# VISITING PROFESSORS

## Clinical Investigators Provide Their Perspectives on Current Cases and Emerging Research in the Management of Hodgkin and Non-Hodgkin Lymphomas and Multiple Myeloma

## CME Information

### TARGET AUDIENCE

This activity is intended for medical oncologists, hematology-oncology fellows and other allied healthcare professionals involved in the treatment of hematologic cancers.

### OVERVIEW OF ACTIVITY

Hematologic cancers include the lymphomas, the leukemias, multiple myeloma and other related disorders (eg, myelodysplastic syndromes, myeloproliferative diseases) stemming from lymphoid and myeloid progenitor cell lines. Taken together, it is estimated that approximately 162,020 new lymphoid, myeloid and leukemic cancer cases will be identified in the United States in the year 2015 and 56,630 individuals will die from these diseases.

More than 60 drug products with more than 70 distinct FDA-approved indications are currently labeled for use in the management of hematologic cancers. 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 video proceedings from a CME symposium held during the 2015 ASCO Annual Meeting feature discussions with leading researchers with an expertise in hematologic cancers regarding actual patient cases and related clinical research findings. By providing information on the latest research developments and their potential application to routine practice, this activity is designed to not only improve clinicians' knowledge of recent data related to the rapidly evolving hematologic oncology treatment landscape but also to provide them with practical perspectives to help them become better and more effective caregivers.

### LEARNING OBJECTIVES

- Incorporate new therapeutic strategies into the best-practice management of Hodgkin lymphoma.
- Review emerging clinical trial data on the efficacy and safety of brentuximab vedotin for patients with CD30-positive lymphomas, and use this information to prioritize protocol and nonresearch options for these patients.
- Consider available clinical research reports in the formulation of therapeutic recommendations for patients with newly diagnosed and relapsed/refractory follicular lymphoma.
- Customize the selection of systemic therapy for patients with newly diagnosed and progressive mantle-cell lymphoma, recognizing the recent addition of bortezomib, lenalidomide and ibrutinib as FDA-endorsed options.
- Appreciate the recent FDA approvals of novel targeted agents — ibrutinib, idelalisib and obinutuzumab — for the treatment of newly diagnosed and relapsed/refractory chronic lymphocytic leukemia, and discern how these therapies can be appropriately integrated into clinical practice.
- Recognize the role of novel agents in the management of T-cell lymphomas, and ensure appropriate supportive care measures to minimize side effects.
- Compare and contrast the benefits and risks of immunomodulatory agents, proteasome inhibitors or both as systemic treatment for newly diagnosed and relapsed/refractory multiple myeloma (MM).
- Customize the use of consolidation and/or maintenance therapeutic approaches for patients with MM in the post-transplant and nontransplant settings based on patient- and disease-related factors.
- Assess investigator perspectives regarding the need for hydration, the incidence of pulmonary and/or cardiac toxicity and the frequency of other side effects associated with carfilzomib, and safely integrate this agent into the clinical care of patients with MM.
- Assess the ongoing clinical trials evaluating novel investigational approaches for Hodgkin and non-Hodgkin lymphoma and MM, and enroll appropriate patients in clinical trials.

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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 at ResearchToPractice.com/ASCOHem15/CME.

## CONTENT VALIDATION AND DISCLOSURES

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

**Stephen M Ansell, MD, PhD**
Professor of Medicine
Division of Hematology
Mayo Clinic
Rochester, Minnesota

**Contracted Research:** Bristol-Myers Squibb Company, Celldex Therapeutics, Seattle Genetics.

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

No real or apparent conflicts of interest to disclose.

**Craig Moskowitz, MD**
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

**Advisory Committee:** Genentech BioOncology, Seattle Genetics; **Contracted Research:** Genentech BioOncology, GlaxoSmithKline, Merck, Seattle Genetics.

**Antonio Palumbo, MD**
Chief, Myeloma Unit
Division of Hematology
University of Torino
Torino, Italy

**Advisory Committee and Consulting Agreements:** Amgen Inc, Bristol-Myers Squibb Company, Celgene Corporation, Janssen Biotech Inc, Onyx Pharmaceuticals, an Amgen subsidiary, Takeda Oncology.

