

Clinical Investigator and Nursing Perspectives on the Management of Multiple Myeloma

OVERVIEW OF ACTIVITY

Multiple myeloma (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) among all the blood cancer subtypes. Patients with smoldering (asymptomatic) myeloma may be cared for by observation only because the course of the disease is often indolent for many years without therapy. However, patients with more advanced, active disease require immediate induction therapy in an effort to prepare eligible candidates for autologous stem cell transplant (ASCT). Optimal initial induction therapy for both ASCT candidates and those not eligible remains an area of clinical controversy, and multiple acceptable treatment options appear to merit consideration. Recent clinical research demonstrates an abundance of treatment options now available to patients with both newly diagnosed and relapsed or refractory MM. To provide oncology nurses with therapeutic strategies to address the disparate needs of patients with MM, the *Oncology Nursing Update* audio series employs one-on-one interviews with medical oncologists and nurses who are experts in caring for patients with MM. Upon completion of this CNE activity, oncology nurses should be able to formulate an up-to-date and more complete approach to the care of patients with MM.

LEARNING OBJECTIVES

- Discuss the benefits and risks associated with evidence-based systemic therapies used in the treatment of MM, including chemotherapy, proteasome inhibitors, corticosteroids and immunomodulatory agents, in the pre- and post-ASCT settings and in patients who are not candidates for ASCT or those with renal insufficiency.
- Develop a plan of care to manage the side effects associated with these therapies to support quality of life and continuation of treatment.
- Evaluate the preliminary safety profiles and response outcomes observed in studies of next-generation proteasome inhibitors, immunomodulatory agents and monoclonal antibodies for patients with relapsed or refractory and previously untreated MM.

- Integrate recent clinical research findings with immunomodulatory agents into the development of individualized maintenance treatment strategies — including factors such as treatment dose and schedule, quality of life and side effects — for patients with MM.

ACCREDITATION STATEMENT

Research To Practice is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

CREDIT DESIGNATION STATEMENT

This educational activity for 1.25 contact hours is provided by Research To Practice during the period of January 2013 through January 2014.

HOW TO USE THIS CNE ACTIVITY

This is an audio CNE program. This website contains CNE information, including learning objectives, faculty disclosures, a Post-test and an Educational Assessment and Credit Form, as well as links to relevant abstracts and full-text articles.

To receive credit, participants should read the learning objectives and faculty disclosures, listen to the audio MP3s and complete the Post-test and Educational Assessment and Credit Form located at ResearchToPractice.com/ONUMM212/CNE. A statement of CNE credit will be issued only upon completion of the Post-test, with a score of 75% or better, and the Educational Assessment and Credit Form. Your statement of credit will be mailed to you within 3 weeks or may be printed online.

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FACULTY — The following faculty (and their spouses/partners) reported real or apparent 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

There is no implied or real endorsement of any product by RTP or the American Nurses Credentialing Center.

INTERVIEW WITH DR LONIAL

- Activity of the newly FDA-approved, irreversible proteasome inhibitor carfilzomib in patients with bortezomib-naïve and bortezomib-resistant multiple myeloma (MM)
- Infrequent carfilzomib-related peripheral neuropathy
- Mechanism(s) of action of proteasome inhibitors
- Synergy of bortezomib with chemotherapy and immunomodulatory drugs (IMiDs) in MM
- Etiology of renal failure in patients with MM and benefit from treatment with bortezomib
- Subcutaneous administration and/or weekly dosing to ameliorate bortezomib-related neuropathy
- Improving long-term outcomes with longer duration of treatment with IMiDs and proteasome inhibitors during initial induction therapy
- Predisposing factors (eg, diabetes) for the development of bortezomib-associated neuropathy
- MLN9708, a next-generation, investigational oral proteasome inhibitor
- Tolerability and side-effect profile of carfilzomib
- Lenalidomide-associated neutropenia, thrombocytopenia and thrombosis
- Perspective on preferred induction therapy in younger patients — lenalidomide, bortezomib and dexamethasone (RVD) versus cyclophosphamide, bortezomib and dexamethasone (CyBORd)
- Role of immediate versus deferred autologous stem cell transplant (ASCT) in the era of novel agents
- Post-transplant maintenance lenalidomide and second primary cancers
- Dose and schedule of maintenance lenalidomide
- Potency and side effects of the third-generation IMiD pomalidomide
- Cereblon expression as a prerequisite for the antimyeloma activity of IMiDs
- Incorporation of carfilzomib into up-front induction therapy regimens for transplant-eligible and transplant-ineligible patients with MM
- Rationale for combining the anti-CS1 monoclonal antibody elotuzumab with lenalidomide and dexamethasone
- Benefits of bisphosphonates and the rank ligand inhibitor denosumab as bone-targeted treatments in MM

- Prevention of bisphosphonate-associated osteonecrosis of the jaw (ONJ)
- Duration of bisphosphonate therapy in patients with active myeloma
- Defining characteristics of smoldering myeloma
- Investigations of risk-adapted treatment approaches for smoldering myeloma

