



# Still there are unmet needs in CML

Shaikha AlOtaibi, Naeem Chaudhri, Feras Alfraih, Syed Osman Ahmed, Marwan Shaheen, Walid Rasheed, Fahd Almohareb, Fahad Al-sharif, Hazzaa Alzharani, Amr Hanbali, Saud Alhayli, Shahrukh K. Hashmi, Mahmoud Aljurf, Riad El fakih  
**Adult Hematology/BMT, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia**

## Background

Bleeding while on TKI therapy for CML is not infrequent, CNS bleed is a serious complication that has been reported in patients taking TKIs even with normal platelet counts and coagulation profile

## Objective

To study the frequency of spontaneous intracranial bleed in CML patients taking TKI and to explore possible risk factors

## Materials & Methods

We retrospectively reviewed our CML database after the introduction of TKIs. We identified patients who developed spontaneous CNS bleed while taking TKIs. Patients older than 14 years, in chronic phase CML were included.

Gender	Current Age	Time of diagnosis	Site of bleeding	Acute treatment	Long-term plan	Last follow up	Current CML treatment and disease status
Female	51	2014	Subdural	Platelet transfusion and tranexamic acid	SCT (refused by the patient) , final plan: Nilotinib	5 <sup>th</sup> april.2018 :had menorrhagia and IDA being treated by Obe/gyne with Iron and tranexamic acid	Bosutinib because of low plt with nilotinib CCR, MMR and CHR
Female	60	1995	SAH	ICU admission for observation and blood pressure control	Imatinib resumed	19 march 2018 : stable no more bleeding	Imatinib CCR , MMR and CHR
Male	29	2017	Subdural	Platelet transfusion	Interferon	12 April 2018 :stable with no more bleeding	Interferon BCR-APL IS:45% from 69 % WBC is 15
Female	61	2010	B/L Subdural hematoma	Platelet transfusion and Evacuation Plavix stopped	Dasatinib Stop plavix	4 <sup>th</sup> Jan 2018 : stable with no more bleeding	Dasatinib CHR , 2.3 log reduction BCR_ABL IS % : 0.0120
Female	76	2003	Subdural hematoma	Surgical evacuation , FFP ,Cryo and Platelet transfusion	Hold TKI and keep monitoring the BCR-ABL	8 <sup>th</sup> April : Doing well with no more episodes of bleeding	Off treatment CHR BCR_ABL IS % : 0.2

## Results

We identified 5 cases of spontaneous CNS bleed out of 854 CML patients treated in our center since 2003 (this number include patients with CML of any age and in any phase and regardless whether they are on TKI or not). 4/5 patients were females (80%), median age was 60.5 (excluding a young patient with Marfan syndrome), 4/5 patients were on imatinib (80%). All patients presented with headache with nausea and/or vomiting. All patients had normal PT/PTT except one patient on warfarin. 1/5 patient was thrombocytopenic (73K) .PFA was prolonged in 2 patients (one in the setting of mildly low VWF antigen and being on antiplatelet, the second patient's PFA normalized while off imatinib). 4/5 had subdural and 1/5 had subarachnoid bleed. 2 patients had mass effect as a result of the bleeding. 3/5 patients had other risk factors for bleeding, one with Marfan syndrome, one taking clopidogrel and one taking warfarin. No patient died as a result of the bleed, all received supportive therapy and 2 patients required surgical evacuation. After controlling the bleeding episode 3 patients were rechallenged with same or different TKIs with no further CNS bleed reported. One patient stopped TKI and the patient with Marfan was treated with interferon.

## Summary

CNS bleed while on TKIs complicates the management of CML. Comprehensive evaluation can reveal an underlying etiology frequently. Mitigating other bleeding risk factors can facilitate the management of these patients. Checking a comprehensive coagulation profile (platelets, PT/PTT, PFA, VWF) before starting therapy could be helpful in patients who develop bleeding complications later on during their treatment course.