Molecular Tumor Board

Biomarker Assessment and Clinical Practice Implications for Patients with Chronic Lymphocytic Leukemia Treated in a Large Regional Oncology Provider

CME Information

TARGET AUDIENCE

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

OVERVIEW OF ACTIVITY

The clinical course of CLL and outcomes for patients with the disease vary widely, largely based on the presence of individual predictive and other risk factors. This heterogeneity has created a need to identify molecular markers that can be used for prognostication and to guide therapeutic decision-making. Current information on how community-based oncologists approach biomarker testing and how they act on the results is limited. This unique CME activity endeavors to develop a more accurate portrait of how practicing clinicians approach biomarker assessment for patients with CLL. This program features expert perspectives on the state of the art of biomarker analysis in CLL and implications for treatment. Upon completion of this CME activity, medical oncologists should be able to formulate an up-to-date and more complete approach to the care of patients with CLL.

LEARNING OBJECTIVES

- Recall the incidence, prognostic significance and clinical implications of biomarkers and genetic alterations that may be associated with a diagnosis of CLL, and use this information to develop evidence-based testing algorithms in general oncology practice.
- Consider current and emerging clinical research data in the formulation of therapeutic recommendations for patients with newly diagnosed and relapsed/refractory CLL.
- Recall published data and the perspectives of clinical investigators on the management of del(17p) CLL, and use this information to guide first- and later-line treatment decision-making.
- Appraise the frequency with which biomarker transformation has been observed in patients with R/R CLL, and consider this information as part of therapeutic decision-making for these individuals.
- Appreciate the recent FDA approval of several novel therapies for newly diagnosed and relapsed/refractory CLL, and discern how these agents can be appropriately integrated into routine clinical practice.

ACCREDITATION STATEMENT

Research To Practice is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

CREDIT DESIGNATION STATEMENT

Research To Practice designates this enduring material for a maximum of 1.25 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

AMERICAN BOARD OF INTERNAL MEDICINE (ABIM) — MAINTENANCE OF CERTIFICATION (MOC)

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 1.25 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 specialty: **medical oncology**.

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HOW TO USE THIS CME ACTIVITY

This CME activity consists of a video component. To receive credit, the participant should review the CME information, watch the video, complete the Post-test with a score of 80% or better and fill out the Educational Assessment and Credit Form located at **ResearchToPractice.com/MolecularTumorBoardCLL18/CME**.

CONTENT VALIDATION AND DISCLOSURES

Research To Practice (RTP) is committed to providing its participants with high-quality, unbiased and state-of-the-art education. We assess conflicts of interest with faculty, planners and managers of CME activities. Conflicts of interest are identified and resolved through a conflict of interest resolution process. In addition, all activity content is reviewed by both a member of the RTP scientific staff and an external, independent physician reviewer for fair balance, scientific objectivity of studies referenced and patient care recommendations.

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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Advisory Committee: Bristol-Myers Squibb Company, Forty Seven Inc; **Consulting Agreement:** Seattle Genetics.

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Consulting Agreement: Sanofi Genzyme; **Contracted Research:** Genentech, Gilead Sciences Inc, GlaxoSmithKline, Pharmacyclics LLC, an AbbVie Company.

MODERATOR — **Dr Love** is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, Adaptive Biotechnologies, Agendia Inc, Agios Pharmaceuticals Inc, Amgen Inc, Ariad Pharmaceuticals Inc, Array BioPharma Inc, Astellas Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Baxalta Inc, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Pharma Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, CTI BioPharma Corp, Dendreon Pharmaceuticals Inc, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech, Genomic Health Inc, Gilead Sciences Inc, Guardant Health, Halozyme Inc, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Kite Pharma Inc, Lexicon Pharmaceuticals Inc, Lilly, Medivation Inc, a Pfizer Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, NanoString Technologies, Natera Inc, Novartis, Novocure, Onyx Pharmaceuticals, an Amgen subsidiary, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sandoz Inc, a Novartis Division, Sanofi Genzyme, Seattle Genetics, Sigma-Tau Pharmaceuticals Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro Inc, Teva Oncology and Tokai Pharmaceuticals Inc.

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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

Anderson MA et al. **Clinicopathological features and outcomes of progression of CLL on the BCL2 inhibitor venetoclax.** *Blood* 2017;129(25):3362-70.