**Noopur Raje, MD**
Director, Center for Multiple Myeloma
Massachusetts General Hospital Cancer Center
Associate Professor of Medicine
Harvard Medical School
Boston, Massachusetts

**Consulting Agreements:** Amgen Inc, Celgene Corporation, Onyx Pharmaceuticals, an Amgen subsidiary, Takeda Oncology.

**Jeff Sharman, MD**
Director of Research
Willamette Valley Cancer Institute
Medical Director of Hematology Research
The US Oncology Network
Eugene, Oregon

**Advisory Committee:** Celgene Corporation, Gilead Sciences Inc, Pharmacyclics Inc; **Consulting Agreement:** Celgene Corporation; **Contracted Research:** Celgene Corporation, Cephalon Inc, Genentech BioOncology, Gilead Sciences Inc, Novartis Pharmaceuticals Corporation, Pharmacyclics Inc, 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, Amgen Inc, Astellas Scientific and Medical Affairs Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Pharma Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Dendreon Corporation, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech BioOncology, Genomic Health Inc, Gilead Sciences Inc, ImmunoGen Inc, Incyte Corporation, Janssen Biotech Inc, Jazz Pharmaceuticals Inc, Lilly, Medivation Inc, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, NanoString Technologies, Novartis Pharmaceuticals Corporation, Novocure, Onyx Pharmaceuticals, an Amgen subsidiary, Pharmacyclics Inc, Prometheus Laboratories Inc, Regeneron Pharmaceuticals, Sanofi, Seattle Genetics, Sigma-Tau Pharmaceuticals Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Teva Oncology, Tokai Pharmaceuticals Inc and VisionGate Inc.

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This activity is supported by educational grants from Celgene Corporation, Genentech BioOncology, Onyx Pharmaceuticals, an Amgen subsidiary, 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 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:** October 2015

**Expiration date:** October 2016

## Select Publications


### Stephen M Ansell, MD, PhD

Ansell SM, Armitage J. **Non-Hodgkin lymphoma: Diagnosis and treatment.** *Mayo Clin Proc* 2005;80(8):1087-97.

Coutré SE et al. **Management of adverse events associated with idelalisib treatment: Expert panel opinion.** *Leuk Lymphoma* 2015;[Epub ahead of print].

Flinn IW et al. **Idelalisib, a selective inhibitor of phosphatidylinositol 3-kinase-∂, as therapy for previously treated indolent non-Hodgkin lymphoma.** *Blood* 2014;123(22):3406-13.

Gopal AK et al. **PI3K∂ inhibition by idelalisib in patients with relapsed indolent lymphoma.** *N Engl J Med* 2014;370(11):1008-18.

Humala K, Younes A. **Current and emerging new treatment strategies for mantle cell lymphoma.** *Leuk Lymphoma* 2013;54(5):912-21.

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

Le Gouill S et al. **Rituximab maintenance versus wait and watch after four courses of R-DHAP followed by autologous stem cell transplantation in previously untreated young patients with mantle cell lymphoma: First interim analysis of the phase III prospective LYMA trial, a LYSA study.** *Proc ASH* 2014;**Abstract 146**.

Martin P et al. **Outcome of deferred initial therapy in mantle-cell lymphoma.** *J Clin Oncol* 2009;27(8):1209-13.

Maurer MJ et al. **Event-free survival at 12 months (EFS12) from diagnosis is a robust endpoint for disease-related survival in patients with follicular lymphoma in the immunochemotherapy era.** *Proc ASH* 2014;**Abstract 1664**.

Robak T et al. **Bortezomib-based therapy for newly diagnosed mantle-cell lymphoma.** *N Engl J Med* 2015;372(10):944-53.

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.

Till BG et al. **Phase II trial of R-CHOP plus bortezomib induction therapy followed by bortezomib maintenance for previously untreated mantle cell lymphoma: SWOG 0601.** *Proc ASH* 2014;**Abstract 149**.

### Jonathan W Friedberg, MD, MMSc

Czuczman MS et al. **A phase 2/3 multicenter, randomized study comparing the efficacy and safety of lenalidomide versus investigator's choice in relapsed/refractory DLBCL.** *Proc ASH* 2014;**Abstract 628**.

Hernandez-Ilizaliturri FJ et al. **Higher response to lenalidomide in relapsed/refractory diffuse large B-cell lymphoma in nongerminal center B-cell-like than in germinal center B-cell-like phenotype.** *Cancer* 2011;117(22):5058-66.

Jacobsen ED et al. **Brentuximab vedotin demonstrates objective responses in a phase 2 study of relapsed/refractory DLBCL with variable CD30 expression.** *Blood* 2015;125(9):1394-402.

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.

Vitolo U et al. **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.

