

NCCN Continuing Education

Target Audience: This journal article is designed to meet the educational needs of oncologists, nurses, pharmacists, and other healthcare professionals who manage patients with cancer.

Accreditation Statements



In support of improving patient care, National Comprehensive Cancer Network (NCCN) is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

Physicians: NCCN designates this journal-based CME activity for a maximum of 1.0 AMA PRA Category 1 Credit™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Nurses: NCCN designates this educational activity for a maximum of 1.0 contact hour.

Pharmacists: NCCN designates this knowledge-based continuing education activity for 1.0 contact hour (0.1 CEUs) of continuing education credit. UAN: JA4008196-0000-26-003-H01-P

PA: NCCN has been authorized by the American Academy of PAs (AAPA) to award AAPA Category 1 CME credit for activities planned in accordance with AAPA CME Criteria. This activity is designated for 1.0 AAPA Category 1 CME credit. Approval is valid

until March 10, 2027. PAs should only claim credit commensurate with the extent of their participation.

All clinicians completing this activity will be issued a certificate of participation. To participate in this journal CE activity: (1) review the educational content; (2) take the posttest with a 66% minimum passing score and complete the evaluation at <https://education.nccn.org/Mar2026>; and (3) view/print certificate.

Pharmacists: You must complete the posttest and evaluation within 30 days of the activity. Continuing pharmacy education credit is reported to the CPE Monitor once you have completed the posttest and evaluation and claimed your credits. Before completing these requirements, be sure your NCCN profile has been updated with your NAPB e-profile ID and date of birth. Your credit cannot be reported without this information. If you have any questions, please email education@nccn.org.

Release date: March 10, 2026; Expiration date: March 10, 2027

Learning Objectives:

Upon completion of this activity, participants will be able to:

- Integrate into professional practice the updates to the NCCN Guidelines for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
- Describe the rationale behind the decision-making process for developing the NCCN Guidelines for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

Disclosure of Relevant Financial Relationships

None of the planners for this educational activity have relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

Individuals Who Provided Content Development and/or Authorship Assistance:

The faculty listed below have no relevant financial relationship(s) with ineligible companies to disclose.

Mary Dwyer, MS, Senior Director, Guidelines Operations, NCCN

Hema Sundar, PhD, Senior Manager, Global Clinical Content, NCCN

The faculty listed below have the following relevant financial relationship(s) with ineligible companies to disclose. All of the relevant financial relationships listed for these individuals have been mitigated.

William G. Wierda, MD, PhD, Panel Chair, has disclosed receiving grant/research support from AbbVie, Inc., AstraZeneca Pharmaceuticals LP, Cyclacel Pharmaceuticals, Inc. (now Bio Green Med Solution, Inc.), Eli Lilly and Company, Genentech, Inc., Gilead Sciences, Inc., GSK plc, Janssen Pharmaceutica Products, LP, Juno Therapeutics, Inc., Kite Pharma, miRagen Therapeutics, Inc., Oncernal Therapeutics, Pharmacyclics LLC, Sunesis Pharmaceuticals, Inc., and Xencor, Inc.

Jennifer Brown, MD, PhD, Panel Vice Chair, has disclosed receiving grant/research support from BeiGene, Ltd., Gilead Sciences, Inc., iOnctura, Lilly, Nagoon Therapeutics, Inc., and Nurix Therapeutics, Inc.; and receiving consulting fees from AbbVie, Inc., Acerta Pharma, Alloplex Biotherapeutics, BeiGene, Ltd., Bristol Myers Squibb, EcoR1 Capital, Lilly, Galapagos NV, Genentech, Inc., Grifols, InnoCare Pharma Limited, Magnet Biomedicine, Merck & Co., Inc., Nurix Therapeutics, Inc., and Pharmacyclics LLC.

Larry Cripe, MD, Panel Member, has disclosed receiving grant/research support from AstraZeneca Pharmaceuticals LP.

