Chronic Myeloid Leukemia (CML) Treatment Regimens


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.

<table>
<thead>
<tr>
<th>REGIMEN</th>
<th>DOSING</th>
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<tbody>
<tr>
<td>Primary Treatment(^1)</td>
<td></td>
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<tr>
<td>Low-risk Score</td>
<td>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).</td>
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<tr>
<td>Intermediate- or High-risk Score</td>
<td>Bosutinib 400mg orally daily (Category 1). OR Dasatinib 100mg orally daily (Category 1). OR Imatinib (or generic imatinib) 400mg orally daily. OR Nilotinib 300mg orally twice daily (Category 1).</td>
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3 Month Evaluation\(^1\)\(^-\)\(^8\)

<table>
<thead>
<tr>
<th>BCR-ABL1 transcripts ≤10% by QPCR (IS)</th>
<th>Monitor response and side effects.</th>
<th>Continue same tyrosine kinase inhibitor (TKI).(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCR-ABL1 transcripts &gt;10% by QPCR (IS)(^9)(^-)(^10)</td>
<td>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.</td>
<td>Switch to alternate TKI. OR Continue same TKI (other than imatinib). OR Increase imatinib dose to a maximum of 800mg (if primary treatment with imatinib) AND Consider evaluation for allogeneic hematopoietic cell transplantation (HCT).</td>
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6 Month Evaluation\(^1\)\(^-\)\(^8\)

<table>
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<tr>
<th>BCR-ABL1 transcripts ≤10% by QPCR (IS)</th>
<th>Monitor response and side effects.</th>
<th>Continue same TKI.(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCR-ABL1 transcripts &gt;10% by QPCR (IS)(^9)(^-)(^10)</td>
<td>Evaluate patient compliance and drug interactions, and consider mutational analysis.</td>
<td>Switch to alternate TKI AND Evaluate for allogeneic HCT.</td>
</tr>
</tbody>
</table>

12 Month Evaluation\(^1\)\(^-\)\(^6\)\(^,\)\(^1\)

| BCR-ABL1 transcripts ≤1% by QPCR (IS) | Monitor response and side effects. | Continue same TKI.\(^c\) |

continued
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### Chronic Phase CML\(^1\) (continued)

<table>
<thead>
<tr>
<th>REGIMEN</th>
<th>DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>12 Month Evaluation</strong>(^{16}) (continued)</td>
<td></td>
</tr>
</tbody>
</table>
| BCR-ABL1 transcripts \(\leq 10\%\) but \(>1\%\) by QPCR (IS)\(^a\) 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 imatinib).\(^a\)  
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)\(^a\) Evaluate patient compliance and drug interactions, consider mutational analysis. | Switch to alternate TKI.  
AND  
Evaluate for allogeneic HCT. |
| **\(\geq 15\) Month Evaluation**\(^{16}\) | |
| BCR-ABL1 transcripts \(\leq 1\%\) by QPCR (IS) Monitor response and side effects. | Continue same TKI.\(^c\) |
| BCR-ABL1 transcripts >1\% by QPCR (IS)\(^a\) 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\(^a\) | 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 ENESTind trials, second generation TKIs (dasatinib, nilotinib, 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 dasatinib, bosutinib, 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.

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\(^{16}\) Based on preliminary data from the BFORE trial and long-term follow-up data from the DASISION and ENESTind trials, second generation TKIs (dasatinib, nilotinib, 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.
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3. Omacetaxine is a treatment option for patients with disease that is resistant and/or intolerant to 2 or more TKIs.

4. 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.

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

6. Followed by evaluation for allogeneic HCT as indicated.

References

2. 17. Kim DD, Lee H, Kamel-Reid S, Lipton JH. BCR-ABL1 transcript at 3 months predicts
9. 1. NCCN Clinical Practice Guidelines in Oncology™. Chronic Myeloid Leukemia.
10. 1. O'Brien SG, Guilhot F, Larson RA, et al. Imatinib compared with interferon and
11. 1. O'Brien SG, Guilhot F, Larson RA, et al. Imatinib compared with interferon and
12. 1. O'Brien SG, Guilhot F, Larson RA, et al. Imatinib compared with interferon and
15. 1. O'Brien SG, Guilhot F, Larson RA, et al. Imatinib compared with interferon and
17. 1. O'Brien SG, Guilhot F, Larson RA, et al. Imatinib compared with interferon and
18. 1. O'Brien SG, Guilhot F, Larson RA, et al. Imatinib compared with interferon and
20. 1. O'Brien SG, Guilhot F, Larson RA, et al. Imatinib compared with interferon and
22. 1. O'Brien SG, Guilhot F, Larson RA, et al. Imatinib compared with interferon and
23. 1. O'Brien SG, Guilhot F, Larson RA, et al. Imatinib compared with interferon and
25. 1. O'Brien SG, Guilhot F, Larson RA, et al. Imatinib compared with interferon and
27. 1. O'Brien SG, Guilhot F, Larson RA, et al. Imatinib compared with interferon and
crisis treated with imatinib 600 mg: outcome of the patients alive after a 6-year
responses in patients with accelerated phase chronic myeloid leukemia treated with
imatinib 600 mg: the GIMEMA CML Working Party experience after a 7-year
32. Silver RT, Cortes J, Waltzman R, et al. Sustained durability of responses and
improved progression-free and overall survival with imatinib treatment for
accelerated phase and blast crisis chronic myeloid leukemia: long-term follow-up of
33. Ohanian M, Kantarjian HM, Quintas-Cardama A, et al. Tyrosine kinase inhibitors as
initial therapy for patients with chronic myeloid leukemia in accelerated phase.
myeloid leukemia in accelerated phase after imatinib failure: the START A trial.
35. Cortes J, Kim DW, Raffoux E, et al. Efficacy and safety of dasatinib in imatinib-
resistant or –intolerant patients with chronic myeloid leukemia in blast phase.
36. Cortes J, Kim DW, Raffoux E, et al. Efficacy and safety of dasatinib in imatinib-
resistant or –intolerant patients with chronic myeloid leukemia in blast phase.
37. Ohanian M, Kantarjian HM, Quintas-Cardama A, et al. Tyrosine kinase inhibitors as
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47. Cortes J, Kim DW, Raffoux E, et al. Efficacy and safety of dasatinib in imatinib-
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48. Cortes J, Kim DW, Raffoux E, et al. Efficacy and safety of dasatinib in imatinib-
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49. Ohanian M, Kantarjian HM, Quintas-Cardama A, et al. Tyrosine kinase inhibitors as
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