Introducing Diagnostic Testing for Chronic Myeloid Leukemia in a Public Hospital Setting in Western Kenya

Millicent Orido, BS; Teresa Cherop Lotodo, MD; Nicholas Kigen, BS; Ryan Stohler, BS; Terry A. Vik, MD; Gail H. Vance, MD

• ***Context.***—**Chronic myeloid leukemia (CML) is a myeloproliferative disorder characterized by proliferation of the granulocytic cell line. The incidence of CML in Kenya is estimated at near 2000 cases annually. The disorder is associated with a poor prognosis without treatment. Tyrosine kinase inhibitors are approved for treatment in adults and children with confirmed disease. Diagnostic testing for CML in the public setting in Kenya is limited and not covered by the Kenyan National Health Insurance Fund.**

Objective.—**To establish a clinical fluorescence in situ hybridization assay for the diagnosis of CML in the Academic Model Providing Access to Healthcare (AMPATH) Reference Laboratory in Eldoret, Kenya.**

Design.—**Peripheral blood and bone marrow smears were split between the AMPATH Reference Laboratory and the Indiana University Cytogenetics Laboratory for concordance studies.**

Results.—**Seventeen specimens from patients with a provisional diagnosis of CML were studied by fluorescence in situ hybridization in both the AMPATH and Indiana University Cytogenetics laboratories. The analysis for 1 specimen could not be completed by both laboratories, and the results for 1 other specimen were discordant. The interpretations of 15 of 16 specimens (93.7%) were concordant. Normal specimens were also studied to establish the normal range for the assay.**

Conclusions.—**We report the establishment of diagnostic testing for CML in the AMPATH Reference Laboratory and the Moi Teaching and Referral Hospital in Eldoret, Kenya.**

(*Arch Pathol Lab Med*. 2025;149:613–617; doi: 10.5858/arpa.2024-0264-OA)

Chronic myeloid leukemia (CML) is a stem cell disorder and one of the classic myeloproliferative neoplasms.[1] The disease is characterized by t(9;22)(q34;q11.2), a reciprocal translocation first suggested in 1960 and delineated in 1973.[2,3] The translocation juxtaposes BCR activator of RhoGEF and GTPase (*BCR*) on chromosome 22 with ABL proto-oncogene 1, non-receptor tyrosine kinase (*ABL1*) from chromosome 9, resulting in a fusion gene on chromosome 22 and transcript with constitutive tyrosine kinase signaling.[4,5] The derivative chromosome 22 is also referred to as the Philadelphia chromosome in acknowledgement of the first identification by Nowell and Hungerford.[2]

The t(9;22) translocation is identified in approximately 90% to 95% of CML cases by conventional cytogenetics.[1] The remaining cases result from complex 3- or 4-way translocations involving chromosomes 9 and 22 and other chromosomes or cryptic rearrangements not identified at the resolution of bright-field microscopy.[6,7] Cryptic rearrangements are typically not identified by conventional cytogenetics but are usually identified by fluorescence in situ hybridization (FISH).[8]

A typical diagnostic workup for CML in the United States includes a complete blood cell count with differential; bone marrow (BM) aspirate and biopsy for morphologic review and cytogenetic evaluation; and quantitative polymerase chain reaction (qPCR) using the International Scale for *BCR-ABL1* transcripts.[9] FISH is usually routine at diagnosis but may be used as an alternative strategy when cytogenetic evaluation is not possible or a cryptic rearrangement is suspected.[8,9]

The disorder is associated with a poor prognosis without treatment.[10] Tyrosine kinase inhibitors (TKIs) are approved for treatment in adults and children with confirmed disease.[10,11] Imatinib is a first-generation TKI and generally available internationally, including in Kenya.[12,13] The drug targets the adenosine triphosphate–binding pocket of *ABL1*, rendering its kinase activity null.[14]

Worldwide, the incidence of CML is approximately 1 to 2 cases per 100 000 population.[1] Typical onset occurs around age 50 to 55 years with a reported earlier age of onset in low- and middle-income countries.[1] The incidence of CML in Kenya is estimated at near 2000 cases per year with children 0 to 19 years representing approximately 10% of the total cases.[15] Moi Teaching and Referral Hospital (MTRH), a public hospital, in partnership with Academic Model Providing Access to Healthcare (AMPATH), is the only tertiary care hospital in western Kenya providing comprehensive

Accepted for publication December 17, 2024.
Published online January 30, 2025.

