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

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

PRETREATMENT WORKUP[2,3]

Comprehensive patient history

- Assessment of blood pressure, ECG, and concomitant medications

CV risk level assessment

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

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

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

TREATMENT SELECTION

Refer to Prescribing Information for recommended starting dosage of BTK inhibitor[4-7]

Patients without baseline CV risk factors[3]

- BTK inhibitors are appropriate

Patients with well-managed CV risk[3]

- BTK inhibitors can be appropriate
- More selective BTK inhibitors are preferred

Patients with high and/or unmanaged CV risk[2,3]

- Second-generation covalent BTK inhibitors and noncovalent BTK inhibitors can be appropriate with multidisciplinary team involved
- First-generation covalent BTK inhibitors should be avoided

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

BTK, Bruton tyrosine kinase; CRD, chronic renal disease; CV, cardiovascular; ECG, electrocardiogram; FRS-CVD, Framingham risk score-cardiovascular disease; 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. Package insert. Janssen Biotech, Inc; 2022. 5. Calquence. Package insert. AstraZeneca, Inc; 2017. 6. Brukinsa. Package insert. BeiGene, Ltd; 2023. 7. Jaypirca. Package insert. Eli Lilly and Company, Inc; 2023. 8. Shah NN, et al. Presented at: American Society of Hematology; December 10-13, 2022; New Orleans, LA. 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.

MONITORING AND MANAGEMENT[1,2]

Monitor patients regularly and manage toxicities with the goal of maintaining BTK inhibitor treatment

- Patients with established CV disease require more detailed monitoring
- International consensus statement on the management of CV risk of BTK inhibitors in patients with CLL has recently been published

CV adverse events reported with BTK inhibitor treatment[2,3]

Hypertension

Atrial fibrillation

Major bleeding

Proposed management of cardiac events in patients with history of cardiac comorbidities[1-3]

CV adverse event	Proposed management
Hypertension 	• Begin regular home blood pressure monitoring • Manage treatment decisions with a multidisciplinary team • Treatment of BP should follow published guidelines • If systolic persists >160 or diastolic >100 mmHg despite medical therapy, consider holding BTK inhibitor and/or reducing dose until BP is better controlled
Atrial fibrillation 	• Manage treatment decisions with a multidisciplinary team • If other risk factors are limited (eg, CHA2DS2-VASc 0 or 1), continue BTK inhibitor • If CHA2DS2-VASc >1, anticoagulate with DOAC, hold BTK inhibitor • Once AF is controlled, use more selective BTK inhibitor or reduce dose
Major bleeding 	• If a patient has a history of major bleeding, further risk-benefit analysis may be needed if anticoagulation is considered for patients with AF on BTK inhibitor • BTK inhibitor should be held for 7 days prior to planned major surgery and can be restarted 1 to 3 days postoperatively

- **If grade 3 or 4 toxicity occurs, interrupt BTK inhibitor, reduce the dose, or permanently discontinue[4-7]**

More selective BTK inhibitors have demonstrated fewer CV events than less selective BTK inhibitors, thereby enabling, with appropriate monitoring and management, their safe administration to a broader patient population[1,8,9]

This presentation was commissioned by Lilly Medical and is intended to be used by HCPs for medical, scientific and educational purposes.

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 leukemia; CV, cardiovascular; DOAC, direct oral anticoagulant.

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. Imbruvica. Package insert. Janssen Biotech, Inc; 2022. 5. Calquence. Package insert. AstraZeneca, Inc; 2017. 6. Brukinsa. Package insert. BeiGene, Ltd; 2023. 7. Jaypirca. Package insert. Eli Lilly and Company, Inc; 2023. 8. Seymour JF, et al. *Blood*. 2023;142(8):687-699. 9. Dimopoulos MA, et al. *J Clin Oncol*. 2023;41(33):5099-5106.