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For Hematology and Oncology Centers Using iKnowMed™

Help With Identifying Ph+ CML-CP Patients for Treatment Evaluation

This Guide Provides an Overview for Using Patient Reports and Alerts to Identify Ph+ CML-CP Patients for Evaluation.

Ph+ CML-CP, Philadelphia Chromosome Positive Chronic Myeloid Leukemia Chronic Phase.

Using This Guide and EHR Worksheets

This Guide is not intended to provide any clinical advice or recommendations, which are solely the responsibility of the health system. Please see the important statistics on the following page that highlight the unmet needs of CML patients who are struggling with drug resistance, unmanageable side effects, or other suboptimal results with treatment.

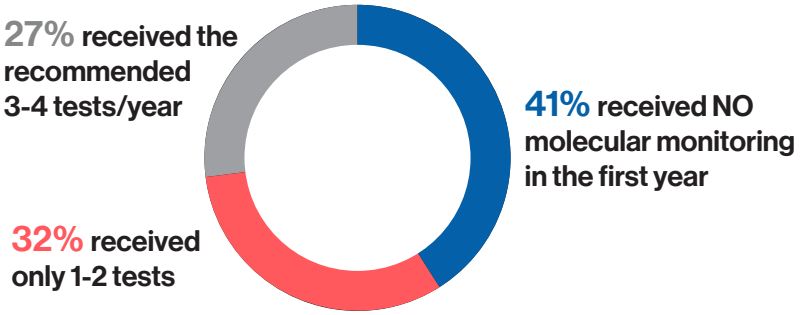
This Guide can help clinical decision makers implement automated EHR functionalities to identify and evaluate care for Ph+ CML-CP patients who may benefit from a treatment switch. It provides examples of Patient List Reports and Chart Alerts, along with EHR Worksheets. The EHR Worksheets provide a list of criteria and/or actions to consider including when creating Patient List Reports and Chart Alerts. The EHR Worksheet can be customized, saved, and reused. It does not constitute guidance for medical advice or treatment.

The information listed in this Guide is based upon the most recent version of iKnowMed. Functions and features may change as new software versions are released. The Guide and EHR Worksheet are meant to serve as educational examples only and should not replace detailed instructions provided to you by your internal or external EHR support resources. Screen images shown within represent hypothetical screens in iKnowMed. Novartis makes no claims or warranties about the applicability or appropriateness of this information and does not endorse specific EHR systems.

EHR, Electronic Health Record.

Real-world evidence reveals significant underutilization of molecular monitoring

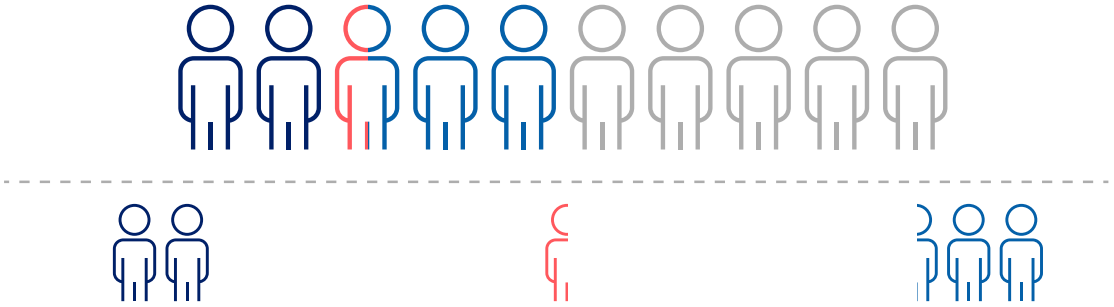
A claims database review of 1205 patients with newly diagnosed CML found that[1]:



Studies suggest that <30% of patients with CML are monitored according to clinical practice guidelines during the first year of TKI treatment.[1]

Lack of initial response, resistance, and intolerance are key drivers of treatment discontinuation of TKI therapy

In a study of 119 patients with CML-CP treated with 2L TKIs, 52% discontinued 2L TKI due to resistance or intolerance[2]



19% discontinued due to primary resistance (lack of initial response)[2,a]

7% discontinued due to secondary resistance[2,b]

26% discontinued due to intolerance[2,c]

TKI, Tyrosine Kinase Inhibitor.

