Best Practices for Managing BTK Inhibitors in Patients With a History of Cardiac Comorbidities

Appropriate assessment, monitoring, and management of cardiotoxicity-associated complications are necessary for optimal use of BTK inhibitors, particularly in patients with baseline risk factors.[1-3]

Pretreatment Workup[3]

Comprehensive patient history

- Assessment of blood pressure, ECG, and concomitant medications

CV risk level assessment

- Presence of diabetes, obesity, hypertension, dyslipidemia, and CRD
- History of VHD, arrhythmias, HF, or LV dysfunction/reduced ejection fraction and ischemic heart disease

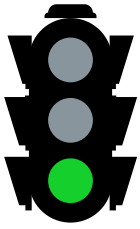
More detailed screening in patients with high CV risk/ established CV disease

- Echocardiogram, baseline cardiac biomarkers
- Consider FRS-CVD score for stratification

BTK Inhibitor Treatment Selection Based on CV Risk

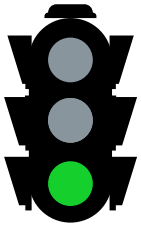
Refer to the summary of product characteristics for the recommended starting dosage of BTK inhibitors.[4-7]

Patients without baseline CV risk factors[3]



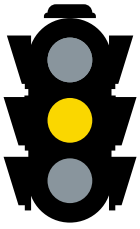
- BTK inhibitors are appropriate

Patients with well-managed CV risk[3,7]



- BTK inhibitors can be appropriate
- More selective BTK inhibitors (eg, second-generation agents) are preferred

Patients with high CV risk[2,3,7]



- Second-generation covalent BTK inhibitors and noncovalent BTK inhibitors can be appropriate with a multidisciplinary team involved

Patients who were intolerant to a prior BTK inhibitor due to cardiac events may be able to tolerate more selective BTK inhibitors.[8-10]

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BTK=Bruton tyrosine kinase; CRD=chronic renal disease; CV=cardiovascular; ECG=electrocardiogram; FRS-CVD=Framingham risk score-cardiovascular disease; HCP=healthcare professional; HF=heart failure; LV=left ventricular; VHD=valvular heart disease.

1. Fleming MR, et al. *Circ Res*. 2021;128(12):1973-1987. 2. Quartermaine C, et al. *JACC CardioOncol*. 2023;5(5):570-590. 3. Awan FT, et al. *Blood Adv*. 2022;6(18):5516-5525. 4. Imbruvica [SmPC]. Beerse, Belgium: Janssen-Cilag International NV, 2019. 5. Calquence [SmPC]. Södertälje, Sweden: AstraZeneca AB, 2020. 6. Brukinsa [SmPC]. Dublin, Ireland: BeOne Medicines Ireland Limited, 2021. 7. Jaypirca [SmPC]. Utrecht, The Netherlands: Eli Lilly Nederland B.V., 2025. 8. Shah NN, et al. Poster presented at: ASH 2022. Poster 17972. 9. Shadman M, et al. *Lancet Haematol*. 2023;10(1):e35-e45. 10. Rogers KA, et al. *Haematologica*. 2021;106(9):2364-2373.

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Monitor patients regularly and manage toxicities with the goal of maintaining BTK inhibitor treatment.[1,2]

- Patients with established CV disease require more detailed monitoring[1,2]
- An international consensus statement on the management of CV risk of BTK inhibitors in patients with CLL has been published[1]

Proposed management of common BTK inhibitor-associated cardiac events in patients with a history of cardiac comorbidities[1-4]:

CV Adverse Event	Proposed Management
Hypertension	▪ Begin regular home BP monitoring ▪ Manage treatment decisions with a multidisciplinary team ▪ Treatment of BP should follow published guidelines ▪ If systolic BP >160 mmHg or diastolic BP >100 mmHg persists despite antihypertensive therapy, consider BTK inhibitor interruption and/or dose reduction until BP is better controlled
Atrial fibrillation	▪ Manage treatment decisions with a multidisciplinary team ▪ If other risk factors are limited (eg, CHA_2DS_2-VASc score is 0 or 1), continue BTK inhibitor ▪ If CHA_2DS_2-VASc score >1, initiate DOAC and hold BTK inhibitor ▪ Once AF is controlled, use a more selective BTK inhibitor or reduce dose
Major bleeding	▪ Further risk-benefit analysis may be needed if anticoagulation is considered for patients with AF on BTK inhibitor therapy who have a history of major bleeding ▪ BTK inhibitor should be held for 7 days prior to planned major surgeries and can be restarted 1-3 days postoperatively

If Grade 3 or 4 toxicity occurs, interrupt or reduce the dose of the BTK inhibitor, or permanently discontinue it.[5-8]

More selective BTK inhibitors have demonstrated fewer CV events than less selective BTK inhibitors, enabling their safe administration to a broader patient population with appropriate monitoring and management.[1,9-11]

AF=atrial fibrillation; BP=blood pressure; BTK=Bruton tyrosine kinase; CHA2DS2-VASc=congestive heart failure, hypertension, age ≥75 [doubled], diabetes, stroke [doubled], vascular disease, age 65 to 74 and sex category [female] score; CLL=chronic lymphocytic leukaemia; CV=cardiovascular; DOAC=direct oral anticoagulant; HCP=healthcare professional.

1. Awan FT, et al. *Blood Adv*. 2022;6(18):5516-5525. 2. Quartermaine C, et al. *JACC CardioOncol*. 2023;5(5):570-590. 3. Fleming MR, et al. *Circ Res*. 2021;128(12):1973-1987. 4. Lenihan D, et al. *Oncologist*. 2025;30(9):oyaf237. 5. Imbruvica [SmPC]. Beerse, Belgium: Janssen-Cilag International NV, 2019. 6. Calquence [SmPC]. Södertälje, Sweden: AstraZeneca AB, 2020. 7. Brukinsa [SmPC]. Dublin, Ireland: BeOne Medicines Ireland Limited, 2021. 8. Jaypirca [SmPC]. Utrecht, The Netherlands: Eli Lilly Nederland B.V., 2025. 9. Seymour JF, et al. *Blood*. 2023;142(8):687-699. 10. Shadman M, et al. *Lancet Haematol*. 2023;10(1):e35-e45. 11. Shah NN, et al. Poster presented at: ASH 2022. Poster 17972.