



Antifungal Activity of Isavuconazole against *Candida* Species and Filamentous Fungi in a Tertiary Hospital in Hong Kong

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Background

Invasive fungal infections are one of the growing global health concerns. Isavuconazole is considered an agent of choice for the treatment of invasive aspergillosis along with voriconazole, but with the advantages of better tolerability and pharmacokinetic profiles than the latter. Antifungal susceptibility data for isavuconazole are sparse in Hong Kong and are urgently needed to guide appropriate antifungal therapy.

Materials and Methods

A total of 57 archived fungal isolates from clinical samples, including 31 *Candida* species and 26 filamentous fungi, were included. The Thermo Scientific Sensititre ITAMYUCC Plate was used to determine the minimum inhibitory concentration (MIC) of isavuconazole, along with eight other commonly used antifungal agents. Results were read after 24 and 48 hours for a colorimetric change, with 72-hour results also being read for filamentous fungi.

Invitro susceptibility of fungal species with Scientific™ Sensititre™ YeastOne™ ITAMYUCC susceptibility plate										
Fungi		Candida species			Aspergillus species				Non-Aspergillus species	
		<i>Candida albicans</i>	<i>Candida glabrata</i>	other candida species	<i>Aspergillus flavus</i>	<i>Aspergillus niger</i>	<i>Aspergillus fumigatus</i>	<i>Aspergillus terreus</i>	<i>Scedosporium species</i>	
Amphotericin B	Nº isolates	7	15	9	5	3	1	1	6	
	MIC range	24h 0.5-1	0.5-1	0.25-1	1 to 4	≤0.12-2	1	-	-	
		48h 0.5-2	1 to 2	1 to 4	4->8	2	2	4	0.5-8	
		72h -	-	-	4->8	2 to 4	2	4	4->8	
	ECV (CLSI) µg/mL	2	2	1 to 2	4	0.5	0.5	4	-	
Anidulafungin	ECOFFs WT (EUCAST) mg/L	-	-	-	≤4	(≤0.5) Tentative	≤1	≤8	-	
	MIC range	24h ≤0.015-0.12	≤0.015-0.12	0.03-1	>8	≤0.015->8	≤0.015	-	-	
		48h ≤0.015-0.12	0.03-0.12	0.06-2	>8	>8	>8	≤0.015	1->8	
		72h -	-	-	>8	>8	>8	0.03	>8	
	ECV (CLSI) µg/mL	0.12	0.25	0.12-4	ND	ND	ND	ND	-	
Caspofungin	ECOFFs WT (EUCAST) mg/L	-	-	-	-	-	-	-	-	
	MIC range	24h 0.03-0.12	0.06-0.12	0.12-1	>8	≤0.008->8	0.03	-	-	
		48h 0.06-0.12	0.06-0.5	0.12-2	>8	>8	>8	≤0.008	0.25->8	
		72h -	-	-	>8	>8	>8	0.06	>8	
	ECV (CLSI) µg/mL	-	-	1	0.5	0.25	0.5	0.12	-	
Fluconazole	ECOFFs WT (EUCAST) mg/L	-	-	-	-	-	-	-	-	
	MIC range	24h 0.25-1	2 to 16	0.5-32	128->256	>256	>256	-	-	
		48h 0.5-1	8-256	1-128	>256	>256	>256	>256	≤0.12-32	
		72h -	-	-	>256	>256	>256	>256	32-64	
	ECV (CLSI) µg/mL	0.5	8	1 to 2	-	-	-	-	-	
Isavuconazole	ECOFFs WT (EUCAST) mg/L	-	-	-	ND	ND	ND	ND	-	
	MIC range	24h ≤0.008	≤0.008-0.25	≤0.008-0.25	0.25-1	1	0.5	-	-	
		48h ≤0.008-0.06	0.25-4	≤0.008-8	0.5-1	1 to 2	0.5	0.25	≤0.008-0.5	
		72h -	-	-	0.5-2	2	0.5	0.5	0.5-8	
	ECV (CLSI) µg/mL	-	-	-	1	4	1	1	-	
Itraconazole	ECOFFs WT (EUCAST) mg/L	-	-	-	≤2	≤4	≤2	≤1	-	
	MIC range	24h ≤0.015-0.06	0.12-0.5	0.03-0.25	0.12-0.25	0.5	0.25	-	-	
		48h ≤0.015-0.12	0.5->16	0.06->16	0.25	0.5	0.25	0.12	≤0.15-0.5	
		72h -	-	-	0.25-0.5	0.5	0.25	0.12	0.25-1	
	ECV (CLSI) µg/mL	-	4	0.5-1	1	4	1	2	-	
Micafungin	ECOFFs WT (EUCAST) mg/L	-	-	-	≤1	≤2	≤1	≤0.5	-	
	MIC range	24h ≤0.008-0.015	≤0.008-0.015	0.03-1	>8	≤0.008->8	≤0.008	-	-	
		48h ≤0.008-0.015	0.015	0.03-2	>8	>8	>8	≤0.008	0.12->8	
		72h -	-	-	>8	>8	>8	0.12	>8	
	ECV (CLSI) µg/mL	0.03	0.03	0.06-2	-	-	-	-	-	
Posaconazole	ECOFFs WT (EUCAST) mg/L	-	-	-	ND	ND	ND	ND	-	
	MIC range	24h 0.015-0.03	0.12-1	0.015-0.25	0.06-0.25	0.12	0.06	-	-	
		48h 0.015-0.06	0.5->8	0.03->8	0.12-0.25	0.12-0.25	0.06	0.06	≤0.008-0.25	
		72h -	-	-	0.25-0.5	0.12-0.25	0.06	0.06	0.25-1	
	ECV (CLSI) µg/mL	0.06	1	0.12-0.5	0.5	2	-	1	-	
Voriconazole	ECOFFs WT (EUCAST) mg/L	-	-	-	≤0.5	≤0.5	≤0.25	≤0.25	-	
	MIC range	24h ≤0.008-0.015	0.03-0.5	≤0.008-0.25	0.25-1	0.5-1	0.25	-	-	
		48h ≤0.008-0.015	0.25-4	0.015-8	0.5-1	0.5-1	0.25	0.25	≤0.008-0.25	
		72h -	-	-	0.5-2	1	0.5	0.5	0.25-0.5	
	ECV (CLSI) µg/mL	0.03	0.25	0.06-0.25	2	2	1	2	-	