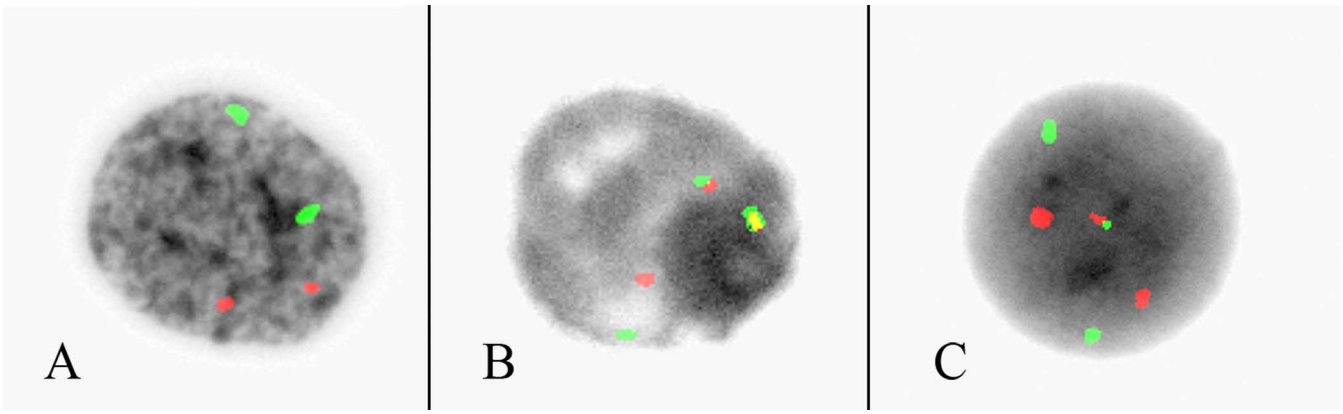
From the Academic Model Providing Access to Healthcare (AMPATH) Reference Laboratory, Eldoret, Kenya (Orido, Kigen); the Department of Pathology, School of Medicine, Moi University, Eldoret, Kenya (Lotodo); and the Departments of Medical and Molecular Genetics (Stohler, Vance) and Pediatrics (Vik), Indiana University School of Medicine, Indianapolis.

Work by Vance is supported by the Sutphin Family Professorship.

The authors have no relevant financial interest in the products or companies described in this article.

Some content was presented during a poster session during the SIOP—International Society of Pediatric Oncology meeting; September 30, 2022; Barcelona, Spain.

Corresponding author: Gail H. Vance, MD, Department of Medical and Molecular Genetics, Indiana University School of Medicine, 975 W Walnut St IB 130, Indianapolis, IN 46202 (email: ghvance@iu.edu).



*A, A nucleus with normal (unrearranged) signal pattern of RRGG (2 signals for ABL proto-oncogene 1, non-receptor tyrosine kinase [*ABL1*] and 2 signals for BCR activator of RhoGEF and GTPase [*BCR*]). B, A nucleus with an abnormal signal pattern, RGFF, representative of t(9;22). C, A variant signal pattern with RRGGF (2 signals for* ABL1*, 2 signals for* BCR*, and a single fusion signal). Abbreviations: F, fusion (*ABL1 *and* BCR *fused); G, green signal (*BCR*); R, red signal (*ABL1*) (original magnification ×100).*

care.[16–18] A 10-year review of the Eldoret Cancer Registry, which captures data from the western region of Kenya, showed that CML was the third common hematologic malignancy after non-Hodgkin lymphoma and lymphoblastic leukemia, accounting for approximately 12% of all cases.[19] The number of patients seen for leukemia at MTRH, Eldoret, Kenya is approximately 70 per month.[19]

In a low- and middle-income country setting, like Kenya, the diagnosis of hematologic malignancies is largely based on morphology. Morphologic diagnosis is limited to a description of the tissue and cells under the microscope. In CML, patient diagnosis has been based on history and physical examination to check for splenomegaly, complete blood count, peripheral blood (PB) film, and BM aspirate/trephine biopsy. Diagnostic testing for CML in the public setting in Kenya is limited and not covered by the Kenyan National Health Insurance Fund. Recently, MTRH established qPCR diagnostic testing in the hematology laboratory. However, this testing is available only to patients who pay out of pocket. Conventional cytogenetic analysis is not available at either MTRH or the AMPATH Reference Laboratory (ARL).

