

Chronic myeloid leukaemia: tests, treatment by setting, options and problems during treatment

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A. Diagnosis, staging and baseline tests

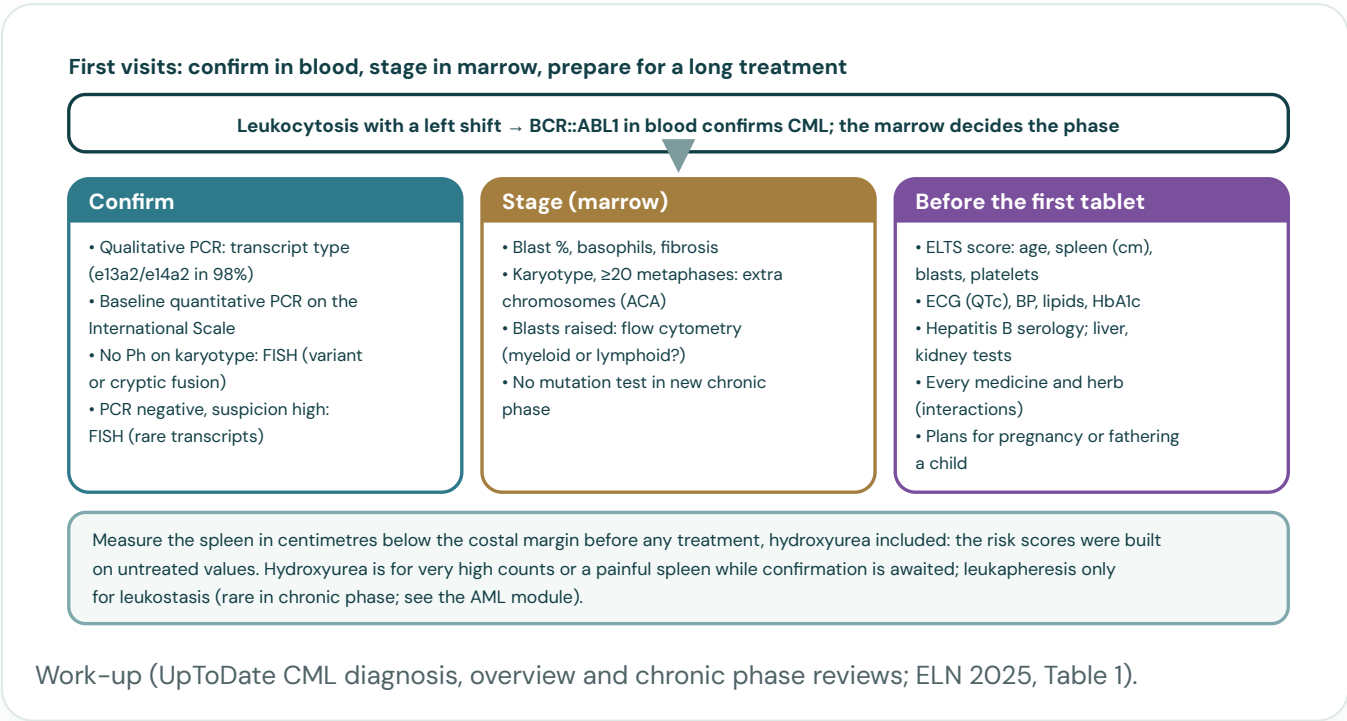


Table A. Diagnosis, staging and baseline tests, and what they change

Test	When	What it changes	Pitfalls
CBC + blood film	Every suspected case; every 2 weeks until CHR	Left-shifted granulocytes, basophils, blasts; phase clues	Leukemoid reaction looks similar: BCR::ABL1 decides
Qualitative PCR (transcript type) + quantitative PCR (IS)	At diagnosis, blood	Confirms CML; sets the baseline for all later monitoring	Routine kits detect p210 and p190 only: p230 and rarer types need FISH or a personalised assay
Marrow: morphology + karyotype (≥20 metaphases)	At diagnosis; at resistance or progression	Phase (blasts, basophils, fibrosis); extra chromosomes (ACA)	FISH alone misses ACA; not needed for routine follow-up

Test	When	What it changes	Pitfalls
FISH for BCR::ABL1	No Ph on karyotype; atypical transcripts	Finds variant or cryptic fusions	Interphase FISH ≥200 nuclei can document CCyR
Flow cytometry	Blasts raised	Myeloid vs lymphoid blast phase → AML-type vs ALL-type induction	Any lymphoblasts should raise suspicion of lymphoid BP
ELTS score	Before any treatment	High risk → 2G TKI or asciminib; ELN "warning"	Spleen in cm below the costal margin; values after hydroxyurea are not valid
ECG (QTc), BP, lipids, HbA1c	Baseline; lipids/HbA1c every 6–12 months on nilotinib or ponatinib	Avoid nilotinib with high CV risk; QT drugs	Repeat ECG 1–2 weeks after starting nilotinib or dasatinib
Hepatitis B serology; liver, kidney tests; lipase as indicated	Baseline	Reactivation risk; bosutinib dose; pancreatitis	Lipase may rise without pancreatitis
Kinase-domain mutation (NGS or Sanger)	Warning or unfavourable response, progression, blast phase; not at diagnosis in CP	Which TKI can still work (mutation figure, section 06)	Not needed after loss of MMR during TFR
HLA typing (patient and siblings)	Blast phase, transformed AP, resistance to a 2G TKI	Early donor search	Haploidentical donors widen access

