FOR ADULT PATIENTS WITH Ph+ CML[1]

DISCOVER the POTENTIAL with BOSULIF

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)[2]

Bosutinib (BOSULIF) is recommended by the NCCN Guidelines as a primary treatment option for patients with newly diagnosed CML (category 1) and as an option for CML patients in need of 2nd- or later-line TKI therapy (category 2A).

INDICATIONS

BOSULIF® (bosutinib) is indicated for the treatment of adult patients with

- Newly diagnosed chronic phase (CP) Ph+ chronic myelogenous leukemia (CML). This indication is approved under accelerated approval based on molecular and cytogenetic response rates. Continued approval for this indication may be contingent upon verification and confirmation of clinical benefit in an ongoing long-term follow-up trial
- Chronic, accelerated, or blast phase Ph+ CML with resistance or intolerance to prior therapy

SELECTED SAFETY INFORMATION

Contraindication: History of hypersensitivity to BOSULIF. Reactions have included anaphylaxis. Anaphylactic shock occurred in less than 0.2% of treated patients in single-agent cancer studies with BOSULIF.

Gastrointestinal Toxicity: Diarrhea, nausea, vomiting, and abdominal pain occur with BOSULIF. In the study of patients with newly diagnosed CP Ph+ CML, the median time to onset for diarrhea (all grades) was 3 days and the median duration per event was 3 days. In the study of patients with CML who were resistant or intolerant to prior therapy, median time to onset of diarrhea (all grades) was 2 days, median duration was 2 days, and the median number of episodes per patient was 3 (range 1-268). Monitor and manage patients using standards of care, including antidiarrheals, antiemetics, and/or fluid replacement. Withhold, dose reduce, or discontinue BOSULIF as necessary.

NCCN=National Comprehensive Cancer Network;
Ph+=Philadelphia chromosome–positive; TKI=tyrosine kinase inhibitor.

Please see additional Important Safety Information on page 19 and accompanying full Prescribing Information in pocket.

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Expectations in CML treatment are evolving[3]

The value of achieving molecular milestones

In today's treatment of CML, CCyR remains a satisfactory and acceptable response; however, increasing emphasis has been placed on achieving MMR as well as molecular responses beyond MMR.[3]

Response criteria[2]

	MR level	% *BCR-ABL1*
Early MR	1.0	≤10% at 3 and 6 months
Major MR	3.0	≤0.1% or ≥3-log reduction in *BCR-ABL1* from baseline
Subsequent responses	4.0 4.5	MR[4]: ≤0.01% MR[4.5]: ≤0.0032%

Early molecular response may impact future outcomes[4]

- It has been shown that patients with *BCR-ABL1* ≤10% at 3 and 6 months may achieve better outcomes (OS, PFS, CCyR)*

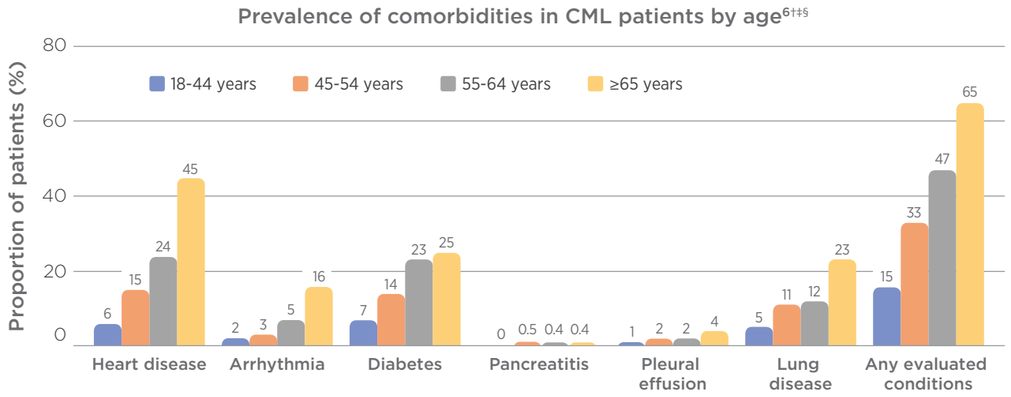
Patients reaching MMR and responses beyond MMR may be more likely to achieve improved long-term clinical outcomes[5]

- Reaching MMR, MR[4], and MR[4.5] are important milestones for patients, as they may minimize the risk of loss of CCyR or MMR*

*Bosutinib was not included in the study.

Considering comorbidities is important throughout CML treatment[6]

The increase in comorbidities with age underscores the importance of adverse reaction profiles when prescribing CML treatment.[2,6]



†Bosutinib was not included in the study.

‡A real-world analysis in which 2296 patients who had CML and initiated TKI treatment were identified from the MarketScan® Commercial and Medicare Supplemental databases (January 1, 2006, to June 30, 2012). Demographics and prevalence of comorbid conditions relevant to TKI treatment choice per NCCN Guidelines® (heart disease, arrhythmia, diabetes, pancreatitis, pleural effusion, lung disease) were assessed among the overall study population and among subgroups.

§Mean age in this study was 56 years old.

CCyR=complete cytogenetic response; CML=chronic myelogenous leukemia; MMR=major molecular response; MR=molecular response; NCCN=National Comprehensive Cancer Network; OS=overall survival; PFS=progression-free survival; TKI=tyrosine kinase inhibitor.

SELECTED SAFETY INFORMATION

Myelosuppression: Thrombocytopenia, anemia, and neutropenia occur with BOSULIF. Perform complete blood counts weekly for the first month and then monthly thereafter, or as clinically indicated. Withhold, dose reduce, or discontinue BOSULIF as necessary.

PATIENT PROFILE

Consider Tracey
A newly diagnosed CML patient

Tracey, 58

Nurse (actively employed)

Tracey is not an actual patient.

DIAGNOSIS

CP Ph+ CML, diagnosed a month ago. Routine CBC by PCP showed a WBC count of 100 × 10^9/L. Hem/onc confirmed diagnosis after PCP referral.

MEDICAL HISTORY

History of diabetes (controlled) and smoking.

SOKAL RISK SCORE

0.9 (intermediate risk).‖

‖Intermediate risk=Sokal score of 0.8 to 1.2.

CBC=complete blood count; CP=chronic phase; PCP=primary care physician; Ph+=Philadelphia chromosome–positive; WBC=white blood cell.

SELECTED SAFETY INFORMATION

Hepatic Toxicity: BOSULIF may cause elevations in serum transaminases (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]). In a study of BOSULIF in combination with letrozole, one drug-induced liver injury occurred without alternative causes. In the study of patients with newly diagnosed CP Ph+ CML, the incidence of ALT/AST elevations was 31% and 23%, respectively. In patients with CML who were resistant or intolerant to prior therapy, the incidence of ALT/AST elevations was 18% and 15%, respectively. Twenty percent of the patients resistant or intolerant to prior therapy experienced an increase in either ALT or AST. Perform hepatic enzyme tests at least monthly for the first 3 months and as clinically indicated. In patients with transaminase elevations, monitor liver enzymes more frequently. Withhold, dose reduce, or discontinue BOSULIF as necessary. In patients with mild, moderate, or severe hepatic impairment, the recommended starting dose is 200 mg daily.

