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

Clarence Adoo, MD  
Medical Oncology and Hematology  
Arizona Center for Cancer Care, Honor Health  
Scottsdale, Arizona

P. Leif Bergsagel, MD  
Mayo Clinic College of Medicine  
Scottsdale, Arizona

William Brown  
Arizona Myeloma Network  
Scottsdale, Arizona

Suzanne Hyde, MSW, LCSW  
Licensed Clinical Social Worker  
Scottsdale, Arizona

Barbara Kavanagh, MSW  
Arizona Myeloma Network  
Glendale, Arizona

Jonathan Keats, PhD  
Translational Genomics Research Institute  
Phoenix, Arizona

Joan Koerber-Walker  
Arizona Bioindustry Association, Inc. (AzBio)  
Chandler, Arizona

Paul Long  
Navajo Nation Healer and Health Disparities Liaison  
Navajo Nation, Arizona

Sumit Madan, MD  
Banner MD Anderson Cancer Center  
Gilbert, Arizona

Jonathan Keats, PhD  
Translational Genomics Research Institute  
Phoenix, Arizona

Joan Koerber-Walker  
Arizona Bioindustry Association, Inc. (AzBio)  
Chandler, Arizona

Paul Long  
Navajo Nation Healer and Health Disparities Liaison  
Navajo Nation, Arizona

Sumit Madan, MD  
Banner MD Anderson Cancer Center  
Gilbert, Arizona
Summit Agenda

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<td>Welcome</td>
<td>Joan Koerber-Walker, CEO, AzBio</td>
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<td>9:45 – 10:15 AM</td>
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<td>P. Leif Bergsagel, MD</td>
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<td>High-Dose Chemotherapy and Stem Cell Transplantation, Maintenance Therapy, and Treatment Goals</td>
<td>Clarence Adoo, MD</td>
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<td>Relapsed/Refractory Multiple Myeloma</td>
<td>Sumit Madan, MD</td>
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<td>Arizona Myeloma Network Virtual Cancer Caregiver’s Education Program</td>
<td>William Brown, Suzanne Hyde, MSW, LCSW</td>
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<td>2:30 – 3:30 PM</td>
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<td>Panel</td>
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<tr>
<td>3:30 – 3:45 PM</td>
<td>Closing Remarks</td>
<td>Barbara and Jack Kavanagh, Mary DeRome, MS</td>
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</table>

MMRF Introduction

Mary DeRome, MS
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 and CureCloud Research Study

MyDRUG Trial

Functional high-risk patients
Profiling for alterations (NCT02884102)

- No detectable actionable alterations
  - Daratumumab + IPd
- RAF/RAS mutations
  - Cobimetinib + dex
  - Abemaciclib + IPd*
- CDK pathway–activating alterations
  - Cobimetinib + IPd*
- FGFR3–activating alterations
  - Erdafitinib + IPd*
- t(11;14)
  - 2:1
  - Venetoclax + IPd
  - IPd control

*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 with the results placed in the CureCloud along with their clinical information.

- Patients can sign up for CureCloud from home and will soon 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 that 15 sites will be approved for on-site enrollment.

- For now, patients will still provide their blood samples 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. Sign up on the MMRF CureCloud website or in person at a CureCloud participating clinic and see if you are eligible.
2. Convenient at-home blood test. A medical professional will come to you.
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%

941 Patients enrolled

685 Patient samples sequenced

247 Patient health records pulled
Welcome!

Joan Koerber-Walker
Arizona Bioindustry Association, Inc.
Chandler, Arizona
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.
Question

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

Question

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

Is this your first Summit?
A. Yes
B. No

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.
Newly Diagnosed Multiple Myeloma: Diagnosis and Induction Therapy

P. Leif Bergsagel, MD
Mayo Clinic College of Medicine
Scottsdale, Arizona

Normal Bone Marrow

Normal plasma cells
Light chain (kappa $\kappa$ or lambda $\lambda$)
Heavy chains (IgG, IgA, IgM, IgD, IgE)
Antibodies
Bone
Bone marrow
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

- **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

M proteins

Multiple myeloma cells

MM, multiple myeloma
Multiple Myeloma Affects Your Bones, Blood, and 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

- 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

MMRF. Multiple myeloma symptoms, side effects, and complications. themmrf.org/multiple-myeloma/symptoms-side-effects-and-complications/.
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)

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**

- **Available resources**
  - Connect with a myeloma specialist—a doctor who diagnoses and treats a high number of myeloma patients
  - Seek a second opinion at any point in your journey

- **MMRF’s online myeloma treatment locator:** [themmrf.org/resources/find-a-treatment-center](http://themmrf.org/resources/find-a-treatment-center)

- **Contact the MMRF Patient Navigation Center:** [themmrf.org/resources/patient-navigation-center](http://themmrf.org/resources/patient-navigation-center)
  - 1-888-841-MMRF (6673)
The Right Tests

Common laboratory tests conducted

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

**Urine tests**
- Urine protein electrophoresis 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

Determines how advanced the myeloma is and identifies the myeloma subtype

Learn Your Labs!

**Blood Tests**

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

Urine tests

• Detect Bence Jones proteins (otherwise known as myeloma light chains)

UPEP

• Determine the presence and levels of M protein and Bence Jones protein

24-hr urine analysis

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

- **Bone marrow**
  - Hip bone
  - Skin

- **Chromosome**

- **Myeloma cell**

- **DNA**

- **Karyotyping**

- **FISH (fluorescence in situ hybridization)**

- **Genomic sequencing**
Putting the Results Together

Staging, prognosis, and risk assessment

Multiple Myeloma Prognosis and Risk

<table>
<thead>
<tr>
<th>Revised International Staging System (R-ISS)</th>
<th>Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSMART) Consensus Guidelines</th>
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<tbody>
<tr>
<td><strong>R-ISS stage</strong></td>
<td><strong>High risk</strong></td>
</tr>
<tr>
<td>I</td>
<td>• High-risk genetic abnormalities</td>
</tr>
<tr>
<td></td>
<td>• t(4;14)</td>
</tr>
<tr>
<td></td>
<td>• t(14;16)</td>
</tr>
<tr>
<td></td>
<td>• t(14;20)</td>
</tr>
<tr>
<td></td>
<td>• del 17p</td>
</tr>
<tr>
<td></td>
<td>• p53 mutation</td>
</tr>
<tr>
<td></td>
<td>• gain 1q</td>
</tr>
<tr>
<td></td>
<td>• R-ISS Stage 3</td>
</tr>
<tr>
<td></td>
<td>• High plasma cell S phase</td>
</tr>
<tr>
<td></td>
<td>• GEP: high-risk signature</td>
</tr>
<tr>
<td>I</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td></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>
<tr>
<td>*High-risk chromosomal abnormality (CA) by FISH: del(17p) and/or t(4;14) and/or t(14;16)</td>
<td></td>
</tr>
</tbody>
</table>

