Questions from the Community

Clinical Investigators Provide Their Perspectives on Challenging Issues and Ongoing Research in the Management of Lymphomas and Multiple Myeloma

A special audio supplement to a CME symposia series held during the 2015 American Society of Hematology Annual Meeting featuring expert comments on the application of emerging research to patient care

FACULTY INTERVIEWS

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EDITOR

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Questions from the Community: Clinical Investigators Provide Their Perspectives on Challenging Issues and Ongoing Research in the Management of Lymphomas and Multiple Myeloma

A Continuing Medical Education Audio Program

OVERVIEW OF ACTIVITY

Hematologic oncology and related blood disorders are some of the most rapidly evolving fields in all of medicine. Results presented at major conferences from a plethora of ongoing clinical trials lead to the continual emergence of new therapeutic agents and changes in the indications for existing treatments. In order to offer optimal patient care, the practicing hematologist-oncologist must be well informed of these advances. To bridge the gap between research and patient care, this CME program uses one-on-one interviews with 4 leading investigators to discuss key data sets in addition to cases and questions submitted by attendees at a satellite symposium. This program will assist practicing clinicians in formulating up-to-date and appropriate clinical management strategies.

LEARNING OBJECTIVES

- Develop a rational plan to incorporate B-cell receptor signaling inhibitors and anti-CD20 monoclonal antibodies into the treatment of chronic lymphocytic leukemia and other B-cell neoplasms.
- Incorporate newly approved agents and strategies in the treatment of newly diagnosed and relapsed or refractory multiple myeloma (MM).
- Develop an understanding of the biologic rationale for and early efficacy and toxicity data with the use of immunotherapeutic approaches for patients with various lymphoma subtypes and MM.
- Develop an understanding of emerging efficacy and side-effect data with novel agents and combination regimens under evaluation for indolent and aggressive B-cell non-Hodgkin lymphomas.
- Customize the selection of systemic therapy for patients with newly diagnosed and progressive mantle-cell lymphoma, recognizing the recent addition of bortezomib, lenalidomide and ibrutinib as FDA-endorsed options.
- Review emerging clinical trial data on the efficacy and safety of brentuximab vedotin for patients with CD30-positive lymphomas, and use this information to prioritize protocol and nonresearch options for these patients.

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Other participants at Research To Practice symposia series at ASH, from top left: Lymphoma faculty Drs Anas Younes, Owen A O'Connor, Christopher Flowers, Martin Dreyling and consulting oncologist Dr Margaret A Deutsch and multiple myeloma faculty Drs Xavier Leleu, Rafael Fonseca, Philip L McCarthy and consulting oncologist Dr Neil I Morganstein

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Interview with Michael E Williams, MD, ScM

Tracks 1-14

Track 1 Selection of front-line therapy for elderly patients with chronic lymphocytic leukemia (CLL)

Track 2 Efficacy and tolerability of obinutuzumab as up-front treatment for CLL

Track 3 Use of fludarabine/cyclophosphamide/rituximab (FCR) in younger patients with newly diagnosed, standard-risk CLL

Track 4 Perspective on the up-front use of ibrutinib for patients with untreated CLL

Track 5 Ibrutinib in patients with del(17p) CLL

Track 6 Venetoclax in relapsed CLL

Track 7 Atrial fibrillation in patients receiving ibrutinib

Track 8 Efficacy of idelalisib with rituximab for relapsed CLL

Track 9 "Watch and wait" approach for indolent mantle-cell lymphoma (MCL)

Track 10 Therapeutic options for younger patients with MCL

Track 11 Sequencing of ibrutinib, lenalidomide and bortezomib for relapsed MCL

Track 12 Effectiveness of lenalidomide with rituximab (R^2) in MCL

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Track 14 CD30 testing and the role of brentuximab vedotin in DLBCL

Interview with Sonali M Smith, MD

Tracks 1-14

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Track 3 GADOLIN: Results of a Phase III trial of bendamustine alone or in combination with obinutuzumab for rituximab-refractory indolent non-Hodgkin lymphoma

Track 4 Similarities and differences between rituximab and obinutuzumab

Track 5 Perspective on the role of obinutuzumab for relapsed/refractory FL

Track 6 Second-line therapeutic options for patients with FL

Track 7 Integration of idelalisib into the therapeutic algorithm for patients with FL

Track 8 Risks and benefits associated with idelalisib in FL

Track 9 Brentuximab vedotin as a bridge to transplant for patients with relapsed Hodgkin lymphoma (HL)

Track 10 Viewpoint on the use of brentuximab vedotin in the up-front treatment of HL

Track 11 Brentuximab vedotin as consolidation therapy after autologous stem cell transplant (ASCT) for patients with recurrent HL

