SECOND OPINION: NEW AGENTS AND EMERGING TRIAL DATA IN THE MANAGEMENT OF MULTIPLE MYELOMA

CME Information

TARGET AUDIENCE

This activity is intended for medical oncologists, hematologists and other healthcare providers involved in the treatment of multiple myeloma (MM).

OVERVIEW OF ACTIVITY

MM is a plasma cell neoplasm that accounts for approximately 10% of all hematologic cancers and carries with it the worst death to new cases ratio (3:4). In addition, the disease course for advanced myeloma is uniformly aggressive. However, the introduction of new agents with substantial activity has improved outcomes and allowed patients to experience longer periods of remission. Both novel proteasome inhibitors and immunomodulatory agents have effectively transformed standard care for patients with newly diagnosed and relapsed/refractory MM. Therefore, the current challenge facing the oncology community is identification of those patients who will enjoy the greatest benefit from a specific regimen while incurring the least toxicity. In this regard, hematologic oncologists must be apprised of the unique risks and benefits accompanying each evidence-based treatment strategy, as well as the acceptable monitoring and supportive management techniques that enable early recognition of safety concerns and effective interventions to address side effects. Several consensus- and evidence-based treatment guidelines are available and aim to assist clinicians with making clinical management decisions related to these diseases. But despite the existence of these tools, many areas of controversy persist within academic and community settings.

To bridge the gap between research and patient care, this video presentation by Dr Noopur Raje uses a review of recent relevant publications and presentations, ongoing clinical trials and clinical investigator treatment preferences to assist medical oncologists, hematologists and other healthcare providers involved in the treatment of MM with the formulation of up-to-date clinical management strategies.

LEARNING OBJECTIVES

- Appraise recent data on therapeutic advances and changing practice standards in MM, and integrate this information, as appropriate, into current clinical care.
- Compare and contrast the benefits and risks of immunomodulatory agents, proteasome inhibitors or both as systemic treatment for active MM.
- Use patient- and disease-related factors, including cytogenetic profile, to customize the use of induction and maintenance therapeutic approaches in the post-transplant and nontransplant settings.
- Consider available research data and other clinical factors in the best-practice selection, sequencing or combining of carfilzomib and pomalidomide in the nonresearch care of patients with relapsed or refractory MM.
- Recognize the recent FDA approvals of panobinostat, elotuzumab, ixazomib and daratumumab, and effectively identify patients for whom treatment with these novel agents may be appropriate.
- Develop an understanding of emerging efficacy and safety data with novel monoclonal antibodies under evaluation for MM.
- Assess the ongoing clinical trials evaluating innovative developmental approaches for MM, and obtain consent from appropriate patients for study participation.

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FACULTY — The following faculty (and their spouses/partners) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process:

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Hardware/Software Requirements:
A high-speed Internet connection
A monitor set to 1280 x 1024 pixels or more
Internet Explorer 7 or later, Firefox 3.0 or later, Chrome, Safari 3.0 or later
Adobe Flash Player 10.2 plug-in or later
Adobe Acrobat Reader
(Optional) Sound card and speakers for audio

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Select Publications

Attal M et al. **Autologous transplantation for multiple myeloma in the era of new drugs: A phase III study of the Intergroupe Francophone du Myélome (IFM/DFCI 2009 trial).** *Proc ASH* 2015;**Abstract 391**.

Avet-Loiseau H et al. **Evaluation of minimal residual disease (MRD) by next generation sequencing (NGS) is highly predictive of progression free survival in the IFM/DFCI 2009 trial.** *Proc ASH* 2015;**Abstract 191**.

Berenson J et al. **Weekly carfilzomib with dexamethasone for patients with relapsed or refractory multiple myeloma: Updated results from the phase 1/2 study CHAMPION-1 (NCT01677858).** *Proc ASH* 2015;**Abstract 373**.

Chari A et al. **Open-label, multicenter, phase 1b study of daratumumab in combination with pomalidomide and dexamethasone in patients with at least 2 lines of prior therapy and relapsed or relapsed and refractory multiple myeloma.** *Proc ASH* 2015;**Abstract 508**.

