ELN European LeukemiaNet

Management of chronic myeloid leukemia (CML): recommendations from the European LeukemiaNet (ELN)

Definitions of failure, suboptimal response, warnings and optimal response

Table 1. Proposed criteria for failure, suboptimal response, and warnings for previously untreated patients with early chronic phase CML who are treated with imatinib 400 mg daily

Time	Failure	Suboptimal response	Warnings	Optimal response
Diagnosis	N/A	N/A	High risk, del9q+, ACAs in Ph+ cells	N/A
3 months after diagnosis	No HR (stable disease or disease progression)	Less than CHR	N/A	CHR
6 months after diagnosis	Less than CHR, no CgR (Ph+ > 95%)	Less than PCgR (Ph+ > 35%)	N/A	At least PCgR (Ph+ ≤ 35%)
12 months after diagnosis	Less than PCgR (Ph+ > 35%)	Less than CCgR	Less than MMolR	CCgR
18 months after diagnosis	Less than CCgR	Less than MMolR	N/A	MMolR
Any time	Loss of CHR* Loss of CCgR† Mutation‡	ACA in Ph+ cells§ Loss of MMolR§ Mutation#	Any rise in transcript level Other chromosomal abnormalities in Ph– cells	N/A

N/A, not applicable; ACA, additional chromosomal abnormalities; HR, hematologic response; CCgR, complete cytogenetic response; PCgR, partial CgR;
* To be confirmed on two occasions unless associated with progression to accelerated phase/blast crisis;
† To be confirmed on two occasions unless associated with CHR loss or progression to accelerated phase/blast crisis;
‡ High level of insensitivity to imatinib;
§ To be confirmed on two occasions unless associated with CHR or CCgR loss;
# Low level of insensitivity to imatinib

- 'Failure' indicates that continuing imatinib treatment at the current dose is no longer appropriate for the patient.
- 'Suboptimal response' indicates the patient may gain benefit from continuing imatinib therapy but long-term outcomes may not be favorable.
- 'Warnings' are indications that standard-dose imatinib treatment may not be the best option for a particular patient, and careful monitoring is required.

Response definitions and monitoring

Most published reports use the same definitions of hematologic and cytogenetic responses, with minor variations. The definitions proposed by ELN are summarized in Table 2.

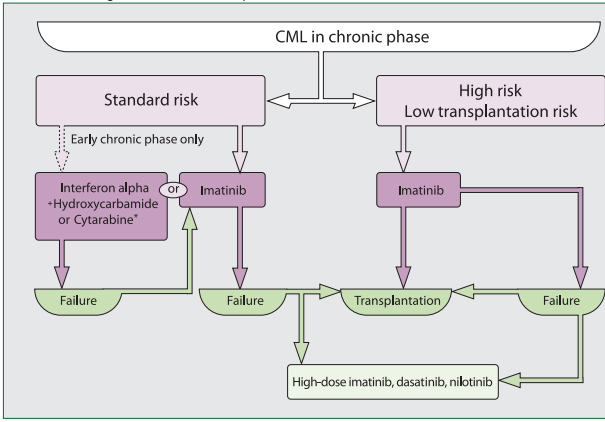
Table 2. Definitions of responses to CML therapy and recommended monitoring activity

	Definition	Monitoring
Hematologic response (complete)	Platelet count < 450 x 109/L WBC count < 10 x 109/L Differential: without immature granulocytes and with < 5% basophils Non-palpable spleen	Check every 2 weeks until complete response achieved and confirmed, then every 3 months unless otherwise specified
Cytogenetic response	Complete: Ph+ none Partial: Ph+ 1–35% Minor: Ph+ 36–65% Minimal: Ph+ 66–95% None: Ph+ > 95%	Check every 6 months until complete response achieved and confirmed
Molecular response **(BCR-ABL: control gene ratio according to an international scale)**	'Complete' : transcript non-detectable Major: ≤ 0,1 %	Check every 3 months; mutational analysis only in case of failure, suboptimal response or increased level of transcript

WBC, white blood cells

Treatment recommendations

Table 3. Treatment algorithm for CML in chronic phase in 2007 (Hehlmann et al., Lancet 2007)



* First-line IFN is usually limited to special indications such as imatinib intolerance, pregnancy or patients' preference. The algorithm accounts for the long survival times of patients who have a complete cytogenetic response with interferon alfa and that those who have complete cytogenetic response with interferon alfa or imatinib have identical survival rates.

References

1. Baccarani M, Saglio G, Goldman J, et al. Evolving concepts in the management of chronic myeloid leukemia: recommendations from an expert panel on behalf of the European LeukemiaNet. Blood 2006;108:1809–20.
2. Druker BJ, Guilhot F, O'Brien SG, Gathmann I, Kantarjian H, Gattermann N, Deininger MW, Silver RT, Goldman JM, Stone RM, Cervantes F, Hochhaus A, Powell BL, Gabrilove JL, Rousselot P, Reiffers J, Cornelissen JJ, Hughes T, Agis H, Fischer T, Verhoef G, Shepherd J, Saglio G, Gratwohl A, Nielsen JL, Radich JP, Simonsson B, Taylor K, Baccarani M, So C, Letvak L, Larson RA; IRIS Investigators. Five-year follow-up of patients receiving imatinib for chronic myeloid leukemia.N Engl J Med. 2006;355:2408-17. 3. Hehlmann R, Hochhaus A, Baccarani M on behalf of the European LeukemiaNet: Chronic myeloid leukaemia, Lancet 2007;370:342-50.