Track 12 Promising activity with anti-PD-1 antibodies in relapsed/refractory HL

Track 13 Up-front therapy options for patients with peripheral T-cell lymphoma (PTCL)

Track 14 Sequencing of belinostat, romidepsin and pralatrexate for PTCL

Interview with Irene M Ghobrial, MD

Tracks 1-13

Track 1 Role of ASCT in younger patients with newly diagnosed multiple myeloma (MM)

Track 2 Progression-free survival benefit with ASCT after RVD induction therapy

Track 3 Therapeutic options for patients with MM not eligible for transplant

Track 4 Use of carfilzomib as up-front therapy for patients with MM

Track 5 Role of the recently FDA-approved oral proteasome inhibitor ixazomib for patients with MM

Track 6 Choice of induction regimen for patients with adverse cytogenetics

Track 7 Perspective on maintenance therapy for patients who have achieved a complete response

Track 8 Importance of minimal residual disease detection in MM

Track 9 Tailoring up-front therapy on the basis of cytogenetic risk status

Track 10 Investigation of BRAF/MEK inhibitors for patients with BRAF mutation-positive MM

Track 11 Role of chimeric antigen receptor T-cell therapy and checkpoint inhibitors in MM

Track 12 Integration of the recently approved monoclonal antibodies elotuzumab and daratumumab into the treatment algorithm for patients with MM

Track 13 Clinical experience with and tolerability of panobinostat

Interview with Ola Landgren, MD, PhD

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Track 1 Perspective on bortezomib and the newer-generation proteasome inhibitors ixazomib and carfilzomib

Track 2 Cardiac monitoring for patients initiating carfilzomib

Track 3 Carfilzomib-associated cardiopulmonary adverse events

Track 4 Mechanisms of action of elotuzumab and daratumumab in MM

Track 5 Efficacy of elotuzumab versus daratumumab for relapsed/refractory MM

Track 6 Perspective on the integration of elotuzumab into the treatment algorithm for patients with relapsed/refractory MM

Track 7 Tolerability of elotuzumab and daratumumab

Track 8 Mode of action, activity and side effects of panobinostat

Track 9 Updated criteria for the diagnosis of smoldering MM

Track 10 Response to carfilzomib, lenalidomide and dexamethasone (KRd) in high-risk smoldering MM

Track 11 Therapeutic options for patients with AL amyloidosis

Track 12 Approach to patients with relapsed/refractory Waldenström macroglobulinemia

Track 13 Emerging research and novel agents for Waldenström macroglobulinemia

Visit **www.ResearchToPractice.com/CommunityQuestions15/Video** for the full video proceedings from the related CME events at the 2015 ASH Annual Meeting.

SELECT PUBLICATIONS

A randomized, phase III study comparing conventional dose treatment using a combination of lenalidomide, bortezomib, and dexamethasone (RVD) to high-dose treatment with peripheral stem cell transplant in the initial management of myeloma in patients up to 65 years of age. NCT01208662

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Ruan J et al. **Lenalidomide plus rituximab as initial treatment for mantle-cell lymphoma.** *N Engl J Med* 2015;373(19):1835-44.

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Sehn L et al. **GADOLIN: Primary results from a phase III study of obinutuzumab plus bendamustine compared with bendamustine alone in patients with rituximab-refractory indolent non-Hodgkin lymphoma.** *Proc ASCO* 2015;**Abstract LBA8502**.

POST-TEST

Questions from the Community: Clinical Investigators Provide Their Perspectives on Challenging Issues and Ongoing Research in the Management of Lymphomas and Multiple Myeloma

QUESTIONS (PLEASE CIRCLE ANSWER):

1. **The Phase III IFM 2009 trial evaluating RVD induction with or without immediate ASCT for younger patients with newly diagnosed MM demonstrated a significant improvement in _____ with the addition of ASCT.**
   a. Overall survival
   b. Progression-free survival
   c. Both a and b

2. **_____ is an anti-CD38 monoclonal antibody with single-agent activity that recently received FDA approval as treatment for MM in patients who have received at least 3 prior lines of therapy.**
   a. Elotuzumab
   b. Daratumumab
   c. Ixazomib

3. **The Phase III ENDEAVOR trial comparing carfilzomib/dexamethasone to bortezomib/dexamethasone for patients with relapsed or refractory MM demonstrated a significant difference in progression-free survival in favor of the bortezomib/dexamethasone arm.**
   a. True
   b. False

4. **Patients with the activated B-cell subtype of DLBCL have a decreased response to _____ in comparison to those with the germinal center B-cell subtype.**
   a. R-CHOP
   b. Ibrutinib
   c. Lenalidomide

