INTERNATIONAL SECOND OPINION

# Part I: Case-Based Discussions Focused on the Management of Non-Hodgkin Lymphoma and Chronic Lymphocytic Leukemia

## TARGET AUDIENCE

This activity is intended for hematologists, medical oncologists, hematology-oncology fellows and other healthcare providers involved in the treatment of non-Hodgkin lymphoma (NHL)/chronic lymphocytic leukemia (CLL).

## OVERVIEW OF ACTIVITY

Taken together, it is estimated that approximately 148,040 new lymphoid and myeloid cancer cases were identified in the United States in the year 2012, and 54,380 individuals died from these diseases. Of importance, currently more than 50 drug products are labeled for use in the management of hematologic cancers, with more than 60 distinct FDA-approved indications. Although this extensive list of available treatment options is reassuring for patients and oncology healthcare professionals, it poses a challenge to the practicing clinician who must maintain up-to-date knowledge of appropriate clinical management strategies across a vast spectrum of liquid and solid tumors.

These proceedings from a CME symposium during the 54th ASH Annual Meeting use the perspectives of renowned experts in the field of hematologic oncology on cases provided by an international panel of community oncologists from the United States, India, Italy and Spain to frame a relevant discussion of the optimal management of various forms of NHL. By providing information on the latest research developments and their potential application to routine practice, this activity is designed to assist hematologists, medical oncologists and hematology-oncology fellows with the formulation of up-to-date clinical management strategies for NHL and CLL.

## LEARNING OBJECTIVES

- Appraise recent data on therapeutic advances and changing practice standards in NHL, including CLL, and integrate this information, as appropriate, into current clinical care.
- Use prognostic and predictive clinical and molecular markers to aid in treatment decision-making for NHL.
- Apply the results of emerging clinical research to the selection of optimal systemic therapy for patients with newly diagnosed and relapsed or refractory CLL.
- Identify patients with NHL who may benefit from maintenance systemic treatment.
- Recognize the role of romidepsin, pralatrexate, brentuximab vedotin and other novel agents in the management of peripheral T-cell lymphoma and/or advanced-stage cutaneous T-cell lymphoma, and educate patients about their associated benefits and risks.
- Recall new data with investigational agents demonstrating promising activity in NHL.
- Assess ongoing clinical trials evaluating innovative investigational approaches for NHL, and counsel appropriate patients for study participation.

## ACCREDITATION STATEMENT

Research To Practice is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

## CREDIT DESIGNATION STATEMENT

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## HOW TO USE THIS CME ACTIVITY

This CME activity consists of a video component. To receive credit, the participant should watch the video, complete the Post-test with a score of 70% or better and fill out the Educational Assessment and Credit Form located on our website at ResearchToPractice.com/ASHNHL13/Video/CME.

## CONTENT VALIDATION AND DISCLOSURES

Research To Practice (RTP) is committed to providing its participants with high-quality, unbiased and state-of-the-art education. We assess potential conflicts of interest with faculty, planners and managers of CME activities. Real or apparent conflicts of interest are identified and resolved through a conflict of interest resolution process. In addition, all activity content is reviewed by both a member of the RTP scientific staff and an external, independent physician reviewer for fair balance, scientific objectivity of studies referenced and patient care recommendations.

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**Hardware/Software Requirements:**
A high-speed Internet connection
A monitor set to 1280 x 1024 pixels or more
Internet Explorer 7 or later, Firefox 3.0 or later, Chrome, Safari 3.0 or later
Adobe Flash Player 10.2 plug-in or later
Adobe Acrobat Reader
(Optional) Sound card and speakers for audio

**Last review date:** March 2013

**Expiration date:** March 2014

## Select Publications


### John P Leonard, MD

Ardeshna KM et al. **An Intergroup randomised trial of rituximab versus a watch and wait strategy in patients with Stage II, III, IV, asymptomatic, non-bulky follicular lymphoma (Grades 1, 2 and 3a). A preliminary analysis.** *Proc ASH* 2010;**Abstract 6**.

