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Antifungal prophylaxis in AML patients receiving intensive induction chemotherapy. A prospective observational study from the Acute Leukemia French Association (ALFA) group

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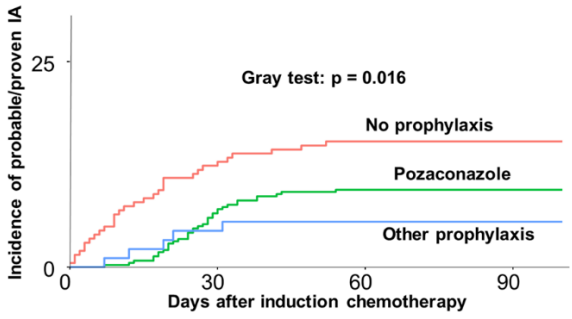
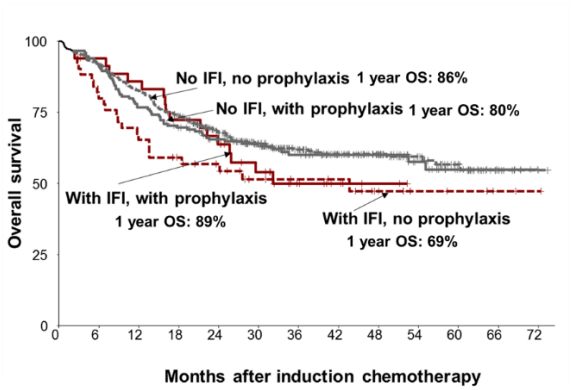
Background: The objective of this study was to describe the IFI prophylaxis strategies used in the prospective clinical trial of intensive chemotherapy within the Acute Leukemia French Association (ALFA 0702 study, NCT00932412), calculate the cumulative incidence of IFI according to different strategies, and evaluate the overall survival and IFI related mortality.

Material/methods: The trial protocol recommended posaconazole suspension as AF prophylaxis of 200 mg three times/day from day 4 after induction chemotherapy until neutrophils recovery according to ECIL recommendations. Patients were considered evaluable if they received posaconazole for a minimum duration of 7 days. IFI were classified by local investigators and reviewed later by an independent expert according to the EORTC classification, scanner images were requested for further investigations when needed.

Results: Among 677 patients, 383 (57%) received posaconazole for a median duration of 25 days (7-253). Posaconazole was introduced after a median time of 3 days after induction chemotherapy. We distinguished 4 groups, Group 1: patients without prophylaxis (n = 203, 30%), Group 2: posaconazole alone (n=241, 36%), Group 3: posaconazole plus other prophylaxis (n=142, 21%), and Group 4: patients receiving other prophylaxis (n= 91, 13%). Overall, there were 72 IA [34 (47%) possible, 38 (53%) probable/proven], 17 IC (all probable/proven) and 7 IM [1 possible, 6 probable/proven]. The median delay between posaconazole prophylaxis and IFI occurrence was 22 days (7-50) for IA, 18 days (15-60) for IC and 26 days (13-28) for IM compared to 10 days (3-180), 8 days (3-32) and 21 days (10-32) in case of other prophylaxis. The cumulative incidence of IFI was 2.4% at 10 days (IA: 2.4%, IC : 0%, IM : 0%), 11,2% at 30 days (IA: 8.4%, IC: 2%, IM: 0.7%), 14.2% at 60 days (IA: 10.6%, IC : 2.5%, IM : 1%), and 14.2% at 100 days (IA:10.6%, IC : 2.5%, IM : 1%). The cumulative incidence of probable/proven IA at day 60 was 8.37% for Group 1; 4.7% for Groups 2 and 3 combined and 3.3% for Group 4. After a median follow-up of 27.5 months (0.4- 73.4), 418 patients are alive and 259 (38.3%) died with 5.4% from IFI. We observed a better survival without any IFI whatever the AF prophylaxis was and in case of AF prophylaxis there was an improvement of 2-years survival. The multivariate analysis showed the negative impact of 2 factors on the mortality at day 100: Unfavorable cytogenetics: HR= 3.34 (1-11.20) p=0.05 and presence of IFI: HR = 5.63 (2.62-12.08) p<0.001.

Conclusions: Despite the trial protocol recommendations, this study shows that the ECIL recommendations are followed only in 57% of patients. AF prophylaxis has a significant impact on IFI incidence and overall survival with an IFI related mortality rate of 5.4%.


Incidence of probable/proven IA
25
0
Gray test: p = 0.016
No prophylaxis
Pozaconazole
Other prophylaxis
0
30
60
90
Days after induction chemotherapy


Overall survival
100
75
50
25
0
No IFI, no prophylaxis 1 year OS: 86%
No IFI, with prophylaxis 1 year OS: 80%
With IFI, with prophylaxis
1 year OS: 89%
With IFI, no prophylaxis
1 year OS: 69%
0
6
12
18
24
30
36
42
48
54
60
66
72
Months after induction chemotherapy