other candida species: included *Candida parapsilosis*, *Candida tropicalis* and *Candida krusei*.

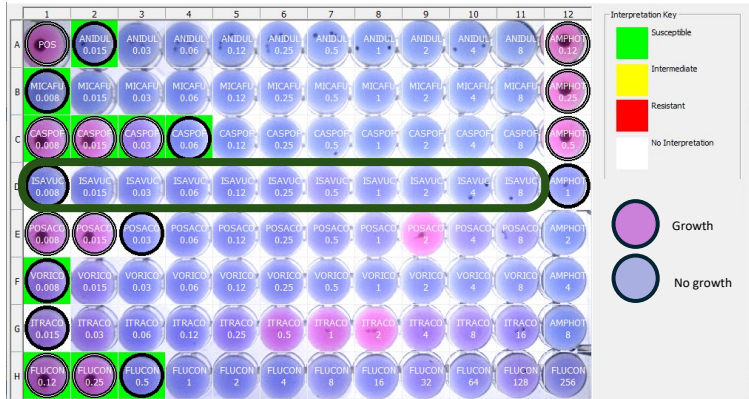
Results

Isavuconazole exhibited a good *in vitro* activity against all *Candida* species isolate, with low MIC of ≤0.008µg/mL to 2µg/mL, and at least 8-fold lower in comparison to fluconazole. Isavuconazole displayed effective in vitro activity against all molds tested, including *Aspergillus flavus*, *Aspergillus niger*, *Aspergillus fumigatus*, and *Aspergillus terreus* (mode MIC: 0.12µg/mL - 2µg/mL), *Scedosporium species*, and *Purpureocillium lilacinum*. A discrepancy was noted between 24- and 48-hour readings in *Candida* species, with the 48-hour reading showing at least a 2-fold increase in mode MIC for almost all azoles.

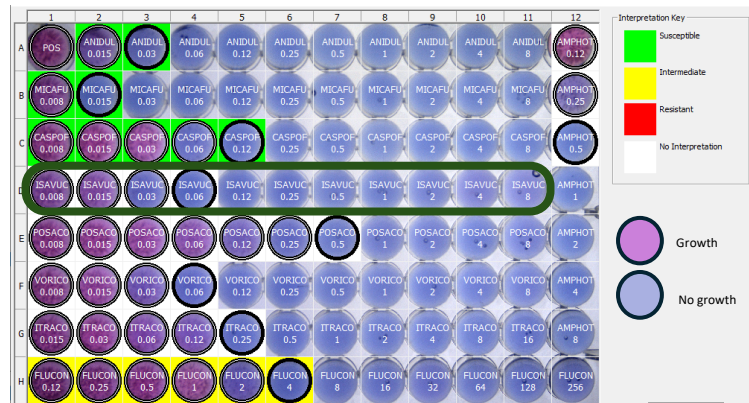
Conclusion

Isavuconazole demonstrated good in vitro activity against all *Candida*, *Aspergillus species*, *Scedosporium species*, and *Purpureocillium lilacinum* indicating it is a possible substitution for traditional azoles administration in Hong Kong.