**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
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

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

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*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

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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

<table>
<thead>
<tr>
<th>Year</th>
<th>Percentage</th>
<th>Available Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1975</td>
<td>26.5%</td>
<td>Chemotherapy + dexamethasone + stem cell transplantation</td>
</tr>
<tr>
<td>1985</td>
<td>27.4%</td>
<td>Velcade (bortezomib), Revlimid (lenalidomide)</td>
</tr>
<tr>
<td>1995</td>
<td>33.5%</td>
<td>Kyprolis (carfilzomib), Pomalyx (pomalidomide)</td>
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<tr>
<td>2005</td>
<td>47.2%</td>
<td>Ninlaro (ixazomib), Empliciti (elotuzumab)</td>
</tr>
<tr>
<td>2013</td>
<td>56.9%</td>
<td>Darzalex (daratumumab), Xpovio (selinexor)</td>
</tr>
<tr>
<td>2014 and beyond</td>
<td></td>
<td>Sarclisa (isatuximab), Blenrep (belantamab mafodotin)</td>
</tr>
</tbody>
</table>

Available treatments:
- Ninlaro (ixazomib)
- Empliciti (elotuzumab)
- Darzalex (daratumumab)
- Xpovio (selinexor)
- Sarclisa (isatuximab)
- Blenrep (belantamab mafodotin)
- Abecma (idecabtagene vicleucel)
- Carvykti (ciltaclabtagene autoleucel)
- Tecvayli (teclistamab)
Current Treatment Paradigm for Newly Diagnosed Multiple Myeloma

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

No

• Any of the regimens used for transplant candidates*
  • Clinical trial
  • 2-drug regimen may be considered for frail patients

Supportive care

*In certain circumstances, consideration for a tandem transplant
Induction Therapy Regimens

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

**Recommended**
- Darzalex-Revlimid-Velcade-dex (D-RVd)
- Kyprolis-Revlimid-dex (KRd)
- Ninlaro-Revlimid-dex (IRd)
- Velcade-Thalomid-dex (VTd)*
- Velcade-Cytoxan-dex (VCd)
- Velcade-Doxil-dex (VDd)
- Kyprolis-Cytoxan-dex (KCd)
- Revlimid-Cytoxan-dex (RCd)
- Darzalex-Velcade-Thalomid-dex (D-VTd)
- Darzalex-Kyprolis-Revlimid-dex (D-KRd)
- Ninlaro-Revlimid-dex (IRd)
- Ninlaro-Cytoxan-dex (ICd)
- VTD-PACE

**Certain circumstances**
- Velcade-dex (Vd)*
- Revlimid-dex (Rd)*
- Velcade-Cytoxan-dex (VCd)
- Velcade-Cytoxan-dex (RCd)
- Kyprolis-Cytoxan-dex (KCd)
- Velcade-Thalomid-dex (VTd)-lite

*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 cycles
   - Stem cell mobilization
     - Neupogen, Neulasta, Leukine, Cytoxan, Mozobil
2. **Collection of stem cells from the bloodstream**
3. **Freezing of stem cells**
4. **High-dose chemotherapy**
   - Melphalan
     - Alkeran, Evomea
5. **Thawing and infusion of stem cells**
   - Day 0
6. **Recovery**
   - 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 eligible | • Revlimid* | • Ninlaro  
|                     |           | • Velcade  
|                     |           | • Darzalex  
| Transplant ineligible | • Revlimid* | • Ninlaro  
|                              |           | • Velcade  
|                              |           | • Velcade-Revlimid ± dex  
|                              |           | • Kyprolis-Revlimid  
| Transplant ineligible | • Velcade-Revlimid | • Velcade-Revlimid |

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


Measuring Response to Therapy

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

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!
Please take a moment to answer two questions about this presentation.
Overview of Treatment Approach for Active Multiple Myeloma

Is the patient a candidate for autologous stem cell transplantation?

Yes
- 3–4 treatment cycles
- 3 or 4 drugs

Stem cell collection and storage

High-dose melphalan + stem cell transplant*

No
- 6 or more treatment cycles
- 3 or 4 drugs.

*In certain circumstances, consideration for a tandem transplant

Maintenance treatment

High-Dose Chemotherapy and Stem Cell Transplantation

• Remission lasts longer
• Can be done early on or later (or both)
• Most patients will qualify,
  – including older patients,
  – patients with kidney disease
  – Insurance coverage.
What does transplant mean?

Understanding the basics of autologous stem cell transplantation

- Blood-forming cells 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 like hair follicles and taste buds recover.

Autologous Stem Cell Transplantation

1. Induction therapy
   ≥2 cycles
   Stem cell mobilization
   • Neupogen, Neulasta, Leukine, Cytoxan, Mozobil

2. Collection of stem cells from the bloodstream
   -2 to -3 weeks*

3. Freezing of stem cells

4. High-dose chemotherapy
   Melphalan
   • Alkeran, Evomelea

5. Thawing and infusion of stem cells
   Day 0

6. Recovery
   Days +1 to +100†

*The weeks leading up to the transplant; †The days after the transplant.
Side Effects of High-Dose Chemotherapy

- **Fatigue**
  - Expected
  - May last 1–3 months

- **Nausea & vomiting**
  - 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

- **Diarrhea**
  - 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 cells count- risk for infection
  - Hemoglobin drop. Fatigue
  - Platelet count drop bleeding risk
  - Blood transfusion
  - Platelet transfusion
  - Antibiotics
  - WBC and platelets recover in 2 weeks

---

Transplant or 3-drug treatment?

**Comparative trial of Transplant vs continued 3 drug treatment: DETERMINATION Trial**

<table>
<thead>
<tr>
<th>Newly diagnosed myeloma patients</th>
<th>EARLY TRANSPLANT ARM</th>
<th>LATE TRANSPLANT ARM</th>
</tr>
</thead>
<tbody>
<tr>
<td>365 patients</td>
<td>Revlimid + Velcade + dex (RVd)</td>
<td>Revlimid + Velcade + dex (RVd)</td>
</tr>
<tr>
<td>357 patients</td>
<td>Induction</td>
<td>Stem cell collection</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ASCT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RVd</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Consolidation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RVd</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maintenance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R</td>
</tr>
</tbody>
</table>

**The study enrolled 19% Black myeloma patients.**

Comparative Study of Early Transplant vs continuation of Bortezomib, Lenalidomide and dexamethasone.

