# MEET THE PROFESSORS

## Clinical Investigator Perspectives on Key Questions and Emerging Research in the Management of Lymphoma, Chronic Lymphocytic Leukemia and Multiple Myeloma

## CME Information

### TARGET AUDIENCE

This program is intended for medical oncologists, hematologists, 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 (MM) and other related disorders stemming from lymphoid and myeloid progenitor cell lines. Taken together, it is estimated that approximately 176,200 new lymphoid, myeloid and leukemic cancer cases will be identified in the United States in the year 2019, and 56,770 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 appropriate clinical management strategies across a vast spectrum of liquid and solid tumors. This is particularly true, however, within the realm of Hodgkin and non-Hodgkin lymphoma (including chronic lymphocytic leukemia [CLL]) and MM, where the past several years have seen a staggering number of important clinical and research advances.

These video proceedings from a CME symposium held during the 2019 ASCO Annual Meeting feature discussions with leading researchers with an expertise in hematologic cancers regarding actual cases from their practices and the published data that drive clinical decision-making for patients in those and diverse other situations. By providing information on the latest research developments and their potential application to routine practice, this activity is designed to assist medical oncologists, hematologists, hematology-oncology fellows and other healthcare providers 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 clinical presentation, biomarker profile and psychosocial status.
- Evaluate existing and emerging clinical research data to formulate therapeutic recommendations for patients with newly diagnosed and R/R diffuse large B-cell lymphoma, follicular lymphoma, mantle cell lymphoma and T-cell lymphoma.
- Incorporate new therapeutic strategies into the best-practice management of newly diagnosed and R/R Hodgkin lymphoma (HL).
- Customize induction, consolidation and maintenance therapeutic approaches for MM in the post-transplant and nontransplant settings, considering patient- and disease-related factors, including cytogenetic profile.
- 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 R/R MM.
- Compare and contrast the mechanisms of action, efficacy and safety of approved and investigational immunotherapeutic approaches (eg, immune checkpoint inhibitors, chimeric antigen receptor-directed T-cell therapy) for the treatment of HL, non-Hodgkin lymphoma (NHL), CLL and MM to determine the current and/or potential utility of each in clinical practice.
- Design and implement a plan of care to recognize and manage side effects and toxicities associated with the use of existing and recently approved systemic therapies in the management of HL, NHL, CLL and MM to support quality of life and continuation of treatment.
- Assess the ongoing clinical trials evaluating other novel investigational approaches for HL, NHL, CLL and MM, and obtain consent from appropriate patients for study participation.

## ACCREDITATION STATEMENT

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Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 2.75 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 specialties: **medical oncology** and **hematology**.

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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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**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

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**Expiration date:** July 2020

# Select Publications

## Module 1: Newly Diagnosed and Relapsed/Refractory Multiple Myeloma


Costa LJ et al. **Phase 2 study of venetoclax plus carfilzomib and dexamethasone in patients with relapsed/refractory multiple myeloma.** ASCO 2018;**Abstract 8004**.

Delforoush M et al. **In vitro and in vivo activity of melflufen (J1) in lymphoma.** *BMC Cancer* 2016;16:263.

Dimopoulos M et al. **Oral ixazomib maintenance following autologous stem cell transplantation (TOURMALINE-MM3): A double-blind, randomised, placebo-controlled phase 3 trial.** *Lancet* 2019;393(10168):253-64.

Dimopoulos MA et al. **Elotuzumab plus pomalidomide and dexamethasone for multiple myeloma.** *N Engl J Med* 2018;379(19):1811-22.

Facon T et al. **Phase 3 randomized study of daratumumab plus lenalidomide and dexamethasone (D-Rd) versus lenalidomide and dexamethasone (Rd) in patients with newly diagnosed multiple myeloma (NDMM) ineligible for transplant (MAIA).** *Proc ASH* 2018;**Abstract LBA-2**.

Flinn IW et al. **DYNAMO: A phase II study of duvelisib (IPI-145) in patients with refractory indolent non-hodgkin lymphoma.** *J Clin Oncol* 2019;37(11):912-22.

Gay F et al. **Efficacy of carfilzomib lenalidomide dexamethasone (KRd) with or without transplantation in newly diagnosed myeloma according to risk status: Results from the FORTE trial.** ASCO 2019;**Abstract 8002**.

Kumar S et al. **Efficacy of venetoclax as targeted therapy for relapsed/refractory t(11;14) multiple myeloma.** *Blood* 2017;130(22):2401-9.

Lonial S et al. **E3A06: Randomized phase III trial of lenalidomide versus observation alone in patients with asymptomatic high-risk smoldering multiple myeloma.** ASCO 2019;**Abstract 8001**.

