Meet The Professor
Management of Multiple Myeloma

S Vincent Rajkumar, MD
Edward W and Betty Knight Scripps Professor of Medicine
Mayo Clinic
Rochester, Minnesota
Commercial Support

This activity is supported by educational grants from Adaptive Biotechnologies Corporation, Celgene Corporation, GlaxoSmithKline, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, and Takeda Oncology.
Potential Conflicts of Interest

USF Health endorses the standards of the ACCME that require everyone in a position to control the content of an accredited educational activity to disclose all financial relationships with commercial interests that are related to the content of the educational activity. All accredited activities must be balanced, independent of commercial bias, and promote improvements or quality in healthcare. All recommendations involving clinical medicine must be based on evidence accepted within the medical profession.

USF Health will identify, review, and resolve all conflicts of interest that speakers, authors, or planners disclose prior to an educational activity being delivered to learners. Disclosure of a relationship is not intended to suggest or condone bias in any presentation, but is made to provide participants with information that might be of potential importance to their evaluation of a presentation.
Non-Faculty Disclosures

USF Health CPD Staff and Research To Practice CME Planning Committee Members, Staff, and Reviewers have no relevant conflicts to disclose.
Accreditation

USF Health is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

USF Health designates this live activity for a maximum of 1 AMA PRA Category 1 Credit™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.
Successful completion of this CME activity, which includes participation in the evaluation component and a short post-test, enables the participant to earn up to 1 Medical Knowledge MOC point in the American Board of Internal Medicine’s (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider’s responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

Please note, this program has been specifically designed for the following ABIM specialties: medical oncology and hematology.
Dr Love — Disclosures

Dr Rajkumar — Disclosures

No financial interests or affiliations to disclose
Joseph Mikael, MD — Disclosures

| Consulting Agreements | Amgen Inc, Celgene Corporation, GlaxoSmithKline, Janssen Biotech Inc, Karyopharm Therapeutics, Sanofi Genzyme, Takeda Oncology |
We Encourage Clinicians in Practice to Submit Questions

You may submit questions using the Zoom Chat option below.

Feel free to submit questions now before the program begins and throughout the program.
Familiarizing Yourself with the Zoom Interface

How to answer poll questions

When a poll question pops up, click your answer choice from the available options. Results will be shown after everyone has answered.
Upcoming Live Webinars

Thursday, October 1, 2020
12:00 PM – 1:00 PM ET
Meet The Professor: Management of Ovarian Cancer

Faculty
Ursula Matulonis, MD

Moderator
Neil Love, MD

Friday, October 2, 2020
12:00 PM – 1:00 PM ET
Meet The Professor: Management of Chronic Lymphocytic Leukemia

Faculty
William G Wierda, MD, PhD

Moderator
Neil Love, MD
Upcoming Live Webinars

Monday, October 5, 2020
12:00 PM – 1:00 PM ET
Meet The Professor: Management of Lung Cancer

Faculty
Professor Tony SK Mok, MD

Moderator
Neil Love, MD

Wednesday, October 7, 2020
12:00 PM – 1:00 PM ET
Meet The Professor: Management of Chronic Lymphocytic Leukemia

Faculty
Mitchell R Smith, MD, PhD

Moderator
Neil Love, MD
Upcoming Live Webinars

Thursday, October 8, 2020
12:00 PM – 1:00 PM ET

Meet The Professor: Management of Gynecologic Cancers

Faculty
Brian M Slomovitz, MD

Moderator
Neil Love, MD
Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 days.
ONCOLOGY TODAY
WITH DR NEIL LOVE

Listen on
Apple Podcasts

Listen on
Spotify

Listen on
Google Podcasts
Meet The Professor
Management of Multiple Myeloma

S Vincent Rajkumar, MD
Edward W and Betty Knight Scripps Professor of Medicine
Mayo Clinic
Rochester, Minnesota
Meet The Professor Program Participating Faculty

Rafael Fonseca, MD
Getz Family Professor of Cancer
Director for Innovation and Transformational Relationships
Interim Executive Director of the Mayo Clinic Comprehensive Cancer Center
Chair, Department of Internal Medicine
Distinguished Mayo Investigator
Mayo Clinic in Arizona
Phoenix, Arizona

Shaji K Kumar, MD
Mark and Judy Mullins Professor of Hematological Malignancies
Consultant, Division of Hematology
Professor of Medicine, Mayo Clinic
Rochester, Minnesota

Jonathan L Kaufman, MD
Associate Professor of Hematology and Medical Oncology
Winship Cancer Institute of Emory University
Atlanta, Georgia

Ola Landgren, MD, PhD
Professor of Medicine
Chief, Myeloma Service
Department of Medicine
Memorial Sloan Kettering Cancer Center
New York, New York
Meet The Professor Program Participating Faculty

Sagar Lonial, MD
Chair and Professor
Department of Hematology and Medical Oncology
Anne and Bernard Gray Family Chair in Cancer
Chief Medical Officer
Winship Cancer Institute
Emory University School of Medicine
Atlanta, Georgia

Nikhil C Munshi, MD
Kraft Family Chair
Director of Basic and Correlative Science
Jerome Lipper Multiple Myeloma Center
Professor of Medicine
Harvard Medical School
Dana-Farber Cancer Institute
Boston, Massachusetts

Joseph Mikhael, MD
Professor, Applied Cancer Research and Drug Discovery
Translational Genomics Research Institute
City of Hope Cancer Center
Phoenix, Arizona

Robert Z Orlowski, MD, PhD
Florence Maude Thomas Cancer Research Professor
Department of Lymphoma and Myeloma
Professor, Department of Experimental Therapeutics
Director, Myeloma Section
Division of Cancer Medicine
The University of Texas
MD Anderson Cancer Center
Houston, Texas
Meet The Professor Program Participating Faculty

Noopur Raje, MD
Director
Center for Multiple Myeloma
Massachusetts General Hospital Cancer Center
Professor of Medicine
Harvard Medical School
Boston, Massachusetts

Nina Shah, MD
Associate Professor of Medicine
University of California, San Francisco
Division of Hematology-Oncology
San Francisco, California

S Vincent Rajkumar, MD
Edward W and Betty Knight Scripps Professor of Medicine
Mayo Clinic
Rochester, Minnesota

Project Chair
Neil Love, MD
Research To Practice
Miami, Florida
We Encourage Clinicians in Practice to Submit Questions

You may submit questions using the Zoom Chat option below.

