touch™ HAEMATOLOGY

Innovations and advances in CML:

A focus on navigating early-line options and maintaining QoL

Practice aid for healthcare professionals

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This practice aid is part of an independent medical education activity supported by Novartis and provided by touchIME.
It is for healthcare professionals outside of the USA and UK.

Overview of approved TKIs for managing CML-CP

TKI	MoA	EMA indication	Selected special warnings/precautions
Imatinib[1]	Binds to the ATP binding site of ABL1; agents differ in their potency and off-target effect profile[7]	Adult and paediatric patients with newly diagnosed Ph+ CML-CP in the 1L, where HSCT is not an option	**Risk of** fluid retention, GI haemorrhage, TLS, TMA **Monitor** patients with hepatic dysfunction, cardiac risk factors, history of renal failure or thyroidectomy
Dasatinib[2]		Adult patients with newly diagnosed Ph+ CML-CP or CML (-CP/-AP/-BP) following resistance/ intolerance to prior therapy, including imatinib	**Risk of** bleeding, fluid retention, PAH, CV AEs, QT prolongation, TMA
Nilotinib[3]		Adult/paediatric patients with newly diagnosed Ph+ CML-CP; adult patients with CML-CP/-AP following resistance/intolerance to prior therapy including imatinib	**Risk of** QT prolongation, sudden death, fluid retention/oedema, CV AEs
Bosutinib[4]		Adult/paediatric (≥6 years) patients with newly diagnosed Ph+ CML-CP or following resistance/intolerance to ≥1 TKI where imatinib/nilotinib/dasatinib are not suitable	**Risk of*** liver function abnormalities, diarrhoea/vomiting, fluid retention, serum lipase, infections, CV toxicity, proarrhythmic potential, severe skin reactions, TLS, renal impairment
Ponatinib[5]		Adult patients with CML (-CP/-AP/-BP) who are resistant to dasatinib/nilotinib; are intolerant to dasatinib/nilotinib and, for clinical reasons, cannot be treated with imatinib; or have the *T315I* mutation	**Risk of** AOEs, VTEs, hypertension, aneurysms and artery dissections, congestive heart failure, pancreatitis and serum lipase, hepatotoxicity, haemorrhage, PRES, QT prolongation
Asciminib[6]	Allosteric inhibitor, specifically targeting the myristoyl pocket of the BCR::ABL1 protein[7]	Adult patients with Ph+ CML-CP treated with ≥2 TKIs • CHMP positive opinion (17 October 2025) for the treatment of adult patients with Ph+ CML-CP[8]	**Risk of** pancreatic toxicity, QT prolongation, hypertension

- Caution should be exercised with the concomitant administration of *BCR::ABL1*-targeting TKIs and other drugs
- Patients should be tested for HBV infection before starting treatment with a BCR::ABL1 TKI, since these agents can reactivate the HBV
- Key low-grade side effects include fatigue, rash, peripheral oedema, pain (headache, myalgia, muscle cramp, arthralgia, bone pain) and GI side effects (diarrhoea, nausea, vomiting)[9]
- Grade 2 side effects, such as fatigue or GI side effects, can seriously impact patient QoL, potentially leading to treatment non-adherence[9]
- Haematologic side effects are very common to all TKIs; the relevant labels carry a special warning for myelosuppression

*Asian patients should be monitored closely due to a lower clearance rate and increased exposure.

Therapeutic strategies to improve treatment tolerability

ASC4START (NCT05456191), phase IIIb, asciminib vs nilotinib in the first line: interim analysis (median follow-up: 9.7 months)[10]

Primary endpoint: time to treatment discontinuation due to AEs (TTDAE), defined as time from first dose of study treatment to discontinuation due to AEs (including death due to AE)[10,11]

Primary endpoint was met at interim analysis, showing a statistically significant difference in TTDAE in favour of asciminib: HR (95% CI): 0.45 (0.25–0.81), p=0.004[10]

Interim analysis supported by primary analysis: HR (95% CI): 0.46 (0.27–0.76), p=0.001[11]