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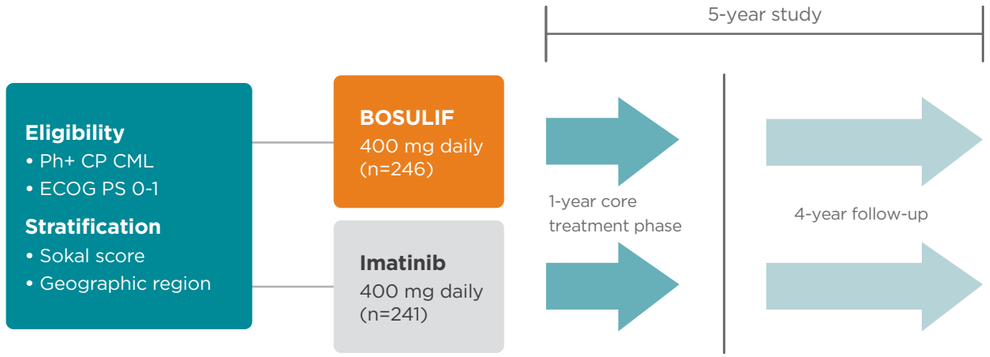
BFORE: an ongoing phase 3 study of BOSULIF in newly diagnosed adult patients with CP Ph+ CML[1]

A randomized, 2-arm, open-label, multicenter trial conducted to investigate the efficacy and safety of BOSULIF vs imatinib

- 536 patients were randomized to receive 400 mg of BOSULIF® (bosutinib) or imatinib once daily
- The primary endpoint was evaluated in a modified intent-to-treat (mITT) population of patients with Ph+ CML (n=487)

STUDY DESIGN: mITT POPULATION (1:1)[1,3]



Primary endpoint
- MMR at 12 months

Secondary endpoints
- CCyR by month 12
- MMR by month 18
- Duration of CCyR and MMR
- EFS
- OS

Exploratory endpoints
- MMR at 12 months (ITT population; N=536)
- MMR at 3, 6, and 9 months
- MR^4 and $MR^{4.5}$ at 3, 6, 9, and 12 months
- Time to MMR and CCyR
- Time to on-treatment transformation to AP or BP CML

MMR at 12 months was defined as ≤0.1% *BCR-ABL* ratio on the International Scale (corresponding to a ≥3-log reduction from standardized baseline) with a minimum of 3000 *ABL* transcripts assessed by the central laboratory. CCyR was defined as the absence of Ph+ metaphases in chromosome banding analysis of ≥20 metaphases derived from bone marrow aspirate, or MMR if an adequate cytogenetic assessment was unavailable. MR^4 was defined as ≤0.01% *BCR-ABL1* transcripts on the International Scale with ≥9800 *ABL1* assessed; $MR^{4.5}$ was defined as ≤0.0032% *BCR-ABL1* transcripts on the International Scale with ≥30,990 *ABL1* assessed.[1,3]

AP=accelerated phase; BFORE=**B**osutinib Trial in **F**irst-Line Chr**o**nic Myelogenous Leukemia T**re**atment; BP=blast phase; CCyR=complete cytogenetic response; CML=chronic myelogenous leukemia; CP=chronic phase; ECOG PS=Eastern Cooperative Oncology Group performance status; EFS=event-free survival; MMR=major molecular response; MR=molecular response; OS=overall survival; Ph+=Philadelphia chromosome–positive.

SELECTED SAFETY INFORMATION

Cardiac Failure: Cardiac failure and left ventricular dysfunction have been reported in patients taking BOSULIF. These events occurred more frequently in previously treated patients than in patients with newly diagnosed CML and were more frequent in patients with advanced age or risk factors, including previous medical history of cardiac failure. In a randomized study with newly diagnosed CML, cardiac failure occurred in 1.5% of patients treated with BOSULIF compared to 0.8% of patients treated with imatinib. In a single-arm study in patients with CML who were resistant or intolerant to prior therapy, cardiac failure was observed in 5.3% of patients treated with BOSULIF. Monitor patients for signs and symptoms consistent with cardiac failure and treat as clinically indicated. Interrupt, dose reduce, or discontinue BOSULIF as necessary.

BOSULIF was studied in a population representing a clinical spectrum of patients with CP CML[1,3]

BFORE included patients with comorbidities and across all Sokal risk groups

Characteristic*	BOSULIF (n=246)	Imatinib (n=241)	Total (N=487)
Age, n (%)			
Median (range), years	52 (18-84)	53 (19-84)	53 (18-84)
Age ≤64 years	198 (80.5)	199 (82.6)	397 (81.5)
Age ≥65 years	48 (19.5)	42 (17.4)	90 (18.5)
Sokal risk group, n (%)			
Low	94 (38.2)	95 (39.4)	189 (38.8)
Intermediate	101 (41.1)	95 (39.4)	196 (40.2)
High	51 (20.7)	51 (21.2)	102 (20.9)
ECOG PS,† n (%)			
0	174 (70.7)	170 (70.5)	344 (70.6)
1	72 (29.3)	70 (29.0)	142 (29.2)
Extramedullary disease, n (%)	14 (5.7)	8 (3.3)	22 (4.5)
History of cardiac disease,‡ n (%)	28 (11.4)	29 (12.0)	57 (11.7)
History of cardiac procedures, n (%)	15 (6.1)	16 (6.6)	31 (6.4)

Patients with uncontrolled or significant cardiovascular disease, including prolonged QT interval, were excluded by protocol.[1]
*NOTE: Data are n (%) unless noted otherwise. mITT population includes Ph+ patients with typical (e13a2 and/or e14a2) *BCR-ABL1* transcript types.
†Data missing for 1 patient in the imatinib arm.
‡Per case report form collected at screening if the patient had history of coronary disease.

SELECTED SAFETY INFORMATION

Fluid Retention: Fluid retention occurs with BOSULIF and may cause pericardial effusion, pleural effusion, pulmonary edema, and/or peripheral edema. Monitor and manage patients using standards of care. Interrupt, dose reduce, or discontinue BOSULIF as necessary.

Renal Toxicity: An on-treatment decline in estimated glomerular filtration rate has occurred in patients treated with BOSULIF. Monitor renal function at baseline and during therapy, with particular attention to patients with preexisting renal impairment or risk factors for renal dysfunction. Lower starting doses are recommended for patients with renal impairment. For patients who have declining renal function while on BOSULIF or who cannot tolerate the starting dose, follow dose adjustment recommendations for toxicity.

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Patients taking BOSULIF had higher rates of molecular and cytogenetic responses vs imatinib[1,7]

BOSULIF significantly improved MMR and CCyR[1]

MMR AT 12 MONTHS
PRIMARY ENDPOINT

47%
BOSULIF
(95% CI, 40.9-53.4)
n=246

37%
Imatinib
(95% CI, 30.8-43.0)
n=241

P=0.0200*

CCyR BY 12 MONTHS
SECONDARY ENDPOINT

77%
BOSULIF
(95% CI, 72.0-82.5)
n=246

66%
Imatinib
(95% CI, 60.4-72.4)
n=241

P=0.0075*

The 24-month data analysis, while not prespecified in the protocol, is from the ongoing BFORE trial and is presented to provide additional information about BOSULIF and its use in newly diagnosed Ph+ CML patients.[3]

24-month MMR and CCyR were post hoc exploratory analyses

These analyses were not powered to detect statistical significance. No conclusion of efficacy can be drawn from these data. Lack of multiplicity adjustments can be a limitation of these analyses.

