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Prophylaxis (Px) and Response to Treatment (Tx) of Invasive Mold Infections (IMI) in Hematopoeitic Cell Transplantation (HCT)

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Abstract

Background: Background: Breakthrough IMI despite antifungal Px and poor responses to Tx continue to be a problem in HCT.
Methods: Chart review of HCT patients were identified by pathology and microbiology database as having a probable or proven IMI as defined by the European Organization for Research and Treatment of Cancer/Mycoses Study Group from 1998 to 2008. Evaluation included: Px, Tx, and response to Tx at 90-days post onset.
Results: 214 cases were evaluable: 83% probable and 17% proven. 73% of cases were due to Aspergillus (IA), and 8% Zygomycetes (ZY). 90% were allogeneic HCT. 30% (65/214) of IMI cases were not on Px prior to onset. However, IMI cases due to multiple organisms, 82% (9/11) were not on Px prior to onset. For ZY, 88% (15/17) were not on ZY active Px.

Breakthrough IMI	IA N=156 (%)	ZY N=17 (%)
No Px	47 (30)	1 (6)
Echinocandin (EC)	36 (23)	5 (29)
Fluconazole/Itraconazole	36 (23)	6 (36)
Amphotericin B product (AB)	28 (18)	1 (6)
Voriconazole (V)	5 (3)	4 (24)
Posaconazole (P)	4 (3)	0

Overall 90-day response to Tx for all IMI was 29% (61/214). Overall response for IA was 30% (46/156). Tx for ZY: overall response was 18% (3/17), and 25% (3/12) if AB was in the regimen. Response rates for other IMI were 20% or less, and most were treated with an azole.

Response to Tx			P-value
IA	V (alone or with EC) 26/36 (72%)	AB (alone or with EC) 4/16 (25%)	0.002
ZY	AB alone 3/9 (33%)	No AB in regimen 0/5 (all 5/5 died)	NS

Conclusion: IMI occurred in cases where no Px was used or where Px may not have provided adequate coverage, specifically, there were no breakthrough ZY on P Px. Response rates were highest if V regimen was used for IA and AB regimen for ZY.

Study Objectives

- To review the antifungal regimens patients with IMI received as prophylaxis and treatment
- To evaluate the 90-day response to therapy

Introduction

- The number of IMI has continued to persist due primarily to the increased numbers of patients subjected to severe immunosuppression, such as HCT.
- Despite the use of prophylaxis, breakthrough IMI continue, and the resulting IMI may vary depending on the antifungal agent [1,2]
- IMI continues to be a significant factor in HCT outcomes resulting in high mortality rates [3].

Methods

•Patient Selection:
•Microbiology records and hematology database from 1998 to 2008 were used to identify patients with IMI and HCT

•Data Collection:
•Retrospective review using medical record and chart review
•Patient information collected: age, gender, hematological diagnosis, type of transplant, prophylaxis, treatment, and response at 90-days.

•Definitions/Criteria:
•Patients with proven and probable fungal infection were included. Criteria for probable and proven IFI were based on the definitions established by the European Organization for Research and Treatment of Cancer/Mycoses Study Group (EORTC/MSG) [4].
•Definitions of responses and outcomes were also based on those established by EORTC/MSG [5].

Responders = patients with complete or partial response to therapy
Non-Responder = patients with stable or failed response to therapy

GVHD = graft-versus-host disease

Results

Table 1: Patient Demographics

Patient Characteristics	N=214 (%)
Type of HCT	
Autologous HCT	21 (10)
Allogeneic HCT	192 (90)
MRD	104 (47)
MUD	76 (35)
Cord	12 (6)
Hematologic Malignancy	
Acute leukemia	109 (51)
Chronic leukemia	25 (12)
Lymphoma	41 (19)
Myelodysplastic syndrome	11 (5)
Multiple Myeloma	12 (6)
Other	16 (7)
GVHD (Allogeneic recipients)	N=192
Acute	34/192 (18)
Chronic	72/192 (38)
None	14/192 (7)

Figure 1: Proportion not on Prophylaxis

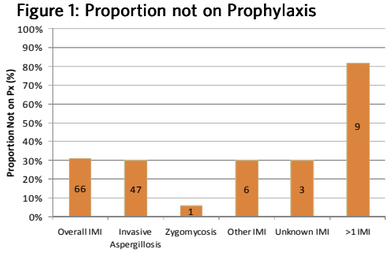


Table 2: Proportion of Breakthrough IMI on Prophylaxis

Prophylactic Agent	IA N=156 (%)	ZY N=17 (%)	Other* N=41 (%)
Echinocandin (EC)	36 (23)	5 (29)	8 (20)
Fluconazole/Itraconazole	36 (23)	6 (36)	7 (17)
Amphotericin B product (AB)	28 (18)	1 (6)	7 (17)
Voriconazole (V)	5 (3)	4 (24)	1 (2)
Posaconazole (P)	4 (3)	0	0

*IMI caused by other organisms &multiple organisms including IA or ZY

Figure 2: Proportion of Fungal Organisms

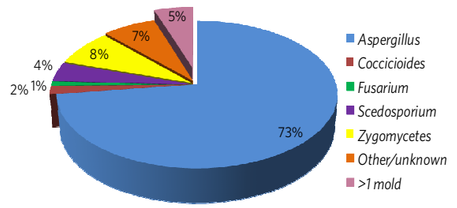


Figure 4: IA Response to Therapy at 90-Days

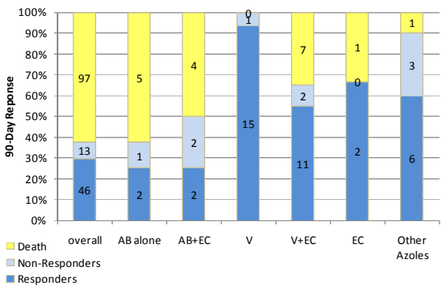


Figure 4: Response to Therapy by IMI at 90-Days

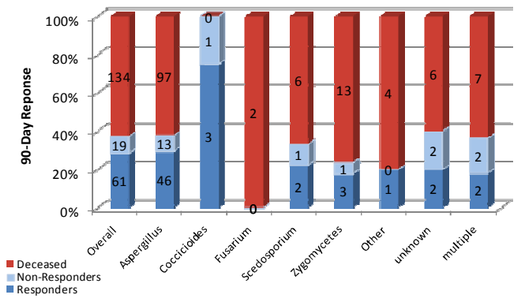
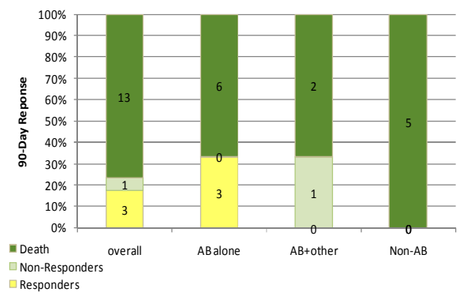


Figure 5: ZY Response to Therapy at 90-Days



Conclusion

1. IMI occurred in cases where no Px was used or where Px may not have provided adequate coverage, specifically, there were no breakthrough ZY on P Px and only 1 breakthrough on AB Px..
2. Response rates were lowest for IMI caused by *Fusarium spp*, (0%), followed by ZY (21%), and multiple IMI (22%).
3. Response rates were highest if V regimen (72%) was used for IA and AB regimen (33%) for ZY.

References

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4. De Pauw et al. *Clin Infect Dis* 2008; 46:1813-21.
5. Segal et al. *Clin Infect Dis* 2008; 47:674-83.