Addressing Current Questions and Controversies in the Management of Lymphoma and Chronic Lymphocytic Leukemia

CME Information

TARGET AUDIENCE

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

OVERVIEW OF ACTIVITY

Hematologic cancers include the lymphomas, the leukemias, multiple myeloma and other related disorders stemming from lymphoid and myeloid progenitor cell lines. Taken together, it is estimated that approximately 174,250 new lymphoid, myeloid and leukemic cancer cases will be identified in the United States in the year 2018, and 56,100 individuals will die from these diseases. Importantly, nearly 70 drug products are currently labeled for use in the management of hematologic cancers with more than 120 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 their appropriate application across a vast spectrum of tumor types. This is particularly true within the realm of Hodgkin and non-Hodgkin lymphoma, including CLL, where the past several years have yielded a staggering number of important clinical and research advances.

These proceedings from a CME symposium during the ASH Annual Meeting use the perspectives of a group of community oncologists gathered during a daylong working group to establish and subsequently address some of the most frequently encountered questions and controversies facing clinicians involved in the management of these diseases. By providing information on the latest research developments and their potential application to routine practice, this activity is designed to assist hematologists, medical oncologists, hematology-oncology fellows and other healthcare providers involved in the treatment of Hodgkin and non-Hodgkin lymphoma, including CLL, with the formulation of up-to-date clinical management strategies.

LEARNING OBJECTIVES

- Individualize the selection and sequence of systemic therapy for patients with newly diagnosed and relapsed/refractory (R/R) CLL, considering the patient's clinical presentation, biomarker profile and psychosocial status.
- Consider existing and emerging clinical research data in the formulation of therapeutic recommendations for patients with newly diagnosed and R/R diffuse large B-cell lymphoma, follicular lymphoma and mantle cell lymphoma.
- Incorporate new therapeutic strategies into the best-practice management of newly diagnosed and R/R Hodgkin lymphoma (HL).
- Assess the benefits and risks of evidence-based systemic treatment options to individualize and optimize the care of patients with T-cell lymphoma.
- Compare and contrast the mechanisms of action, efficacy and safety of approved and investigational immune checkpoint inhibitors for the treatment of HL and non-Hodgkin lymphoma (NHL) to determine the current and/or potential utility of each in clinical practice.
- Develop an understanding of the biologic rationale for and appreciate available efficacy and safety data with chimeric antigen receptor T-cell therapy, and identify patients with R/R B-cell cancers for whom this approach may be appropriate.
- Assess the ongoing clinical trials evaluating other novel investigational approaches for HL, NHL and CLL, and obtain consent from 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

Research To Practice designates this enduring material for a maximum of 3 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

AMERICAN BOARD OF INTERNAL MEDICINE (ABIM) — MAINTENANCE OF CERTIFICATION (MOC)

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 3 Medical Knowledge MOC points in the American Board of Internal Medicine's (ABIM) Maintenance

of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

Please note, this program has been specifically designed for the following ABIM specialty: **medical oncology**.

Personal information and data sharing: Research To Practice aggregates deidentified user data for program-use analysis, program development, activity planning and site improvement. We may provide aggregate and deidentified data to third parties, including commercial supporters. We do not share or sell personally identifiable information to any unaffiliated third parties or commercial supporters. Please see our privacy policy at **ResearchToPractice.com/Privacy-Policy** for more information.

HOW TO USE THIS CME ACTIVITY

This CME activity consists of a video component. To receive credit, the participant should review the CME information, watch the video, complete the Post-test with a score of 80% or better and fill out the Educational Assessment and Credit Form located at **ResearchToPractice.com/ASHNHL2017/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 conflicts of interest with faculty, planners and managers of CME activities. 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.

