotherapy and Stem Cell Transplantation

Remission lasts longer
Can be done early on or later (or both)

Some patients will not qualify
- Older/frail patients
- Comorbidities

Dose-reduced melphalan
- Age >75
- Kidney disease

Supportive care is given throughout treatment.

*If you have high-risk markers, additional agents may be given with Revlimid; if you cannot tolerate Revlimid, another treatment (for example, a proteasome inhibitor) may be given.
*In the U.S., maintenance is typically given until progression, but studies are evaluating stopping treatments for patients with deep responses. If you have little or no evidence of disease but are experiencing side effects, discuss with your doctor whether to continue until progression. Dose adjustments are also options.
IFM 2009/DETERMINATION Phase 3 Study

Q: Should I get a transplant up front or not?

Is transplant still required in newly diagnosed myeloma?

Q: Should I get a transplant up front or not?
IFM 2009: ASH 2020 Updated Results

Updated PFS (primary end point)

- Median follow-up: 93 months

- 30% reduction in the risk of progression or death in patients receiving transplant

- 8-year OS 62.2% for RVd-ASCT and 60.2% for RVd alone (60% alive in both arms after 8 years)

PFS, progression-free survival; OS, overall survival; HR, hazard ratio; CI, confidence interval


Phase 3 Study of ASCT for NDMM: Survival Analysis

- Primary end point
  - PFS for RVd + ASCT: approximately 5.5 years
  - PFS for RVd alone: approximately 4 years

- Transplant extended time to progression by 20 months

- Risk of progression or death 53% higher in RVd alone group

- Length of OS: no difference (with a median follow-up time of 76 months).

- High risk PFS 17.1 vs 55.5 mo PFS (n=66 vs 66); HR 1.99

NDMM, newly diagnosed multiple myeloma

Phase 3 Study of ASCT for NDMM: Survival Analysis by MRD Status

**Survival Analysis by MRD Status**

<table>
<thead>
<tr>
<th>MRD-neg status</th>
<th>5-year PFS, %</th>
<th>HR (unadjusted 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVd alone</td>
<td>59.2</td>
<td>0.91 (0.46–1.79)</td>
</tr>
<tr>
<td>RVd + ASCT</td>
<td>53.5</td>
<td></td>
</tr>
</tbody>
</table>

**Probability of Progression-Free Survival**

- Time Since MRD Evaluation at Start of Maintenance (Months)

**HR (unadjusted 95% CI) Median PFS, mos**

- MRD-pos status
  - RVd alone: 1.67 (0.98–2.85) 33.4 mos
  - RVd + ASCT: 50.6 mos

Phase 3 Study of ASCT for NDMM: Best Response to Treatment and Duration of Response

**All patients**

- Response Rate (%)
  - 2PR: 97.5, 95
  - ≥VGPR: 82.7, 79.6
  - ≥CR: 46.8, 42

- Median duration of response was 38.9 mo in RVd vs 56.4 mo in ASCT group

**All patients by race**

- Solid bars = Black
- Stippled bars = White

**Patients (%)**

- ORR
  - RVd alone: 92.4, 95.5
  - RVd + ASCT: 81.9, 78.7

- ≥VGPR
  - RVd alone: 45.5, 41.6
  - RVd + ASCT: 93.9, 77.3

- ≥CR
  - RVd alone: 30.3
  - RVd + ASCT: 51.5
Phase 3 Study of ASCT for NDMM: Quality of Life


Phase 3 Study of ASCT for NDMM: Subsequent Therapy and Rate of ASCT in RVD-Alone Arm (Late ASCT)

<table>
<thead>
<tr>
<th>Subsequent therapy in patients off protocol therapy (%)</th>
<th>RVd alone (N=279) late transplant</th>
<th>RVd + ASCT (N=276) early transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any treatment*</td>
<td>79.8</td>
<td>69.6</td>
</tr>
<tr>
<td>Subsequent therapy</td>
<td>n=222</td>
<td>n=192</td>
</tr>
<tr>
<td>Any immunomodulatory drug</td>
<td>55.9</td>
<td>58.3</td>
</tr>
<tr>
<td>Pomalyst (pomalidomide)</td>
<td>30.2</td>
<td>29.2</td>
</tr>
<tr>
<td>Revlimid (lenalidomide)</td>
<td>25.7</td>
<td>29.2</td>
</tr>
<tr>
<td>Any proteasome inhibitor</td>
<td>55.9</td>
<td>50.0</td>
</tr>
<tr>
<td>Velcade (bortezomib)</td>
<td>27.5</td>
<td>25.5</td>
</tr>
<tr>
<td>Kyprolis (carfilzomib)</td>
<td>21.2</td>
<td>16.7</td>
</tr>
<tr>
<td>Ixazomib</td>
<td>8.1</td>
<td>7.8</td>
</tr>
<tr>
<td>Marizomib</td>
<td>0</td>
<td>0.5</td>
</tr>
<tr>
<td>Any monoclonal antibody</td>
<td>16.2</td>
<td>27.6</td>
</tr>
<tr>
<td>Darzalex (daratumumab)</td>
<td>11.3</td>
<td>21.4</td>
</tr>
<tr>
<td>Empliciti (elotuzumab)</td>
<td>4.5</td>
<td>6.3</td>
</tr>
<tr>
<td>Sarclisa (isatuximab)</td>
<td>0.5</td>
<td>0</td>
</tr>
</tbody>
</table>

