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Management of chronic myeloid leukemia that is intolerant or resistant to front-line treatment.

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Introduction

With advances in treatment for chronic myeloid leukemia (CML), the natural history of chronic phase (CP) CML has changed, with most individuals expected to live a normal life expectancy.[1] The goal of therapy for most is to achieve a long-term deep molecular response (DMR) with the potential for medication discontinuation and treatment-free remission (TFR).[1] Currently, six oral therapies have been approved for CP-CML in Canada: (1) imatinib, a first-generation tyrosine kinase inhibitor (TKI); (2) dasatinib, (3) nilotinib, and (4) bosutinib, the second-generation TKIs (2G-TKIs); (5) ponantinib, a third-generation TKI; and (6) asciminib, specifically targeting the ABL Myristoyl pocket (STAMP) inhibitor. Classically, treatment for CP-CML has consisted of front-line imatinib and switching to a 2G-TKI upon treatment resistance or intolerance. Increasingly, patients are being prescribed an upfront 2G-TKI with the goal of achieving quicker and deeper molecular remissions and a TFR.[2] Challenges arise in CML when treatment with either two TKIs (imatinib + 2G-TKI) or one 2G-TKI fails, given the lack of evidence to inform clinical decision-making at this juncture. This paper aims to define TKI failure and help guide the selection of second-line treatment after failure of front-line therapy.

Defining treatment failure in CP-CML

TKI failure can be defined as either (1) resistance: a lack of hematologic response or failure to achieve molecular milestones or (2) intolerance: any adverse events or hematological toxicities mandating a switch in therapy.

The European LeukemiaNet 2020 guideline outlines milestones for molecular response in CP-CML at 3, 6, and 12 months during front- and second-line treatment with a TKI.[1] Molecular response is assessed as the ratio of BCR-ABL1 transcripts to ABL1 transcripts on the International Scale (IS) and reported as BCR-ABL1% on a log scale. Responses are divided into three zones: (1) optimal: treatment can be continued without modification; (2) warning: concerns for treatment resistance, with careful consideration as to continuing versus switching therapy; and (3) failure: defined treatment resistance mandating a switch in therapy **(Table 1)**.[1] The NCCN 2021 guideline offers similar milestones.[3]

Long-term outcomes of the pivotal trials that led to the approval of the first and second-generation TKIs in front-line treatment of CP-CML highlight the rates and reasons for treatment discontinuation **(Table 2)**.[4-7] Ten-year follow-up from the IRIS trial examining imatinib in front-line CP-CML demonstrated a discontinuation rate of 49.2%, 16% due to resistance, and 7% due to intolerance.[4] In contrast, five-to-ten-year follow-up of the 2G-TKIs in front-line CP-CML demonstrated lower discontinuation rates for resistance (5-6%), but higher discontinuation due to intolerance (19-34%).[5-7]

Selection of second-line therapy at the time of treatment failure is determined by: (1) the initial TKI used, (2) patient co-morbidities, and (3) the reason for drug discontinuation – resistance vs. intolerance. While several studies support the switch from front-line imatinib to a 2G-TKI, there is limited data to inform on the next best treatment post-front-line 2G-TKI. A summary of our approach to treatment failure can be found in **Figure 1**.

Second-line therapy post-imatinib

Switching to a 2G-TKI post-imatinib failure can provide long-term responses with complete cytogenetic remissions (CCyRs) of 40-50% and major molecular responses (MMRs) of 30-50%.[8-10]

	Optimal	Warning	Failure
3 months	≤10%	>10%	>10% if confirmed within 1-3 months
6 months	≤1%/CCyR	>1-10%	>10%
12 months	≤0.1%/MMR	>0.1-1%	>1%
Any time	≤0.1%/MMR	>0.1-1%, Loss of ≤0.1%	>1%, resistance mutations, high-risk cytogenetics

