Multiple Myeloma Update

Issue 1, 2018 (Video Program)

CME Information

TARGET AUDIENCE

This activity is intended for medical oncologists, hematologists, hematology-oncology fellows and other healthcare providers involved in the treatment of hematologic cancers.

OVERVIEW OF ACTIVITY

Multiple myeloma (MM) is a plasma cell neoplasm that accounts for approximately 12% of all hematologic cancers and carries with it one of the worst death to new cases ratios. Although MM only represented 1.8% of all new cancer cases diagnosed in the United States in 2017, practicing clinicians would be hard pressed to identify another area of oncology in which the research database — and available treatments — has evolved more rapidly over the past decade. In addition to significantly altering the natural history of MM, novel agents, including proteasome inhibitors, immunomodulatory agents and BTK inhibitors, have contributed to recent treatment gains for 2 related blood disorders — Waldenström macroglobulinemia (WM) and amyloidosis. Featuring the latest research developments along with expert perspectives, this CME activity will deliver to community-based oncology clinicians highly applicable, current clinical information delving into the individualized and multifaceted management of these disorders.

LEARNING OBJECTIVES

- Use patient and disease characteristics, including cytogenetic profile, to customize induction and maintenance therapeutic approaches in the transplant and nontransplant settings.
- Consider available research data and other clinical factors in the best-practice selection, sequencing and combination of current and recently approved novel agents in the nonresearch care of patients with relapsed/refractory MM.
- Design and implement a plan of care to recognize and manage side effects and toxicities associated with recently approved systemic therapies to support quality of life and continuation of treatment.
- Develop an evidence-based algorithm for the use of stem cell transplantation, chemotherapy and/or novel targeted agents for the management of amyloidosis.
- Consider clinical and other patient-related factors in the sequence and selection of systemic therapy for WM requiring active treatment.
- Develop risk-adapted treatment plans for patients with smoldering MM, considering the roles of observation and active treatment.

ACCREDITATION STATEMENT

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of Penn State College of Medicine and Research To Practice. Penn State College of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

CREDIT DESIGNATION STATEMENT

Penn State College of Medicine designates this enduring material for a maximum of 5.25 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

HOW TO USE THIS CME ACTIVITY

This CME activity consists of a video component. To receive credit, the participant should review the CME information, watch the video, complete the Post-test with a score of 80% or better and fill out the Educational Assessment and Credit Form located at **ResearchToPractice.com/MMUpdate118/Video/CME**. The corresponding audio program is available as an alternative at **ResearchToPractice.com/MMUpdate118**.

CONTENT VALIDATION AND DISCLOSURES

It is the policy of Research To Practice and Penn State College of Medicine to ensure balance, independence, objectivity and scientific rigor in all their educational programs. All faculty, planners and managers participating in this activity are required to disclose any relevant financial relationship(s) they (or spouse/partner) have with a commercial interest that benefits the individual in any financial amount that has occurred within the past 12 months; and the opportunity to affect the content of CME about the products or services of the commercial interest. Research To Practice and Penn State College of Medicine ensured that any conflicts of interest were resolved before the educational activity occurred.

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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PENN STATE COLLEGE OF MEDICINE — Faculty and staff involved in the development and review of this activity have disclosed no relevant financial relationships.

RESEARCH TO PRACTICE STAFF AND EXTERNAL REVIEWERS — The scientific staff and reviewers for Research To Practice have no relevant conflicts of interest to disclose.