Peter Riedell, MD, Panel Member, has disclosed receiving grant/research support from AbbVie, Inc., Bristol Myers Squibb, Genentech, Inc., Gilead Sciences, Inc., and Novartis Pharmaceuticals Corporation; receiving consulting fees from AbbVie, Inc., Bristol Myers Squibb, Genentech, Inc., Gilead Sciences, Inc., and Pfizer Inc.; and receiving honoraria from AbbVie, Inc., Bristol Myers Squibb, Genentech, Inc., Johnson & Johnson, Miltenyi Biotec, and Novartis Pharmaceuticals Corporation.

Meghan Thompson, MD, Panel Member, has disclosed receiving grant/research support from AbbVie, Inc., Adaptive Biotechnologies, AstraZeneca Pharmaceuticals LP, BeiGene, Ltd., Genentech, Inc., Genmab A/S, and Nurix Therapeutics, Inc.; receiving consulting fees from AbbVie, Inc., AstraZeneca Pharmaceuticals LP, BeiGene, Ltd., Lilly, Genentech, Inc., and Janssen Pharmaceutica Products, LP; receiving honoraria from DAVA Oncology; and serving as a scientific advisor for BeiGene, Ltd. and Lilly.

To view disclosures of external relationships for the NCCN Guidelines Panel, go to [NCCN.org/guidelines/guidelines-panels-and-disclosure/disclosure-panels](https://www.nccn.org/guidelines/guidelines-panels-and-disclosure/disclosure-panels)

This activity is supported by educational grants from AstraZeneca, Johnson & Johnson, Lantheus, Lilly, Novartis, and Recordati Rare Diseases Inc. This activity is supported by an independent medical education grant from GSK. This activity is supported by a medical education grant from Exelixis, Inc.

Chronic Lymphocytic Leukemia/ Small Lymphocytic Lymphoma, Version 2.2026

Featured Updates to the NCCN Guidelines

William G. Wierda, MD, PhD^{1,*}; Jennifer Brown, MD, PhD^{2,*}; Jeremy S. Abramson, MD, MMSc³; Farrukh Awan, MD⁴; Greg Bociek, MD, MSc⁵; Daniel Boyer, MD, PhD⁶; Matthew Cortese, MD, MPH⁷; Larry Cripe, MD^{8,*}; Christopher D'Angelo, MD⁵; Elijah Darnell, MD⁹; Randall S. Davis, MD¹⁰; Herbert Eradat, MD, MS¹¹; Naseem Esteghamat, MD, MS¹²; Lindsey Fitzgerald, MD¹³; Christopher D. Fletcher, MD¹⁴; Sameh Gaballa, MD¹⁵; Scott Huntington, MD, MPH, MSc¹⁶; Brad Kahl, MD¹⁷; Manali Kamdar, MD¹⁸; Thomas J. Kipps, MD, PhD¹⁹; Shuo Ma, MD, PhD²⁰; Claudio A. Mosse, MD, PhD²¹; Shazia Nakhoda, MD²²; Sameer A. Parikh, MBBS²³; Peter Riedell, MD^{9,*}; Andrew Schorr, MS²⁴; Stephen Schuster, MD²⁵; Madhav Seshadri, MD²⁶; Tait Shanafelt, MD²⁷; Tanya Siddiqi, MD²⁸; Andrea Sitlinger, MD²⁹; Meghan Thompson, MD^{30,*}; Chaitra Ujjani, MD³¹; Nina Wagner-Johnston, MD³²; Jennifer A. Woyach, MD³³; Mary Dwyer, MS^{34,*}; and Hema Sundar, PhD^{34,*}

Abstract

Bruton tyrosine kinase inhibitors (BTKis) and BCL2 inhibitor (BCL2i)-containing regimens significantly improve survival outcomes in patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL). Results from randomized clinical trials have demonstrated that time-limited treatment with BCL2i-containing regimens resulted in higher rates of undetectable measurable residual disease (uMRD) than BTKi monotherapy or chemoimmunotherapy (CIT). Pirtobrutinib (a noncovalent BTKi) and lisocabtagene maraleucl (CD19-directed CAR T-cell therapy) are newer options for relapsed or refractory disease after prior therapy with BTKi and BCL2i-containing regimens. Histologic transformation of CLL/SLL to diffuse large B-cell lymphoma (Richter transformation) is associated with a poor prognosis. Molecular analysis to determine whether there is clonal relationship between CLL/SLL and transformed diffuse large B-cell lymphoma is useful to select an appropriate treatment option. These NCCN Guideline Insights highlight significant updates to the NCCN Guidelines for the treatment of CLL/SLL and Richter transformation.

