Antifungal Activity of Isavuconazole and Comparator Agents against Contemporaneous Mucorales Isolates from USA, Europe, and Asia-Pacific

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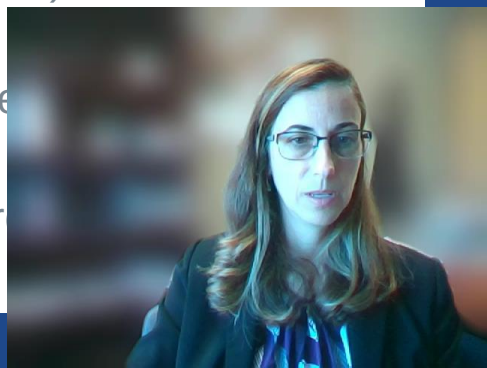
Objective

To evaluate isavuconazole activity against a global collection of contemporary Mucorales isolates

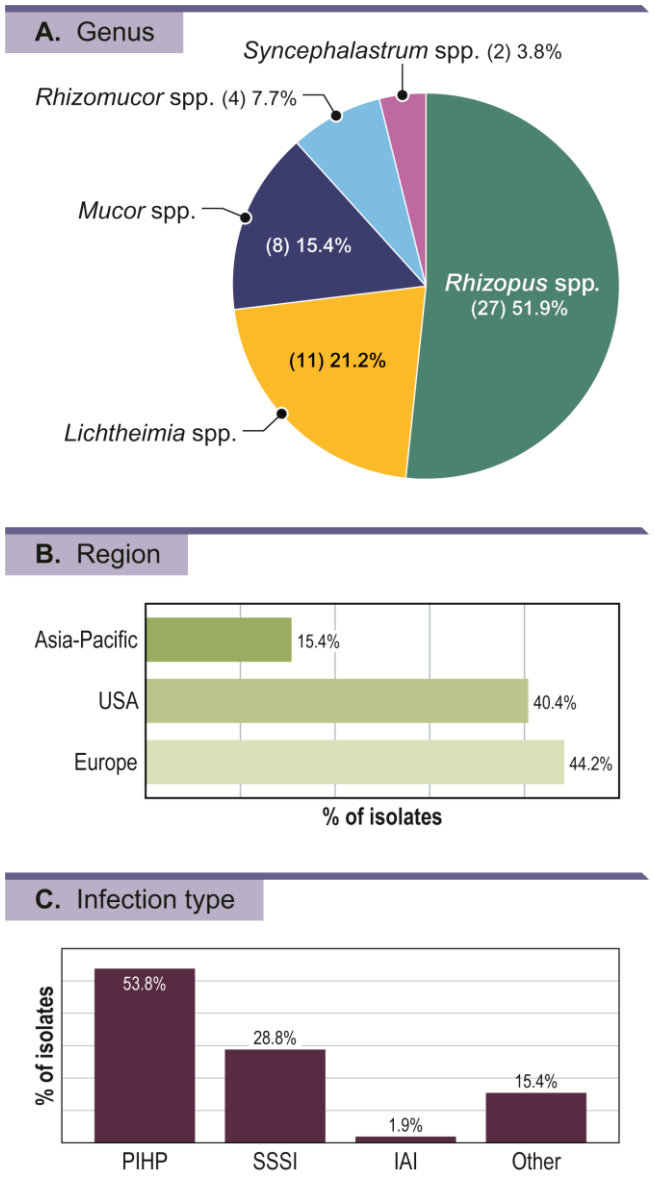
Methods

- A total of 52 Mucorales isolates that caused invasive fungal infection were collected (1/patient) during 2017-2020.
- Isolates were recovered from hospitals located in the USA (11 centres), Europe (6 centres in 5 countries), and the Asia-Pacific region (3 centres in 3 countries).
- Isolates were recovered from pneumonia in hospitalized patients (PIHP; 53.8%), skin and skin structure infections (SSSI; 28.8%), and other sites of infection (17.3%).
- Isolates were identified by MALDI-TOF followed by se
  MALDI score ≥2.0 was not achieved.
- Isolates were susceptibility tested by CLSI broth micr