At ARL in Eldoret, Kenya, a FISH platform was established in 2018 in collaboration with the pediatric oncology program and the Indiana University (IU) Cytogenetics Laboratory, Indianapolis. Since then, FISH has been clinically validated for clinical use for Burkitt lymphoma for the *MYC* and t(8;14) probes.[20] The goal of this study was to establish a FISH assay for CML for rapid diagnosis to enable local treatment with a TKI. We report here the establishment of diagnostic testing for CML at the ARL in collaboration with MTRH in Eldoret, Kenya.

METHODS

FISH methodology with a dual-color/dual-fusion (DC/DF) *BCR*::*ABL1* probe set was applied to both PB and BM smears. MRTH patients with an elevated white count and granulocytic proliferation were identified. There were 12 PB and 5 BM specimens studied. Two slides of each specimen type were split for concordance studies between the ARL and the IU Cytogenetics Laboratory. Likewise, 16 MRTH specimens from patients with normal white blood cell counts and a diagnosis of fever, anemia, or rule out leukemia were handled in an identical manner and studied as normal (negative for t[9;22]) controls. Both laboratories followed the same protocol using direct-labeled DC/DF *BCR*::*ABL1* probes from the same vendor (Abbott Molecular, Des Plaines, Illinois). The Abbott/Vysis LSI *BCR*::*ABL1* DC/DF FISH probes consist of a mixture of the LSI *BCR* probe (22q11.2) labeled with Spectrum Green and the LSI *ABL1* (9q34) probe labeled with Spectrum Orange (Abbott Molecular) This probe set will detect both major and minor breakpoints but cannot distinguish the 2.

Briefly, unstained slides of PB or BM smears were fixed in 3:1 methanol and acetic acid and allowed to air-dry. They were pretreated in 2× SSC followed by 1 to 2 minutes of 0.005% pepsin, both at 37°C. Denaturation, ethanol dehydration, and hybridization with the LSI DC/DF *BCR*::*ABL1* probe set were carried out per a previously validated IU Cytogenetics Laboratory procedure. Cells were counterstained with 4′,6-diamidino-2-phenylindole (Abbott/Vysis, Des Plaines, Illinois) and observed under Leica DM2000 LED (ARL) and Leica DM6B (IU) fluorescence microscopes (Leica Microsystems, Wetzlar, Germany). One hundred cells were scored for each specimen at the respective laboratory.

Microscopists at the ARL laboratory (NK and TL) had been trained on the IU FISH scoring protocol for CML using the DC/DF *BCR*::*ABL1* probe set.[17] A normal interphase cell (lacking the t(9;22) translocation) will exhibit a pattern of 2 red (*ABL1*) and 2 green (*BCR*) signals (Figure, A). In a nucleus containing a single balanced t(9;22), 1 red (*ABL1*) and 1 green (*BCR*) signal from the normal chromosomes 9 and 22 and 2 red/green (yellow) fusion signals, 1 each from the derivative chromosomes 9 and 22, will be observed (Figure, B). The fusion signals may be overlapped, touching, or adjacent with less than 1 signal width separation between signals. In some instances, deletions or complex rearrangements will create variant signal patterns.[7,8]

RESULTS

Seventeen cases of patients with an elevated white blood cell count and a provisional pathologic diagnosis of CML were studied by FISH in both the AMPATH and IU FISH laboratories (Table 1). Cells from 5 BM and 12 PB specimens were studied with the *BCR*::*ABL1* probe set. The IU laboratory was unable to complete the study of 1 PB specimen (CML-04), leaving 16 total specimens with results from both laboratories. FISH results were concordant in 15 of 16 specimens (93.8%). The 1 discordant result (CML-07) was a PB specimen interpreted as negative in the ARL and positive with a variant pattern in the IU FISH laboratory. The signal pattern was RRGGF, indicating 2 signals for *ABL1* (red) and 2 signals for *BCR* (green) with a single fusion signal. The variant pattern was most likely due to a complex 3-way translocation with a *BCR*::*ABL1* fusion at

