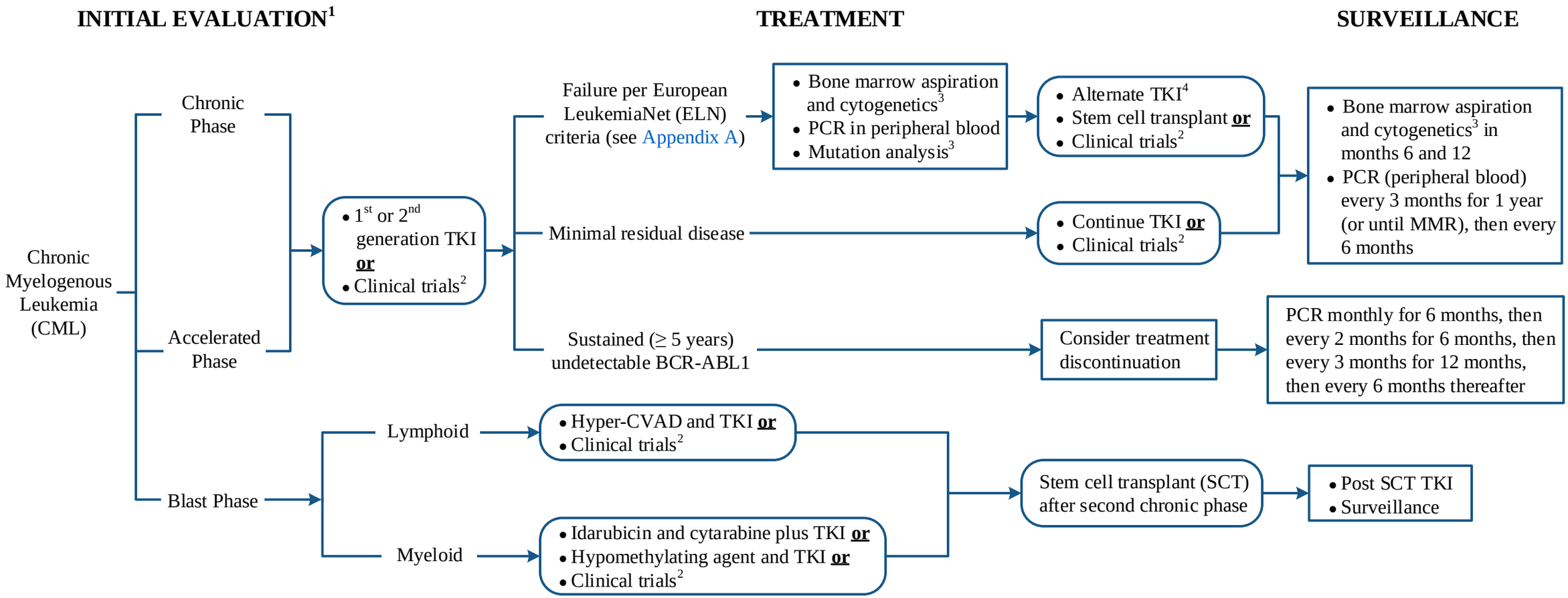
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center Making Cancer History®

Chronic Myelogenous Leukemia - Adult (Age ≥ 18 years)

Disclaimer: *This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.*

Notes: Consider Clinical Trials as treatment options for eligible patients. Leukemia patients should be referred and treated at a comprehensive cancer center.



Hyper-CVAD = hyper-fractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone
TKI = tyrosine kinase inhibitors
PCR = polymerase chain reaction
MMR = major molecular response
BCR-ABL1 = gene sequence in an abnormal chromosome 22

[1] See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice
[2] See Leukemia Clinical Trials
[3] Consider MD Anderson approved biomarkers
[4] If T315I, consider ponatinib

Department of Clinical Effectiveness V5
Approved by The Executive Committee of the Medical Staff 09/15/2020

Chronic Myelogenous Leukemia - Adult (Age ≥ 18 years)

APPENDIX A: Definition of the Response of TKIs (any TKI) as First-line Treatment[1]

	Optimal	Warning	Failure
Baseline	NA	High risk or CCA/Ph+, major route	NA
3 months	BCR-ABL1 ≤ 10% and/or Ph+ ≤ 35%	BCR-ABL1 > 10% and/or Ph+ = 36-95%	Non-CHR and/or Ph+ > 95%
6 months	BCR-ABL1 < 1% and/or Ph+ = 0	BCR-ABL1 = 1-10% and/or Ph+ = 1-35%	BCR-ABL1 > 10% and/or Ph+ > 35%
12 months	BCR-ABL1 ≤ 0.1%	BCR-ABL1 = 0.1-1%	BCR-ABL1 > 1% and/or Ph+ > 0
Then, and at any time	BCR-ABL1 ≤ 0.1%	CCA/Ph- (-7 or 7q-)	Loss of CHR, loss of CCyR, confirmed loss of MMR[2], mutations and CCA/Ph+