[a]Primary resistance is defined as lack of efficacy (failure to achieve landmark responses) from the onset of treatment.[3]
[b]Secondary resistance, also known as acquired resistance, is considered loss of response to treatment.[4]
[c]Intolerance is considered when a patient develops an adverse event that cannot be managed through dose reduction or treatment of symptoms.[5]

Treatment intolerance may lead to nonadherence in patients receiving TKI therapy

Treatment intolerance may lead to nonadherence in patients receiving TKI therapy

Some patients are intolerant to TKIs,

with up to ~25% of patients discontinuing treatment due to an adverse event[6]

Up to ~30% of patients with CML are nonadherent.[7]

Nonadherence may be a factor associated with higher health care costs, suboptimal response, disease progression, and mortality[8-10]

EHR Capabilities Can Help to Stratify CML Patients

Clinical champions within an organization can advocate for the configuration of EHR capabilities such as Patient List Reports and Chart Alerts.

Role of Patient List Reports

Patient List Reports are iKnowMed system reports that can be used to stratify CML patients. Patient List Reports can be generated using the Patient List widget on the User Dashboard.

Patient List Reports can be used to demonstrate and champion the need for follow-up care within an organization. They can also be used for planning purposes to understand for which patients a Chart Alert would display.

Available criteria to generate these reports can include patient gender, age, diagnosis, lab result values, and medications.

Creating a Patient List Report

- Access the **Patient List widget**, from the widget Library on the user Dashboard
- When **Create List** is selected, criterion options display
- Select a problem, medication, and lab value that provide a representative group of the Ph+ CML-CP BCR::ABL positive patient population. For example:

ICD-10	C92.10
Medication	TKI Medication
Lab Analyte	BCR::ABL Operation / Range value (eg > 0.1%)

Note: *Uncheck "Include Any Match" to require a match on all criteria.*

BCR, breakpoint cluster region; ABL, Abelson.

EHR Capabilities Can Help to Stratify CML Patients (continued)

Role of Patient List Reports (continued)

Upon selecting **Search**, the matching population displays on the screen

- Navigate to each patient's chart directly from the resulting list to review the chart for additional inclusion or exclusion criteria
- Review exclusion criteria, for example:
  - TKI history
  - Recent BCR::ABL ordered within timeframe

Patient List Search *required

From: 04/01/2023 12:00 AM
To: 11/29/2023 12:00 AM
Problem: C92.10
Medication: Search Medications
Allergy:
Gender:
Age From:
Age To:
Clinical Trial Study ID:
Preferred Method of Contact:
MRN:
Up to 1000 comma separated
ADD LAB ANALYTE

Lab Analyte Name	Operation	Result Value
BCR::ABL	>	0.1%

1-1 of 0

Exclude: Include Any Match; Inactive Patients; Test Patients; Deceased Patients
CLEAR SEARCH IMPORT MRN LIST
CSV or Excel Only

Patient Name - DOB - MRN	Age/Gender	Active	Test	Deceased	Date	Result Value
Smith, Betty - MRN 8013335459	58/F	Y	N	N	4/3/2023	0.0178
Jones, Sam - MRN 8013345789	62/M	Y	N	N	6/20/2023	0.0137
Abner, Darlene - MRN 8013238521	72/F	Y	N	N	9/20/2023	0.0142
Carlson, Sandra - MRN 8013208132	43/F	Y	N	N	11/14/2023	0.0165

Hypothetical example of Patient List Report

EHR Capabilities Can Help to Stratify CML Patients (continued)

Role of Chart Alerts

Chart Alerts are displayed at the point of care to remind or alert.

