

Clinical Investigator and Nursing Perspectives on the Management of Non-Hodgkin Lymphoma and Chronic Lymphocytic Leukemia

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 2012, the numbers of estimated new cases of NHL and chronic lymphocytic leukemia (CLL) in the United States were 70,130 and 16,060, respectively, with approximately 23,000 deaths estimated from these diseases. Increasingly, the age of patients diagnosed with NHL has risen during the past 2 decades, which may result in more significant comorbid conditions that will complicate treatment. Published results from ongoing clinical trials lead to the continual emergence of new therapeutic agents and changes in the use of existing treatments. To provide oncology nurses with therapeutic strategies to address the disparate needs of patients with NHL/CLL, the Oncology Nursing Update audio series employs one-on-one interviews with medical oncologists and nurses who are experts in caring for patients with NHL/CLL. Upon completion of this CNE activity, oncology nurses should be able to formulate an up-to-date and more complete approach to the care of patients with NHL/CLL.

LEARNING OBJECTIVES

- Relate therapeutic algorithms for the management of indolent and aggressive forms of B-cell NHL to appropriate patient-focused education to enhance clinical decisionmaking.
- Apply the results of emerging clinical research to the therapeutic and supportive care of patients with newly diagnosed and relapsed/refractory CLL.
- Explain the risks and benefits of evidence-based treatment approaches and agents to patients with T-cell lymphoma requiring systemic therapy.
- Evaluate the preliminary safety profiles and response outcomes of investigational agents and treatment strategies undergoing evaluation in NHL and CLL, and counsel appropriately selected patients about the potential for enrollment in clinical trials.

ACCREDITATION STATEMENT

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CREDIT DESIGNATION STATEMENT

This educational activity for 3 contact hours is provided by Research To Practice during the period of March 2013 through March 2014.

HOW TO USE THIS CNE ACTIVITY

This is an audio CNE program. This website contains CNE information, including learning objectives, faculty disclosures, a Post-test and an Educational Assessment and Credit Form, as well as links to relevant abstracts and full-text articles.

To receive credit, participants should read the learning objectives and faculty disclosures, listen to the audio MP3s and complete the Post-test and Educational Assessment and Credit Form located at ResearchToPractice. com/ONUNHL113/CNE. A statement of CNE credit will be issued only upon completion of the Post-test, with a score of 70% or better, and the Educational Assessment and Credit Form. Your statement of credit will be mailed to you within 3 weeks or may be printed online.

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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

There is no implied or real endorsement of any product by RTP or the American Nurses Credentialing Center.

TOPICS DISCUSSED DURING THE PROGRAM

INTERVIEW WITH MS GOODRICH

- Case discussion: A 70-year-old woman with a prior history of breast cancer presents with asymptomatic Stage IIIA nonbulky follicular lymphoma (FL) and subsequently undergoes treatment with rituximab (R) on the RESORT study
 - Phase III ECOG-E4402 (RESORT) study comparing R maintenance to R re-treatment upon disease progression for low tumor burden indolent non-Hodgkin lymphoma (NHL)
 - Hypogammaglobulinemia and chronic infections in patients receiving maintenance R
 - Bendamustine-R (BR) as front-line therapy for FL
 - Counseling patients with FL about the similarities and differences between BR and R-CHOP
 - PRIMA: Maintenance R in patients with FL who achieve a response to R-chemotherapy
 - Use of R-lenalidomide (R²) in patients with FL who are intolerant to chemotherapy
- Case discussion: A 63-year-old woman with widespread adenopathy and aggressive, high-risk diffuse large B-cell lymphoma (DLBCL)
 - Monitoring and treatment of tumor lysis syndrome
 - Use of rasburicase prophylaxis for tumor lysis syndrome
 - CNS prophylaxis for patients with DLBCL
- Case discussion: A 64-year-old man with Stage IVA, Grade I FL is observed off treatment for 5 years and subsequently receives R in the face of progressive disease. The patient achieves a complete response to R followed by transformation to DLBCL
 - Treatment of transformed FI