Feel free to submit questions now before the program begins and throughout the program.
Familiarizing Yourself with the Zoom Interface

How to answer poll questions

When a poll question pops up, click your answer choice from the available options. Results will be shown after everyone has answered.
Meet The Professor
Management of Ovarian Cancer

Thursday, October 1, 2020
12:00 PM – 1:00 PM ET

Faculty
Ursula Matulonis, MD

Moderator
Neil Love, MD
Meet The Professor
Management of Lung Cancer

Monday, October 5, 2020
12:00 PM – 1:00 PM ET

Faculty
Professor Tony SK Mok, MD

Moderator
Neil Love, MD
Meet The Professor
Management of Chronic Lymphocytic Leukemia

Wednesday, October 7, 2020
12:00 PM – 1:00 PM ET

Faculty
Mitchell R Smith, MD, PhD

Moderator
Neil Love, MD
Meet The Professor
Management of Gynecologic Cancers

Thursday, October 8, 2020
12:00 PM – 1:00 PM ET

Faculty
Brian M Slomovitz, MD

Moderator
Neil Love, MD
Meet The Professor
Management of Multiple Myeloma

S Vincent Rajkumar, MD
Edward W and Betty Knight Scripps Professor of Medicine
Mayo Clinic
Rochester, Minnesota
Joseph Mikhael, MD
Professor, Applied Cancer Research and Drug Discovery
Translational Genomics Research Institute
City of Hope Cancer Center
Phoenix, Arizona
Meet The Professor with Dr Rajkumar

Module 1: Cases from Dr Mikhael

- Questions and Comments: Intermediate- or high-risk smoldering myeloma
- An active 79-year-old woman with newly diagnosed standard-risk multiple myeloma
- Questions and Comments: Dosing of dexamethasone for older patients
- Questions and Comments: Triple-class refractory disease
- Questions and Comments: Belantamab mafodotin-associated keratopathy
- A 55-year-old woman with newly diagnosed multiple myeloma and chronic kidney disease
- A 65-year-old woman with relapsed, high-risk multiple myeloma
- Questions and Comments: Future biomarkers to identify patients for whom therapy may be discontinued
- Questions and Comments: Subcutaneous daratumumab

Module 2: Myeloma Journal Club with Dr Rajkumar

Module 3: Beyond the Guidelines — Clinical Investigator Approaches to Common Clinical Scenarios

Module 4: Key Papers and Recent Approvals
Questions and Comments: Intermediate- or high-risk smoldering myeloma

Joseph Mikhael, MD
Case Presentation – Dr Mikhael: An active 79-year-old woman with newly diagnosed standard-risk multiple myeloma

- Presents with ongoing fatigue, anemia and back pain
  - Multiple back fractures
  - Significant M-spikes
- Diagnosed with standard-risk myeloma; 40% plasma cells in bone marrow
- Daratumumab, lenalidomide, and dexamethasone (DRd)

Questions

- In a patient such as this, for whom an ASCT is not planned, what would be your preferred front-line regimen for her — VRd or DRd?
- What criteria do you use to determine transplant eligibility? How much of a geriatric assessment do you include in your strategy?
Questions and Comments: Dosing of dexamethasone for older patients

Joseph Mikael, MD
Questions and Comments: Triple-class refractory disease

Joseph Mikhael, MD
Questions and Comments: Belantamab mafodotin-associated keratopathy

Joseph Mikhael, MD
Case Presentation – Dr Mikhael: A 55-year-old woman with newly diagnosed multiple myeloma and chronic kidney disease

- Presents with standard-risk multiple myeloma
- Chronic kidney disease from vascular disease
  - Creatinine clearance < 30 mL/min but stable

Questions

- What is your approach when you’re planning to give VRd in a patient whose creatinine clearance is less than 30? What dosing strategy do you choose for the lenalidomide?
- Currently, would you use plasmapheresis in a patient with extremely high light chains and acute kidney injury because of those light chains?
Case Presentation – Dr Mikhael: A 65-year-old woman with relapsed, high-risk multiple myeloma

- 2018: Diagnosed with high-risk multiple myeloma
- Presented with significant renal dysfunction, requiring dialysis for a period of time
- VRd, with not quite VGPR, p53 deletion → ASCT (1/2020) → Maintenance lenalidomide/ixazomib
- Six months post-ASCT: Significant increase in light chains
- Daratumumab/weekly carfilzomib/dexamethasone

Questions
- In this high-risk patient, relapsing 6 months post-ASCT, while on ixazomib and lenalidomide maintenance, would you choose daratumumab/pomalidomide/dex or daratumumab/carfilzomib/dex, or perhaps even a different regimen?
- What is the role of ixazomib in the management of patients with multiple myeloma?
Questions and Comments: Future biomarkers to identify patients for whom therapy may be discontinued