Table 1. Study Specimen Clinical Information and Fluorescence In Situ Hybridization (FISH) Results						
Study No./Specimen	Age, y/Sex	WBC, K/ul	Hgb, g/dL	Plt, mcL	FISH (AMPATH) *BCR*::*ABL1*	FISH (IU) *BCR*::*ABL1*
CML-01/PB	30/M	252	6.7	175	+	+
CML-02/PB	NA/M	754	12.8	729	+	+
CML-03/PB	71/M	150	12.8	129	−	−
CML-04/PB	NA/F	300	NA	NA	+	ns
CML-05/PB	NA	NA	NA	NA	+	+
CML-06/PB	43/M	170	12	198	+	+
CML-07/PB	46/M	160	11	136	−	+ variant signal
CML-08/PB	24/F	169	10	810	+	+
CML-09/PB	34/M	68	10	73	+	+
CML-10/PB	32/F	86	6	24	+	+
CML-11/PB	16/M	170	9	76	+	+
CML-12/PB	NA/M	NA	NA	NA	+	+
CML-13/BM	80/F	410	9	45	+	+
CML-14/BM	NA/M		M:E ratio 10:1		+	+
CML-15/BM	NA/M	23	13.4	962	+	+
CML-16/BM	39/M	NA	NA	NA	+	+
CML-17/BM	15/M	NA	NA	NA	+	+

Abbreviations: *ABL1*, ABL proto-oncogene 1, non-receptor tyrosine kinase; AMPATH, AMPATH Reference Laboratory (Eldoret, Kenya); *BCR*, BCR activator of RhoGEF and GTPase; BM, bone marrow; CML, chronic myeloid leukemia; Hgb, hemoglobin; IU, Indiana University Cytogenetics Laboratory (Indianapolis); M:E, myeloid to erythroid; NA, not available; ns, no signal; PB, peripheral blood; Plt, platelet count; WBC, white blood cell count; +, positive FISH results; −, negative FISH results.

22q11.2, a small *ABL1* signal on the abnormal chromosome 9, a small BCR signal on the (non–chromosome 9 or 22) translocated chromosome, a *BCR* signal at 22q11.2 on the normal chromosome 22 and an *ABL1* signal at 9q34.1 on the normal chromosome 9 (Figure, C).[7] The nomenclature was written as: nuc ish (ABL1x3,BCRx3)(ABL1 con BCRx1)[92/100]. Conventional cytogenetics was not available to confirm the rearrangement. Also noted was a ribbonlike artifact over a small area of the slide, which, along with the variant pattern, may have contributed to the interpretation discordance and normal interpretation in the ARL.

Further, PB and BM aspirate specimens were collected from an additional 16 study patients and split between the 2 laboratories. All had white blood cell counts within normal limits with diagnoses including fever, anemia, or rule out leukemia. There were 7 PB and 9 BM specimens studied. A minimum of 200 cells were scored per specimen by 2 observers. All were interpreted as normal in both FISH laboratories for 100% concordance (Table 2). In total, 33 specimens were studied. One PB specimen was a failure in the IU laboratory. Thirty-two specimens were studied in both laboratories, with 31 of 32 (96.9%) concordant results.

As part of the FISH probe validation, each laboratory must establish its own normal and abnormal range cutoffs for each specimen type.[21] The number of false-positive nuclei on normal specimens is determined for each specimen, allowing for calculation of the maximum number of abnormal nuclei encountered in any patient. This number is used to calculate the upper bound of 1-sided 95% CI using a beta inverse calculation from Microsoft Excel (Microsoft, Redmond, Washington) beta inverse function, _BETAINV (confidence level, false-positive cells plus 1, number of cells analyzed).

