ISSUE 1 • 2013

Striving for Consensus: The Application of Existing and Emerging Research Findings to the Practical Management of Hodgkin and Non-Hodgkin Lymphoma

Proceedings from a Clinical Investigator Think Tank

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Striving for Consensus: The Application of Existing and Emerging Research Findings to the Practical Management of Hodgkin and Non-Hodgkin Lymphoma

A Continuing Medical Education Audio Program

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 for 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

- Develop an understanding of emerging efficacy and side-effect data with novel agents and combination regimens under evaluation for indolent and aggressive B-cell and T-cell NHL.
- Incorporate new therapeutic strategies into the best-practice management of HL.
- Develop an algorithm for the evaluation and treatment of newly diagnosed and relapsed/refractory CLL.
- Devise an evidence-based approach for the sequential systemic treatment of peripheral T-cell lymphoma.
- Communicate the existing and emerging roles of proteasome inhibitors and IMiDs to patients with relapsed/refractory mantle-cell lymphoma.
- Utilize available research evidence and understand the controversies surrounding the use of CNS prophylaxis to guide treatment decision-making for patients with diffuse large B-cell lymphoma.

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

Last review date: December 2013; Release date: December 2013; Expiration date: December 2014

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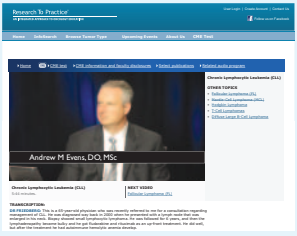
Video Highlights of the Clinical Investigator Think Tank



Visit www.ResearchToPractice.com/HOUTT113/Video to access a number of short video segments and corresponding transcripts from the Think Tank featuring the faculty discussing and debating some of the key clinical management and research issues in Hodgkin and non-Hodgkin lymphoma.

SELECT PUBLICATIONS

A randomized, open-label, Phase 3 trial of A+AVD versus ABVD as frontline therapy in patients with advanced classical Hodgkin lymphoma. NCT01712490

Brown JR et al. **Final results of a phase 1 study of idelalisib (GS-1101), a selective inhibitor of phosphatidylinositol 3-kinase p110 delta, in patients with relapsed or refractory CLL.** *Proc ASCO* 2013;**Abstract 7003**.

Chen R et al. **Two-year follow-up of patients with relapsed/refractory Hodgkin treated with brentuximab vedotin prior to reduced intensity allogeneic hematopoietic cell transplantation.** *Proc ICML* 2013;**Abstract 140**.

Chiappella A et al. **Rituximab-CHOP21 plus lenalidomide is effective and feasible in elderly untreated diffuse large B-cell lymphoma: Results of Phase II REAL07 study of the Fondazione Italiana Linfomi (FIL).** *Proc ASH* 2012;**Abstract 903**.

ECOG-E2408: A 3-arm randomized Phase II trial of bendamustine-rituximab (BR) followed by rituximab vs bortezomib-BR followed by rituximab vs BR followed by lenalidomide/rituximab in high-risk follicular lymphoma. NCT01216683

Friedberg JW et al. **Phase II study of alisertib, a selective Aurora A kinase inhibitor, in relapsed and refractory aggressive B- and T-cell non-Hodgkin lymphomas.** *J Clin Oncol* 2013;[Epub ahead of print].

Goede V et al. **Obinutuzumab (GA101) + chlorambucil (Clb) or rituximab + Clb versus Clb alone in patients with chronic lymphocytic leukemia (CLL) and co-existing medical conditions (comorbidities): Final stage 1 results of the CLL11 (BO21004) Phase 3 trial.** *Proc ASCO* 2013;**Abstract 7004**.

Goy A et al. **Single-agent lenalidomide in patients with relapsed/refractory mantle cell lymphoma following bortezomib: Efficacy, safety and pharmacokinetics from the multicenter phase II MCL-001 "EMERGE" trial.** *Proc EHA* 2013;**Abstract S1156**.