Joseph Mikhael, MD
Questions and Comments: Subcutaneous daratumumab

Joseph Mikhael, MD
Meet The Professor with Dr Rajkumar

Module 1: Cases from Dr Mikhael

Module 2: Myeloma Journal Club with Dr Rajkumar

- 2020 update on diagnosis, risk stratification and management of multiple myeloma
- Identification of patients with smoldering myeloma at high risk for disease progression
- Predictors of short-term survival in Waldenström macroglobulinemia
- Venetoclax and t(11:14) AL amyloidosis
- Role of bone marrow biopsy for patients with plasma cell disorders

Module 3: Beyond the Guidelines — Clinical Investigator Approaches to Common Clinical Scenarios

Module 4: Key Papers and Recent Approvals
Multiple myeloma: 2020 update on diagnosis, risk-stratification and management

S. Vincent Rajkumar

Smoldering Myeloma and the Art of War

Sagar Lonial, MD¹; Madhav V. Dhodapkar, MD¹; and S. Vincent Rajkumar, MD²

Genomic Profiling of Smoldering Multiple Myeloma Identifies Patients at a High Risk of Disease Progression

Mark Bustoros, MD¹,²,³; Romanos Sklavenitis-Pistofidis, MD¹,²,³; Jihye Park, PhD¹,³; Robert Redd, MS⁴; Benny Zhitomirsky, PhD⁵; Andrew J. Dunford, BS²; Karma Salem, MD¹; Yu-Tzu Tai, PhD¹; Shankara Anand, MS³; Tarek H. Mouhieddine, MD¹,²,³; Selina J. Chavda, MBBS, BSc⁶; Cody Boehner, BS¹,²; Liudmila Elagina, MS²; Carl Jannes Neuse, MD¹,⁶; Justin Cha, BS³; Mahshid Rahmat, PhD¹,²,³; Amaro Taylor-Weiner, PhD³; Eliezer Van Allen, MD¹,³; Shaji Kumar, MD⁷; Efstathios Kastritis, MD⁸; Ignaty Leshchiner, PhD³; Elizabeth A. Morgan, MD³; Jacob Laubach, MD, MPP¹; Tineke Casneuf, PhD¹⁰; Paul Richardson, MD¹; Nikhil C. Munshi, MD¹; Kenneth C. Anderson, MD¹; Lorenzo Trippa, PhD⁴,¹¹; François Aguet, PhD³; Chip Stewart, PhD³; Meletios-Athanasios Dimopoulos, MD⁸; Kwee Yong, PhD³; P. Leif Bergsagel, MD¹²; Salomon Manier, MD, PhD¹³; Gad Getz, PhD₃,¹⁴; and Irene M. Ghobrial, MD¹,²,³

J Clin Oncol 2020;38:2380-9
Predictors of short-term survival in Waldenström Macroglobulinemia


Leuk Lymphoma 2020;14:1-5
Venetoclax for the treatment of translocation (11;14) AL amyloidosis

M. Hasib Sidiqi1,2, Abdullah S. Al Saleh1, Nelson Leung1,3, Dragan Jevremovic4, Mohammed A. Aljama5, Wilson I. Gonsalves1, Francis K. Buadi1, Taxiarchis V. Kourelis1, Rahma Warsame1, Eli Muchtar1, Miriam A. Hobbs1, Martha Q. Lacy1, David Dingli1, Ronald S. Go1, Suzanne R. Hayman1, S. Vincent Rajkumar1, Angela Dispenzieri1, Morie A. Gertz1, Shaji K. Kumar1, Rafael Fonseca6 and Prashant Kapoor1

Blood Cancer J 2020;10(5):55
The role of bone marrow biopsy in patients with plasma cell disorders: should all patients with a monoclonal protein be biopsied?

M. Hasib Sidiqi1,2, Mohammed Aljama3, Shaji K. Kumar1, Dragan Jevremovic4, Francis K. Buadi1, Rahma Warsame1, Martha Q. Lacy1, David Dingli1, Wilson I. Gonsalves1, Amie L. Fonder1, Miriam A. Hobbs1, Yi Lisa Hwa1, Prashant Kapoor1, Taxiarchis Kourelis1, Nelson Leung1,5, Eli Muchtar1, John A. Lust1, Robert A. Kyle1, Ronald S. Go6, Vincent S. Rajkumar1, Morie A. Gertz1 and Angela Dispenzieri1

Blood Cancer J 2020;10(5):52
Meet The Professor with Dr Rajkumar

Module 1: Cases from Dr Mikhael

Module 2: Myeloma Journal Club with Dr Rajkumar

Module 3: Beyond the Guidelines: Clinical Investigator Approaches to Common Clinical Scenarios

Module 4: Key Papers and Recent Approvals

- TOURMALINE-MM3 trial: Maintenance ixazomib
- FDA approval of carfilzomib and daratumumab with dexamethasone for relapsed/refractory (R/R) disease
- Phase I study of novel CELMoD agent CC-92480
- BOSTON: Initial results of a Phase III trial of selinexor, bortezomib and dexamethasone
- OPTIMISSM: Phase III trial of pomalidomide with bortezomib and dexamethasone for R/R myeloma
- COLUMBA: Phase III noninferiority trial of subcutaneous daratumumab
- FDA approval of isatuximab in combination with pomalidomide and dexamethasone in R/R myeloma
- Clinical trial data with and FDA approval of belantamab mafodotin in multiple regimen-relapsed myeloma
- Anti-BCMA CAR T-cell therapy trials: KarMMa, CARTITUDE-1 and EVOLVE

Co-provided by USF Health
Currently, what is your usual pretransplant induction regimen for a 65-year-old patient with MM and no high-risk features?

