

Addressing Current Questions and Controversies in the Management of Lymphomas 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 lymphomas 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 58,100 individuals will die from these diseases. Importantly, more than 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/hematologists 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 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).
- 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) and CLL 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 current and recently approved systemic therapies in the management of HL, NHL and CLL to support quality of life and continuation of treatment.
- Assess the ongoing clinical trials evaluating other novel investigational approaches for HL, NHL and CLL, and obtain consent from appropriate patients for study participation.

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No relevant conflicts of interest to disclose.

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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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Select Publications

Brad S Kahl, MD

- Barr P et al. **Updated efficacy and safety from the phase 3 Resonate-2 study: Ibrutinib as first-line treatment option in patients 65 years and older with chronic lymphocytic leukemia/small lymphocytic leukemia.** *Proc ASH 2016*;Abstract 234.
- Brander DM et al. **Durability of responses on continuous therapy and following drug cessation in deep responders with venetoclax and rituximab.** *Proc ASH 2018*;Abstract 183.
- 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 chronic lymphocytic leukemia: Updated results from the phase 1/2 ACE-CL-001 study.** *Proc ASH 2017*;Abstract 498.
- Byrd JC et al. **Three-year follow-up of treatment-naïve and previously treated patients with CLL and SLL receiving single-agent ibrutinib.** *Blood 2015*;125(16):2497-506.
- Furman R et al. **Ibrutinib resistance in chronic lymphocytic leukemia.** *N Engl J Med 2014*;370(24):2352-4.
- Moreno C et al. **Ibrutinib + obinutuzumab versus chlorambucil + obinutuzumab as first-line treatment in patients with chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL): Results from phase 3 iLLUMINATE.** *Proc ASH 2018*;Abstract 691.
- Rogers KA et al. **Phase 2 study of combination obinutuzumab, ibrutinib, and venetoclax in treatment-naïve and relapsed/refractory chronic lymphocytic leukemia.** *Proc ASH 2018*;Abstract 693.
- Seymour JF et al. **MURANO trial establishes feasibility of time-limited venetoclax-rituximab (VenR) combination therapy in relapsed/refractory (R/R) chronic lymphocytic leukemia (CLL).** *Proc ASH 2018*;Abstract 184.
- Seymour JF et al. **Venetoclax-rituximab in relapsed or refractory chronic lymphocytic leukemia.** *N Engl J Med 2018*;378(12):1107-20.
- Shanafelt T 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.
- Shanafelt T. **Treatment of older patients with chronic lymphocytic leukemia: Key questions and current answers.** *ASH Education Book 2013*;2013:158-67.
- Stilgenbauer S et al. **Venetoclax in relapsed or refractory chronic lymphocytic leukaemia with 17p deletion: A multicentre, open-label, phase 2 study.** *Lancet Oncol 2016*;17(6):768-78.
- Wierda WG et al. **Phase 2 CAPTIVATE results of ibrutinib (ibr) plus venetoclax (ven) in first-line chronic lymphocytic leukemia (CLL).** *Proc ASCO 2018*;Abstract 7502.
- Woyach JA et al. **Ibrutinib alone or in combination with rituximab produces superior progression free survival (PFS) compared with bendamustine plus rituximab in untreated older patients with chronic lymphocytic leukemia (CLL): Results of Alliance North American Intergroup study A041202.** *Proc ASH 2018*;Abstract 6.

Jonathan W Friedberg, MD, MMSc

- Borchmann P et al. **PET-guided treatment in patients with advanced-stage Hodgkin's lymphoma (HD18): Final results of an open-label, international, randomised phase 3 trial by the German Hodgkin Study Group.** *Lancet 2017*;390(10114):2790-802.
- 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.
- Johnson P et al. **Adapted treatment guided by interim PET-CT scan in advanced Hodgkin's lymphoma.** *New Engl J Med 2016*;374(25):2419-29.
- Press OW et al. **US Intergroup trial of response-adapted therapy for stage III to IV Hodgkin lymphoma using early interim fluorodeoxyglucose-positron emission tomography imaging: Southwest Oncology Group S0816.** *J Clin Oncol 2016*;34(17):2020-7.
- Radford J et al. **Frontline brentuximab vedotin plus chemotherapy exhibits superior modified progression-free survival vs chemotherapy alone in patients with stage III or IV Hodgkin lymphoma.** *Proc ISHL 2018*;Abstract P072.
- Ramchandren R et al. **Brentuximab vedotin (BV) plus chemotherapy in patients with newly diagnosed advanced stage Hodgkin lymphoma (HL): North American results.** *Proc ASCO 2018*;Abstract 7541.

