VOL 2 · ISSUE 1 · 2012

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

Proceedings from a Clinical Investigator Think Tank

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

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 rarer 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 diffuse large B-cell lymphoma.
- Appraise 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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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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HODGKIN LYMPHOMA, DIFFUSE LARGE B-CELL LYMPHOMA AND FOLLICULAR LYMPHOMA

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CHRONIC LYMPHOCYTIC LEUKEMIA, MANTLE-CELL LYMPHOMA, T-CELL LYMPHOMAS AND RADIOIMMUNOTHERAPY IN NHL

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Track 4 Initial results with fludarabine/rituximab followed by lenalidomide maintenance in untreated CLL

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Track 6 Age-appropriate up-front treatment options for CLL

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Track 8 Role of allogeneic transplant for younger patients with CLL with adverse cytogenetics

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Track 14 Efficacy, toxicity and schedule of bortezomib — alone and in combination — in relapsed MCL

Track 15 **Case discussion:** A 58-year-old woman with mycosis fungoides/Sézary syndrome, erythroderma and blood involvement previously treated with multiple lines of skin-directed therapy receives vorinostat followed by romidepsin

Track 16 Response to sequential histone deacetylase (HDAC) inhibitor therapy

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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

Chen R et al. **Results of a pivotal Phase 2 study of brentuximab vedotin (SGN-35) in patients with relapsed or refractory Hodgkin lymphoma.** *Proc ASH* 2010;**Abstract 283**.

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Erin-Siobhain R et al. **Treatment strategies for Hodgkin lymphoma recurring following autologous hematopoietic stem cell transplantation.** *Korean J Hematol* 2012;47(1):8-16.

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GAUSS: A study of RO5072759 in patients with indolent non-Hodgkin's lymphoma. NCT00576758

Hernandez-Ilizaliturri FJ et al. **Higher response to lenalidomide in relapsed/refractory diffuse large B-cell lymphoma in nongerminal center B-cell-like than in germinal center B-cell-like phenotype.** *Cancer* 2011;117(22):5058-66.

Kahl BS et al. **Results of Eastern Cooperative Oncology Group protocol E4402 (RESORT): A randomized Phase III study comparing two different rituximab dosing strategies for low tumor burden follicular lymphoma.** *Proc ASH* 2011;**Abstract LBA-6**.

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Moskowitz C et al. **Diffuse large B cell lymphoma: How can we cure more patients in 2012?** *Best Pract Res Clin Haematol* 2012;25(1):41-7.

Pro B et al. **Durable remissions with brentuximab vedotin (SGN-35): Updated results of a phase II study in patients with relapsed or refractory systemic anaplastic large cell lymphoma (sALCL).** *Proc ASCO* 2011;**Abstract 8032**.

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

Sehn LH et al. **Randomized Phase II trial comparing GA101 (obinutuzumab) with rituximab in patients with relapsed CD20+ indolent B-cell non-Hodgkin lymphoma: Preliminary analysis of the GAUSS study.** *Proc ASH* 2011;**Abstract 269**.

Tomás JF. **The challenge of recurrent follicular lymphoma.** *Lancet Oncol* 2011;12(8):714-6.

Witzig TE et al. **An international phase II trial of single-agent lenalidomide for relapsed or refractory aggressive B-cell non-Hodgkin's lymphoma.** *Ann Oncol* 2011;22(7):1622-7.

Younes A et al. **Phase 2 study of rituximab plus ABVD in patients with newly diagnosed classical Hodgkin lymphoma.** *Blood* 2012;119(18):4123-8.

Younes A et al. **Brentuximab vedotin (SGN-35) for relapsed CD30-positive lymphomas.** *N Engl J Med* 2010;363(19):1812-21.

POST-TEST

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

QUESTIONS (PLEASE CIRCLE ANSWER):

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

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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

	BEFORE	AFTER
Activity and toxicity of brentuximab vedotin in HL/sALCL	4 3 2 1	4 3 2 1
Maintenance rituximab for patients with FL	4 3 2 1	4 3 2 1
Response to sequential HDAC inhibitor therapy in CTCL	4 3 2 1	4 3 2 1
Role of RIT as initial treatment and consolidation therapy for FL	4 3 2 1	4 3 2 1
Awareness of the possibility of tumor flare and tumor lysis in the treatment of CLL	4 3 2 1	4 3 2 1
Intergroup study of BR versus BVR with rituximab with or without lenalidomide maintenance therapy for older patients with newly diagnosed MCL	4 3 2 1	4 3 2 1

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 case-based learning to formulate individualized strategies for the care of patients with lymphoma. . . . . 4 3 2 1 N/M N/A
- 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. . . . . 4 3 2 1 N/M N/A
- Utilize available research evidence on the use of CNS prophylaxis to guide treatment decision-making for patients with diffuse large B-cell lymphoma. . . . . 4 3 2 1 N/M N/A
- Appraise recent data on therapeutic advances and changing practice standards in follicular lymphoma, and apply this information to clinical practice. . . . . 4 3 2 1 N/M N/A
- Develop an algorithm for the evaluation and treatment of newly diagnosed and relapsed/refractory CLL.. . . . . 4 3 2 1 N/M N/A
- Devise an approach for the sequential systemic treatment of cutaneous T-cell lymphoma. . . . . 4 3 2 1 N/M N/A
- Communicate the existing and emerging roles of proteasome inhibitors and IMiDs to patients with mantle-cell lymphoma. . . . . 4 3 2 1 N/M N/A
- Facilitate patient access to clinical trial participation through communication of ongoing research opportunities.. . . . . 4 3 2 1 N/M N/A

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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

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.....

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

Faculty	Knowledge of subject matter				Effectiveness as an educator			
Jonathan W Friedberg, MD, MMSc	4	3	2	1	4	3	2	1
Steven M Horwitz, MD	4	3	2	1	4	3	2	1
Brad S Kahl, MD	4	3	2	1	4	3	2	1
Mark S Kaminski, MD	4	3	2	1	4	3	2	1
John P Leonard, MD	4	3	2	1	4	3	2	1
Craig Moskowitz, MD	4	3	2	1	4	3	2	1
Mitchell R Smith, MD, PhD	4	3	2	1	4	3	2	1
Anas Younes, MD	4	3	2	1	4	3	2	1
Moderator	**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 moderator for this activity:

.....

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This activity is supported by educational grants from
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Last review date: June 2012
Release date: June 2012
Expiration date: June 2013
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