Chronic Myelogenous Leukemia - Adult (Age ≥ 18 years)

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson’s specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient’s care. This algorithm should not be used to treat pregnant women.

**Notes:** Consider Clinical Trials as treatment options for eligible patients. Leukemia patients should be referred and treated at a comprehensive cancer center.

### INITIAL EVALUATION

- **Chronic Phase**
  - Chronic Myelogenous Leukemia (CML)
  - 1° or 2nd generation TKI or Clinical trials

- **Accelerated Phase**
  - Minimal residual disease
  - Sustained (≥ 5 years) undetectable BCR-ABL1
  - Hyper-CVAD and TKI or Clinical trials

- **Blast Phase**
  - Lymphoid
  - Myeloid
  - Idarubicin and cytarabine plus TKI or Hypomethylating agent and TKI or Clinical trials

### TREATMENT

- Failure per European LeukemiaNet (ELN) criteria (see Appendix A)
  - Bone marrow aspiration and cytogenetics
  - PCR in peripheral blood
  - Mutation analysis

- Alternate TKI
  - Stem cell transplant or Clinical trials

- Continue TKI or Clinical trials

- Consider treatment discontinuation

### SURVEILLANCE

- Bone marrow aspiration and cytogenetics in months 6 and 12
- PCR (peripheral blood) every 3 months for 1 year (or until MMR), then every 6 months

- Continue TKI or Clinical trials

- Stem cell transplant (SCT) after second chronic phase

- Bone marrow aspiration and cytogenetics in months 6 and 12
- PCR (peripheral blood) every 3 months for 1 year (or until MMR), then every 6 months thereafter

- Post SCT TKI or Surveillance

Hyper-CVAD = hyper-fractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone

TKI = tyrosine kinase inhibitors

PCR = polymerase chain reaction

MMR = major molecular response

BCR-ABL1 = gene sequence in an abnormal chromosome 22

1 See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

2 See Leukemia Clinical Trials

3 Consider MD Anderson approved biomarkers

4 If T315I, consider ponatinib

Approved by The Executive Committee of the Medical Staff 09/15/2020
APPENDIX A: Definition of the Response of TKIs (any TKI) as First-line Treatment

<table>
<thead>
<tr>
<th></th>
<th>Optimal</th>
<th>Warning</th>
<th>Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>NA</td>
<td>High risk or CCA/Ph+, major route</td>
<td>NA</td>
</tr>
<tr>
<td>3 months</td>
<td>BCR-ABL1 ≤ 10% and/or Ph+ ≤ 35%</td>
<td>BCR-ABL1 &gt; 10% and/or Ph+ = 36-95%</td>
<td>Non-CHR and/or Ph+ &gt; 95%</td>
</tr>
<tr>
<td>6 months</td>
<td>BCR-ABL1 &lt; 1% and/or Ph+ = 0</td>
<td>BCR-ABL1 = 1-10% and/or Ph+ = 1-35%</td>
<td>BCR-ABL1 &gt; 10% and/or Ph+ &gt; 35%</td>
</tr>
<tr>
<td>12 months</td>
<td>BCR-ABL1 ≤ 0.1%</td>
<td>BCR-ABL1 = 0.1-1%</td>
<td>BCR-ABL1 &gt; 1% and/or Ph+ &gt; 0</td>
</tr>
<tr>
<td>Then, and at any time</td>
<td>BCR-ABL1 ≤ 0.1%</td>
<td>CCA/Ph- (-7 or 7q-)</td>
<td>Loss of CHR, loss of CCyR, confirmed loss of MMR, CCA/Ph+</td>
</tr>
</tbody>
</table>

Note: The definitions are the same for patients in chronic phase, accelerated phase, and blastic phase, and also apply to second-line treatment when first-line treatment was changed for intolerance. The response can be assessed with either a molecular or a cytogenetic test, but both are recommended whenever possible. Cutoff values have been used to define the boundaries between optimal and warning, and between warning and failures. Because cutoff values are subjected to fluctuations, in case of cytogenetic or molecular data close to the indicated values, a repetition of the tests is recommended. After 12 months, if an MMR is achieved, the response can be assessed by real quantitative polymerase chain reaction (RQ-PCR) every 3 to 6 months, and cytogenetic is required only in case of failure or if standardized molecular testing is not available. Note that MMR (MR\textsuperscript{3.0} or better) is optimal for survival but that a deeper response is likely to be required for a successful discontinuation of treatment.

CCA/Ph+ = clonal chromosome abnormalities in Ph+ cells
CCA/Ph- = clonal chromosome abnormalities in Ph- cells
CCyR = complete cytogenetic response
CHR = complete hematologic response
MMR, BCR-ABL1 ≤ 0.1% = MR\textsuperscript{3.0} or better
NA = not applicable
Ph = philadelphia chromosome

1 Per European LeukemiaNet (ELN) criteria
2 In 2 consecutive tests, of which one with a BCR-ABL1 transcripts level ≥ 1%
SUGGESTED READINGS


This practice algorithm is based on majority expert opinion of the Leukemia Center Faculty at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following:

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