

Bruton tyrosine kinase (BTK) inhibitors such as ibrutinib are associated with atrial fibrillation (AFib), ventricular arrhythmias and sudden cardiac death.



- ✘ The median time from initiation of ibrutinib to onset of AFib is 3.8 months.
- ✘ AFib can persist despite stopping or reducing the dose of ibrutinib.
- ✘ Drug interactions can occur between ibrutinib and several antiarrhythmic agents (amiodarone, verapamil and diltiazem) due to CYP3A4.
- ✘ Ibrutinib is associated with approximately 50% risk of bleeding.
- ✘ The mechanisms of ICI-related cardiovascular events are not well-known.



- ✓ Anticoagulation is still recommended for CHA2DS2-VASc >2 if not at high risk of bleeding.
- ✓ Hold anticoagulation prior to procedures and administer reversal agents prior to urgent/emergent procedures given high risk of procedural bleeding with ibrutinib.
- ✓ Consider holding ibrutinib if significantly symptomatic AFib despite rate/rhythm control strategies.

TREATMENT TABLE

Institute monitoring and management strategies outlined in the treatment table

BTK Inhibitors	<ul style="list-style-type: none"> - Acalabrutinib (A) - Ibrutinib (I) - Zanubrutinib (Z) 	
Cardiotoxic Effects	<ul style="list-style-type: none"> - AFib - Ventricular arrhythmia - Sudden cardiac death 	<p>Severe AFib/atrial flutter I > Z > A</p> <p>Hypertension I = Z > A</p>
Monitoring Strategies	<ul style="list-style-type: none"> - Electrocardiography - Blood pressure (BP) 	
Management Strategies	<p>Cardiac arrhythmias</p> <ul style="list-style-type: none"> - Interrupt for symptomatic arrhythmia requiring urgent intervention - Reinitiate once asymptomatic/baseline 	<p>Hypertension</p> <ul style="list-style-type: none"> - Interrupt: Systolic BP > 160 mmHg or diastolic BP > 100 mmHg - Reinitiate once resolved: Systolic BP 120-139 mmHg or diastolic BP 80-89 mmHg/baseline - Manage: Initiate/adjust hypertension therapy throughout treatment

BEST PRACTICES



- ✓ Establish cardio-oncology clinic in collaboration with oncology.
- ✓ Clinical judgment based on detailed history and physical examination, in combination with cardiac biomarkers and imaging modalities, can aid in the evaluation of patients at risk of cardiovascular complications.
- ✓ For BTK inhibitors, consider a dose reduction or interruption of the drug and addition of anticoagulation and/or antiarrhythmic agents.

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