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

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</td>
<td></td>
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<tr>
<td>Low-risk Score</td>
<td>Imatinib (or generic imatinib) 400mg orally daily (Category 1) OR Bosutinib 400mg orally daily (Category 1) OR Dasatinib 100mg 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 Nilotinib 300mg orally twice daily (Category 1) OR Imatinib (or generic imatinib) 400mg orally daily.</td>
</tr>
</tbody>
</table>

3 Month Evaluation

<table>
<thead>
<tr>
<th>BCR-ABL1 transcripts ≤10% by QPCR (IS)</th>
<th>Continue same tyrosine kinase inhibitor (TKI).</th>
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<tbody>
<tr>
<td>BCR-ABL1 transcripts &gt;10% by QPCR (IS)</td>
<td>Switch to alternate TKI OR Continue same TKI (other than imatinib) OR Dose escalation of imatinib 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

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<thead>
<tr>
<th>BCR-ABL1 transcripts ≤10% by QPCR (IS)</th>
<th>Continue same TKI.</th>
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<tbody>
<tr>
<td>BCR-ABL1 transcripts &gt;10% by QPCR (IS)</td>
<td>Switch to alternate TKI AND Evaluate for allogeneic HCT.</td>
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</table>

12 Month Evaluation

| BCR-ABL1 transcripts ≤1% by QPCR (IS) | Continue same TKI. |

continued
# Chronic Myeloid Leukemia (CML) Treatment Regimens

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

### REGIMEN

<table>
<thead>
<tr>
<th>12 Month Evaluation(^{16a}) (continued)</th>
<th>DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BCR-ABL1 transcripts ≤10% but &gt;1% by QPCR (IS)(^1)</strong>&lt;br&gt;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.</td>
<td>Switch to alternate TKI&lt;br&gt;<strong>OR</strong>&lt;br&gt;Continue same TKI (other than imatinib)(^a)&lt;br&gt;<strong>OR</strong>&lt;br&gt;Dose escalation of imatinib to a maximum of 800mg (if primary treatment with imatinib) <strong>AND</strong>&lt;br&gt;Consider evaluation for allogeneic HCT.</td>
</tr>
<tr>
<td><strong>BCR-ABL1 transcripts &gt;10% by QPCR (IS)(^1)</strong>&lt;br&gt;Evaluate patient compliance and drug–drug interactions, consider mutational analysis.</td>
<td>Switch to alternate TKI&lt;br&gt;<strong>AND</strong>&lt;br&gt;Evaluate for allogeneic HCT.</td>
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### >15 Month Evaluation\(^1\-14\)

| **BCR-ABL1 transcripts ≤1% by QPCR (IS)**<br>Monitor response and side effects. | Continue same TKI. |
| **BCR-ABL1 transcripts >1% by QPCR (IS)\(^1\)**<br>Evaluate patient compliance and drug–drug interactions, consider mutational analysis. | Switch to alternate TKI<br>**AND**<br>Evaluate for allogeneic HCT. |

## Advanced Phase CML\(^{1,19-38}\)

### Accelerated phase\(^{a,b}\)

| **Imatinib 600mg orally daily**<br>**OR**<br>**Dasatinib 140mg orally daily**<br>**OR**<br>**Nilotinib 400mg orally twice daily**<br>**OR**<br>**Bosutinib 500mg orally daily**<br>**OR**<br>**Ponatinib 45mg orally daily**<br>**OR**<br>**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.** | **Acute lymphoblastic leukemia (ALL)-type induction chemotherapy + TKI\(^b\)**<br>**OR**<br>**TKI + steroids.**<br>Or<br>**Acute myeloid leukemia (AML)-type induction chemotherapy + TKI**<br>**OR**<br>**TKI.** |

**Blast phase—lymphoid**

| **Acute lymphoblastic leukemia (ALL)-type induction chemotherapy + TKI\(^b\)**<br>**OR**<br>**TKI + steroids.** | **Acute myeloid leukemia (AML)-type induction chemotherapy + TKI**<br>**OR**<br>**TKI.** |

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\(^1\) Based on long-term follow-up data from the DASISION and ENESTnd trials and preliminary data from the BFORTE trial, second-generation TKIs (dasatinib, nilotinib, or bosutinib) are preferred for patients with an intermediate- or high-risk Sokal or Hasford score, especially for young women whose goal is to achieve a deep and rapid molecular response and eventual drug discontinuation of TKI for fertility purposes.

\(^a\) Imatinib may be preferred for older patients with comorbidities such as cardiovascular disease.

\(^b\) 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, nilotinib, or bosutinib for another 3 months. Continuation of imatinib 400 mg is not recommended.

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

\(^f\) Dasatinib is the recommended treatment option for patients with a Y253H, E255K/V, or F359V/C/I mutation.

\(^g\) Nilotinib is the recommended treatment option for patients with F317L/V/I/C, T315A, or V299L mutation.

\(^h\) Bosutinib is the recommended treatment option for patients with E255K/V, F359V/C/I, T315I, 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.

\(^\text{continued}\)
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1. 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 may facilitate discontinuation of TKI therapy.
2. Omacetaxine is a treatment option for patients with disease that is resistant and/or intolerant to 2 or more TKIs.
3. 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.
4. Patients who present with accelerated phase at diagnosis should be treated with a TKI, followed by evaluation for allogeneic HCT.
5. Followed by evaluation for allogeneic HCT.

References


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