Progression-Free Survival (PFS)

Early transplant (median PFS, 67.5 mos)

3-drug treatment (median PFS, 46.2 mos)

PFS for early transplant: 5 and one half years
PFS for 3 drug treatment: 4 years.

Length of overall survival was same.

Transplant extended time to progression by 20 months


Comparative Study of Transplantation in Patients With Newly Diagnosed Multiple Myeloma

Best Response to Treatment and Duration of Response

<table>
<thead>
<tr>
<th>Response to Treatment</th>
<th>RVd alone (late transplant)</th>
<th>RVd + ASCT (early transplant)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥PR</td>
<td>97.5</td>
<td>95</td>
<td>0.55</td>
</tr>
<tr>
<td>≥VGPR</td>
<td>82.7</td>
<td>79.6</td>
<td>0.99</td>
</tr>
<tr>
<td>≥CR</td>
<td>46.8</td>
<td>42</td>
<td>0.99</td>
</tr>
<tr>
<td>Duration of response</td>
<td>38.9</td>
<td>56.4</td>
<td>0.003*</td>
</tr>
<tr>
<td>5-year duration of ≥CR, %</td>
<td>52.9</td>
<td>60.6</td>
<td>0.698</td>
</tr>
</tbody>
</table>

Phase 3 Study of Early vs Late Autologous Stem Cell Transplantation in Patients With Newly Diagnosed Multiple Myeloma

<table>
<thead>
<tr>
<th>Side effect, %</th>
<th>RVd-alone (N=357)</th>
<th>RVd+ASCT (N=365)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>78.2</td>
<td>94.2</td>
</tr>
<tr>
<td>Blood count problems</td>
<td>60.5</td>
<td>89.9</td>
</tr>
<tr>
<td>Fatal side effects</td>
<td>0.3</td>
<td>1.6 *</td>
</tr>
<tr>
<td>Very low white cell count</td>
<td>42.6</td>
<td>86.3</td>
</tr>
<tr>
<td>Low platelet count</td>
<td>19.9</td>
<td>82.7</td>
</tr>
<tr>
<td>Low white cell count</td>
<td>19.6</td>
<td>39.7</td>
</tr>
<tr>
<td>Anemia</td>
<td>18.2</td>
<td>29.6</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>9.0</td>
<td>10.1</td>
</tr>
<tr>
<td>Infections with low WBC</td>
<td>4.2</td>
<td>9.0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3.9</td>
<td>4.9</td>
</tr>
<tr>
<td>Nausea</td>
<td>0.6</td>
<td>6.6</td>
</tr>
<tr>
<td>Mouth sores</td>
<td>0</td>
<td>5.2</td>
</tr>
<tr>
<td>Fatigue</td>
<td>2.8</td>
<td>6.0</td>
</tr>
<tr>
<td>Fever</td>
<td>2.0</td>
<td>5.2</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>5.0</td>
<td>9.0</td>
</tr>
<tr>
<td>Low phosphate</td>
<td>9.5</td>
<td>8.2</td>
</tr>
<tr>
<td>Numbness, tingling nerve</td>
<td>5.6</td>
<td>7.1</td>
</tr>
</tbody>
</table>

Severe side effects were more common with transplant.

*Includes one death related to ASCT


Autologous Stem Cell Transplantation in Patients With Newly Diagnosed Multiple Myeloma

Quality of Life

Phase 3 Study of Early vs Late Autologous Stem Cell Transplantation in Patients With Newly Diagnosed Multiple Myeloma

### Second Cancers

- 5-year cumulative incidence of SPMs (RVd-alone vs RVd+ASCT):
  - All: 9.7% vs 10.8%
  - Invasive: 4.9% vs 6.5%
  - Hematologic: 1.59% vs 3.52%

### Transplant

- RVd+ASCT (N=365)
- RVd-alone (N=357)

#### Another cancer, %

<table>
<thead>
<tr>
<th></th>
<th>RVd-alone (N=357)</th>
<th>Transplant RVd+ASCT (N=365)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>10.4</td>
<td>10.7</td>
</tr>
<tr>
<td>Any invasive SPM</td>
<td>5.3</td>
<td>6.8</td>
</tr>
<tr>
<td>Any hematologic SPM</td>
<td>2.5</td>
<td>3.6</td>
</tr>
<tr>
<td>ALL, n</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>AML/MDS, n</td>
<td>0*</td>
<td>10*</td>
</tr>
<tr>
<td>CLL/CML, n</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Any solid tumor SPM</td>
<td>3.4</td>
<td>3.3</td>
</tr>
<tr>
<td>Any non-invasive solid tumor SPM</td>
<td>0</td>
<td>0.5</td>
</tr>
<tr>
<td>Any non-melanoma skin cancer</td>
<td>5.9</td>
<td>4.1</td>
</tr>
</tbody>
</table>

*S* = 0.002

---

**Subsequent Therapy and Rate of ASCT in RVD-Alone Arm (Late ASCT)**

### Subsequent therapy in patients off protocol therapy, %

<table>
<thead>
<tr>
<th></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>79.6</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>0.5</td>
</tr>
</tbody>
</table>

*Including IMiDs, PiTs, mAbs, HDACi (panobinostat), ASCT, chemotherapy, 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 Delayed Transplant

#### Pros

**Early ASCT**
- Youngest you are going to be
- Healthiest you are going to be
- Allows for fewer cycles of initial treatment
- Deeper and more durable response

**Delayed ASCT**
- Conserve quality of life in the early part of disease journey
- PFS may be shorter with delayed (vs early) hematopoietic cell transplantation (HCT), but OS is the same
- Better drugs or treatments could be available later on

#### Cons

**Early ASCT**
- 20% of patients still relapse within 2 years
- 1% risk of serious life-threatening complications
- 3 months of full clinical recovery
- No proven impact on overall survival

**Delayed ASCT**
- 60%–70% of patients will relapse and may need it as salvage
- Not all patients relapsing are able to undergo salvage HCT
- May need longer duration of chemotherapy to replace its effects

---

### What is maintenance therapy?

- A prolonged, and often low-dose, treatment given to myeloma patients after achieving a desired response to initial therapy
- To prevent disease progression for as long as possible while maintaining favorable quality of life
- To deepen responses by reducing minimal residual disease (MRD) or maintaining the response achieved, reduce the risk of relapse, and prolong survival
Successful Maintenance Therapy Must...

