Clinical Studies
May 5, 2023

Tech Support
1-719-234-7952
Resources

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

Submit your questions throughout the program!
MMRF Research Initiatives

For more information, visit themmrf.org

Speakers

Elizabeth O'Donnell, MD
Dana-Farber Cancer Institute
Harvard University
Boston, Massachusetts

Andrew J. Yee, MD
Harvard Medical School
Massachusetts General Cancer Center
Boston, Massachusetts
Clinical Studies: What Are They?

Andrew J. Yee, MD
Harvard Medical School
Massachusetts General Cancer Center
Boston, Massachusetts

Goal of Clinical Trials:
Making Progress Against Myeloma

Participants in clinical trials receive specific treatments according to the research plan or protocol created by the investigators to determine the safety and efficacy of the treatment.

- Improve the way we use currently available drugs and regimens
- Develop new medications
- Identify rational selection of existing drugs
- Increase the understanding of the disease and how the treatment works
Impact of Clinical Trials in Myeloma

Survival rates have nearly doubled; further improvements expected in near future.

Many new drugs approved since 2003.

Many new drugs being studied in clinical trials.

Understanding of the biology of myeloma improving, with the eventual goal of personalized medicine.

Therapeutic Options in Myeloma: The Current Landscape

<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>Antibodies (monoclonal or bispecific)</th>
<th>Cellular therapy (CAR T cells)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thalomid (thalidomide)</td>
<td>Velcade (bortezomib)</td>
<td>Adriamycin (cytotoxic)</td>
<td>Cytoxan (cyclophosphamide)</td>
<td>Dexamethasone</td>
<td>XPOVIO (veloclax)</td>
<td>Empicit (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 (cilatamab)</td>
</tr>
<tr>
<td>Pomalyst (pomalidomide)</td>
<td>Ninlaro (ixazomib)</td>
<td>Melphalan</td>
<td></td>
<td></td>
<td></td>
<td>Sarclisa (satulimab)</td>
<td>Tecvayli (teclistamab)*</td>
</tr>
</tbody>
</table>

*Not yet FDA-approved for patients with multiple myeloma; *Bispecific antibody

New formulations, new dosing, and new combinations, too!
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>Treatment</th>
<th>Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1975</td>
<td>Chemotherapy + dexamethasone +</td>
<td>26.5%</td>
</tr>
<tr>
<td></td>
<td>stem cell transplantation</td>
<td></td>
</tr>
<tr>
<td>1985</td>
<td>Velcade (bortezomib)</td>
<td>27.4%</td>
</tr>
<tr>
<td>1995</td>
<td>Revlimid (lenalidomide)</td>
<td>33.5%</td>
</tr>
<tr>
<td>2005</td>
<td>Kyprolis (carfilzomib)</td>
<td>47.2%</td>
</tr>
<tr>
<td>2013</td>
<td>Pomalyst (pomalidomide)</td>
<td>56.9%</td>
</tr>
<tr>
<td>2014+</td>
<td>Ninlaro (ixazomib)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Empliciti (elotuzumab)</td>
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<td>Carvykti (ciltaclibagene autoleucel)</td>
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<td>Tecvayli (teclistamab)</td>
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</tr>
</tbody>
</table>

Available treatments

New Drug Development

**STEP 1**
Identify a target for therapy in the laboratory

**STEP 2**
Confirm the anti-cancer activity in laboratory and animal studies

**STEP 3**
Clinical trials (human studies) to determine safety, dosing, and effectiveness

The whole process costs millions of dollars and years of effort!
Designing Clinical Studies

When a treatment is ready to be tested, researchers design a research plan called a protocol that includes such details as:

• How many patients will be enrolled
• How the treatment will be administered
• When and how participants will be monitored
• The goals of the trial: determine safety, identify the right dose, measure the efficacy

Clinical studies pass high standards of scientific design as well as an ethics review to ensure that the trial protects the rights and welfare of all participants.