Table 1. Milestones for treating BCR-ABL1 on the international scale (IS). *Courtesy of Lisa Bilston, MD, FRCPC and Kareem Jamani, MD, FRCPC*
Abbreviations: CCyR: complete cytogenetic response; **MMR:** major molecular response

	Imatinib	Dasatinib	Nilotinib		Bosutinib
Trial	IRIS[4] (10-year, n=553)	DASISION[5] (5-year, n=258)	ENESTnd[6] (10-year)		BFORE[7] (5-year, n=268)
			300 BID (n=282)	400 BID (n=281)	
Rate of discontinuation	49.2% (n=272)	39% (n=100)	62% (n=175)	65% (n=182)	40% (n=108)
Treatment failure/ resistance	16% (n=88)	11% (n=28)	5% (n=13)	6% (n=17)	5% (n=15)
Intolerance	7% (n=38)	16% (n=42)	21% (n=62)	34% (n=98)	19% (n=53)

Table 2. Rates and reasons for discontinuation of front-line treatment with imatinib or a 2G-TKI. *Courtesy of Lisa Bilston, MD, FRCPC and Kareem Jamani, MD, FRCPC*
Abbreviations: 2g-TKI: second-generation tyrosine kinase inhibitor; **BID:** twice daily

Second-line dasatinib has demonstrated a seven-year progression-free survival (PFS) and overall survival (OS) of 30-50% and 60-70%, respectively, with higher rates in patients intolerant as opposed to resistant to imatinib.[8] Similar data favouring a switch to either nilotinib or bosutinib is outlined in **Table 3**.[9,10] Rates of discontinuation of 2G-TKI post-imatinib therapy due to treatment resistance range from 20-30%.[8-10]

While these data support a switch from imatinib to a 2G-TKI, selecting a 2G-TKI is based on the patient's co-morbidities to minimize intolerance.[2] Dasatinib is associated with an increased risk of pleural effusions, pulmonary arterial hypertension (PAH) and bleeding; avoiding use in patients with existing cardiopulmonary disease, uncontrolled hypertension, PAH, or at increased bleeding risk is recommended.[2,5]

Nilotinib can cause hyperglycemia, pancreatitis, QTc prolongation, and arterial occlusive events (AOE), with a ten-year follow-up from the ENESTnd trial demonstrating AOE rates of 24.8%.[2,6] Nilotinib should be avoided in patients with cardiovascular risk factors, a history of AOE's, or uncontrolled diabetes. Bosutinib's main side effect is diarrhea, and it should not be used in patients with inflammatory bowel disease or other conditions associated with chronic diarrhea.[2,7]

Treatment post-2G-TKI

Limited data exists to guide therapy after the use of a 2G-TKI in the front- or second-line setting. If treatment failure is due to resistance (as opposed to intolerance) mutational analysis should be done via Sanger Sequencing or next-

generation sequencing to help guide the selection of second-line therapy, with treatment tailored to the mutation found.[1] In the absence of a mutation to guide treatment, two options exist:

1. Switch to a different 2G-TKI:

The cohort studies SIMPLICITY and AIFA examined rates of switching from upfront 2G-TKI in a real-world setting.[11,12] SIMPLICITY demonstrated that at two years, rates of switching from dasatinib and nilotinib were 23.8% and 21.1%, respectively,[11] whereas AIFA had a rate of switching from front-line 2G-TKI of 13.2% at six years.[12] Neither study reported on clinical outcomes after switching.