INTERVIEW WITH DR SMITH

- Case discussion: A 58-year-old woman with asymptomatic chronic lymphocytic leukemia (CLL) and WBC rising to 200,000/mm³
 - Detection, diagnosis and prognosis of CLL
 - Indications to initiate treatment for CLL
 - Hypersplenism in CLL
 - Management of tumor lysis syndrome hydration, allopurinol and rasburicase
 - Undefined role of R maintenance in CLL
 - Overview of the similarities and differences between FL and CLL

- Educating patients with indolent lymphoma about a "watch-and-wait" approach versus active treatment
- Promising investigational agents in CLL: ibrutinib, idelalisib (GS1101) and the Bcl-2 inhibitor ABT-199
- Evolving role of lenalidomide ± R in CLL and other lymphomas
- Avoidance of lenalidomide-associated tumor flare in CLI
- Mechanisms of action of R and lenalidomide and rationale for their synergy when used in combination
- Use of R monotherapy in CLL
- Radioimmunotherapy (RIT) as a treatment option in indolent lymphomas
- Case discussion: A 63-year-old man with massive splenomegaly and progressively worsening fatigue is diagnosed with mantle-cell lymphoma (MCL) and undergoes treatment with modified hyper-CVAD
 - Diagnostic workup for MCL
 - Treatment approaches for younger and older patients with MCL
 - Maintenance R in patients with MCL responding to R-CHOP
 - BR followed by maintenance R for relapsed MCL
 - Promising investigational agents in MCL: mTOR inhibitors everolimus and temsirolimus
- Case discussion: A 60-year-old man with low-risk, germinal-center DLBCL receives R-CHOP-14, relapses 1 year later and receives R-ICE followed by HDT and ASCT followed by a second relapse 9 months later
 - Perspective on dose-dense R-CHOP-14 versus R-CHOP-21 in DLBCL
 - Phase III study of pixantrone/R versus gemcitabine/R for aggressive, relapsed NHL not eligible for stem cell transplant

INTERVIEW WITH DR HORWITZ

• Case discussion: A 69-year-old woman who responded well to initial treatment with EPOCH for angioimmunoblastic T-cell lymphoma (TCL) undergoes allogeneic stem cell transplant for a biopsy-proven recurrence and achieves remission

TOPICS DISCUSSED DURING THE PROGRAM

- Overview of angioimmunoblastic TCL
- Key clinical differences between B-cell and T-cell lymphomas
- Activity and tolerability of EPOCH in angioimmunoblastic TCL
- Common subtypes of systemic TCL
- Perspective on allogeneic transplant for older patients with relapsed/refractory angioimmunoblastic TCL
- Treatment options for relapsed/refractory angioimmunoblastic TCL
- Mechanisms of action, efficacy and toxicity profiles of the novel agents romidepsin and pralatrexate used in the treatment of TCL
- Activity and side effects of the antibody-drug conjugate brentuximab vedotin in CD30-positive lymphomas
- Promising investigational agents in TCL: belinostat, bendamustine, KW-0761 and BTK inhibitors
- Potential role of lenalidomide in the treatment of TCL
- Case discussion: An 81-year-old man with Stage 1B mycosis fungoides is enrolled in a clinical trial of pralatrexate and bexarotene after disease transformation
 - Presentation and symptomatology of mycosis fungoides
 - Educating patients about phototherapy for the treatment of cutaneous TCL (CTCL)
 - Treatment options for patients with relapsed/ refractory CTCL
 - Phase I study of pralatrexate in combination with bexarotene for patients with relapsed or refractory CTCL