B. Treatment by setting

Molecular milestones (BCR::ABL1 IS) for 1st, 2nd and 3rd line: ELN 2025 wording

	Favourable: no switch	Warning: switch may be needed	Unfavourable: switch preferred
Baseline	—	High-risk ACA or high ELTS	—
3 months	≤10%	>10%	>10% confirmed within 1–3 months
6 months	≤1%	>1–10%	>10%
12 months	≤0.1%	>0.1–1%	>1%
Any time	≤0.1%	>0.1–1%; loss of ≤0.1% (MMR)	Loss of response; resistance mutation; high-risk ACA

Decide on the trend, never on one result: repeat near a threshold within 1–2 months, ask about missed doses and interacting drugs first. "Late responders" whose values keep falling may not need a switch, especially older people with comorbidity: in CML Study IV, 10-year survival was about 80% even when the 3-, 6- or 12-month milestones were missed, but 55% if BCR::ABL1 was still >10% at 12 months.

A rising PCR without an obvious cause → karyotype, kinase-domain mutation test and a switch.

Milestones (ELN 2025, Table 4; UpToDate overview and chronic phase reviews; Lauseker 2023).

Table B. Treatment by setting

Setting	Usual approach	Alternatives	Key points
Chronic phase, ELTS low or intermediate	Imatinib (generic), a 2G TKI or asciminib	—	Same long-term survival; 2G/asciminib reach deep responses faster
Chronic phase, ELTS high	A 2G TKI or asciminib	Imatinib if nothing else is affordable	Fewer early progressions than imatinib
Very high count or painful spleen before confirmation	Hydroxyurea for days	Leukapheresis only for leukostasis	Start the TKI as soon as BCR::ABL1 is confirmed
Warning at a milestone	Check adherence and interactions; repeat PCR in 1–2 months	Switch TKI if the trend does not fall	Late responders may stay on the same TKI
Unfavourable / resistant after imatinib	Mutation test; a 2G TKI or asciminib	Higher-dose imatinib if no other option	Choice by mutation, comorbidity and cost
Resistant after a 2G TKI	Ponatinib or asciminib	Another 2G TKI rarely works	Start donor search now
T315I	Ponatinib or asciminib	Allogeneic HCT if inadequate response	Asciminib for T315I needs a higher dose than usual

Setting	Usual approach	Alternatives	Key points
Intolerance with a good response	Dose reduction with close monitoring	Switch by side-effect profile	Some toxicities always need a switch
Stable deep response	TFR attempt if ELN criteria met	Dose halving for a year first (DESTINY)	Monitor every 6–8 weeks for 6 months
Planning pregnancy (woman)	Deep response, then stop as for TFR	Stop at first positive test (MMR, regular cycles)	Interferon if counts need control; TKI only after week 16
De novo accelerated phase	A 2G TKI	—	No TFR attempts
Transformed accelerated phase	TKI by mutation, then allogeneic HCT	TKI alone if not eligible	Adherence and mutation test first
Myeloid blast phase	TKI + AML-type induction (intensive or HMA ± venetoclax), then HCT	TKI alone (palliative)	See the AML module
Lymphoid blast phase	TKI + Ph+ ALL regimen (or TKI + blinatumomab/inotuzumab), then HCT	TKI + steroid if frail	Lumbar puncture; see the ALL module

C. Treatment options: evidence and best fit

Kinase-domain mutation → which TKI may still work (ELN 2025, Table 5)

	Dasatinib	Nilotinib	Bosutinib	Ponatinib	Asciminib
T315I	—	—	—	✓	✓
Y253H	✓	—	✓	✓	✓
E255K/V	✓	—	—	✓	✓
V299L	—	✓	—	✓	✓
F317L/V/I/C, T315A	—	✓	✓	✓	✓
F359V/I/C	✓	—	—	✓	—
M244V	✓	✓	✓	✓	—
Myristoyl-pocket (A337V/T, P465S...)	✓	✓	✓	✓	—

Imatinib is not listed: most kinase-domain mutations resist it. Compound mutations (two in the same molecule) resist most TKIs, and some T315I-inclusive ones resist both ponatinib and asciminib. Rare transcripts without ABL1 exon 2 (e13a3, e14a3) are expected to resist asciminib.

The UpToDate in-vitro table agrees on T315I, Y253H, V299L and F317, but also lists bosutinib as an option for E255K/V and F359V, and adds A244V and A465S as asciminib-resistant: read the laboratory report with both tables.

Mutation-guided choice (ELN 2025, Table 5; UpToDate after-failure, accelerated and blast phase reviews).
✓ = recommended option; — = not recommended. In vitro data, not trials.