Several studies have attempted to examine outcomes after treatment with a 2G-TKI in the front- or second-line setting. In an Albertan retrospective review, 232 patients were initiated on nilotinib (n=45) or dasatinib (n=187) in front-line treatment of CP-CML.[13] A total of 76 patients switched therapy, with rates of CCyR, MMR (without MR4.5 – 4.5 log reduction), and MR4.5 being 17%, 28%, and 13%, respectively. Of the 76 patients who switched therapy, only 6% (n=16) switched due to resistance. Rates of MMR (without MR4.5) and MR4.5 were 35% and 53% in the intolerant group vs. 44% and 6% in the resistant group, respectively. A similar study examining the long-term outcomes after front-line treatment with a 2G-TKI in CP-CML demonstrated comparable results, with 42.4% of patients requiring a switch in therapy, 26.4% due to intolerance and 16% due to resistance.[14] While intolerant patients could obtain a DMR, outcomes were inferior in resistant patients; resistant patients not responding to second-line 2G-TKI had a 7-year-OS of 66.1% compared to an OS of 100% in intolerant patients. Several other studies, which included small

	Dasatinib (100 mg OD)		**Nilotinib (400 mg BID)**		**Bosutinib (500 mg OD)**	
Trial	CA180-034[8] (n= 167)		Giles *et al.* (2013)[9] (n=321)		Brummendorf *et al.* (2020)[10] (n=284)	
Reason for imatinib discontinuation	Intolerant (n= 43)	Resistant (n=124)	Intolerant (n=90)	Resistant (n=226)	Intolerant (n=89)	Resistant (n=195)
Follow-up	7 years		48+ months		8+ years	
CCyR	44%		45%		42 (53%)	88 (48%)
MMR	22 (55%)	51 (43%)	NA		25 (36%)	58 (46%)
PFS	51%	39%	4 year - 57%		NA	NA
OS	70%	63%	4 year- 78%		9 year - 74%	
Rate of discontinuation	166 (includes study closure)		224		NA	
Resistance/progression	35 (21%)		96 (30%)		27%	
Intolerance/AEs	39 (24%)		66 (21%)		NA	
Adverse events	• Pleural effusions • Pulmonary arterial HTN • Bleeding		• Arterio-occlusive events (AOEs) • Elevated blood glucose • Pancreatitis • QTc prolongation		• Diarrhea • Nausea • Elevated liver enzymes	

Table 3. Second-line treatment with a 2G-TKI after imatinib failure. *Courtesy of Lisa Bilston, MD, FRCPC and Kareem Jamani, MD, FRCPC*

Abbreviations: AE: adverse event; **BID:** twice daily; **CCyR:** complete cytogenetic response; **HTN:** hypertension; **MMR:** major molecular response; **PFS:** progression-free survival; **OD:** once daily; **OS:** overall survival

numbers of patients, have examined 2G-TKI's in the third-line setting.[15] Results of the Phase 4 BYOND study examining bosutinib in the second, third, and fourth line of treatment demonstrated a progressive reduction in rates of MMR at two years with each successive line of therapy (second-line: 82.6%, third-line: 74.5%, and fourth-line: 56.3%), with rates of response at 2 years being higher in patients intolerant (MMR of 80.8%) vs. resistant (MMR of 61.8%) to treatment.[16] These studies highlight that patients who have demonstrated resistance to a 2G-TKI are a particularly high-risk group of individuals; if the choice is made to pursue a 2G-TKI in this setting, it should only be done with close monitoring and response assessments at 3-6 months, with a prompt switch to third-line therapy (asciminib or ponatinib) if molecular targets are not being met.

2. Switch to Asciminib vs. Ponatinib:

CP-CML that is resistant to two or more TKIs is eligible for therapy with either ponatinib or asciminib.

Ponatinib is a potent third-generation TKI, with activity against several clinically relevant BCR-ABL1 kinase domain mutations, including the T315I mutation.[1] Ponatinib was studied in the Phase 2 PACE trial, which demonstrated the efficacy of ponatinib in the treatment of CP-CML that was resistant or intolerant to dasatinib, nilotinib, or in the presence of the BCR-ABL1 T315I mutation.[17] The major limitation of ponatinib was the high rates of AOEs at 31%. The OPTIC trial subsequently examined the efficacy of ponatinib at starting doses of 45 mg/day, 30 mg/day or 15 mg/day, with a dose reduction to 15 mg/day at MR2 (2-log reduction) (BCR-ABL1 <1%).[18] The OPTIC trial demonstrated that upfront high-dose ponatinib followed by dose de-escalation was both highly efficacious and superior to the lower dose arms (MR2 at 12 months of 52% vs. 36% vs. 25% in the 45 mg, 30 mg, and 15 mg cohort, respectively). Dose de-escalation reduced AOEs compared to the PACE data, with AOEs of 9.6%, 5.3%, and 3.2% in the 45 mg, 30 mg, and 15 mg cohorts, respectively. In the T315I group, upfront treatment with 45 mg/day was superior to 30 mg/day with MR2 rates of 60% and 25% at 12 months, respectively. Without resistance or a documented KD mutation, the advantage of higher dose ponatinib was less apparent.