*Including immunomodulatory drugs (IMiDs), protease inhibitors (PIs), monoclonal antibodies (mAbs), HDACi (panobinostat), ASCT, chemotherapy, radiation therapy (RT), steroids, other

Only 28.0% of RVd alone (late transplant) patients had received ASCT at any time following end of study treatment.

Early vs Late Transplant

Pros and Cons

Pros

Early ASCT
- Deeper and more durable response
- Youngest/healthiest you are going to be
- Allows for fewer cycles of induction treatment

Late ASCT
- PFS may be shorter, but currently appears OS is the same
- Fewer side effects without high-dose chemotherapy
- Conserve quality of life in the early part of disease journey

Cons

Early ASCT
- No proven impact on overall survival
- 20% of patients still relapse within 2 years
- More side effects, including a small risk of serious life-threatening complications
- 3 months to full clinical recovery

Late ASCT
- Need more cycles of induction
- May need next treatment sooner, including (late) transplant
- Not all patients relapsing are able to undergo salvage ASCT

Early vs Late ASCT Summary

- ASCT is a standard of care for frontline therapy of myeloma.
- ASCT safety has been established, and it induces long progression-free survival.
- Decision of ASCT should be individualized in every patient and deserves a thorough discussion between the patient and provider.
  - Emerging data suggests patients with an extremely good response (that is, complete response and ideally minimal residual disease negative) to induction therapy may have a long PFS. Studies are ongoing to determine whether these patients require ASCT.
Please take a moment to answer two questions about this presentation.

Questions?
Treatment for Relapsed/Refractory Multiple Myeloma

Santiago Thibaud, MD
Icahn School of Medicine at Mount Sinai
New York, New York

Disclosures

• Santiago Thibaud, MD, has no relevant financial information to disclose.
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**: increase 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

Approved therapies

- Clinical trials
  - Proteasome inhibitor/immunomodulatory drug/antibody-based therapy
  - DKd, Isa-Kd, DPd, Elo-Pd, Isa-Pd, or KPd
  - DVd, SVd, Ven-Vd (for t[11;14])
  - Refractory to Velcade and Revlimid
  - Refractory to an IMiD but sensitive to a PI

Treatment Approach

**First relapse**

- Any options for first relapse not tried

**>1 Relapse**

- Approved therapies
- Clinical trials
- Triple-class refractory

- Sd, Tecvayli, Talvey, Elrexfio
- 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); ide-cel, idecabtagene vicleucel (Abecma); cilt-a-cel, cilta-cel, autoleucel (Carvykti)

*Not approved for use in myeloma patients; †At least 1 prior line of therapy, including a PI and an IMiD, and are refractory to Revlimid; ‡After two or more prior lines of therapy including an IMiD, a PI, and an anti-CD38 monoclonal antibody.
### Currently Available 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 Pomalyist 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 Pomalyist 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 Pomalyist 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</td>
<td>• For relapsed/refractory myeloma</td>
</tr>
<tr>
<td></td>
<td>• SC injection</td>
<td>• For relapsed/refractory myeloma as a single agent, as a doublet with dexamethasone, and as a triplet with Revlimid or Darzalex plus dexamethasone</td>
</tr>
<tr>
<td>Kyprolis (carfilzomib)</td>
<td>• IV infusion</td>
<td>• For relapsed/refractory myeloma as a triplet with Revlimid and dexamethasone</td>
</tr>
<tr>
<td></td>
<td>• Weekly dosing</td>
<td>• For relapsed/refractory myeloma in combination with dexamethasone</td>
</tr>
<tr>
<td>Ninlaro (ixazomib)</td>
<td>Once-weekly pill</td>
<td>• For relapsed/refractory myeloma in combination with dexamethasone</td>
</tr>
<tr>
<td>Revlimid (lenalidomide)*</td>
<td>Once-daily pill</td>
<td>• For relapsed/refractory myeloma in combination with dexamethasone</td>
</tr>
<tr>
<td>Pomalyist (pomalidomide)*</td>
<td>Once-daily pill</td>
<td>• For relapsed/refractory myeloma in combination with dexamethasone</td>
</tr>
<tr>
<td>XPOVIO (selinexor)</td>
<td>Once-weekly pill</td>
<td>• For relapsed/refractory myeloma as a triplet with Velcade and dexamethasone</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Class</th>
<th>Drug</th>
<th>Formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chimeric antigen receptor (CAR) T cell</td>
<td>Abecma (idecabtagene vicleucel)*</td>
<td>300 to 510 × 10^6 genetically modified autologous CAR T cells in one or more infusion bags</td>
</tr>
<tr>
<td>CAR T cell</td>
<td>Carvykti (ciltaclabtagene autoleucel)†</td>
<td>0.5 to 1.0 × 10^6 genetically modified autologous CAR T cells/kg of body weight</td>
</tr>
</tbody>
</table>

*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

Abecma, Carvykti, Tecvayli, Talvey, and Elrexfio are available only through a restricted distribution program.