Fowler N et al. T**he Btk inhibitor, PCI-32765, induces durable responses with minimal toxicity in patients with relapsed/refractory B-cell malignancies: Results from a Phase I study.** *Proc ASH* 2010;**Abstract 964**.

Furman RR et al. **CAL-101, an isoform-selective inhibitor of phosphatidylinositol 3-kinase P110 δ, demonstrates clinical activity and pharmacodynamic effects in patients with relapsed or refractory chronic lymphocytic leukemia.** *Proc ASH* 2010;**Abstract 65**.

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**.

Kahl BS et al. **Clinical safety and activity in a Phase 1 study of CAL-101, an isoform-selective inhibitor of phosphatidylinositol 3-kinase P110δ, in patients with relapsed or refractory non-Hodgkin lymphoma.** *Proc ASH* 2010;**Abstract 1777**.

Leonard J et al. **CALGB 50401: A randomized trial of lenalidomide alone versus lenalidomide plus rituximab in patients with recurrent follicular lymphoma.** *Proc ASCO* 2012;**Abstract 8000**.

Rummel MJ et al. **Bendamustine plus rituximab (B-R) versus CHOP plus rituximab (CHOP-R) as first-line treatment in patients with indolent and mantle cell lymphomas (MCL): Updated results from the StiL NHL1 study.** *Proc ASCO* 2012;**Abstract 3**.

Stevenson FK et al. **B-cell receptor signaling in chronic lymphocytic leukemia.** *Blood* 2011;118(16):4313-20.

Van Meerten T, Hagenbeek A. **CD20-targeted therapy: A breakthrough in the treatment of non-Hodgkin's lymphoma.** *Neth J Med* 2009;67(7):251-9.

### Myron S Czuczman, MD

Dunleavy K et al. **Differential efficacy of bortezomib plus chemotherapy within molecular subtypes of diffuse large B-cell lymphoma.** *Blood* 2009;113(24):6069-76.

Gisselbrecht C et al. **Salvage regimens with autologous transplantation for relapsed large B-cell lymphoma in the rituximab era.** *J Clin Oncol* 2010;28(27):4184-90.

Lenz G et al. **Stromal gene signatures in large-B-cell lymphomas.** *N Engl J Med* 2008;359(22):2313-23.

Lossos IS. **Molecular pathogenesis of diffuse large B-cell lymphoma.** *J Clin Oncol* 2005;23(26):6351-7.

Roschewski M et al. **Diffuse large B cell lymphoma: Molecular targeted therapy.** *Int J Hematol* 2012;96(5):552-61.

Thieblemont C et al. **The germinal center/activated B-cell subclassification has a prognostic impact for response to salvage therapy in relapsed/refractory diffuse large B-cell lymphoma: A bio-CORAL study.** *J Clin Oncol* 2011;29(31):4079-87.

### Martin Dreyling, MD, PhD

Fernandez V et al. **Genomic and gene expression profiling defines indolent forms of mantle cell lymphoma.** *Cancer Res* 2010;70(4):1408-18.

Goy A et al. **Bortezomib in patients with relapsed or refractory mantle cell lymphoma: Updated time-to-event analyses of the multicenter phase 2 PINNACLE study.** *Ann Oncol* 2009;20(3):520-5.

Hess G et al. **Phase III study to evaluate temsirolimus compared with investigator's choice therapy for the treatment of relapsed or refractory mantle cell lymphoma.** *J Clin Oncol* 2009;27(23):3822-9.

Hoster E et al. **A new prognostic index (MIPI) for patients with advanced-stage mantle cell lymphoma.** *Blood* 2008;111(2):558-65.

Hoster E et al. **Autologous stem cell transplantation and addition of rituximab independently prolong response duration in advanced stage mantle cell lymphoma.** *Proc ASH* 2009;**Abstract 880**.

Jares P et al. **Genetic and molecular pathogenesis of mantle cell lymphoma: Perspectives for new targeted therapeutics.** *Nature Reviews Cancer* 2007;7(10):750-62.