1. RVD (lenalidomide/bortezomib/dexamethasone)
2. KRd (carfilzomib/lenalidomide/dexamethasone)
3. CyBorD
4. MVP, MPR or MPT (M = melphalan, P = prednisone, V = bortezomib, R = lenalidomide, T = thalidomide)
5. MVP/daratumumab
6. Rd/daratumumab
7. VTd (bortezomib/thalidomide/dexamethasone) with daratumumab
8. RVD/daratumumab
9. KRd/daratumumab
10. Other
Currently, what is your usual pretransplant induction regimen for a 65-year-old patient with multiple myeloma (MM) and no high-risk features?

- RVD
- RVD/daratumumab
- KRd
- RVD
- RVD/daratumumab
- RVD
- KRd
- RVD/daratumumab
- RVD
Currently, what is your usual pretransplant induction regimen for a 65-year-old patient with \textit{del(17p)} MM?
Regulatory and reimbursement issues aside, what is your preferred induction regimen for an 85-year-old patient with ISS Stage II MM who is transplant ineligible with normal renal function and no high-risk features?

<table>
<thead>
<tr>
<th>Name</th>
<th>Regimen</th>
<th>Name</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAFAEL FONSECA, MD</td>
<td>Rd/dara</td>
<td>NIKHIL C MUNSHI, MD</td>
<td>Rd</td>
</tr>
<tr>
<td>JONATHAN L KAUFMAN, MD</td>
<td>Rd/dara</td>
<td>ROBERT Z ORLOWSKI, MD PHD</td>
<td>Rd/dara</td>
</tr>
<tr>
<td>SHAJI K KUMAR, MD</td>
<td>Rd/dara</td>
<td>NOOPUR RAJE, MD</td>
<td>Rd or RVD or RVD lite or Rd/dara</td>
</tr>
<tr>
<td>OLA LANDGREN, MD, PHD</td>
<td>Rd/dara</td>
<td>S VINCENT RAJKUMAR, MD</td>
<td>RVD or RVD lite</td>
</tr>
<tr>
<td>SAGAR LONIAL, MD</td>
<td>Rd/dara</td>
<td>NINA SHAH, MD</td>
<td>RVD or RVD lite or Rd/dara</td>
</tr>
<tr>
<td>JOSEPH R MIKHAEL, MD</td>
<td>Rd/dara</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Dara = daratumumab
Regulatory and reimbursement issues aside, what is your preferred induction regimen for an 85-year-old patient with del(17p) MM?

- RAFAEL FONSECA, MD: KRd
- JONATHAN L KAUFMAN, MD: RVD lite
- SHAJI K KUMAR, MD: RVD lite
- OLA LANDGREN, MD, PHD: RVD lite + dara
- SAGAR LONIAL, MD: RVD lite
- JOSEPH R MIKAEL, MD: RVD
- NIKHIL C MUNSHI, MD: RVD lite
- ROBERT Z ORLOWSKI, MD, PHD: RVD lite
- NOOPUR RAJE, MD: RVD lite
- S VINCENT RAJKUMAR, MD: RVD lite
- NINA SHAH, MD: RVD lite
Are there situations in which you believe community-based oncologists/hematologists should be ordering minimal residual disease (MRD) assessment to guide treatment decision-making for patients with MM?

<table>
<thead>
<tr>
<th>RAFAEL FONSECA, MD</th>
<th>Yes – Pts in long-term CR or with plasmacytomas; monitoring amyloidosis</th>
<th>NIKHIL C MUNSHI, MD</th>
<th>Yes – Post-transplant, at CR, before and during maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>JONATHAN L KAUFMAN, MD</td>
<td>No</td>
<td>ROBERT Z ORLOWSKI, MD, PHD</td>
<td>Yes, timing the number of induction cycles prior to stem cell collection for patients in CR</td>
</tr>
<tr>
<td>SHAJI K KUMAR, MD</td>
<td>Yes – Pts with high-risk disease</td>
<td>NOOPUR RAJE, MD</td>
<td>No</td>
</tr>
<tr>
<td>OLA LANDGREN, MD, PHD</td>
<td>Yes – After combination therapy for decision of stem cell collection and maintenance</td>
<td>S VINCENT RAJKUMAR, MD</td>
<td>No</td>
</tr>
<tr>
<td>SAGAR LONIAL, MD</td>
<td>No</td>
<td>NINA SHAH, MD</td>
<td>No</td>
</tr>
<tr>
<td>JOSEPH R MIKAEL, MD</td>
<td>No</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Co-provided by USFHealth
What is your usual recommendation for post-ASCT maintenance therapy for patients with MM and **no high-risk features** who received RVD induction therapy?

| RAFAEL FONSECA, MD | Lenalidomide | NIKHIL C MUNSHI, MD | Lenalidomide + dex |
| JONATHAN L KAUFMAN, MD | Lenalidomide | ROBERT Z ORLOWSKI, MD | Lenalidomide |
| SHAJI K KUMAR, MD | Lenalidomide | NOOPUR RAJE, MD | Lenalidomide |
| OLA LANDGREN, MD, PhD | Lenalidomide | S VINCENT RAJKUMAR, MD | Lenalidomide |
| SAGAR LONIAL, MD | Lenalidomide | NINA SHAH, MD | Lenalidomide |
| JOSEPH R MIKAEL, MD | Lenalidomide | | |

*Dex = dexamethasone*
What is your usual recommendation for post-ASCT maintenance therapy for patients with del(17p) MM who received RVD induction therapy?

