



	Time	Optimal Response	Failure	Warnings
ELN	Baseline	NA	NA	High risk Major route CCA/Ph+
NCCN		NA	NA	NA
ELN	3 Months	<i>BCR-ABL1</i> (IS) ≤10% and/or Ph+ ≤35% (PCyR)	No CHR and/or Ph+ >95%	<i>BCR-ABL1</i> (IS) >10% and/or Ph+ 36-95%
NCCN		<i>BCR-ABL1</i> ≤10% by QPCR (IS) or PCyR on bone marrow cytogenetics, if QPCR (IS) is not available	<i>BCR-ABL1</i> >10% by QPCR (IS) or lack of PCyR on bone marrow cytogenetics, if QPCR (IS) is not available	NA
ELN	6 Months	<i>BCR-ABL1</i> (IS) <1% and/or Ph+ 0% (CCyR)	<i>BCR-ABL1</i> (IS) >10% and/or Ph+ >35%	<i>BCR-ABL1</i> (IS) 1-10% and/or Ph+ 1-35%
NCCN		<i>BCR-ABL1</i> ≤10% (IS) or ≥PCyR on bone marrow cytogenetics, if QPCR (IS) is not available	<i>BCR-ABL1</i> >10% (IS) or lack of PCyR on bone marrow cytogenetics, if QPCR (IS) is not available	NA
ELN	12 Months	<i>BCR-ABL1</i> (IS) ≤0.1% (MMR)	<i>BCR-ABL1</i> (IS) >1% and/or Ph+ >0	<i>BCR-ABL1</i> >0.1-1%
NCCN	12 Months and beyond ^b	CCyR or <i>BCR-ABL1</i> ≤1% but >0.1% by QPCR (IS)	PCyR or <i>BCR-ABL1</i> ≤10% but >1% by QPCR (IS); <PCyR or <i>BCR-ABL1</i> >10% by QPCR (IS); Cytogenetic relapse	NA
ELN	Then, and at any time	MMR or better	Loss of CHR Loss of CCyR Confirmed loss of MMR ^c Mutations CCA/Ph+	CCA/Ph- (-7, or 7q-) NA
NCCN	See 12 Months and beyond ^b	See 12 Months and beyond ^b	See 12 Months and beyond ^b	NA

Abbreviations: CCA/Ph+=clonal chromosome abnormalities in Ph+ cells; CCA/Ph-=clonal chromosome abnormalities in Ph- cells; CCyR=complete cytogenetic response; CHR=complete hematologic response; CML=chronic myeloid or myelogenous leukemia; CyR=cytogenetic response; ELN=European LeukemiaNet; IS=International Scale; MMR=major molecular response *BCR-ABL1* ≤0.1% = MR or better; NA=not applicable; NCCN=National Comprehensive Cancer Network; PCyR=partial cytogenetic response; QPCR=quantitative real time polymerase chain reaction.

^aELN criteria as described in this section refer to the response to TKIs (any TKI) as first-line treatment. ELN has eliminated suboptimal response definitions in its latest recommendations for the management of chronic myeloid leukemia: 2013. At baseline, ELN warning includes high risk or CCA/Ph+, major route. NCCN criteria refer to previously untreated patients with chronic-phase Ph+ or *BCR-ABL1* + CML who are treated with imatinib, 400 mg daily; nilotinib, 300 mg twice daily; or dasatinib, 100 mg daily.

^bNCCN states 12-month evaluation and beyond with bone marrow cytogenetics if neither CCyR nor MMR has been previously achieved. Each of the three definitions of failure have their own specific recommended course of action.

^cBaccarani M, et al. *Blood*. 2013;122(6):872-884. In 2 consecutive tests, of which one with a *BCR-ABL1* transcripts level ≥1%.

Notes from ELN: The definitions are the same for patients in CP, AP, and BP 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 or better) is optimal for survival but that a deeper response is likely to be required for a successful discontinuation of treatment.

References: Baccarani M, et al. European LeukemiaNet recommendations for the management of chronic myeloid leukemia: 2013. *Blood*. 2013;122(6):872-884; Radich JP, et al. *NCCN Clinical Practice Guidelines in Oncology: Chronic Myelogenous Leukemia*. Version 1.2016 (09/09/2015). Accessed March 8, 2016 at http://www.nccn.org/professionals/physician_gls/pdf/cml.pdf.