Posaconazole prophylaxis in patients with acute myeloid leukemia: A real life experience from a prospective multicenter observational study

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Background: We aimed to investigate the effectivity of posaconazole prophylaxis (PP) in patients receiving induction chemotherapy for acute myeloid leukemia (AML) at Turkish hospitals.

Patients and methods: Patients ≥18-years who received chemotherapy for AML with a duration of neutropenia (<500 cells/mm³) ≥10 days were included in a prospective multicenter observational study. Patients were followed until one week after recovery from neutropenia or discharge from hospital (for patients who were not recovered from neutropenia) to define the success of PP. Survival was followed up to six months. Each patient was allowed to be included for only one chemotherapy cycle. Prophylaxis failure was defined as; (1) the occurrence of invasive fungal diseases (IFDs) identified according to European Organization for Research and Treatment of Cancer and the Mycoses Study Group (EORTC/MSG) criteria¹, (2) receipt of any other systemic antifungal agent for 4 days or more during febrile neutropenia episode without any identified IFDs, (3) the occurrence of an adverse event related to the posaconazole resulting in the discontinuation of posaconazole, (4) Death for any cause under PP. Each patient was allowed to be included for only one chemotherapy cycle. The exclusion criteria were as; previous history of IFD, switch to an other antifungal before 7-days of PP except in case of toxicity related to posaconazole and duration of neutropenia <10 days. Groups (according to the outcome of PP) were compared with the use of Chi square and Fisher's exact tests for categorical variables, and Mann–Whitney U test for continuous variables

Results:

- A total of 115 patients were recruited from 18 centers between 21 November 2015 and 01 June 2016 (Table 1)
- Ninety-nine patients received first induction chemotherapy..
- Daunorubicin/idarubicin combined with cytarabine was the choice of chemotherapy in 98 patients
- All patients received 200 mg of posaconazole in an oral suspension three times daily.
- Median duration of PP was 25 days (Inter quartile range IQR; 17-35).
- PP was successful in 76 (66.1%) patients.
- The reasons for failure were as; initiation of an other antifungal drug for persistent neutropenic fever in 7 patients, breakthrough IFDs in 15 patients (possible IFD in 8 patients, probable invasive aspergillosis in 5 patients, proven IFDs in 2 patients), unable to take oral drug in 2 patients, Non-specific pulmonary findings with prolonged fever in 3 patients and death under PP in 8 patients. Adverse events related to PP were reported in 6 patients.
- The overall mortality was 15.7% (18 out of 115 patients) 12-weeks after initiation of PP

Table 1. Clinical and demographic characteristics of the patients

	Success (n=76)%	Failure (n=39)%	p
Age (median(IQR)) (years)	46,0 (32,0-60,75)	51,0 (37,0-60,0)	NS
Male	41 (53,9)	22 (56,4)	NS
Duration of neutropenia (median(IQR)) days	22,0 (18,0-29,0)	26,5 (19,75-37,5)	NS
Patients who did not recover from neutropenia	-	13 (33.3)	
Factors related to the posaconazole absorbtion			
- Fatigue	22 (28,9)	15 (38,5)	NS
- Vomitting	5 (6,6)	7 (17,9)	NS
- Diarrhea	10 (13,2)	8 (20,5)	NS
- Gastrointestinal mucositis	16 (21,0)	7 (17,9)	NS
- Lipid rich diet	13 (17,1)	9 (23,1)	NS
- Use of H2 receptor blocker	13 (17,1)	5 (12,8)	NS
- Use of proton pump inhibitor	39 (51,3)	16(41,0)	NS
- Smoking	18/ (23,7)	10(25,6)	NS
- Duration of smoking (pack- years) (median, (IQR))	27,5 (20,0-40,0)	17,5 (10,0-30,0)	NS
Leaving in a rural area	14/(18,4)	3 (7,7)	NS
Receipt of care at HEPA filtered room	26 (34,2)	6 (15,4)	0.047
Receipt of care at a positive –pressured and HEPA filtered room	18 (23,7)	5 (12,8)	NS
Construction close to the ward when patient was neutropenic	25 (32,9)	16 (41,0)	NS
Number of erythrocyte transfusions (median, (IQR))	8,0 (4,25-12,0)	6,0 (4,0-10,0)	NS
Exposure outside the hematology or stem cell transplantation ward during neutropenic period (median(IQR))	4,0 (2,0-7,0)	2,0 (1,0-7,0)	NS
Nystatin suspension prophylaxis	46 (60,5)	24 (61,5)	NS
Duration of PP (median, IQR) (days)	26,0 (22,0-34,75)	16,0 (9,0-36,0)	<0.001
Initiation of PP after cytotoxic chemotherapy	26 (34,2)	17 (43,6)	NS
12-weeks mortality after initiation of PP	3/76 (14,0)	15 (39,5)	<0.001
24-weeks mortality after initiation of PP	4/73 (4,2)	2/24 (8,3)	NS

IQR; Interquartile range, NS; not significant, PP; posaconazole prophylaxis

Conclusion

PP is widely used in our hospitals. Despite the acceptable rate of efficacy, better standardized strategies are required to improve the overall success of

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