FACULTY — The following faculty (and their spouses/partners) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process:

Martin Dreyling, MD, PhD
Professor of Medicine
Department of Medicine III
University Hospital – LMU Munich
Munich, Germany

Advisory Committee: Bayer HealthCare Pharmaceuticals, Celgene Corporation, Gilead Sciences Inc, Janssen Biotech Inc, Pfizer Inc, Roche Laboratories Inc; **Speakers Bureau:** Bayer HealthCare Pharmaceuticals, Celgene Corporation, Gilead Sciences Inc, Janssen Biotech Inc, Roche Laboratories Inc; **Other Remunerated Activities:** Celgene Corporation, Janssen Biotech Inc, Mundipharma International Limited, Roche Laboratories Inc.

Jonathan W Friedberg, MD, MMSc
Samuel E Durand Professor of Medicine
Director, James P Wilmot Cancer Institute
University of Rochester
Rochester, New York

Data and Safety Monitoring Board: Bayer HealthCare Pharmaceuticals.

Craig Moskowitz, MD
Stephen A Greenberg Chair in Lymphoma Research
Clinical Director, Division of Hematologic Oncology
Attending Physician, Lymphoma and Adult BMT Services
Member, Memorial Sloan Kettering Cancer Center
Professor of Medicine, Weill Medical College of
Cornell University
New York, New York

Consulting Agreements: Celgene Corporation, Genentech BioOncology, Merck, Seattle Genetics; **Contracted Research:** Merck, Pharmacyclics LLC, an AbbVie Company, Seattle Genetics.

Owen A O'Connor, MD, PhD
Professor of Medicine and Developmental Therapeutics
Director, Center for Lymphoid Malignancies
Columbia University Medical Center
College of Physicians and Surgeons
NewYork-Presbyterian Hospital
New York, New York

Consulting Agreements: Celgene Corporation, Mundipharma International Limited; **Contracted Research:** Celgene Corporation, Mundipharma International Limited, Spectrum Pharmaceuticals Inc.

Laurie H Sehn, MD, MPH
Centre for Lymphoid Cancer
BC Cancer Agency and University of British Columbia
Vancouver, British Columbia, Canada

Consulting Agreements: AbbVie Inc, Amgen Inc, Celgene Corporation, Genentech BioOncology, Gilead Sciences Inc, Janssen Biotech Inc, Roche Laboratories Inc, Seattle Genetics, Takeda Oncology.

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: AbbVie Inc, Acerta Pharma, Adaptive Biotechnologies, Agendia Inc, Agios Pharmaceuticals Inc, Amgen Inc, Ariad Pharmaceuticals Inc, Array BioPharma Inc, Astellas Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Baxalta Inc, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Pharma Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, CTI BioPharma Corp, Dendreon Pharmaceuticals Inc, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech BioOncology, Genomic Health Inc, Gilead Sciences Inc, Halozyme Inc, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Kite Pharma Inc, Lexicon Pharmaceuticals Inc, Lilly, Medivation Inc, a Pfizer Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, NanoString Technologies, Natera Inc, Novartis, Novocure, Onyx Pharmaceuticals, an Amgen subsidiary, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceu-

ticals Inc, Sanofi Genzyme, Seattle Genetics, Sigma-Tau Pharmaceuticals Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro Inc, Teva Oncology and Tokai Pharmaceuticals Inc.

RESEARCH TO PRACTICE STAFF AND EXTERNAL REVIEWERS — The scientific staff and reviewers for Research To Practice have no relevant conflicts of interest to disclose.

This educational activity contains discussion of published and/or investigational uses of agents that are not indicated by the Food and Drug Administration. Research To Practice does not recommend the use of any agent outside of the labeled indications. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications and warnings. The opinions expressed are those of the presenters and are not to be construed as those of the publisher or grantors.

This activity is supported by educational grants from AbbVie Inc, Adaptive Biotechnologies, AstraZeneca Pharmaceuticals LP/Acerta Pharma, Bayer HealthCare Pharmaceuticals, Celgene Corporation, Genentech BioOncology, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Pharmacyclics LLC, an AbbVie Company, Seattle Genetics and Takeda Oncology.