1. Be convenient
2. Be safe and well tolerated long term
3. Not interfere with the use of other future treatments
   Not obscure disease measurement

Continuous or Maintenance Therapy Options

<table>
<thead>
<tr>
<th>Transplant status</th>
<th>Preferred</th>
<th>Recommended</th>
<th>Certain circumstances</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transplant eligible</td>
<td>Revlimid*</td>
<td>Velcade, Darzalex, Ninlaro</td>
<td>Velcade-Revlimid ± dex, Kyprolis-Revlimid</td>
</tr>
<tr>
<td>Transplant ineligible</td>
<td>Revlimid*</td>
<td>Velcade, Ninlaro</td>
<td>Velcade-Revlimid</td>
</tr>
</tbody>
</table>

*Category 1 recommendation. Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate. National Comprehensive Cancer Network Guidelines Version 2.2023. Multiple Myeloma.
**Revlimid Maintenance Therapy: Improves Depth of Response**

**Disease Response**

![Graph showing disease response](image)


**At maximal response during or after maintenance treatment with Revlimid**

**Revlimid Maintenance Duration**

**STAMINA Trial (BMT-CTN0702)**

![Diagram of STAMINA trial](image)

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

MEL, melphalan; RVD, Revlimid-Velcade-dex; REV, Revlimid

**Revlimid Maintenance: Cumulative Incidence of Second Primary Malignancies**

**Hematologic**

<table>
<thead>
<tr>
<th>Time to Hematologic SPM Onset, mos</th>
<th>Lenalidomide</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulative Incidence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>0.2</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>0.4</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>0.6</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>0.8</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>1.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

HR (95% CI): 2.03 (1.14–3.61)  
\( P = 0.015 \)

**Solid Tumor**

<table>
<thead>
<tr>
<th>Time to Solid Tumor SPM Onset, mos</th>
<th>Lenalidomide</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulative Incidence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>0.2</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>0.4</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>0.6</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>0.8</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>1.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

HR (95% CI): 1.71 (1.04–2.79)  
\( P = 0.032 \)

---

**Minimal Residual Disease Negativity as a Multiple Myeloma Treatment Goal**
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

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

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

- The presence of small amounts of myeloma cells in the body after treatment
- MRD tests can detect at least 1 cell in 100,000

Why do we need to MRD?

- With new and more effective treatments, more patients achieve CR
- However, achieving a CR does not necessarily mean that all myeloma cells are gone
- Routine blood tests are not sensitive enough to detect these remaining cells
How is MRD measured?

Right now, measurement of MRD depends on counting cells in bone marrow samples.

What about other areas of the body?

Imaging (with PET/CT scan) is also required to detect residual disease outside of the bone marrow.
Why is it important to achieve MRD negativity?

Patients who achieve MRD negativity following treatment experience longer remission than those who are still MRD positive after treatment.

MRD by next-generation sequencing (sensitivity $1 \times 10^{-5}$)

Patients Who Achieve MRD Negativity Following Treatment Live Longer Than Those Who Are MRD Positive

Key points from 14 studies analyzed*

- Being MRD negative is correlated with longer progression-free and overall survival.
- MRD negativity may not (?) carry the same weight in patients with standard-risk vs high-risk disease.

*5 trials included stem cell transplantation/10 studies included maintenance

**MRD Is Important for Clinical Care and New Drug Registration**

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

- A surrogate for patient outcome in clinical trials

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

- Many clinical trials are using MRD-driven strategies

- Accelerate innovative trials leading to regulatory approval

---

**Summary**

**Autologous Stem Cell Transplantation**

- ASCT remains the standard of care for frontline therapy of myeloma; its safety has been established and it induces long remissions.

**Continuous or Maintenance Therapy**

- The body of evidence from phase 3 trials indicates that maintenance (or “continuous”) therapy improves PFS and likely OS and should be given until progression.
- Most patients should receive maintenance who are thought to be Revlimid responsive and able to tolerate the side effects.
- For patients who are unable to tolerate Revlimid there are other agents such as Ninlaro, Kyprolis, and Darzalex that are effective, but they are not yet FDA-approved for use as maintenance. Several clinical trials are under way.

**Minimal Residual Disease**

- 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 has been associated with longer progression-free and overall survival to predict lower risk of progression. Modern combination therapies show increasingly higher MRD negativity rate.
- MRD response–directed therapy has been applied in more and more clinical trials to explore how to guide treatment decisions in myeloma.
- MRD is also useful as an end point in clinical trials helping to expedite new drug approval in myeloma.
Please take a moment to answer two questions about this presentation.
Effects of Myeloma

- Low blood counts
- Bone damage
- Decreased kidney function

Bone damage

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

Fracture caused by lesion
Lesions
Bone Strengthening Agents for Myeloma Bone Disease

**How they work**
- Prevent bone disease from getting worse

**Benefits**
- Decrease pain and reduce skeletal-related fractures

**Medication types**
- Zometa (zoledronic acid): 15-minute infusion
- Aredia (pamidronate): 2-hour infusion
- Xgeva (denosumab): injection

**Dosing**
- Zometa/Aredia: IV infusion in doctor’s office every 3–4 weeks
- Xgeva: injection once every 4 weeks

**Side effects**
- 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)

Vertebroplasty  Kyphoplasty

Radiation Therapy for Pain Management
### Pain Management Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen (Tylenol)</td>
<td>Will not hurt your kidneys; high dosage can hurt your liver</td>
</tr>
<tr>
<td>NSAIDs (nonsteroidal</td>
<td>Prefer to avoid with MM due to increased risk of kidney injury</td>
</tr>
<tr>
<td>anti-inflammatory drugs)</td>
<td></td>
</tr>
<tr>
<td>Opioids</td>
<td>Will not hurt kidneys, liver, stomach; potential for constipation, sedation, confusion,</td>
</tr>
<tr>
<td></td>
<td>dependence, addiction</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Will not hurt kidneys; can raise blood sugar; short- and long-term effects</td>
</tr>
<tr>
<td>(dexamethasone, prednisone)</td>
<td></td>
</tr>
<tr>
<td>Gabapentin</td>
<td></td>
</tr>
</tbody>
</table>

### 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

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

**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**
- Low red blood cells (anemia): Identify and treat causes other than myeloma; supplements; medications to increase number of red blood cells; blood transfusions
- Low white blood cells (leukopenia): Medications to stimulate production of white blood cells; antibiotics; antifungal medications; infection prevention
- Low platelets (thrombocytopenia): 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

- Myeloma patients are at increased risk of developing blood clots
- Several myeloma 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 myeloma or its treatments
- Cardiovascular side effects (including high blood pressure or congestive heart failure) can occur with some myeloma drugs
- Commonly used myeloma drugs may cause a variety of gastrointestinal problems, such as constipation, diarrhea, and nausea/vomiting
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.