Traditional Clinical Study Types

<table>
<thead>
<tr>
<th>Treatment dose</th>
<th>Number of patients</th>
<th>Questions answered*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Different doses</td>
<td>Small</td>
<td>What is the best dose? Is the drug safe? What are the side effects?</td>
</tr>
<tr>
<td>Same dose</td>
<td>Moderate</td>
<td>Does the drug work? What are the side effects?</td>
</tr>
</tbody>
</table>

*The FDA approves treatments that are safe, effective, and shown to be better than the standard treatments available.
†When no standard treatment is available, the FDA may approve drugs based on study results of phase 2 studies.
Examples of Phase 1 and Phase 2 Clinical Studies

New drugs for triple-class refractory patients

**Phase 1 MajesTEC-1 Study**

- Relapsed/refractory multiple myeloma and progression after ≥2 prior treatment regimens
- Tecvayli (teclistamab) (73 patients treated)

- Part 1: Dose escalation
  - 80 μg/kg (n=6)
  - 240 μg/kg (n=7)
  - 720 μg/kg (n=15)
  - 1,500 μg/kg (n=40)
  - 3,000 μg/kg (n=4)
- Randomized phase 2 dose
- Part 2: Dose expansion

**Best drug and combinations**

**Phase 2 RVD-Lite Study**

- Transplant-ineligible newly diagnosed myeloma patients
- 50 patients
- Induction: Revlimid + Velcade + dex (RVd)
- Consolidation: RV

**Phase 2 GRIFFIN Study**

- Newly diagnosed myeloma patients
- 104 patients
- Induction: Revlimid + Velcade + dex (RVd)
- Consolidation: RVd
- Maintenance: R

Traditional Clinical Study Types

- **Phase 3**
  - Treatment dose
  - Number of patients
  - Questions answered:
    - Is the treatment safe?
    - Does this treatment work better than other treatments?
    - Does this treatment cause fewer side effects than other treatments?

*The FDA approves treatments that are safe, effective, and shown to be better than the standard treatments available.

†Conducted to receive FDA approval of new drugs, in most cases.
Examples of Phase 3 Clinical Studies

**Finding the better drug combination**

**IKEMA Study**
- Patients with relapsed/refractory myeloma who received 1-3 prior therapies, no prior therapy with Kyprolis, and were not refractory to prior anti-CD38 antibody
- EARLY TRANSPLANT ARM: 179 patients
- LATE TRANSPLANT ARM: 123 patients
- Drug: Sarcis-Kd

**The timing of ASCT**

**Phase 3 DETERMINATION Study**
- Newly diagnosed myeloma patients
- 365 patients vs. 357 patients
- EARLY TRANSPLANT ARM: 365 patients
- LATE TRANSPLANT ARM: 357 patients
- Drug: Revlimid + Velcade + dex (RVd)

**Actionable Alterations in MM**

- Personalized medicine efforts have identified molecular alterations for which there are drugs in the clinic
- **KRAS and NRAS** (40%)
- **IDH1/2** (5%)
- **IGF1R and ALK** (5%)
- **FGFR3** (5%)
- **PI3K-AKT** (5%)
- **CDKN2A and CCND1** (18%)
- **MYD88** (3%)
- **Others** (11%)
- **Others** (11%)

Innovative Trial Designs: Guiding the Future of Cancer Research Toward Personalized Medicine

Umbrella/platform trials: patients have the same cancer but different genetic mutations

Basket/bucket trials: patients have different cancers but the same genetic mutation

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

Standard of care
- Agent targeted to A
- Agent targeted to B
- Agent targeted to C

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

• Long-term studies with a large number of patients
• Patients are treated using available therapies
• Efficacy and safety are analyzed following treatment
• Typically involve a large number of patients

Other Types of Clinical Studies

- Longitudinal Studies
- Registry Studies
- Expanded-Access Programs

• Allow early access to experimental therapies when no alternatives are available

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Participation in a Clinical Study
Elizabeth O’Donnell, MD
Dana-Farber Cancer Institute
Harvard University
Boston, Massachusetts

Aren’t clinical studies for people who are running out of options?

• Today, clinical studies are used at all stages of disease
  – Clinical studies are available for induction (first) therapy, maintenance therapy, all stages of relapsed disease, and myeloma precursor conditions
• If you have become resistant to standard therapies, clinical studies may offer you another type of treatment—but that is not the only situation in which they are useful
If I go on this clinical study, will I be cured?

Patients who participate in clinical studies are the first to receive the newest therapies.

However, it is important to remember that the treatments studied in clinical studies may or may not be more effective than existing treatments, and they do not come with any guarantee as to the outcome.

The treatments may also have side effects.

By participating in a clinical study, you not only give hope to yourself but also to other myeloma patients, including those who will be diagnosed with multiple myeloma in the future.

How is my treatment on a clinical study going to be different from standard treatment?

Clinical studies may have fairly strict rules for timing and procedures.

You will work with a clinical study coordinator in addition to your regular providers.

You may have additional office visits or lab work depending upon the requirements of the study.
How do I know if I qualify to participate?

