

The role of molecular biology in the diagnosis and monitoring of chronic myeloid leukemia: Experience from the hematology laboratory of Avicenna hospital in Marrakech

Awati-El Mehdi *, Mounib-Yassine, Marjane-Yassine, Dergaoui-Hanane and Chakour Mohamed

Hematology Laboratory Avicenna Hospital in Marrakech, Morocco.

World Journal of Biological and Pharmaceutical Research, 2025, 08(02), 036-040

Publication history: Received on 09 April 2025; revised on 23 June 2025; accepted on 26 June 2025

Article DOI: <https://doi.org/10.53346/wjbpr.2025.8.2.0020>

Abstract

Background: Advances in molecular biology have transformed the diagnosis and therapeutic monitoring of chronic myeloid leukemia (CML), particularly through the implementation of rapid, standardized testing such as GeneXpert. This study, conducted at the Hematology Laboratory of Avicenna Hospital in Marrakech, highlights the clinical impact of these innovations in a resource-limited setting.

Methods: We conducted a retrospective analysis of 10 patients diagnosed with CML between 2015 and 2021. BCR-ABL1 transcript levels were monitored using the GeneXpert assay, with data collected from laboratory records and clinical charts.

Results: A major molecular response (MMR) was achieved in 70% of patients by 12 months, with rapid early molecular responses observed in most cases. Imatinib was used as first-line therapy in all patients. Treatment escalation to nilotinib and masitinib was necessary in cases of suboptimal response or resistance. The presence of resistance-associated mutations, including T315I, was identified as a key therapeutic challenge.

Conclusions: The integration of molecular diagnostic tools such as GeneXpert significantly improves disease monitoring and response assessment in CML. However, disparities in access to modern treatments and limitations in mutation-guided therapy remain major challenges. Strengthening public-private partnerships is essential to expand access to advanced diagnostics and reduce inequities in care delivery.

Keywords: Chronic Myeloid Leukemia; BCR-ABL1; Gene Xpert; Molecular Response; Tyrosine Kinase Inhibitors; Resource-Limited Settings

1. Introduction

Chronic myeloid leukemia (CML) is a rare hematologic malignancy and a classic model of oncogenesis driven by a specific chromosomal abnormality: the Philadelphia chromosome (Ph1). This abnormality results from a reciprocal translocation, t(9;22)(q34;q11), which gives rise to the BCR-ABL1 fusion gene. The constitutive tyrosine kinase activity of the BCR-ABL1 protein is central to the pathogenesis of CML [1,2].

The advent of tyrosine kinase inhibitors (TKIs), in conjunction with advances in molecular biology, has revolutionized the management of CML. These innovations have enabled not only the rapid confirmation of diagnosis but also precise therapeutic monitoring through quantification of BCR-ABL1 transcripts [3,4].

* Corresponding author: Awati-El Mehdi

The introduction of reverse transcription–polymerase chain reaction (RT-PCR) techniques has greatly enhanced the sensitivity of diagnostic and monitoring tools [5]. Among them, the GeneXpert assay stands out for its ability to deliver standardized, rapid results based on the international scale (IS) [6]. However, access to such technologies remains limited in many regions, impeding optimal patient management.

This study presents the experience of the Hematology Laboratory at Avicenna Hospital in Marrakech (HMA), focusing on the contributions of modern molecular diagnostics—particularly GeneXpert—to the diagnosis and follow-up of CML.

2. Patients and Methods

This descriptive, observational, and retrospective study was conducted over a six-year period (April 2015 to February 2021) and included 10 patients referred for the diagnosis and biological follow-up of chronic myeloid leukemia (CML) at the Hematology Laboratory of Avicenna Hospital (HMA) in Marrakech.

2.1. Inclusion and Exclusion Criteria

Patients were eligible if they had a confirmed diagnosis of CML based on molecular or cytogenetic testing and were monitored using quantitative RT-PCR for BCR-ABL1 transcript levels. Patients with incomplete data or lacking molecular follow-up were excluded from the study.

2.2. Molecular Analysis

Quantification of BCR-ABL1 transcripts was performed using the GeneXpert assay on peripheral blood samples. The assay provided standardized results expressed on the International Scale (IS).

2.3. Data Collection and Statistical Analysis

Clinical and laboratory data were retrieved from patient medical records and the laboratory's internal database. Statistical analysis was conducted using Excel and SPSS software. Quantitative variables were expressed as means with standard deviations. Due to the small sample size, descriptive statistics were primarily used.

3. Results

3.1. Patient Characteristics

Among the 10 patients included in the study, the mean age was 59.2 years (± 8.6), with a male predominance (70%; male-to-female ratio: 2.3). All patients were covered by a social security system.