<table>
<thead>
<tr>
<th>RAFAEL FONSECA, MD</th>
<th>Len/ixa ± dex</th>
<th>NIKHIL C MUNSHI, MD</th>
<th>Len/bortez ± dex</th>
</tr>
</thead>
<tbody>
<tr>
<td>JONATHAN L KAUFMAN, MD</td>
<td>Len/bortez ± dex</td>
<td>ROBERT Z ORLOWSKI, MD</td>
<td>Len/ixa ± dex</td>
</tr>
<tr>
<td>SHAJI K KUMAR, MD</td>
<td>Len/bortez ± dex</td>
<td>NOOPUR RAJE, MD</td>
<td>Len/ixa ± dex or Len/bortez ± dex</td>
</tr>
<tr>
<td>OLA LANDGREN, MD, PHD</td>
<td>Lenalidomide</td>
<td>S VINCENT RAJKUMAR, MD</td>
<td>Lenalidomide + bortezomib</td>
</tr>
<tr>
<td>SAGAR LONIAL, MD</td>
<td>Len/bortez ± dex</td>
<td>NINA SHAH, MD</td>
<td>Len/K ± dex</td>
</tr>
<tr>
<td>JOSEPH R MIKAEL, MD</td>
<td>Lenalidomide + bortezomib</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Len = lenalidomide; ixa = ixazomib; dex = dexamethasone; bortez = bortezomib; K = carfilzomib
What is your usual treatment recommendation for a patient with MM who receives RVD followed by ASCT and maintenance lenalidomide for 1.5 years who then experiences an asymptomatic biochemical relapse?

1. Carfilzomib +/- dexamethasone
2. Pomalidomide +/- dexamethasone
3. Carfilzomib + pomalidomide +/- dexamethasone
4. Elotuzumab + lenalidomide +/- dexamethasone
5. Elotuzumab + pomalidomide +/- dexamethasone
6. Daratumumab + lenalidomide +/- dexamethasone
7. Daratumumab + pomalidomide +/- dexamethasone
8. Daratumumab + bortezomib +/- dexamethasone
9. Ixazomib + Rd
10. Other
What is your usual treatment recommendation for a patient with MM who receives RVD followed by ASCT and maintenance lenalidomide for 1.5 years who then experiences an asymptomatic biochemical relapse?

Dara/pom ± dex

Dara/pom ± dex

Dara/pom ± dex

Dara/pom ± dex

Dara/pom ± dex

Dara/pom ± dex

Dara/pom ± dex ± dex if high risk

Dara/pom ± dex

Dara/pom ± dex

Dara/pom ± dex

Dara/pom ± dex

Dara/pom ± dex

Dara/len ± dex

Dara/pom ± dex

Dara = daratumumab; pom = pomalidomide; Elo = elotuzumab
What is your usual treatment recommendation for a patient with MM who receives RVD followed by ASCT and maintenance lenalidomide for 3 years who then experiences an asymptomatic biochemical relapse?

- Rafael Fonseca, MD: Dara/pom ± dex
- Jonathan L Kaufman, MD: Dara/pom ± dex
- Sha Ji K Kumar, MD: Dara/pom ± dex
- Ola Landgren, MD, PhD: Dara/pom ± dex
- Sagar Lonial, MD: Dara/pom ± dex
- Joseph R Mikhail, MD: Dara/pom ± dex
- Nikhil C Munshi, MD: Dara/pom ± dex
- Robert Z Orloffski, MD, PhD: Pom ± dex or dara/pom ± dex
- Noopur Raje, MD: Ixazomib + Rd
- S Vincent Rajkumar, MD: Dara/len + dex
- Nina Shah, MD: Dara/pom ± dex

Dara = daratumumab; pom = pomalidomide; Elo = elotuzumab
In general, when do you refer patients for possible inclusion in trials of BCMA-targeted CAR T-cell therapy?

<table>
<thead>
<tr>
<th>RAFAEL FONSECA, MD</th>
<th>Refractory to all drugs</th>
<th>NIKHIL C MUNSHI, MD</th>
</tr>
</thead>
<tbody>
<tr>
<td>JONATHAN L KAUFMAN, MD</td>
<td>2-3 prior lines, good PS, counts OK</td>
<td>ROBERT Z ORLOWSKI, MD, PHD</td>
</tr>
<tr>
<td>SHAJI K KUMAR, MD</td>
<td>Triple-class refractory</td>
<td>NOOPUR RAJE, MD</td>
</tr>
<tr>
<td>OLA LANDGREN, MD, PHD</td>
<td>Per protocol eligibility criteria</td>
<td>S VINCENT RAJKUMAR, MD</td>
</tr>
<tr>
<td>SAGAR LONIAL, MD</td>
<td>Few treatment options, slow relapse to wait the time to get cells</td>
<td>NINA SHAH, MD</td>
</tr>
<tr>
<td>JOSEPH R MIKAEL, MD</td>
<td>Triple-class refractory, reasonable PS, especially high-risk pts</td>
<td></td>
</tr>
</tbody>
</table>

- Having received combo of PI, IMiD and anti-CD38 Ab and disease progressing
- Multiply R/R setting; more recently in earlier settings if trial available
- As early as possible
- >3 prior regimens
- After failure of 3rd-line treatment
Meet The Professor with Dr Rajkumar

Module 1: Cases from Dr Mikhael

Module 2: Myeloma Journal Club with Dr Rajkumar

Module 3: Beyond the Guidelines: Clinical Investigator Approaches to Common Clinical Scenarios