INTERVIEW WITH MS RICHARDS

- Counseling patients who are about to initiate induction therapy
- Impact of subcutaneous administration and/or weekly dosing of bortezomib on the incidence of peripheral neuropathy
- Importance of hydration prior to carfilzomib administration
- Thromboembolic prophylaxis in patients receiving RVD induction therapy
- Educating patients who are about to undergo ASCT
- Defining autologous and allogeneic stem cell transplants and graft versus host disease
- Conventional cytogenetics and FISH to identify patients with a poor prognosis
- Monitoring and management of patients receiving post-transplant maintenance lenalidomide
- Treatment approach for relapsed MM
- Newly approved (carfilzomib) and promising novel (pomalidomide and elotuzumab) agents in MM
- Selection of up-front treatment for patients with MM who are ineligible for transplant — MPV versus MPR
- Dosing and duration of initial treatment for elderly patients
- Treatment and reversibility of renal dysfunction in MM
- Selection and duration of bone-targeted treatment in MM
- Importance of dental evaluation for patients prior to receiving bisphosphonates to ameliorate risk of ONJ
- Local treatments for bone disease — radiation therapy and kyphoplasty
- Counseling patients with MM about their expected prognosis

SELECT PUBLICATIONS

- Arnulf B et al. **Updated survival analysis of a randomized, phase 3 study of subcutaneous versus intravenous bortezomib in patients with relapsed multiple myeloma.** *Haematologica* 2012;[Epub ahead of print]. **Abstract**
- Attal M et al. **Lenalidomide maintenance after stem-cell transplantation for multiple myeloma.** *N Engl J Med* 2012;366(19):1782-91. **Abstract**
- Jakubowiak AJ et al. **A phase 1/2 study of carfilzomib in combination with lenalidomide and low-dose dexamethasone as a frontline treatment for multiple myeloma.** *Blood* 2012;120(9):1801-9. **Abstract**
- Jakubowiak AJ et al. **Stringent complete response (sCR) in patients (pts) with newly diagnosed multiple myeloma (NDMM) treated with carfilzomib (CFZ), lenalidomide (LEN), and dexamethasone (DEX).** *Proc ASCO* 2012;Abstract 8011.
- Lacy MQ et al. **Pomalidomide plus low-dose dexamethasone in myeloma refractory to both bortezomib and lenalidomide: Comparison of 2 dosing strategies in dual-refractory disease.** *Blood* 2011;118(11):2970-5. **Abstract**
- McCarthy PL et al. **Lenalidomide after stem-cell transplantation for multiple myeloma.** *N Engl J Med* 2012;366(19):1770-81. **Abstract**
- Morgan GJ et al. **Effects of induction and maintenance plus long-term bisphosphonates on bone disease in patients with multiple myeloma: The Medical Research Council Myeloma IX trial.** *Blood* 2012;119(23):5374-83. **Abstract**
- Morgan GJ et al. **Effects of zoledronic acid versus clodronic acid on skeletal morbidity in patients with newly diagnosed multiple myeloma (MRC Myeloma IX): Secondary outcomes from a randomised controlled trial.** *Lancet Oncol* 2011;12(8):743-52. **Abstract**
- Moreau P et al. **A randomized phase II study of elotuzumab with lenalidomide and low-dose dexamethasone in patients with relapsed/refractory multiple myeloma.** *Proc ASCO* 2012;Abstract 8020.
- Moreau P et al. **Subcutaneous versus intravenous administration of bortezomib in patients with relapsed multiple myeloma: A randomised, phase 3, non-inferiority study.** *Lancet Oncol* 2011;12(5):431-40. **Abstract**
- Palumbo A et al. **Continuous lenalidomide treatment for newly diagnosed multiple myeloma.** *N Engl J Med* 2012;366(19):1759-69. **Abstract**
- Reeder CB et al. **Once- versus twice-weekly bortezomib induction therapy with CyBorD in newly diagnosed multiple myeloma.** *Blood* 2010;115(16):3416-7. **Abstract**
- Reeder CB et al. **Cyclophosphamide, bortezomib and dexamethasone induction for newly diagnosed multiple myeloma: High response rates in a phase II clinical trial.** *Leukemia* 2009;23(7):1337-41. **Abstract**
- Richardson PG et al. **Oral weekly MLN9708, an investigational proteasome inhibitor, in combination with lenalidomide and dexamethasone in patients (pts) with previously untreated multiple myeloma (MM): A phase I/II study.** *Proc ASCO* 2012;Abstract 8033.
- Richardson PG et al. **Lenalidomide, bortezomib, and dexamethasone combination therapy in patients with newly diagnosed multiple myeloma.** *Blood* 2010;116(5):679-86. **Abstract**
- Vij R et al. **An open-label, single-arm, phase 2 study of single-agent carfilzomib in patients with relapsed and/or refractory multiple myeloma who have been previously treated with bortezomib.** *Br J Haematol* 2012;158(6):739-48. **Abstract**
- Vij R et al. **Pomalidomide (POM) with or without low-dose dexamethasone (LoDEX) in patients (pts) with relapsed/refractory multiple myeloma (RRMM): Outcomes in pts refractory to lenalidomide (LEN) and/or bortezomib (BORT).** *Proc ASCO* 2012;Abstract 8016.
- Zhu YX et al. **Cereblon expression is required for the antimyeloma activity of lenalidomide and pomalidomide.** *Blood* 2011;118(18):4771-9. **Abstract**