CAR T: Expected Toxicities

<table>
<thead>
<tr>
<th>CRS</th>
<th>Onset</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1–9 days after CAR T-cell infusion</td>
<td>5–11 days</td>
</tr>
<tr>
<td>ICANS</td>
<td>2–9 days after CAR T-cell infusion</td>
<td>3–17 days</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>Actemra (tocilizumab)</td>
</tr>
<tr>
<td>Difficult breathing</td>
<td>Corticosteroids</td>
</tr>
<tr>
<td>Dizziness</td>
<td>Supportive care</td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>Antiseizure medications</td>
</tr>
<tr>
<td>Rapid heartbeat</td>
<td>Corticosteroids</td>
</tr>
<tr>
<td>Low blood pressure</td>
<td></td>
</tr>
</tbody>
</table>

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

ICANS, immune effector cell-associated neurotoxicity syndrome
Ongoing Clinical Studies With Ide-Cel and Cilta-Cel

**Ide-Cel Studies**
- KarMMa-2
  - Phase 2 study in RRMM and high-risk myeloma (relapse early after induction)
- KarMMa-4
  - Phase 1 study in newly diagnosed high-risk myeloma

**Cilta-Cel Studies**
- CARTITUDE-2
  - Phase 2 study in RRMM and high-risk myeloma (relapse early after induction)
    - Arm D: len/dex after CAR
    - Arm E: dara-RVd induction, CAR then dara-R consolidation
- CARTITUDE-6
  - Phase 3 study in NDMM
  - Replaces transplant with CAR-T

**Triple-Class Refractory**
- 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

**Proteasome inhibitors**
- Velcade (bortezomib)
- Kyprolis (carfilzomib)
- Ninlaro (ixazomib)

**Immunomodulatory drugs**
- Revlimid (lenalidomide)
- Pomalyst (pomalidomide)

**Anti-CD38 monoclonal antibodies**
- Darzalex (daratumumab)
- Sarclisa (isatuximab)
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>
</tbody>
</table>

<table>
<thead>
<tr>
<th>XPOVIO + dexamethasone in relapsed/refractory myeloma</th>
<th>No. patients with ≥PR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>32 (26)</td>
</tr>
<tr>
<td>Previous therapies to which the disease was refractory, n (%)</td>
<td></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


Currently Available Drugs for Triple-Class Refractory Myeloma

<table>
<thead>
<tr>
<th>Class</th>
<th>Drug</th>
<th>Formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bispecific antibody</td>
<td>Tecvayli (tecristamab)*†</td>
<td>Step-up dosing† the first week then once weekly thereafter by subcutaneous injection</td>
</tr>
<tr>
<td>Bispecific antibody</td>
<td>Talvey (talquetamab)*†</td>
<td>Step-up dosing† the first week then once weekly thereafter by subcutaneous injection</td>
</tr>
<tr>
<td>Bispecific antibody</td>
<td>Elrefio (elranatamab)*</td>
<td>Step-up dosing† the first week then once weekly thereafter by subcutaneous injection</td>
</tr>
</tbody>
</table>

And, CAR T-cell therapies: Abecma, Carvykti

*Black box warning: cytokine release syndrome; neurologic toxicities
† Patients are hospitalized for 48 hours after administration of all step-up doses.
‡ Patients are hospitalized for 48 hours after administration first step-up dose and for 24 hours after second step-up dose.
Abecma, Carvykti, Tecvayli, Talvey, and Elrefio are available only through a restricted distribution program.
Now Approved: Three Bispecific Antibodies!

**Tecvayli**
- Patients (%)
  - ≥CR: 39.4%
  - CR: 6.7%
  - VGPR: 19.4%
  - PR: 19.4%

**Talvey**
- Patients Responding (%)
  - PR: 23.8%
  - VGPR: 9.8%
  - CR: 25.9%
  - sCR: 14.7%

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

**Median duration of response**
- **18.4 months**


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

- **Cytokine release syndrome (CRS)**
- **Infections**
- **Cytopenias**
- **Neurotoxicity (ICANS)**
- **Cytokeratin changes/rash**
- **Dysgeusia**
- **Off-target effects (with GPRC5D-targeted agents)**

ICANS, immune effector cell-associated neurotoxicity syndrome
**GPRC5D-Associated Side Effects**