Bulian P et al. **CD49d is the strongest flow cytometry-based predictor of overall survival in chronic lymphocytic leukemia.** *J Clin Oncol* 2014;32(9):897-904.

Damle RN et al. **Ig V gene mutation status and CD38 expression as novel prognostic indicators in chronic lymphocytic leukemia.** *Blood* 1999;94(6):1840-7.

Dohner H et al. **Genomic aberrations and survival in chronic lymphocytic leukemia.** *N Engl J Med* 2000;343(26):1910-6.

Hamblin TJ et al. **Unmutated Ig V(H) genes are associated with a more aggressive form of chronic lymphocytic leukemia.** *Blood* 1999;94(6):1848-54.

Kipps TJ et al. **Chronic lymphocytic leukaemia.** *Nat Rev Dis Primers* 2017;3:17008.

Kovacs G et al. **Minimal residual disease assessment improves prediction of outcome in patients with chronic lymphocytic leukemia (CLL) who achieve partial response: Comprehensive analysis of two phase III studies of the German CLL Study Group.** *J Clin Oncoi* 2016;34(31):3758-65.

International CLL-IPI Working Group. **An international prognostic index for patients with chronic lymphocytic leukaemia (CLL-IPI): A meta-analysis of individual patient data.** *Lancet Oncol* 2016;17(6):779-90.

Landau DA et al. **Mutations driving CLL and their evolution in progression and relapse.** *Nature* 2015;526(7574):525-30.

Maddocks KJ et al. **Etiology of ibrutinib therapy discontinuation and outcomes in patients with chronic lymphocytic leukemia.** *JAMA Oncol* 2015;1(1):80-7.

O'Brien SM et al. **Five-year experience with single-agent ibrutinib in patients with previously untreated and relapsed/refractory chronic lymphocytic leukemia/small lymphocytic leukemia.** *Proc ASH* 2016;**Abstract 233**.

Parikh SA, Shanafelt TD. **Prognostic factors and risk stratification in chronic lymphocytic leukemia.** *Semin Oncol* 2016;43(2):233-40.

Rawstron AC et al. **A complementary role of multiparameter flow cytometry and high-throughput sequencing for minimal residual disease detection in chronic lymphocytic leukemia: An European Research Initiative on CLL study.** *Leukemia* 2016;30(4):929-36.

Sutton LA, Rosenquist R. **Deciphering the molecular landscape in chronic lymphocytic leukemia: Time frame of disease evolution.** *Haematologica* 2015;100(1):7-16.

Thompson PA et al. **β2-microglobulin normalization within 6 months of ibrutinib-based treatment is associated with superior progression-free survival in patients with chronic lymphocytic leukemia.** *Cancer* 2016;122(4):565-73.

Thompson PA et al. **Fludarabine, cyclophosphamide, and rituximab treatment achieves long-term disease-free survival in IGHV-mutated chronic lymphocytic leukemia.** *Blood* 2016;127(3):303-9.

Thompson PA, Wierda WG. **Eliminating minimal residual disease as a therapeutic end point: Working toward cure for patients with CLL.** *Blood* 2016;127(3):279-86.

Thompson PA et al. **Complex karyotype is a stronger predictor than del(17p) for an inferior outcome in relapsed or refractory chronic lymphocytic leukemia patients treated with ibrutinib-based regimens.** *Cancer* 2015;121(20):3612-21.

Wierda W et al. **Venetoclax in relapsed/refractory chronic lymphocytic leukemia (CLL) with 17p deletion: Outcomes and minimal residual disease (MRD) from the full population of the pivotal M13-982 trial.** *Proc SOHO* 2017;**Abstract CLL-102**.

Wierda WG et al. **Multivariable model for time to first treatment in patients with chronic lymphocytic leukemia.** *J Clin Oncol* 2011;29(31):4088-95.

Woyach JA et al. **BTKC481S-mediated resistance to ibrutinib in chronic lymphocytic leukemia.** *J Clin Oncol* 2017;35(13):1437-43.

Woyach JA et al. **The development and expansion of resistant subclones precedes relapse during ibrutinib therapy in patients with CLL.** *Proc ASH* 2016;**Abstract 55**.

Yeh P et al. **Circulating tumour DNA reflects treatment response and clonal evolution in chronic lymphocytic leukaemia.** *Nat Commun* 2017;8:14756.