Dimopoulos MA et al. **An open-label, randomised Phase 3 study of daratumumab, lenalidomide, and dexamethasone (DRD) versus lenalidomide and dexamethasone (RD) in relapsed or refractory multiple myeloma (RRMM): POLLUX.** *Proc EHA* 2016;**Abstract LB2238**.

Dimopoulos MA et al. **ELOQUENT-2 update: A phase 3, randomized, open-label study of elotuzumab in combination with lenalidomide/dexamethasone in patients with relapsed/refractory multiple myeloma — 3-year safety and efficacy follow-up.** *Proc ASH* 2015;**Abstract 28**.

Durie B et al. **Bortezomib, lenalidomide and dexamethasone versus lenalidomide and dexamethasone in patients (pts) with previously untreated multiple myeloma without an intent for immediate autologous stem cell transplant (ASCT): Results of the randomized phase III trial SWOG S0777.** *Proc ASH* 2015;**Abstract 25**.

ENDURANCE: Randomized phase III trial of bortezomib, lenalidomide and dexamethasone (VRd) versus carfilzomib, lenalidomide, dexamethasone (CRd) followed by limited or indefinite lenalidomide maintenance in patients with newly diagnosed symptomatic multiple myeloma. NCT01863550

Lokhorst HM et al. **Targeting CD38 with daratumumab monotherapy in multiple myeloma.** *N Engl J Med* 2015;373(13):1207-19.

Lonial S et al. **Elotuzumab therapy for relapsed or refractory multiple myeloma.** *N Engl J Med* 2015;373(7):621-31.

Lonial S et al. **Phase II study of daratumumab (DARA) monotherapy in patients with ≥ 3 lines of prior therapy or double refractory multiple myeloma (MM): 54767414MMY2002 (SIRIUS).** *Proc ASCO* 2015;**Abstract LBA8512**.

Moreau P et al. **Ixazomib, an investigational oral proteasome inhibitor (PI), in combination with lenalidomide and dexamethasone (IRd), significantly extends progression-free survival (PFS) for patients (pts) with relapsed and/or refractory multiple myeloma (RRMM): The phase 3 TOURMALINE-MM1 study (NCT01564537).** *Proc ASH* 2015;**Abstract 727**.

Palumbo A et al. **Phase III randomized controlled study of daratumumab, bortezomib, and dexamethasone (DVd) versus bortezomib and dexamethasone (Vd) in patients (pts) with relapsed or refractory multiple myeloma (RRMM): CASTOR study.** *Proc ASCO* 2016;**Abstract LBA4**.

Plesner T et al. **Daratumumab in combination with lenalidomide and dexamethasone in patients with relapsed or relapsed and refractory multiple myeloma: Updated results of a phase 1/2 study (GEN503).** *Proc ASH* 2015;**Abstract 507**.

Rosenthal A et al. **Carfilzomib and the cardiorenal system in myeloma: An endothelial effect?** *Blood Cancer J* 2016;6:e384.

San Miguel J et al. **Pembrolizumab in combination with lenalidomide and low-dose dexamethasone for relapsed/refractory multiple myeloma (RRMM): Keynote-023.** *Proc ASH* 2015;**Abstract 505**.

San-Miguel JF et al. **Panobinostat plus bortezomib and dexamethasone versus placebo plus bortezomib and dexamethasone in patients with relapsed or relapsed and refractory multiple myeloma: A multicentre, randomised, double-blind phase 3 trial.** *Lancet Oncol* 2014;15(11):1195-206.

Stewart AK et al. **Carfilzomib, lenalidomide, and dexamethasone for relapsed multiple myeloma.** *N Engl J Med* 2015;372(2):142-52.

TOURMALINE-MM2: A phase 3, randomized, double-blind, multicenter study comparing oral ixazomib (MLN9708) plus lenalidomide and dexamethasone versus placebo plus lenalidomide and dexamethasone in adult patients with newly diagnosed multiple myeloma. NCT01850524