As part of an organization's care quality EHR initiative, Chart Alerts can help proactively identify at-risk

Ph+ CML-CP patients when they come in for an appointment.

Chart Alerts can be configured in a meaningful way which specifies the patient criteria and milestones within the EHR workflow.

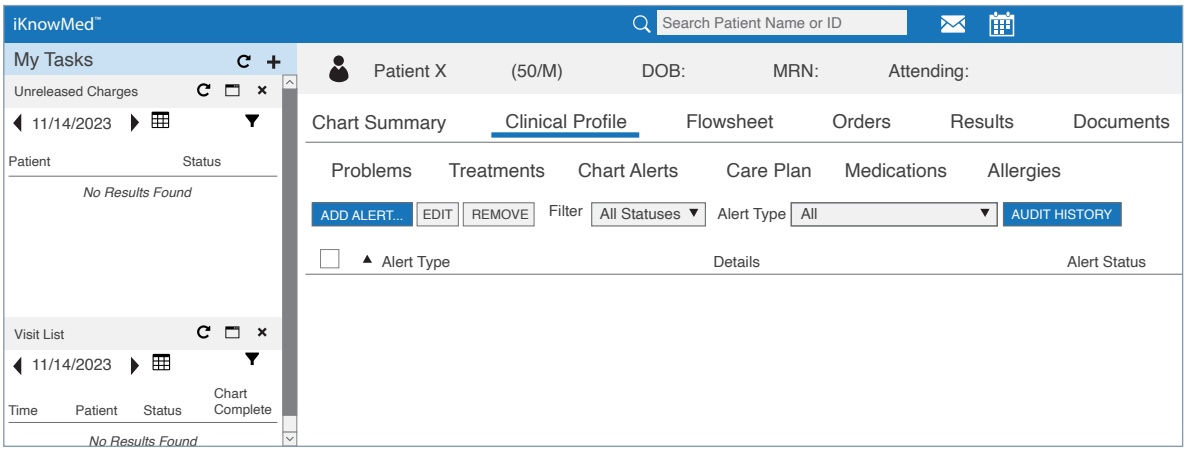
iKnowMed enables the setup of Chart Alerts using a Patient List Report to determine which charts should be reviewed for potential alert notification.

- Navigate to the **Patient List Search**
- Select a date range, and set additional criteria as desired to target specific patient groups
- From the resulting **Patient List** display, navigate to patient chart by selecting a patient
- Review the chart for exclusion or additional inclusion data points
- Add a **Chart Alert** to appropriate patient charts

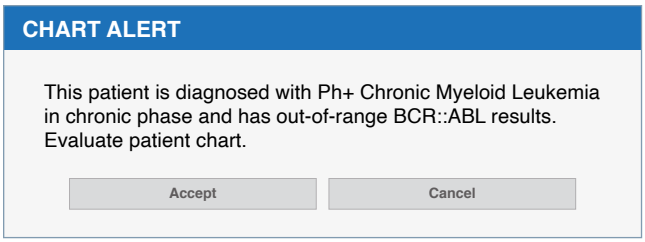
EHR Capabilities Can Help to Stratify CML Patients (continued)