Witzig TE et al. **An international phase II trial of single-agent lenalidomide for relapsed or refractory aggressive B-cell non-Hodgkin's lymphoma.** *Ann Oncol* 2011;22(7):1622-7.

### Craig Moskowitz, MD

Armand P et al. **Nivolumab in patients with relapsed or refractory Hodgkin lymphoma — Preliminary safety, efficacy and biomarker results of a Phase I study.** *Proc ASCO* 2014;**Abstract 289**.

Chemnitz JM et al. **RNA fingerprints provide direct evidence for the inhibitory role of TGFbeta and PD-1 on CD4+ T cells in Hodgkin lymphoma.** *Blood* 2007;110(9):3226-33.

Chen BJ et al. **PD-L1 expression is characteristic of a subset of aggressive B-cell lymphomas and virus-associated malignancies.** *Clin Cancer Res* 2013;19(13):3462-73.

Chen RW et al. **Results of a Phase II trial of brentuximab vedotin as first line salvage therapy in relapsed/refractory HL prior to AHCT.** *Proc ASCO* 2014;**Abstract 501**.

## Select Publications


Green MR et al. **Constitutive AP-1 activity and EBV infection induce PD-L1 in Hodgkin lymphomas and posttransplant lymphoproliferative disorders: Implications for targeted therapy**. *Clin Cancer Res* 2012;18(6):1611-8.

Green MR et al. **Integrative analysis reveals selective 9p24.1 amplification, increased PD-1 ligand expression, and further induction via JAK2 in nodular sclerosing Hodgkin lymphoma and primary mediastinal large B-cell lymphoma.** *Blood* 2010;116(17):3268-77.

LaCasce A et al. **Brentuximab vedotin in combination with bendamustine for patients with Hodgkin lymphoma who are relapsed or refractory after frontline therapy.** *Proc ASCO* 2014;**Abstract 293**.

Moskowitz AJ et al. **PET-adapted sequential salvage therapy with brentuximab vedotin followed by augmented ifosfamide, carboplatin, and etoposide for patients with relapsed and refractory Hodgkin's lymphoma: A non-randomised, open-label, single-centre, phase 2 study.** *Lancet Oncol* 2015;16(3):284-92.

Moskowitz CH et al. **Brentuximab vedotin as consolidation therapy after autologous stem-cell transplantation in patients with Hodgkin's lymphoma at risk of relapse or progression (AETHERA): A randomised, double-blind, placebo-controlled, phase 3 trial.** *Lancet* 2015;385(9980):1853-62.

Moskowitz C et al. **PD-1 blockade with the monoclonal antibody pembrolizumab (MK-3475) in patients with classical Hodgkin lymphoma after brentuximab vedotin failure: Preliminary results from a Phase 1b study (KEYNOTE-013).** *Proc ASCO* 2014;**Abstract 290**.

Yamamoto R et al. **PD-1-PD-1 ligand interaction contributes to immunosuppressive microenvironment of Hodgkin lymphoma.** *Blood* 2008;111(6):3220-4.


### Antonio Palumbo, MD


Stewart AK et al. **Carfilzomib, lenalidomide, and dexamethasone for relapsed multiple myeloma.** *N Engl J Med* 2015;372(2):142-52.


### Noopur Raje, MD


Attal M et al. **Lenalidomide maintenance after stem-cell transplantation for multiple myeloma: Follow-up analysis of the IFM 2005-02 trial.** *Proc ASH* 2013;**Abstract 406**.

Attal M et al. **Lenalidomide maintenance after stem-cell transplantation for multiple myeloma.** *N Engl J Med* 2012;366(19):1782-91.

Dimopoulos M et al. **Myeloma in the octogenarians: Disease characteristics and clinical outcomes in the era of modern anti-myeloma therapy.** *Proc ASH* 2014;**Abstract 4738**.

Facon T et al. **Initial phase 3 results of the FIRST (Frontline Investigation of Lenalidomide + Dexamethasone versus Standard Thalidomide) trial (MM-020/IFM 07 01) in newly diagnosed multiple myeloma (NDMM) patients (Pts) ineligible for stem cell transplantation (SCT).** *Proc ASH* 2013;**Abstract 2**.

Facon T et al. **Melphalan and prednisone plus thalidomide versus melphalan and prednisone alone or reduced-intensity autologous stem cell transplantation in elderly patients with multiple myeloma (IFM 99-06): A randomised trial.** *Lancet* 2007;370(9594):1209-18.

Gay F et al. **Complete response correlates with long-term progression-free and overall survival in elderly myeloma treated with novel agents: Analysis of 1175 patients.** *Blood* 2011;117(11):3025-31.