The score sheets from the AMPATH laboratory were reviewed, and there was a maximum of 2 RGFF false-positive nuclei in a PB specimen. The beta inverse calculations for this would be 3.5% for 200 cells counted, or 7 cells. There were no BM specimens with a false-positive RGFF signal

Table 2. Establishing Normal Range for Peripheral Blood and Bone Marrow Specimens[a]							
	Abnormal Signal Pattern						
	RGG	RRG	RGF	RG	RGFF	RGGF	RFF
Peripheral blood (n = 7 specimens)							
Cells[b]	3	4	5	3	2	0	0
Beta inverse, %	4	4.5	5.5	4	3.5	1.5	1.5
Bone marrow (n = 9 specimens)							
Cells[b]	5	4	4	2	0	1	1
Beta inverse, %	5.5	4.5	4.5	3.5	1.5	2.5	2.5

Abbreviations: F, fusion signal (ABL proto-oncogene 1, non-receptor tyrosine kinase [*ABL1*] and BCR activator of RhoGEF and GTPase [*BCR*] fused); G, green signal (*BCR*); R, red signal (*ABL1*).

[a] The table reflects application of the beta inverse calculation to the highest number of false-positive or alternate signal patterns in normal specimens. In a peripheral blood specimen, up to 2 cells (3.5%) with an RGFF signal pattern would be considered within normal limits.

[b] A total of 200 cells were counted per specimen.

pattern. Using the beta inverse calculation for 200 cells would equal 1.5% or up to 3 false-positive cells assessed in a BM specimen. The highest alternate pattern observed on PB specimens was 5 cells with an RGF signal pattern. For BM specimens, an RGG alternate pattern was most frequently encountered (Table 2).

The abnormal reference range (percentage of cells with an abnormal signal pattern) is defined as the lowest and highest percentage of cells with an abnormal signal pattern for patients with untreated disease. These values may be calculated using data from specimens of untreated patients with CML. The range of cells with a positive FISH fusion pattern in patients with suspected CML was from 52 to 199 of 200 cells observed for PB and 26 to 190 for BM specimens.

DISCUSSION

Establishing a clinical FISH assay in the United States requires validation as established by US law.[22] For CML, these studies were performed on both PB and BM cells as part of the validation of the DC/DF *BCR*::*ABL1* assay by the IU Cytogenetics Laboratory. The *BCR*::*ABL1* probes and the IU Cytogenetics Laboratory's standard operating procedure were shared with the ARL for this concordance study. Both laboratories followed the same protocol.

Seventeen specimens from Kenyan patients with a provisional diagnosis of CML were studied by FISH in both the AMPATH Reference and IU FISH laboratories. The analysis for 1 specimen could not be completed by both laboratories and the results for 1 other specimen were discordant. The interpretation of 15 of 16 specimens (93.7%) were concordant. Normal specimens were also studied to establish the normal range for the assay. For the 16 provisionally normal specimens (7 PB and 9 BM specimens), there was 100% concordance between the ARL and IU Cytogenetics Laboratory. Further, using ARL data from 200 cells analyzed per specimen, the normal range was established, indicating that fusion signals greater than 1.5% in a BM specimen and 3.5% in a PB specimen should require additional analysis and may be determined to be abnormal.

Going forward, the ARL must also run controls with each batch of patients clinically tested for CML. Controls may be made by using leftover cells obtained from patients with CML that were studied by FISH in clinical practice. Quality control parameters must be established in the ARL by graphing data from the studies of the standard control specimens over time. Further, the laboratory should enroll in an external quality assurance program for assessment of its performance compared with other laboratories across the globe.[21,22]

FISH is a powerful diagnostic tool for screening, early detection, tumor classification, and monitoring the efficacy of interventions in leukemia and lymphoma.[23,24] A major advantage of FISH is that it can be performed on smears of both PB and BM specimens.[24] qPCR is the preferred method to monitor response to TKI therapy in CML.[9] However, FISH also may be used to monitor cytogenetic response when conventional cytogenetics is not available, as is the case in Eldoret.[9] FISH can also detect cryptic and complex cytogenetic rearrangements, which may number between 5% and 10% of cases, or 100 to 200 Kenyan CML cases annually. Pretreatment specimens, as those studied here, provide an opportunity to establish the signal pattern for accurate scoring for subsequent posttherapy specimens.