Eligibility

- Each study has specific requirements for patients to be eligible

Challenges to Eligibility*

- Renal failure
- Low blood counts
- Recent diagnosis with another type of cancer
- Myeloma that is hard to measure

*This is specific to each study, however, so don’t automatically count yourself out!

The Finances of Participating in a Clinical Study

You may receive medications at no cost as part of the study.

Other standard-of-care treatment will be billed to your insurance as usual.

You may be able to receive money for hotel stays, gas, food, and airfare to defray some of the cost if you are traveling to participate in the study.

Ask your coordinator for details on who is responsible for what costs and discuss any areas of financial concern, as assistance may be available.
Will I be treated like a guinea pig?

*No!*

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**Three influential documents**

- The Nuremberg Code
- The Declaration of Helsinki
- The Belmont Report

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**Benefits of Clinical Trials**

- You will have normal standard of care in terms of office visits, lab work, etc.
- You may even have additional care and investigation as a part of the clinical trial.
- You will generally see your health care providers and will also have a research coordinator involved in your care.
- You will likely even have a higher standard of care than normal!
Will I be obligated to continue this study no matter what?

- Most studies have predefined criteria for *progressive disease*, after which patients are taken off the trial
- If a drug is not working, you will not remain on it and can move on to other options for therapy
- Most studies also have criteria for side effects that require discontinuation if they are severe enough
- YOU are still ALWAYS in charge of what goes into your body, and you always have the right to discontinue participation; you will still receive quality care and respectful treatment and will in no way be punished for deciding not to participate

Considering Entering Clinical Trials

- Find a clinical trial
  - Contact the MMRF Patient Navigator Center at 1-888-841-6673
  - Visit themmrfr.org/resources/clinical-trial-finder/
  - Ask your treating hematologist-oncologist about any available trials
  - Check with any academic medical centers close to your home
- Talk to your doctor about your eligibility
- Meet with the research nurse to learn more
- Carefully review the informed consent paperwork
Questions to Ask Your Care Team

- How does the study work? How often will I need to see my doctor or visit the cancer center?
- Will I need to undergo additional tests?
- What is currently known about the new drug or combination?
- What benefits can I expect?
- What side effects should I expect? Who should I notify if I have side effects?
- Can I take my vitamins or other medications?
- Can I get the treatment with my local doctor?
- Will my insurance pay for my participation in the clinical study?

Summary

- Myeloma survival rates have nearly doubled; further improvements are expected.
- Many new drugs approved in the last two decades.
- The drive of research and clinical trials has brought us to where we are.

    Clinical trials are available for patients at all stages of myeloma, including those who have precursor conditions, those who are newly diagnosed, and those who have received previous treatments and whose myeloma has relapsed.

- No one is expected to be a guinea pig; research and clinical trials are under very tight supervision and standards.
- Open, clear communication between the physician and the patient is essential.
MMRF Patient Resources

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

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

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

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

Join us today!

Endurance Events  

5K Walk/Run Events  

Independent Events

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

Upcoming Patient Education Events

Save the Date

<table>
<thead>
<tr>
<th>Topic</th>
<th>Date and Time (ET)</th>
<th>Speakers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facebook Live FAQs</td>
<td>Wednesday, May 17 11:00 AM to 12:00 PM</td>
<td>Noopur Raje, MD, Kathleen J. Lively, RN</td>
</tr>
<tr>
<td>Patient Summit</td>
<td>Saturday, May 20 9:00 AM to 3:45 PM</td>
<td>Saad Usmani, MD, Faith Davies, MBBCh, Justina Kiernan, PA, Neha Korde, MD, Sham Mailankody, MBBS, Gunjan Shah, MD</td>
</tr>
</tbody>
</table>

For more information or to register, please visit themmrf.org/resources/education-program
Resources

- Resource tab includes
  - Speaker bios
  - Copy of the slide presentation
  - Exhibit Hall
Need help with travel to a clinical study?

- The MMRF has partnered with the Lazarex Cancer Foundation to help provide more equitable access to clinical studies for multiple myeloma patients
- This partnership is one facet of the MMRF’s commitment to improve diversity and representation in myeloma clinical trials
- MMRF has provided $100,000 over 2 years to Lazarex to fund travel, lodging, and food for patients (and a travel companion) so that they can participate in clinical studies that are appropriate for them
- Patients are funded according to income guidelines and will be reimbursed for allowed expenses
- For more information on this program and to be connected with Lazarex, call our Patient Navigation Center at 1-888-841-6673

Thank you!