INTERVIEW WITH MS MORAN

- Case discussion: A 59-year-old man with MCL achieves a complete remission after treatment with R-hyper-CVAD
 - Overview of MCL
 - Educating patients about the side effects and toxicities of R-hyper-CVAD
 - Treatment options for recurrent MCL
 - Activity and side effects of bortezomib in MCL
 - Benefits and risks of lenalidomide in MCL
- Case discussion: A 63-year-old woman with Stage IVB DLBCL receives R-EPOCH on a Phase III trial and remains in complete remission after 2 years
 - CNS prophylaxis in DLBCL
- Case discussion: A 65-year-old man with FL who achieves a complete response to BR experiences disease relapse 2 years later and receives R²
 - Response and tolerability of BR versus R-CHOP as front-line therapy in FL
 - Consideration of R up front or as maintenance therapy for FL
 - Use of R² in patients with relapsed/refractory FL
 - Lenalidomide-associated tumor flare in FL
 - RIT as a treatment option in FL
- Case discussion: A 64-year-old man with CLL whose disease progresses through multiple lines of therapy is now under consideration for a clinical trial of the oral BTK inhibitor ibrutinib
 - Risk for infections in patients with CLL
 - Counseling patients with indolent lymphomas about their diagnosis, treatment and prognosis

SELECT PUBLICATIONS

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.

Armitage JO. The aggressive peripheral T-cell lymphomas: 2012 update on diagnosis, risk stratification, and management. *Am J Hematol* 2012;87(5):511-9. **Abstract**

Armitage JO et al. Clinical roundtable monograph. T-cell lymphoma: Therapeutic overview and disease state awareness. Clin Adv Hematol Oncol 2010;8(12 Suppl 22):1-15. Abstract

Badoux XC et al. Fludarabine, cyclophosphamide, and rituximab chemoimmunotherapy is highly effective treatment for relapsed patients with CLL. *Blood* 2011;117(11):3016-24. **Abstract**

Beckers MM et al. Therapy refractory angioimmunoblastic T-cell lymphoma in complete remission with lenalidomide. *Eur J Haematol* 2012;[Epub ahead of print]. **Abstract**

Byrd JC et al. The Bruton's tyrosine kinase (BTK) inhibitor ibrutinib PCI-32765 (P) is highly active and tolerable in treatment-naive (TN) chronic lymphocytic leukemia (CLL) patients (pts): Interim results of a phase Ib/II study. *Proc ASCO* 2012:Abstract 6507.

Chanan-Khan A et al. Tumor flare reaction associated with lenalidomide treatment in patients with chronic lymphocytic leukemia predicts clinical response. *Cancer* 2011;117(10):2127-35. **Abstract**

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. Abstract

Coiffier B et al. Bortezomib plus rituximab versus rituximab alone in patients with relapsed, rituximab-naive or rituximab-sensitive, follicular lymphoma: A randomised phase 3 trial. *Lancet Oncol* 2011;12(8):773-84. Abstract

Coiffier B et al; Groupe d'Etude des Lymphomes de l'Adulte Trial on Rasburicase Activity in Adult Lymphoma. Efficacy and safety of rasburicase (recombinant urate oxidase) for the prevention and treatment of hyperuricemia during induction chemotherapy of aggressive non-Hodgkin's lymphoma: Results of the GRAAL1 (Groupe d'Etude des Lymphomes de l'Adulte Trial on Rasburicase Activity in Adult Lymphoma) study. *J Clin Oncol* 2003;21(23):4402-6. Abstract

Cortes J et al. Control of plasma uric acid in adults at risk for tumor lysis syndrome: **Efficacy and safety of rasburicase alone** and rasburicase followed by allopurinol compared with allopurinol alone — Results of a multicenter phase III study. *J Clin Oncol* 2010;28(27):4207-13. **Abstract**

Cunningham D et al. R-CHOP14 versus R-CHOP21: Result of a randomized phase III trial for the treatment of patients with newly diagnosed diffuse large B-cell non-Hodgkin lymphoma. *Proc ASCO* 2011;Abstract 8000.