Kluin-Nelemans HC et al. **Treatment of older patients with mantle-cell lymphoma.** *N Engl J Med* 2012;367(6):520-31.

Kluin-Nelemans JC et al. **R-CHOP versus R-FC followed by maintenance with rituximab versus interferon-alfa: Outcome of the first randomized trial for elderly patients with mantle cell lymphoma.** *Proc ASH* 2011;**Abstract 439**.

Rummel MJ et al. **Bendamustine plus rituximab (B-R) versus CHOP plus rituximab (CHOP-R) as first-line treatment in patients with indolent and mantle cell lymphomas (MCL): Updated results from the StiL NHL1 study.** *Proc ASCO* 2012;**Abstract 3**.

Wang M et al. **Interim results of an international, multicenter, phase 2 study of Bruton's tyrosine kinase (BTK) inhibitor, ibrutinib (PCI-32765), in relapsed or refractory mantle cell lymphoma (MCL): Durable efficacy and tolerability with longer follow-up.** *Proc ASH* 2012;**Abstract 904**.

### Steven M Horwitz, MD

Coiffier B et al. **Results from a pivotal, open-label, phase II study of romidepsin in relapsed or refractory peripheral T-cell lymphoma after prior systemic therapy.** *J Clin Oncol* 2012;30(6):631-6.

D'Amore F et al. **Up-front autologous stem-cell transplantation in peripheral T-cell lymphoma: NLG-T-01.** *J Clin Oncol* 2012;30(25):3093-9.

Dueck G et al. **Interim report of a phase 2 clinical trial of lenalidomide for T-cell non Hodgkin's lymphoma.** *Cancer* 2010;116(19):4541-8.

Mahadevan D et al. **Phase 2 trial of combined cisplatin, etoposide, gemcitabine, and methylprednisolone (PEGS) in peripheral T-cell non-Hodgkin lymphoma: Southwest Oncology Group Study S0350.** *Cancer* 2013;119(2):371-9.

O'Connor OA et al. **Pralatrexate in patients with relapsed or refractory peripheral T-cell lymphoma: Results from the pivotal PROPEL study.** *J Clin Oncol* 2011;29(9):1182-9.

Reimer P et al. **Autologous stem-cell transplantation as first-line therapy in peripheral T-cell lymphomas: Results of a prospective multicenter study.** *J Clin Oncol* 2009;27(1):106-13.

Schmitz N et al. **Treatment and prognosis of mature T-cell and NK-cell lymphoma: An analysis of patients with T-cell lymphoma treated in studies of the German High-Grade Non-Hodgkin Lymphoma Study Group.** *Blood* 2012;116(18):3418-25.

Vose J et al. **International peripheral T-cell and natural killer/T-cell lymphoma study: Pathology findings and clinical outcomes.** *J Clin Oncol* 2008;26(25):4124-30.

### Mitchell R Smith, MD, PhD

Badoux XC et al. **Lenalidomide as initial therapy of elderly patients with chronic lymphocytic leukemia.** *Blood* 2011;118(13):3489-98.

Fabbri M et al. **Association of a microRNA/TP53 feedback circuitry with pathogenesis and outcome of B-cell chronic lymphocytic leukemia.** *JAMA* 2011;305(1):59-67.

Hallek M et al. **Addition of rituximab to fludarabine and cyclophosphamide in patients with chronic lymphocytic leukaemia: A randomised, open-label, phase 3 trial.** *Lancet* 2010;376(9747):1164-74.

Hillmen P et al. **Alemtuzumab compared with chlorambucil as first-line therapy for chronic lymphocytic leukemia.** *J Clin Oncol* 2007;25(35):5616-23.

James DF et al. **Lenalidomide and rituximab for the initial treatment of patients with chronic lymphocytic leukemia (CLL): A multicenter study of the CLL research consortium.** *Proc ASH* 2011;**Abstract 291**.

Wierda WG. **Making advances in first-line chronic lymphocytic leukemia treatment.** *J Clin Oncol* 2012;30(26);3162-4.