Antifungal susceptibility patterns (AFSP) of 300 *Scedosporium* strains from a wide variety of clinical/environmental sources

Mag. Dr. rer. nat. Michaela Lackner
Division of Hygiene and Medical Microbiology
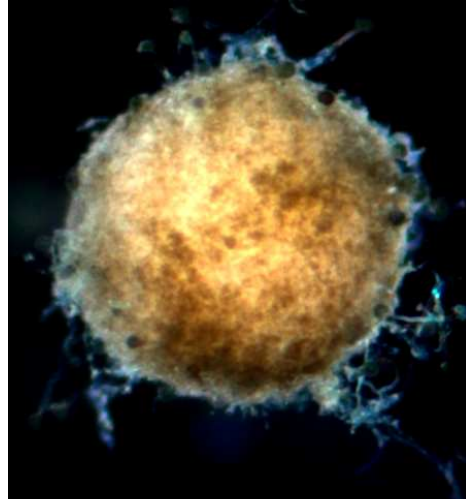Medical University Innsbruck
Austria

About the fungus

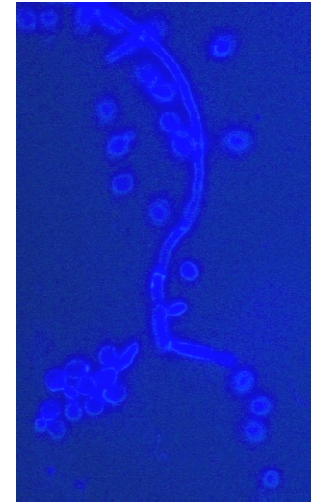**Anamorph**

Scedosporium

Teleomorph

Pseudallescheria

Systematics

Ascomycota
-Microascales

Morchella

Candida
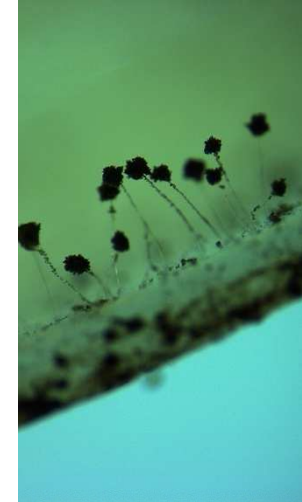
Aspergillus

Infections

COSMOPOLITAN

http://img.medscape.com

2

Strain set

25 %

74 %

N=322

9 % unknown

5 % 68 % 10 %

2 %

5 %

1 %

1 isolate Antarctica
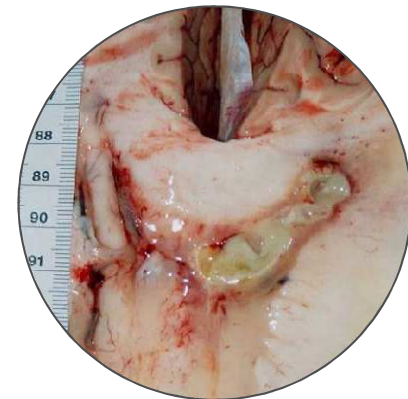
Identification: **AFLP + type strains**
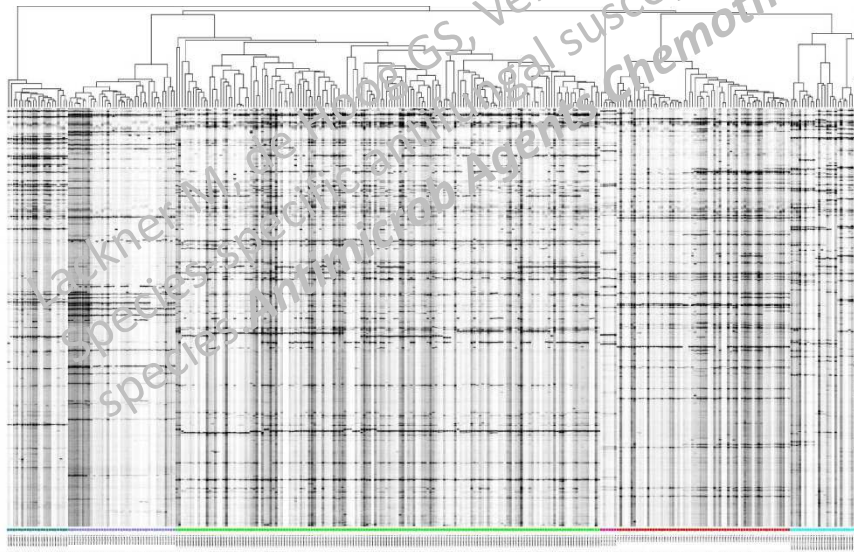
P. apiosperma (n = 154)
P. boydii (n = 60)
S. prolificans (n = 37)
S. aurantiacum (n = 22)

