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First-Line Flumatinib in Newly Diagnosed Chronic-Phase Chronic Myeloid Leukemia: A 3-Month Landmark-Evaluable Real-World Experience

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To the editor.

Flumatinib is a second-generation BCR::ABL1 tyrosine kinase inhibitor used for chronic-phase chronic myeloid leukemia (CP-CML). Although randomized and large real-world studies have established its activity, small regional cohorts may remain informative when reported transparently, particularly regarding patient selection, baseline disease burden, molecular monitoring, treatment modification, and tolerability in routine practice.[1-6]

We retrospectively reviewed consecutive patients with newly diagnosed CML who initiated first-line flumatinib at Anqing Municipal Hospital between January 2020 and December 2025. During this period, 45 consecutive patients with newly diagnosed CML started first-line flumatinib. One patient was excluded because of accelerated-phase CML at diagnosis. The remaining 44 consecutive patients with newly diagnosed CP-CML constituted the present cohort. All 44 patients reached the 3-month landmark and had BCR::ABL1 molecular testing available. At the data cutoff, 39 and 34 patients had reached the 6- and 12-month treatment landmarks, respectively. No CP-CML patient who initiated first-line flumatinib during the study period was excluded because of early discontinuation, intolerance, progression, death, transfer, loss to follow-up, immature follow-up, or missing baseline data before the 3-month landmark. No patient was lost to follow-up, and one patient died during follow-up because of cardiac disease unrelated to flumatinib.

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Anqing Municipal Hospital (approval No. 2026-082). Written informed consent was waived because the study was retrospective and used de-identified clinical data. The waiver applied to all included patients. A 17-year-old adolescent patient was included because of near-adult body size and routine clinical practice considerations and received flumatinib 600 mg once daily with close hematologic and organ-function monitoring. No unusual or unexpected toxicity was observed in this patient. This observation should be regarded as a factual description of local practice and should not be interpreted as evidence supporting routine pediatric use of adult-dose flumatinib.

Cytogenetic response was assessed by conventional G-banding karyotype analysis of bone marrow aspirates; at least 20 metaphases were analyzed when adequate metaphases were available. Complete cytogenetic response (CCyR) was defined as 0% Philadelphia chromosome-positive metaphases. For patients with typical p210 transcripts, molecular monitoring was performed according to the routine standardized BCR::ABL1 quantitative testing pathway and reported as BCR:ABL1 on the International Scale (IS) in the laboratory report. Major molecular response (MMR) was defined as BCR::ABL1^{IS} <=0.1%. For the patient with the atypical e14a3/b3a3 transcript, quantitative monitoring was performed by fluorescence quantitative reverse-transcription PCR on an ABI 7500 system using Thermo Fisher FastMix reagents. Because this atypical-transcript assay was not the same standardized IS-calibrated assay used for typical p210 monitoring and transcript-specific IS calibration was not available, the e14a3/b3a3 patient was not included in standard BCR::ABL1^{IS} molecular-response denominators and was described separately.

Baseline disease characteristics are summarized in **Table 1**. Diagnostic reports identified typical p210 transcript(s) in 43 patients; the reports did not further distinguish e13a2/b2a2 from e14a2/b3a2. One patient had an atypical e14a3/b3a3 transcript. ABL1 kinase-domain mutation testing was not routinely performed in all patients and was not based on a predefined testing protocol. In real-world practice, mutation testing was performed at the discretion of the treating physicians: some physicians requested baseline testing, whereas others deferred testing unless intolerance, inadequate

Table 1. Baseline clinical and disease characteristics of the 44 patients with newly diagnosed CP-CML.

Variable	Category or summary	Result
Age, years	Median (range)	58 (17-85)
Sex	Male	20 (45.5%)
	Female	24 (54.5%)
ECOG performance status	0-1	42 (95.5%)
	2-3	2 (4.5%)
Sokal score (n=43)	Low risk	9 (20.9%)
	Intermediate risk	16 (37.2%)
	High risk	18 (41.9%)
ELTS score (n=43)	Low risk	17 (39.5%)
	Intermediate risk	18 (41.9%)
	High risk	8 (18.6%)
Comorbidities (multiple allowed)	Hypertension	4 (9.1%)
	Diabetes mellitus	3 (6.8%)
	Pulmonary disease	2 (4.5%)
	Cardiovascular disease	5 (11.4%)
	Renal disease	6 (13.6%)
	Other malignancy or rheumatic/immune disease	2 (4.5%)
Bone marrow fibrosis	MF grade 0-1	41 (93.2%)
	MF grade 2-3	3 (6.8%)
White blood cell count, x10^9/L	Median (range)	120.92 (9.41-441.99)
Hemoglobin, g/L	Median (range)	97 (45-132)
Platelet count, x10^9/L	Median (range)	361.5 (121-1708)
Peripheral blood basophils, %	Median (range)	5.7 (2.5-9.9)
Spleen size below costal margin, cm	Median (range)	6.4 (0-20)
Peripheral blood blasts, %	Median (range)	2 (0-5)
Bone marrow blasts, %	Median (range)	3 (1-5)
Philadelphia chromosome-positive karyotype	t(9;22)(q34;q11)	44/44 (100.0%)
BCR::ABL1 transcript type	Typical p210 transcript(s): e13a2/b2a2 and/or e14a2/b3a2	43/44 (97.7%)
	Atypical transcript: e14a3/b3a3	1/44 (2.3%)
Baseline BCR::ABL1^{IS}, %	Median (range)	64.73 (35.29-91.80)
Follow-up, months	Median (range)	24 (4-73)