J Natl Compr Canc Netw 2026;24(3):68–80
doi:10.6004/jnccn.2026.0012

First-Line Therapy for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Measurable Residual Disease Assessment

Measurable residual disease (MRD) is a highly sensitive indicator of disease burden in patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), and assessment of MRD as part of response evaluation is incorporated into some clinical trials.

MRD detection can be performed using different methods with associated sensitivities, using cells obtained from either blood or bone marrow. A commercial next-generation sequencing (NGS)-based assay was reported to achieve a limit of CLL detection down to $\leq 10^{-6}$ (MRD6), and currently is the only assay in the United States with FDA regulatory clearance.^{1–4} NGS-based assays require collection of a pretreatment sample. Multicolor (≥ 4) flow cytometry and allele-specific oligonucleotide PCR (ASO-PCR) are the 2 other methods used to detect

MRD at the level of $\leq 10^{-4}$ (MRD4) or $\leq 10^{-5}$ (MRD5), and have significantly more supporting data from clinical trials. Flow cytometry methodology was standardized by the European Research Initiative on CLL (ERIC) and is the most widely used approach due to its extensive availability and reliable detection sensitivity down to MRD5; it also does not require a pretreatment sample for analysis.⁵ ASO-PCR is less widely used because it is expensive, requires a pretreatment sample, and is more labor-intensive.⁶

Consensus recommendations on MRD determination methodology, assay requirements, tissue selection (blood vs bone marrow), and the use of MRD in clinical trials have been published.^{7,8} Few clinical trials have evaluated MRD-guided treatment protocols to determine treatment duration.^{9–11} The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for CLL/SLL recommend serial MRD evaluations every 3 to 6 months during active treatment (using either flow cytometry [MRD flow]

¹The University of Texas MD Anderson Cancer Center; ²Dana-Farber/Brigham and Women's Cancer Center; ³Mass General Cancer Center; ⁴UT Southwestern Simmons Comprehensive Cancer Center; ⁵Fred & Pamela Buffett Cancer Center; ⁶University of Michigan Rogel Cancer Center; ⁷Roswell Park Comprehensive Cancer Center; ⁸Indiana University Melvin and Bren Simon Comprehensive Cancer Center; ⁹The UChicago Medicine Comprehensive Cancer Center; ¹⁰O'Neal Comprehensive Cancer Center at UAB; ¹¹UCLA Jonsson Comprehensive Cancer Center; ¹²UC Davis Comprehensive Cancer Center; ¹³Huntsman Cancer Institute at the University of Utah; ¹⁴University of Wisconsin Carbone Cancer Center; ¹⁵Moffitt Cancer Center; ¹⁶Yale Cancer Center/Smilow Cancer Hospital; ¹⁷Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine; ¹⁸University of Colorado Cancer Center; ¹⁹UC San Diego Moores Cancer Center; ²⁰Robert H. Lurie Comprehensive Cancer Center of Northwestern University; ²¹Vanderbilt-Ingram Cancer Center; ²²Fox Chase Cancer Center; ²³Mayo Clinic Comprehensive Cancer Center; ²⁴Patient Advocate; ²⁵Abramson Cancer Center at the University of Pennsylvania; ²⁶UCSF Helen Diller Family Comprehensive Cancer Center; ²⁷Stanford Cancer Institute; ²⁸City of Hope National Medical Center; ²⁹Duke Cancer Institute; ³⁰Memorial Sloan Kettering Cancer Center; ³¹Fred Hutchinson Cancer Center; ³²Johns Hopkins Kimmel Cancer Center; ³³The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute; and ³⁴National Comprehensive Cancer Network.

*Provided content development and/or authorship assistance.

The full and most current version of these NCCN Guidelines is available at [NCCN.org](https://www.nccn.org).