TARGET AUDIENCE
This activity is intended for medical oncologists, hematologists and other healthcare providers involved in the treatment of chronic lymphocytic leukemia (CLL).

OVERVIEW OF ACTIVITY
CLL is a lymphoid neoplasm in the family of the non-Hodgkin lymphomas. In the United States, an estimated 14,620 new cases of CLL will be diagnosed in 2015, with 4,650 deaths attributed to the disease. The clinical course and outcomes of patients vary widely, largely based on the presence of individual predictive and other risk factors. In recent years, the identification of cytogenetic abnormalities and their subsequent incorporation into traditional clinical staging systems has further refined clinicians’ ability to determine patient prognosis. Of significance, although risk stratification plays an important role in treatment decision-making, the disease remains incurable. Despite the availability of numerous effective agents and regimens, the inevitable mortality associated with CLL has led many to seek new and better management approaches. To this end, and based on an improved understanding of the biology of CLL, in recent years a number of novel agents and strategies have been investigated in the disease, and a number of these efforts have proven successful and have yielded therapeutic options that are already available for use in the clinic.

This is a watershed moment in the management of CLL, but with the many exciting advances that are rapidly occurring, a number of vexing questions and clinical challenges are simultaneously emerging as well. To bridge the gap between research and patient care, this video presentation by Dr John P Leonard uses a review of recent relevant publications and presentations, ongoing clinical trials and clinical investigator treatment preferences to assist medical oncologists, hematologists and other healthcare providers involved in the treatment of CLL with the formulation of up-to-date clinical management strategies.

LEARNING OBJECTIVES
• Appraise recent data on therapeutic advances and changing practice standards in CLL, and integrate this information, as appropriate, into current clinical care.
• Develop an algorithm for the evaluation and treatment of newly diagnosed and relapsed/refractory CLL, taking into consideration the availability of novel agents and innovative research protocols.
• Appreciate the recent FDA approval of obinutuzumab, and develop strategies to appropriately incorporate this agent into the management of CLL.
• Communicate the efficacy and safety of ibrutinib in patients with CLL, and consider its potential integration into nonprotocol management.
• Describe recently presented Phase III data illustrating the efficacy and safety of idelalisib in patients with CLL.
• Consider the biologic rationale for targeting Bcl-2 in CLL, and recognize the similarities and differences between ABT-199 and first-generation Bcl-2 inhibitors.
• Identify ongoing clinical trials evaluating innovative investigational approaches for CLL, and obtain consent from appropriate patients for study participation.

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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:

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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

Last review date: November 2015
Expiration date: November 2016
A multicenter, open-label, single-arm, phase IIIb, international study evaluating the safety of obinutuzumab alone or in combination with chemotherapy in patients with previously untreated or relapsed/refractory chronic lymphocytic leukemia. NCT01905943

A study of GDC-0199 (ABT-199) plus MabThera/Rituxan (rituximab) compared with bendamustine plus MabThera/Rituxan (rituximab) in patients with relapsed or refractory chronic lymphocytic leukemia. NCT02005471


Bosch F et al. Preliminary safety results from the phase IIIb GREEN study of obinutuzumab (GA101) alone or in combination with chemotherapy for previously untreated or relapsed/refractory chronic lymphocytic leukemia (CLL). Proc ASH 2014;Abstract 3345.

Brown JR et al. Safety and efficacy of obinutuzumab (GA101) with fludarabine/cyclophosphamide (G-FC) or bendamustine (G-B) in the initial therapy of patients with chronic lymphocytic leukemia (CLL): Results from the Phase 1b Galton trial (GA04779g). Proc ASH 2013;Abstract 523.


Efficacy and safety of idelalisib in combination with bendamustine and rituximab in subjects with previously untreated chronic lymphocytic leukemia. NCT01980888

Eichhorst B et al. Frontline chemoimmunotherapy with fludarabine (F), cyclophosphamide (C), and rituximab (R) (FCR) shows superior efficacy in comparison to bendamustine (B) and rituximab (BR) in previously untreated and physically fit patients (pts) with advanced chronic lymphocytic leukemia (CLL): Final analysis of an international, randomized study of the German CLL Study Group (GCLLSG) (CLL10 study). Proc ASH 2014;Abstract 19.


Porter DL et al. Chimeric antigen receptor modified T cells directed against CD19 (CTL019 cells) have long-term persistence and induce durable responses in relapsed, refractory CLL. Proc ASH 2013;Abstract 4162.

Porter DL et al. Randomized, phase II dose optimization study of chimeric antigen receptor modified T cells directed against CD19 (CTL019) in patients with relapsed, refractory CLL. Proc ASH 2013;Abstract 873.
Select Publications

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

Seymour JF et al. ABT-199 (GDC-0199) in relapsed/refractory (R/R) chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL): High complete-response rate and durable disease control. Proc ASCO 2014;Abstract 7015.
