

Dissecting the Decision:

Documenting and Discussing the Clinical Practice Patterns of Hematologic Oncology Investigators in the Management of Follicular Lymphoma

CME Information

TARGET AUDIENCE

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

OVERVIEW OF ACTIVITY

FL is an indolent form of non-Hodgkin lymphoma that can vary significantly in its clinical presentation. As such, no single standard approach to the initial management of the disease has been established, and available options range from watchful waiting, radiation therapy and rituximab monotherapy to various combinations of chemoimmunotherapy. In general, the decision to employ one of these approaches versus another is made based on a number of established criteria as well as patient preferences. Despite active treatment in the up-front setting, FL remains incurable, and as patients relapse it becomes more difficult to treat their disease, as durability and duration of response to therapy tend to diminish over time. Notably, recent data sets and corresponding FDA actions have ushered in an era in which additional evidence-based options must now be considered. Thus, a significant need exists to ensure that clinicians and patients are made aware of the risks and benefits associated with all available therapeutic options so that they may make informed and personalized treatment choices.

These proceedings from a CME/CNE symposium held during the 2018 Pan Pacific Lymphoma Conference use an innovative strategy to formally document and present the perspectives, experiences and preferred treatment approaches of 25 lymphoma-specific investigators. 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 FL with the formulation of up-to-date clinical management strategies.

LEARNING OBJECTIVES

- Explore the self-reported practice patterns employed by lymphoma clinical investigators, and apply this knowledge to the diagnosis and treatment of patients with FL.
- Recognize emerging research data and recent FDA authorizations when designing an optimal therapeutic approach for patients with newly diagnosed FL requiring active therapy.

- Appreciate emerging Phase III data with rituximab/lenalidomide as front-line treatment for patients with FL, and assess investigator perspectives on the current utility of this novel therapeutic approach in the nonresearch management of previously untreated and relapsed/refractory FL.
- Individualize the use of maintenance therapeutic approaches in the care of patients with previously untreated FL who have completed induction chemoimmunotherapy.
- Consider published research data and other clinical factors in the best-practice selection, sequencing or combining of available therapeutic agents in the nonresearch care of patients with relapsed/refractory FL.
- Develop practical strategies to prevent, recognize and/or ameliorate the toxicities associated with therapies routinely used in the management of FL.
- Identify ongoing clinical trials evaluating innovative investigational approaches for FL, and obtain consent from appropriate patients for study participation.

CME/CNE ACCREDITATION AND CREDIT DESIGNATION STATEMENTS

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education through the joint providership of the University of Nebraska Medical Center, Center for Continuing Education (UNMC CCE), University of Nebraska Medical Center College of Nursing Continuing Nursing Education (UNMC CON CNE) and Research To Practice.

PHYSICIANS: The University of Nebraska Medical Center, Center for Continuing Education is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

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NURSES: The University of Nebraska Medical Center College of Nursing Continuing Nursing Education is accredited with distinction as a provider of continuing nursing education by

the American Nurses Credentialing Center's Commission on Accreditation.

This activity is provided for 2.25 contact hours under ANCC criteria.

FOR SUCCESSFUL COMPLETION

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

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MODERATOR — **Dr Love** is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, 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, Bodesix 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, Genomic Health Inc, Gilead Sciences Inc, Guardant Health, 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 Pharmaceuticals Inc, Sandoz Inc, a Novartis Division, 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.

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— Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

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This activity is supported by educational grants from Bayer HealthCare Pharmaceuticals Inc, Celgene Corporation and Genentech.

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

Release date: August 2018

Expiration date: August 2019

Select Publications

Nathan H Fowler, MD

Evens AM et al. **A 3-arm randomized phase II trial with bendamustine/rituximab therapy in untreated high risk (HR) follicular lymphoma (FL): Bortezomib induction or novel IMiD® continuation (BIONIC) study from the ECOG-ACRIN Cancer Research Group.** *Proc ASH 2017*;Abstract 482.