Adding a Chart Alert

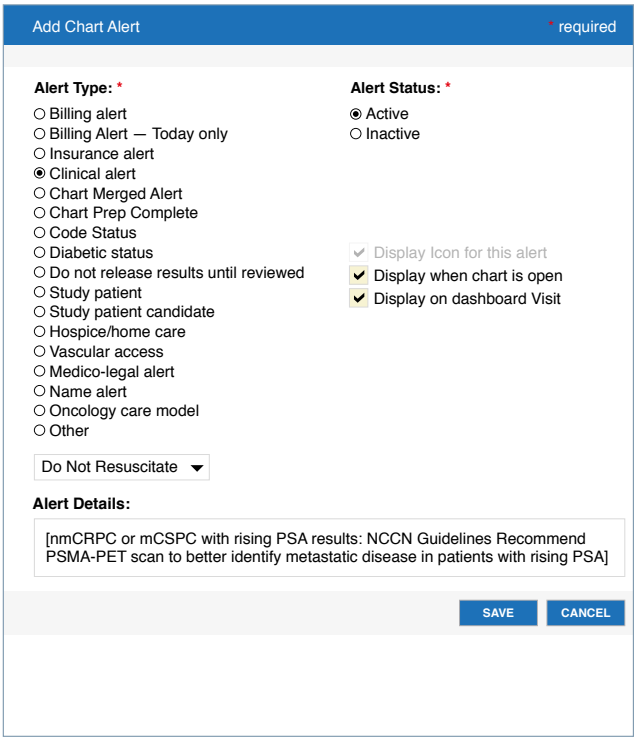
- While in the patient chart, navigate to **Clinical Profile**, **Chart Alerts**, **Add Alert**...
- Select the **Alert Type Clinical Alert**, and appropriate options, such as **Display when Chart is Opened**
- Enter **Alert Details**, such as "This patient is diagnosed with Ph+ Chronic Myeloid Leukemia in chronic phase and has out-of-range BCR::ABL results. Evaluate patient chart."
- Select **Save**



Hypothetical example of the navigation to Add Alert...



Hypothetical example of the Chart Alert display



Hypothetical example of Add Chart Alert options

Optional Use of EHR Worksheets in This Guide

An interactive, digital EHR Worksheet that follows is intended to assist health systems in configuring their EHR capabilities to help identify Ph+ CML-CP patients in need of additional care. It outlines the criteria that need to be defined in an IT request for creating Patient List Reports and Chart Alerts.

The EHR Worksheet can help translate desired clinical parameters for identifying CML patients with suboptimal results from CML treatment into categories and values for EHR functions. Once the EHR Worksheet is completed, it can be saved under a new name. Then, the EHR Worksheet can be reused or edited if the criteria selected results in a patient population that is too broad or too narrow.

The codes are provided for reference purposes only and may not be all inclusive. The responsibility to determine coverage and reimbursement parameters, and appropriate coding for a particular patient and/or procedure, is always the responsibility of the physician. The EHR Worksheet includes categories of selection criteria for health systems to consider when seeking to identify and evaluate appropriate patients.

Actions for a clinical champion:

1

Start by selecting the inclusion and exclusion criteria to define the specific search parameters for finding and evaluating CML patients with suboptimal results from CML treatment.

2

Then, specify the data that will be displayed on the Patient List Report by selecting columns for provider evaluation and review. After reviewing the Patient List Report, clinical champions may wish to broaden or narrow the criteria and values to refine the list of patients according to their preferences.

3

Utilizing the criteria in Step 1, choose the language, display restrictions, and clinical actions for the Chart Alert, that will appear to prompt treatment evaluation by care team members.

The following pages help identify TKI-resistant and/or intolerant patients with specific criteria:

Patients with a missing or overdue BCR::ABL test	Patients who are non-compliant with TKI medication prescriptions that have lapsed	Patients who are not meeting treatment milestones and may be TKI-resistant

Patient With a Missing or Overdue BCR::ABL Test

Before you begin to build on this topic, it's important to consider several key technical questions that will influence the impact of your BCR::ABL program.

Technical Considerations:

Are results interfaced back to your EHR?

OPTION	ACTIONS
Yes – our results interface returns BCR::ABL results and completes the original order	Proceed with EHR report and Chart Alert build
No – we don't receive results digitally to our EHR	Do not proceed with build – pursue an interfaced result option with your interfaces team before moving forward

If yes above, are interfaced results filed to discrete result values in your EHR?

OPTION	ACTIONS
Yes – our results interface returns BCR::ABL results and completes the original order	Proceed with EHR report and Chart Alert build
No – we don't receive results digitally to our EHR	Do not proceed with build – pursue an interfaced result option with your interfaces team before moving forward

Operational Impact:

If you are not receiving discrete results for your BCR::ABL tests, the build is still possible but there is a greater operational burden placed upon the program.

