A Continuing Medical Education Activity

OVERVIEW OF ACTIVITY
Non-Hodgkin lymphoma (NHL) comprises a heterogeneous group of lymphoproliferative disorders and is one of the most rapidly evolving fields in hematology and oncology. In contrast, Hodgkin lymphoma (HL) is a rare disease that is relatively chemosensitive and often curable when treated appropriately. However, care for patients who do not respond to primary treatment or those with relapsed or refractory HL remains a significant challenge for oncology clinicians. Published results from ongoing clinical trials lead to the continual emergence of new therapeutic agents and changes in the use of existing treatments. To offer optimal patient care — including the option of clinical trial participation — practicing medical oncologists, hematologists and hematology-oncology fellows must be well informed of these advances. This program uses a roundtable discussion with leading clinical investigators to assist practicing clinicians in formulating up-to-date clinical management strategies for NHL, HL and chronic lymphocytic leukemia (CLL).

LEARNING OBJECTIVES
• Use case-based learning to formulate individualized strategies for the care of patients with lymphoma.
• Integrate practice-changing clinical trial results recently reported with the antibody-drug conjugate brentuximab vedotin into the evidence-based treatment algorithm for patients with relapsed/refractory HL and systemic anaplastic large cell lymphoma.
• Utilize available research evidence on the use of CNS prophylaxis to guide treatment decision making for patients with relapsed refractory HL.
• Apportion recent data on therapeutic advances and changing practice standards in follicular lymphoma, and apply this information to clinical practice.
• Develop an algorithm for the evaluation and treatment of newly diagnosed and relapsed/refractory CLL.
• Devise an approach for the sequential systemic treatment of cutaneous T-cell lymphoma.
• Communicate the existing and emerging roles of proteasome inhibitors and IMiDs to patients with mantle-cell lymphoma.
• Facilitate patient access to clinical trial participation through communication of ongoing research opportunities.

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CREDIT DESIGNATION STATEMENT
Research To Practice designates this enduring material for a maximum of 2.5 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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This CME activity contains an audio component. To receive credit, the participant should review the CME information, listen to the CDs, complete the Post-test with a score of 70% or better and fill out the Educational Assessment and Credit Form located in the back of this booklet or on our website at ResearchToPractice.com/HOUTT112/CME.

This activity is supported by educational grants from Celgene Corporation, Genentech BioOncology/Biogen Idec, Millennium: The Takeda Oncology Company, Seattle Genetics and Spectrum Pharmaceuticals Inc.

Last review date: June 2012; Release date: June 2012; Expiration date: June 2013
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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: Dr Friedberg — Advisory Committee: Cephalon Inc, Genentech BioOncology; Consulting Agreement: Mundipharma International Limited; Data and Safety Monitoring Board: Lilly USA LLC; Paid Research: Millennium: The Takeda Oncology Company, Onyx Pharmaceuticals Inc. Dr Horwitz — Advisory Committee: Allos Therapeutics, Celgene Corporation; Consulting Agreements: Allos Therapeutics, Bristol-Myers Squibb Company, Celgene Corporation, Kyowa Hakko Kirin Co Ltd, Seattle Genetics, Spectrum Pharmaceuticals Inc; Paid Research: Allos Therapeutics, Celgene Corporation, Kyowa Hakko Kirin Co Ltd, Millennium: The Takeda Oncology Company, Seattle Genetics, Spectrum Pharmaceuticals Inc. Dr Kahl — Advisory Committee: Celgene Corporation, Cephalon Inc, Genentech BioOncology, GlaxoSmithKline, Millennium: The Takeda Oncology Company. Dr Kaminski — Consulting Agreement: Allos Therapeutics; Paid Research and Patent Holder: GlaxoSmithKline. Dr Leonard — Consulting Agreements: Celgene Corporation, Cephalon Inc, Genentech BioOncology, GlaxoSmithKline, Millennium: The Takeda Oncology Company. Dr Moskowitz — Advisory Committee: Cephalon Inc, Genentech BioOncology, Seattle Genetics; Paid Research: Cephalon Inc, Genentech BioOncology, Lilly USA LLC, Plexxikon Inc, Seattle Genetics. Dr Smith — Advisory Committee: Cephalon Inc; Speakers Bureau: Allos Therapeutics, Cephalon Inc, Genentech BioOncology, Millennium: The Takeda Oncology Company, Spectrum Pharmaceuticals Inc. Dr Younes — Advisory Committee: Allos Therapeutics, Boehringer Ingelheim Pharmaceuticals Inc, Celgene Corporation, Millennium: The Takeda Oncology Company, Novartis Pharmaceuticals Corporation, Sanofi, Spectrum Pharmaceuticals Inc; Paid Research: Novartis Pharmaceuticals Corporation, Sanofi.