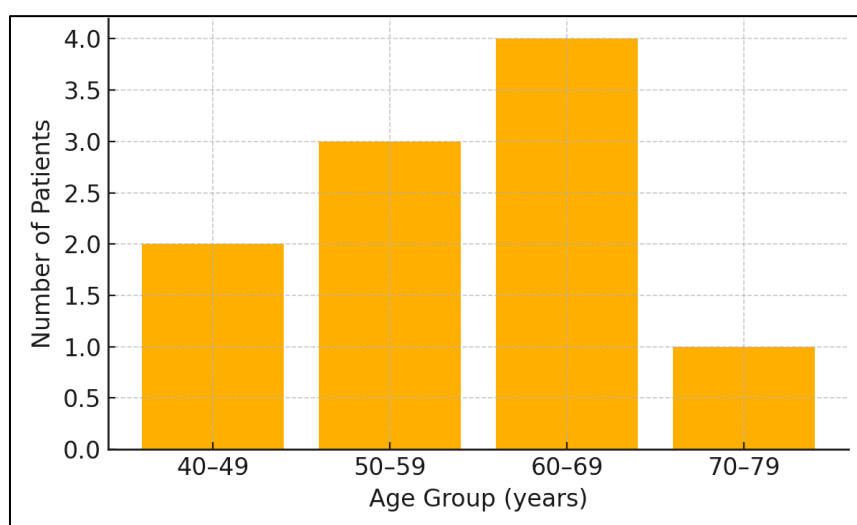


Figure 1 Age distribution of patients

3.2. Biological Diagnosis

All patients presented with marked leukocytosis at diagnosis, with a mean white blood cell count of $166.9 \times 10^9/L$. Thrombocytosis was observed in 80% of cases, with a mean platelet count of $482.2 \times 10^9/L$.

Molecular analysis confirmed the presence of BCR-ABL1 transcripts in all patients, with a median BCR-ABL1/ABL1 ratio of 68%, confirming the diagnosis of CML.

3.3. Treatment and Molecular Follow-up

All patients received first-line treatment with imatinib at a dose of 400 mg/day. A favorable early response, defined as BCR-ABL1 $\leq 10\%$ at 3 months, was observed in 60% of patients.

- Four patients required escalation to second-line therapy with nilotinib (400 mg twice daily).
- Two patients were further treated with third-line dasatinib (140 mg/day) due to resistance or intolerance.

3.4. Molecular Response

A major molecular response (MMR) was achieved in 70% of patients by 12 months. Patients who responded favorably exhibited a rapid decline in BCR-ABL1 transcript levels, with MMR reached between 6 and 9 months in most cases.

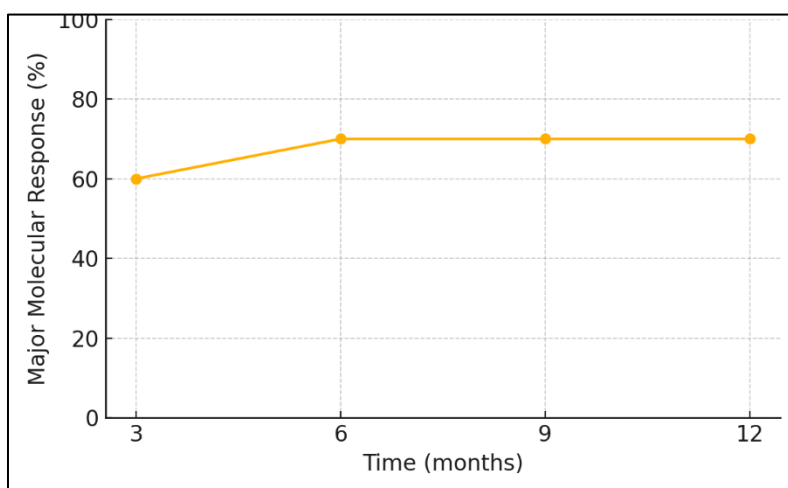


Figure 2 Molecular response rate over time

4. Discussion

This study underscores the effectiveness of the GeneXpert assay in the diagnosis and monitoring of chronic myeloid leukemia (CML). With a major molecular response (MMR) achieved in 70% of patients by 12 months, our findings align with previous studies emphasizing the importance of early BCR-ABL1 transcript quantification [3]. For example, a recent multicenter trial reported similar MMR rates at 12 months among patients treated with first- and second-generation tyrosine kinase inhibitors (TKIs) [4].

However, unlike those studies, our cohort primarily received imatinib as first-line therapy—reflecting local limitations in access to newer TKIs. In resource-limited settings, delayed diagnosis and poor treatment adherence often result in lower response rates [2]. These constraints highlight the critical need to expand access to molecular diagnostics and patient education initiatives.