Class: Proteasome Inhibitors
Side Effects and Management

Velcade
- PN (numbness, tingling, burning sensations and/or pain due to nerve damage)
- Low platelets
- GI problems: nausea, diarrhea, vomiting, loss of appetite
- Fatigue
- Rash

Kyprolis
- Fatigue
- Anemia
- Nausea
- Low platelets
- Shortness of breath
- Diarrhea
- Fever
- Hypertension
- Cardiac toxicity

Ninlaro
- Diarrhea
- Constipation
- Low platelets
- PN
- Nausea
- Peripheral edema
- Vomiting
- Back pain

Management
- PN occurs less often when subcutaneous or once weekly dosing is used for Velcade
- Other PN prevention:
  - Vitamins and other supplements*
  - Certain medications such as gabapentin, pregabalin, duloxetine, opioids
  - Acupuncture
  - Physical therapy
  - Shingles-prevention pills
  - Blood thinners

*Do not take any supplements without consulting with your doctor.
PN, peripheral neuropathy; GI, gastrointestinal
Class: Monoclonal Antibodies
Side Effects and Management

**Empliciti**
- Low blood counts
- Infusion reactions

**Darzalex*/Sarclisa**
- Infusion reactions
- Fatigue
- Upper respiratory tract infection

*Now approved as subcutaneous injection with fewer side effects.

**Management**
- Premedication in anticipation of infusion reactions
- Post-infusion medications (Darzalex)

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

---

**CRS With Bispecifics Severity Is Typically Mild: Early Recognition and Treatment Is Key**

**Mitigation and monitoring for 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 |
| HEPATIC     | • Altered liver function tests in the blood |
| RENAL       | • ↑ Serum creatinine | • Renal insufficiency |
| HEMATOLOGIC | • Anemia | • Thrombocytopenia | • Neutropenia |
| CONSTITUTIONAL | • Fever | • Fatigue | • Headache |
| NEUROLOGIC  | • Tremors | • Altered wakefulness | • Difficulty speaking |
| CARDIOVASCULAR | • Rapid heart rate | • Low blood pressure | • Arrhythmias |
| GASTROINTESTINAL | • Nausea | • Vomiting | • Diarrhea |
| MUSCULOSKELETAL | • Weakness |

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


Infection Can be Serious for Patients With Myeloma

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)

As recommended by your health care team


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
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.

Personalized Medicine

Jonathan Keats, PhD
Translational Genomics Research Institute
Phoenix, Arizona
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 needed to address high-risk patients

What We Need

• Evolving definitions of high-risk, beyond historic markers such as translocation 4;14, 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>Age</td>
<td>72</td>
<td>71</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Caucasian</td>
<td>Caucasian</td>
</tr>
<tr>
<td>ISS stage</td>
<td>II</td>
<td>II</td>
</tr>
<tr>
<td>Baseline treatment</td>
<td>VRD</td>
<td>VRD</td>
</tr>
<tr>
<td>Cytogenetics</td>
<td>t(4;14), del13</td>
<td>t(4;14), del13</td>
</tr>
<tr>
<td>Time of progression</td>
<td>11 months</td>
<td>36 months</td>
</tr>
<tr>
<td>Overall Survival</td>
<td>1.6 years</td>
<td>6.3 years</td>
</tr>
</tbody>
</table>

How did their clinical courses compare?

[Graphs showing treatment lines and quantities for MMRF_2172 and MMRF_2250]
How do the patients’ tumors compare?

An Example of the Importance of Personalized Medicine

<table>
<thead>
<tr>
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<th>CoMMpass MMRF2172</th>
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<tr>
<td><strong>Overall Survival</strong></td>
<td>1.6 years</td>
<td>6.3 years</td>
</tr>
<tr>
<td><strong>Other Genetic Events</strong></td>
<td>1q21, del17p + TP53 mut</td>
<td>No 1q21, No 17p or TP53 mut</td>
</tr>
</tbody>
</table>
**Actionable Alterations in MM**

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.**

<table>
<thead>
<tr>
<th>KRAS and NRAS</th>
<th>40%</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDH1/2</td>
<td>(5%)</td>
</tr>
<tr>
<td>MYD88</td>
<td>(3%)</td>
</tr>
<tr>
<td>IGF1R and ALK</td>
<td>(5%)</td>
</tr>
<tr>
<td>FGFR3</td>
<td>(5%)</td>
</tr>
<tr>
<td>PI3K-AKT</td>
<td>(5%)</td>
</tr>
<tr>
<td>CDKN2C and CCND1</td>
<td>(18%)</td>
</tr>
<tr>
<td>Others</td>
<td>(11%)</td>
</tr>
<tr>
<td>BRAF</td>
<td>(8%)</td>
</tr>
</tbody>
</table>

BRAF mutations are driver mutations (eg, in melanoma) and can be important in multiple myeloma.

**Personalized Medicine Agents Under Clinical Investigation**

<table>
<thead>
<tr>
<th>Clinical phase</th>
<th>Novel agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 3</td>
<td>Venetoclax*</td>
</tr>
<tr>
<td>Phase 1, 2</td>
<td>Abemaciclib*</td>
</tr>
</tbody>
</table>

*Being studied in the MyDRUG trial
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


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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

Venetoclax and t(11;14)

Venetoclax and bortezomib dex vs placebo bortezomib dex; 1–3 prior lines

Median follow up 18.7 m mPFS
22.4 m venetoclax
11.5 m placebo

Venetoclax especially active in t(11;14) or BCL2high MM


Innovative Trial Designs: Shaping the Future of Cancer Research Toward Precision Medicine

Umbrella/platform trials

Basket/bucket trials

MyDRUG Trial

Functional high-risk patients

Profile for alterations (NCT02884102)

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

- Daratumumab + IPd
- Cobimetinib + IPd
- Abemaciclib + IPd
- Erdafitinib + IPd

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

2 cycles

2:1

Cobimetinib + dex
Cobimetinib + IPd
Abemaciclib + Dex
Abemaciclib + IPd
Erdafitinib + Dex
Erdafitinib + IPd

Precision Medicine in Myeloma: MyDRUG (NCT03732703)

Case study: Man, age 59

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

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

Precision 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 trials to provide bone marrow and peripheral blood is paramount.

Personalized medicine provides the right treatment at the right time for each myeloma patient.
Relapsed/Refractory Multiple Myeloma

Sumit Madan, MD
Banner MD Anderson Cancer Center
Gilbert, Arizona

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>Other mechanisms of action</th>
<th>Monoclonal antibodies</th>
<th>Cellular therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thalidomide (thalidomide)</td>
<td>Velcade (bortezomib)</td>
<td>Adriamycin (cylophosphamide)</td>
<td>Cytoxan (cyclodiphosphamide)</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 (ciltaclabtagene autoleucel)</td>
</tr>
<tr>
<td>Pomalyst (pomalidomide)</td>
<td>Ninlaro (ixazomib)</td>
<td>Melphalan</td>
<td></td>
<td></td>
<td>Egydak (Panobinostat)†</td>
<td>Sarcida (isatuximab)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Elepaxto (melillufen)†‡</td>
<td>Blenrep (belantamab mafodotin)†</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Tescvayli (teclistamab)†</td>
<td>Tescvayli (teclistamab)†</td>
<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!
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.

