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 health care 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 provided only to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data become 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.

Chronic Phase CML[1]

Primary Treatment[1]

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

REGIMEN	DOSING
Low-risk Score[2-9a]	Imatinib 400mg orally daily (Category 1) **OR** Nilotinib 300mg orally twice daily (Category 1) **OR** Dasatinib 100mg orally daily (Category 1).
Intermediate- or High-risk Score[2-9a]	Dasatinib 100mg orally daily (preferred) **OR** Nilotinib 300mg orally twice daily (preferred) **OR** Imatinib 400mg orally daily.
3 Month Evaluation[1]	
BCR-ABL1 transcripts ≤10% by QPCR (IS)[2-9b]	Continue same tyrosine kinase inhibitor (TKI).
BCR-ABL1 transcripts >10% by QPCR (IS)[9-12c-j] Evaluate patient compliance and drug–drug interactions, consider mutational analysis and bone marrow cytogenetics	Switch to alternate TKI (other than imatinib) **OR** Continue same TKI **OR** Dose escalation of imatinib to a maximum of 800mg (if primary treatment with imatinib) **AND** Evaluate for hematopoietic cell transplantation (HCT) depending on response to TKI therapy.
6 Month Evaluation[1]	
BCR-ABL1 transcripts ≤10% by QPCR (IS)[2-9b]	Continue same TKI.
BCR-ABL1 transcripts >10% by QPCR (IS)[13c, e-j] 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 HCT depending on response to TKI therapy.
12 Month Evaluation[1]	
BCR-ABL1 transcripts <1% by QPCR (IS)[2-9b]	Continue same TKI.
BCR-ABL1 transcripts ≤10% but ≥1% by QPCR (IS)[10d-j] Evaluate patient compliance and drug–drug interactions, consider mutational analysis and bone marrow cytogenetics	Switch to alternate TKI **OR** Continue same TKI **OR** Dose escalation of imatinib to a maximum of 800mg (if primary treatment with imatinib) **AND** Evaluate for HCT depending on response to TKI therapy.
BCR-ABL1 transcripts >10% by QPCR (IS)[10c,e-j] Evaluate patient compliance and drug–drug interactions, consider mutational analysis	Change therapy to alternate TKI (other than imatinib) **and** evaluate for HCT depending on response to TKI

continued

LEUKEMIA TREATMENT REGIMENS: Chronic Myeloid Leukemia (CML) (Part 2 of 3)

Chronic Phase CML[1] (continued)

Evaluations Beyond 12 Months[1]

REGIMEN	DOSING
BCR-ABL1 transcripts <0.1% by QPCR (IS)[2-9b]	Continue same TKI.
BCR-ABL1 transcripts <1% but no less than 0.1% by QPCR (IS)[10d-j] 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 TKI **OR** Dose escalation of imatinib to a maximum of 800mg (if primary treatment with imatinib) **AND** Evaluate for hematopoietic cell transplantation (HCT) depending on response to TKI therapy.
BCR-ABL1 transcripts >10% by QPCR (IS)[10c, e-j] 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 HCT depending on response to TKI therapy.

Advanced Phase CML[1]

Accelerated phase[15-32k]	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/m² SC twice daily on days 1–14 cycled every 28 days until hematologic response, followed by omacetaxine 1.25mg/m² SC twice daily on days 1–7 cycled every 28 days until disease progression or unacceptable toxicity.
Blast phase—lymphoid[15-32]	Acute lymphoblastic leukemia (ALL)-type induction chemotherapy + TKI **OR** TKI + steroids.
Blast phase—myeloid[15-32]	Acute myeloid leukemia (AML)-type induction chemotherapy + TKI **OR** TKI.

[a] Preliminary data suggest that patients with an intermediate- or high-risk Sokal or Hasford score may preferentially benefit from dasatinib or nilotinib.

[b] Discontinuation of TKI with careful monitoring is feasible in selected patients.

[c] Patients with BCR-ABL1 only slightly >10% at 3 months and/or with a steep decline from baseline, may achieve <10% at 6 months and have generally favorable outcomes. Therefore, it is important to interpret the value at 3 months in this context, before making drastic changes to the treatment strategy.

[d] Achievement of response milestones must be interpreted within the clinical context. Patients with more than 50% reduction compared to baseline or minimally above the 10% cutoff can continue the same dose of dasatinib or nilotinib for another 3 months.

[e] Patients with disease that is resistant to primary treatment with imatinib should be treated with nilotinib, dasatinib, or bosutinib in the second-line setting. Patients with disease that is resistant to primary treatment with nilotinib or dasatinib could be treated with an alternate TKI (other than imatinib) in the second-line setting.

[f] Dasatinib is a treatment option for patients with a Y253H, E255K/V, or F359V/C/I mutation

[g] Nilotinib is a treatment option for patients with F317L/V/I/C, T315A, or V299L mutation

[h] Bosutinib is a treatment option for patients with E255K/V, F317L/V/I/C, F359V/C/I, T315A, or Y253H mutation

[i] Ponatinib is a treatment option for patients with T315I mutation or for patients for whom no other TKI is indicated

[j] Omacetaxine is a treatment option for patients with disease that is resistant and/or intolerant to 2 or more TKIs.

[k] Omacetaxine is a treatment option for patients with disease progression to accelerated phase CML. Omacetaxine is not a treatment option for patients that present with accelerated phase CML

continued

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

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