Use of terbinafine in combination with other systemic anti-fungal agents as treatment for invasive mold infections. Experience from a National Cancer Institute designated cancer center.

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BACKGROUND

- Severely Immunocompromised patients are at an increased risk of fatal infection caused by invasive molds.
- In addition to surgery, amphotericin B and triazole agents with anti-mold activity are commonly used in treating invasive mold infections.
- There is some data from in-vitro experiments to suggest an enhanced killing of Aspergillus spp., Fusarium spp. and Scedosporium spp. when terbinafine is used in combination with certain azoles or amphotericin B.
- At our center, terbinafine has sometimes been used in combination with other systemic anti-fungal agents in treating invasive mold infections.

STUDY OBJECTIVE

- To describe the clinical outcomes observed at the Moffitt Cancer Center when oral terbinafine was used in combination with other systemic anti-fungal agents in the treatment of invasive mold infections.

METHODS

- The study was a retrospective review of electronic medical records.
- Our study population composed of sixty-four patients treated for culture confirmed infection with mold isolates at the Moffitt Cancer Center from 1/1/2015 to 6/1/2021.
- Patients were grouped into 2 treatment groups: **Group A** comprised of those treated with a terbinafine containing regimen and **Group B** comprised of patients that received an anti-fungal regimen that did not include terbinafine.

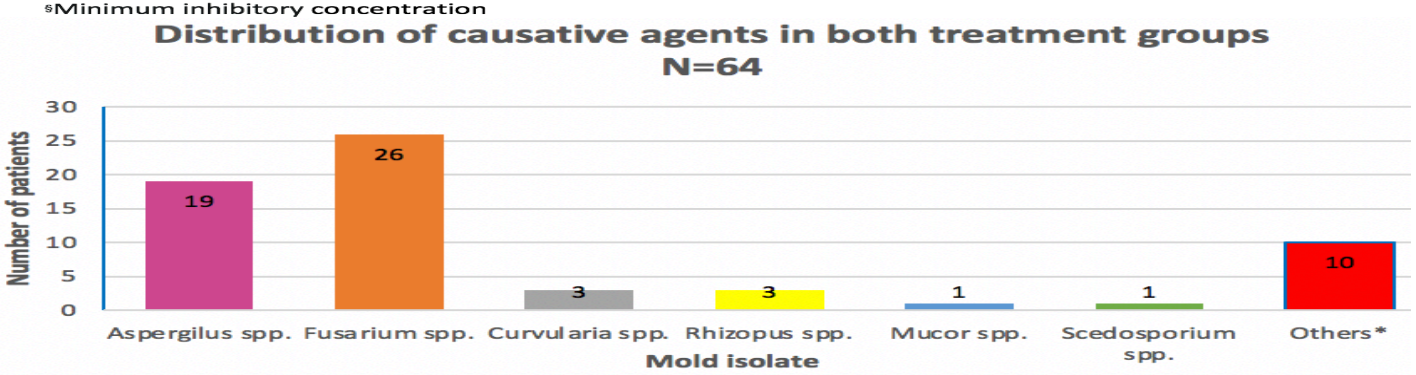
RESULTS

- **Treatment group A:** This comprised of 14 patients.
- Twenty-nine percent of the patients (4/14) had skin/soft tissue infections, 21% (3/14) had rhinosinusitis, 21% (3/14) had pulmonary infections and 4 patients (29%) had disseminated infection with an unclear source.
- Thirty-six percent (5/14) of patients in this group were discharged with clinical with treatment response, 57% (8/14) did not respond to treatment or died due to the invasive mold infection and 7% (1/14) died as a result of malignancy.
- **Treatment group B:** Composed of 50 patients.
- Thirty-eight percent (19/50) of patients this group had pulmonary infections, 28% (14/50) with skin/soft tissue infections, 16% (8/50) had rhinosinusitis, 2% (1/50) were diagnosed with central nervous system infection, 2% (1/50) had gastrointestinal infection, 14% (7/50) had an unclear source of infection.
- Forty-eight percent (24/50) of patients in this group were discharged with treatment response, 42% (21/50) had treatment failure or died due to the invasive mold infection and 10% (5/50) died as a result of malignancy.

Table 1: Demographics and Patient Characteristics N=64

Variable	Treatment Group A (n=14)	Treatment Group B(n=50)	p-value
Median age (IQR) -yrs	64 (55, 69)	60 (48, 70)	0.8
Male sex no. (%)	10 (71)	32 (64)	0.8
Severe neutropenia no. (%)*	10 (71)	27 (54)	0.2
Prolonged severe neutropenia no.(%)†	11 (79)	28 (56)	0.3
Causative Organisms no.(%)			
Fusarium spp.	10 (71)	17(34)	
Aspergillus spp.	1 (7)	17 (34)	
Curvularia spp.	0 (0)	3 (6)	
Rhizopus spp.	0 (0)	3 (6)	
Mucor spp.	0 (0)	1 (2)	
Scedosporium spp.	0	1 (2)	
Others‡	3 (21)	8 (16)	
MIC§ to terbinafine >=2 (n=14)	3	11	
MIC to terbinafine <2 (n= 19)	6	13	
MIC to terbinafine not reported (n=31)	4	27	
Site of infection no.(%)			0.5
Rhino-sinusitis	3 (21)	8 (16)	
Skin and soft tissue infection	4 (29)	14 (28)	
Pulmonary	3 (21)	19 (38)	
Central nervous system	0 (0)	1 (2)	
Gastrointestinal	0 (0)	1 (2)	
Disseminated infection, source unclear	4 (29)	7 (14)	
Hematologic malignancy no.(%)	12 (86)	42 (84)	
Solid organ malignancy no.(%)	2 (14)	8 (16)	
Treatment outcomes no.(%)			0.7
Discharged with clinical with treatment response	5 (36)	24 (48)	
Treatment failure/Died from invasive mold infection	8 (57)	21 (42)	
Malignancy related death	1 (7)	5 (10)	

* Absolute neutrophil count <500/mm³
† Severe neutropenia for 2 weeks or more
‡ Syncephalastrum spp., Apophysomyces spp., Scopulariopsis spp., Phialemonium spp., Colletotrichum spp., Cunninghamella spp., Exophiala spp., Scytalidium spp. and Blastoschizomyces spp.
§ Minimum inhibitory concentration



* Syncephalastrum spp., Apophysomyces spp., Scopulariopsis spp., Phialemonium spp., Colletotrichum spp., Cunninghamella spp., Exophiala spp., Scytalidium spp. and Blastoschizomyces spp.

CONCLUSION

- There was no statistically significant improvement in outcome observed in this study when terbinafine was used in addition to other systemic anti-fungal medications as treatment of invasive mold infections.
- There is need for larger studies to determine if terbinafine has a role in treatment of invasive mold infections.