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Hardware/Software Requirements:
A high-speed Internet connection
A monitor set to 1280 x 1024 pixels or more
Internet Explorer 11 or later, Firefox 56 or later, Chrome 61 or later, Safari 11 or later, Opera 48 or later
Adobe Flash Player 27 plug-in or later
Adobe Acrobat Reader
(Optional) Sound card and speakers for audio

Last review date: February 1, 2018

Expiration date: February 1, 2019

Select Publications

A phase 3, randomized, controlled, open-label, multicenter, safety and efficacy study of dexamethasone plus MLN9708 or physicians choice of treatment administered to patients with relapsed or refractory systemic light chain (AL) amyloidosis. NCT01659658

A phase 3, randomized, multicenter, double-blind, placebo-controlled, 2-arm, efficacy and safety study of NEOD001 plus standard of care versus placebo plus standard of care in subjects with light chain (AL) amyloidosis. NCT02312206

A phase 3 randomized, open-label, multicenter study comparing isatuximab (SAR650984) in combination with pomalidomide and low-dose dexamethasone versus pomalidomide and low-dose dexamethasone in patients with refractory or relapsed and refractory multiple myeloma. NCT02990338

A randomized phase 3 study to evaluate the efficacy and safety of daratumumab in combination with cyclophosphamide, bortezomib and dexamethasone (CyBorD) compared to CyBorD alone in newly diagnosed systemic AL amyloidosis. NCT03201965

A single arm, open-label, phase 2 study of melflufen in combination with dexamethasone in patients with relapsed refractory multiple myeloma who are refractory to pomalidomide and/or daratumumab. NCT02963493

Aggressive smoldering curative approach evaluating novel therapies and transplant (ASCENT): A phase 2 trial of induction, consolidation, and maintenance in subjects with high risk smoldering multiple myeloma (SMM). NCT03289299

Anderson KC et al. **The role of minimal residual disease testing in myeloma treatment selection and drug development: Current value and future applications.** *Clin Cancer Res* 2017;23(15):3980-93.

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

Chng WJ et al. **IMWG consensus on risk stratification in multiple myeloma.** *Leukemia* 2014;28(2):269-77.

Dimopoulos MA et al. **Ibrutinib for patients with rituximab-refractory Waldenström's macroglobulinaemia (iNNOVATE): An open-label substudy of an international, multicentre, phase 3 trial.** *Lancet Oncol* 2017;18(2):241-50.

Dimopoulos MA et al; ENDEAVOR Investigators. **Carfilzomib and dexamethasone versus bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma (ENDEAVOR): A randomised, phase 3, open-label, multicentre study.** *Lancet Oncol* 2016;17(1):27-38.

Fan F et al. **Durable remissions with BCMA specific chimeric antigen receptor (CAR)-modified T cells in patients with refractory/relapsed multiple myeloma.** *Proc ASCO* 2017;**Abstract LBA3001**.

Gertz M et al. **First-in-human phase I/II study of NEOD001 in patients with light chain amyloidosis and persistent organ dysfunction.** *J Clin Oncol* 2016;34(10):1097-103.

Jackson GH et al. **Lenalidomide induction and maintenance therapy for transplant eligible myeloma patients: Results of the Myeloma XI study.** *Proc ASCO* 2017;**Abstract 8009**.

Jackson GH et al. **Response adapted induction treatment improves outcomes for myeloma patients; Results of the phase III Myeloma XI study.** *Proc ASH* 2016;**Abstract 244**.

Kapoor P et al. **Diagnosis and management of Waldenström macroglobulinemia: Mayo Stratification of Macroglobulinemia and Risk-Adapted Therapy (mSMART) Guidelines 2016.** *JAMA Oncol* 2017;3(9):1257-65.

Kourelis TV et al. **Presentation and outcomes of localized immunoglobulin light chain amyloidosis: The Mayo Clinic experience.** *Mayo Clin Proc* 2017;92(6):908-17.

Laubach J et al. **Management of relapsed multiple myeloma: Recommendations of the International Myeloma Working Group.** *Leukemia* 2016;30(5):1005-17.

Lonial S et al; ELOQUENT-2 Investigators. **Elotuzumab therapy for relapsed or refractory multiple myeloma.** *N Engl J Med* 2015;373(7):621-31.