MMR AT 24 MONTHS[7]

62%
BOSULIF
(95% CI, 55.7-67.9)
n=246

53%
Imatinib
(95% CI, 46.8-59.4)
n=241

CCyR BY 24 MONTHS[7]

83%
BOSULIF
(95% CI, 77.8-87.3)
n=246

77%
Imatinib
(95% CI, 71.4-82.1)
n=241

Cumulative transformation rates

- After a minimum of 12 months of follow-up, 5 BOSULIF® (bosutinib) patients and 7 imatinib patients transformed to AP or BP CML while on treatment[1]
- After 24 months of follow-up, 6 and 7 patients transformed to AP or BP CML on BOSULIF and imatinib, respectively[7]

*Derived from Cochran–Mantel–Haenszel test stratified by geographical region and Sokal risk score at randomization; *P* values are 2 sided.
AP=accelerated phase; BFORE=**B**osutinib Trial in **F**irst-Line Chr**o**nic Myelogenous Leukemia T**re**atment; BP=blast phase; CCyR=complete cytogenetic response; CI=confidence interval; CML=chronic myelogenous leukemia; CP=chronic phase; MMR=major molecular response; Ph+=Philadelphia chromosome–positive.

SELECTED SAFETY INFORMATION

Embryofetal Toxicity: BOSULIF can cause fetal harm. Women of childbearing potential should be advised of the potential hazard to the fetus and to use effective contraceptive measures while on treatment and for at least 2 weeks after the final dose.

IN NEWLY DIAGNOSED ADULTS WITH CP Ph+ CML

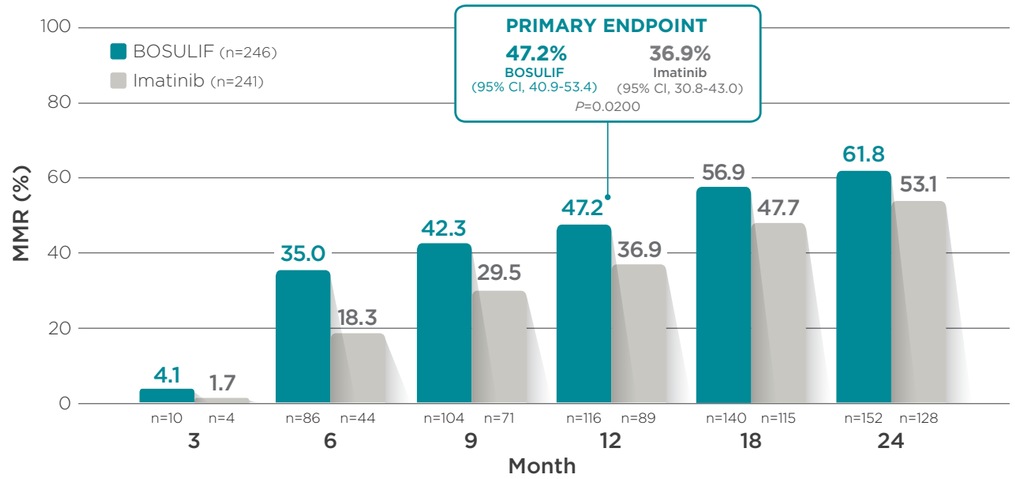
More patients reached the 12-month MMR treatment milestone with BOSULIF vs imatinib[1,3,7]

Primary and secondary endpoints

In the BFORE study, MMR at 12 months was a primary endpoint, and MMR at 18 months was a secondary endpoint.

Exploratory analyses

MMR at 3, 6, and 9 months were prespecified exploratory analyses. MMR at 24 months is a post hoc exploratory analysis of the ongoing BFORE trial. These analyses were not powered to detect statistical significance. No conclusion of efficacy can be drawn from these data. Lack of multiplicity adjustments can be a limitation of these analyses.



SELECTED SAFETY INFORMATION

Adverse Reactions: The most common adverse reactions observed in greater than or equal to 20% of patients with newly diagnosed CML were diarrhea, nausea, thrombocytopenia, rash, increased ALT, abdominal pain, and increased AST. The most common Grade 3/4 adverse reactions and laboratory abnormalities observed in greater than 10% of newly diagnosed CML patients were increased ALT and thrombocytopenia. The most common adverse reactions observed in greater than or equal to 20% of patients with CML who were resistant or intolerant to prior therapy were diarrhea, nausea, abdominal pain, rash, thrombocytopenia, vomiting, anemia, fatigue, pyrexia, cough, headache, increased ALT, and edema. The most common Grade 3/4 adverse reactions and laboratory abnormalities observed in greater than 10% of patients who were resistant or intolerant to prior therapy were thrombocytopenia, neutropenia, and anemia.

CYP3A Inhibitors and Inducers: Avoid concurrent use with strong or moderate CYP3A inhibitors or strong CYP3A inducers.

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MR[4] and MR[4.5] over time[3,7]

Exploratory analyses

MR[4] and MR[4.5] at 3, 6, 9, and 12 months were prespecified exploratory analyses. MR[4] and MR[4.5] at 24 months are post hoc exploratory analyses of the ongoing BFORE trial. These analyses were not powered to detect statistical significance. No conclusion of efficacy can be drawn from these data. Lack of multiplicity adjustments can be a limitation of these analyses.

MR[4]	3 months	6 months	9 months	12 months	24 months
BOSULIF® (bosutinib) (n=246)	**0.4%** (n=1)	**9.8%** (n=24)	**13.8%** (n=34)	**20.7%** (n=51)	**33.3%** (n=82)
Imatinib (n=241)	**0.0%** (n=0)	**4.6%** (n=11)	**8.3%** (n=20)	**12.0%** (n=29)	**26.6%** (n=64)

MR[4.5]	3 months	6 months	9 months	12 months	24 months
BOSULIF (n=246)	**0.0%** (n=0)	**2.0%** (n=5)	**4.5%** (n=11)	**8.1%** (n=20)	**12.6%** (n=31)
Imatinib (n=241)	**0.0%** (n=0)	**0.8%** (n=2)	**2.9%** (n=7)	**3.3%** (n=8)	**11.2%** (n=27)

BFORE=**B**osutinib Trial in **F**irst-Line Chr**o**nic Myelogenous Leukemia T**re**atment; CML=chronic myelogenous leukemia; CP=chronic phase; MR=molecular response; Ph+=Philadelphia chromosome–positive.

SELECTED SAFETY INFORMATION

Proton Pump Inhibitors (PPIs): Consider using short-acting antacids or H2 blockers instead of PPIs to avoid a reduction in BOSULIF exposure. Separate antacid or H2 blocker dosing and BOSULIF dosing by more than 2 hours.

Lactation: Because of the potential for serious adverse reactions in a nursing child, breastfeeding is not recommended during treatment with BOSULIF and for at least 2 weeks after the last dose.

