

**Control Number:** 52

**Abstract Category:** Clinical Science in Cardio-Oncology

**Title:** IBRUTINIB AND THE UNDERRECOGNIZED RISK OF VENTRICULAR TACHYCARDIA: A METANALYSIS AND METAREGRESSION

## **ABSTRACT BODY**

### **Background**

Atrial fibrillation following initiation of Ibrutinib is an increasingly recognized phenomenon. Ibrutinib has emerged as a widely used treatment option for patients with chronic lymphocytic leukemia (CLL), mantle cell lymphoma, and Waldenstrom's macroglobulinemia, especially as salvage therapy for refractory disease. Although the clinical relationship between atrial fibrillation and Ibrutinib is well known, there is very little investigation of the relationship between ventricular arrhythmias and initiation of Ibrutinib. Atrial fibrillation often requires treatment without discontinuation of Ibrutinib, but in many cases ventricular arrhythmias can be fatal. Data comparison between ventricular arrhythmias and Ibrutinib has shown inconsistent results in terms of both incidence and mortality. Our clinical hypothesis is that Ibrutinib is associated with a much higher incidence of ventricular arrhythmias than patients not treated with Ibrutinib and the incidence will increase with longer duration of treatment with Ibrutinib.

### **Methods**

We performed aggregate data meta-analyses on 9 studies with 3,809 patients being treated with Ibrutinib to examine the incidence of ventricular arrhythmias. We also performed a meta-regression analysis to evaluate the effect of duration of therapy on incidence of ventricular arrhythmias. Summary relative risk (RR) and 95% confidence intervals (CI) were estimated using a random-effects model.

### **Results**

In 3,809 patients being treated with Ibrutinib, the incidence of ventricular arrhythmias was almost 5-fold higher in patients being treated with Ibrutinib compared to patients on other treatment regimens (RR 4.82, 95% CI 2.22-10.45,  $p < 0.0001$ ). On meta-regression, when plotting log odds ratio of incidence of ventricular arrhythmias (y-axis) against duration of therapy (x-axis), incidence increased further with longer duration of treatment (coefficient = 0.344,  $p=0.0001$ ).

### **Conclusion**

For patients treated with Ibrutinib, there was a markedly higher rate of ventricular arrhythmias compared to patients on all other treatment regimens. Meta-regression showed a trend towards increased incidence of ventricular arrhythmias with longer duration of treatment reached statistical significance.

### **Clinical Implications**

There needs to be more surveillance for ventricular arrhythmias, and it should be considered a potential major side effect, which can increase morbidity and mortality, for patients initiating Ibrutinib.