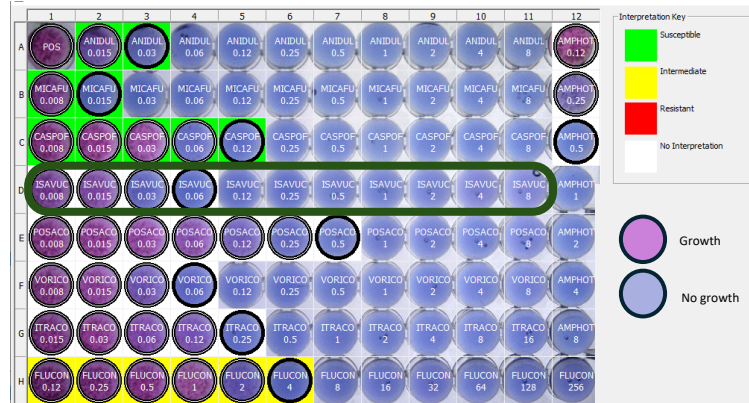
Acknowledgement: The Sensititre plates were provided for free by Pfizer Inc



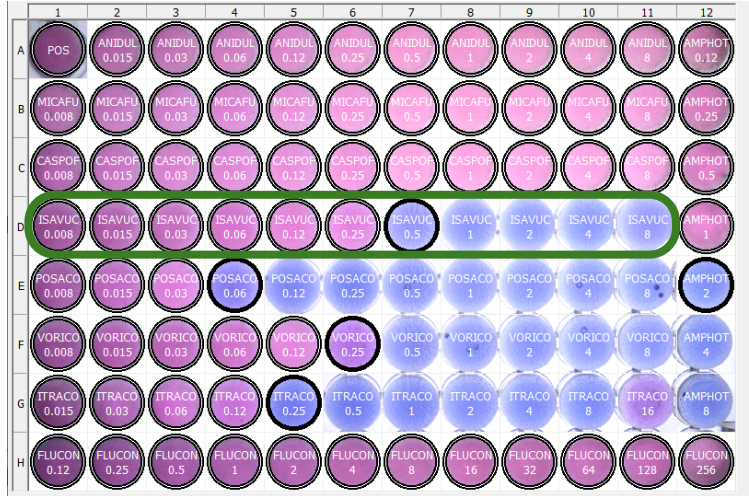
Candida albicans – Isavuconazole MIC: 0.008mcg/ml (@48 hrs)



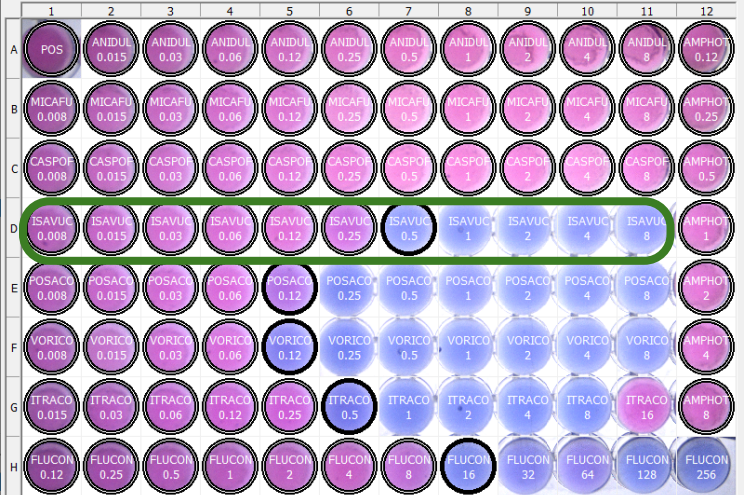
Candida glabrata – Isavuconazole MIC: 0.03mcg/ml (@48hrs)



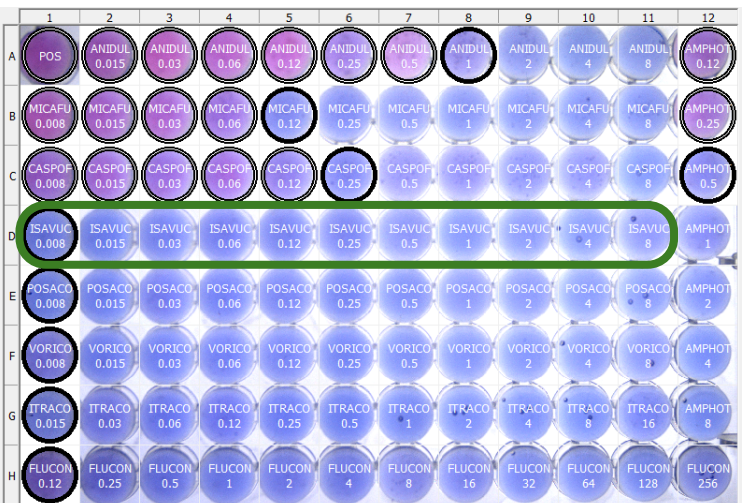
Candida parapsilosis – Isavuconazole MIC: 0.03mcg/ml (@48hrs)



Aspergillus fumigatus – Isavuconazole MIC: 0.5mcg/ml (@72hrs)



Purpureocillium lilacinum – Isavuconazole MIC: 0.5mcg/ml (@72hrs)



Scedosporium apiospermum – Isavuconazole MIC: ≤0.008mcg/ml (@72hrs)