

Are cardiovascular adverse events with Ibrutinib well considered?

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Background

• Chronic lymphocytic leukemia and mantle cell lymphoma have a new standard of care:



Ibrutinib (metabolized by CYP 3A4/5 and P-glycoprotein inhibitor)

Cardiovascular (CV) adverse events are known with



atrial fibrillation (AF) (5-13,8%),

bleeding event (BE) (grade 3 or 4 about 3-4%)

hypertension

CV pre-treatment evaluation is not required in Ibrutinib summary of product characteristics (SPC)

Objectives

Evaluate whether the CV risks are considered regarding the prescription of Ibrutinib

Measure cardiovascular adverse event occurrence during treatment

Material and Methods

A retrospective analyze was conducted including patients with Ibrutinib initiation in our hematology department from May 2014 to July 2017.

A database was constituted consulting all the medical records including:

- demographic, clinical and biological informations
- adverse events
- CV evaluation
- potential drug interactions

The incidence of AF and BE and the CHA₂DS₂-VASc score were calculated

Results



55 medical records were analyzed
The patient's mean age was 70 years old

Risk factors evaluation



65% had at least one CV risk factor 5 patients had more than 3 CV risk factor



38% had CV monitoring during their treatment



25% had at least one initial cardiac exam (ECG/Holter, echocardiography, cardiology consultation)

Other CV adverse events

✓ One patient had myocardial infarction

√ 3 patients developped hypertension

Atrial Fibrillation

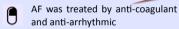


 ✓ 4 patients developped AF
 1 to 7 months after starting treatment

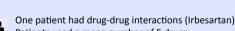


41 patients had no one CV exam

One patient with CHA₂DS₂-VASc < 2 was treated whereas initiation threshold treatment is 2



Ibrutinib dose was decreased for 2 patients, maintained for one and stopped the fourth patient



No potential cause could be identified

Patients used a mean number of 5 drugs > ¼ of patients used 7 or more medications

These adverse events were described in Ibrutinib SPC

Bleeding events

√ 24 patients had at least one BE



One event grade 3 and 8 events grade 2

5 patients were under anti-platelet medication

4 patients had drug-drug interactions (Irbesartan,

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Verapamil, Voriconazole)

Discussion

Our results show that cardiac pre-treatment exam are few performed (25%) despite our patients CV risk factors

With 7,2% of AF, this risk is not negligible considering the limited cohort

Almost half (44%) of patients presented BE. A part of serious BE could have been prevented, as concomitant drugs, especially CYP 3A4 inhibitors, seems to play a role in CV adverse event occurrence. Patients are all the more exposed at BE because of their comorbidities can require anti-platelet medication.

Conclusion

The therapeutic management of adverse event seems to be not standardized.

As a result of drug interactions and CV consequence, which can lead to serious outcomes, a multidisciplinary consultation including hematologist, cardiologist and pharmacist should be established at the initiation and during treatment by Ibrutinib