

# Multiple Myeloma™

U P D A T E

Conversations with Oncology Investigators  
Bridging the Gap between Research and Patient Care

**FACULTY INTERVIEWS**

Edward A Stadtmauer, MD  
Sarah A Holstein, MD, PhD  
Paul G Richardson, MD  
Shaji K Kumar, MD

**EDITOR**

Neil Love, MD

**CONTENTS**

1 Audio CD



# Multiple Myeloma™

U P D A T E

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## Multiple Myeloma Update

### A Continuing Medical Education Audio Series

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#### 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.

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Penn State College of Medicine designates this enduring material for a maximum of 4.5 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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## CME INFORMATION

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## Interview with Edward A Stadtmauer, MD

### Tracks 1-12

Track 1	Evolution of B-cell maturation antigen (BCMA) targeting in multiple myeloma (MM)	Track 8	Subcutaneous delivery of daratumumab
Track 2	Chimeric antigen receptor (CAR) T-cell therapy-associated cytokine release syndrome and neurotoxicity	Track 9	<b>Case:</b> A 56-year-old man with R/R MM and t(11;14) receives venetoclax/bortezomib/dexamethasone
Track 3	Clinical management of cytokine release syndrome	Track 10	<b>Case:</b> A 54-year-old man with R/R MM receives ixazomib/lenalidomide/dexamethasone
Track 4	Durable remissions with BCMA CAR T-cell therapy in relapsed/refractory (R/R) MM	Track 11	Treatment approach for patients who experience relapse while receiving post-transplant lenalidomide maintenance therapy
Track 5	Initial efficacy and safety results with BCMA CAR T-cell therapy	Track 12	<b>Case:</b> A 76-year-old man with previously treated Waldenström macroglobulinemia (WM) experiences a prolonged response to ibrutinib
Track 6	Feasibility of administering CAR T-cell therapy in a community setting		
Track 7	Mechanism of action of monoclonal antibodies; daratumumab-associated infusion-related reactions		

## Interview with Sarah A Holstein, MD, PhD

### Tracks 1-20

Track 1	<b>Case:</b> A 58-year-old man with newly diagnosed high-risk MM experiences a very good partial response and moderate peripheral neuropathy with lenalidomide/bortezomib/dexamethasone (RVd) induction → autologous stem cell transplant (ASCT) but is unwilling to receive bortezomib maintenance therapy because of concerns about further neuropathy	Track 8	Duration of lenalidomide maintenance therapy
Track 2	Ixazomib as a component of maintenance therapy for high-risk MM	Track 9	Early versus delayed ASCT after induction therapy for MM
Track 3	Benefits of post-transplant maintenance therapy	Track 10	Clinical utility of minimal residual disease (MRD) assessment in MM
Track 4	RVd consolidation and maintenance therapy for high-risk MM	Track 11	<b>Case:</b> A 59-year-old man with R/R MM and high-risk cytogenetics receives pomalidomide/daratumumab/dexamethasone
Track 5	Selecting among options for maintenance therapy	Track 12	Triplet therapy options for R/R disease
Track 6	Ixazomib-associated gastrointestinal toxicity	Track 13	Advantages of subcutaneous daratumumab
Track 7	Carfilzomib- versus bortezomib-based induction therapy	Track 14	<b>Case:</b> A 41-year-old woman presents with lambda light chain MM and bone marrow amyloidosis
		Track 15	<b>Case:</b> A 72-year-old man develops myelodysplastic syndrome after receiving post-transplant consolidation RVd and subsequently receives multiple lines of therapy for R/R disease

## Interview with Dr Holstein (continued)

<b>Track 16</b>	<b>Case:</b> A 52-year-old woman initially diagnosed with smoldering MM presents with widespread bone disease	<b>Track 19</b>	Activity and tolerability of panobinostat in combination with carfilzomib/dexamethasone
<b>Track 17</b>	Updated IMWG (International Myeloma Working Group) criteria on risk stratification in MM	<b>Track 20</b>	Status of the Phase III KEYNOTE-183 and 185 trials: Pembrolizumab in combination with an immunomodulatory drug (IMiD) and dexamethasone
<b>Track 18</b>	Management of high-risk R/R MM that progresses rapidly on triplet therapy		