Note: The definitions are the same for patients in chronic phase, accelerated phase, and blastic phase, and also apply to second-line treatment when first-line treatment was changed for intolerance. The response can be assessed with either a molecular or a cytogenetic test, but both are recommended whenever possible. Cutoff values have been used to define the boundaries between optimal and warning, and between warning and failures. Because cutoff values are subjected to fluctuations, in case of cytogenetic or molecular data close to the indicated values, a repetition of the tests is recommended. After 12 months, if an MMR is achieved, the response can be assessed by real quantitative polymerase chain reaction (RQ-PCR) every 3 to 6 months, and cytogenetic is required only in case of failure or if standardized molecular testing is not available. Note that MMR ($MR^{3.0}$ or better) is optimal for survival but that a deeper response is likely to be required for a successful discontinuation of treatment.

CCA/Ph+ = clonal chromosome abnormalities in Ph+ cells
CCA/Ph- = clonal chromosome abnormalities in Ph- cells
CCyR = complete cytogenetic response
CHR = complete hematologic response
MMR, BCR-ABL1 ≤ 0.1% = $MR^{3.0}$ or better
NA = not applicable
Ph = philadelphia chromosome

[1] Per European LeukemiaNet (ELN) criteria
[2] In 2 consecutive tests, of which one with a BCR-ABL1 transcripts level ≥ 1%

SUGGESTED READINGS

Baccarani, M., Deininger, M., Rosti, G., Hochhaus, A., Soverini, S., Apperley, J., . . . Hehlmann, R. (2013). European LeukemiaNet recommendations for the management of chronic myeloid leukemia: 2013. *Blood*, 122(6), 872-884. https://doi.org/10.1182/blood-2013-05-501569

Jabbour, E., & Kantarjian, H. (2016). Chronic myeloid leukemia: 2016 update on diagnosis, therapy, and monitoring. *American Journal of Hematology*, 91(2), 252-265. https://doi.org/10.1002/ajh.24275

National Comprehensive Cancer Network. (2020) *Chronic Myeloid Leukemia* (NCCN Guideline Version 3.2020). Retrieved from https://www.nccn.org/professionals/physician_gls/pdf/cml.pdf

Steegmann, J., Baccarani, M., Breccia, M., Casado, L., García-Gutiérrez, V., Hochhaus, A., . . . Clark, R. (2016). European LeukemiaNet recommendations for the management and avoidance of adverse events of treatment in chronic myeloid leukaemia. *Leukemia*, 30(8), 1648-1671. https://doi.org/10.1038/leu.2016.104

DEVELOPMENT CREDITS

This practice algorithm is based on majority expert opinion of the Leukemia Center Faculty at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following:

Yesid Alvarado, MD (Leukemia)
Michael Andreeff, MD, PhD (Leukemia)
Kapil Bhalla, MD (Leukemia)
Gautam Borthakur, MBBS (Leukemia)
Prithviraj Bose, MD (Leukemia)
Jan Burger, MD (Leukemia)
Naval Daver, MD (Leukemia)
Courtney DiNardo, MD (Leukemia)
Zeev Estrov, MD (Leukemia)
Alessandra Ferrajoli, MD (Leukemia)[Ŧ]
Emil Freireich, MD (Leukemia)
Wendy Garcia, BS[♦]
Guillermo Garcia-Manero, MD (Leukemia)
Ghayas Issa, MD (Leukemia)
Elias Jabbour, MD (Leukemia)
Nitin Jain, MBBS (Leukemia)
Tapan Kadia, MD (Leukemia)
Hagop M. Kantarjian, MD (Leukemia)[Ŧ]
Michael Keating, MD (Leukemia)
Marina Konopleva, MD, PhD (Leukemia)
Steven Kornblau, MD (Leukemia)
Lucia Masarova, MD (Leukemia)
Guillermo Montalban-Bravo, MD (Leukemia)
Kiran Naqvi, MD (Leukemia)
Maro Ohanian, DO (Leukemia)
Naveen Pemmaraju, MD (Leukemia)
Farhad Ravandi-Kashani, MD (Leukemia)
Mary Beth Rios, RN (Leukemia)[Ŧ]
Koji Sasaki, MD, PhD (Leukemia)
Nicholas Short, MD (Leukemia)
Koichi Takahashi, MD (Leukemia)
Philip Thompson, MBBS (Leukemia)
Srdan Verstovsek, MD (Leukemia)
Mary Lou Warren, DNP, APRN, CNS-CC[♦]
William Wierda, MD, PhD (Leukemia)
Musa Yilmaz, MD (Leukemia)

[Ŧ] Core Development Team

[♦] Clinical Effectiveness Development Team