Results

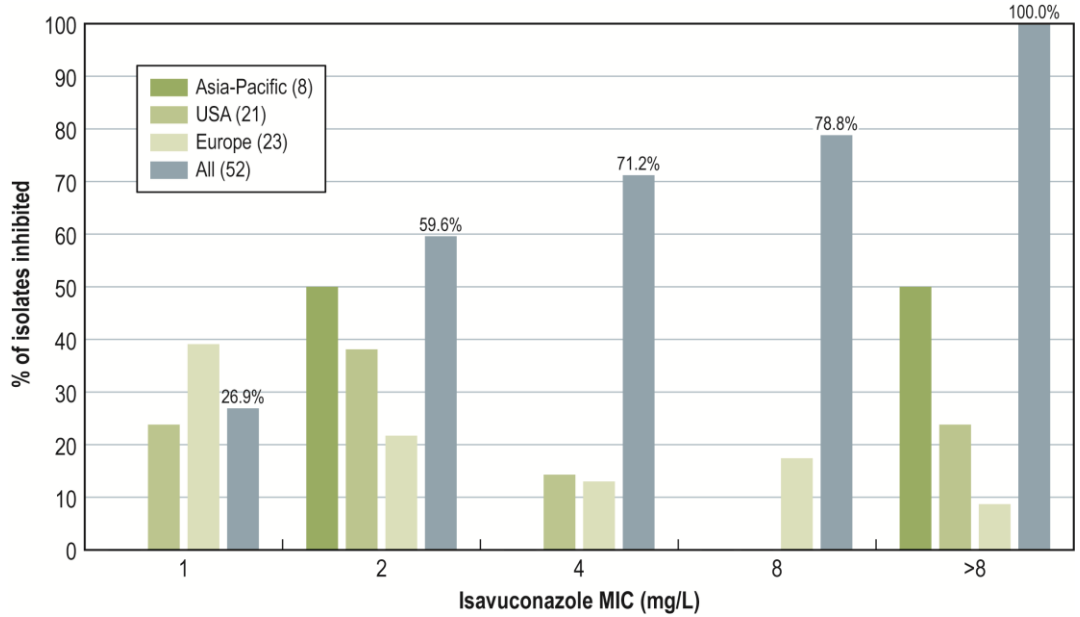
Figure 1. Distribution of Mucorales isolates recovered from IFI worldwide (2017-2020)



PIHP, pneumonia in hospitalized patients; SSSI, skin and skin structure infection; IAI, intra-abdominal infection

- Isavuconazole ($MIC_{50/90}$, 2/>8 mg/L) inhibited 59.6% and 71.2% of all Mucorales isolates at ≤2 mg/L and ≤4 mg/L, respectively.

Figure 2. Activity of isavuconazole tested against Mucorales isolates causing IFI worldwide (2017-2020)