IN NEWLY DIAGNOSED PATIENTS WITH CP Ph+ CML

Most common adverse reactions for BOSULIF vs imatinib[1,7]

Warnings and precautions for BOSULIF include gastrointestinal toxicity, myelosuppression, hepatic toxicity, cardiac failure, fluid retention, renal toxicity, and embryofetal toxicity

Most common (≥20%) all-grade ARs

	12 months		24 months	
	BOSULIF n=268 (%)	Imatinib n=265 (%)	BOSULIF n=268 (%)	Imatinib n=265 (%)
Diarrhea	70	34	72	36
Nausea	35	38	37	40
Thrombocytopenia	35	20	36	19
Rash*	34	21	37	22
ALT increased	31	6	32	5
Abdominal pain	25	15	29	16
AST increased	23	6	23	6
Neutropenia	11	21	12	22
Fatigue	*19*	*19*	*23*	*20*
Anemia	*19*	*19*	*21*	*21*
Headache	*19*	*13*	*21*	*14*

Most common (≥2%) grade 3/4 ARs

	12 months		24 months	
	BOSULIF n=268 (%)	Imatinib n=265 (%)	BOSULIF n=268 (%)	Imatinib n=265 (%)
ALT increased	19	2	21	2
Thrombocytopenia	14	6	14	6
Lipase increased	10	5	11	5
AST increased	10	2	10	2
Diarrhea	8	<1	8	<1
Neutropenia	7	12	7	13
Anemia	3	5	4	5
Abdominal pain	2	<1	2	<1
Rash*	1	2	1	2

*Rash includes the following preferred terms: acne, dermatitis, dermatitis acneiform, dermatitis allergic, dermatitis exfoliative, drug reaction with eosinophilia and systemic symptoms, photosensitivity reaction, rash, rash erythematous, rash generalized, rash macular, rash maculo-papular, rash papular, rash pruritic, urticaria.

ALT=alanine aminotransferase; AR=adverse reaction; AST=aspartate aminotransferase.

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Additional safety information[1,7]

Clinically relevant grade 3/4 laboratory test abnormalities

	12 months		24 months	
	BOSULIF n=268 n (%)	Imatinib n=265 n (%)	BOSULIF n=268 n (%)	Imatinib n=265 n (%)
Hematology parameters				
Platelet count (low) <50 × 10^9/L	38 (14.2)	17 (6.4)	39 (14.6)	16 (6.0)
Absolute neutrophil count <1 × 10^9/L	24 (9.0)	49 (18.5)	24 (9.0)	50 (18.9)
Hemoglobin (low) <80 g/L	19 (7.1)	15 (5.7)	21 (7.8)	15 (5.7)
White blood cell count (low) <2 × 10^9/L	15 (5.6)	20 (7.5)	16 (6)	21 (7.9)
Biochemistry parameters				
SGPT/ALT >5.0 × ULN	62 (23.1)	7 (2.6)	67 (25.0)	7 (2.6)
SGOT/AST >5.0 × ULN	32 (11.9)	8 (3.0)	34 (12.7)	8 (3.0)
Lipase >2 × ULN	35 (13.1)	16 (6.0)	42 (15.7)	19 (7.2)
Phosphorus (low) <0.6 mmol/L	12 (4.5)	45 (17.0)	18 (6.7)	45 (17.0)
Total bilirubin >3.0 × ULN	3 (1.1)	2 (0.8)	4 (1.5)	2 (0.8)
Amylase >2 × ULN	6 (2.2)	4 (1.5)	7 (2.6)	5 (1.9)
Creatinine >3.0 × baseline; >3.0 × ULN	0	2 (0.8)	1 (0.4)	2 (0.8)

- By the 12-month analysis, 1 patient receiving BOSULIF® (bosutinib) died vs 6 patients receiving imatinib[3]
- By 24 months, 3 patients receiving BOSULIF died vs 9 patients receiving imatinib[7]

Discontinuation rates due to ARs[3,7]

	12 months		24 months	
	BOSULIF	Imatinib	BOSULIF	Imatinib
Discontinuation due to ARs	14.2%	10.6%	20%	12%
Most common AR leading to discontinuation	ALT increased 4.9% AST increased 2.2%	Thrombocytopenia 1.5% Myalgia 1.1%	ALT increased 4.5% AST increased 2.6% Lipase increased 1.5% Neutropenia 1.1% Thrombocytopenia 1.1%	Thrombocytopenia 1.5% Myalgia 1.1% Diarrhea 1.1%

Cases of diarrhea occurred early in treatment and discontinuation rates remained low[3,7]

	12 months		24 months	
	BOSULIF	Imatinib	BOSULIF	Imatinib
Diarrhea	70%	34%	72%	36%

Median time to onset in the BOSULIF arm	
12 months	24 months
3 days (range 1-505)	**4 days** (range 1-721)

Median duration of diarrhea in the BOSULIF arm	
12 months	24 months
3 days (range 1-436)	**2 days** (range 1-692)

- At 12 months, 1% of patients discontinued due to diarrhea[3]
- At 24 months, 1% of patients discontinued due to diarrhea[7]
- Diarrhea was manageable (primarily grade 1 or 2). Monitor and manage patients using standards of care, including antidiarrheals, antiemetics, and fluid replacement. Withhold, dose reduce, or discontinue BOSULIF as necessary[1,3]

ALT=alanine aminotransferase; AR=adverse reaction; AST=aspartate aminotransferase; CML=chronic myelogenous leukemia; CP=chronic phase; Ph+=Philadelphia chromosome–positive; SGOT=serum glutamic-oxaloacetic transaminase; SGPT=serum glutamic-pyruvic transaminase; ULN=upper limit of normal.

IN NEWLY DIAGNOSED PATIENTS WITH CP Ph+ CML

Additional safety information (cont'd)

Most cases of transaminase elevations occurred early in treatment[1,3,7]

	12 months		24 months	
	BOSULIF	Imatinib	BOSULIF	Imatinib
Liver function ARs	40%	14%	42%	14%

- Of patients receiving BOSULIF who experienced transaminase elevations of any grade, 79% experienced their first event within the first 3 months[1]
  - The median time to onset of increased ALT and AST was 32 and 43 days, respectively, and the median duration was 20 and 15 days, respectively[1]

Rates of fluid retention[3,7]

	12 months		24 months	
	BOSULIF	Imatinib	BOSULIF	Imatinib
Pleural effusion	1.9%	1.5%	3.7%	1.5%
Peripheral edema	4.1%	13.6%	5.2%	14.3%

- In the first 12 months, 1 patient receiving BOSULIF (0.4%) experienced severe fluid retention of grade 3 pericardial effusion[1]
- At 24 months, severe fluid retention (grade ≥3) was experienced by 2 patients (0.7%) for BOSULIF: grade 3 pericardial effusion and pleural effusion. For imatinib, 1 patient (0.4%) experienced grade 3 peripheral edema[7]

Incidence of cardiac* and vascular† events[1,3,7]

	12 months		24 months	
	BOSULIF	Imatinib	BOSULIF	Imatinib
Cardiac events	5.2%	5.3%	8.2%	5.7%
Grade ≥3	0.7%	0.4%	2.6%	1.1%
Peripheral vascular events	1.5%	1.1%	1.9%	1.1%
Cardiovascular events	3.0%	0.4%	3.4%	0.4%

- In the first 12 months, cardiac events that were grade ≥3 were pericardial effusion (n=1) and supraventricular tachycardia (n=1) in the BOSULIF arm and QTc prolongation (n=1) in imatinib patients[3]
- At 24 months, grade ≥3 cardiac events were electrocardiogram QT prolonged (n=1), atrial fibrillation (n=2), pericardial effusion (n=1), cardiac failure (n=2, one of which was death), cardiorespiratory arrest (n=1), pleuropericarditis (n=1), and supraventricular tachycardia (n=1) for BOSULIF. For imatinib, grade ≥3 cardiac events were electrocardiogram QT prolonged (n=1), atrial fibrillation (n=1), and supraventricular tachycardia (n=1)[7]
- Cardiac failure occurred in 1.5% of patients treated with BOSULIF compared to 0.8% of patients treated with imatinib[1]
- One patient in the group treated with BOSULIF experienced a grade 3 QTc prolongation (>500 msec)[1,7]
- Patients with uncontrolled or significant cardiovascular disease, including prolonged QT interval, were excluded by protocol[1]

*Includes MedDRA HLGTs cardiac arrhythmias, heart failures, and pericardial disorders under the SOC cardiac disorders; the preferred terms cardiac death, sudden cardiac death, sudden death, and ejection fraction decreased; and the standardized MedDRA query torsade de pointes/QT prolongation (narrow).