Withdrawn 2021

Farydak (panobinostat)
- The required clinical studies were not completed within the FDA-specified time frame

Pepaxto (melflufen)
- The phase 3 OCEAN study compared Pepaxto-dex with Pomalyst-dex in patients with relapsed/refractory myeloma
  - 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 U.S.

Withdrawn 2022*

Blenrep (belantamab mafodotin)
- 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
- 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
  - Results are anticipated in the first half of 2023

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

Treatment Approach

First relapse

Proteasome inhibitor/immunomodulatory drug/antibody-based therapy

Any options for first relapse not tried

Refactory to Velcade and Revlimid

DKd, Isa-Kd, DPd, Elo-Pd, Isa-Pd, or KPd

Refactory to an IMiD but sensitive to a PI

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

Approved therapies

Sd, belamaf, ide-cel, cilt-cel, Tecvayli

Clinical trials

Bispecific/trispecific antibodies, cellular therapies (CAR T-cells, NK cells), CELMoDs

>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.
## Triplet Regimens for Early Relapse

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</td>
<td>• For relapsed/refractory myeloma</td>
</tr>
<tr>
<td>Kyprolis (carfilzomib)</td>
<td>• IV infusion • Weekly dosing</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>Ninlaro (ixazomib)</td>
<td>Once-weekly pill</td>
<td>• For relapsed/refractory myeloma as a triplet with Revlimid and 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>Pomalyst (pomalidomide)*</td>
<td>Once-daily pill</td>
<td>• For relapsed/refractory myeloma in combination with dexamethasone</td>
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<tr>
<td>XPOVIO (selinexor)</td>
<td>Once-weekly pill</td>
<td>• For relapsed/refractory myeloma as a triplet with Velcade and dexamethasone</td>
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</table>

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

Monoclonal Antibody–Based Regimens for Early Relapse: Darzalex

<table>
<thead>
<tr>
<th>POLLUX</th>
<th>CASTOR</th>
<th>CANDOR</th>
<th>APOLLO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regimens compared</td>
<td>• Darzalex-Revlimid-dex (DRd) vs Rd</td>
<td>• Darzalex-Velcade-dex (DVd) vs Vd</td>
<td>• Darzalex-Kyprolis-dex (DKd) vs Kd</td>
</tr>
<tr>
<td>Median progression-free survival favored</td>
<td>• DRd: 45 vs 18 months</td>
<td>• DVd: 17 vs 7 months</td>
<td>• DKd: 29 vs 15 months</td>
</tr>
<tr>
<td>Clinical considerations</td>
<td>• Consider for relapses from Revlimid or Velcade maintenance • DRd associated with more upper respiratory infections, low blood white blood cell counts, and diarrhea</td>
<td>• Consider for patients who are Revlimid-refractory without significant neuropathy • DVd associated with more low blood cell counts</td>
<td>• Consider for younger, fit patients who are double-refractory to Revlimid and Velcade • DKd associated with more respiratory infections • Sever side effects (possibly fatal) in intermediate fit patients 65 and older</td>
</tr>
</tbody>
</table>
Monoclonal Antibody–Based Regimens for Early Relapse: Sarclisa and Empliciti

**ELOQUENT-2**
- Regimens compared: Empliciti–Revlimid-dex vs Rd
- Median progression-free survival favored: Empliciti-Rd: 19 vs 15 months
- Clinical considerations:
  - Consider for non-Revlimid refractory, frailer patients
  - Overall survival benefit with Empliciti-Rd
  - Empliciti-Rd associated with more infections

**ELOQUENT-3**
- Regimens compared: Empliciti–Pomalyst-dex vs Pd
- Median progression-free survival favored: Empliciti-Pd: 10 vs 5 mos
- Clinical considerations:
  - Consider for patients refractory to Revlimid and a proteasome inhibitor (Velcade, Kyprolis, Ninlaro)
  - Empliciti-Pd associated with severe low white blood cell counts, more dose reductions, upper respiratory infections, and diarrhea

**ICARIA-MM**
- Regimens compared: Sarclisa–Pomalyst-dex vs Pd
- Median progression-free survival favored: Sarclisa-Pd: 12 vs 7 mos
- Clinical considerations:
  - Consider for patients refractory to Revlimid and a proteasome inhibitor (Velcade, Kyprolis, Ninlaro)

**IKEMA**
- Regimens compared: Sarclisa–Kyprolis-dex vs Kd
- Median progression-free survival favored: Sarclisa-Kd: 42 vs 21 mos
- Clinical considerations:
  - Consider for patients refractory to Revlimid and Velcade

**ELOQUENT-2**
- Regimens compared: Empliciti–Revlimid-dex vs Rd
- Median progression-free survival favored: Empliciti-Rd: 19 vs 15 months
- Clinical considerations:
  - Consider for non-Revlimid refractory, frailer patients
  - Overall survival benefit with Empliciti-Rd
  - Empliciti-Rd associated with more infections

**ELOQUENT-3**
- Regimens compared: Empliciti–Pomalyst-dex vs Pd
- Median progression-free survival favored: Empliciti-Pd: 10 vs 5 mos
- Clinical considerations:
  - Consider for patients refractory to Revlimid and a proteasome inhibitor (Velcade, Kyprolis, Ninlaro)
  - Empliciti-Pd associated with severe low white blood cell counts, more dose reductions, upper respiratory infections, and diarrhea

**ICARIA-MM**
- Regimens compared: Sarclisa–Pomalyst-dex vs Pd
- Median progression-free survival favored: Sarclisa-Pd: 12 vs 7 mos
- Clinical considerations:
  - Consider for patients refractory to Revlimid and a proteasome inhibitor (Velcade, Kyprolis, Ninlaro)

**IKEMA**
- Regimens compared: Sarclisa–Kyprolis-dex vs Kd
- Median progression-free survival favored: Sarclisa-Kd: 42 vs 21 mos
- Clinical considerations:
  - Consider for patients refractory to Revlimid and Velcade

