# Incidence of Cardiotoxicity in Patient's with Leukemia Being Treated with Tyrosine Kinase Inhibitors

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## Introduction

- Tyrosine Kinase Inhibitors (TKIs) are associated with vascular toxicity and heart failure as well as short-term side effects such as nausea, vomiting, edema and others.
- Although Imatinib has a well documented safety profile and is often first line treatment for those who meet indication, 10% of patients do not tolerate their first TKI.
- There are increasing number of long-term side effects with second generation TKIs.

## Objective

- To examine the incidence of cardiac toxicity in a large cohort of cancer patients who received TKIs
- To evaluate the rates of heart failure (HF) hospitalizations, atrial fibrillation, and abnormalities of systolic or diastolic function determined by echocardiography.
- *We hypothesized that TKI's are associated with RV failure from pulmonary hypertension.*

## Methods

- Conduct a retrospective review of 89 patients who received TKIs (Imatinib, Nilotinib, Dasatinib, Bosutinib, Sunitinib, or Ibrutinib) for leukemia (2012-2019).
- A retrospective review was performed manually using the electronic medical records and data was collected and exported to a spreadsheet
- We used statistical percentages to show the incidence of cardiotoxicity among patients taking TKIs

## Results

**Table 1. Demographics of patients with and without clinical cardiotoxicity.**

| | Without clinical cardiotoxicity | Hospitalized for HF/AF/Pulmonary HTN |
|---|---|---|
| **Number of Patients** | 85 | 4 |
| **Average Age** | 58 | 78 |
| **Gender** | | |
| **Male** | 45 (53%) | 2 (50%) |
| **White** | 65 (76%) | 3 (75%) |
| **Black** | 13(15%) | 1 (25%) |
| **Hispanic** | 4 (5%) | 0 |
| **Smoker** | 0 | 0 |
| **Obesity, BMI > 30** | 28% | 1 (25%) |
| | | |
| **Cancer type** | | |
| **B cell ALL** | 8 (9%) | 1 (25%) |
| **CML** | 44 (52%) | 2 (50%) |
| **CLL** | 2 (2%) | 1 (25%) |
| **AML** | 8 (9%) | 0 |
| **GIST** | 16 (19%) | 0 |
| **Other** | 8 | 0 |
| | | |
| **Status** | | |
| **Alive** | 68 (85%) | 2 (50%) |
| **Deceased** | 18 (15%) | 2 (50%) |
| | | |
| **Medications** | | |
| **ACEi** | 28 (33%) | 2 (50%) |
| **Beta Blocker** | 31 (36%) | 2 (50%) |
| **Diuretic** | 44 (52%) | 3 (75%) |
| **Statin** | 22 (26%) | 2 (50%) |
| **TKI** | | |
| **Nilotinib** | 7 (8%) | 3 (75%) |
| **Dasatinib** | 32 (37%) | 1 (25%) |
| **Imatinib** | 23 (27%) | 0 |
| **Bosutinib** | 1 (1%) | 0 |
| **Ibrutinib** | 2 (2%) | 1 (25%) |
| **Sunitinib** | 1 (1%) | 0 |
| **Multiple TKIs** | 20 (24%) | 0 |

- Demographics of patients with and without cardiac events are shown in Table 1.
- EF assessments were available at baseline and during therapy in 27/89 (30%) patients. No patient had HF with reduced EF defined as EF < 50% at baseline.
- During treatment 4/27 (15%) had EF < 50%, mean EF 36% (range 15-45%). All patients' EF recovered to normal within 1 year. 11% had left atrial enlargement defined as either left atrial dimension > 4cm or volume index > 34 ml/m2.
- At long term follow up (4-7 years), the incidence of HF hospitalizations was 2/89 (2%) and atrial fibrillation was 2/89 (2%). Pleural effusion was seen in 2/89 (2%) with Dasatinib.
- Cardiac mortality was 1/89 (1%) due to right HF from pulmonary hypertension and occurred after taking Nilotinib for 6 years.

## Conclusions

- This analysis is from consecutive patients receiving TKIs with long-term follow up referred to the comprehensive cancer center, without any selection bias.
- TKIs are rarely associated with clinically significant HF but the incidence of subclinical HF was much higher.
- Routine echocardiographic monitoring could help in earlier detection and management of HF.
- Continued collaborative investigation may further expose potential cardiovascular toxicities in leukemic patients.

❖ Disclosures: None to report

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