MODERATOR — Dr Love is president and CEO of Research To Practice, which receives funds in the form of educational grants to develop CME activities from the following commercial interests: Abbott Laboratories, Allos Therapeutics, Amgen Inc, ArQule Inc, Astellas, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals/Onyx Pharmaceuticals Inc, Biodesix Inc, Biogen Idec, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Daiichi Sankyo Inc, Dendreon Corporation, Eisai Inc, EMD Serono Inc, Genentech BioOncology, Genomic Health Inc, ImClone Systems, a wholly owned subsidiary of Eli Lilly and Company, Incyte Corporation, Lilly USA LLC, Medivation Inc, Millennium: The Takeda Oncology Company, Mundipharma International Limited, Novartis Pharmaceuticals Corporation, Regeneron Pharmaceuticals, Sanofi, Seattle Genetics, Spectrum Pharmaceuticals Inc and Teva.

RESEARCH TO PRACTICE STAFF AND EXTERNAL REVIEWERS — The scientific staff and reviewers for Research To Practice have no real or apparent conflicts of interest to disclose.
Tracks 1-26

Track 1  Management of early-stage Hodgkin lymphoma (HL) with combined-modality treatment versus a non-radiation therapy (RT)-containing approach

Track 2  Association between gender and incidence of disease relapse in HL

Track 3  Weighing the benefits of RT against long-term treatment-related cardiovascular risks in HL

Track 4  Mechanism of action and responses with the antibody-drug conjugate brentuximab vedotin in HL and other CD30-positive lymphomas

Track 5  AETHERA: A Phase III trial of brentuximab vedotin and best supportive care (BSC) versus placebo and BSC for patients at high risk for residual HL after autologous stem cell transplant (ASCT)

Track 6  Clinical experience with brentuximab vedotin-related peripheral neuropathy

Track 7  Safety of brentuximab vedotin with doxorubicin/bleomycin/vinblastine/dacarbazine (ABVD) or AVD in newly diagnosed advanced HL

Track 8  Case discussion: A 32-year-old woman with advanced-stage HL whose disease recurs 6 months after ASCT experiences a complete response after 4 cycles of brentuximab vedotin and is now considering allogeneic transplant

Track 9  Role of interim PET scanning for patients receiving treatment for diffuse large B-cell lymphoma (DLBCL)

Track 10  Role of transplant for DLBCL in the rituximab era

Track 11  Molecular diagnosis and outcome prediction in the treatment of DLBCL

Track 12  Management of extranodal DLBCL and indications for central nervous system (CNS) prophylaxis

Track 13  Perspective on the use of intrathecal versus intravenous CNS prophylaxis

Track 14  Case discussion: A 48-year-old man with asymptomatic low tumor burden follicular lymphoma (FL) enters the RESORT trial and receives rituximab re-treatment upon disease progression

Track 15  Perspective on initiating therapy versus a “watch and wait” strategy for low tumor burden FL

Track 16  ECOG-E4402: RESORT trial comparing rituximab maintenance to rituximab re-treatment upon disease progression for low tumor burden indolent non-Hodgkin lymphoma (NHL)

Track 17  Efficacy, side effects and preliminary quality-of-life results with the 2 rituximab dosing regimens on the RESORT trial