International data suggest that second-generation TKIs (e.g., nilotinib, masitinib) offer faster and deeper molecular responses, with improved tolerability. For instance, nilotinib has been shown to achieve MR4.5 in up to 50% of patients within 12 months, compared to 30% for imatinib [6]. Nevertheless, such therapies remain difficult to implement in low-resource regions due to financial and logistical barriers.

Our findings also reflect the emerging concern of resistance to TKI therapy, often driven by mutations in the BCR-ABL1 kinase domain. In our cohort, two patients required escalation to second- or third-line treatment due to therapeutic

resistance. These results are consistent with recent literature on resistance-associated mutations, particularly T315I, which poses a major therapeutic challenge [1].

In this context, innovative approaches such as comprehensive mutation profiling and next-generation sequencing (NGS) could enhance risk stratification and treatment selection. One study demonstrated that pre-therapy mutation screening improves early identification of patients likely to benefit from specific TKIs [7].

Moreover, our data highlight the importance of adherence support and psychosocial interventions. Recent programs combining education and structured follow-up have significantly improved adherence rates, directly impacting clinical outcomes.

Addressing the broader challenges requires ambitious public health policies aimed at reducing the cost of TKIs and expanding access to novel therapies. Public-private partnerships involving governments, pharmaceutical companies, and non-governmental organizations (NGOs) may offer sustainable solutions to these economic barriers [8].

Ultimately, this study reinforces the vital role of molecular diagnostics—particularly GeneXpert—in improving CML management. Our findings are consistent with the existing literature and confirm the value of early detection and precise molecular monitoring. Nevertheless, persistent disparities in access to advanced diagnostics and therapies remain a major obstacle, especially in low-resource countries.

Collaborative action between public and private stakeholders, supported by comprehensive health policies, is essential to address these gaps. Targeted education programs and broader availability of second-generation TKIs could significantly improve outcomes and quality of life for patients. With the integration of innovative tools and equitable strategies, healthcare systems can make meaningful progress in the management of CML.

5. Conclusion

This study confirms the essential role of molecular biology techniques—particularly the GeneXpert assay—in the diagnosis and longitudinal monitoring of chronic myeloid leukemia (CML). Our results demonstrate significant improvements in therapeutic management through early detection and precise assessment of molecular response.

However, persistent challenges remain, including disparities in access to advanced therapies and the management of resistance-associated mutations such as T315I. Expanding access to diagnostic tools and next-generation TKIs is imperative for achieving equitable and effective care.

Strengthened collaboration between public and private stakeholders is urgently needed to address these gaps. By adopting context-appropriate strategies that integrate innovative technologies with health system reforms, substantial progress can be made toward optimizing CML outcomes worldwide.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflicts of interest related to this study.

Statement of ethical approval

This study was conducted in accordance with the Declaration of Helsinki. It was approved by the institutional ethics committee of Avicenna Military Hospital, Marrakech, Morocco.

Statement of informed consent

Informed consent was obtained from all participants following a clear explanation of the study's objectives and procedures.

References

- [1] Rowley JD. A new consistent chromosomal abnormality in chronic myelogenous leukemia identified by quinacrine fluorescence and Giemsa staining. *Nature*. 1973;243(5405):290–293.

- [2] Goldman JM, Melo JV. Chronic myeloid leukemia—advances in biology and new approaches to treatment. *N Engl J Med*. 2003;349(15):1451–1464.
- [3] Hehlmann R, Hochhaus A, Baccarani M. Chronic myeloid leukaemia. *Lancet*. 2007;370(9584):342–350.
- [4] Saglio G, et al. Dasatinib versus imatinib in newly diagnosed chronic-phase chronic myeloid leukemia. *N Engl J Med*. 2010;362(24):2260–2270.
- [5] Branford S, et al. Monitoring CML patients responding to tyrosine kinase inhibitors: recommendations for harmonizing BCR-ABL transcript detection and reporting. *Blood*. 2006;108(1):28–37.
- [6] Hughes TP, et al. Frequency of major molecular responses to imatinib or interferon alfa plus cytarabine in newly diagnosed chronic myeloid leukemia. *N Engl J Med*. 2003;349(15):1423–1432.
- [7] Shah NP, et al. Sequential ABL kinase inhibitor therapy selects for compound drug-resistant BCR-ABL mutations with altered oncogenic potency. *J Clin Invest*. 2007;117(9):2562–2569.
- [8] Radich JP, et al. Treatment of chronic myeloid leukemia: current practice and challenges. *Am J Hematol*. 2018;93(2):265–274.
- [9] Kumar S, et al. Public-private partnerships to improve access to tyrosine kinase inhibitors: case studies from developing countries. *Health Policy Plan*. 2022;37(1):45–52.