Lonial S et al. **First clinical (phase 1b/2a) study of iberdomide (CC-220; IBER), a CELMoD, in combination with dexamethasone (DEX) in patients (pts) with relapsed/refractory multiple myeloma (RRMM).** ASCO 2019;**Abstract 8006**.

Mateos M et al. **Efficacy and safety of the randomized, open-label, non-inferiority, phase 3 study of subcutaneous (SC) versus intravenous (IV) daratumumab (DARA) administration in patients (pts) with relapsed or refractory multiple myeloma (RRMM): COLUMBA.** ASCO 2019;**Abstract 8005**.

Miguel J et al. **Updated risk stratification model for smoldering multiple myeloma (SMM) incorporating the revised IMWG diagnostic criteria.** ASCO 2019;**Abstract 8000**.

Mikhael J et al. **A phase Ib study of isatuximab in combination with pomalidomide (Pom) and dexamethasone (Dex) in relapsed/refractory multiple myeloma (RRMM).** ASCO 2017;**Abstract 8007**.

Moreau P et al. **Phase 3 randomized study of daratumumab + bortezomib/thalidomide/dexamethasone (D-VTD) versus VTD in transplant-eligible newly diagnosed multiple myeloma: Part 1 CASSIOPEIA results.** EHA 2019;**Abstract S145**.

Moreau P et al. **Phase 3 randomized study of daratumumab (DARA) + bortezomib/thalidomide/dexamethasone (D-VTd) vs VTd in transplant-eligible (TE) newly diagnosed multiple myeloma (NDMM): CASSIOPEIA part 1 results.** ASCO 2019;**Abstract 8003**.

Moreau P et al. **Promising efficacy and acceptable safety of venetoclax plus bortezomib and dexamethasone in relapsed/refractory MM.** *Blood* 2017;30(132):2392-400.

Munshi NC et al. **Association of minimal residual disease with superior survival outcomes in patients with multiple myeloma: A meta-analysis.** *JAMA Oncol* 2017;3(1):28-35.

Perrot A et al. **Minimal residual disease negativity using deep sequencing is a major prognostic factor in multiple myeloma.** *Blood* 2018;132(23):2456-64.

Raje N et al. **Anti-BCMA CAR T-cell therapy bb2121 in relapsed or refractory multiple myeloma.** *N Engl J Med* 2019;380(18):1726-37.

Richardson P et al. **A phase III randomized, open label, multicenter study comparing isatuximab, pomalidomide, and low-dose dexamethasone versus pomalidomide and low-dose dexamethasone in patients with relapsed/refractory multiple myeloma (RRMM).** ASCO 2019;**Abstract 8004**.

Richardson PG et al. **Pomalidomide, bortezomib, and dexamethasone for patients with relapsed or refractory multiple myeloma previously treated with lenalidomide (OPTIMISMM): A randomised, open-label, phase 3 trial.** *Lancet Oncol* 2019;20(6):781-94.

## Select Publications


Richardson P et al. **OP-106 Horizon — melflufen therapy for RRMM patients refractory to daratumumab and/or pomalidomide; updated results and first report on PFS.** *Proc ASH* 2018;**Abstract 600**.

Richardson P et al. **First report on overall survival (OS) and improved progression free survival (PFS) in a completed phase 2a study of melflufen in advanced relapsed refractory multiple myeloma (RRMM).** *Proc ASH* 2017;**Abstract 3150**.

Shah N et al. **Initial results from a phase 1 clinical study of bb21217, a next-generation anti bcma CAR T therapy.** *Proc ASH* 2018;**Abstract 488**.

Topp M et al. **Evaluation of AMG 420, an anti-BCMA bispecific T-cell engager (BiTE) immunotherapy, in R/R multiple myeloma (MM) patients: Updated results of a first-in-human (FIH) phase I dose escalation study.** ASCO 2019;**Abstract 8007**.

Voorhees PM et al. **Efficacy and updated safety analysis of a safety run-in cohort from Griffin, a phase 2 randomized study of daratumumab (Dara), bortezomib (V), lenalidomide (R), and dexamethasone (D; Dara-Vrd) vs. Vrd in patients (Pts) with newly diagnosed (ND) multiple myeloma (MM) eligible for high-dose therapy (HDT) and autologous stem cell transplantation (ASCT).** *Proc ASH* 2018;**Abstract 151**.


### Module 2: Chronic Lymphocytic Leukemia and Follicular Lymphoma


Barf T et al. **Acalabrutinib (ACP-196): A covalent Bruton tyrosine kinase inhibitor with a differentiated selectivity and in vivo potency profile.** *J Pharmacol Exp Ther* 2017;363(2):240-52.