Module 4: Key Papers and Recent Approvals

- TOURMALINE-MM3 trial: Maintenance ixazomib
- FDA approval of carfilzomib and daratumumab with dexamethasone for relapsed/refractory (R/R) disease
- Phase I study of novel CELMoD agent CC-92480
- BOSTON: Initial results of a Phase III trial of selinexor, bortezomib and dexamethasone
- OPTIMISSM: Phase III trial of pomalidomide with bortezomib and dexamethasone for R/R myeloma
- COLUMBA: Phase III noninferiority trial of subcutaneous daratumumab
- FDA approval of isatuximab in combination with pomalidomide and dexamethasone in R/R myeloma
- Clinical trial data with and FDA approval of belantamab mafodotin in multiple regimen-relapsed myeloma
- Anti-BCMA CAR T-cell therapy trials: KarMMa, CARTITUDE-1 and EVOLVE
Oral ixazomib maintenance following autologous stem cell transplantation (TOURMALINE-MM3): a double-blind, randomised, placebo-controlled phase 3 trial

Meletios A Dimopoulos, Francesca Gay, Fredrik Schjesvold, Meral Bekzac, Roman Hajek, Katja Christina Weisel, Hartmut Goldschmidt, Vladimir Maisnar, Philippe Moreau, Chang Ki Min, Agnieszka Pluta, Wee-Joo Chng, Martin Kaiser, Sonja Zweegman, Maria-Victoria Mateos, Andrew Spencer, Shinsuke Iida, Gareth Morgan, Kaveri Suryanarayan, Zhaoyang Teng, Tomas Skacel, Antonio Palumbo, Ajeeta B Dash, Neeraj Gupta, Richard Labotka, S Vincent Rajkumar, on behalf of the TOURMALINE-MM3 study group

Lancet 2019;393(10168):253-64.
TOURMALINE-MM3 Primary Endpoint: Progression-Free Survival (ITT)

<table>
<thead>
<tr>
<th></th>
<th>Ixazomib (n = 395)</th>
<th>Placebo (n = 261)</th>
<th>HR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median PFS</td>
<td>26.5 mo</td>
<td>21.3 mo</td>
<td>0.72</td>
<td>0.0023</td>
</tr>
</tbody>
</table>

Relapsed/Refractory Myeloma
FDA Approves Carfilzomib and Daratumumab with Dexamethasone for Multiple Myeloma
Press Release – August 20, 2020

“On August 20, 2020, the Food and Drug Administration approved carfilzomib and daratumumab in combination with dexamethasone for adult patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy.

The efficacy of carfilzomib and daratumumab with dexamethasone was evaluated in two clinical trials, CANDOR and EQUULEUS.”

First-in-Human Phase I Study of the Novel CELMoD Agent CC-92480 Combined with Dexamethasone (DEX) in Patients (pts) with Relapsed/Refractory Multiple Myeloma (RRMM)

Richardson PG et al.
ASCO 2020;Abstract 8500.
**CC-92480/Dexamethasone Combined with Bortezomib or Daratumumab or Carfilzomib**

**IMiD®**
- **Thalidomide**
  - Erythema Nodosum
  - Erythema Leprosum
  - Multiple Myeloma
- **Lenalidomide**
  - Mantle Cell Lymphoma
  - Multiple Myeloma
  - Myelodysplastic Syndrome (5q-) (CC-90009)
- **Pomalidomide**
  - Multiple Myeloma
  - Kaposi Sarcoma

**Indication**
- Erythema Nodosum
- Erythema Leprosum
- Multiple Myeloma
- Mantle Cell Lymphoma
- Multiple Myeloma
- Myelodysplastic Syndrome (5q-)
- Kaposi Sarcoma

**Clinical trials**
- **IMiD/CELMoDs**
  - Multiple Myeloma
  - Diffuse Large B-Cell Lymphoma
  - CNS Lymphoma
  - Glioblastoma
  - Hepatocellular Carcinoma
  - Chronic Lymphocytic Leukemia

- **CELMoDs**
  - CC-122
  - CC-220
  - CC-90009
  - CC-92480
  - CC-885

**Activity**
- MDS del 5q
- Anti-Tumor
- Anti-AML,-Lymphoma
- Anti-Myeloma

**Abbreviation:**
- CK1a: casein kinase 1a
- CELMods: Cereblon E3 Ligase Modulation Drugs
- CRL4: culin-4 RING E3 ligase
- CRBN: Cereblon: CNS: Central Nervous System
- CUL4: Cullin-4; DDB1: DNA damage-binding protein 1
- GSPT1: G1 To S Phase Transition 1
- IKZF1: Ikaros zinc-finger protein 1
- IKZF3: Aiolos zinc-finger protein 3
- IMiD: Immunomodulatory Drugs
- MDS: Myelodysplastic Syndrome
- Roc1: Ring finger protein
- Ub: Ubiquitination
- UBE2G1/2D3: Ubiquitin-conjugating enzymes

**Holstein et al, Next-Generation Drugs. Targeting the Cereblon Ubiquitin Ligase. JCO 2018.**
- Lu G et al eLife 2018
- Gandhi AK et al Br Haem 2014
- Krönke J et al Science 2014
- Hansen JD et al J Med Chem 2020
- Uehara, T et al Nat Chem Biol 2017

McCarthy P. ASCO 2020 Discussant

Co-provided by USF Health
Weekly Selinexor, Bortezomib, and Dexamethasone (SVd) versus Twice Weekly Bortezomib and Dexamethasone (Vd) in Patients with Multiple Myeloma (MM) After One to Three Prior Therapies: Initial Results of the Phase III BOSTON Study

Dimopoulos MA et al.
ASCO 2020;Abstract 8501.
OPTIMISMM: Phase III Trial of Pomalidomide with Bortezomib and Dexamethasone in Relapsed/Refractory MM


### Median PFS

<table>
<thead>
<tr>
<th></th>
<th>Pom-bort/dex</th>
<th>Bort/dex</th>
<th>HR (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refractory to lenalidomide (n = 200; 191)</td>
<td>9.5 mo</td>
<td>5.6 mo</td>
<td>0.65 (0.0008)</td>
</tr>
<tr>
<td>Refractory to lenalidomide and 1 prior line of treatment (n = 64; 65)</td>
<td>17.8 mo</td>
<td>9.5 mo</td>
<td>0.55 (0.03)</td>
</tr>
</tbody>
</table>

**All patients with 1-3 prior lines of therapy (including 2 or more cycles of lenalidomide)**

- Median PFS: 11.2 mo for Pomalidomide, bortezomib and dexamethasone (n = 281) vs. 7.1 mo for Bortezomib and dexamethasone (n = 278)
- HR 0.61; two-sided p < 0.0001
COLUMBA: Phase III Noninferiority Trial of Subcutaneous (SC) versus Intravenous (IV) Daratumumab for Relapsed or Refractory MM

Mateos M-V et al. ASCO 2019;Abstract 8005.