Hardware/Software Requirements:
A high-speed Internet connection
A monitor set to 1280 x 1024 pixels or more
Internet Explorer 11 or later, Firefox 56 or later, Chrome 61 or later, Safari 11 or later, Opera 48 or later
Adobe Flash Player 27 plug-in or later
Adobe Acrobat Reader
(Optional) Sound card and speakers for audio

Last review date: March 2018

Expiration date: March 2019

Select Publications

Craig Moskowitz, MD

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

Evens AM et al. **Sequential brentuximab vedotin (Bv) before and after adriamycin, vinblastine, and dacarbazine (Bv-AVD) for older patients with untreated classical Hodgkin Lymphoma (cHL): Final results from a multicenter phase II study.** *Proc ASH* 2017;**Abstract 733**.

Forero-Torres A et al. **Phase 2 study of frontline brentuximab vedotin monotherapy in Hodgkin lymphoma patients aged 60 years and older.** *Blood* 2015;126(26):2798-804.

Friedberg JW et al. **Frontline brentuximab vedotin in combination with dacarbazine or bendamustine in patients aged ≥60 years with HL.** *Blood* 2017;130(26):2829-37.

Gibb A et al. **Results of a phase II study of brentuximab vedotin in the first line treatment of Hodgkin lymphoma patients considered unsuitable for standard chemotherapy (BREVITY).** *Proc ICML* 2017;**Abstract 069**.

Jonathan W Friedberg, MD, MMSc

Anderson MA et al. **Clinicopathological features and outcomes of progression of CLL on the BCL2 inhibitor venetoclax.** *Blood* 2017;129(25):3362-70.

Döhner H et al. **Genomic aberrations and survival in chronic lymphocytic leukemia.** *N Engl J Med* 2000;343(26):1910-6.

Eichhorst B, Hallek M. **Prognostication of chronic lymphocytic leukemia in the era of new agents.** *Hematology Am Soc Hematol Educ Program* 2016;2016(1):149-55.

Hallek M. **Chronic lymphocytic leukemia: 2017 update on diagnosis, risk stratification, and treatment.** *Am J Hematol* 2017;92(9):946-65.

International CLL-IPI working group. **An international prognostic index for patients with chronic lymphocytic leukaemia (CLL-IPI): A meta-analysis of individual patient data.** *Lancet Oncology* 2016;17(6):779-90.

Landau DA et al. **Mutations driving CLL and their evolution in progression and relapse.** *Nature* 2015;526(7574):525-30.

Roberts AW et al. **Targeting BCL2 with venetoclax in relapsed chronic lymphocytic leukemia.** *N Engl J Med* 2016; 374(4):311-22.

Seymour JF et al. **Venetoclax plus rituximab is superior to bendamustine plus rituximab in patients with relapsed/ refractory chronic lymphocytic leukemia — Results from pre-planned interim analysis of the randomized phase 3 Murano Study.** *Proc ASH* 2017;**Abstract LBA-2**.

Shanafelt TD et al. **Prospective evaluation of clonal evolution during long-term follow-up of patients with untreated early-stage chronic lymphocytic leukemia.** *J Clin Oncol* 2006;24(28):4634-41.

Stilgenbauer S et al. **Clonal evolution in chronic lymphocytic leukemia: Acquisition of high-risk genomic aberrations associated with unmutated VH, resistance to therapy, and short survival.** *Haematologica* 2007;92(9):1242-5.

Laurie H Sehn, MD, MPH

A multicenter, phase III, open-label, randomized study in previously untreated patients with advanced indolent non-Hodgkin's lymphoma evaluating the benefit of GA101 (RO5072759) plus chemotherapy compared with rituximab plus chemotherapy followed by GA101 or rituximab maintenance therapy in responders. NCT01332968

Burke JM et al. **Phase IIIb randomized study of lenalidomide plus rituximab (R2) followed by lenalidomide vs. rituximab maintenance in patients with relapsed/refractory NHL: Analysis of follicular lymphoma patients.** *Proc EHA* 2017;**Abstract P634**.

Coutré SE et al. **Management of adverse events associated with idelalisib treatment: Expert panel opinion.** *Leuk Lymphoma* 2015;56(10):2779-86.