This new diagnostic FISH test for CML, performed in the ARL, is available at MTRH in Eldoret, Kenya. To our knowledge, this new test, along with the diagnostic FISH testing for Burkitt lymphoma, are the only available FISH cancer diagnostic tests in the entire country of Kenya. MTRH, a public hospital, serves residents of 23 counties in Kenya, parts of eastern Uganda, South Sudan, Tanzania, and the Democratic Republic of Congo, with a population of more than 25 million.[25]

The rationale for developing the CML FISH assay was multifold. The ARL has extensive experience with research protocols and high-complexity clinical testing.[16,20] Its administration and billing are separate from the MTRH hematology laboratory. Further, the ARL oversees research funding for diagnostic projects that may be subsequently commercialized. The FISH laboratory was established in the ARL initially as part of a US National Institutes of Health–sponsored pediatric oncology clinical trial for which FISH is an established diagnostic test.[20] The equipment and trained personnel reside there. Also, CML FISH may be performed on peripheral and BM smears, reducing the amount of sample necessary for diagnostic testing. Currently, CML FISH testing for children is available as part of a Kenyan program grant, overseen by Fetus Njuguna, MD, PhD, and sponsored by the AFAS Foundation of the Netherlands. To date, 26 children have been tested for CML as part of this study.

Unfortunately, the CML FISH test, like qPCR testing, remains an out-of-pocket expense for patients at 10 000 Kenyan shillings (US $100) and as such is not available to all individuals with a suspected diagnosis of CML outside of research-supported testing or other special circumstances. It is important for the Kenyan National Health Insurance Fund to consider coverage of both tests to support accurate and rapid disease diagnosis to quickly begin treatment in the patient's local setting and subsequently monitor treatment response. An accurate diagnosis will ensure that patients receive appropriate therapy and that imatinib is given to patients who will benefit from the therapy. Before the development of disease-specific diagnostic testing, patients from Eldoret needed to travel approximately 312 km to Nairobi, Kenya, for diagnosis and treatment of CML. Now they may be diagnosed and treated in their local community.

CONCLUSIONS

Here we report the validation of CML FISH as a diagnostic tool for leukemia in a public hospital setting in Eldoret, Kenya. The ARL has demonstrated the ability to implement a standard operating procedure for the testing and establish scoring criteria and normal and abnormal range cutoffs. Validated diagnostic testing is the first step to rapid confirmation of CML and initiation of disease-specific therapy.

References

1. Apperley JF, Godley LA, Radich J, et al. Chronic myeloid leukaemia. In: WHO Classification of Tumours Editorial Board. *Haematolymphoid Tumours*. 5th ed. Lyon, France: International Agency for Research on Cancer; 2024. *WHO Classification of Tumours*; vol 11. https://tumourclassification.iarc.who.int/chapters/63. Accessed June 16, 2024.

2. Nowell P, Hungerford D. A minute chromosome in chronic granulocytic leukemia [abstract. *J. Science*. 1960;132:1497.

3. Rowley JD. A new consistent chromosomal abnormality in chronic myelogenous leukemia identified by quinacrine fluorescence and Giemsa staining [letter. *J. Nature*. 1973;243(5405):290–293. doi:10.1038/243290a0

4. Heisterkamp N, Stephenson JR, Groffen J, et al. Localization of the c-abl oncogene to a translocation breakpoint in chronic myelocytic leukaemia. *Nature*. 1983;306(5940):239–242. doi:10.1038/306239a0

5. Shtivelman E, Lifshitz B, Gale RP, Canaani E. Fused transcript of abl and bcr genes in chronic myelogenous leukaemia. *Nature*. 1985;315(6020):550–554. doi:10.1038/315550a0

6. Faderl S, Talpaz M, Estrov Z, O'Brien S, Kurzrock R, Kantarjian HM. The biology of chronic myeloid leukemia. *N Engl J Med*. 1999;341(3):164–172. doi:10.1056/NEJM199907153410306

7. Dewald GW. Interphase FISH studies of chronic myeloid leukemia. *Methods Mol Biol*. 2002;204:311–342. doi:10.1385/1-59259-300-3:331

