PB1909 A STUDY ON TROUGH LEVELS OF GENERIC DASATINIB AND ITS CORRELATION WITH ADVERSE EVENTS AND EFFICACY.

Topic: 08. Chronic myeloid leukemia - Clinical

Ashwin Nair1, Alka khadwal1, arihant jain1, savita attri2, smita pattnaik3, Shano Naseem4, Neelam verma4, aditya jandial1, deepesh lad1, gaurav prakash1, pankaj malhotra1

1 CLINICAL HEMATOLOGY AND MEDICAL ONCOLOGY, PGIMER, CHANDIGARH, India; 2 pediatric biochemistry, PGIMER, CHANDIGARH, India; 3 CLINICAL PHARMACOLOGY, PGIMER, CHANDIGARH, India; 4 Hematology, PGIMER, CHANDIGARH, India

Background:
Generic dasatinib has flooded the Indian market since April 2020. It has made dasatinib a feasible option as 1st or 2nd line TKI in our patients. Various studies worldwide have shown correlation between Cmin (trough levels) and incidence of pleural effusion. Through this study we try to collect pharmacokinetic data on generic dasatinib in our population.

Aims:
To study the relationship between trough levels of generic dasatinib drugs with adverse events and molecular response in patients with Ph+ve ALL and CML.

Methods: This study was a prospective observational study. It was conducted over a period of fourteen months i.e., from November 2020 to December 2021. Patients of Ph+ve ALL and CML were prospectively screened for inclusion (minimum 1 month of drug intake) and exclusion criteria (poor compliance, inappropriate sample collection). Selected 51 patients were enrolled in the study. Blood samples were collected for doing dasatinib trough levels and the patients were followed up over 6 months from the time of sample collection for adverse events and molecular responses. The dasatinib drug levels were measured by Liquid chromatographic mass spectrometry (LCMS) technique.

Results:
The median age of overall study cohort was 39 years (range 13-74). There were 15 (29.6%) females and 36 (70.4%) males, with Male: Female ratio of 2.4:1. Among the CML patients, 22 patients (68.75%) were in chronic phase, 3 (9.3%) in accelerated phase and 7 (22.8%) in blast phase with all of them being myeloid blast crisis. One patient was on ATT (1.96 %), fifteen on azoles (30.61%), fourteen on PPI/H2RB/Antacid (28.57%), and none on antiepileptics.

Achievement of Early molecular response (EMR), Major molecular response (MMR) or deep molecular response (DMR) was not related to the dose of drug. In ALL patients, there was no statistically significant correlation between dose of dasatinib and achieving MRD negativity (p – 0.794).

The median Cmin in the study population was 1.21 ng/ml (range 0 – 20.5). Cmin was found to be similar across various age groups with a median of 1.17 ng/ml, 1.42 ng/ml and 1.46 ng/ml for age group 20-39 years, 40-59 years and ≥ 60 years respectively (range – 0-22.5, p – 0.346). Median Cmin values were higher in those taking 140mg of dasatinib (3.22 ng/ml), as compared to lower doses but the trough levels for 50 mg and 100 mg were similar (1.46 ng/ml and 1.175 ng/ml) and lowest for those taking 70 mg of dasatinib (0.745 ng/ml), but there was no statistically significant correlation among them.

Pleural effusion was seen in 6 patients (11.76%) with two patients each in grade1, grade 2 and grade 3. Patients with
pleural effusion had higher median Cmin values when compared to those without (2.17 ng/ml vs. 1.18 ng/ml, p value = 0.558). Relation between cytopenias and Cmin was analysed in CML patients, and no statistical significant correlation was found between Cmin and toxicity profile in the overall study cohort. Patients taking azoles, PPI’s, H2-receptor blocker, ATT etc. did not show any statistical significance with their Cmin values as compared to those not taking these drugs.

Summary/Conclusion:

In this prospective study of generic dasatinib Cmin levels in patients with Ph+ve leukemias, there was no statistical significant correlation between Cmin values and incidence of pleural effusion which has been demonstrated in DARIA01 and OPTIMDASATINIB study. Efficacy of dasatinib did not correlate with dosage or with Cmin levels. The small sample size and shorter follow up are the main drawbacks of this study.