<table>
<thead>
<tr>
<th>Affected area</th>
<th>Symptoms and effects</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>Rash, skin peeling</td>
<td>Relatively benign, not painful, self-limiting, and manageable with emollients</td>
</tr>
<tr>
<td>Nails</td>
<td>Nail thinning and loss</td>
<td>Mostly aesthetic but take time to resolve</td>
</tr>
<tr>
<td>Oral</td>
<td>Difficulty swallowing, dry mouth, taste changes</td>
<td>Can lead to weight loss; have longer duration and can affect quality of life. Most successfully managed with dose modification. Supportive measures may be used (e.g., NaCl mouth rinse, artificial saliva spray, diet modification)</td>
</tr>
</tbody>
</table>

*Myloma patients respond well to treatment, and GPRC5D-associated side effects improve over time, becoming more tolerable; notable reduction in side effects is seen with dose modification*


---

**Bispecific Antibodies Under Investigation**

<table>
<thead>
<tr>
<th>Bispecific antibody</th>
<th>Target (on MM cell × T cell)</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tecvayli (teclistamab)</td>
<td>BCMA × CD3</td>
<td>Approved for use in myeloma patients</td>
</tr>
<tr>
<td>Elrexfio (elranatamab)</td>
<td>BCMA × CD3</td>
<td>Approved for use in myeloma patients</td>
</tr>
<tr>
<td>Linvoseltamab</td>
<td>BCMA × CD3</td>
<td>Clinical studies</td>
</tr>
<tr>
<td>Alnuctamab</td>
<td>BCMA × CD3</td>
<td>Clinical studies</td>
</tr>
<tr>
<td>ABBV-383</td>
<td>BCMA × CD3</td>
<td>Clinical studies</td>
</tr>
<tr>
<td>Talvey (talquetamab)</td>
<td>GPRC5D × CD3</td>
<td>Clinical studies</td>
</tr>
<tr>
<td>Forintamig (RG6234)</td>
<td>GPRC5D × CD3</td>
<td>Clinical studies</td>
</tr>
<tr>
<td>Cevostamab</td>
<td>FcRH5 × CD3</td>
<td>Clinical studies</td>
</tr>
</tbody>
</table>

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

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

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

**CD3**: a T-cell receptor

---

GPRC5D, G protein-coupled receptor family C group 5 member D
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 PFS.

We have three different monoclonal antibodies that improve PFS when added to other standard therapies without significantly increasing side effects.

CAR T and bispecific antibodies are very active even in heavily pre-treated patients with unprecedented response rates and durations of response.

Please take a moment to answer two questions about this presentation.
Personalized Medicine
Samir S. Parekh, MD
Icahn School of Medicine at Mount Sinai
New York, New York

Disclosures

- Dr. Parekh discloses consulting relationships with Grail and research support from Amgen, Celgene/BMS Corporation, and Caribou
Multiple Myeloma Is Not Just One Disease!

Multiple myeloma is a heterogeneous disease even within cytogenetically defined molecular subtypes.

In the future, the goal is to go beyond a one-size-fits-all approach.

How do we customize treatment?
Personalized medicine

Treatment of Multiple Myeloma

Where are we now?
• Standard induction with proteasome inhibitors and IMiDs, consolidation with ASCT, and maintenance therapy have benefited the majority of multiple myeloma patients
• A subset of myeloma patients still have poor outcome with standard therapy
• Personalized medicine approaches are needed to address high-risk patients

What we need
• Evolving definitions of high-risk beyond historic markers such as translocation 4;14 and deletion of chromosome 17p
• Advanced molecular diagnostics are key to revealing individual targets and therapies
• Immunotherapies are emerging as promising new weapons in the fight against multiple myeloma

IMiDs, immunomodulatory drugs; ASCT, autologous stem cell transplantation
### An Example of the Importance of Personalized Medicine

<table>
<thead>
<tr>
<th></th>
<th>CoMMpassMMRF2172</th>
<th>CoMMpassMMRF2250</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>72</td>
<td>71</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td>Caucasian</td>
<td>Caucasian</td>
</tr>
<tr>
<td><strong>ISS stage</strong></td>
<td>II</td>
<td>II</td>
</tr>
<tr>
<td><strong>Baseline treatment</strong></td>
<td>VRD</td>
<td>VRD</td>
</tr>
<tr>
<td><strong>Cytogenetics</strong></td>
<td>t(4;14), del13</td>
<td>t(4;14), del13</td>
</tr>
<tr>
<td><strong>Time of progression</strong></td>
<td>11 months</td>
<td>36 months</td>
</tr>
<tr>
<td><strong>Overall survival</strong></td>
<td>1.6 years</td>
<td>6.3 years</td>
</tr>
</tbody>
</table>

- **Other genetic events**: 1q21, del17p + TP53 mut
- No 1q21, no 17p or TP53 mut
Multiple Myeloma Genomics/Precision Medicine at Sinai

Alessandro Lagana, PhD

Joel Dudley, PhD

Lagana A et al. Leukemia. 2018;32:120.