Harousseau JL et al. **Achievement of at least very good partial response is a simple and robust prognostic factor in patients with multiple myeloma treated with high-dose therapy: Long-term analysis of the IFM 99-02 and 99-04 trials.** *J Clin Oncol* 2009;27(34):5720-6.

Hulin C et al. **Efficacy of melphalan and prednisone plus thalidomide in patients older than 75 years with newly diagnosed multiple myeloma: IFM 01/01 trial.** *J Clin Oncol* 2009;27(22):3664-70.

Jakubowiak AJ et al. **A phase 1/2 study of carfilzomib in combination with lenalidomide and low-dose dexamethasone as a frontline treatment for multiple myeloma.** *Blood* 2012;120(9):1801-9.

Jasielec J et al. **Predictors of treatment outcome with the combination of carfilzomib, lenalidomide, and low-dose dexamethasone (CRd) in newly diagnosed multiple myeloma (NDMM).** *Proc ASH* 2013;**Abstract 3220**.

Kapoor P et al. **Importance of achieving stringent complete response after autologous stem-cell transplantation in multiple myeloma.** *J Clin Oncol* 2013;31(36):4529-35.

## Select Publications


Korde N et al. **Phase II clinical and correlative study of carfilzomib, lenalidomide, and dexamethasone followed by lenalidomide extended dosing (CRD-R) induces high rates of MRD negativity in newly diagnosed multiple myeloma (MM) patients.** *Proc ASH* 2013;**Abstract 538**.

McCarthy PL et al. **Lenalidomide after stem-cell transplantation for multiple myeloma.** *N Engl J Med* 2012;366(19):1770-81.

O'Donnell E et al. **A phase II study of modified lenalidomide, bortezomib, and dexamethasone (RVD lite) for transplant-ineligible patients with newly diagnosed multiple myeloma.** *Blood* 2014;124(21):3454.

Palumbo A et al. **Geriatric assessment predicts survival and toxicities in elderly myeloma patients: An International Myeloma Working Group report.** *Blood* 2015;125(13):2068-74.

Palumbo A et al. **Second primary malignancies with lenalidomide therapy for newly diagnosed myeloma: A meta-analysis of individual patient data.** *Lancet Oncol* 2014;15(3):333-42.

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Richardson PG et al. **Lenalidomide, bortezomib, and dexamethasone combination therapy in patients with newly diagnosed multiple myeloma.** *Blood* 2010;116(5):679-86.

Singh PP et al. **Lenalidomide maintenance therapy in multiple myeloma: A meta-analysis of randomized trials.** *Proc ASH* 2013;**Abstract 407**.

Sonneveld P et al. **Bortezomib induction and maintenance treatment improves survival in patients with newly diagnosed multiple myeloma: Extended follow-up of the HOVON-65/GMMG-HD4 trial.** *Proc ASH* 2013;**Abstract 404**.


### Jeff Sharman, MD


Freeman CL et al. **Pattern of cytokine release in patients with chronic lymphocytic leukemia treated with obinutuzumab and possible relationship with development of infusion related reactions.** *Proc ASH* 2014;**Abstract 4674**.

Goede V et al. **Obinutuzumab (GA101) plus chlorambucil (Clb) or rituximab (R) plus Clb versus Clb alone in patients with chronic lymphocytic leukemia (CLL) and preexisting medical conditions (comorbidities): Final stage 1 results of the CLL11 (BO21004) phase III trial.** *Proc ASCO* 2013;**Abstract 7004**.

Jones JA et al. **Pattern of use of anticoagulation and/or antiplatelet agents in patients with chronic lymphocytic leukemia (CLL) treated with single-agent ibrutinib therapy.** *Proc ASH* 2014;**Abstract 1990**.

Roberts AW et al. **Determination of recommended phase 2 dose of ABT-199 (GDC-0199) combined with rituximab (R) in patients with relapsed/refractory (R/R) chronic lymphocytic leukemia (CLL).** *Proc ASH* 2014;**Abstract 325**.

Souers AJ et al. **ABT-199, a potent and selective BCL-2 inhibitor, achieves antitumor activity while sparing platelets.** *Nat Med* 2013;19(2):202-8.

Zelenetz AD et al. **Safety and efficacy of obinutuzumab (GA101) plus CHOP chemotherapy in first-line advanced diffuse large B-cell lymphoma: Results from the phase 2 GATHER study (GAO4915g).** *Proc ASH* 2013;**Abstract 1820**.