Dreyling M et al. **Phosphatidylinositol 3-kinase inhibition by copanlisib in relapsed or refractory indolent lymphoma.** *J Clin Oncol* 2017;35(35):3898-905.

Gopal AK et al. **PI3Kδ inhibition by idelalisib in patients with relapsed indolent lymphoma.** *N Engl J Med* 2014; 370(11):1008-18.

Salles G et al. **Efficacy and safety of idelalisib in patients with relapsed, rituximab- and alkylating agent-refractory follicular lymphoma: A subgroup analysis of a phase 2 study.** *Haematologica* 2017;102(4):e156-9.

Select Publications

Sehn L et al. **Obinutuzumab plus bendamustine versus bendamustine monotherapy in patients with rituximab-refractory indolent non-Hodgkin lymphoma (GADOLIN): A randomised, controlled, open-label, multicentre, phase 3 trial.** *Lancet Oncology* 2016;17(8):1081-93.

Martin Dreyling, MD, PhD

Davids MS et al. **Phase I first-in-human study of venetoclax in patients with relapsed or refractory non-Hodgkin lymphoma.** *J Clin Oncol* 2017;35(8):826-33.

Dreyling M et al. **Ibrutinib versus temsirolimus in patients with relapsed or refractory mantle-cell lymphoma: An international, randomised, open-label, phase 3 study.** *Lancet* 2016;387(10020):770-8.

Dreyling M, Ferrero S; European Mantle Cell Lymphoma Network. **The role of targeted treatment in mantle cell lymphoma: Is transplant dead or alive?** *Haematologica* 2016;101(2):104-14.

Eskelund CW et al. **TP53 mutations identify younger mantle cell lymphoma patients who do not benefit from intensive chemoimmunotherapy.** *Blood* 2017;130(17):1903-10.

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

Le Gouill S et al. **Rituximab after autologous stem-cell transplantation in mantle-cell lymphoma.** *N Engl J Med* 2017;377(13):1250-60.

Ruan J et al. **Lenalidomide plus rituximab as initial treatment for mantle-cell lymphoma.** *N Engl J Med* 2015;373(19):1835-44.

Wang M et al. **Efficacy and safety of acalabrutinib monotherapy in patients with relapsed/refractory mantle cell lymphoma in the phase 2 ACE-LY-004 study.** *Proc ASH* 2017;**Abstract 155**.

Owen A O'Connor, MD, PhD

Hans CP et al. **Confirmation of the molecular classification of diffuse large B-cell lymphoma by immunohistochemistry using a tissue microarray.** *Blood* 2004;103(1):275-82.

Nowakowski GS et al. **Lenalidomide combined with R-CHOP overcomes negative prognostic impact of non-germinal center B-cell phenotype in newly diagnosed diffuse large B-Cell lymphoma: A phase II study.** *J Clin Oncol* 2015;33(3):251-7.

Nowakowski GS et al. **Effect of lenalidomide combined with R-CHOP (R2CHOP) on negative prognostic impact of nongerminal center (non-GCB) phenotype in newly diagnosed diffuse large b-cell lymphoma: A phase 2 study.** *Proc ASCO* 2014;**Abstract 8520**.

Rosenwald A et al; Lymphoma/Leukemia Molecular Profiling Project. **The use of molecular profiling to predict survival after chemotherapy for diffuse large-B-cell lymphoma.** *N Engl J Med* 2002;346(25):1937-47.

Vitolo U et al; Fondazione Italiana Linfomi. **Lenalidomide plus R-CHOP21 in elderly patients with untreated diffuse large B-cell lymphoma: Results of the REAL07 open-label, multicentre, phase 2 trial.** *Lancet Oncol* 2014;15(7):730-7.

Younes A et al. **Combination of ibrutinib with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) for treatment-naive patients with CD20-positive B-cell non-Hodgkin lymphoma: A non-randomised, phase 1b study.** *Lancet Oncology* 2014;15(9):1019-26.