## Interview with Paul G Richardson, MD

### Tracks 1-25

<b>Track 1</b>	Recent therapeutic advances in MM	<b>Track 14</b>	Recent FDA approval of ibrutinib for chronic graft-versus-host disease
<b>Track 2</b>	Changing landscape of smoldering MM	<b>Track 15</b>	Potential of ibrutinib-based combinations for R/R MM
<b>Track 3</b>	Impact of cytogenetics on treatment choice	<b>Track 16</b>	Activity and side effects of CAR T-cell therapy in MM
<b>Track 4</b>	Bisphosphonate therapy in MM	<b>Track 17</b>	Promising therapeutic vaccines and antibodies for MM
<b>Track 5</b>	Role of histone deacetylase inhibitors in the treatment of MM	<b>Track 18</b>	Effectiveness and tolerability of the investigational proteasome inhibitor marizomib for central nervous system MM and malignant glioblastoma
<b>Track 6</b>	Correlation between CD38 expression levels and response to daratumumab	<b>Track 19</b>	Activity of melflufen, a peptidase-activated derivative of melphalan
<b>Track 7</b>	Optimizing the frequency and convenience of daratumumab administration	<b>Track 20</b>	IFM/DFCI 2009 Phase III trial results: RVd with or without ASCT for newly diagnosed MM
<b>Track 8</b>	Clinical experience with the investigational anti-CD38 monoclonal antibody isatuximab	<b>Track 21</b>	<b>Case:</b> A 70-year-old woman with high-risk MM and bone metastases receives daratumumab on a clinical trial after disease progression on multiple lines of therapy
<b>Track 9</b>	ICARIA-MM: An ongoing Phase III trial of pomalidomide and dexamethasone with or without isatuximab for R/R MM	<b>Track 22</b>	<b>Case:</b> A 61-year-old man with R/R MM receives ixazomib/lenalidomide/dexamethasone on a clinical trial
<b>Track 10</b>	Sequencing of therapies to achieve optimal outcomes in MM	<b>Track 23</b>	<b>Case:</b> A 64-year-old man with R/R MM and bone metastases harbors a 13q deletion abnormality
<b>Track 11</b>	Recognition and management of immune paresis	<b>Track 24</b>	Venetoclax for MM with or without t(11;14)
<b>Track 12</b>	Potential utility of elotuzumab in combination with lenalidomide in the maintenance setting	<b>Track 25</b>	Comparison of proteasome inhibitors for MM
<b>Track 13</b>	Toxicities associated with long-term single-agent lenalidomide maintenance therapy; management of lenalidomide-associated diarrhea		