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

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

| Median progression-free survival (months) | 24.7 | 17.2 | 42.7 | 21.9 |
| Overall response rate (%)                | 82   | 82.6 | 90.4 | 86.1 |
| ≥VGPR rate (%)                           | 67.2 | 52.2 | 76   | 58.3 |
| MRD negativity rate (%)                  | 24.6 | 15.2 | 37.5 | 16.7 |
| MRD-negative CR rate (%)                 | 18   | 10.9 | 30.8 | 13.9 |

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

*<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)

## 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>

### OPTIMISMM

- Consider for relapse on Revlimid
- VPd associated with more low blood counts, infections, and neuropathy than Pd

### ASPIRE

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

### TOURMALINE-MM1

- IRd: 21 vs 15 months
- IRd an oral regimen
- Gastrointestinal toxicities and rashes
- Lower incidence of peripheral neuropathy

### BOSTON

- 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

#### Darzalex

- **Infusion reactions**
  - Less with SC use
- **Risk of shingles**
  - Use appropriate vaccination
- **Increased risk of hypogammaglobulinemia** and upper respiratory infections
  - Bactrim prophylaxis
  - IVIG support

#### Empliciti

- **Infusion reactions**
- **Risk of shingles**
  - Use appropriate vaccination

#### Sarclisa

- **Infusion reactions**
- **Risk of shingles**
  - Use appropriate vaccination

---

SC, subcutaneous; IVIG, intravenous immunoglobulin
Important Considerations for Use of Proteasome Inhibitors

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

**Kyprolis**
- 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

**Ninlaro**
- 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
Important Considerations for Use of XPOVIO

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

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

Fatigue
- Stay hydrated and active.

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


Treatment Approach

First relapse
- Proteasome inhibitor/immunomodulatory drug/antibody-based therapy

Any options for first relapse not tried
- Refractory to Velcade and Revlimid
- Refractory to an IMiD, but sensitive to a PI

>1 Relapse
- Triple-class refractory
- Approved therapies
  - Sd, belamaf, ide-cel, cilta-cel, Tecvayli
  - DVd, SVd, Ven-Vd (for t[11;14])*

Clinical trials

Approved therapies
- Bispecific/trispecific antibodies, CAR-T cells, CELMeDs

*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...

**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</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</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>CAR T cell</td>
<td>Carvykti</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>
<tr>
<td>Bispecific antibody</td>
<td>Tecvayli</td>
<td>Step-up dosing1 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, a PI, and an anti-CD38 mAb)</td>
</tr>
</tbody>
</table>

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

1. Black box warning: cytokine release syndrome; neurologic toxicities; hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS); prolonged cytopenia
2. Black box warning: cytokine release syndrome; neurologic toxicities; Parkinsonism and Guillain-Barré syndrome; hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS); prolonged cytopenia
3. Black box warning: cytokine release syndrome; neurologic toxicities
4. 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 ≥PR (%)</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


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)
- Carvykti (cilta-cel)
- CT103A
- Gamma secretase inhibitor followed by CAR T-cells

CAR, chimeric antigen receptor; MM, multiple myeloma

Abecma and Carvykti in Relapsed and Refractory Multiple Myeloma

Abecma

<table>
<thead>
<tr>
<th>Patients (%)</th>
<th>ORR 73%</th>
</tr>
</thead>
<tbody>
<tr>
<td>PR</td>
<td>26</td>
</tr>
<tr>
<td>VGPR</td>
<td>7</td>
</tr>
<tr>
<td>CR or sCR and MRD NE</td>
<td>20</td>
</tr>
<tr>
<td>CR or sCR and MRD-</td>
<td>21</td>
</tr>
</tbody>
</table>

Average PFS 9 months

Carvykti

<table>
<thead>
<tr>
<th>Patients (%)</th>
<th>ORR 97.9%</th>
</tr>
</thead>
<tbody>
<tr>
<td>PR</td>
<td>14.4</td>
</tr>
<tr>
<td>VGPR</td>
<td>3</td>
</tr>
<tr>
<td>CR or sCR and MRD NE</td>
<td>12.4</td>
</tr>
<tr>
<td>CR or sCR and MRD-</td>
<td>3</td>
</tr>
</tbody>
</table>

27-month PFS 55%

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


CAR T: Expected Toxicities

<table>
<thead>
<tr>
<th></th>
<th>CRS</th>
<th>ICANS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>1–9 days after CAR T-cell infusion</td>
<td>2–9 days after CAR T-cell infusion</td>
</tr>
<tr>
<td>Duration</td>
<td>5–11 days</td>
<td>3–17 days</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Fever, difficulty breathing, dizziness, nausea, headache, rapid heartbeat, low blood pressure</td>
<td>Headache, confusion, language disturbance, seizures, delirium, cerebral edema</td>
</tr>
<tr>
<td>Management</td>
<td>Antiseizure medications, corticosteroids, supportive care</td>
<td>Antiseizure medications, corticosteroids</td>
</tr>
</tbody>
</table>

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
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

Now Approved: Tecvayli, the First Bispecific Antibody!

- 63.0% (104/165)
- ≥CR: 39.4%
- 32.7%
- ≥VGPR: 58.8%
- 19.4%
- 4.2%

Patients (%)

- sCR
- CR
- VGPR
- PR

Median duration of response 18.4 months

Tecvayli Side Effects

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>Approved product</td>
<td>Abecma, Carvykti</td>
<td>Tecvayli</td>
</tr>
<tr>
<td>Efficacy</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>How given</td>
<td>One-and-done</td>
<td>IV or SC, weekly to every 3 weeks until progression</td>
</tr>
<tr>
<td>Where given</td>
<td>Academic medical centers</td>
<td>Academic medical centers</td>
</tr>
<tr>
<td>Notable adverse events</td>
<td>CRS and neurotoxicity</td>
<td>CRS and neurotoxicity</td>
</tr>
<tr>
<td>Cytokine release syndrome</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Neurotoxicity</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Availability</td>
<td>Wait time for manufacturing</td>
<td>Off-the-shelf, close monitoring for CRS and neurotoxicity</td>
</tr>
<tr>
<td>Advantages</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>Disadvantages</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>• Dependently 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>
Emerging Treatment Options

- Cereblon E3 ligase modulators (CELMoDs)
- Immunocytokines
- More bispecific antibodies (BCMA, GCPR5D, Fc5H targets)
- More chimeric antigen receptor (CAR) T-cell therapies

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.

CAR T and bispecific antibodies are very active even in heavily pre-treated patients. Many other exciting immunotherapy options are in trials and look very promising.
Please take a moment to answer two questions about this presentation.

A Cancer Patient and Caregiver’s Journey

Cancer Caregiving: Its challenges and celebrations.
An intimate conversation with the England Family

Objective
A look at a cancer caregiving experience and the importance of enhancing the skills and knowledge of the cancer caregivers.
Cancer Caregivers of America

Cancer Caregivers Education Platform
Online Training, Resources, and a Cancer Care Community

HOW DID WE GET HERE?