Byrd JC et al. **Acalabrutinib in treatment-naïve (TN) chronic lymphocytic leukemia (CLL): Updated results from the phase 1/2 ACE-CL-001 study.** *Proc ASH* 2018;**Abstract 692**.

Byrd JC et al. **Acalabrutinib monotherapy in patients with relapsed/refractory (R/R) chronic lymphocytic leukemia: Updated results from the Phase 1/2 ACE-CL-001 study.** *Proc ASH* 2017;**Abstract 498**.

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

Fischer K et al. **Effect of fixed-duration venetoclax plus obinutuzumab (VenG) on progression-free survival (PFS), and rates and duration of minimal residual disease negativity (MRD–) in previously untreated patients (pts) with chronic lymphocytic leukemia (CLL) and comorbidities.** ASCO 2019;**Abstract 7502**.

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

Kater AP et al. **Fixed duration of venetoclax-rituximab in relapsed/refractory chronic lymphocytic leukemia eradicates minimal residual disease and prolongs survival: Post-treatment follow-up of the MURANO phase III study.** *J Clin Oncol* 2019;37(4):269-77.

Leonard JP et al. **AUGMENT: A phase III study of lenalidomide plus rituximab versus placebo plus rituximab in relapsed or refractory indolent lymphoma.** *J Clin Oncol* 2019;37(14):1188-99.

Moreno C et al. **Ibrutinib plus obinutuzumab versus chlorambucil plus obinutuzumab in first-line treatment of chronic lymphocytic leukaemia (iLLUMINATE): A multicentre, randomised, open-label, phase 3 trial.** *Lancet Oncol* 2019;20(1):43-56.

Morschhauser F et al. **Rituximab plus lenalidomide in advanced untreated follicular lymphoma.** *N Engl J Med* 2018;379(10):934-47.

Seymour JF et al. **Venetoclax-rituximab in relapsed or refractory chronic lymphocytic leukemia.** *N Engl J Med* 2018;378(12):1107-20.

Shanafelt TD et al. **A randomized phase III study of ibrutinib (PCI-32765)-based therapy vs standard fludarabine, cyclophosphamide, and rituximab (FCR) chemoimmunotherapy in untreated younger patients with chronic lymphocytic leukemia (CLL): A trial of the ECOG-ACRIN Cancer Research Group (E1912).** *Proc ASH* 2018;**Abstract LBA-4**.

Siddiqi T et al. **TRANSCEND CLL 004: Minimal residual disease (MRD) negative responses after lisocabtagene maraleucel (Liso-Cel; JCAR017), a CD19-directed CAR T cell product, in patients (pts) with relapsed/refractory chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL).** ASCO 2019;**Abstract 7501**.

Townsend W et al. **Obinutuzumab-based immunochemotherapy prolongs progression-free survival and time to next anti-lymphoma treatment in patients with previously untreated follicular lymphoma: Four-year results from the phase III GALLIUM study.** *Proc ASH* 2018;**Abstract 1597**.

## Select Publications


Wierda WG et al. **Phase 2 CAPTIVATE results of ibrutinib (ibr) plus venetoclax (ven) in first-line chronic lymphocytic leukemia (CLL).** ASCO 2018;**Abstract 7502**.

Woyach JA et al. **Acalabrutinib with obinutuzumab (Ob) in treatment-naïve (TN) and relapsed/refractory (R/R) chronic lymphocytic leukemia (CLL): Three-year follow-up.** ASCO 2019;**Abstract 7500**.

Woyach JA et al. **Ibrutinib regimens versus chemoimmunotherapy in older patients with untreated CLL.** *N Engl J Med* 2018;379(26):2517-28.

Zinzani PL et al. **DYNAMO: A phase 2 study demonstrating the clinical activity of duvelisib in patients with double-refractory follicular lymphoma.** *Proc EHA* 2017;**Abstract S777**.


### Module 3: Hodgkin and Other Lymphomas


Abramson JS et al. **Updated safety and long term clinical outcomes in TRANSCEND NHL 001, pivotal trial of lisocabtagene maraleucel (JCAR017) in R/R aggressive NHL.** *Proc ASCO* 2018;**Abstract 7505**.

Armand P et al. **Nivolumab for relapsed/refractory classic Hodgkin lymphoma after failure of autologous hematopoietic cell transplantation: Extended follow-up of the multicohort single-arm phase II CheckMate 205 trial.** *J Clin Oncol* 2018;36(14):1428-39.

Armand P et al. **Pembrolizumab in patients with relapsed or refractory primary mediastinal large B-cell lymphoma (PMBCL): Data from the Keynote-013 and Keynote-170 Studies.** *Proc ASH* 2018;**Abstract 228**.