Preliminary PRO data from ASC4FIRST for three PROMs also favour asciminib vs IS-TKI indicating better QoL and reduced symptom burden[12]

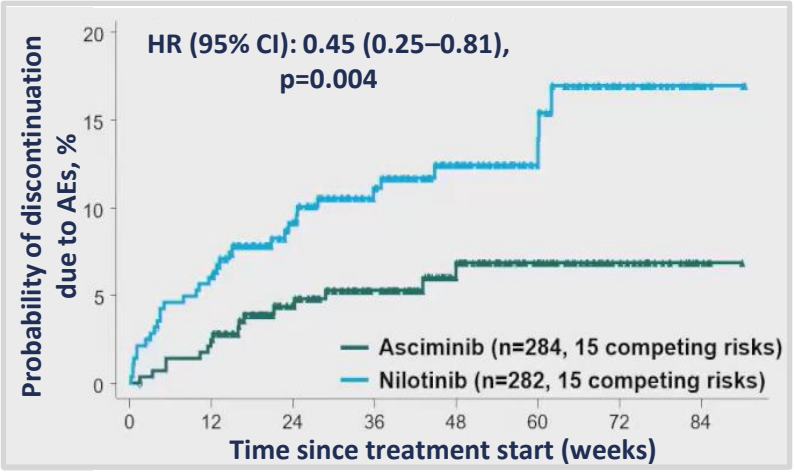


Figure from Hochhaus A, et al. ASCO 2025, reproduced with permission.

Approaches for managing patients with treatment intolerance

"The most important point is to identify that our patient is having issues with their TKI… and understanding how much these symptoms are really bothering them… these are relative to the patient, their QoL and what they do"

Dr Ehab Atallah, Medical College of Wisconsin, Milwaukee, WI, USA[13]

1	**Supportive measures**	Patients should be educated about side effects and their time course; side effects may improve over time[14]
2	**Dose reductions**	May be considered, if the patient has a good sustained response; data have shown it can reduce side effects and improve QoL[15]
3	**Treatment switching**	A balance must be struck between switching too quickly or too slowly;[16,17] the patient must be involved in the decision[18]
4	**Treatment discontinuation**	Suitable for a select group of patients,* who are willing to be monitored; they must understand the available data before starting[16]

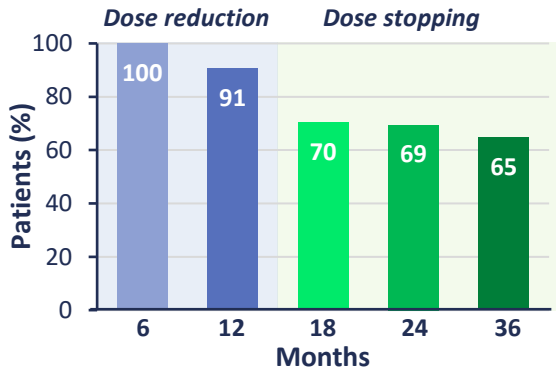
*Optimally the patient will have been on a TKI for >5 years and have a DMR for >3 years if MR4 or >2 years if MR4.5.[16]

Recent data for strategies to optimize dosing and improve patient QoL in CML

HALF (NCT04147533), phase II, N=207[19,20]

To evaluate the efficacy and safety of TKI discontinuation following a two-step reduction in dosing in patients in DMR*

MRFS (median follow-up: 35.9 months)



TKI withdrawal syndrome: 12%

- The majority of patients experienced musculoskeletal pain

RODEO (EUCT: 2024-516511-24-00), N=148[21]

To evaluate the effectiveness of patient-guided dose reduction at 6 months (interim analysis) in patients with CML in stable remission

Dose reduction, median (IQR): 25% (8.4)

Dose reduction failure at 6 months

- 6/146† patients (4%) re-escalated dosing
- MRFS (95% CI): 0.972 (0.946–0.999)

Changes in QoL at 6 months

- Statistically significant improvements were observed on several scales, particularly for women and patients treated with dasatinib