Delarue R et al. R-CHOP14 compared to R-CHOP21 in elderly patients with diffuse large B-cell lymphoma (DLBCL): Final analysis of the LNH03-6B GELA study. *Proc ASCO* 2012; Abstract 8021.

Delfau-Larue MH et al. Targeting intratumoral B-cells with rituximab in addition to CHOP in angioimmunoblastic T-cell lymphoma. A clinicobiological study of the GELA. Haematologica 2012;97(10):1594-602. Abstract

Dueck G et al. Interim report of a phase 2 clinical trial of lenalidomide for T-cell non-Hodgkin lymphoma. *Cancer* 2010;116(19):4541-8. Abstract

Federico M et al. R-CVP versus R-CHOP versus R-FM as first-line therapy for advanced-stage follicular lymphoma: Final results of FOLL05 trial from the Fondazione Italiana Linfomi. *Proc ASCO* 2012; Abstract 8006.

Fischer K et al. Bendamustine combined with rituximab in patients with relapsed and/or refractory chronic lymphocytic leukemia: A multicenter phase II trial of the German Chronic Lymphocytic Leukemia Study Group. *J Clin Oncol* 2011;29(26):3559-66. Abstract

Fowler N et al. Bortezomib, bendamustine, and rituximab in patients with relapsed or refractory follicular lymphoma: The phase II VERTICAL study. *J Clin Oncol* 2011;29(25):3389-95. Abstract

Friedberg JW et al. Effectiveness of first-line management strategies for stage I follicular lymphoma: Analysis of the National LymphoCare study. *J Clin Oncol* 2012;30(27):3368-75. Abstract

Friedberg JW et al. The combination of bendamustine, bortezomib, and rituximab for patients with relapsed/refractory indolent and mantle cell non-Hodgkin lymphoma. *Blood* 2011;117(10):2807-12. **Abstract**

Gisselbrecht C et al. Rituximab maintenance therapy after autologous stem-cell transplantation in patients with relapsed CD20+ diffuse large B-cell lymphoma: Final analysis of the collaborative trial in relapsed aggressive lymphoma. *J Clin Oncol* 2012:[Epub ahead of print]. Abstract

Guirguis HR et al. Impact of central nervous system (CNS) prophylaxis on the incidence and risk factors for CNS relapse in patients with diffuse large B-cell lymphoma treated in the rituximab era: A single centre experience and review of the literature. Br J Haematol 2012:159(1):39-49. Abstract

Gunnellini M, Falchi L. Therapeutic activity of lenalidomide in mantle cell lymphoma and indolent non-Hodgkin's lymphomas. *Adv Hematol* 2012;2012;523842. Abstract

Hallek M et al; International Group of Investigators; German Chronic Lymphocytic Leukaemia Study Group. **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. **Abstract**

Hermine O et al. Alternating courses of 3x CHOP and 3x DHAP plus rituximab followed by a high dose ARA-C containing myeloablative regimen and autologous stem cell transplantation (ASCT) is superior to 6 courses CHOP plus rituximab followed by myeloablative radiochemotherapy and ASCT in mantle cell lymphoma: Results of the MCL Younger Trial of the European Mantle Cell Lymphoma Network (MCL net). *Proc ASH* 2010; Abstract 110.

Jaglowski SM et al. A phase Ib/II study evaluating activity and tolerability of BTK inhibitor PCI-32765 and ofatumumab in patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) and related diseases. *Proc ASCO* 2012:Abstract 6508.

Joly B et al. Rituximab in combination with CHOP regimen in angioimmunoblastic T-cell lymphoma: Results of the phase II RAIL trial — A prospective study of the Groupe d'Etude des Lymphomes de l'Adulte (GELA). *Proc ASCO* 2010; Abstract 8049

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.