Asciminib is a novel, first-in-class STAMP inhibitor that inhibits the kinase activity of BCR-ABL1 via allosteric binding. Asciminib was studied in the Phase 3 ASCEMBL trial, which compared asciminib 40 mg twice daily (BID) to bosutinib 500 mg once daily (OD) in CP-CML previously treated with two or more TKIs.[19] Asciminib was found to have superior

	Ponatinib 45 mg OD	Asciminib 40 mg BID
Trial	OPTIC (n= 92)	ASCEMBL (n=157)
Follow-up	32 months	19 months
≥3 prior TKI lines	53%	48%
Resistant to the last TKI	98%	61%
Intolerant to prior TKI	2%	38%
MR2 at 12 months	44%	42%
Discontinuation due to resistance/progression	19%	24%
Discontinuation due to intolerance/AE's	17%	6%
AOEs per 100 patient years	9.6	3.4

Table 4. Choice of TKI after use of prior 2G-TKI. *Courtesy of Lisa Bilston, MD, FRCPC and Kareem Jamani, MD, FRCPC*
Abbreviations: 2G-TKI: second-generation tyrosine kinase inhibitor; **AOE:** arterial occlusive events; **BID:** twice daily; **MR2:** 2-log molecular response; **OD:** once daily; **TKI:** tyrosine kinase inhibitor

MR2 rates at 12 months compared to bosutinib at 42% vs. 19%, respectively.

Randomized controlled trials comparing the efficacy of asciminib to ponatinib in the third-line setting are lacking, but a comparison of the trials leading to their approval can inform decision-making **(Table 4)**.[20] The OPTIC trial included more patients with TKI resistance or documented kinase domain mutations than the ASCEMBL trial, which included more patients intolerant to prior therapies.[18,19] Molecular response rates at 12 months were similar for ponatinib vs. asciminib, with MR2 rates of 44% vs. 42%, respectively. Both drugs have demonstrated activity against the T315I mutation at higher doses. In a Phase 1 trial, asciminib at 200 mg BID demonstrated efficacy against the T315I mutation, with MMR rates at six months of 57% in ponatinib-naïve patients and 29% in ponatinib resistant/intolerant patients.[21] Toxicity appeared comparable to standard dose therapy. The OPTIC trial demonstrated the efficacy of ponatinib at 45 mg OD against the T315I mutation, but with dose de-escalation to prevent AOEs, loss of response exceeded 30%.[18] Despite both asciminib and ponatinib having efficacy against the T315I mutation and in CP-CML resistant to prior 2G-TKIs, current recommendations favour the use of ponatinib in CP-CML resistant to a 2G-TKI, especially in the setting of low cardiovascular disease risk. In contrast, asciminib is preferred when there has been intolerance to prior TKIs or when cardiovascular risk is high.[2,20,22] In addition, the higher dose of asciminib that has demonstrated efficacy against the T315I mutation (200 mg) is not routinely available/funded in Canada, limiting its utility in this setting.

