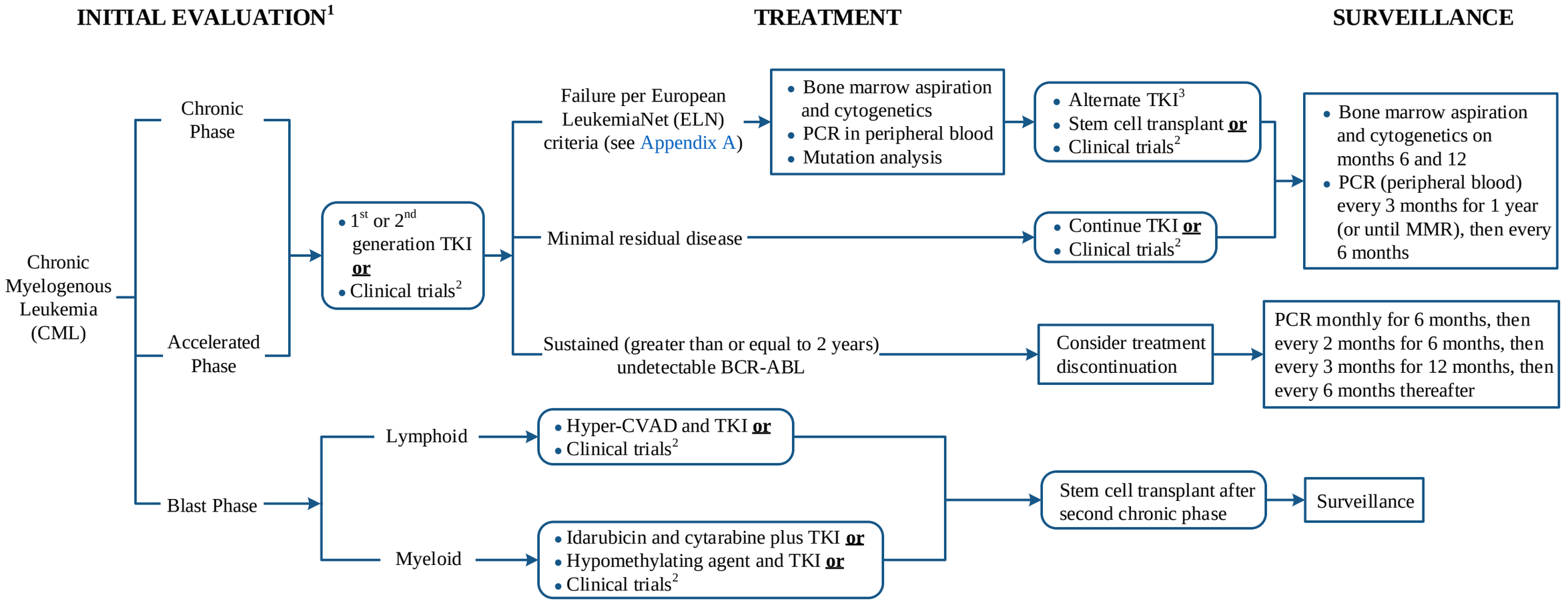
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center Making Cancer History®

Chronic Myelogenous Leukemia - Adult (Greater than or equal to 18 years old)

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
MMR = major molecular response
TKI = tyrosine kinase inhibitors

[1] See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice
[2] Leukemia newsletter: http://www.mdanderson.org/leukemia (Available programs-treatment priorities)
[3] If T315I, consider ponatinib

Department of Clinical Effectiveness V4
Approved by The Executive Committee of the Medical Staff 09/25/2018

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

Chronic Myelogenous Leukemia - Adult (Greater than or equal to 18 years old)

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 less than or equal to 10% and/or Ph+ less than or equal to 35%	BCR-ABL1 greater than 10% and/or Ph+ equals 36-95%	Non-CHR and/or Ph+ greater than 95%
6 months	BCR-ABL1 less than 1% and/or Ph+ equals 0	BCR-ABL1 equals 1-10% and/or Ph+ equals 1-35%	BCR-ABL1 greater than 10% and/or Ph+ greater than 35%
12 months	BCR-ABL1 less than or equal to 0.1%	BCR-ABL1 greater than 0.1-1%	BCR-ABL1 greater than 1% and/or Ph+ greater than 0
Then, and at any time	BCR-ABL1 less than or equal to 0.1%	CCA/Ph- (-7 or 7q-)	Loss of CHR, loss of CCyR, confirmed loss of MMR[2], mutations and CCA/Ph+

The definitions are the same for patients in chronic phase, accelerated phase, and blastic phase and apply also 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 cytogenetics 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 less than or equal to 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 greater than or equal to 1%

Chronic Myelogenous Leukemia - Adult (Greater than or equal to 18 years old)

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.

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

National Comprehensive Cancer Network. Chronic Myelogenous Leukemia (Version 3.2018). https://www.nccn.org/professionals/physician_gls/pdf/cml.pdf. Accessed January 19, 2018.

Steegmann, J. L., Baccarani, M., Breccia, M., Casado, L. F., García-Gutiérrez, V., Hochhaus, A., … Mayer, J. (2016). European LeukemiaNet recommendations for the management and avoidance of adverse events of treatment in chronic myeloid leukaemia. *Leukemia,* 30(8), 1648-1671.

Chronic Myelogenous Leukemia - Adult (Greater than or equal to 18 years old)

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, PhD, MD (Leukemia)
Kapil Bhalla, MD (Leukemia)
Christopher Benton, MD (Leukemia)
Gautam Borthakur, MBBS (Leukemia)
Prithviraj Bose, MD (Leukemia)
Jan Burger, MD (Leukemia)
Jorge Cortes, MD (Leukemia)[Ŧ]
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)
Elias Jabbour, MD (Leukemia)
Kiran Naqvi, MD (Leukemia)
Nitin Jain, MBBS (Leukemia)
Hagop M. Kantarjian, MD (Leukemia)[Ŧ]
Tapan Kadia, MD (Leukemia)
Michael Keating, MD (Leukemia)
Marina Konopleva, PhD, MD (Leukemia)
Steven Kornblau, MD (Leukemia)
Maro Ohanian, DO (Leukemia)
Naveen Pemmaraju, MD (Leukemia)
Farhad Ravandi-Kashani, MD (Leukemia)
Mary Beth Rios, RN (Leukemia)[Ŧ]
Michael Rytting, MD (Pediatrics)
Koichi Takahashi, MD (Leukemia)
Philip Thompson, MBBS (Leukemia)
Srdan Verstovsek, MD (Leukemia)
William Wierda, PhD, MD (Leukemia)

[Ŧ] Core Development Team
[♦] Clinical Effectiveness Development Team