Reports that are built to identify patients with missing or overdue results will return patients who have had the order completed but the EHR won't be able to return that data. This places the onus of follow-up onto whoever is managing the reports and the population. In other words, operational owners running these reports will need to do manual follow-up in the chart or with the patient directly to determine if the result was completed and then manually key those results into the patient's chart.

Given the relatively small size of the population who would be doing this testing, this may not be a significant lift and may be worth it for your organization. However, it's important to plan for the additional workload.

Patient With a Missing or Overdue BCR::ABL Test

Inclusion Criteria for Patient List Report and Chart Alert

INCLUSION CRITERIA

CATEGORY ("AND" CRITERIA)	✓	VALUES		
Patient Status		Alive		
Population (select one)		Only my patients		
		Seen in my department		
		All patients who meet the criteria		
		Other		
Age (eg ≥18)		> <		
Diagnosis/ Clinical Findings (select ≥ 1) "or" criteria	✓	**Description**	**Code Set**	**Code[11,12]**
		chronic myeloid leukemia, BCR::ABL positive	ICD-10	C92.10
		chronic myeloid leukemia, BCR::ABL positive, in remission	ICD-10	C92.11
		chronic myeloid leukemia, BCR::ABL positive, in relapse	ICD-10	C92.12
		chronic myeloid leukemia, disease; disorder	SNOMED	92818009
		myeloid leukemia in relapse; disorder	SNOMED	122901000119109
		relapsing chronic myeloid leukemia; disorder	SNOMED	415287001
		chronic myeloid leukemia category; morphologic abnormality	SNOMED	413841000
		chronic phase chronic myeloid leukemia; disorder	SNOMED	413847001
Lab tests missing or overdue (select a lab test and specify a date range)	✓	**Description**	**Code Set**	**Code[13]**
		t(9,22)(ABL1,BCR) Translocation [Presence] in Blood or Tissue by Molecular genetics method	LOINC	21821-4
			Local	
	BCR::ABL Date Range Date of BCR::ABL lab result (eg, greater than 6 months is [>m-6])		Date range: -	

Patient With a Missing or Overdue BCR::ABL (continued)

Chart Alert Content

	CATEGORY	✓	VALUES
CHART ALERT	Message to include in Chart Alert (eg, "This patient with CML has missing BCR::ABL lab tests.")		

Noncompliant Patient

Before you begin to build on this topic, it's important to consider several key technical questions that will influence the impact of your BCR::ABL program.

Technical Considerations:

Is medication adherence data returned by your e-prescribing vendor (ie, Surescripts)?

OPTION	ACTIONS
Yes – we receive data back from our eRx vendor on fills and other adherence items	Proceed with EHR report and Chart Alert build
No – we don't receive any med adherence data	Proceed with EHR report and Chart Alert build but note operational impact below

Operational Impact:

If you are not receiving TKI medication adherence data back from your vendor, the build is still possible but there is a greater operational burden placed upon the program.

Reports that are built to identify patients with late or missing medication fill data will return patients who may have had the medication filled despite data showing the opposite. This places the onus of follow-up onto whoever is managing the reports and the population. In other words, operational owners running these reports will need to do manual follow-up in the chart or with the patient directly to determine if the medication was filled.

Given the relatively small size of the population, this may not be a significant lift and may be worth it for your organization. However, it's important to plan for the additional workload.