8. Dewald GW, Wyatt WA, Juneau AL, et al. Highly sensitive fluorescence in situ hybridization method to detect double BCR/ABL fusion and monitor response to therapy to chronic myeloid leukemia. *Blood*. 1998;91(9):3357–3365. doi:10.1182/blood.V91.3357

9. Shah N, Bhatia R, Altman JK, et al. Chronic myeloid leukemia, version 2.2024, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2024;22(1):43–69. doi:10.6004/jnccn.2024.0007

10. Jabbour E, Kantarjian H, O'Brien S, et al. The achievement of an early complete cytogenetic response is a major determinant for outcome in patients with early chronic phase chronic myeloid leukemia treated with tyrosine kinase inhibitors. *Blood*. 2011;118:4541–4546. doi:10.1182/blood-2011-04-349110

11. Andolina JR, Neudorf SM, Corey SJ. How I treat childhood CML. *Blood*. 2012;19:1821–1830. doi:10.1182/blood-2011-10-380774.

12. Druker BJ, Tamura S, Buchdunger E, et al. Effects of a selective inhibitor of the Abl tyrosine kinase on the growth of Bcr-Abl positive cells. *Nat Med*. 1996;2(5):561–566. doi:10.1038/nm0596-561

13. O'Brien SG, Guilhot F, Larson RA, et al. Imatinib compared with interferon and low dose cytarabine for newly diagnosed chronic-phase chronic myeloid leukemia. *N Engl J Med*. 2003;348(11):994–1004. doi:10.1056/NEJMoa022457

14. Rossari F, Minutolo F, Orciuolo E. Past, present, and future of Bcr-Abl inhibitors: from chemical development to clinical efficacy. *J Hematol Oncol*. 2018;11(1):84. doi: 10.1186/s13045–018-0624-2

15. Bray F, Ferlay J, Soejomataram I, Siegal RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2018;68(6):394–424. doi:10.3322/caac.21492

16. Einterz RM, Kimaiyo S, Mengech HN, et al. Responding to the HIV pandemic: the power of an academic medical partnership. *Acad Med*. 2007;82:812–818. doi:10.1097/ACM.0b013e3180cc29f1

17. Einterz RM, Kelley CR, Mamlin JJ, et al. Partnerships in international health. the Indiana University–Moi University experience. *Infect Dis Clin North Am*. 1995;9(2):453–455.

18. Mercer T, Gardner A, Andama B, et al. Leveraging the power of partnerships: spreading the vision for a population health care delivery model in western Kenya. *Global Health*. 2018;14(1):44. doi:10.1186/s12992-018-0366-5

19. Lotodo T, Burziba N, Chsumbai G, et al. Geographical distribution of hematological malignancies managed at Moi Teaching and Referral hospital. *East Afr Med J*. 2022;99(3):4604–4616.

20. Vance GH, Lotodo T, Kigen N, et al. Improvement in diagnosis in children with Burkitt lymphoma in Kenya: Implementation of fluorescence in situ hybridization testing for *MYC* and the *MYC/IGH* translocation. *Ecancermedicalscience*. 2023;17:1505. doi:10.3332/ecancer.2023.1505

21. Wiktor AE, Van Dyke DL, Stupca PJ, et al. Preclinical validation of fluorescence in situ hybridization assays for clinical practice. *Genet Med*. 2006;8(1):16–23. doi:10.1097/01.gim.0000195645.00446.61

22. Standard: Establishment and verification of performance specifications. 42 CFR §493. 1253. https://www.govregs.com/regulations/title42_chapterIV-i3_part493_subpartK_subjgrp40_section493.1253. Accessed June 23, 2024.

23. Gozetti A, Le Beau MM. Fluorescence in situ hybridization: uses and limitations. *Semin Hematol*. 2000;37(4):320–333. doi:10.1016/s0037-1963(00)90013-1

24. Vance GH, Khan WA. Utility of fluorescence in situ hybridization in clinical and research applications. *Clin Lab Med*. 2022;42(4):573–586. doi:10.1016/j.cll.2022.09.020

25. Moi Teaching and Referral Hospital. https://www.mtrh.go.ke/. Accessed September 30, 2024.