clinical relevant

S. dehoogii (n = 22)
P. elliposidea (n = 16)
P. angusta (n = 15)
P. minutispora (n = 6)

environmental

3

Susceptibility testing

CLSI document M38-A2

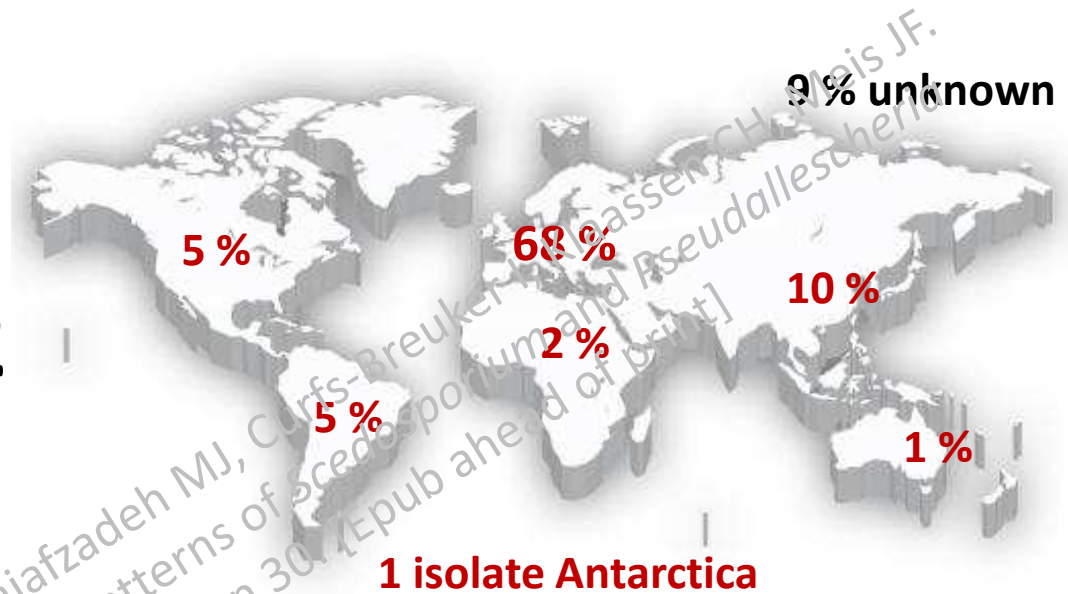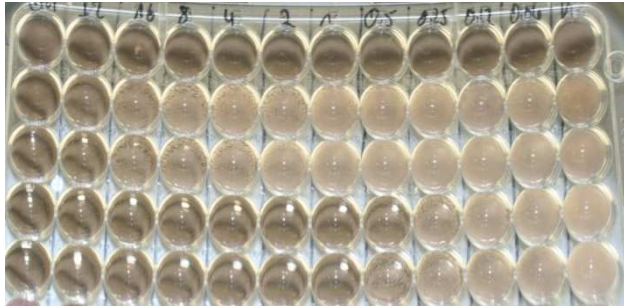**Compounds tested**

Isavuconazole
Itraconazole
Posaconazole
Voriconazole

Amphotericin B

MIC
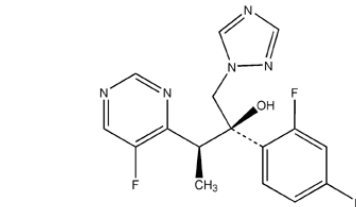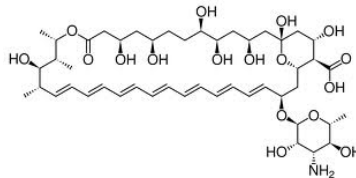
Anidulafungin
Caspofungin
Micafungin
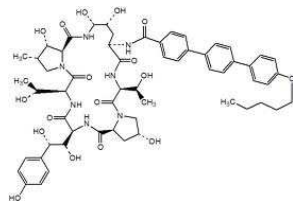
MEC

Statistical Analyses

Minimal Inhibitory/Effective Concentration (MIC/MEC)
MIC_{50}/MEC_{50}
MIC_{90}/MEC_{90}

MIC/MEC distribution per species and antifungal

MIC/MEC distribution **environmental/clinical** with Mann-Whitney test
(significant if p-value <0.05)

Cross resistance test
Spearman rank correlation
(significant if p-value <0.01)