McCarthy PL et al. **CALGB/ECOG 100104 (Alliance) study: Lenalidomide (LEN) vs placebo (PBO) maintenance (maint) after stem cell transplant (SCT) for patients (pts) with multiple myeloma—Overall survival (OS) and progression-free survival (PFS) adjusted for treatment (tx) crossover (XO).** *Proc ASCO* 2017;**Abstract 8037**.

Moreau P et al; TOURMALINE-MM1 Study Group. **Oral ixazomib, lenalidomide, and dexamethasone for multiple myeloma.** *N Engl J Med* 2016;374(17):1621-34.

Morgan GJ et al. **Long-term follow-up of MRC Myeloma IX trial: Survival outcomes with bisphosphonate and thalidomide treatment.** *Clin Cancer Res* 2013;19(21):6030-8.

Select Publications

Muchtar E et al. **Diagnosis and management of smoldering multiple myeloma: The razor's edge between clonality and cancer.** *Leuk Lymphoma* 2018;59(2):288-99.

Muchtar E et al. **Improved outcomes for newly diagnosed AL amyloidosis between 2000 and 2014: Cracking the glass ceiling of early death.** *Blood* 2017;129(15):2111-9.

Muchtar E et al. **The prognostic value of multiparametric flow cytometry in AL amyloidosis at diagnosis and at the end of first-line treatment.** *Blood* 2017;129(1):82-7.

Nijhof IS et al. **CD38 expression and complement inhibitors affect response and resistance to daratumumab therapy in myeloma.** *Blood* 2016;128(7):959-70.

Nooka AK et al. **Consolidation and maintenance therapy with lenalidomide, bortezomib and dexamethasone (RVD) in high-risk myeloma patients.** *Leukemia* 2014;28(3):690-3.

Paludo J et al. **Survival trends in young patients with Waldenström macroglobulinemia: Over 5 decades of experience.** *Proc ASH* 2016;**Abstract 1810**.

Palumbo A et al; CASTOR Investigators. **Daratumumab, bortezomib, and dexamethasone for multiple myeloma.** *N Engl J Med* 2016;375(8):754-66.

Voorhees PM et al. **Efficacy of melflufen, a peptidase targeted therapy, and dexamethasone in an ongoing open-label phase 2a study in patients with relapsed and relapsed-refractory multiple myeloma (RRMM) including an initial report on progression free survival.** *Proc ASH* 2015;**Abstract 3029**.

San Miguel JF et al. **Final analysis of overall survival from the Phase 3 Panorama 1 trial of panobinostat plus bortezomib and dexamethasone versus placebo plus bortezomib and dexamethasone in patients with relapsed or relapsed and refractory multiple myeloma.** *Proc ASH* 2015;**Abstract 3026**.

Sidana S et al. **Factors predicting organ response in light chain amyloidosis (AL).** *Proc ASCO* 2017;**Abstract 8048**.

Sidana S et al. **Bortezomib versus non-bortezomib based treatment for transplant ineligible patients with light chain amyloidosis.** *Proc ASH* 2016;**Abstract 3317**.

Stadtmauer et al. **B-cell maturation antigen (BCMA)-specific chimeric antigen receptor T cells (CART-BCMA) for multiple myeloma (MM): Initial safety and efficacy from a phase I study.** *Proc ASH* 2016;**Abstract 1147**.

Stadtmauer et al. **Pilot study of anti-CD19 chimeric antigen receptor T cells (CTL019) in conjunction with salvage autologous stem cell transplantation for advanced multiple myeloma.** *Proc ASH* 2016;**Abstract 974**.

Treon SP et al. **Ibrutinib in previously treated Waldenström's macroglobulinemia.** *N Engl J Med* 2015;372(15):1430-40.

Usmani SZ et al. **Open-label, multicenter, dose escalation phase 1b study to assess the subcutaneous delivery of daratumumab in patients (pts) with relapsed or refractory multiple myeloma (PAVO).** *Proc ASH* 2016;**Abstract 1149**.