Role of allogeneic-hematopoietic stem cell transplant (allo-HSCT)

Allo-HSCT remains the only true curative treatment for CML. However, with second- and third-generation TKIs, it is far less commonly utilized in CP-CML. The ELN-2020 guides indications for allo-HSCT in CP-CML.[1] Allo-HSCT should be considered in CP-CML that has demonstrated:

1. Resistance or intolerance to 2+ TKI's
2. Inadequate recovery of hematopoiesis
3. Resistance to a 2G-TKI used either in the front- or second-line setting
4. Resistance to ponatinib or failure to respond to ponatinib after three months of treatment
5. Emergence of high-risk cytogenetics

The timing of allo-HSCT is critical. Outcomes are best in early CP-CML compared to late CP-CML, with the latter at an increased risk of progression to accelerated phase CML. The goal of therapy prior to transplant is to return to chronic phase CML if the patient had transformed prior to transplant.[1,20]

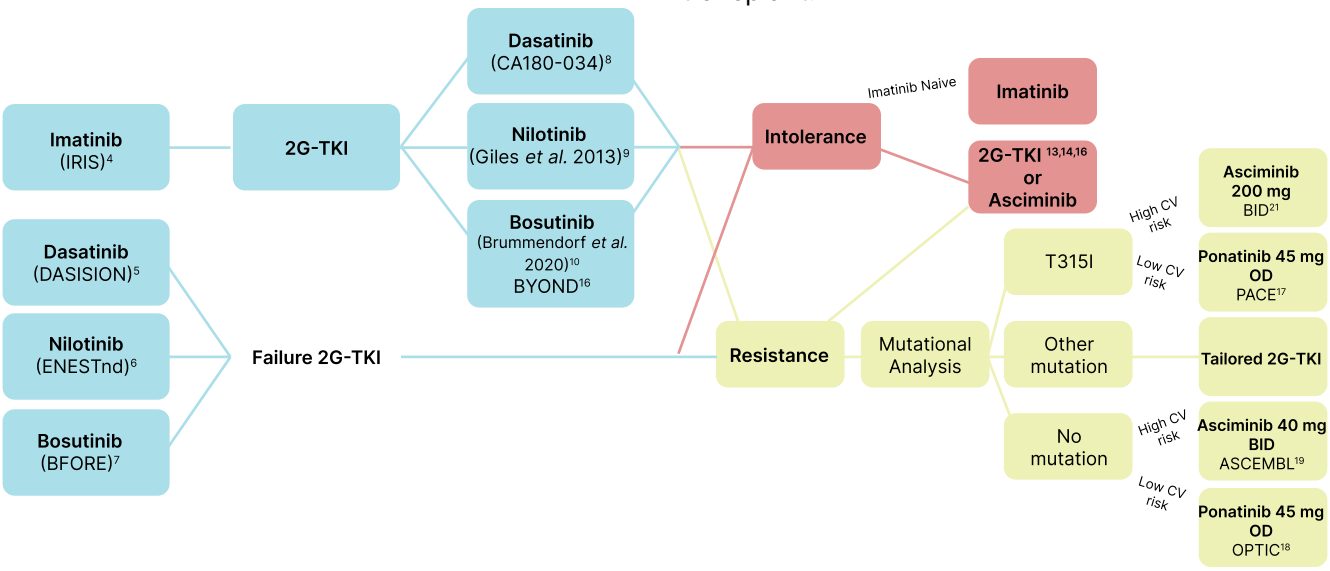

Figure 1. Choice of tyrosine kinase inhibitor after resistance or intolerance to upfront treatment with imatinib or a 2G-TKI. *Courtesy of Lisa Bilston, MD, FRCPC and Kareem Jamani, MD, FRCPC*

Abbreviations: 2G-TKI: second-generation tyrosine kinase inhibitor; **allo-HSCT:** allogeneic hematopoietic stem cell transplant; **BID:** twice daily; **OD:** once daily

Conclusion:

