

# 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<sup>1-3</sup>

## PRETREATMENT WORKUP<sup>2,3</sup>



### 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<sup>4-7</sup>

### Patients **without** baseline CV risk factors<sup>3</sup>



- BTK inhibitors are appropriate

### Patients **with well-managed** CV risk<sup>3</sup>



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

### Patients **with high and/or unmanaged** CV risk<sup>2,3</sup>



- 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<sup>8-10</sup>

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.

VV-MED-158864 ©2024 Lilly USA, LLC. All rights reserved.



## MONITORING AND MANAGEMENT<sup>1,2</sup>



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<sup>2,3</sup>



**Hypertension**



**Atrial fibrillation**



**Major bleeding**

### Proposed management of cardiac events in patients with history of cardiac comorbidities<sup>1-3</sup>

#### 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<sup>4-7</sup>

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<sup>1,8,9</sup>

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  $\geq 75$  [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.