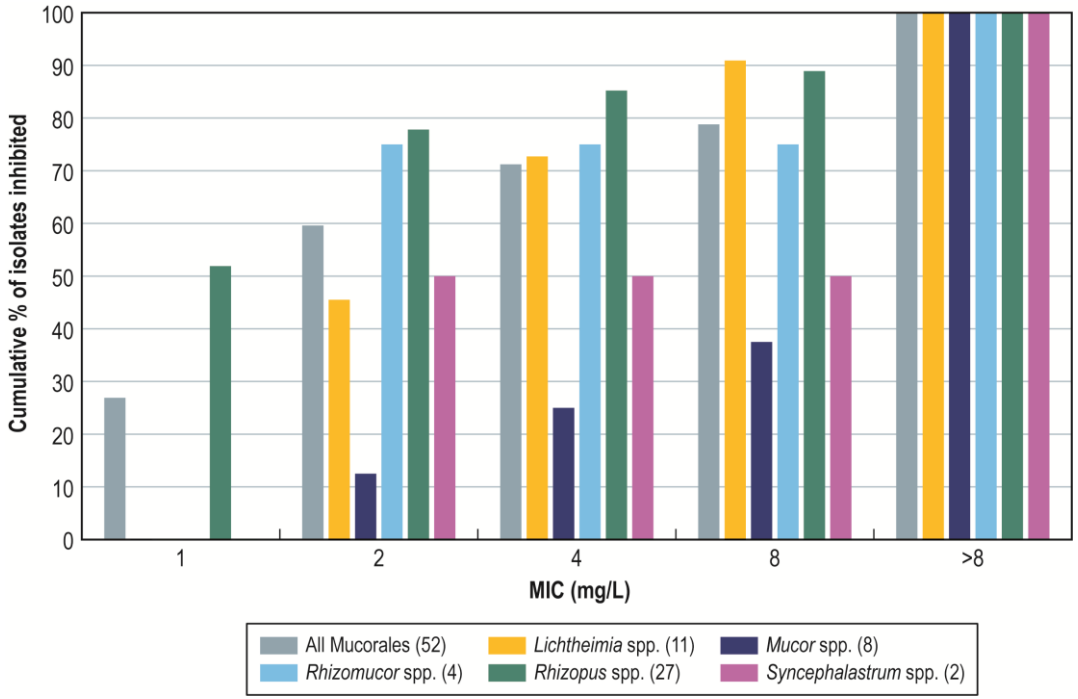
Results

Table 1. Activity of isavuconazole and comparator agents against Mucorales isolates causing IFI (2017-2020)

Antimicrobial agent	MIC_{50} / MEC_{50} (mg/L)	MIC_{90} / MEC_{90} (mg/L)	Range (mg/L)
Isavuconazole	2	>8	1 to >8
Itraconazole	2	8	0.5 to >8
Voriconazole	>8	>8	4 to >8
Posaconazole	0.5	8	0.25 to >8
Amphotericin B	0.5	1	0.25 to 2
Anidulafungin	>4	>4	>4 to >4
Caspofungin	>4	>4	>4 to >4
Micafungin	>4	>4	>4 to >4

- The most active agents were amphotericin B ($MIC_{50/90}$, 0.5/1 mg/L), posaconazole ($MIC_{50/90}$, 0.5/8 mg/L), isavuconazole ($MIC_{50/90}$, 2/>8 mg/L), and itraconazole ($MIC_{50/90}$, 2/8 mg/L).
- Limited activity was displayed by voriconazole ($MIC_{50/90}$, >8/>8 mg/L) and the echinocandins ($MIC_{50/90}$, >4/>4 mg/L).

Figure 3. Cumulative % of Mucorales isolates inhibited at isavuconazole MIC (mg/L), by genus



- Isavuconazole at ≤4 mg/L inhibited 85.2%, 72.7%, and 25% of *Rhizopus* spp. (*n*=27; $MIC_{50/90}$, 1/>8 mg/L), *Lichtheimia* spp. (*n*=11; $MIC_{50/90}$, 4/8 mg/L), and *Mucor* spp. (*n*=8; MIC_{50}, >8 mg/L) isolates, respectively.

Results

- Isavuconazole, posaconazole, itraconazole, and amphotericin B displayed low MIC_{50} values against *Rhizopus*, *Rhizomurcor*, and *Syncephalastrum* spp.
- Posaconazole exhibited a lower MIC_{50} against *Lichtheimia* spp. and *Mucor* spp. than other azoles.

Table 2. Activity of azoles against Mucorales isolates causing IFI (2017-2020)

	MIC_{50}/MIC_{90} in mg/L			
Organism (no. isolates)	Isavuconazole	Voriconazole	Posaconazole	Itraconazole
Mucorales group (52)	2/>8	>8/>8	0.5/8	2/8
Rhizopus spp. (27)	1/>8	8/>8	0.5/>8	2/>8
Lichtheimia spp. (11)	4/8	>8/>8	0.5/1	1/2
Mucor spp. (8)	>8/-	>8/-	2/-	4/-
Rhizomucor spp. (4)	2/-	>8/-	0.5/-	1/-
Syncephalastrum spp. (2)	2/-	>8/-	0.5/-	1/-

Conclusions

- The activity of azoles vary by Mucorales genus.
- Isavuconazole exhibited activity against most of the Mucorales isolates causing invasive infections regardless of geographic region.
- Isavuconazole inhibited most isolates of *Rhizopus*, *Rhizomucor*, and *Lichtheimia* spp. from this collection at an MIC ≤4 mg/L.
- Further studies are warranted to monitor the activity of antifungal agents against a larger collection of this rare and highly resistant organism group.

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