Kane RC et al. **Bortezomib for the treatment of mantle cell lymphoma.** Clin Cancer Res 2007;13(18 Pt 1):5291-4. **Abstract** Kluin-Nelemans HC et al. **Treatment of older patients with mantle-cell lymphoma.** N Engl J Med 2012;367(6):520-31. **Abstract**

Korfel A et al. Prevention of central nervous system relapses in diffuse large B-cell lymphoma: Which patients and how? *Curr Opin Oncol* 2011;23(5):436-40. **Abstract**

Kridel R, Dietrich PY. **Prevention of CNS relapse in diffuse large B-cell lymphoma.** *Lancet Oncol* 2011;12(13):1258-66. **Abstract**

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.

Nooka AK et al. Examination of the follicular lymphoma international prognostic index (FLIPI) in the National LymphoCare study (NLCS): A prospective US patient cohort treated predominantly in community practices. *Ann Oncol* 2013;24(2):441-8. Abstract

O'Brien S, Kay NE. **Maintenance therapy for B-chronic lymphocytic leukemia.** Clin Adv Hematol Oncol 2011;9(1):22-31. **Abstract**

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

Pettitt AR et al. Alemtuzumab in combination with methylprednisolone is a highly effective induction regimen for patients with chronic lymphocytic leukemia and deletion of TP53: Final results of the national cancer research institute CLL206 trial. *J Clin Oncol* 2012;30(14):1647-55. Abstract

Piekarz RL et al. **Phase 2 trial of romidepsin in patients with peripheral T-cell lymphoma.** *Blood* 2011;177(22):5827-34. **Abstract**

Press OW et al. A phase III randomized intergroup trial (S0016) comparing CHOP plus rituximab with CHOP plus iodine-131-tositumomab for front-line treatment of follicular lymphoma: Results of subset analyses and a comparison of prognostic models. *Proc ASCO* 2012; Abstract 8001.

Pro B et al. Brentuximab vedotin (SGN-35) in patients with relapsed or refractory systemic anaplastic large-cell lymphoma: Results of a phase II study. *J Clin Oncol* 2012;30(18):2190-6. Abstract

Récher C et al; Groupe d'Etude des Lymphomes de l'Adulte. Intensified chemotherapy with ACVBP plus rituximab versus standard CHOP plus rituximab for the treatment of diffuse large B-cell lymphoma (LNH03-2B): An open-label randomised phase 3 trial. *Lancet* 2011;378(9806):1858-67. Abstract

Ruan J et al. Bortezomib plus CHOP-rituximab for previously untreated diffuse large B-cell lymphoma and mantle cell lymphoma. *J Clin Oncol* 2011;29(6):690-7. Abstract

Rule S et al. The addition of rituximab to fludarabine and cyclophosphamide (FC) improves overall survival in newly diagnosed mantle cell lymphoma (MCL): Results of the randomised UK National Cancer Research Institute (NCRI) trial. *Proc ASH* 2011; Abstract 440.

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.

Salles G et al. Rituximab maintenance for 2 years in patients with high tumour burden follicular lymphoma responding to rituximab plus chemotherapy (PRIMA): A phase 3, randomised controlled trial. *Lancet* 2011;377(9759):42-51. Abstract

Sehn LH et al. Bortezomib ADDED to R-CVP is safe and effective for previously untreated advanced-stage follicular lymphoma: A phase II study by the National Cancer Institute of Canada Clinical Trials Group. *J Clin Oncol* 2011;29(25):3396-401. Abstract

Siegal T et al. CNS prophylaxis in diffuse large B-cell lymphoma: If, when, how and for whom? *Blood Rev* 2012;26(3):97-106. Abstract

Wang M et al. Lenalidomide in combination with rituximab for patients with relapsed or refractory mantle-cell lymphoma: A phase 1/2 clinical trial. Lancet Oncol 2012;13(7):716-23. Abstract

Wang LY et al. Recombinant urate oxidase (rasburicase) for the prevention and treatment of tumor lysis syndrome in patients with hematologic malignancies. *Acta Haematol* 2006;115(1-2):35-8. **Abstract**