QT Prolongation - All Kinase Inhibitors[1,2]

Kinase Inhibitor	QT-interval prolongation? (Yes/ No)	Recommendations on how DDIs can be managed
Afatinib	No	
Axitinib	No	
Bosutinib	No	Bosutinib should be administered with caution to patients with a history of or predisposition for QT prolongation, uncontrolled or significant cardiac disease including recent MI, CHF, unstable angina or clinically significant bradycardia, or taking medicinal products known to prolong the QT interval Monitoring is advisable and a baseline ECG is recommended prior to initiating therapy and as clinically indicated Hypokalemia or hypomagnesemia must be corrected prior to bosutinib administration and should be monitored periodically during therapy
Cabozantinib	No	Cabozantinib should be used with caution in patients with a history of QT interval prolongation, those taking antiarrhythmics, or those with relevant pre-existing cardiac disease, bradycardia, or electrolyte disturbances When using cabozantinib, periodic monitoring with on-treatment ECGs and electrolytes (serum calcium, potassium, and magnesium) should be considered
Ceritinib	Yes	Avoid use in patients with congenital long QT syndrome Conduct periodic monitoring with ECGs and elecotrolytes in patients with congestive heart failure, bradyarrhythmias, electrolyte abnormalities or taking medications that prolong the QT interval Withhold in patients who develop a QT interval greater than 500 msec on at least 2 separate ECGs until the QT interval is less than 481 msec or recovery to baseline if the QTc interval is greater than or equal to 481 msec, then resume at a reduced dose. Permanently discontinue in patients who develop QTc interval prolongation in combination with Torsade de pointes or polymorphic ventricular tachycardia or signs/symptoms of serious arrhythmia
Crizotinib	Yes	Monitor with ECGs and electrolytes in patients who have a history of or predisposition for QT prolongation, or who are taking medications that prolong QT Temporarily suspend (Grade 3 QTc prolongation), dose reduce, or permanently discontinue (Grade 4 QTc prolongation) crizotinib

5HT3, serotonin; CHF, congestive heart failure; ECG, electrocardiogram; MI, myocardial infarction; QTc, correct QT.

References

1. Food and Drug Administration. 2015. http://www.fda.gov/
2. European Medicines Agency. 2015. http://www.ema.europa.eu/ema/

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Kinase Inhibitor	QT-interval prolongation? (Yes/ No)	Recommendations on how DDIs can be managed
Dabrafenib	Yes	Treatment with dabrafenib is not recommended in patients with uncorrectable electrolyte abnormalities (including magnesium), long QT syndrome or those taking medicines known to prolong QT interval ECG and electrolytes must be monitored in all patients before treatment, after 1 month of treatment, and after dose modification Further monthly monitoring is recommended in patients with moderate to severe hepatic impairment during the first 3 months of treatment, followed by every 3 months thereafter If QTc exceeds 500 msec, dabrafenib should be temporarily interrupted, electrolyte abnormalities corrected, and cardiac risk factors for QT prolongation (e.g. CHF, bradyarrhythmias) controlled Permanent discontinuation of dabrafenib is recommended if QTc >500 msec and there is a >60 msec change from pre-treatment values
Dasatinib	No	Dasatinib should be used with caution in patients who have or may develop prolongation of the QT interval, including patients with hypokalemia or hypomagnesemia, patients with congenital long QT syndrome, patients taking anti-arrhythmic medicines or other medicinal products that lead to QT prolongation, and cumulative high-dose anthracycline therapy Correct hypokalemia or hypomagnesemia prior to dasatinib initiation
Erlotinib	No	
Gefitinib	Yes	
Ibrutinib	Yes	Clinicians are cautioned to use clinical judgment when assessing whether to prescribe ibrutinib to patients at risk from further shortening QTc duration (e.g., congenital short QT syndrome or a family history of the syndrome)
Idelalisib	Yes	Concurrent administration of salmeterol and idelalisib is not recommended. The combination may result in increased risk of cardiovascular adverse events associated with salmeterol, including QT prolongation.
Imatinib	No	

5HT3, serotonin; CHF, congestive heart failure; ECG, electrocardiogram; MI, myocardial infarction; QTc, correct QT.

References

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Kinase Inhibitor	QT-interval prolongation? (Yes/ No)	Recommendations on how DDIs can be managed
Lapatinib	Yes	Lapatinib should be administered with caution to patients who have or may develop prolongation of QTc (e.g., hypokalemia, hypomagnesemia, congenital long QT syndrome, co-administration of anti-arrhythmic medicines or other medicinal products that lead to QT prolongation, and cumulative high-dose anthracycline therapy) Hypokalemia or hypomagnesemia should be corrected prior to lapatinib administration ECG and electrolyte monitoring should be considered
Lenvatinib	Yes	Withhold lenvatinib for the development of Grade 3 or greater QT interval prolongation Resume lenvatinib at a reduced dose when QT prolongation resolves to Grade 0 or 1 or baseline.
Nilotinib	Yes	Prior to nilotinib administration and periodically, patients should be monitored for hypokalemia or hypomagnesemia and deficiencies corrected ECGs should be obtained at baseline, 7 days after initiation, and periodically thereafter, and following any dose adjustments Nilotinib should not be administered to patients with hypokalemia, hypomagnesemia, or long QT syndrome Concomitant use of drugs known to prolong the QT interval should be avoided
Nintedanib	No	Caution should be exercised when administering nintedanib in patients who may develop QTc prolongation
Pazopanib	Yes	Pazopanib should be used with caution in patients with a history of QT interval prolongation, in those taking antiarrhythmics or other medications that may prolong QT interval, and those with relevant pre-existing cardiac disease Baseline and periodic monitoring of ECGs and maintenance of electrolytes (e.g., calcium, magnesium, potassium) within the normal range should be performed
Ponatinib	No	
Regorafenib	No	
Ruxolitinib	No	
Sorafenib	Yes	If a drug is indicated which also prolongs the QTc interval, an ECG should be obtained 24-48 hours before and 1 week after initiating the concomitant therapy. Pharmacists should also routinely check for concomitant use of such QT prolonging drugs such as 5HT3 antagonists, antibiotics, antifungals and over the counter drugs such as domperidone

5HT3, serotonin; CHF, congestive heart failure; ECG, electrocardiogram; MI, myocardial infarction; QTc, correct QT.

References

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2. European Medicines Agency. 2015. http://www.ema.europa.eu/ema/

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Kinase Inhibitor	QT-interval prolongation? (Yes/ No)	Recommendations on how DDIs can be managed
Sunitinib	Yes	Sunitinib should not be administered with QTc interval-prolonging drugs (e.g. 5HT3 antagonists, antibiotics, antifungals and over-the-counter drugs (e.g. domperidone) If co-administration of QTc interval-prolonging drugs is necessary, an ECG should be obtained 24-48 hours before, and 1 week after, the start of treatment
Trametinib	No	
Vandetanib	Yes	Concomitant administration with products known to prolong the QT interval should be avoided Co-administration with ondasetron has a small additive effect on prolongation of the QTc interval
Vemurafenib	Yes	

5HT3, serotonin; CHF, congestive heart failure; ECG, electrocardiogram; MI, myocardial infarction; QTc, correct QT.

References

1. Food and Drug Administration. 2015. http://www.fda.gov/
2. European Medicines Agency. 2015. http://www.ema.europa.eu/ema/