†Cardiovascular includes the MedDRA HLGT coronary artery disorders. Cerebrovascular includes the high-level terms central nervous system hemorrhages and cerebrovascular accidents, central nervous system vascular disorders NEC, transient cerebrovascular events, vascular imaging procedures NEC, and vascular therapeutic procedures NEC. Peripheral vascular includes the HLGTs arteriosclerosis, stenosis, vascular insufficiency and necrosis, and embolism and thrombosis as well as the high-level terms arterial therapeutic procedures (excluding aortic), nonsite-specific vascular disorders NEC, and peripheral vascular disorders NEC (excluding flushing and hot flash).

HLGT=high-level group term; MedDRA=Medical Dictionary for Regulatory Activities; NEC=not elsewhere classified; SOC=system organ class.

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PATIENT PROFILE

Consider Michael
A patient with resistance or intolerance to prior therapy

Michael, 62

Accountant (retiring in 3 years)

Michael is not an actual patient.

DIAGNOSIS
CP Ph+ CML, diagnosed 4 years ago.

MEDICAL HISTORY
Currently being treated with a 2nd-generation TKI since diagnosis; dose adjusted due to ARs and patient intolerance to treatment.

COMORBIDITIES
History of COPD; mild hypertension (controlled); hyperlipidemia (controlled).

SOKAL RISK SCORE
0.9 (intermediate risk).*

RESPONSE
Recent routine blood work shows an increase in *BCR-ABL1* levels and signals a loss of response to current therapy. Noncompliance was ruled out as a cause and mutational analysis was performed. No known *BCR-ABL1* kinase domain mutations were detected.

*Intermediate risk=Sokal score of 0.8 to 1.2.

AR=adverse reaction; CML=chronic myelogenous leukemia; COPD=chronic obstructive pulmonary disease; CP=chronic phase; Ph+=Philadelphia chromosome–positive; TKI=tyrosine kinase inhibitor.

SELECTED SAFETY INFORMATION

Contraindication: History of hypersensitivity to BOSULIF. Reactions have included anaphylaxis. Anaphylactic shock occurred in less than 0.2% of treated patients in single-agent cancer studies with BOSULIF.

Gastrointestinal Toxicity: Diarrhea, nausea, vomiting, and abdominal pain occur with BOSULIF. In the study of patients with newly diagnosed CP Ph+ CML, the median time to onset for diarrhea (all grades) was 3 days and the median duration per event was 3 days. In the study of patients with CML who were resistant or intolerant to prior therapy, median time to onset of diarrhea (all grades) was 2 days, median duration was 2 days, and the median number of episodes per patient was 3 (range 1-268). Monitor and manage patients using standards of care, including antidiarrheals, antiemetics, and/or fluid replacement. Withhold, dose reduce, or discontinue BOSULIF as necessary.

IN PATIENTS WITH RESISTANCE OR INTOLERANCE TO PRIOR THERAPY

The efficacy and safety of BOSULIF as a 2nd-line treatment were evaluated in a long-term follow-up study[1]

The long-term analysis was based on a minimum of 60 months of follow-up for patients with CP CML treated with 1 prior TKI (imatinib) and a minimum of 48 months of follow-up for patients with CP CML treated with imatinib and at least 1 additional TKI (nilotinib and/or dasatinib).

Trial population of patients with CML (N=546)

2nd-line treatment with a minimum follow-up of 60 months (n=284)

CP CML previously treated with 1 TKI (imatinib)

Primary endpoints (n=262 evaluable):
- Rate of attaining MCyR by 6 months
- Duration of MCyR

3rd-line treatment with a minimum follow-up of 48 months (n=119)

CP CML previously treated with imatinib and 1 additional TKI

Primary endpoints (n=112 evaluable):
- Cumulative rate of attaining MCyR by 6 months
- Duration of MCyR

AdvP CML treatment with a minimum follow-up of 48 months (n=143)

AP and BP CML previously treated with at least imatinib

Primary endpoints (n=132 evaluable):
- Confirmed CHR and OHR

AP CML (n=79) | BP CML (n=64)

BOSULIF was studied in 546 patients with Ph+ CML with resistance or intolerance to previous therapy

BOSULIF® (bosutinib) was studied in a single-arm, phase 1/2, open-label, multicenter trial in 546 patients with CP, AP, and BP CML who had developed resistance or intolerance to either 1st-line imatinib or 1st-line imatinib and then dasatinib and/or nilotinib.

- Patients were treated with BOSULIF 500 mg once daily
- Of the 546 treated patients, 506 were considered evaluable for efficacy. Patients were evaluable for efficacy if they had received at least 1 dose of BOSULIF and had a valid baseline efficacy assessment

AdvP CML=advanced phase chronic myelogenous leukemia; AP=accelerated phase; BP=blast phase; CHR=complete hematologic response; MCyR=major cytogenetic response; OHR=overall hematologic response.

SELECTED SAFETY INFORMATION

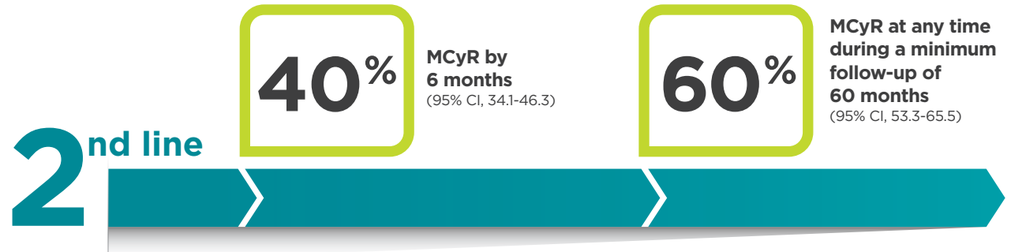
Myelosuppression: Thrombocytopenia, anemia, and neutropenia occur with BOSULIF. Perform complete blood counts weekly for the first month and then monthly thereafter, or as clinically indicated. Withhold, dose reduce, or discontinue BOSULIF as necessary.

Please see additional Important Safety Information on page 19 and accompanying full Prescribing Information in pocket.

Bosulif® bosutinib tablets 500 mg | 400 mg | 100 mg

BOSULIF helped patients achieve a durable response in the 2nd-line setting[1]

BOSULIF helped patients achieve MCyR after treatment with imatinib (n=262 evaluable)*



- 65% of responders had an MCyR lasting at least 18 months
- 43% of responders had an MCyR lasting at least 54 months

Median duration of MCyR was not reached at the time of analysis[1]

62% (n=96) of patients who achieved MCyR at any time (n=156) stayed on BOSULIF for at least 5 years[1]

Treatment with BOSULIF helps keep transformation rates low[7†]

- 95% of patients remained in CP while taking BOSULIF® (bosutinib) (n=269 out of 284)
  - 5% of patients in CP had confirmed disease transformation to AP or BP disease while taking BOSULIF (n=15 out of 284)

*Median duration of treatment was 26 months for evaluable patients.
†Transformation rates for CP 2nd-line patients.
AP=accelerated phase; BP=blast phase; CI=confidence interval; CP=chronic phase; MCyR=major cytogenetic response.