<table>
<thead>
<tr>
<th></th>
<th>DARA IV (n = 258)</th>
<th>DARA SC (n = 260)</th>
<th>Odds ratio (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate of infusion-related reactions</td>
<td>34.5%</td>
<td>12.7%</td>
<td>0.28 (&lt;0.00001)</td>
</tr>
</tbody>
</table>
Anti-CD38 Antibodies: Mechanism of Action, Structural and Pharmacologic Similarities and Differences

Mechanism of action

<table>
<thead>
<tr>
<th>Mechanism of action</th>
<th>Daratumumab</th>
<th>Isatuximab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Origin, isotype</td>
<td>Human IgG-kappa</td>
<td>Chimeric IgG1-kappa</td>
</tr>
<tr>
<td>CDC</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>ADCC</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>ADCP</td>
<td>+++</td>
<td>Not determined</td>
</tr>
<tr>
<td>PCD direct</td>
<td>—</td>
<td>++</td>
</tr>
<tr>
<td>PCD cross linking</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Modulation ectoenzyme function</td>
<td>+</td>
<td>+++</td>
</tr>
</tbody>
</table>

Direct effects
Alteration in intracellular signaling
CD38 enzymatic inhibition
Inhibition of adhesion

Immunomodulatory effects

FDA Approves New Therapy for Patients with Previously Treated Multiple Myeloma
Press Release – March 02, 2020

“Today, the US Food and Drug Administration approved isatuximab-irfc, in combination with pomalidomide and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.

The FDA approved isatuximab-irfc based on the results of a clinical trial involving 307 patients with relapsed and refractory multiple myeloma who had received at least two prior therapies, including lenalidomide and a proteasome inhibitor.

Patients who received isatuximab-irfc in combination with pomalidomide and low-dose dexamethasone showed improvement in PFS with a 40% reduction in the risk of disease progression or death compared to patients who received pomalidomide and dexamethasone. These patients also had an overall response rate of 60.4%. In comparison, the patients who only received pomalidomide and low-dose dexamethasone had an overall response rate of 35.3.”

The Food and Drug Administration granted accelerated approval to belantamab mafodotin-blmf for adult patients with relapsed or refractory multiple myeloma who have received at least 4 prior therapies, including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent.

Belantamab mafodotin-blmf was evaluated in DREAMM-2 (NCT 03525678), an open-label, multicenter trial. Patients received either belantamab mafodotin-blmf, 2.5 mg/kg or 3.4 mg/kg intravenously, once every 3 weeks until disease progression or unacceptable toxicity.

Efficacy was based on overall response rate (ORR) and response duration, as evaluated by an independent review committee using the International Myeloma Working Group uniform response criteria. The ORR was 31%. Seventy-three percent of responders had response durations ≥6 months. These results were observed in patients receiving the recommended dose of 2.5 mg/kg.

The prescribing information includes a Boxed Warning stating belantamab mafodotin-blmf causes changes in the corneal epithelium resulting in alterations in vision, including severe vision loss and corneal ulcer, and symptoms, such as blurred vision and dry eyes. Ophthalmic exams at baseline, prior to each dose, and promptly for worsening symptoms should be conducted.”
DREAMM-2 Randomized Phase II Study Design

Key eligibility:
- Relapsed or refractory MM
- PD on at least 3 prior therapies
- Refractory to IMiDs and proteasome inhibitors
- Refractory and/or intolerant to an anti-CD38 antibody

Primary endpoint: Overall response in the intent-to-treat population as determined by an independent review committee

DREAMM-2: Response and Duration of Response

2.5 mg/kg

- Overall response: 30 (31%)
- ≥VGPR: 18 (19%)

3.4 mg/kg

- Overall response: 34 (34%)
- ≥VGPR: 20 (20%)

# DREAMM-2: Select Adverse Events

<table>
<thead>
<tr>
<th>Adverse events (AEs) of special interest, any grade</th>
<th>Belantamab mafodotin 2.5 mg/kg (n = 95)</th>
<th>Belantamab mafodotin 3.4 mg/kg (n = 99)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia</td>
<td>35%</td>
<td>59%</td>
</tr>
<tr>
<td>Infusion-related reactions</td>
<td>21%</td>
<td>16%</td>
</tr>
<tr>
<td>Corneal events</td>
<td>71%</td>
<td>75%</td>
</tr>
<tr>
<td>Drug-related serious AEs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infusion-related reactions</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>6%</td>
<td>5%</td>
</tr>
<tr>
<td>Sepsis</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>4%</td>
<td>12%</td>
</tr>
</tbody>
</table>

DREAMM-6: Safety and Tolerability of Belantamab Mafodotin in Combination with Bortezomib/Dexamethasone in Relapsed/Refractory Multiple Myeloma (RRMM)