5. **Idelalisib has been approved by the FDA for which of the following indications?**
   a. Relapsed CLL in combination with rituximab
   b. Relapsed FL
   c. Relapsed MCL
   d. All of the above
   e. Both a and b

6. **A recent Phase II study of lenalidomide and rituximab for MCL demonstrated a response rate of 92% with this regimen in the _____ setting.**
   a. First-line
   b. Second-line
   c. Late-line

7. **Results from a Phase III trial comparing ibrutinib to chlorambucil in older patients with previously untreated CLL or small lymphocytic lymphoma demonstrated a significant difference in favor of ibrutinib in terms of _____.**
   a. Overall response rate
   b. Progression-free survival
   c. Overall survival
   d. All of the above

8. **Which of the following is true of venetoclax in the treatment of CLL?**
   a. It acts by inhibiting Bcl-2
   b. It is not effective in patients with del(17p) CLL
   c. It can cause tumor lysis syndrome
   d. All of the above
   e. Both a and c

9. **Elotuzumab was recently FDA approved _____ for patients with MM who have received 1 to 3 prior therapies.**
   a. As a single agent
   b. In combination with lenalidomide/dexamethasone
   c. In combination with bortezomib/dexamethasone

10. **Common adverse events associated with obinutuzumab include:**
    a. Atrial fibrillation
    b. Infusion reactions
    c. Neutropenia
    d. All of the above
    e. Both b and c

EDUCATIONAL ASSESSMENT AND CREDIT FORM

Questions from the Community: Clinical Investigators Provide Their Perspectives on Challenging Issues and Ongoing Research in the Management of Lymphomas and Multiple Myeloma

Research To Practice is committed to providing valuable continuing education for oncology clinicians, and your input is critical to helping us achieve this important goal. Please take the time to assess the activity you just completed, with the assurance that your answers and suggestions are strictly confidential.

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

	BEFORE	AFTER
Results of the IFM 2009 trial on the role of ASCT in younger patients with newly diagnosed MM	4 3 2 1	4 3 2 1
Responses with and tolerability of anti-PD-1 antibodies for patients with various lymphoma subtypes and MM	4 3 2 1	4 3 2 1
Selection of optimal up-front treatment for elderly patients with CLL	4 3 2 1	4 3 2 1
Efficacy of ixazomib in the front-line setting for MM	4 3 2 1	4 3 2 1
Management of atrial fibrillation in patients receiving ibrutinib	4 3 2 1	4 3 2 1
Activity of obinutuzumab with bendamustine in patients with relapsed FL	4 3 2 1	4 3 2 1

Practice Setting:

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

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:

- Develop a rational plan to incorporate B-cell receptor signaling inhibitors and anti-CD20 monoclonal antibodies into the treatment of chronic lymphocytic leukemia and other B-cell neoplasms. . . . . 4 3 2 1 N/M N/A
- Incorporate newly approved agents and strategies in the treatment of newly diagnosed and relapsed or refractory multiple myeloma (MM). . . . . 4 3 2 1 N/M N/A
- Develop an understanding of the biologic rationale for and early efficacy and toxicity data with the use of immunotherapeutic approaches for patients with various lymphoma subtypes and MM. . . . . 4 3 2 1 N/M N/A
- Develop an understanding of emerging efficacy and side-effect data with novel agents and combination regimens under evaluation for indolent and aggressive B-cell non-Hodgkin lymphomas. . . . . 4 3 2 1 N/M N/A
- Customize the selection of systemic therapy for patients with newly diagnosed and progressive mantle-cell lymphoma, recognizing the recent addition of bortezomib, lenalidomide and ibrutinib as FDA-endorsed options. . . . . 4 3 2 1 N/M N/A
- Review emerging clinical trial data on the efficacy and safety of brentuximab vedotin for patients with CD30-positive lymphomas, and use this information to prioritize protocol and nonresearch options for these patients. . . . . 4 3 2 1 N/M N/A

EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)

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: .....

Additional comments about this activity:

.....

PART 2 — Please tell us about the faculty and editor for this educational activity

4 = Excellent 3 = Good 2 = Adequate 1 = Suboptimal

Faculty	Knowledge of subject matter	Effectiveness as an educator
Michael E Williams, MD, ScM	4 3 2 1	4 3 2 1
Sonali M Smith, MD	4 3 2 1	4 3 2 1
Irene M Ghobrial, MD	4 3 2 1	4 3 2 1
Ola Landgren, MD, PhD	4 3 2 1	4 3 2 1
Editor	**Knowledge of subject matter**	**Effectiveness as an educator**
Neil Love, MD	4 3 2 1	4 3 2 1

Please recommend additional faculty for future activities:

.....

Other comments about the faculty and editor for this activity:

.....

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Hematologic Oncology™
UPDATE

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