Note: Data are shown as n (%) unless otherwise indicated. Continuous variables are reported as median (range). Sokal and ELTS scores were available for 43 patients; one 17-year-old adolescent patient was not included in risk-score assessment. Comorbidities were not mutually exclusive, and percentages were calculated using the full cohort (N=44) as the denominator. For typical p210 BCR::ABL1 transcripts, diagnostic reports did not further distinguish e13a2/b2a2 from e14a2/b3a2. e14a3/b3a3 was classified as an atypical BCR::ABL1 transcript. ECOG, Eastern Cooperative Oncology Group; ELTS, EUTOS long-term survival; MF, myelofibrosis; CP-CML, chronic-phase chronic myeloid leukemia.

response, or disease progression was suspected. In total, 18 patients underwent ABL1 kinase-domain mutation testing, and no mutation was detected among those tested.

Landmark responses are shown in **Table 2**. For hematologic and cytogenetic responses, all patients available at each landmark were included in the denominator. For standard molecular-response categories, only patients with typical p210 transcripts were included in the BCR::ABL1^{IS} denominators. Among typical p210 patients, BCR::ABL1^{IS} <=10% was achieved in 36/43 (83.7%) at 3 months, BCR::ABL1^{IS} <=1% in 27/38 (71.1%) at 6 months, and MMR in 23/33 (69.7%) at 12 months. The atypical e14a3/b3a3 patient had molecular levels corresponding descriptively to >1% to <=10% at 3 months, >0.1% to <=1% at 6 months, and <=0.1% at 12 months, but was not included in standard BCR::ABL1^{IS} denominators. Because the 3-, 6-, and 12-month denominators were not identical, these findings should not be interpreted as true

Table 2. Landmark responses after initiation of flumatinib.

Response	3 months	6 months	12 months
CHR	43/44 (97.7%)	38/39 (97.4%)	34/34 (100.0%)
CCyR	29/44 (65.9%)	34/39 (87.2%)	33/34 (97.1%)
Standard BCR::ABL1IS molecular categories, typical p210 only	n=43	n=38	n=33
BCR::ABL1IS >10%	7 (16.3%)	4 (10.5%)	1 (3.0%)
BCR::ABL1IS >1% to <=10%	18 (41.9%)	7 (18.4%)	2 (6.1%)
BCR::ABL1IS >0.1% to <=1%	10 (23.3%)	9 (23.7%)	7 (21.2%)
BCR::ABL1IS <=0.1%	8 (18.6%)	18 (47.4%)	23 (69.7%)
Atypical e14a3/b3a3 patient, descriptive only	>1% to <=10%	>0.1% to <=1%	<=0.1%

Note: CHR, complete hematologic response; CCyR, complete cytogenetic response; BCR::ABL1^{IS}, BCR::ABL1 transcript level on the International Scale; MMR, major molecular response. Standard BCR::ABL1^{IS} molecular-response categories were calculated using patients with typical p210 transcripts only. The patient with e14a3/b3a3 was excluded from standard molecular-response denominators and described separately. The 6- and 12-month denominators were smaller because some patients had not yet reached those treatment durations by the data cutoff.

Table 3. Cohort flow, treatment modification, and selected safety summary.