- Patient-guided dose reduction, supported by SDM and a patient decision aid, appears to be a safe and well-accepted approach

Shared decision-making with patients with CML[22]

1. Inform the patient of a change and emphasize the importance of their input
2. Discuss the pros and cons of potential treatment options
3. Explore the patient's personal preferences
4. Discuss the patient's decision/need for more time for further reflection

- Patient decision aids enhance patient knowledge, reduce decisional conflict and improve understanding of risks, benefits and personal values; they foster more informed and collaborative treatment decisions[23]

*Half of the standard dose during the first 6 months, followed by the same reduced dose given every other day during the next 6 months.
†Patients included in the analysis.

Abbreviations and references

Abbreviations

1L, first-line; AE, adverse event; AOE, arterial occlusive event; AP, accelerated phase; ATP, adenosine triphosphate; BID, twice a day; BL, baseline; BP, blast phase; CHMP, Committee for Medicinal Products for Human Use; CI, confidence interval; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; DMR, deep MR; EMA, European Medicines Agency; GI, gastrointestinal; HBV, hepatitis B virus; HR, hazard ratio; HSCT, haemopoietic stem cell transplant; IQR, interquartile range; IS-TKI, investigator-selected-TKI; MoA, mechanism of action; MR, molecular response; MMR, major MR; MRFS, molecular response-free survival; PAH, pulmonary arterial hypertension; Ph+, Philadelphia chromosome-positive; PRES, posterior reversible encephalopathy syndrome; PRO, patient-reported outcomes; PROM, PRO measures; QD, every day; QoL, quality of life; SDM, shared decision-making; TKI tyrosine kinase inhibitor; TLS, tumour lysis syndrome; TMA, thrombotic microangiopathy; VTE, venous thromboembolism.

References

1. EMA. Imatinib SmPC.*
2. EMA. Dasatinib SmPC.*
3. EMA. Nilotinib SmPC.*
4. EMA. Bosutinib SmPC.*
5. EMA. Ponatinib SmPC.*
6. EMA. Asciminib SmPC.*
7. Lee H, et al. *Int J Hematol*. 2021;113:632–41.
8. CHMP. Asciminib–variation to marketing authorisation.*
9. Apperley JF. *Lancet*. 2015;385:1447–59.
10. Hochhaus A, et al. Presented at: The American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, IL, USA. 30 May–3 June 2025. #6501.
11. Mahon F-X, et al. Presented at: The 27th Annual John Goldman Conference on CML in Estoril, Portugal. 10–12 October 2025.
12. Hochhaus A, et al. Presented at: EHA 2025, Milan, Italy. 12–15 June 2025. #PS1588.
13. touchHAEMATOLOGY. Innovations and advances in CML: Focus on navigating early-line options and maintaining QoL (part 3). Available at: https://touchhaematologyime.org/advances-in-CML-quality-of-life (accessed 20 November 2025).
14. Steegman JL, et al. *Leukemia*. 2016;30:1648–71.
15. Chen J, et al. *Clin Pharmacol*. 2025;17:211–25.
16. Apperley JF, et al. *Leukemia*. 2025;39:1797–813.
17. Busque L, et al. *Blood Cancer J*. 2025;15:35.
18. Lang F, et al. *Haematologica*. 2025;doi:10.3324/haematol.2025.287772.
19. ClinicalTrials.gov. NCT04147533. Available at: http://bit.ly/49sCwhl (accessed 20 November 2025).
20. Žácková D, et al. Presented at: The 27th Annual John Goldman Conference on CML in Estoril, Portugal. 10–12 October 2025.
21. Lokhorst DN, et al. *Haematologica*. 2025;doi: 10.3324/haematol.2025.288516.
22. Stiggelbout AM, et al. *Patient Educ Couns*. 2015;98:1172–9.
23. Stacey D, et al. *Cochrane Database Syst Rev*. 2024;1:CD001431.

***All SmPCs and CHMP opinion on asciminib are available at: www.ema.europa.eu according to the product name (accessed 20 November 2025).**

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