

**Control Number:** 41

**Abstract Category:** Clinical Case Challenge in Cardio-Oncology

**Title:** Severe Recurrent Pulmonary Arterial Hypertension from Bosutinib After Dasatinib Toxicity

## **ABSTRACT BODY**

### **Background and Purpose**

Pulmonary arterial hypertension (PAH) is a well described toxicity of dasatinib, a BCR-ABL tyrosine kinase inhibitor (TKI) used to treat chronic myelogenous leukemia (CML). We present a case of severe PAH during treatment with bosutinib, another 2nd generation TKI.

### **Case Description and Outcomes**

A 41 year old woman with a history of migraine and CML on dasatinib therapy presented with progressive shortness of breath. Chest imaging revealed pleural and pericardial effusions, and mild PAH was diagnosed by right heart catheterization [PA 42/20 (mean 27), PCWP 7, PVR 3.3 WU]. Both resolved after switching to imatinib, but due to intolerable diarrhea she was transitioned to bosutinib. After 17 months of bosutinib, she developed recurrent dyspnea and signs of right heart failure. CT angiography and ventilation/perfusion studies were negative for pulmonary embolism. An echocardiogram showed RVSP > 100mmHg and right heart catheterization confirmed severe pre-capillary PAH (PA 85/45, PCWP 10, PVR 16.6 WU) unresponsive to oxygen or nitric oxide. Bosutinib was discontinued, and PAH responded to treatment with treprostinil followed by tadalafil and ambrisentan. After 12 months of treatment, right heart catheterization showed complete reversal of PAH [PA 26/8, PCWP 5, PVR 2.36 WU]. Nilotinib was prescribed for further CML treatment with plans for close echocardiographic surveillance.

### **Discussion**

BCR-ABL TKIs such as dasatinib dramatically improve prognosis of CML, but are associated with important vascular toxicities including hypertension, thrombosis, arterial ischemia, and PAH. Proposed mechanisms of PAH include Src kinase inhibition in the lungs and direct endothelial damage. Bosutinib is used in the second line setting, often for patients with intolerance to other TKIs. Bosutinib also inhibits Src kinase and has been associated with recurrent PAH in patients previously exposed to dasatinib. Shared Src kinase inhibition may mediate pathogenesis of dasatinib and bosutinib induced PAH, although further investigation is needed. PAH should be recognized as a possible toxicity of bosutinib among patients previously treated with dasatinib, and close cardiac surveillance with echocardiography may be warranted in patients with prior history of TKI induced pulmonary or vascular toxicity.

### **References**

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