Our Journey

Jack Kavanagh diagnosed with Multiple Myeloma (1991)

Arizona Multiple Myeloma Network Non-profit created (2004)

Cancer Caregivers AZ, Cancer Caregivers Education Program created (2014)

WELCOME
CancerCaregivers of America, Online Cancer Caregivers Education Platform Launch (2023)
Cancer Caregivers Education
The NEED

Today we **LAUNCH!!!**

Online Cancer Caregivers Education Platform

Available in the U.S. and Canada
Cancer Caregivers are a vital part of the cancer care continuum. **OUR VISION** is that they are Knowledgeable and skillful cancer caregivers.
What is the Online Cancer Caregivers Education Platform?

Online Cancer Caregivers Education Platform includes, online Education/Training, Resources, and a Cancer Care Community

The program also has the option to provide In-Person Training Sessions

The program is designed for **ALL CANCERS and CANCER CAREGIVERS**

The program focuses on **INCREASING your KNOWLEDGE and BUILDING your cancer caregiving SKILLS**

The program is developed using actual Cancer Caregivers and Patients knowledge and experiences

The program is designed with a **360° view** of what the cancer caregiver and patient will experience. The psychological, physical, social, emotional, financial and the many other circumstances that will arise on your journey.

---

**Online Cancer Caregivers Education Program Assets**

<table>
<thead>
<tr>
<th>Program Assets</th>
<th>Cancer Caregivers/Patients</th>
<th>Cancer Care Professionals</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Cancer Caregivers Online Training</td>
<td>8 Education modules</td>
<td>Interactive and engaging Pre/post assessments</td>
</tr>
<tr>
<td></td>
<td>Interactive and engaging Pre/post assessments</td>
<td>4 Education modules</td>
</tr>
<tr>
<td></td>
<td>Data collection Certificate of completion</td>
<td>CME/CEU available 2023/24</td>
</tr>
<tr>
<td>2 Cancer Care Resource Library</td>
<td>Only cancer related resources Clinical trials, finance support, etc.</td>
<td>Not Available</td>
</tr>
<tr>
<td></td>
<td>Additional videos, links, documents from the program and other sources</td>
<td></td>
</tr>
<tr>
<td>3 Cancer Care Community</td>
<td>National cancer caregiver’s network where you can share information in a closed network</td>
<td>Not Available</td>
</tr>
<tr>
<td></td>
<td>Share resources and more in a supportive environment</td>
<td></td>
</tr>
<tr>
<td>4 Cancer Caregivers In-person Training</td>
<td>Same benefits / access as Online Training</td>
<td>Available</td>
</tr>
</tbody>
</table>

Cancer Care Professionals' Education Modules will be available 9/1/23
Online Cancer Caregivers Education Platform

Cancer Caregivers Education Training Modules (8)

**Cancer Caregivers Education Program Introduction**
- Program Overview
  - Navigating through the platform
  - Benefits
  - What you can expect

**Who You Are as A Cancer Caregiver**
- Understand what it means to assume responsibilities of being a Cancer Caregiver
- Know the common frustrations
- Understand resilience

**Circle of Responsibilities**
- Understand the scope of work
- Understand the amount of time you spend cancer caregiving
- Learn how to build your Cancer Care Team
- Learn how to effectively plan caregiving work

**Managing Stress In The Cancer Caregiving Role**
- Understand what stress is
- Learn how to recognize your stress triggers
- Build your self care plan to manage stress

**Cancer Caregiving Survivorship**
- Understand what cancer survivorship is
- How the impacts of cancer caregiving affects you
- Learn how to manage your overall well-being as a cancer caregiver

**Communications with Family in your Cancer Caregiving Role**
- Learn the types of communication needs and challenges in your cancer caregiving role
- Provide you with tools to enhance your communication skills

**Communications with Medical Professionals**
- Build your skills to effectively communicate with your Medical Care Professionals
- Learn how to be organized to get the most out of time spent with Medical care professionals

**Navigating the Healthcare System**
- Understand the many functions involved with delivering care and support for your loved one.
- Learn strategies that will enhance your ability to navigate the healthcare system
Online Cancer Caregivers Education Platform

[Image of the Online Cancer Caregivers Education Platform]

FREQUENTLY ASKED QUESTIONS

- **SET-UP 2-FACTOR AUTHENTICATION (2FA)**
  a. From the dashboard select “My Account” then select “Account profile”
  b. Inside the “login information” box select “Set-up 2-factor authentication (2FA)”
  c. Type in your password
  d. Select “Install Google Authenticator”
  e. Install the Google Authenticator app from the app or android store
  f. Scan QR code from your phone on the website and enter the code from the Google Authenticator App

- **RESET PASSWORD**

- **CREATING A TICKET AND REPLYING**

- **UPLOAD A PROFILE ACCOUNT PHOTO**

- **DOMINICAN AN INVOICE**

- **EDIT, PAY OR DEACTIVATE SUBSCRIPTION**
In Summary

Cancer Caregivers Education Program was developed with Cancer Patients and Cancer Caregivers input and guidance

Cancer Caregivers Education Platform Assets

Cancer Caregivers Online Education/Training

Cancer Care Resource Library

Cancer Care Community

The program is designed with a 360° view of what the cancer caregiver and patient will experience. The psychological, physical, social, emotional, financial and the many other circumstance that will arise on your journey.

Our Mission is to educate, build skills, provide resources that will improve quality of life, treatment, and healthcare outcomes for the cancer patient, caregivers, and family.
A Gift for YOU

We are giving away 100 free, 1-year subscriptions
The code is only good through midnight Monday March 27, 2023

CODE: CCEP!

Directions:
Go to Cancer Caregivers of America Website; https://cancercaregiversofamerica.com/
Register for the Cancer Caregivers Education Program using promotion code: CCEP!

Start taking advantage of the Cancer Caregivers Education Platform right away

Online Cancer Caregivers Education Platform
Available in the U.S. and Canada

We are officially LAUNCHED!!!
Please take a moment to answer a few questions about this presentation.

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 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>
</tr>
<tr>
<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>
</tr>
</tbody>
</table>

For more information or to register, please visit themmrf.org/resources/education-program
Myeloma Mentors® allows patients and caregivers the opportunity to connect with trained mentors. This is a phone-based program offering an opportunity for a patient and/or caregiver to connect one-on-one with a trained patient and/or caregiver mentor to share his or her patient journeys and experiences.

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

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

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

Endurance Events 5K Walk/Run Events Independent Events

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