Actionable Alterations in Multiple Myeloma

Precision medicine efforts have identified molecular alterations for which there are drugs in the clinic.

These alterations may be the Achilles' heel of myeloma cells.
Innovative Study Designs: Shaping the Future of Cancer Research Toward Personalized Medicine

Umbrella/platform studies

Myeloma patients:
- No specific lesion
- Molecular lesion A
- Molecular lesion C

Basket/bucket studies

All patients with molecular lesion A:
- Patient with myeloma
- Patient with cancer X
- Patient with cancer Y
- Patient with cancer Z

MyDRUG Study

Functional high-risk patients

Profiling for alterations (NCT02884102)

- No detectable Actionable alterations
- RAF/RAF mutations
- CDK pathway-activating alterations
- FGFR3-activating alterations
- t(11;14)

- Daratumumab + IPd
- Cobimetinib + dex
- Abemaciclib + Dex
- Erdafitinib + Dex

- 2 cycles

*Assess single-agent activity after 2 cycles; after cycle 2, add backbone to single agent

Venetoclax + IPd
IPd control
Case study: man, age 59

**Treatments**

**1st Line**
- VRd/KRd induction, ASCT, Rev maintenance
- Best response: CR
- Progressed in 30 months (22 months post-ASCT/maint.)

**2nd Line**
- EPd
- Best response: MR
- Progressed in 4 months

**3rd Line**
- MyDRUG

---

**Response on MyDRUG**

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>M-Spike (g/dL)</th>
<th>kappa sFLC (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

**Genomics**
- Hyperdiploid, del13q, del1p, Myc ampl.
- NRAS Q61H, 56% allelic fraction

---

**Personalized Medicine Agents Under Clinical Investigation**

<table>
<thead>
<tr>
<th>Clinical phase</th>
<th>Novel agents</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Personalized medicine</td>
</tr>
<tr>
<td>Phase 3</td>
<td>Venetoclax*</td>
</tr>
<tr>
<td>Phase 1, 2</td>
<td>Abemaciclib*</td>
</tr>
<tr>
<td></td>
<td>Cobimetinib*</td>
</tr>
<tr>
<td></td>
<td>Dabrafenib</td>
</tr>
<tr>
<td></td>
<td>Enasidenib</td>
</tr>
<tr>
<td></td>
<td>Erdaftinib*</td>
</tr>
<tr>
<td></td>
<td>Idasanutlin</td>
</tr>
<tr>
<td></td>
<td>Trametinib</td>
</tr>
<tr>
<td></td>
<td>Vemurafenib</td>
</tr>
</tbody>
</table>

*Being studied in the MyDRUG trial
64-Year-Old With Relapsed Myeloma After CAR T With BRAF V600E

Venetoclax and t(11;14)

Venetoclax is a Bcl-2 inhibitor

- BCL2 inhibitor
- Induces cancer cell death
- t(11;14) multiple myeloma → ↑BCL2 and ↓MCL1
- t(11;14): first predictive marker in multiple myeloma, indicating susceptibility to BCL2 inhibition
**BRAF and MEK**

- **PET CT before and after 2 months of vemurafenib (a BRAF inhibitor) treatment in patient with BRAF V600E mutation**

  **Before**

  **After**

  **Significant improvement in bone lesions.**

  **A phase 2 study evaluating combined BRAF and MEK inhibition in relapsed/refractory multiple myeloma patients with activating BRAF V600E mutations**


- **12 patients treated with**
  - BRAFTOVI (encorafenib)
  - MEKTOVI (binimetinib)
- **83% of patients responded to treatment**
- **Common side effects included** blurred vision, macular edema, cramps, arthralgia, diarrhea, rash, and decreased left ventricular function
- **Serious side effects included** low blood counts and hypertension

---

**Venetoclax and t(11;14)**

- **Venetoclax bortezomib dexamethasone vs placebo bortezomib dexamethasone; 1–3 prior lines**
- **Median follow up 18.7 months**
- **PFS: all patients**
  - Venetoclax + Velcade-dex vs Placebo + Velcade-dex
  - HR 0.11 (95% CI 0.02-0.56); P = 0.0040
- **OS: all patients**
  - Venetoclax + Velcade-dex vs Placebo + Velcade-dex
  - HR 0.24 (95% CI 0.12-0.48); P < 0.0001

- **Venetoclax especially active in t(11;14) or BCL2-high MM**

Next-Generation BCL-2 Inhibitors

Lisaftoclax

- 30 patients
  - 22 RRMM, lisaftoclax + pom-dex
  - 3 RRMM, lisaftoclax + dara-Rd
  - 5 RR AL, lisaftoclax + pom-dex
  - Median 4 prior lines of therapy
  - 18 patients triple-class exposed

Safety
- TRAEs: neutropenia 16.7%, nausea 16.7%
- Grade ≥3 TRAEs: neutropenia 10%