Noncompliant Patient

Inclusion Criteria for Patient List Report and Chart Alert

INCLUSION CRITERIA

CATEGORY ("AND" CRITERIA)	✓	VALUES		
Patient Status		Alive		
Population (select one)		Only my patients		
		Seen in my department		
		All patients who meet the criteria		
		Other		
Age (eg ≥18)		> <		
Diagnosis/ Clinical Findings (select ≥ 1) "or" criteria	✓	**Description**	**Code Set**	**Code[11,12]**
		chronic myeloid leukemia, BCR::ABL positive	ICD-10	C92.10
		chronic myeloid leukemia, BCR::ABL positive, in remission	ICD-10	C92.11
		chronic myeloid leukemia, BCR::ABL positive, in relapse	ICD-10	C92.12
		chronic myeloid leukemia, disease; disorder	SNOMED	92818009
		myeloid leukemia in relapse; disorder	SNOMED	122901000119109
		relapsing chronic myeloid leukemia; disorder	SNOMED	415287001
		chronic myeloid leukemia category; morphologic abnormality	SNOMED	413841000
		chronic phase chronic myeloid leukemia; disorder	SNOMED	413847001
Medications (to identify patients who have lapsed TKI therapies and may be struggling with side effects) "or" criteria **Note: Insert FDA approved TKIs (or other medications) here.**	✓	**Description**	**Code Set**	**Code**
	Patients who have TKI medications that have lapsed (eg, 30-day prescription + 2 refills = 90 days supply, current date is >90 days from the original prescription, and not renewed with additional refills)		Lookback period: (starting today) or Date range: -	

Noncompliant Patient (continued)

Chart Alert Content

	CATEGORY	✓	VALUES
CHART ALERT	Message to include in Chart Alert (eg, "This patient with CML has TKI medications that have lapsed.")		

Patient Not Meeting Milestones

Before you begin to build on this topic, it's important to consider several key technical questions that will influence the impact of your BCR::ABL program.

Technical Considerations:

Are results interfaced back to your EHR?

OPTION	ACTIONS
Yes – our results interface returns BCR::ABL results and completes the original order	Proceed with EHR report and Chart Alert build
No – we don't receive results digitally to our EHR	Do not proceed with build – pursue an interfaced result option with your interfaces team before moving forward

If yes above, are interfaced results filed to discrete result values in your EHR?

OPTION	ACTIONS
Yes – results file to discrete components in the patients chart in a usable data format	Proceed with EHR report and Chart Alert build
No – results file as a PDF/image to the chart in a generic, non-reportable format	Proceed with EHR report and Chart Alert build but note operational impact below

Operational Impact:

If you are not receiving discrete results for your BCR::ABL tests, the build is still possible but there is a greater operational burden placed upon the program.

Reports that are built to identify patients with missing or overdue results will return patients who have had the order completed but the EHR won't be able to return that data. This places the onus of follow-up onto whoever is managing the reports and the population. In other words, operational owners running these reports will need to do manual follow-up in the chart or with the patient directly to determine if the result was completed and then manually key those results into the patients chart.

Given the relatively small size of the population who would be doing this testing, this may not be a significant lift and may be worth it for your organization. However, it's important to plan for the additional workload.

Patient Not Meeting Milestones

Inclusion Criteria for Patient List Report and Chart Alert

	CATEGORY ("AND" CRITERIA)	✓	VALUES		
INCLUSION CRITERIA	**Patient Status**		Alive		
	Population (select one)		Only my patients		
			Seen in my department		
			All patients who meet the criteria		
			Other		
	Age (eg ≥18)		> <		
	Diagnosis/ Clinical Findings (select ≥ 1) "or" criteria	✓	**Description**	**Code Set**	**Code[11,12]**
			chronic myeloid leukemia, BCR::ABL positive	ICD-10	C92.10
			chronic myeloid leukemia, BCR::ABL positive, in remission	ICD-10	C92.11
			chronic myeloid leukemia, BCR::ABL positive, in relapse	ICD-10	C92.12
			chronic myeloid leukemia, disease; disorder	SNOMED	92818009
			myeloid leukemia in relapse; disorder	SNOMED	122901000119109
			relapsing chronic myeloid leukemia; disorder	SNOMED	415287001
			chronic myeloid leukemia category; morphologic abnormality	SNOMED	413841000
			chronic phase chronic myeloid leukemia; disorder	SNOMED	413847001