SELECTED SAFETY INFORMATION

Hepatic Toxicity: BOSULIF may cause elevations in serum transaminases (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]). In a study of BOSULIF in combination with letrozole, one drug-induced liver injury occurred without alternative causes. In the study of patients with newly diagnosed CP Ph+ CML, the incidence of ALT/AST elevations was 31% and 23%, respectively. In patients with CML who were resistant or intolerant to prior therapy, the incidence of ALT/AST elevations was 18% and 15%, respectively. Twenty percent of the patients resistant or intolerant to prior therapy experienced an increase in either ALT or AST. Perform hepatic enzyme tests at least monthly for the first 3 months and as clinically indicated. In patients with transaminase elevations, monitor liver enzymes more frequently. Withhold, dose reduce, or discontinue BOSULIF as necessary. In patients with mild, moderate, or severe hepatic impairment, the recommended starting dose is 200 mg daily.

IN PATIENTS WITH RESISTANCE OR INTOLERANCE TO PRIOR THERAPY

The most common ARs with BOSULIF are well established[1]

Warnings and precautions for BOSULIF include gastrointestinal toxicity, myelosuppression, hepatic toxicity, cardiac failure, fluid retention, renal toxicity, and embryofetal toxicity

Most common ARs (≥20%; all grades) based on long-term follow-up (N=546)

Adverse reaction	CP CML (n=403)	Advanced phase CML (n=143)
Diarrhea	85	76
Nausea	47	48
Abdominal pain	42	31
Rash	42	38
Thrombocytopenia	40	45
Vomiting	37	43
Anemia	27	38
Fatigue	26	21
Pyrexia	23	37
Cough	22	22
Headache	21	17
ALT increased	20	10
Edema	20	17
Neutropenia	18	22
Dyspnea	12	20

Diarrhea (all grades) was the most common AR, occurring in 82% of patients receiving BOSULIF (N=450)[1,7]

- 90% (406 out of 450) of patients who developed diarrhea had a maximum severity of grade 1 or 2, and there were no grade 4 cases[7]
- More than half of these patients (249 out of 450) had a maximum severity of grade 1[7]
- Monitor and manage patients using standards of care, including antidiarrheals, antiemetics, and fluid replacement. Withhold, dose reduce, or discontinue BOSULIF as necessary[1]

ALT=alanine aminotransferase; AR=adverse reaction.

SELECTED SAFETY INFORMATION

Cardiac Failure: Cardiac failure and left ventricular dysfunction have been reported in patients taking BOSULIF. These events occurred more frequently in previously treated patients than in patients with newly diagnosed CML and were more frequent in patients with advanced age or risk factors, including previous medical history of cardiac failure. In a randomized study with newly diagnosed CML, cardiac failure occurred in 1.5% of patients treated with BOSULIF compared to 0.8% of patients treated with imatinib. In a single-arm study in patients with CML who were resistant or intolerant to prior therapy, cardiac failure was observed in 5.3% of patients treated with BOSULIF. Monitor patients for signs and symptoms consistent with cardiac failure and treat as clinically indicated. Interrupt, dose reduce, or discontinue BOSULIF as necessary.

Please see additional Important Safety Information on page 19 and accompanying full Prescribing Information in pocket.

Bosulif®
bosutinib tablets
500 mg | 400 mg | 100 mg

BOSULIF has long-term cardiac and vascular safety data

Patients with uncontrolled or significant cardiovascular disease, including prolonged QT interval, were excluded by protocol[1]

Long-term follow-up of adult patients with CP Ph+ CML and with advanced leukemias[7]

- The long-term follow-up data analysis was based on a minimum of ~8 years (94 months) for patients with CP CML treated with 1 prior TKI (imatinib) and a minimum of 7 years (84 months) for patients with CP CML treated with imatinib and at least 1 additional TKI and for patients with advanced phase CML
- Total extended safety population (N=570) included patients with CP Ph+ CML (n=403) and advanced Ph+ leukemias (AP CML [n=79], BP CML [n=64], and ALL [n=24])*

Patients	CP2L† (n=284)	CP3L‡ (n=119)	AdvP‡ (n=167)	Total (N=570)
Cardiac cluster§				
Any TEAEs	14.1%	15.1%	13.2%	14.0%
Grade 3-4 TEAEs	5.6%	7.6%	3.6%	5.4%
Grade 5 TEAEs‖	1.1%	0%	0.6%	0.7%
Vascular cluster¶				
Any TEAEs	9.5%	7.6%	9.0%	8.9%
Cardiovascular	5.6%	4.2%	3.0%	4.6%
Cerebrovascular	3.2%	0.8%	4.8%	3.2%
Peripheral vascular	2.5%	3.4%	1.2%	2.3%
Grade 3-4 TEAEs	5.3%	4.2%	2.4%	4.2%
Grade 5 TEAEs‖	0.4%	1.7%	4.2%	1.8%
Hypertension cluster#				
Any TEAEs	10.2%	9.2%	7.8%	9.3%
Grade 3-4 TEAEs	3.5%	2.5%	3.0%	3.2%
Grade 5 TEAEs‖	0%	0%	0%	0%

Cardiac failure and left ventricular dysfunction have been reported in patients taking BOSULIF® (bosutinib). These events occurred more frequently in previously treated patients than in patients with newly diagnosed CML and were more frequent in patients with advanced age or risk factors, including previous medical history of cardiac failure.[1]

In a single-arm study in patients with CML who were resistant or intolerant to prior therapy, cardiac failure was observed in 5.3% of patients treated with BOSULIF. Monitor patients for signs and symptoms consistent with cardiac failure and treat as clinically indicated. Interrupt, dose reduce, or discontinue BOSULIF as necessary.[1]

*BOSULIF is not indicated for the treatment of ALL.[1]

†8-year follow-up.

‡7-year follow-up.

§Cardiac includes MedDRA HLGTs in cardiac arrhythmias, heart failures, pericardial disorders; SOC in general disorders and administration site conditions and MedDRA PT in cardiac death, sudden cardiac death, sudden death; MedDRA SOC in investigations and MedDRA PT in ejection fraction decreased or PT MedDRA (SMQ) torsade de pointes/QT prolongation (narrow).

‖Grade 5 TEAEs are deaths.

¶Vascular includes MedDRA HLGTs in coronary artery disorders, arteriosclerosis, stenosis, vascular insufficiency and necrosis, embolism and thrombosis, HLT in arterial therapeutic procedures (excluding aortic), central nervous system hemorrhages and cerebrovascular accidents, central nervous system vascular disorders NEC, nonsite-specific vascular disorders NEC, peripheral vascular disorders NEC (excluding the 2 PTs flushing and hot flash), transient cerebrovascular events, vascular imaging procedures NEC, vascular therapeutic procedures NEC, PT in intestinal ischemia, subarachnoid hemorrhage, transcatheter arterial chemoembolization.

#Hypertension includes MedDRA SOC in investigations and HLGT in cardiac and vascular investigations (excluding enzyme tests) and HLT in vascular tests NEC (including blood pressure) and PT of blood pressure abnormal, blood pressure ambulatory abnormal, blood pressure ambulatory increased, blood pressure diastolic abnormal, blood pressure diastolic increased, blood pressure increased, blood pressure systolic abnormal, blood pressure systolic increased; SOC in vascular disorders and HLGT in vascular hypertensive disorders.