ORR, lisaftoclax + pom-dex in RRMM: 67%

Sonrotoclax

- 19 patients
  - Median age 68 years
  - 21% R-ISS III; 16% high-risk cytogenetics
  - Median 4 prior lines of therapy
  - All patients received prior IMiD and prior PI

Safety
- Hematologic AEs 21%, infections 32%
- Grade ≥3 AEs 26%, SAEs 11%

The Road Ahead

- Comprehensive translational and clinical research to find the best combinations of targeted and immune therapies for each group of myeloma patient
- Deliver on the promise of personalized medicine for every patient
Personalized Medicine Summary

- Efforts are under way to better understand the nature of the disease and to provide patients with a more personalized approach to treatment.

- Genomic sequencing and data from myeloma patients are key to identifying subtype: our goal is to help individualize treatment for better outcomes.

- Participation in clinical studies to provide bone marrow and peripheral blood is paramount.

- Personalized medicine provides the right treatment at the right time for each myeloma patient.

Supportive Care

Leora A. Giacoia, MS, FNP-BC, ACHPN
Mount Sinai Hospital
New York, NY
Disclosures

- Leora A. Giacoia, MS, FNP-BC, ACHPN, has no relevant financial information to disclose.

Myeloma Affects Your…

- Blood counts
- Bones
- Kidney function
Multiple Myeloma Affects Your Bones

BONES
- Surrounding bone where myeloma cells grow is affected
- Myeloma cells activate bone destruction
- Cord compression, lesions, pathologic fracture, bone pain, hypercalcemia

Medications for Myeloma Bone Disease

Recommendation
- Vitamin D 600–1,000 IU daily
- Calcium 1,000–1,200 mg daily
- Monitor renal function

How they work
- Prevent bone disease from getting worse

Benefits
- Decrease pain and reduce skeletal-related fractures

Medication types
- Zometa* (zoledronic acid): 30-minute infusion
- Aredia* (pamidronate): 2-hour infusion
- Xgeva (denosumab): injection

Dosing
- Zometa: IV over 15 min every 3–4 weeks
- Aredia: IV over 2 hours every 3–4 weeks
- Xgeva: injection once every 4 weeks

Side effects
- Reduced kidney function
- Fracture of the femur
- Osteonecrosis of the jaw (ONJ)*

*Dose adjust for renal function
OC, osteoclast (inhibited, halting bone breakdown); BP, bisphosphonate
Recommendations for Reducing the Risk of ONJ and Infection

• Complete major dental work before beginning treatment for bone disease
• Practice good oral hygiene
• Schedule regular dental visits/antibiotic prophylaxis
• 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

Procedures for Bone Pain Radiation and Surgical Intervention

• 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)

Vertebroplasty  Kyphoplasty

• Destroys myeloma cells
• Stops bone destruction
• Pain control
• Targeted and localized therapy
• Can affect bone marrow function
• Can affect adjacent tissues
### Pain Management Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Effect/Warning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen (Tylenol)</td>
<td>High dosage can hurt your liver; caution with elevated liver function tests (LFTs)</td>
</tr>
<tr>
<td>NSAIDs (nonsteroidal anti-inflammatory drugs)</td>
<td>Prefer to avoid with multiple myeloma due to increased risk of kidney injury</td>
</tr>
<tr>
<td></td>
<td>Topical NSAIDS may be acceptable on case by case basis</td>
</tr>
<tr>
<td>Opioids</td>
<td>Potential for constipation, sedation, confusion, physiologic dependence</td>
</tr>
<tr>
<td>Corticosteroids (dexamethasone, prednisone)</td>
<td>Has myeloma-fighting effects. Can raise blood sugar and cause insomnia; short- and long-term effects</td>
</tr>
<tr>
<td>GABA analogues (gabapentin and Lyrica)</td>
<td>For use of neuropathic pain. Potential for drowsiness and dizziness</td>
</tr>
</tbody>
</table>

### Multiple Myeloma Affects Your…

**Blood**

- Myeloma is a cancer of the blood
- Myeloma crowds out normal blood cells
- Anemia, low platelets
- Weakness, fatigue, and infection

M proteins

Multiple myeloma cells
Effects of Myeloma: Low Blood Counts

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

- **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

**Low red blood cells (anemia)**

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

**Low white blood cells (leukopenia)**

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

**Low platelets (thrombocytopenia)**

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

Infection Can be Serious for Patients With Myeloma

- **General infection-prevention tips**
  - Good personal hygiene (skin, oral)
  - Environmental control (wash hands, avoid crowds and sick people, etc)
  - Growth factor (Neupogen, Neulasta)
  - IV gamma globulin infusion (Gamunex)
    - 4-hour infusion every 4 weeks IV
  - Immunizations
    - COVID-19 vaccination + booster(s)
    - Pneumococcal 20-valent conjugate vaccine
    - Seasonal inactivated influenza vaccine
    - Shingles vaccine: zoster vaccine recombinant, adjuvanted
  - Prophylactic medications (antibacterial, antiviral)
    - Valacyclovir/acyclovir
    - Hepatitis B virus nucleoside reverse transcriptase inhibitors
    - Bactrim, Mepron, or dapsone

- **Multiple myeloma**

  **Immune dysfunction**

  **Treatment**

  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.