Track 18  SAKK-35/98: Long-term follow-up from a randomized trial of prolonged versus short-course rituximab for FL

Track 19  Reconciling the RESORT and SAKK-35/98 trial results

Track 20  Activity of lenalidomide alone and in combination with rituximab in indolent and aggressive lymphomas

Track 21  Use of single-agent lenalidomide in relapsed or refractory transformed FL

Track 22  Utility of lenalidomide monotherapy in DLBCL

Track 23  LYM-3001: Results from a Phase III trial of bortezomib and rituximab versus rituximab alone for patients with relapsed, rituximab-naïve or rituximab-sensitive FL

Track 24  Ongoing investigation of the combination of bendamustine, bortezomib and rituximab (BVR) in FL

Track 25  ECOG-E2408: A Phase II trial of bendamustine and rituximab (BR) with or without bortezomib followed by rituximab with or without lenalidomide for patients with high-risk Stage II, Stage III or Stage IV FL

Track 26  Case discussion: A highly anxious 44-year-old man with high tumor burden Stage II FL receives R-CHOP followed by rituximab maintenance on a clinical trial
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<td><strong>Track 23</strong> <strong>Case discussion:</strong> A 30-year-old man with Grade I/II FL achieves a durable complete remission with front-line radioimmunotherapy (RIT) on a clinical trial</td>
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SELECT PUBLICATIONS

A 3-arm randomized phase II trial of bendamustine-rituximab (BR) followed by rituximab vs bortezomib-BR (BVR) followed by rituximab vs BR followed by lenalidomide/rituximab in high risk follicular lymphoma. NCT01216683

A multi-center, randomized, phase III study of rituximab versus iodine I 131 tositumomab therapy for patients with relapsed follicular non-Hodgkin’s lymphoma. NCT00078598

A Phase III study of brentuximab vedotin (SGN-35) in patients at high risk of residual Hodgkin lymphoma following stem cell transplant (the AETHERA trial). NCT01100502

Bendamustine hydrochloride and rituximab with or without bortezomib followed by rituximab with or without lenalidomide in treating patients with high-risk stage II, stage III, or stage IV follicular lymphoma. NCT01216683


GAUSS: A study of RO5072759 in patients with indolent non-Hodgkin’s lymphoma. NCT00573578


Monoclonal antibody therapy in treating patients with follicular or mantle cell lymphoma. NCT0003280


Randomized phase III trial comparing two different rituximab dosing regimens for patients with low tumor burden indolent non-Hodgkin’s lymphoma. NCT00075946

Rituximab in treating patients with low tumor burden indolent non-Hodgkin’s lymphoma. NCT00075946


1. The RESORT trial demonstrated that at 3 years more than 80% of patients with previously untreated, low tumor burden FL who received 4 doses of rituximab on the control arm had not received chemotherapy for relapse.
   a. True
   b. False

2. The SAKK-35/98 clinical trial, which evaluated a short course (4 weekly doses) of rituximab versus prolonged rituximab for patients with newly diagnosed or relapsed FL, did not report an improved progression-free survival for patients who received prolonged rituximab.
   a. True
   b. False

3. Brentuximab vedotin is an antibody-drug conjugate that targets ______ tumor cells.
   a. CD20-positive
   b. CD30-positive
   c. CD5-positive

4. What is the mechanism of action of romidepsin?
   a. Antimetabolite
   b. Alkylating agent
   c. Histone deacetylase inhibitor
   d. None of the above

5. Data from the pivotal trial that led to the approval of brentuximab vedotin in the treatment of HL after failure of ASCT reported a 75% response rate for patients undergoing treatment in this setting.
   a. True
   b. False

6. Results from a Phase II study of lenalidomide and rituximab in patients with previously untreated indolent lymphomas indicated a response rate of approximately 90% with this combination.
   a. True
   b. False

