Hematologic Oncology Update

Issue 2, 2016 (Video Program)

CME Information

TARGET AUDIENCE

This activity is intended for medical oncologists and other healthcare providers involved in the treatment of hematologic cancers.

OVERVIEW OF ACTIVITY

The term hematologic cancer is applicable to any neoplasm originating in the blood, lymph or marrow, but the unique clinical characteristics and treatment considerations of the many individual diseases culminating from this single body system necessitate the further subdivision of these disorders by common etiologic pathway. As such, hematologic cancers include the lymphomas, the leukemias, multiple myeloma and other related disorders such as myelodysplastic syndrome and myeloproliferative diseases stemming from lymphoid and myeloid progenitor cell lines. Taken together, it is estimated that 171,550 new lymphoid, myeloid and leukemic cancer cases will be identified in the United States in the year 2016 and 58,320 individuals will die from these diseases.

The treatment of hematologic cancer remains a challenge for many healthcare professionals and patients despite recent gains made in the management of this group of diseases. Determining which treatment approach is most appropriate for a given patient requires careful consideration of patient-specific characteristics, physician expertise and available health system resources. By providing information on the latest clinical developments in the context of expert perspectives, this activity assists medical oncologists, hematologists and hematology-oncology fellows with the formulation of evidence-based and current therapeutic strategies, which in turn facilitates optimal patient care.

LEARNING OBJECTIVES

- Consider available clinical research reports on the formulation of therapeutic recommendations for patients with newly diagnosed follicular lymphoma.
- Appreciate the FDA approvals of novel targeted agents — ibrutinib, obinutuzumab and venetoclax — for the treatment of newly diagnosed and relapsed/refractory chronic lymphocytic leukemia, and discern how these therapies can be appropriately integrated into the clinical management of standard- and high-risk disease.
- Recognize the recent FDA approvals of daratumumab, elotuzumab, ixazomib and panobinostat, and effectively identify where and how these agents should be integrated into the clinical management of relapsed or refractory multiple myeloma.
- 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.
- Incorporate new therapeutic strategies into the best-practice management of newly diagnosed and relapsed/refractory Hodgkin lymphoma.
- Assess the benefits of ongoing clinical trials for patients with hematologic cancers, and inform appropriately selected patients about these options for treatment.

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

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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 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

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Select Publications

A Phase I/II study evaluating brentuximab vedotin in combination with nivolumab in patients with relapsed or refractory Hodgkin lymphoma after failure of frontline therapy. NCT02572167

A phase III, randomized, placebo-controlled, double-blind study of oral ixazomib maintenance therapy after initial therapy in patients with newly diagnosed multiple myeloma not treated with stem cell transplantation. NCT02312258

Ansell SM et al. **Nivolumab in patients (pts) with relapsed or refractory classical Hodgkin lymphoma (R/R cHL): Clinical outcomes from extended follow-up of a phase 1 study (CA209-039).** *Proc ASH* 2015;**Abstract 583**.

Ansell SM et al. **PD-1 blockade with nivolumab in relapsed or refractory Hodgkin's lymphoma.** *N Engl J Med* 2015;372(4):311-9.

Armand P et al. **A phase 2 study of a nivolumab (nivo)-containing regimen in patients (pts) with newly diagnosed classical Hodgkin lymphoma (cHL): Study 205 Cohort D.** *Proc ASCO* 2016;**Abstract TPS7573**.

Armand P et al. **PD-1 blockade with pembrolizumab in patients with classical Hodgkin lymphoma after brentuximab vedotin failure: Safety, efficacy, and biomarker assessment.** *Proc ASH* 2015;**Abstract 584**.

Attal M et al. **Autologous transplantation for multiple myeloma in the era of new drugs: A phase III study of the Intergroupe Francophone Du Myelome (IFM/DFCI 2009 trial).** *Proc ASH* 2015;**Abstract 391**.

Avet-Loiseau H et al. **Evaluation of minimal residual disease (MRD) by next generation sequencing (NGS) is highly predictive of progression free survival in the IFM/DFCI 2009 trial.** *Proc ASH* 2015;**Abstract 191**.

Bashey A et al. **CTLA4 blockade with ipilimumab to treat relapse of malignancy after allogeneic hematopoietic cell transplantation.** *Blood* 2009;113:1581-8.

Berenson JR et al. **CHAMPION-1: A phase 1/2 study of once-weekly carfilzomib and dexamethasone for relapsed or refractory multiple myeloma.** *Blood* 2016;127(26):3360-8.

Berenson JR et al. **Weekly carfilzomib with dexamethasone for patients with relapsed or refractory multiple myeloma: Updated results from the phase 1/2 study Champion-1 (NCT01677858).** *Proc ASH* 2015;**Abstract 373**.

Byrd JC et al. **Acalabrutinib (ACP-196) in relapsed chronic lymphocytic leukemia.** *N Engl J Med* 2016;374(4):323-32.