Multiple Myeloma Affects Your... **Kidneys**

KIDNEYS
- Large amounts of M proteins can overwork or cause damage to the kidneys
- Weakness, fatigue, foamy urine

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 nephrotoxic substances
    - Nonsteroidal anti-inflammatory drugs (NSAIDs) such as Aleve, Advil/Motrin
    - CT contrast
  - Plasmapheresis
  - Treat other causes
  - Dialysis (severe)
# Side Effects and Management of Myeloma Therapies

<table>
<thead>
<tr>
<th>Immunomodulatory medications</th>
<th>Proteasome inhibitors</th>
<th>Monoclonal antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revlimid, Pomalyx</td>
<td>Velcade, Kyprolis, Ninlaro</td>
<td>Darzalex/Sarclisa, Empliciti</td>
</tr>
<tr>
<td>• Fatigue and weakness</td>
<td>• Peripheral neuropathy</td>
<td>• Infusion reactions</td>
</tr>
<tr>
<td>• Blood clots</td>
<td>• Low platelets</td>
<td>• Fatigue</td>
</tr>
<tr>
<td>• GI effects: diarrhea</td>
<td>• GI problems</td>
<td>• Low platelets</td>
</tr>
<tr>
<td>• Muscle cramping and back pain</td>
<td>• Styes</td>
<td>• Hepatitis B reactivation</td>
</tr>
<tr>
<td>• Drug rash</td>
<td>• Fatigue</td>
<td>• Upper respiratory tract infections</td>
</tr>
<tr>
<td>• Shortness of breath</td>
<td>• Rash</td>
<td></td>
</tr>
<tr>
<td>• Upper respiratory infections</td>
<td>• Hypertension</td>
<td></td>
</tr>
<tr>
<td>• Mental fogginess</td>
<td>• Cardiac toxicity</td>
<td></td>
</tr>
<tr>
<td>• Birth defects</td>
<td>• Shortness of breath</td>
<td></td>
</tr>
<tr>
<td>Management</td>
<td>Management</td>
<td>Management</td>
</tr>
<tr>
<td>Blood thinners for potential clots; tonic water/hydration for cramps; avoid dairy; fiber Imodium; cholestyramine for GI toxicities; sleep hygiene, regular exercise, dose reduction for fatigue</td>
<td>Dose or frequency decrease, vitamins and supplements, gabapentin, pregabalin, duloxetine, opioids, acupuncture, anticoagulants, antivirals, stop meds if needed</td>
<td>Premedication in anticipation of infusion reactions, post-infusion medications (dex), antivirals</td>
</tr>
</tbody>
</table>

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# Side Effects of Steroids (Dexamethasone)

<table>
<thead>
<tr>
<th>Insomnia</th>
<th>Fluid retention</th>
<th>Mood changes</th>
<th>Dyspepsia-heartburn</th>
<th>Elevation in glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Healthy sleep habits</td>
<td>• Monitor for swelling of extremities and “puffy” face</td>
<td>• Irritable, anxiety, difficulty concentrating</td>
<td>• Dietary modifications (avoid spicy, acidic foods)</td>
<td>• Monitor glucose and refer/treat as needed</td>
</tr>
<tr>
<td>• Timing</td>
<td>• Monitor weight changes/gain</td>
<td>• Severe cases → depression, euphoria</td>
<td>• Avoid NSAIDs</td>
<td></td>
</tr>
<tr>
<td>• Medication to assist with sleeping as needed</td>
<td></td>
<td></td>
<td>• Acid-blocking medications</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Take steroid with food; use enteric-coated aspirin with food</td>
<td></td>
</tr>
</tbody>
</table>

---
Bispecific Antibodies

Tecvayli, Talvey, Elrexfio
- Tecvayli (teclistamab) and Elrexfio (elranatamab)
  - BCMA target: CRS, neurotoxicities/ICANS, infections, decreased blood counts, injection-related reactions
- Talvey (talquetamab)
  - GPRC5D target: CRS, neurotoxicities/ICANS, neutropenia, hypogammaglobulinemia, taste changes, oral and skin effects, nail changes

Management
- Patients receive step-up dosing and are monitored in an inpatient setting
- CRS is managed with tocilizumab
- Neurological toxicities managed with anakinra and/or steroids
- Supportive care (oral, skin, and nail care)
- Injection reactions are managed with oral antihistamines and topical steroids
- Infection prevention!