7. The Phase II ECOG-E2408 trial is evaluating BR with or without ___________ followed by rituximab with or without lenalidomide for patients with high-risk Stage II to Stage IV FL.
   a. Bortezomib
   b. Carfilzomib
   c. Both of the above

8. The GAUSS study evaluated obinutuzumab (GA101) versus _____________ for patients with relapsed CD20-positive indolent B-cell NHL.
   a. Bortezomib
   b. Brentuximab vedotin
   c. Rituximab

9. A trial evaluating maintenance rituximab after induction therapy with R-CHOP or R-FC for elderly patients with MCL reported a benefit in remission duration for patients receiving rituximab maintenance versus interferon maintenance.
   a. True
   b. False

10. In the Phase III FIT trial of consolidation therapy with ibritumomab tiuxetan after first remission in patients with advanced FL, patients who received consolidation therapy experienced ___________ compared to patients who received no additional therapy.
    a. A progression-free survival (PFS) advantage
    b. An overall survival (OS) advantage
    c. No PFS or OS advantage
**EDUCATIONAL ASSESSMENT AND CREDIT FORM**

**Striving for Consensus: The Application of New Research Findings in the Management of Hodgkin and Non-Hodgkin Lymphoma**

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?

<table>
<thead>
<tr>
<th>Activity and toxicity of brentuximab vedotin in HL/sALCL</th>
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<tr>
<td>Response to sequential HDAC inhibitor therapy in CTCL</td>
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<td>Role of RIT as initial treatment and consolidation therapy for FL</td>
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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:**

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<th>As a result of this activity, I will be able to:</th>
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<td>Use case-based learning to formulate individualized strategies for the care of patients with lymphoma.</td>
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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:

As part of our ongoing, continuous quality-improvement effort, we conduct postactivity follow-up surveys to assess the impact of our educational interventions on professional practice. Please indicate your willingness to participate in such a survey.
- [ ] Yes, I am willing to participate in a follow-up survey.
- [ ] No, I am not willing to participate in a follow-up survey.

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

<table>
<thead>
<tr>
<th>Faculty</th>
<th>Knowledge of subject matter</th>
<th>Effectiveness as an educator</th>
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<tr>
<td>Jonathan W Friedberg, MD, MMSc</td>
<td>4 3 2 1</td>
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<tr>
<td>Steven M Horwitz, MD</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
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<tr>
<td>Brad S Kahl, MD</td>
<td>4 3 2 1</td>
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<tr>
<td>Mark S Kaminski, MD</td>
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<tr>
<td>John P Leonard, MD</td>
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<tr>
<td>Craig Moskowitz, MD</td>
<td>4 3 2 1</td>
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<tr>
<td>Mitchell R Smith, MD, PhD</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
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<tr>
<td>Anas Younes, MD</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
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</table>

Moderator

<table>
<thead>
<tr>
<th>Knowledge of subject matter</th>
<th>Effectiveness as an educator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neil Love, MD</td>
<td>4 3 2 1</td>
</tr>
</tbody>
</table>

Please recommend additional faculty for future activities:

Other comments about the faculty and moderator for this activity:

REQUEST FOR CREDIT — Please print clearly

Name: .................................................. Specialty: ..................................

Professional Designation:  
- [ ] MD  
- [ ] DO  
- [ ] PharmD  
- [ ] NP  
- [ ] RN  
- [ ] PA  
- [ ] Other  

Street Address: .......................................................... Box/Suite: ..................................

City, State, Zip: ..........................................................

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Signature: ............................................................ Date: ..........................................................

The expiration date for this activity is June 2013. To obtain a certificate of completion and receive credit for this activity, please complete the Post-test, fill out the Educational Assessment and Credit Form and fax both to (800) 447-4310, or mail both to Research To Practice, One Biscayne Tower, 2 South Biscayne Boulevard, Suite 3600, Miami, FL 33131. You may also complete the Post-test and Educational Assessment online at www.ResearchToPractice.com/HOUTT112/CME.

Proceedings from a Clinical Investigator Think Tank

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MODERATOR
Neil Love, MD

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