Introduction to the Review Series. Chronic myeloid leukemia in 2026

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Introduction

In this issue of *Haematologica* we present a series of papers outlining the outstanding, compelling clinical and biological questions about chronic myeloid leukemia (CML).

We can hear you asking: "Why should I ever read *anything* about CML again? Haven't we finished with it?"

No, *we haven't*, and learning more about CML is worthwhile for several reasons. First, it is an intensely interesting leukemia. CML is the prime example of the "bench to bedside" paradigm. CML was the first disease with a pathognomonic chromosomal marker (the Philadelphia chromosome), the first with a defined genetic lesion (the *BCR::ABL1* rearrangement), the first for which allogeneic transplant was established as the upfront treatment of choice, the first disease with a specific small molecular inhibitor directed at the core molecular lesion (tyrosine kinase inhibitors), and the first and best demonstration of the clinical utility of molecular tracking of disease burden (the detection of *BCR-ABL* mRNA in the peripheral blood). Twenty years ago, without allogeneic transplantation, patients would inevitably progress from chronic to lethal blast phase in 5-7 years. Now, CML patients treated with tyrosine kinase inhibitors experience essentially a normal lifespan. Can there be a better example of the power and promise of science to intervene in pathology?

Second, CML is still relevant. The concept and utilization of minimal residual disease (MRD) are becoming more common across hematologic malignancies, and one could argue that CML has blazed the trail. The principles of understanding response and resistance and using MRD as guideposts for therapeutic milestones is being approached in acute lymphoblastic leukemia, acute myeloid leukemia and myeloma as well as CML. The use of MRD to prompt treatment discontinuation has been established in CML, and lessons learned are bound to be applied to other leukemias. Moreover, the biology of CML constitutes a genetic clock whereby unopposed BCR-ABL signaling will inevitably lead to progression to either a myeloid or lymphoid leukemia. Surely this is a unique disease to study the biology of differentiation, stem cell and lineage determination, genetic instability, and mechanisms of disease resistance (since blast crisis is very poorly responsive to any treatment modalities, including ablative transplantation).

Third, a deeper understanding of CML is practical. At steady state, the prevalence of any event is determined by the incidence and mean duration of the event (P = I x D). Thus, while CML is a rare leukemia (1-3 cases per 100,000 people), the fact that patients with CML now live normal lifespans means the number of CML patients followed by physicians must climb steadily over the years. Even if complications of CML such as resistance and progression are relatively unusual, the sheer volume of cases means that physicians will encounter these problems more and more often. To be ready and equipped, knowledge is power.

We have brought together an all-star lineup for your education and enjoyment. Jorge Cortes' team discusses the factors that go into picking a first-line tyrosine kinase inhibitor,[1] while the groups of S. Tiong Ong[2] and Michael Deininger[3] offer two different angles to examine and explain resistance. Kathryn Flynn and Ehab Atallah discuss quality-of-life strategies,[4] and Vivian Oehler *et al*. review preventing and managing tyrosine kinase inhibitor toxicities.[5] Lastly, Delphine Rea educates us on the possibility of treatment-free remissions in CML cases with long and deep responses.[6] Together these six reviews cover the horizon of the CML experience and should leave you convinced that CML (in homage to Monty Python) is *not dead yet*.

Haematologica hopes you enjoy the series and, as always, we welcome your comments and suggestions.

Disclosures

No conflicts of interest to disclose.

References

1. Jain AG, Dalgetty M, Cortes JE. Is there a best frontline therapy in chronic myeloid leukemia? Haematologica 2026;111(7):2216-2226.
2. Krishnan V, Shyamsunder P, Ong ST. Understanding drug resistance in chronic myeloid leukemia through the lens of leukemic stem cell states: insights from single-cell analyses. Haematologica 2026;111(7):2227-2243.
3. Cruz-Rodriguez N, Torres-Llanos Y, Deininger MW. Intrinsic cellular resistance to BCR::ABL1 inhibitors. Haematologica 2026;111(7):2244-2265.
4. Flynn KE, Atallah E. Improving quality of life for patients with chronic myeloid leukemia through supportive care, low-dose therapy, switching, and treatment-free remission. Haematologica 2026;111(7):2281-2290.
5. Oehler VG, Berman E, Huang IJ. Management of chronic myeloid leukemia with tyrosine kinase inhibitors: adverse events, toxicities and therapy dosing. Haematologica 2026;111(7):2266-2280.
6. Rea D. Prognostic factors in chronic myeloid leukemia: at diagnosis and for treatment-free remission. Haematologica 2026;111(7):2207-2215.