Chen RW et al. **Pembrolizumab for relapsed/refractory classical Hodgkin lymphoma (R/R cHL): Phase 2 KEYNOTE-087 study.** *Proc ASCO* 2016;**Abstract 7555**.

Dartigeas C et al. **Rituximab maintenance after induction with abbreviated FCR in previously untreated elderly (≥ 65 years) CLL patients: Results of the randomized CLL 2007 SA trial from the French FILO Group (NCT00645606).** *Proc ASCO* 2016;**Abstract 7505**.

Davids MS et al. **Ipilimumab for patients with relapse after allogeneic transplantation.** *N Engl J Med* 2016;375(2):143-53.

Dimopoulos MA et al. **Carfilzomib and dexamethasone versus bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma (ENDEAVOR): A randomised, phase 3, open-label, multicentre study.** *Lancet Oncol* 2016;17(1):27-38.

Dimopoulos MA et al. **Daratumumab, lenalidomide, and dexamethasone for multiple myeloma.** *N Engl J Med* 2016;375(14):1319-31.

Durie B et al. **Bortezomib, lenalidomide and dexamethasone vs lenalidomide and dexamethasone in patients (pts) with previously untreated multiple myeloma without an intent for immediate autologous stem cell transplant (ASCT): Results of the randomized phase III trial SWOG S0777.** *Proc ASH* 2015;**Abstract 25**.

ECOG-E1A11: A randomized phase III trial of bortezomib, lenalidomide and dexamethasone (VRd) versus carfilzomib, lenalidomide, dexamethasone (CRd) followed by limited or indefinite lenalidomide maintenance in patients with newly diagnosed symptomatic multiple myeloma. NCT01863550

Eichhorst B et al. **First-line chemoimmunotherapy with bendamustine and rituximab versus fludarabine, cyclophosphamide, and rituximab in patients with advanced chronic lymphocytic leukaemia (CLL10): An international, open-label, randomised, phase 3, non-inferiority trial.** *Lancet Oncol* 2016;17(7):928-42.

Evens AM et al. **Effect of bortezomib on complete remission (CR) rate when added to bendamustine-rituximab (BR) in previously untreated high-risk (HR) follicular lymphoma (FL): A randomized phase II trial of the ECOG-ACRIN Cancer Research Group (E2408).** *Proc ASCO* 2016;**Abstract 7507**.

Flinn IW et al. **Randomized trial of bendamustine-rituximab or R-CHOP/R-CVP in first-line treatment of indolent NHL or MCL: The BRIGHT study.** *Blood* 2014;123(19):2944-52.

Goede V et al. **Obinutuzumab plus chlorambucil in patients with CLL and coexisting conditions.** *N Engl J Med* 2014;370(12):1101-10.

Hunter ZR et al. **Transcriptome sequencing reveals a profile that corresponds to genomic variants in Waldenström macroglobulinemia.** *Blood* 2016;128(6):827-38.

Ibrutinib and rituximab compared with fludarabine phosphate, cyclophosphamide, and rituximab in treating patients with untreated chronic lymphocytic leukemia or small lymphocytic lymphoma. NCT02048813.

Issa JP et al. **Safety and tolerability of guadecitabine (SGI-110) in patients with myelodysplastic syndrome and acute myeloid leukaemia: A multicentre, randomised, dose-escalation phase 1 study.** *Lancet Oncol* 2015;16(9):1099-110.

Jabbour E et al. **Combination of hyper-CVAD with ponatinib as first-line therapy for patients with Philadelphia chromosome-positive acute lymphoblastic leukaemia: A single-centre, phase 2 study.** *Lancet Oncol* 2015;16(15):1547-55.

Kantarjian HP et al. **Overall survival in relapsed/refractory B-cell acute lymphoblastic leukemia patients receiving inotuzumab ozogamicin vs standard care in the Phase 3 INO-VATE study.** *Proc EHA* 2016;**Abstract LB2233**.

Kumar S et al. **International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma.** *Lancet Oncol* 2016;17(8):e328-46.

Leoni V et al. **Tyrosine kinase inhibitors in BCR-ABL positive acute lymphoblastic leukemia.** *Haematologica* 2015;100(3):295-99.

Lesokhin AM et al. **Nivolumab in patients with relapsed or refractory hematologic malignancy: Preliminary results of a phase Ib study.** *J Clin Oncol* 2016;34(23):2698-704.

Lin TL et al. **Phase Ib/2 study of venetoclax with low-dose cytarabine in treatment-naive patients age ≥ 65 with acute myelogenous leukemia.** *Proc ASCO* 2016;**Abstract 7007**.

Lokhorst H et al. **Dose-dependent efficacy of daratumumab (DARA) as monotherapy in patients with relapsed or refractory multiple myeloma (RR MM).** *Proc ASCO* 2014;**Abstract 8513**.