## Interview with Shaji K Kumar, MD

### Tracks 1-26

<b>Track 1</b>	Improving outcomes for newly diagnosed amyloid light chain (AL) amyloidosis	<b>Track 13</b>	Advances in the treatment of R/R MM
<b>Track 2</b>	Investigational strategies for the treatment of AL amyloidosis; factors predicting organ response	<b>Track 14</b>	Principles guiding the sequencing of therapies for R/R MM
<b>Track 3</b>	Presentation and treatment of localized AL amyloidosis	<b>Track 15</b>	Treatment approach for lenalidomide-refractory relapsed MM
<b>Track 4</b>	Advances in the treatment of WM	<b>Track 16</b>	Incorporating ixazomib into the treatment algorithm for R/R MM
<b>Track 5</b>	Incorporation of ibrutinib into the treatment of WM	<b>Track 17</b>	ELOQUENT-2 Phase III trial of elotuzumab/lenalidomide and dexamethasone for R/R MM
<b>Track 6</b>	Guiding principles in the treatment of WM	<b>Track 18</b>	Evaluation of elotuzumab as part of induction and/or maintenance therapy
<b>Track 7</b>	Diagnosis and management of smoldering MM	<b>Track 19</b>	Therapeutic options for patients with disease that is not refractory to lenalidomide or bortezomib or both
<b>Track 8</b>	ASCENT Phase II study of carfilzomib/lenalidomide/ dexamethasone and daratumumab with or without ASCT for patients with high-risk smoldering MM	<b>Track 20</b>	Choice of proteasome inhibitor in the relapsed setting
<b>Track 9</b>	MRD testing in MM and its application in clinical trials and practice	<b>Track 22</b>	Options for patients with “double-refractory” MM
<b>Track 10</b>	MRD negativity after induction therapy and prediction of benefit from transplant	<b>Track 23</b>	Venetoclax for patients with heavily pretreated t(11;14) MM
<b>Track 11</b>	Importance of risk stratification in the selection of initial therapy for MM	<b>Track 24</b>	PCR-based assay for Bcl-2 and association with response to venetoclax
<b>Track 12</b>	Carfilzomib-associated cardiac dysfunction and dyspnea	<b>Track 25</b>	BCMA CAR T-cell therapy in MM
		<b>Track 26</b>	Combining immune checkpoint inhibitors with IMiDs
		<b>Track 26</b>	ASCT for relapsed MM

## Video Program

View the corresponding video interviews with (from left) Drs Stadtmauer, Holstein, Richardson and Kumar by Dr Love at [www.ResearchToPractice.com/MMUpdate118/Video](http://www.ResearchToPractice.com/MMUpdate118/Video)



## QUESTIONS (PLEASE CIRCLE ANSWER):

1. Because it is universally expressed on malignant plasma cells, which of the following antigens is an attractive target for CAR T-cell-directed therapy in MM?\*
  - a. BCMA
  - b. CD19
  - c. CD33
2. A study presented at the 2016 ASH Annual Meeting demonstrated that daratumumab \_\_\_\_\_ safely be administered via subcutaneous injection.\*
  - a. Could
  - b. Could not
3. Which of the following proteasome inhibitors has demonstrated activity in myeloma affecting the central nervous system?\*
  - a. Bortezomib
  - b. Ixazomib
  - c. Carfilzomib
  - d. Marizomib
4. Ibrutinib is FDA approved for the treatment of \_\_\_\_\_.
  - a. Chronic graft-versus-host disease
  - b. WM
  - c. Both a and b
  - d. Neither a nor b
5. Infusion-related reactions associated with the administration of daratumumab tend to persist over the course of the patient's treatment.
  - a. True
  - b. False
6. Which of the following side effects is NOT associated with ixazomib therapy?
  - a. Arthralgia
  - b. Gastrointestinal toxicity
  - c. Peripheral neuropathy
  - d. All of the above
7. Sensitivity to venetoclax for MM has primarily been observed in patients with t(11;14) disease.\*
  - a. True
  - b. False
8. The Phase III randomized ELOQUENT-2 study evaluating elotuzumab/lenalidomide/dexamethasone versus lenalidomide/dexamethasone \_\_\_\_\_ a significant improvement in progression-free survival with the addition of elotuzumab for patients with R/R MM.
  - a. Demonstrated
  - b. Did not demonstrate
9. Which of the following categories reflects the mechanism of action of isatuximab?\*
  - a. Anti-CD38 monoclonal antibody
  - b. Anti-PD-1/PD-L1 antibody
  - c. IMiD
  - d. Proteasome inhibitor
10. Recent data presented from the Myeloma X and XI trials demonstrated that lenalidomide maintenance therapy improved outcomes for transplant-eligible patients with \_\_\_\_\_.
  - a. High-risk MM
  - b. Standard-risk MM
  - c. Both a and b
  - d. Neither a nor b

\* The content of this question refers to drugs or the use of drugs that have not yet received FDA approval.



