LEUKEMIA TREATMENT REGIMENS:
Chronic Myeloid Leukemia (CML) (Part 1 of 3)

Clinical Trials: The NCCN recommends cancer patient participation in clinical trials as the gold standard for treatment.

Cancer therapy selection, dosing, administration, and the management of related adverse events can be a complex process that should be handled by an experienced healthcare team. Clinicians must choose and verify treatment options based on the individual patient; drug dose modifications and supportive care interventions should be administered accordingly. The cancer treatment regimens below may include both U.S. Food and Drug Administration-approved and unapproved indications/regimens. These regimens are only provided to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data becomes available. The NCCN Guidelines® are a consensus statement of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

Primary Treatment[1]

Note: All recommendations are Category 2A unless otherwise indicated.

REGIMEN	DOSING
Ph positive or BCR-ABL positive[2-9]	Imatinib 400mg orally daily (Category 1) **OR** Nilotinib 300mg orally twice daily (Category 1) **OR** Dasatinib 100mg orally daily (Category 1).
3 Month Evaluation	
BCR-ABL1/ABL1<10% (IS) or PCyR, if QPCR (IS) not available[2-9]	Continue current regimen.
If response of BCR-ABL1 transcripts >10% (IS) or lack of PCyR on bone marrow cytogenetics, if QPCR (IS) not available[9-12]* Evaluate patient compliance and drug–drug interactions, consider mutational analysis and bone marrow cytogenetics	**Primary Treatment with Imatinib** Change therapy to alternate TKI **OR** Imatinib dose may be increased to a maximum of 800 mg, if tolerated **and** evaluate for hematopoietic stem cell transplantation (HSCT) depending on response to tyrosine kinase inhibitor (TKI) therapy. **Primary Treatment with Nilotinib or Dasatinib** Continue same dose of nilotinib or dasatinib **OR** Change therapy to alternate TKI (other than imatinib) **and** evaluate for HSCT depending on response to TKI therapy.
6 Month Evaluation[1]	
BCR-ABL1/ABL1 ≤ 10% by QPCR (IS) or ≥ PCyR , if QPCR (IS) not available[2-9]	Continue current regimen.
If response of BCR-ABL1 transcripts >10% (IS) or lack of PCyR on bone marrow cytogenetics, if QPCR (IS) not available[13]* Evaluate patient compliance and drug–drug interactions, consider mutational analysis and bone marrow cytogenetics	Change therapy to alternate TKI (other than imatinib) and evaluate for HSCT depending on response to TKI therapy.
12 Month Evaluation and Beyond[1†]	
Complete cytogenetic response or BCR-ABL1 transcripts ≤1% but >0.1% by QPCR (IS)[2-9]	Continue current regimen.
PCyR or BCR-ABL1 transcripts ≤ 10% but > 1% by QPCR (IS)[10]* Evaluate patient compliance and drug–drug interactions, consider mutational analysis and bone marrow cytogenetics	Change therapy to alternate TKI (preferred) (other than imatinib) **OR** Continue same dose of TKI **OR** Increase dose of imatinib to a maximum dose of 800 mg, as tolerated (if not candidate for alternate TKI or omacetaxine).

continued

LEUKEMIA TREATMENT REGIMENS:
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12 Month Evaluation and Beyond[1†] (continued)

REGIMEN	DOSING
Less than PCyR or BCR-ABL1 transcripts > 10% by QPCR (IS)[10]* Evaluate patient compliance and drug–drug interactions, consider mutational analysis	Change therapy to alternate TKI (other than imatinib) **and** evaluate for HSCT depending on response to TKI
Cytogenetic relapse[10]* Evaluate patient compliance and drug-drug interactions, mutational analysis	Change therapy to alternate TKI (preferred) (other than imatinib) **OR** Increase dose of imatinib to a maximum dose of 800 mg, as tolerated (if not candidate for alternate TKI or omacetaxine) and evaluate for HSCT depending on response to TKI therapy.

Advanced Phase[1]

Accelerated phase[15-32]‡	Imatinib 600mg orally daily **OR** Dasatinib 140mg orally daily (70mg twice daily) **OR** Nilotinib 400mg orally twice daily **OR** Bosutinib 500mg orally daily **OR** Ponatinib 45mg orally daily **OR** Omacetaxine 1.25mg/m^2 SC twice daily on days 1–14 cycled every 28 days until hematologic response, followed by omacetaxine 1.25mg/m^2 SC twice daily on days 1–7 cycled every 28 days until disease progression or unacceptable toxicity **AND** Consider HSCT based on response.
Blast phase—lymphoid[15-32]	ALL-type induction chemotherapy, **plus** TKI followed by HSCT, if feasible **OR** TKI followed by HSCT, if feasible.
Blast phase—myeloid[15-32]	AML-type induction chemotherapy, **plus** TKI followed by HSCT, if feasible. **OR** TKI followed by HSCT, if feasible.

* Alternate TKIs include dasatinib, nilotinib, bosutinib, and ponatinib.
† Repeat bone marrow evaluation at 3 months to document CCyR, if <CCyR, treat as per <PCrR.
‡ Ponatinib is a treatment option for patients with a T315I mutation or for patients with disease that has not responded to 2 or more TKI therapies.

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LEUKEMIA TREATMENT REGIMENS:
Chronic Myeloid Leukemia (CML) (Part 3 of 3)

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