Table C. Treatment options: evidence and best fit

Option	Best fit	Evidence	Watch for
Imatinib (generic)	Lower-risk CP; cost-limited care; CV disease	IRIS, IRIS 10-year; generic = innovator in India	Cramps, periorbital oedema, fluid retention, nausea, diarrhoea
Dasatinib	High-risk CP; second line; pancreatitis history	CA180-O34	Effusions, pulmonary hypertension, bleeding, QTc; avoid in lung disease
Nilotinib	High-risk CP without CV risk; second line	ENESTnd	Arterial events, glucose and lipids, QTc, pancreatitis; twice daily, food rules
Bosutinib	CV disease; second line	Gambacorti-Passerini 2014	Early diarrhoea, liver enzymes; avoid in GI, liver or kidney disease
Asciminib	First line (FDA); after ≥2 TKIs; T315I	ASC4FIRST, ASCEMBL	Lipase, hypertension; take without food; myristoyl-pocket mutations resist
Ponatinib	T315I; failure of a 2G TKI; blast phase	PACE, OPTIC	Arterial occlusion, hypertension, liver; reduce the dose once BCR::ABL1 <1%
Interferon alfa	Pregnancy (any trimester)	Chelysheva 2024	Slow count control; molecular response not assured

Option	Best fit	Evidence	Watch for
Hydroxyurea	Short cytoreduction before confirmation	Kockerols 2022	Does not change milestones; teratogenic in animals
Allogeneic HCT	Blast phase, transformed AP, failure of ponatinib/asciminib	Lübking 2019 , Nicolini 2017	Early mortality 10–20%; GVHD; lifelong PCR after

D. Managing problems during treatment

Heart, vessels and lungs: the late side effects that change the choice of TKI

Nilotinib

- Coronary, cerebral, leg artery disease
- QTc; rare sudden death
- Higher glucose and cholesterol
- Avoid with diabetes or high CV risk

Ponatinib

- Arterial occlusion, dose-related
- Hypertension, heart failure, liver
- Lower dose once BCR::ABL1 <1%
- Not for most with CV disease

Dasatinib

- Pleural/pericardial effusion: up to 1 in 3
- Pulmonary arterial hypertension: stop for good
- Bleeding (platelet defect)
- QTc

Lower arterial risk

- Imatinib and bosutinib
- Asciminib: hypertension, lipase rise
- Imatinib: fluid retention
- Bosutinib: diarrhoea, liver

Before and during treatment (ELN 2025): ECG and blood pressure for everyone; lipids and HbA1c before and every 6–12 months on nilotinib or ponatinib; thyroid tests on ponatinib. Risk is highest in older people and with hypertension, diabetes, high lipids or smoking, whatever the TKI, and in the first years. Treat the risk factors; many clinicians add low-dose aspirin with nilotinib, dasatinib or ponatinib, although benefit is unproven.

Stop for good, do not just reduce: symptomatic or progressive arterial disease on nilotinib or dasatinib; pulmonary arterial hypertension on dasatinib; recurrent effusions despite dose reduction.

Cardiovascular and lung toxicity (UpToDate chronic phase and after-failure reviews; ELN 2025, Table 9; Jain 2019; Cortes 2018 PACE; Cortes 2021 OPTIC).

Table D. Managing problems during treatment

Problem	First steps	Then	Points
Nausea, cramps, rash, oedema, diarrhoea, fatigue (early)	Symptomatic care; take imatinib and bosutinib with food; correct electrolytes	Brief interruption (5–7 days) or dose adjustment	Usually settle; ask about lactose intolerance with diarrhoea
Low counts in the first weeks	Continue if mild: it is the leukaemia clearing	Hold or reduce for severe cytopenias; growth factors rarely	Avoid ESAs; transfusion for symptomatic anaemia
Breathless or coughing on dasatinib	Chest X-ray; look for effusion, pneumonitis, infection, heart failure	Interrupt or reduce; drain if large	Recurrent effusions or pulmonary hypertension: switch for good
Chest pain, claudication, TIA on nilotinib or ponatinib	Urgent CV assessment	Stop that TKI; switch (imatinib, bosutinib or TFR if eligible)	Control BP, glucose, lipids, smoking from the start
QTc prolongation	Correct potassium and magnesium; stop QT-prolonging drugs	Dose adjustment or switch	ECG 1–2 weeks after starting nilotinib or dasatinib
Raised lipase or abdominal pain	Check lipase; image if symptomatic	Reduce or hold; switch if it persists	Nilotinib, bosutinib, asciminib, ponatinib

Problem	First steps	Then	Points
Bleeding or bruising on dasatinib	Platelet count; review antiplatelets and anticoagulants	Drug holiday usually enough	Qualitative platelet defect with normal counts
Aches after stopping the TKI	Simple analgesia or an NSAID	Short steroid course occasionally	Withdrawal syndrome in 20–30%; usually self-limiting
Missed doses, cost or travel problems	Ask at every visit; involve family; patient-assistance programmes	Simplify the schedule; generic options	Adherence $\leq$ 80%: no MMR (Marin 2010)
New medicine or herb	Check CYP3A4 interactions and QT effect	Choose an alternative	PPIs reduce dasatinib and nilotinib absorption (special formulations exist)