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**PART 1 — Please tell us about your experience with this educational activity**

**How would you characterize your level of knowledge on the following topics?**

	4 = Excellent	3 = Good	2 = Adequate	1 = Suboptimal
	<b>BEFORE</b>		<b>AFTER</b>	
Biologic rationale for and efficacy and tolerability of CAR T cells targeting BCMA in MM	4	3	2	1
Activity and ongoing investigation of the anti-CD38 antibody isatuximab for R/R MM	4	3	2	1
Biologic rationales for the effectiveness of venetoclax in patients with MM and for the lower risk of associated tumor lysis syndrome compared to chronic lymphocytic leukemia	4	3	2	1
Safety and effectiveness of subcutaneous daratumumab	4	3	2	1
Emerging research data with and nonresearch role, if any, of ixazomib as a component of induction and maintenance therapy	4	3	2	1

**Practice Setting:**

- Academic center/medical school     
  Community cancer center/hospital     
  Group practice  
 Solo practice     
  Government (eg, VA)     
  Other (please specify).....

**Approximately how many new patients with multiple myeloma do you see per year?** ..... patients

**Was the activity evidence based, fair, balanced and free from commercial bias?**

- Yes     
  No     
 If no, please explain: .....

**Please identify how you will change your practice as a result of completing this activity (select all that apply).**

- This activity validated my current practice  
 Create/revise protocols, policies and/or procedures  
 Change the management and/or treatment of my patients  
 Other (please explain): .....

**If you intend to implement any changes in your practice, please provide 1 or more examples:**

.....  
 .....

**The content of this activity matched my current (or potential) scope of practice.**

- Yes     
  No     
 If no, please explain: .....

**Please respond to the following learning objectives (LOs) by circling the appropriate selection:**

4 = Yes    3 = Will consider    2 = No    1 = Already doing    N/M = LO not met    N/A = Not applicable

**As a result of this activity, I will be able to:**

- Use patient and disease characteristics, including cytogenetic profile, to customize induction and maintenance therapeutic approaches in the transplant and nontransplant settings. .... 4 3 2 1 N/M N/A
- 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. .... 4 3 2 1 N/M N/A
- 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. .... 4 3 2 1 N/M N/A
- Develop an evidence-based algorithm for the use of stem cell transplantation, chemotherapy and/or novel targeted agents for the management of amyloidosis. .... 4 3 2 1 N/M N/A

**EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)**

**As a result of this activity, I will be able to:**

- Consider clinical and other patient-related factors in the sequence and selection of systemic therapy for WM requiring active treatment. . . . . 4 3 2 1 N/M N/A
- Develop risk-adapted treatment plans for patients with smoldering MM, considering the roles of observation and active treatment. . . . . 4 3 2 1 N/M N/A

**Please describe any clinical situations that you find difficult to manage or resolve that you would like to see addressed in future educational activities:**

.....

.....

**Would you recommend this activity to a colleague?**

Yes       No

If no, please explain: .....

<b>PART 2 — Please tell us about the faculty and editor for this educational activity</b>									
		4 = Excellent		3 = Good		2 = Adequate		1 = Suboptimal	
<b>Faculty</b>		<b>Knowledge of subject matter</b>				<b>Effectiveness as an educator</b>			
Edward A Stadtmauer, MD		4	3	2	1	4	3	2	1
Sarah A Holstein, MD, PhD		4	3	2	1	4	3	2	1
Paul G Richardson, MD		4	3	2	1	4	3	2	1
Shaji K Kumar, MD		4	3	2	1	4	3	2	1
<b>Editor</b>		<b>Knowledge of subject matter</b>				<b>Effectiveness as an educator</b>			
Neil Love, MD		4	3	2	1	4	3	2	1

**Please recommend additional faculty for future activities:**

.....

.....

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Professional Designation:  
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# Multiple Myeloma™

U P D A T E

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