Florida CHAPTER

Arrhythmias and QT Prolongation in Cancer Patients

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CANCER BACKGROUND

While much of the focus of cardio-oncology has been on heart failure and left ventricular dysfunction, it is increasingly recognized that many traditional and novel cancer therapeutics are associated with various arrythmias which can range from benign to potentially life-threatening. Management of these issues in cancer patients requires a thoughtful and nuanced approach to ensure optimal outcomes.

ADVERSE EFFECTS

Atrial Arrhythmias are quite common in cancer patients, especially atrial fibrillation. In fact, there is a 20% higher adjusted risk of AF in patients with cancer, especially within the first year of diagnosis. Various cancer therapeutics are associated with an increased incidence of atrial fibrillation including anthracyclines. Melphalan, an alkylating agent, also has significantly increased rates of atrial fibrillation especially when used as a stem cell transplant preconditioning chemotherapeutic. Finally, various tyrosine kinase inhibitors (TKI) are associated with atrial arrhythmias. Ibrutinib, a small molecule inhibitor of Bruton's tyrosine kinase is associated with atrial fibrillation with an incidence of 10-15%.

QT Prolongation and Ventricular Arrhythmias: A great deal of attention is paid to the QT prolonging potential of cancer therapeutics, however the risk of fatal arrhythmias is quite low. In particular, arsenic, tyrosine kinase inhibitors, and the cyclin dependent 4/6 inhibitor ribociclib have been implicated for the QT prolonging effects. Other agents associated with ventricular arrhythmias include anthracyclines and fluoropyrimidines, generally resulting from other toxicities such as cardiomyopathy and ischemia. Ibrutinib has been associated with increased ventricular arrhythmias. The mechanism is unclear and is likely related to direct arrhythmogenic effects on the myocardium.

Bradyarrhythmias are relatively uncommon and rarely symptomatic. There are seen most commonly with ALK (anaplastic lymphoma kinase) inhibitors, a group of TKISs primary used for non-small cell lung cancer and taxanes. Bradyarrhythmias can also be the presenting manifestation of checkpoint inhibitor (immunotherapy) myocarditis.

RECOMMENDATIONS

Diagnosis of arrhythmias are often based on physical exam findings, patient reported symptoms and then electrocardiographic (ECG) confirmation. An ECG should be obtained if patients report palpitations or syncope/pre-syncope or if physical exam reveals tachycardia or an irregular pulse. Various cancer treatments have specified ECG monitoring for QT interval prolongation based on FDA and manufacturer recommendations. Treatment of arrhythmias should follow the same algorithms for these conditions in the general population. Special consideration should be given to potential drug-drug interactions as well as the risk of bleeding (especially with ibrutinib or due to hematologic abnormalities) if anticoagulation is required.

DATA TO SUPPORT

Rhea et al. Arrhythmogenic anticancer drugs in cardio-oncology. Cardiol Clin. 2019; 37(4): 459-468.

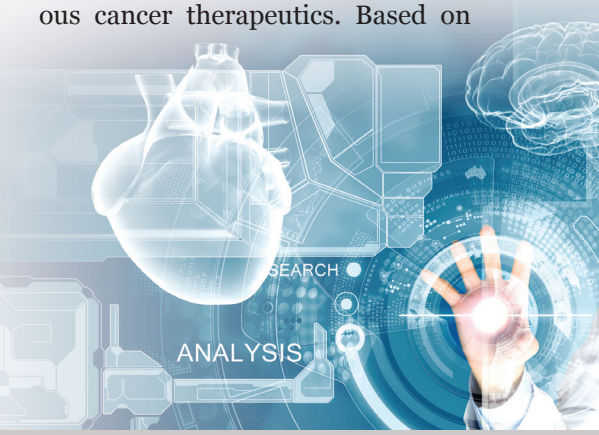
Armanious et al. Electrophysiologic toxicity of chemoradiation. Curr Oncol Rep. 2018; 20(6): 45.

INDICATIONS

Arrhythmias are associated with various cytotoxic, targeted and immunotherapies used to treat various solid and liquid tumors.

ONCOLOGY COMMENTS

Oncologists must be aware of the arrhythmogenic potential of various cancer therapeutics. Based on



Arrhythmias *continued*

clinical suspicion, an ECG should be obtained. In addition, careful attention should be paid to QT monitoring recommendations and employ appropriate risk mitigation strategies including electrolyte repletion and dose adjustment when necessary. Finally, drug-drug interactions may limit the available treatment options in certain patients.