TKIs have markedly changed the landscape of CP-CML treatment, with ten-year OS rates approaching 80%.[22] Most patients require a change in TKI at some point in the treatment of CP-CML, with rates of switching from imatinib or a 2G-TKI approaching 50% and 60%, respectively.[4-7] Clinical outcomes diverge based on the reason for treatment discontinuation, with intolerance in the form of adverse events or hematological toxicities having better long-term outcomes with switching to a 2G-TKI compared to treatment resistance.[13,14,16] In the event of treatment resistance to imatinib, switching to a 2G-TKI confers good outcomes.[8-10] In the event of resistance to a 2G-TKI, kinase domain mutations should be assessed to help guide further therapies.[1] Inferior outcomes are found in patients resistant to a 2G-TKI; an early switch in therapy to either ponatinib or asciminib should be considered and guided by cardiovascular risk.[2,20,22] Allo-HSCT remains a treatment consideration for all patients refractory to at least one 2G-TKI.[20]

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References:

1. Hochhaus A, Baccarani M, Silver RT, Schiffer C, Apperley JF, Cervantes F, et al. European LeukemiaNet 2020 recommendations for treating chronic myeloid leukemia. Leukemia. 2020 Mar 3;34(34).
2. Jabbour E, Kantarjian H. Chronic myeloid leukemia: 2022 update on diagnosis, therapy, and monitoring. American Journal of Hematology. 2022 Jul 6;97(9).
3. Deininger MW, Shah NP, Altman JK, Berman E, Bhatia R, Bhatnagar B, et al. Chronic Myeloid Leukemia, Version 2.2021, NCCN Clinical Practice Guidelines in Oncology. Journal of the National Comprehensive Cancer Network [Internet]. 2020 Oct 1;18(10):1385–415.
4. Hochhaus A, Larson RA, Guilhot F, Radich JP, Branford S, Hughes TP, et al. Long-Term Outcomes of Imatinib Treatment for Chronic Myeloid Leukemia. New England Journal of Medicine. 2017 Mar 9;376(10):917–27.
5. Cortes JE, Saglio G, Kantarjian HM, Baccarani M, Mayer J, Boqué C, et al. Final 5-Year Study Results of DASISION: The Dasatinib Versus Imatinib Study in Treatment-Naïve Chronic Myeloid Leukemia Patients Trial. Journal of Clinical Oncology [Internet]. 2016 Jul 10;34(20):2333–40.
6. Kantarjian HM, Hughes TP, Larson RA, Kim DW, Issaragrisil S, le Coutre P, et al. Long-term outcomes with frontline nilotinib versus imatinib in newly diagnosed chronic myeloid leukemia in chronic phase: ENESTnd 10-year analysis. Leukemia [Internet]. 2021 Jan 7;35(2):440–53.
7. Brümmendorf TH, Cortes JE, Milojkovic D, Gambacorti-Passerini C, Clark RE, le Coutre P, et al. Bosutinib versus imatinib for newly diagnosed chronic phase chronic myeloid leukemia: final results from the BFORE trial. Leukemia. 2022 May 28;36(7):1825–33.
8. Shah NP, Rousselot P, Schiffer C, Rea D, Cortes JE, Milone J, et al. Dasatinib in imatinib-resistant or -intolerant chronic-phase, chronic myeloid leukemia patients: 7-year follow-up of study CA180-034. American Journal of Hematology. 2016 Jun 20;91(9):869–74.
9. Giles FJ, le Coutre PD, Pinilla-Ibarz J, Larson RA, Gattermann N, Ottmann OG, et al. Nilotinib in imatinib-resistant or imatinib-intolerant patients with chronic myeloid leukemia in chronic phase: 48-month follow-up results of a phase II study. Leukemia. 2012 Jul 5;27(1):107–12.
10. Brümmendorf TH, Cortes JE, Goh YT, Yilmaz M, Klisovic RB, Purcell S, et al. Bosutinib (BOS) for chronic phase (CP) chronic myeloid leukemia (CML) after imatinib (IMA) failure: ≥8-y update of a phase I/II study. Journal of Clinical Oncology. 2020 May 20;38(15_ suppl):7549–9.
11. Hehlmann R, Cortes JE, Zyczynski T, Gambacorti-Passerini C, Goldberg SL, Mauro MJ, et al. Tyrosine kinase inhibitor interruptions, discontinuations and switching in patients with chronic-phase chronic myeloid leukemia in routine clinical practice: SIMPLICITY. American Journal of Hematology. 2018 Oct 31;94(1):46–54.
12. Massimo Breccia, Pier Paolo Olimpieri, Odoardo Olimpieri, Pane F, Iurlo A, Paolo Foggi, et al. How many chronic myeloid leukemia patients who started a frontline second-generation tyrosine kinase inhibitor have to switch to a second-line treatment? A retrospective analysis from the monitoring registries of the italian medicines agency (AIFA). Cancer medicine. 2020 Apr 22;9(12):4160–5.
13. Ma CE, Ghosh S, Leyshon C, Blosser N, Deonne Dersch-Mills, Jupp J, et al. Clinical outcome of chronic myeloid leukemia patients who switch from first-line therapy with a second generation tyrosine kinase inhibitor to an alternative TKI. Leukemia research. 2021 Dec 1;111:106674–4.
14. Claudiani S, Chughtai F, Khan A, Hayden C, Fernando F, Khorashad J, et al. Long-term outcomes after upfront second-generation tyrosine kinase inhibitors for chronic myeloid leukemia: managing intolerance and resistance. Leukemia [Internet]. 2024 Apr 1 [cited 2024 Apr 15];38(4):796–802.
15. Hochhaus A, Breccia M, Saglio G, García-Gutiérrez V, Réa D, Janssen J, et al. Expert opinion—management of chronic myeloid leukemia after resistance to