Patient Not Meeting Milestones (continued)

Inclusion Criteria for Patient List Report and Chart Alert (continued)

	CATEGORY ("AND" CRITERIA)	✓	VALUES		
INCLUSION CRITERIA	**Lab Tests**	✓	**Description**	**Code Set**	**Code[13]**
			BCR::ABL1 kinase domain targeted mutation analysis	LOINC	55135-8
				Local	
			BCR::ABL Date Range Date of BCR::ABL lab result (eg, greater than 6 months is [>m-6])	Lookback period: (starting today) or Date range: -	
			BCR::ABL Lab Value Range Capturing out-of-range BCR::ABL lab test (eg, >0.1%, 0.1% - 1%, >1%)	Value: > <	
	Patients TKI activity	✓	**# of Current and Previous TKI Therapies**		
			≥		

Patient Not Meeting Milestones (continued)

Chart Alert Content

	CATEGORY	✓	VALUES
CHART ALERT	Message to include in Chart Alert (eg, "This patient with CML has outdated lab values or This patient has out-of-range lab values.")		

References: 1. Goldberg SL. Monitoring chronic myeloid leukemia in the real world: gaps and opportunities. *Clin Lymphoma Myeloma Leuk.* 2015;15(12):711-714. **2.** Milojkovic D, Apperley J, Gerrard G, et al. Responses to second-line tyrosine kinase inhibitors are durable: an intention-to-treat analysis in chronic myeloid leukemia patients. *Blood* 2012;119(8):1838–1843. **3.** Jabbour E, Parikh SA, Kantarjian H, et al. Chronic myeloid leukemia: mechanisms of resistance and treatment. *Hematol Oncol Clin North Am.* 2011;25(5):981-995 **4.** Patel AB, O'Hare T, Deininger MW. Mechanisms of resistance to ABL kinase inhibition in chronic myeloid leukemia and the development of next generation ABL kinase inhibitors. *Hematol Oncol Clin North Am.* 2017;31(4):589-612. **5.** Deangelo DJ. Managing chronic myeloid leukemia patients intolerant to tyrosine kinase inhibitor therapy. *Blood Cancer J.* 2012;19;2(10):e95. **6.** Hochhaus A, Saglio G, Hughes TP, et al. Long-term benefits and risks of frontline nilotinib vs imatinib for chronic myeloid leukemia in chronic phase: 5-year update of the randomized ENESTnd trial. *Leukemia.* 2016;30(5):1044-1054. **7.** Noens L, van Lierde MA, De Bock R, et al. Prevalence, determinants, and outcomes of nonadherence to imatinib therapy in patients with chronic myeloid leukemia: the ADAGIO study. *Blood.* 2009;113(22):5401-5411. **8.** Boons CCLM, Timmers L, Janssen JJWM, et al. Response and adherence to nilotinib in daily practice (RAND study): an in-depth observational study of chronic myeloid leukemia patients treated with nilotinib. *Eur J Clin Pharmacol.* 2020;76(9):1213-1226. **9.** Ibrahim AR, Eliasson L, Apperley JF, et al. Poor adherence is the main reason for loss of CCyR and imatinib failure for chronic myeloid leukemia patients on long-term therapy. *Blood.* 2011;117(14):3733-3736. **10.** Chen TC, Chen LC, Huang YB, Chang CS. Imatinib adherence associated clinical outcomes of chronic myeloid leukaemia treatment in Taiwan. *Int J Clin Pharm.* 2014;36(1):172-181. **11.** Medical billing codes search. Codify by AAPC. Accessed February 1, 2024. https://www.aapc.com/codes/code-search/ **12.** Health terminology code search. SNOMED CT Browser: National Library of Medicine. Accessed February 1, 2024. https://browser.ihtsdotools.org/? **13.** Clinical observation codes search. SearchLOINC: LOINC Regenstrief Institute, Inc. Accessed February 1, 2024. https://loinc.org/search/

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