Chimeric Antigen Receptor T Cell (CAR T)
- Cytokine release syndrome (CRS)
- Neurotoxicity/ICANS
  - Caregiver role
- Low blood counts
- Infection risk
  - Prophylactic medications
    - Levaquin
    - Mepron
    - Bactrim

How CAR T-cell therapy is used to treat cancer
- Healthcare providers collect blood to obtain T-cells
- Providers return remaining blood
- New CAR T-cells introduced into bloodstream
- Chemotherapy is given before CAR T-cell therapy
- T-cells are genetically altered to have special receptors called chimeric antigen receptors (CAR)
- Millions of CAR T-cells are grown
- T-cells are separated and removed
- T-cells are genetically altered to have special receptors called chimeric antigen receptors (CAR)
- Receptor
- CAR T-cells
CRS With Bispecifics and CAR T: Early Recognition and Treatment Is Key

- **Respiratory**
  - Difficulty breathing
  - Shortness of breath

- **Neurologic**
  - Tremors
  - Altered wakefulness
  - Difficulty speaking

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

- **Gastrointestinal**
  - Nausea
  - Vomiting
  - Diarrhea

- **Musculoskeletal**
  - Weakness

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

- **Hematologic**
  - Anemia
  - Thrombocytopenia
  - Neutropenia

- **Constitutional**
  - Fever
  - Fatigue
  - Headache

**Mitigation and monitoring for CRS**

- Step-up dosing with hospitalization for monitoring
- Frequent vital signs
- Rule out infection
- Laboratory monitoring
- Early intervention with tocilizumab

---

**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.

Questions?
Patient Experience
Roger Rawlings

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 (ET)</th>
<th>Speakers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autologous Stem Cell Transplantation FAQs</td>
<td>Monday, May 6, 2024 4:00 PM</td>
<td>Amrita Krishnan, MD Cherry Lou Rudge, NP-C Todd Kennedy</td>
</tr>
<tr>
<td>Understanding Your Lab Report Webinar</td>
<td>Monday, May 13, 2024 3:30 PM</td>
<td>Craig Emmitt Cole, MD Amy Blake, NP-C</td>
</tr>
<tr>
<td>Understanding Lab Report FAQs Livestream</td>
<td>Friday, June 7, 2024 3:00 PM</td>
<td>Joshua Richter, MD Michelle Lyn, NP</td>
</tr>
<tr>
<td>Patient Summit Hybrid</td>
<td>Saturday, August 17, 2024 Los Angeles, California</td>
<td>Amrita Krishnan, MD—Host</td>
</tr>
</tbody>
</table>

For more information or to register, visit [themmrf.org/educational-resources](http://themmrf.org/educational-resources)

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### MMRF Patient Resources

**MMRF Patient Navigation Center**

- **Expect Guidance.**
- **Information & Resources**
- **Expert Advice**
- **Support**

**THE RIGHT TRACK**

- **Right Team**
  - Healthcare professionals and centers who have oncology-certified training, expertise, and experience.
- **Right Tests**
  - Genetic information, lab results, and physician guidelines to make the right treatment decisions.
- **Right Treatment**
  - Help you plan the best care and treatment plan that’s right for you.

Contact the Patient Navigation Center Today

- **Looking for guidance?**
- **Learn more here.**
  - **Monday - Friday:** 9:00 a.m. – 5:00 p.m. (ET)
  - **Phone:** 1-888-MMRF-NAV (667-3628)
  - **Online:** [themmrf.org/PatientNavigationCenter](http://themmrf.org/PatientNavigationCenter)
  - **Email:** patientnavigation@themmrf.org

Supported by:
- Immunocore
- Genentech
- Amgen
- and others.
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.

Join the MMRF Community!

**National Walk/Run Program**
- Atlanta | 10.26.24
- Boston | 10.12.24
- Chicago | 9.8.24
- Dallas | 11.16.24
- Houston | 11.23.24
- Los Angeles | 8.17.24
- National Virtual | 12.14.24
- New York City | 10.5.24
- Philadelphia | 10.19.24
- San Francisco | 8.24.24
- Scottsdale | 12.7.24
- Southeast Michigan | TBD
- Tampa | TBD
- Washington, D.C. | 9.28.24

**Other MMRF Event Programs**
- Moving Mountains for Multiple Myeloma
- Half and Full Marathons
- Bike/Road to Victories
- Create Your Own Fundraiser
Need help with travel to a clinical study?

• The MMRF has partnered with the Lazarex Cancer Foundation to help provide more equitable access to clinical studies for multiple myeloma patients

• This partnership is one facet of the MMRF’s commitment to improve diversity and representation in myeloma clinical trials

• MMRF has provided $100,000 over 2 years to Lazarex to fund travel, lodging, and food for patients (and a travel companion) so that they can participate in clinical studies that are appropriate for them

• Patients are funded according to income guidelines and will be reimbursed for allowed expenses

• For more information on this program and to be connected with Lazarex, call our Patient Navigation Center at 1-888-841-6673