Fowler N et al. **RELEVANCE: Phase III randomized study of lenalidomide plus rituximab (R2) versus chemotherapy plus rituximab, followed by rituximab maintenance, in patients with previously untreated follicular lymphoma.** *Proc ASCO 2018*;Abstract 7500.

Fowler N et al. **Safety and activity of lenalidomide and rituximab in untreated indolent lymphoma: An open-label, phase 2 trial.** *Lancet Oncol 2014*;15(12):1311-8.

Fowler N et al. **High response rates with lenalidomide plus rituximab for untreated, indolent, B cell NHL.** *Proc ICML 2011*;Abstract 137.

Hiddemann W et al. **Immunochemotherapy with obinutuzumab or rituximab for previously untreated follicular lymphoma in the GALLIUM Study: Influence of chemotherapy on efficacy and safety.** *J Clin Oncol 2018*;[Epub ahead of print].

Marcus R et al. **Obinutuzumab for the first-line treatment of follicular lymphoma.** *N Engl J Med 2017*;377(14):1331-44.

Rummel MJ et al. **Four versus two years of rituximab maintenance (R-maintenance) following bendamustine plus rituximab (B-R): Initial results of a prospective, randomized multicenter phase 3 study in first-line follicular lymphoma (the StiL NHL7-2008 MAINTAIN study).** *Proc ASH 2017*;Abstract 483.

Rummel MJ et al. **Bendamustine plus rituximab versus CHOP plus rituximab as first-line treatment for patients with indolent and mantle-cell lymphomas: An open-label, multicentre, randomised, phase 3 non-inferiority trial.** *Lancet 2013*;381(9873):1203-10.

Salles GA et al. **Long term follow-up of the PRIMA study: Half of patients receiving rituximab maintenance remain progression free at 10 years.** *Proc ASH 2017*;Abstract 486.

Andrew D Zelenetz, MD, PhD

Cheson B et al. **Obinutuzumab plus bendamustine followed by obinutuzumab maintenance prolongs overall survival compared with bendamustine alone in patients with rituximab-refractory indolent non-Hodgkin lymphoma: Updated results of the GADOLIN Study.** *Proc ASH 2016*;Abstract 615.

Fischer T et al. **Natural history of hypogammaglobulinemia in patients with follicular lymphoma and the impact of anti-CD20-based therapy.** *Proc ASH 2017*;Abstract 4054.

Kahl BS et al. **Rituximab extended schedule or re-treatment trial for low-tumor burden follicular lymphoma: Eastern Cooperative Oncology Group Protocol E4402.** *J Clin Oncol 2014*;32(28):3096-102.

Marcus R et al. **Obinutuzumab for the first-line treatment of follicular lymphoma.** *N Engl J Med 2017*;377(14):1331-44.

Marcus R et al. **Obinutuzumab-based induction and maintenance prolongs progression-free survival (PFS) in patients with previously untreated follicular lymphoma: Primary results of the randomized phase 3 GALLIUM study.** *Proc ASH 2016*;Abstract 6.

Morschhauser F et al. **Phase III trial of consolidation therapy with yttrium-90-ibritumomab tiuxetan compared with no additional therapy after first remission in advanced follicular lymphoma.** *J Clin Oncol 2008*;26(32):5156-64.

Salles GA et al. **Long term follow-up of the PRIMA study: Half of patients receiving rituximab maintenance remain progression free at 10 years.** *Proc ASH 2017*;Abstract 486.

Vidal L et al. **Rituximab maintenance improves overall survival of patients with follicular lymphoma — Individual patient data meta-analysis.** *Eur J Cancer 2017*;76:216-25.

Stephen M Ansell, MD, PhD

Daivdas 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. **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.