AdvP CML=advanced phase chronic myelogenous leukemia; ALL=acute lymphoblastic leukemia; AP=accelerated phase; BP=blast phase; CML=chronic myelogenous leukemia; CP=chronic phase; HLGT=high-level group term; HLT=high-level term; MedDRA=Medical Dictionary for Regulatory Activities; NEC=not elsewhere classified; Ph+=Philadelphia chromosome–positive; PT=preferred term; SMQ=standardized MedDRA query; SOC=system organ class; TEAE=treatment-emergent adverse event; TKI=tyrosine kinase inhibitor.

Convenient once-daily dosing[1]

BOSULIF is available in 400-, 500-, and 100-mg tablets

RECOMMENDED STARTING DOSE		ADDITIONAL OPTIONS FOR DOSE ADJUSTMENTS
Newly diagnosed patients	Patients with resistance or intolerance to prior therapy	
		
Orange tablets are **400 mg**, taken orally once daily with food	Red tablets are **500 mg**, taken orally once daily with food	Yellow tablets are **100 mg**, taken orally once daily with food

Tablets shown are not actual size.

ADMINISTRATION

Taken with food

Daily 1X

Once-daily, oral administration

- Continue treatment with BOSULIF until disease progression or intolerance to therapy
- If a dose is missed beyond 12 hours, the patient should skip the dose and take the usual prescribed dose on the following day

Dose escalation

- In clinical studies of adult Ph+ CML patients, dose escalation by increments of 100 mg once daily to a maximum of 600 mg once daily was allowed in patients who did not achieve or maintain a hematologic, cytogenetic, or molecular response and who did not have grade 3 or higher adverse reactions at the recommended starting dose

Additional starting dose recommendations

	Newly diagnosed CP Ph+ CML	CP, AP, or BP Ph+ CML with resistance or intolerance to prior therapy
Renal impairment		
Creatinine clearance 30-50 mL/min	300 mg daily	400 mg daily
Creatinine clearance <30 mL/min	200 mg daily	300 mg daily
Hepatic impairment (mild [Child-Pugh A], moderate [Child-Pugh B], or severe [Child-Pugh C])	200 mg daily**	200 mg daily**

**There are no clinical data for efficacy at the dose of 200 mg once daily in patients with CML.

SELECTED SAFETY INFORMATION

Fluid Retention: Fluid retention occurs with BOSULIF and may cause pericardial effusion, pleural effusion, pulmonary edema, and/or peripheral edema. Monitor and manage patients using standards of care. Interrupt, dose reduce, or discontinue BOSULIF as necessary.

Please see additional Important Safety Information on page 19 and accompanying full Prescribing Information in pocket.

Bosulif® bosutinib tablets 500 mg | 400 mg | 100 mg

PATIENT SUPPORT SERVICES

Making your patients' support needs a priority. Together.

Pfizer is committed to supporting your patients throughout their treatment journey. With Pfizer Oncology Together, BOSULIF® (bosutinib) patients get personalized support, including help identifying financial assistance options and connections to resources that may help with some of their day-to-day challenges.

Voucher program*

30-day free trial offer to help new patients initiate therapy.

Pfizer Oncology together™
Patient Support. Financial Assistance. Together.

Pfizer Oncology Together†

At Pfizer Oncology Together, patient support is at the core of everything we do. From identifying financial assistance options to connecting patients to resources for emotional support, your patients' needs are our priority.

Co-pay assistance‡

Eligible commercially insured patients may pay as little as $0 per month for BOSULIF.

*Limits, terms, and conditions apply. Visit BosulifHCP.com to learn more.

†Some services are provided through third-party organizations that operate independently and are not controlled by Pfizer. Availability of services and eligibility requirements are determined solely by these organizations.

‡Limits, terms, and conditions apply. Patients are not eligible to use this card if they are enrolled in a state or federally funded insurance program, including but not limited to Medicare, Medicaid, TRICARE, Veterans Affairs health care, a state prescription drug assistance program, or the Government Health Insurance Plan available in Puerto Rico. Patients may receive up to $25,000 in savings annually. **The offer will be accepted only at participating pharmacies. This offer is not health insurance.** No membership fees apply. Pfizer reserves the right to rescind, revoke, or amend this offer without notice. For full Terms and Conditions, please see PfizerOncologyTogether.com/terms. For any questions, please call 1-877-744-5675, visit PfizerOncologyTogether.com/terms or write: Pfizer Oncology Together Co-Pay Savings Program, 2250 Perimeter Park Drive, Suite 300, Morrisville, NC 27560.

To learn more about patient support and services, please visit www.BosulifHCP.com.

References: 1. BOSULIF Prescribing Information. New York, NY: Pfizer Inc. **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Chronic Myeloid Leukemia V.2.2020. © National Comprehensive Cancer Network, Inc. 2019. All rights reserved. Accessed November 6, 2019. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content or its use or application and disclaims any responsibility for its use or application in any way. **3.** Cortes JE, Gambacorti-Passerini C, Deininger MW, et al. Bosutinib versus imatinib for newly diagnosed chronic myeloid leukemia: results from the randomized BFORE trial. *J Clin Oncol*. 2018;36(3):231-237. **4.** Marin D, Ibrahim AR, Lucas C, et al. Assessment of *BCR-ABL1* transcript levels at 3 months is the only requirement for predicting outcome for patients with chronic myeloid leukemia treated with tyrosine kinase inhibitors. *J Clin Oncol*. 2012;30(3):232-238. **5.** Falchi L, Kantarjian HM, Wang X, et al. Significance of deeper molecular responses in patients with chronic myeloid leukemia in early chronic phase treated with tyrosine kinase inhibitors. *Am J Hematol*. 2013;88(12):1024-1029. **6.** Jabbour E, Makenbaeva D, Linghor-Smith M, Lin J. Use of real-world claim databases to assess prevalence of comorbid conditions relevant to the treatment of chronic myelogenous leukemia based on National Comprehensive Network treatment guidelines. *Clin Lymphoma Myeloma Leuk*. 2015;15(12):797-802. **7.** Data on file. Pfizer Inc., New York, NY.

IMPORTANT SAFETY INFORMATION

Contraindication: History of hypersensitivity to BOSULIF. Reactions have included anaphylaxis. Anaphylactic shock occurred in less than 0.2% of treated patients in single-agent cancer studies with BOSULIF.

Gastrointestinal Toxicity: Diarrhea, nausea, vomiting, and abdominal pain occur with BOSULIF. In the study of patients with newly diagnosed CP Ph+ CML, the median time to onset for diarrhea (all grades) was 3 days and the median duration per event was 3 days. In the study of patients with CML who were resistant or intolerant to prior therapy, median time to onset of diarrhea (all grades) was 2 days, median duration was 2 days, and the median number of episodes per patient was 3 (range 1-268). Monitor and manage patients using standards of care, including antidiarrheals, antiemetics, and/or fluid replacement. Withhold, dose reduce, or discontinue BOSULIF as necessary.

Myelosuppression: Thrombocytopenia, anemia, and neutropenia occur with BOSULIF. Perform complete blood counts weekly for the first month and then monthly thereafter, or as clinically indicated. Withhold, dose reduce, or discontinue BOSULIF as necessary.