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Stephens DM et al. **Long-term follow-up of SWOG S0816: Response-adapted therapy for stage III/IV Hodgkin lymphoma demonstrates limitations of PET-adapted approach.** *Proc ASH* 2018;Abstract 929.

Martin Dreyling, MD, PhD

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.

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. **Updated safety and efficacy from the copanlisib CHRONOS-1 trial in patients with relapsed or refractory indolent B-cell lymphoma: Low incidence of late-onset severe toxicities.** *Proc ASH* 2017;Abstract 2777.

Dreyling M et al. **Newly diagnosed and relapsed follicular lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up.** *Ann Oncol* 2016;27(Supp 5):v83-v90.

Fowler NH 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.

Gribben JG et al. **Mechanisms of action of lenalidomide in B-cell non-Hodgkin lymphoma.** *J Clin Oncol* 2015;33(25):2803-11.

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;36(23):2395-404.

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

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

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.

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Zinzani PL et al. **Idelalisib efficacy and safety in follicular lymphoma patients from a phase 2 study.** *Proc EHA* 2017;Abstract P689.

Michael E Williams, MD, ScM

Dauids MS et al. **Revised dose ramp-up to mitigate the risk of tumor lysis syndrome when initiating venetoclax in patients with mantle cell lymphoma.** *J Clin Oncol* 2018;[Epub ahead of print].

Dauids M 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.

Herman SEM et al. **The Bruton tyrosine kinase (BTK) inhibitor acalabrutinib demonstrates potent on-target effects and efficacy in two mouse models of chronic lymphocytic leukemia.** *Clin Cancer Res* 2017;23(11):2831-41.

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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.

Sonali M Smith, MD

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.

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Aukema SM et al. **Double-hit B-cell lymphomas.** *Blood* 2011;117(8):2319-31.

Select Publications

- Carreau NA et al. **Checkpoint blockade therapy may sensitize aggressive and indolent non-Hodgkin lymphoma to subsequent therapy.** *Proc ASH* 2018;Abstract 93.
- Castellino A et al. **Lenalidomide plus R-CHOP21 in newly diagnosed diffuse large B-cell lymphoma (DLBCL): Long-term follow-up results from a combined analysis from two phase 2 trials.** *Blood Cancer J* 2018;8(11):108.
- Chamuleau MED et al. **Successful Treatment of MYC rearrangement positive large B cell lymphoma patients with R-CHOP21 plus lenalidomide: Results of a multicenter phase II HOVON trial.** *Proc ASH* 2018;Abstract 786.
- Chen YB et al. **PD-1 blockade for diffuse large B-cell lymphoma after autologous stem cell transplantation.** *Proc ASH* 2018;Abstract 706.
- Chow VA et al. **Outcomes of patients with large B-cell lymphomas and progressive disease following CD19-specific CAR T-cell therapy.** *Proc ASH* 2018;Abstract 94.
- 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.
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- Jacobson CA et al. **Axicabtagene ciloleucel in the real world: Outcomes and predictors of response, resistance and toxicity.** *Proc ASH* 2018;Abstract 92.
- Johnson NA et al. **Concurrent expression of MYC and BCL2 in diffuse large B-cell lymphoma treated with rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone.** *J Clin Oncol* 2012;30(28):3452-9.
- Kline J et al. **PD-L1 gene alterations identify a unique subset of diffuse large B cell lymphoma that harbors a T cell inflamed phenotype.** *Proc ASH* 2018;Abstract 673.
- 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.
- Locke FL et al. **Outcomes by prior lines of therapy (LoT) 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 3039.
- Morschhauser F et al. **Venetoclax plus rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone (R-CHOP) improves outcomes in BCL2-positive first-line diffuse large B-cell lymphoma (DLBCL): First safety, efficacy and biomarker analyses from the phase II CAVALLI study.** *Proc ASH* 2018;Abstract 782.
- 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.
- 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.
- 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.
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- Strout M. **Sugar-coated signaling in follicular lymphoma.** *Blood* 2015;126(16):1871-2.
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