Select Publications

- Gribben JG et al. **Mechanisms of action of lenalidomide in B-cell non-Hodgkin lymphoma.** *J Clin Oncol* 2015;33(25):2803-11.
- Kershaw MH et al. **Gene-engineered T cells for cancer therapy.** *Nat Rev Cancer* 2016;13(8):525-41.
- Leonard JP et al. **Randomized trial of lenalidomide alone versus lenalidomide plus rituximab in patients with recurrent follicular lymphoma: CALGB 50401 (Alliance).** *J Clin Oncol* 2015;33(31):3635-40.
- Magee MS, Snook AE. **Challenges to chimeric antigen receptor (CAR)-T cell therapy for cancer.** *Discov Med* 2014;18(100):265-71.
- Majchrzak A et al. **Inhibition of the PI3K/Akt/mTOR signaling pathway in diffuse large B-cell lymphoma: Current knowledge and clinical significance.** *Molecules* 2014;19(9):14304-15.
- Morschhauser F et al. **Preliminary results of a phase II randomized study (ROMULUS) of polatuzumab vedotin (PoV) or pinatuzumab vedotin (PiV) plus rituximab (RTX) in patients with relapsed/refractory non-Hodgkin lymphoma.** *Proc ASCO* 2014;Abstract 8519.
- Palanca-Wessels MC et al. **Safety and activity of the anti-CD79B antibody-drug conjugate polatuzumab vedotin in relapsed or refractory B-cell non-Hodgkin lymphoma and chronic lymphocytic leukaemia: A phase 1 study.** *Lancet Oncol* 2015;16(6):704-15.
- Roberts AW et al. **Venetoclax in patients with previously treated chronic lymphocytic leukemia.** *Clin Cancer Res* 2017;23(16):4527-33.
- 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.
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- Strout MP. **Sugar-coated signaling in follicular lymphoma.** *Blood* 2015;126(16):1871-2.
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- Laurie H Sehn, MD, MPH**
- Al-Tourah AJ et al. **Population-based analysis of incidence and outcome of transformed non-Hodgkin's lymphoma.** *J Clin Oncol* 2008;26(32):5165-9.
- Bodet-Milin C et al. **Investigation of FDG-PET/CT imaging to guide biopsies in the detection of histological transformation of indolent lymphoma.** *Haematologica* 2008;93(3):471-2.
- Casulo C et al. **Autologous transplantation in follicular lymphoma with early therapy failure: A National LymphoCare Study and Center for International Blood and Marrow Transplant Research analysis.** *Biol Blood Marrow Transplant* 2018;24(6):1163-71.
- Casulo C et al. **Early relapse of follicular lymphoma after rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone defines patients at high risk for death: An analysis from the National LymphoCare Study.** *J Clin Oncol* 2015;33(23):2516-22.
- Cheson B et al. **Obinutuzumab plus bendamustine followed by obinutuzumab maintenance prolongs overall survival compared with bendamustine alone in patients with rituximab-refractory indolent non-Hodgkin lymphoma: Updated results of the GADOLIN study.** *Proc ASH* 2016;Abstract 615.
- Jurinic V et al. **Autologous stem cell transplantation for patients with early progression of follicular lymphoma: A follow-up study of 2 randomized trials from the German Low Grade Lymphoma Study Group.** *Biol Blood Marrow Transplant* 2018;24(6):1172-9.
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- Montoto S, Fitzgibbon J. **Transformation of indolent B-cell lymphomas.** *J Clin Oncol* 2011;29(14):1827-34.
- Noy A et al. **The majority of transformed lymphomas have high standardized uptake values (SUVs) on positron emission tomography (PET) scanning similar to diffuse large B-cell lymphoma (DLBCL).** *Ann Oncol* 2009;20(3):508-12.
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Select Publications

Schöder H et al. **Intensity of ¹⁸fluorodeoxyglucose uptake in positron emission tomography distinguishes between indolent and aggressive non-Hodgkin's lymphoma.** *J Clin Oncol* 2005;23(21):4643-51.

Sehn LH 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.

Villa D et al. **Autologous and allogeneic stem-cell transplantation for transformed follicular lymphoma: A report of the Canadian Blood and Marrow Transplant Group.** *J Clin Oncol* 2013;31(9):1164-71.

Wagner-Johnston ND et al. **Outcomes of transformed follicular lymphoma in the modern era: A report from the National LymphoCare Study (NLCS).** *Blood* 2015;126(7):851-7.