Hepatic Toxicity: BOSULIF may cause elevations in serum transaminases (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]). In a study of BOSULIF in combination with letrozole, one drug-induced liver injury occurred without alternative causes. In the study of patients with newly diagnosed CP Ph+ CML, the incidence of ALT/AST elevations was 31% and 23%, respectively. In patients with CML who were resistant or intolerant to prior therapy, the incidence of ALT/AST elevations was 18% and 15%, respectively. Twenty percent of the patients resistant or intolerant to prior therapy experienced an increase in either ALT or AST. Perform hepatic enzyme tests at least monthly for the first 3 months and as clinically indicated. In patients with transaminase elevations, monitor liver enzymes more frequently. Withhold, dose reduce, or discontinue BOSULIF as necessary. In patients with mild, moderate, or severe hepatic impairment, the recommended starting dose is 200 mg daily.

Cardiac Failure: Cardiac failure and left ventricular dysfunction have been reported in patients taking BOSULIF. These events occurred more frequently in previously treated patients than in patients with newly diagnosed CML and were more frequent in patients with advanced age or risk factors, including previous medical history of cardiac failure. In a randomized study with newly diagnosed CML, cardiac failure occurred in 1.5% of patients treated with BOSULIF compared to 0.8% of patients treated with imatinib. In a single-arm study in patients with CML who were resistant or intolerant to prior therapy, cardiac failure was observed in 5.3% of patients treated with BOSULIF. Monitor patients for signs and symptoms consistent with cardiac failure and treat as clinically indicated. Interrupt, dose reduce, or discontinue BOSULIF as necessary.

Fluid Retention: Fluid retention occurs with BOSULIF and may cause pericardial effusion, pleural effusion, pulmonary edema, and/or peripheral edema. Monitor and manage patients using standards of care. Interrupt, dose reduce, or discontinue BOSULIF as necessary.

Renal Toxicity: An on-treatment decline in estimated glomerular filtration rate has occurred in patients treated with BOSULIF. Monitor renal function at baseline and during therapy, with particular attention to patients with preexisting renal impairment or risk factors for renal dysfunction. Lower starting doses are recommended for patients with renal impairment. For patients who have declining renal function while on BOSULIF or who cannot tolerate the starting dose, follow dose adjustment recommendations for toxicity.

Embryofetal Toxicity: BOSULIF can cause fetal harm. Women of childbearing potential should be advised of the potential hazard to the fetus and to use effective contraceptive measures while on treatment and for at least 2 weeks after the final dose.

Adverse Reactions: The most common adverse reactions observed in greater than or equal to 20% of patients with newly diagnosed CML were diarrhea, nausea, thrombocytopenia, rash, increased ALT, abdominal pain, and increased AST. The most common Grade 3/4 adverse reactions and laboratory abnormalities observed in greater than 10% of newly diagnosed CML patients were increased ALT and thrombocytopenia. The most common adverse reactions observed in greater than or equal to 20% of patients with CML who were resistant or intolerant to prior therapy were diarrhea, nausea, abdominal pain, rash, thrombocytopenia, vomiting, anemia, fatigue, pyrexia, cough, headache, increased ALT, and edema. The most common Grade 3/4 adverse reactions and laboratory abnormalities observed in greater than 10% of patients who were resistant or intolerant to prior therapy were thrombocytopenia, neutropenia, and anemia.

CYP3A Inhibitors and Inducers: Avoid concurrent use with strong or moderate CYP3A inhibitors or strong CYP3A inducers.

Proton Pump Inhibitors (PPIs): Consider using short-acting antacids or H2 blockers instead of PPIs to avoid a reduction in BOSULIF exposure. Separate antacid or H2 blocker dosing and BOSULIF dosing by more than 2 hours.

Lactation: Because of the potential for serious adverse reactions in a nursing child, breastfeeding is not recommended during treatment with BOSULIF and for at least 2 weeks after the last dose.

INDICATIONS

BOSULIF is indicated for the treatment of adult patients with

- Newly diagnosed chronic phase (CP) Ph+ chronic myelogenous leukemia (CML). This indication is approved under accelerated approval based on molecular and cytogenetic response rates. Continued approval for this indication may be contingent upon verification and confirmation of clinical benefit in an ongoing long-term follow-up trial
- Chronic, accelerated, or blast phase Ph+ CML with resistance or intolerance to prior therapy

Please see accompanying full Prescribing Information in pocket.

Bosulif® bosutinib tablets 500 mg | 400 mg | 100 mg

FOR NEWLY DIAGNOSED ADULT PATIENTS WITH CP Ph+ CML[1]

DISCOVER the POTENTIAL with BOSULIF

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)[2]

Bosutinib (BOSULIF) is recommended by the NCCN Guidelines as a primary treatment option for patients with newly diagnosed CML (category 1) and as an option for patients in need of 2nd- or later-line TKI therapy (category 2A).

Greater molecular and cytogenetic responses vs imatinib[1]

- **47% of BOSULIF® (bosutinib) patients** achieved MMR at 12 months vs **37% with imatinib** (*P*=0.0200)
- **77% of patients in the BOSULIF arm** achieved CCyR by 12 months vs **66% of patients in the imatinib arm** (*P*=0.0075)

Safety in newly diagnosed CP Ph+ CML patients[1,3]

Warnings and precautions for BOSULIF include gastrointestinal toxicity, myelosuppression, hepatic toxicity, cardiac failure, fluid retention, renal toxicity, and embryofetal toxicity. Please see Important Safety Information on page 19 for additional details.

- At 12 months, the most common ARs observed in ≥20% of patients with newly diagnosed CML were diarrhea, nausea, thrombocytopenia, rash, increased ALT, abdominal pain, and increased AST. The most common grade 3/4 ARs and laboratory abnormalities observed in >10% of newly diagnosed CML patients were increased ALT and thrombocytopenia
- At 12 months, rates of cardiac and peripheral vascular events were 5.2% and 1.5% for BOSULIF and 5.3% and 1.1% for imatinib, respectively

Patients with uncontrolled or significant cardiovascular disease, including prolonged QT interval, were excluded by protocol.

Convenient once-daily dosing[1]

The recommended starting dose for newly diagnosed patients with CP Ph+ CML is 400 mg once daily with food.

The recommended starting dose for patients with resistance or intolerance to prior therapies is 500 mg once daily with food.

100-mg tablets allow for flexible dosing.

EXPECTATIONS FOR TREATING CML PATIENTS ARE EVOLVING.

There's more to consider when choosing a treatment for your patients.[2,3]

Visit **BosulifHCP.com** to learn more.

ALT=alanine aminotransferase; AR=adverse reaction; AST=aspartate aminotransferase; CCyR=complete cytogenetic response; CML=chronic myelogenous leukemia; CP=chronic phase; MMR=major molecular response; NCCN=National Comprehensive Cancer Network; Ph+=Philadelphia chromosome–positive; TKI=tyrosine kinase inhibitor.

SELECTED SAFETY INFORMATION

Gastrointestinal Toxicity: Diarrhea, nausea, vomiting, and abdominal pain occur with BOSULIF. In the study of patients with newly diagnosed CP Ph+ CML, the median time to onset for diarrhea (all grades) was 3 days and the median duration per event was 3 days. In the study of patients with CML who were resistant or intolerant to prior therapy, median time to onset of diarrhea (all grades) was 2 days, median duration was 2 days, and the median number of episodes per patient was 3 (range 1-268). Monitor and manage patients using standards of care, including antidiarrheals, antiemetics, and/or fluid replacement. Withhold, dose reduce, or discontinue BOSULIF as necessary.

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