Category	Item	Patients, n (%)
Cohort flow	Consecutive newly diagnosed CML patients initiating first-line flumatinib, 2020-2025	45
	Excluded: accelerated-phase CML at diagnosis	1
	Included: newly diagnosed CP-CML patients	44
	Available for 3-month landmark analysis	44
	Patients with BCR::ABL1 molecular testing available	44
	Available for 6-month landmark analysis	39
	Available for 12-month landmark analysis	34
	Lost to follow-up	0
	Deaths during follow-up: cardiac disease, unrelated to flumatinib	1 (2.3%)
Treatment switching or treatment-plan adjustment	Severe thrombocytopenia requiring switch to another TKI, after 3 months	1 (2.3%)
	Drug-induced liver injury requiring switch to another TKI, after 9 months	1 (2.3%)
	Inadequate response requiring treatment-plan adjustment at 12 months	2 (4.5%)
	Total treatment switching or treatment-plan adjustment	4 (9.1%)
Dose management	Dose interruption	3 (6.8%)
	Dose reduction	8 (18.2%)
Grade 3-4 hematologic adverse events	Neutropenia	4 (9.1%)
	Thrombocytopenia	3 (6.8%)
	Anemia	1 (2.3%)
Grade 1-2 nonhematologic adverse events	Gastrointestinal events	11 (25.0%)
	Rash or pruritus	7 (15.9%)
	Edema	5 (11.4%)
	Abnormal liver function	4 (9.1%)
	Bone, joint, or muscle pain	3 (6.8%)
	Renal impairment	2 (4.5%)
	Respiratory tract infection	1 (2.3%)
ABL1 kinase-domain mutation testing	Tested at treating physician discretion	18 (40.9%)
	Detected ABL1 kinase-domain mutation	0/18 (0.0%)

Note: Percentages use the full cohort (N=44) as the denominator unless otherwise indicated. A patient could experience more than one adverse event, so percentages should not be summed. No grade 3-4 nonhematologic adverse events were recorded. ABL1 kinase-domain mutation testing was performed at the discretion of treating physicians rather than according to a predefined protocol. TKI, tyrosine kinase inhibitor.

longitudinal improvement in the original baseline cohort.

Seven patients had BCR::ABL1^{IS} >10% at 3 months. These patients continued flumatinib with repeat molecular monitoring and clinical review. Among these patients, molecular levels decreased during follow-up; however, two patients had inadequate response by 12 months and subsequently underwent treatment-plan adjustment. No ABL1 kinase-domain mutation was detected among the tested patients.

During a median follow-up of 24 months (range, 4-73), 4 patients (9.1%) underwent treatment switching or treatment-plan adjustment (**Table 3**). One patient switched to another TKI after 3 months because of severe thrombocytopenia, one switched after 9 months because of drug-induced liver injury, and two underwent treatment-plan adjustment at 12 months because of inadequate response. One death occurred during follow-up because of cardiac disease and was considered unrelated to flumatinib. Because complete numbers at risk, confidence intervals, and detailed event-time displays were not available for robust survival analysis in this Scientific Letter format, formal FFS/OS estimates and Kaplan-Meier curves are not presented.

Grade 3-4 hematologic adverse events included neutropenia in 4 patients (9.1%), thrombocytopenia in 3 (6.8%), and anemia in 1 (2.3%). No grade 3-4 nonhematologic adverse events were recorded. Dose interruption occurred in 3 patients (6.8%), and dose reduction occurred in 8 (18.2%). The most frequent grade 1-2 nonhematologic events were gastrointestinal events in 11 patients (25.0%), rash or pruritus in 7 (15.9%), edema in 5 (11.4%), abnormal liver function in 4 (9.1%), and bone, joint, or muscle pain in 3 (6.8%). The safety observations should be interpreted descriptively because adverse-event capture was based on available clinical records and not on a prospective toxicity-reporting protocol.

This report has important limitations. It is a single-center retrospective experience without a comparator cohort. Molecular assessment was restricted to available routine clinical reports; typical p210 transcripts were not further separated into e13a2/b2a2 and e14a2/b3a2, and the atypical e14a3/b3a3 patient was excluded from standard BCR::ABL1^{IS} denominators because transcript specific IS calibration was not available. ABL1 kinase-domain mutation testing was performed only in 18 patients at physician discretion rather than according to a predefined protocol, and undetected mutations in untested patients cannot be excluded. Toxicity information did not include a complete prospective grade-by-grade inventory with onset, duration, recurrence, and detailed management for every event. The data describe local clinical experience and should not be interpreted as comparative evidence of effectiveness or superiority over other TKIs.

In summary, this Scientific Letter provides a concise single-center description of first-line flumatinib use in consecutive newly diagnosed CP-CML patients treated at our institution. The findings support the feasibility of reporting local flumatinib practice but underscore the need for larger intention-to-treat cohorts with complete molecular, safety, and survival datasets.

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Data Availability. De-identified summary data supporting the findings of this report are available from the corresponding author upon reasonable request, subject to institutional requirements.

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Competing interests: The authors declare no competing interest.

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