Kim YH et al. **Phase 3 study of brentuximab vedotin versus physician's choice of methotrexate or bexarotene in patients with CD30-positive cutaneous T-cell lymphoma. The ALCANZA study.** *Proc ICML* 2013;**Abstract 572**.

Moskowitz AJ et al. **PET-adapted sequential therapy with brentuximab vedotin and augmented-ICE induces FDG-PET normalization in 92% of patients with relapsed and refractory Hodgkin lymphoma.** *Proc ICML* 2013;**Abstract 141**.

Nowakowski GS et al. **Combination of lenalidomide with R-CHOP is well tolerated and effective as initial therapy for aggressive B-cell lymphomas — A phase II study.** *Proc ASH* 2012;**Abstract 689**.

O'Brien SM et al. **A phase 2 study of the selective phosphatidylinositol 3-kinase delta inhibitor idelalisib in combination with rituximab in treatment-naive patients ≥65 years with chronic lymphocytic leukemia or small lymphocytic lymphoma.** *Proc ASCO* 2013;**Abstract 7005**.

O'Connor OA et al. **Belinostat, a novel pan-histone deacetylase inhibitor in relapsed or refractory peripheral T-cell lymphoma: Results from the BELIEF trial.** *Proc ASCO* 2013;**Abstract 8507**.

O'Connor OA et al. **ECHELON-2: Phase 3 trial of brentuximab vedotin and CHP versus CHOP in the frontline treatment of patients with CD30+ mature T-cell lymphomas.** *Proc ICML* 2013;**Abstract 138**.

Press OW et al. **Phase III randomized intergroup trial of CHOP plus rituximab compared with CHOP chemotherapy plus (131)iodine-tositumomab for previously untreated follicular non-Hodgkin lymphoma: SWOG S0016.** *J Clin Oncol* 2013;31(3):314-20.

Randomized Phase II open-label study of lenalidomide R-CHOP vs R-CHOP in patients with newly diagnosed diffuse large B-cell lymphoma. NCT01856192

Salles GA et al. **Obinutuzumab (GA101) in patients with relapsed/refractory indolent non-Hodgkin lymphoma: Results from the phase II GAUGUIN study.** *J Clin Oncol* 2013;31(23):2920-6.

Scholz CW et al. **(90)Yttrium-ibritumomab-tiuxetan as first-line treatment for follicular lymphoma: 30 months of follow-up data from an international multicenter phase II clinical trial.** *J Clin Oncol* 2013;31(3):308-13.

Witzig TE. **Moving radioimmunotherapy forward for follicular lymphoma.** *J Clin Oncol* 2013;31(3):294-6.

Younes A et al. **Phase III study of brentuximab vedotin plus doxorubicin, vinblastine, and dacarbazine versus doxorubicin, bleomycin, vinblastine, and dacarbazine as front-line treatment for advanced classical Hodgkin lymphoma.** *Proc ASCO* 2013;**Abstract TPS8612**.

POST-TEST

Striving for Consensus: The Application of Existing and Emerging Research Findings to the Practical Management of Hodgkin and Non-Hodgkin Lymphoma

QUESTIONS (PLEASE CIRCLE ANSWER):

1. **A planned interim analysis of the CLL11 trial by an independent data monitoring committee indicated that obinutuzumab/chlorambucil significantly improved progression-free survival compared to rituximab/chlorambucil for patients with previously untreated CLL.**
   a. True
   b. False

2. **Which of the following agents is classified as a BTK inhibitor?**
   a. AVL-292
   b. Ibrutinib
   c. Idelalisib
   d. Both a and b
   e. Both a and c
   f. All of the above

3. **Brentuximab vedotin is an antibody-drug conjugate that targets _____.**
   a. CD20
   b. CD30
   c. CD5

