Chronic Myeloid Leukemia (CML) Treatment Regimens

Clinical Trials: The National Comprehensive Cancer Network 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 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 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.

▶Chronic Phase CML[1]

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

REGIMEN	DOSING
Primary Treatment[1-13]	
Low-risk Score	Bosutinib 400mg orally daily (Category 1). **OR** Dasatinib 100mg orally daily (Category 1). **OR** Imatinib (or generic imatinib) 400mg orally daily (Category 1). **OR** Nilotinib 300mg orally twice daily (Category 1).
Intermediate- or High-risk Score	Bosutinib 400mg orally daily (Category 1).[a] **OR** Dasatinib 100mg orally daily (Category 1).[a] **OR** Imatinib (or generic imatinib) 400mg orally daily.[b] **OR** Nilotinib 300mg orally twice daily (Category 1).[a]
3 Month Evaluation[1-18]	
BCR-ABL1 transcripts ≤10% by QPCR (IS) Monitor response and side effects.	Continue same tyrosine kinase inhibitor (TKI).[c]
BCR-ABL1 transcripts >10% by QPCR (IS)[d,f-k] Evaluate patient compliance and drug interactions, consider mutational analysis, and consider bone marrow cytogenetic analysis to assess for major cytogenetic response (MCyR) at 3 months or complete cytogenetic response (CCyR) at 12 months.	Switch to alternate TKI. **OR** Continue same TKI (other than imatinib).[e] **OR** Increase imatinib dose to a maximum of 800mg (if primary treatment with imatinib) **AND** Consider evaluation for allogeneic hematopoietic cell transplantation (HCT).
6 Month Evaluation[1-18]	
BCR-ABL1 transcripts ≤10% by QPCR (IS) Monitor response and side effects.	Continue same TKI.[c]
BCR-ABL1 transcripts >10% by QPCR (IS)[d,f-k] Evaluate patient compliance and drug interactions, and consider mutational analysis.	Switch to alternate TKI **AND** Evaluate for allogeneic HCT.
12 Month Evaluation[1-16,l]	
BCR-ABL1 transcripts ≤1% by QPCR (IS) Monitor response and side effects.	Continue same TKI.[c]

continued

Chronic Myeloid Leukemia (CML) Treatment Regimens

▶Chronic Phase CML[1] (continued)

REGIMEN	DOSING
12 Month Evaluation[1-16,j] (continued)	
BCR-ABL1 transcripts ≤10% but >1% by QPCR (IS)[f-k] Evaluate patient compliance and drug interactions, consider mutational analysis, and consider bone marrow cytogenetic analysis to assess for MCyR at 3 months or CCyR at 12 months.	Switch to alternate TKI. **OR** Continue same TKI (other than imatinb).[e] **OR** Increase dose of imatinib to a maximum of 800mg (if primary treatment with imatinib). **AND** Consider evaluation for allogeneic HCT.
BCR-ABL1 transcripts >10% by QPCR (IS)[f-k] Evaluate patient compliance and drug interactions, consider mutational analysis.	Switch to alternate TKI. **AND** Evaluate for allogeneic HCT.
≥15 Month Evaluation[1-16]	
BCR-ABL1 transcripts ≤1% by QPCR (IS) Monitor response and side effects.	Continue same TKI.[c]
BCR-ABL1 transcripts >1% by QPCR (IS)[f-k] Evaluate patient compliance and drug interactions, and consider mutational analysis.	Switch to alternate TKI. **AND** Evaluate for allogeneic HCT.

▶Advanced Phase CML[1,19-38]

Accelerated phase[l-o]	Bosutinib 500mg orally daily (preferred). **OR** Dasatinib 140mg orally daily (preferred). **OR** Imatinib (or generic imatinib) 600mg orally daily. **OR** Nilotinib 400mg orally twice daily (preferred). **OR** Omacetaxine 1.25mg/m^2 SC twice daily on days 1–14 cycled every 28 days until hematologic response, followed by omacetaxine maintenance therapy 1.25mg/m^2 SC twice daily on days 1–7 cycled every 28 days until disease progression or unacceptable toxicity. **OR** Ponatinib 45mg orally daily (preferred).
Blast phase—lymphoid	Acute lymphoblastic leukemia (ALL)-type induction chemotherapy + TKI.[p] **OR** TKI + steroids.[p]
Blast phase—myeloid	Acute myeloid leukemia (AML)-type induction chemotherapy + TKI.[p] **OR** TKI.[p]

[a] Based on preliminary data from the BFORE trial and long-term follow-up data from the DASISION and ENESTnd trials, second generation TKIs (dasatinib, nitlotinib, bosutinib) are preferred by patients with an intermediate- or high-risk score, especially for young women whose goal is to achieve a deep and rapid molecular response and eventual drug discontinuation for TKI therapy for family planning purposes.

[b] Imatinib may be preferred for older patients with comorbidities such as cardiovascular disease.

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

[d] 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.

[e] 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, nilotinib, or bosutinib for another 3 months. Continuation of imatinib 400 mg is not recommended.

[f] Patients with disease that is resistant to primary treatment with imatinib should be treated with bosutinib, dasatinib, or nilotinib in the second-line setting taking into account *BCR-ABL1* mutation status. The durability of these responses is frequently limited. Patients with disease that is resistant to primary treatment with bosutinib, dasatinib, or nilotinib can be treated with an alternate TKI (other than imatinib) in the second-line setting.

[g] Bosutinib is contraindicated for patients with a T315I, V299L, G250E, E317L mutation.

[h] Bosutinib has minimal activity against F317L mutation. Nilotinib may be preferred over bosutinib in patients with F317L mutation.

[i] Dasatinib is contraindicated for patients with a T315I/A, F317L/V/I/C, V299L mutation.

[j] Nilotinib is contraindicated for patients with a T315I, Y253H, E255K/V, F359V/C/I, G250E mutation.

continued

[k] BCR-ABL1 0.1% at 12 months is associated with a very low probability of subsequent disease progression and a high likelihood of achieving a subsequent MR4.0, which is a prerequisite for a trial of treatment-free remission.

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

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

[n] 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.

[o] Patients who present with accelerated phase at diagnosis should be treated with a TKI, followed by evaluation for allogeneic HCT.

[p] Followed by evaluation for allogeneic HCT as indicated.

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