second-generation tyrosine kinase inhibitors. Leukemia [Internet]. 2020 May 4;1–8.
16. Hochhaus A, Gambacorti-Passerini C, Abboud C, Gjertsen BT, Brümmendorf TH, Smith BD, et al. Bosutinib for pretreated patients with chronic phase chronic myeloid leukemia: primary results of the phase 4 BYOND study. Leukemia. 2020 Jun 22;34(8):2125–37.
17. Cortes JE, Kim DW, Pinilla-Ibarz J, le Coutre PD, Paquette R, Chuah C, et al. Ponatinib efficacy and safety in Philadelphia chromosome–positive leukemia: final 5-year results of the phase 2 PACE trial. Blood [Internet]. 2018 Jul 26;132(4):393–404.
18. Cortes J, Apperley J, Lomaia E, Moiraghi B, Undurraga Sutton M, Pavlovsky C, et al. Ponatinib dose-ranging study in chronic-phase chronic myeloid leukemia: a randomized, open-label phase 2 clinical trial. Blood [Internet]. 2021 Nov 25;138(21):2042–50.
19. Réa D, Mauro MJ, Boquimpani C, Minami Y, Lomaia E, Voloshin S, et al. A Phase 3, Open-Label, Randomized Study of Asciminib, a STAMP Inhibitor, vs Bosutinib in CML After ≥2 Prior TKIs. Blood [Internet]. 2021 Aug 20;138(21).
20. Hughes TP, Naranie Shanmuganathan. Management of TKI-resistant chronic phase CML. 2022 Dec 9;2022(1):129–37.
21. Cortes JE, Hughes TP, Mauro MJ, Hochhaus A, Rea D, Goh YT, et al. Asciminib, a First-in-Class STAMP Inhibitor, Provides Durable Molecular Response in Patients (pts) with Chronic Myeloid Leukemia (CML) Harboring the T315I Mutation: Primary Efficacy and Safety Results from a Phase 1 Trial. Blood [Internet]. 2020 Nov 5 [cited 2023 Feb 17];136(Supplement 1):47–50.
22. Uhm J. Treatment after failure of frontline therapy of chronic myeloid leukemia in chronic phase including allogeneic hematopoietic stem cell transplantation. Blood research. 2023 Apr 30;58(S1):S109–13.