Nooka AK et al.
ASCO 2020;Abstract 8502.
Novel Agents in Late-Stage Development
Idecabtagene Vicleucel (ide-cel; bb2121), a BCMA-Targeted CAR T-Cell Therapy, in Patients with Relapsed and Refractory Multiple Myeloma (RRMM): Initial KarMMa Results

Munshi NC et al.
ASCO 2020;Abstract 8503.
Update of CARTITUDE-1: A Phase Ib/II Study of JNJ-4528, A B-cell Maturation Antigen (BCMA)-Directed CAR-T-Cell Therapy, in Relapsed/Refractory Multiple Myeloma

Berdeja JG et al.
ASCO 2020;Abstract 8505.
Orvacabtagene Autoleucel (orva-cel), a B-cell Maturation Antigen (BCMA)-Directed CAR T Cell Therapy for Patients (pts) with Relapsed/Refractory Multiple Myeloma (RRMM): Update of the Phase 1/2 EVOLVE Study (NCT03430011)

Mailankody S et al.
ASCO 2020;Abstract 8504.
## Characteristics Summary

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>KarMMa: idecabtagene vicleucel (n = 128)</th>
<th>EVOLVE: orvacabtagene autoleucel (n = 62)</th>
<th>CARTITUDE-1: JNJ-4528 (n = 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>61 (33-78)</td>
<td>61 (33-77)</td>
<td>60 (50-75)</td>
</tr>
<tr>
<td>High risk cytogenetics, %</td>
<td>35</td>
<td>41*</td>
<td>27</td>
</tr>
<tr>
<td>Tumor burden in BM, %</td>
<td>&gt;50% PC = 51</td>
<td>—</td>
<td>≥60% PC = 24</td>
</tr>
<tr>
<td>Extramedullary PCs, %</td>
<td>39</td>
<td>23</td>
<td>10</td>
</tr>
<tr>
<td>Median prior line of therapy</td>
<td>6 (3-16)</td>
<td>6 (3-18)</td>
<td>5 (3-18)</td>
</tr>
<tr>
<td>Triple refractory, %</td>
<td>84</td>
<td>94</td>
<td>86</td>
</tr>
<tr>
<td>Bridging therapy, %</td>
<td>88</td>
<td>63</td>
<td>79</td>
</tr>
<tr>
<td>Unique properties</td>
<td>Human BCMA, 4-1BB, CD3z</td>
<td>Modified spacer, CD4: CD8 enriched for CM</td>
<td>Median cell dose 0.72x106 cells/kg 2 BCMA single chain antibodies</td>
</tr>
</tbody>
</table>

* Included +1q21
## ASCO 2020: 3 BCMA CAR-T Studies

### Safety

<table>
<thead>
<tr>
<th></th>
<th>KarMMa</th>
<th>EVOLVE</th>
<th>CARTITUDE-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANC ≥G3, %</td>
<td>89</td>
<td>90</td>
<td>100</td>
</tr>
<tr>
<td>plts ≥G3, %</td>
<td>52</td>
<td>47</td>
<td>69</td>
</tr>
<tr>
<td>CRS: all, ≥G3, %</td>
<td>84, 6</td>
<td>89, 3</td>
<td>93, 7</td>
</tr>
<tr>
<td>Med. time to CRS, duration, days</td>
<td>1 (1-12) 5 (1-63)</td>
<td>2 (1-4) 4 (1-10)</td>
<td>7 (2-12) 4 (2-64)</td>
</tr>
<tr>
<td>ICANS: all, ≥G3, %</td>
<td>17, 3</td>
<td>13, 3</td>
<td>10, 3</td>
</tr>
<tr>
<td>HLH/MAS, %</td>
<td>—</td>
<td>5</td>
<td>? (lfts)</td>
</tr>
<tr>
<td>Infections: all, ≥G3</td>
<td>69, —</td>
<td>40, 13</td>
<td>—, 19</td>
</tr>
<tr>
<td>Toci/steroid/anakinra use, %</td>
<td>52/15/0</td>
<td>76/52/23</td>
<td>79/21/21</td>
</tr>
</tbody>
</table>

? This was not listed at MAS/HLH, I am just speculating → could this have been early MAS

### Efficacy

<table>
<thead>
<tr>
<th></th>
<th>KarMMa (n = 128)</th>
<th>EVOLVE (n = 62)</th>
<th>CARTITUDE-1 (n = 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR, %</td>
<td>73 (66-81)</td>
<td>92</td>
<td>100</td>
</tr>
<tr>
<td>sCR/CR, %</td>
<td>33</td>
<td>36</td>
<td>86</td>
</tr>
<tr>
<td>MRD neg ≥10⁻⁵, % (of evaluable)</td>
<td>94</td>
<td>84</td>
<td>81</td>
</tr>
<tr>
<td>PFS, DoR, months</td>
<td>8.8/10.7</td>
<td>NR*</td>
<td>NR**</td>
</tr>
<tr>
<td>Screened Apheresed Treated</td>
<td>150</td>
<td>140</td>
<td>128</td>
</tr>
</tbody>
</table>

* 300 x 10⁶ cell dose cohort (lowest) = PFS 9.3 months, other med F/U = 8.8 and 2.3 month
** 9 mo PFS = 86%
EVOLVE BCMA CAR-T Study

Look at that waterfall!

EVOLVE: Deep tumor burden reduction across dose levels

Serological responses* were observed in all patients treated at 450 x 10^6 and 600 x 10^8DLs

* Involved serum or urine paraprotein, free light chains. ^ Patient with baseline extramedullary plasmacytoma.
Meet The Professor
Management of Ovarian Cancer

Thursday, October 1, 2020
12:00 PM – 1:00 PM ET

Faculty
Ursula Matulonis, MD

Moderator
Neil Love, MD
Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 days.