Borchmann P et al. **An updated analysis of JULIET, a global pivotal phase 2 trial of tisagenlecleucel in adult patients with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL).** *Proc EHA* 2018;**Abstract S799**.

Castellino A et al. **High efficacy of lenalidomide plus R-CHOP (R2CHOP) combination in first line treatment of activated B-cell (ABC) DLBCL defined using gene-expression prophyling: A combined analysis from two phase 2 trials.** *Proc ASH* 2018;**Abstract 2962**.

Chen R et al. **Phase II study of the efficacy and safety of pembrolizumab for relapsed/refractory classic Hodgkin lymphoma.** *J Clin Oncol* 2017;35(19):2125-32.

Connors JM et al. **Brentuximab vedotin with chemotherapy for stage III or IV Hodgkin's lymphoma.** *N Engl J Med* 2018;378(4):331-44.

Eyre T et al. **Efficacy of venetoclax monotherapy in patients with relapsed, refractory mantle cell lymphoma post BTK inhibition therapy.** *Proc EHA* 2018;**Abstract S855**.

Horwitz S et al. **Brentuximab vedotin with chemotherapy for CD30-positive peripheral T-cell lymphoma (ECHELON-2): A global, double-blind, randomised, phase 3 trial.** *Lancet* 2019;393(10168):229-40.

Jain P et al. **Four-year follow-up of a single arm, phase II clinical trial of ibrutinib with rituximab (IR) in patients with relapsed/refractory mantle cell lymphoma (MCL).** *Br J Haematol* 2018;182(3):404-11.

Locke FL et al. **Long-term safety and activity of axicabtagene ciloleucel in refractory large B-cell lymphoma (ZUMA-1): A single-arm, multicentre, phase 1-2 trial.** *Lancet Oncol* 2019;20(1):31-42.

Locke FL et al. **Durability of response in ZUMA-1, the pivotal phase 2 study of axicabtagene ciloleucel (Axi-Cel) in patients (Pts) with refractory large B cell lymphoma.** *Proc ASCO* 2018;**Abstract 3003**.

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.** ASCO 2014;**Abstract 8519**.

Moskowitz CH et al. **Five-year PFS from the AETHERA trial of brentuximab vedotin for Hodgkin lymphoma at high risk of progression or relapse.** *Blood* 2018;132(25):2639-42.

Nastoupil LJ et al. **Axicabtagene ciloleucel (Axi-cel) CD19 chimeric antigen receptor (CAR) T-cell therapy for relapsed/refractory large B-cell lymphoma: Real world experience.** *Proc ASH* 2018;**Abstract 91**.

Ramchandren R et al. **Brentuximab vedotin plus chemotherapy in North American subjects with newly diagnosed stage III or IV Hodgkin lymphoma.** *Clin Cancer Res* 2019;25(6):1718-26.

Ruan J et al. **Five-year follow-up of lenalidomide plus rituximab as initial treatment of mantle cell lymphoma.** *Blood* 2018;132(19):2016-25.

## Select Publications


Rule S et al. **Ibrutinib for the treatment of relapsed/refractory mantle cell lymphoma: Extended 3.5-year follow up from a pooled analysis.** *Haematologica* 2019;104(5):e211-4.

Schuster SJ et al; JULIET Investigators. **Tisagenlecleucel in adult relapsed or refractory diffuse large B-cell lymphoma.** *N Engl J Med* 2019;380(1):45-56.

Sehn LH et al. **Polatuzumab vedotin (Pola) plus bendamustine (B) with rituximab (R) or obinutuzumab (G) in relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL): Updated results of a phase (Ph) Ib/II study.** *Proc ASH* 2018;**Abstract 1683**.

Sehn LH et al. **Randomized phase 2 trial of polatuzumab vedotin (pola) with bendamustine and rituximab (BR) in relapsed/refractory (r/r) FL and DLBCL.** ASCO 2018;**Abstract 7507**.

Tam CS et al. **Ibrutinib plus venetoclax for the treatment of mantle-cell lymphoma.** *N Engl J Med* 2018;378(13):1211-23.

Wang M et al. **Acalabrutinib in relapsed or refractory mantle cell lymphoma (ACE-LY-004): A single-arm, multicentre, phase 2 trial.** *Lancet* 2018;391(10121):659-67.

Wang M et al. **Long-term follow-up of acalabrutinib monotherapy in patients with relapsed/refractory mantle cell lymphoma.** *Proc ASH* 2018;**Abstract 2876**.

Younes A et al. **A global, randomized, placebo-controlled, phase 3 study of ibrutinib plus rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (RCHOP) in patients with previously untreated non-germinal center B-cell-like (GCB) diffuse large B-cell lymphoma (DLBCL).** *Proc ASH* 2018;**Abstract 784**.