Lokhorst HM et al. **Targeting CD38 with daratumumab monotherapy in multiple myeloma.** *N Engl J Med* 2015;373(13):1207-19.

Lonial S et al. **Daratumumab monotherapy in patients with treatment-refractory multiple myeloma (SIRIUS): An open-label, randomised, phase 2 trial.** *Lancet* 2016;387(10027):1551-60.

Lonial S et al. **Elotuzumab therapy for relapsed or refractory multiple myeloma.** *N Engl J Med* 2015;373(7):621-31.

Moreau P et al. **Oral ixazomib, lenalidomide and dexamethasone for multiple myeloma.** *N Engl J Med* 2016;374(17):1621-34.

Moreau P et al. **Prospective evaluation of MRI and PET-CT at diagnosis and before maintenance therapy in symptomatic patients with multiple myeloma included in the IFM/DFCI 2009 trial.** *Proc ASH* 2015;**Abstract 395**.

Moskowitz AJ et al. **PET-adapted sequential salvage therapy with brentuximab vedotin followed by augmented ifosamide, 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.

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Moskowitz C et al. **Multicohort phase 2 study of pembrolizumab for relapsed/refractory classical Hodgkin lymphoma (R/R cHL): KEYNOTE-087.** *Proc EHA* 2016;**Abstract S794**.

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.

Palumbo A et al. **Daratumumab, bortezomib and dexamethasone for multiple myeloma.** *N Engl J Med* 2016;375(8):754-66.

Palumbo A et al. **Phase III randomized controlled study of daratumumab, bortezomib, and dexamethasone (DVd) versus bortezomib and dexamethasone (Vd) in patients (pts) with relapsed or refractory multiple myeloma (RRMM): CASTOR study.** *Proc ASCO* 2016;**Abstract LBA4**.

Pieri L et al. **JAK2V617F complete molecular remission in polycythemia vera/essential thrombocythemia patients treated with ruxolitinib.** *Blood* 2015;125(21):3352-3.

Rajkumar SV. **Daratumumab in multiple myeloma.** *Lancet* 2016;387(10027):1490-2.

Rajkumar SV. **Myeloma today: Disease definitions and treatment advances.** *Am J Hematol* 2016;91(1):90-100.

Rituximab and bendamustine hydrochloride, rituximab and ibrutinib, or ibrutinib alone in treating older patients with previously untreated chronic lymphocytic leukemia. NCT01886872

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

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Rubenstein JL et al. **Phase I investigation of lenalidomide plus rituximab and outcomes of lenalidomide maintenance in recurrent CNS lymphoma.** *Proc ASCO* 2016;**Abstract 7502**.

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San-Miguel JF et al. **Overall survival of patients with relapsed multiple myeloma treated with panobinostat or placebo plus bortezomib and dexamethasone (the PANORAMA 1 trial): A randomised, placebo-controlled, phase 3 trial.** *Lancet Haematol* 2016;[Epub ahead of print].

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 Oncol* 2016;17(8):1081-93.

Stone RM et al. **The multi-kinase inhibitor midostaurin prolongs survival compared with placebo in combination with daunorubicin cytarabine induction high-dose C consolidation and as maintenance therapy in newly diagnosed acute myeloid leukemia patients age 18-60 with FLT3 mutations: An international prospective randomized P-controlled double-blind trial (CALGB 10603/RATIFY [Alliance])** *Proc ASH* 2015;**Abstract 6**.

Tam CS et al. **Long-term results of first salvage treatment in CLL patients treated initially with FCR (fludarabine, cyclophosphamide, rituximab).** *Blood* 2014;124(20):3059-64.

Topp MS et al. **Blinatumomab improved overall survival in patients with relapsed or refractory Philadelphia negative B-cell precursor acute lymphoblastic leukemia in a randomized, open-label phase 3 study (TOWER).** *Proc EHA* 2016;**Abstract S149**.

Treon SP et al. **Ibrutinib in previously treated Waldenström's macroglobulinemia.** *N Engl J Med* 2015;372(15):1430-40.

Yasenchak CA et al. **Brentuximab vedotin in combination with dacarbazine or bendamustine for frontline treatment of Hodgkin lymphoma in patients aged 60 years and above: Interim results of a multi-cohort phase 2 study.** *Proc ASH* 2015;**Abstract 587**.

Younes A et al. **Checkmate 205: Nivolumab (nivo) in classical Hodgkin lymphoma (cHL) after autologous stem cell transplant (ASCT) and brentuximab vedotin (BV) — A phase 2 study.** *Proc ASCO* 2016;**Abstract 7535**.

Younes A et al. **Nivolumab for classical Hodgkin's lymphoma after failure of both autologous stem-cell transplantation and brentuximab vedotin: A multicentre, multicohort, single-arm phase 2 trial.** *Lancet Oncol* 2016;17(9):1283-94.