4. **Data from the pivotal trial that led to the approval of brentuximab vedotin in the treatment of HL after failure of ASCT reported a response rate exceeding 70% for patients undergoing treatment in this setting.**
   a. True
   b. False

5. **Which of the following statements is true with regard to the results of the Phase II BELIEF trial of single-agent belinostat for patients with relapsed or refractory PTCL?**
   a. Incidence of thrombocytopenia with belinostat seemed to be attenuated versus rates reported with other HDAC inhibitors evaluated in PTCL
   b. The activity of belinostat was higher in patients with angioimmunoblastic T-cell lymphoma compared to the overall patient population
   c. Both a and b
   d. Neither a nor b

6. **A Phase II trial published by Scholz and colleagues evaluating _____ as first-line therapy for patients with FL reported high response rates (56% complete response and 31% partial response) with this agent.**
   a. ^{90}Yttrium-ibritumomab tiuxetan
   b. ^{131}I-tositumomab
   c. R-CHOP

7. **What is the mechanism of action of alisertib (MLN8237)?**
   a. Antimetabolite
   b. Alkylating agent
   c. Aurora A kinase inhibitor
   d. None of the above

8. **The Phase III ECHELON-2 trial is evaluating _____ in combination with CHP versus CHOP as first-line therapy for patients with CD30-positive mature T-cell lymphomas.**
   a. Brentuximab vedotin
   b. Pralatrexate
   c. Romidepsin
   d. All of the above

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

10. **Preliminary analyses of data from studies evaluating lenalidomide for patients with relapsed/refractory DLBCL suggest that this agent has significantly more activity in which of the following DLBCL subtypes?**
    a. Activated B-cell DLBCL
    b. Germinal center B-cell DLBCL
    c. Neither of the above

EDUCATIONAL ASSESSMENT AND CREDIT FORM

Striving for Consensus: The Application of Existing and Emerging Research Findings to the Practical 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?

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

	BEFORE	AFTER
Initial results from the Phase III CLL11 trial of obinutuzumab (GA101) with chlorambucil or rituximab with chlorambucil versus chlorambucil alone in previously untreated CLL	4 3 2 1	4 3 2 1
Responses and tolerability of the novel pan-histone deacetylase inhibitor belinostat for relapsed/refractory PTCL on the Phase II BELIEF trial	4 3 2 1	4 3 2 1
Differential responses to lenalidomide in the germinal center B-cell and activated B-cell subtypes of DLBCL	4 3 2 1	4 3 2 1
Results from a Phase II trial of the novel Aurora A kinase inhibitor alisertib (MLN8237) in patients with aggressive B- and T-cell non-Hodgkin lymphoma	4 3 2 1	4 3 2 1
Ongoing trials evaluating brentuximab vedotin-based therapies in CD30-positive T-cell lymphoma	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

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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 an understanding of emerging efficacy and side-effect data with novel agents and combination regimens under evaluation for indolent and aggressive B-cell and T-cell NHL. . . . . 4 3 2 1 N/M N/A
- Incorporate new therapeutic strategies into the best-practice management of HL. . . . . 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 evidence-based approach for the sequential systemic treatment of peripheral 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 relapsed/refractory mantle-cell lymphoma. . . . . 4 3 2 1 N/M N/A
- Utilize available research evidence and understand the controversies surrounding 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

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:

.....

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☐ 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

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

Faculty	Knowledge of subject matter	Effectiveness as an educator
Andrew M Evens, DO, MSc	4 3 2 1	4 3 2 1
Christopher Flowers, MD, MS	4 3 2 1	4 3 2 1
Jonathan W Friedberg, MD, MMSc	4 3 2 1	4 3 2 1
Julie M Vose, MD, MBA	4 3 2 1	4 3 2 1
Michael E Williams, MD, ScM	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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Last review date: December 2013
Release date: December 2013
Expiration date: December 2014
Estimated time to complete: 2.75 hours

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