4

Overview

Species	n	AMB				CAS				ANI				MICA			
		Range	MIC$_{50}$	MIC$_{90}$	GM	Range	MEC$_{50}$	MIC$_{90}$	GM	Range	MEC$_{50}$	MIC$_{90}$	GM	Range	MEC$_{50}$	MEC$_{90}$	GM
P. apiosperma	154					0.5 - > 8	1	8	1.5	0.125 - > 8	0.5	8	0.8	0.016 - > 8	0.125	4	0.2
P. boydii	60					1 - > 8	2	8	2.3	0.25 - > 8	1	8	1.4	0.062 - > 8	0.250	> 8	0.5
S. prolificans	37									0.5 - > 8	4	> 8	4.8	0.125 - > 8	> 8	> 8	7.9
S. aurantiacum	22																

Species	n	ITC				VRC				POS				ISA			
		Range	MIC$_{50}$	MIC$_{90}$	GM	Range	MIC$_{50}$	MIC$_{90}$	GM	Range	MIC$_{50}$	MIC$_{90}$	GM	Range	MIC$_{50}$	MIC$_{90}$	GM
P. apiosperma	154					0.25 - 8	1	2	0.9	0.25 - > 16	1	> 16	2.4				
P. boydii	60					0.125 - 2	1	1	0.7	0.125 - > 16	1	4	1.3	0			
S. prolificans	37																
S. aurantiacum	22					0.5 - 1	0.5	1	0.6								

Lackner M, de Hoog GS, Verweij PE, Najafzadeh MJ, Curfs-Breuker I, Klaassen CH, Meis JF. Species-specific antifungal susceptibility patterns of Scedosporium and Pseudallescheria species. Antimicrob Agents Chemother. 2012 Jan 30. [Epub ahead of print]

Population distribution

P. apiosperma

P. boydii

6
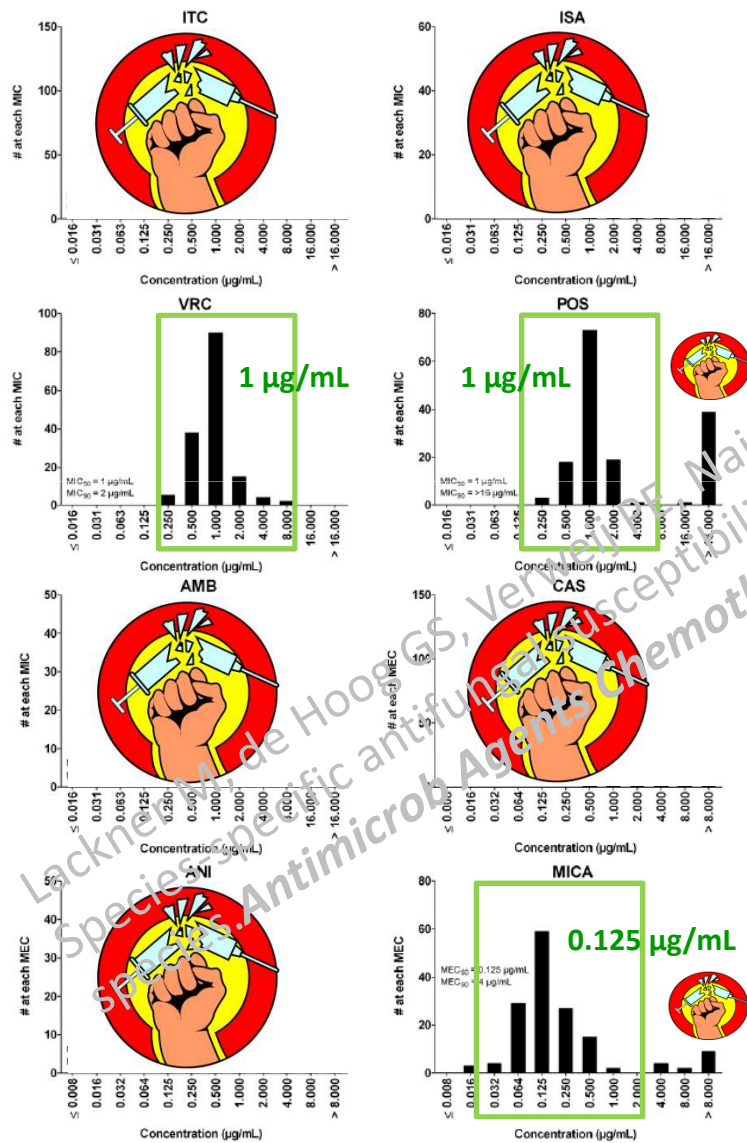
Cross resistance

Image http://www.usc.edu/hsc/i

P. apiosperma

Azoles	ITC	VRC	POS	ISA		Echinocandins	CAS	ANI	MICA
ITC	1	0.37*	0.52*	0.44*	CAS	1	0.73*	0.66*
VRC		1	0.70*	0.72*	ANI		1	0.78*
POS			1	0.76*	MICA			1
ISA				1				

P. boydii

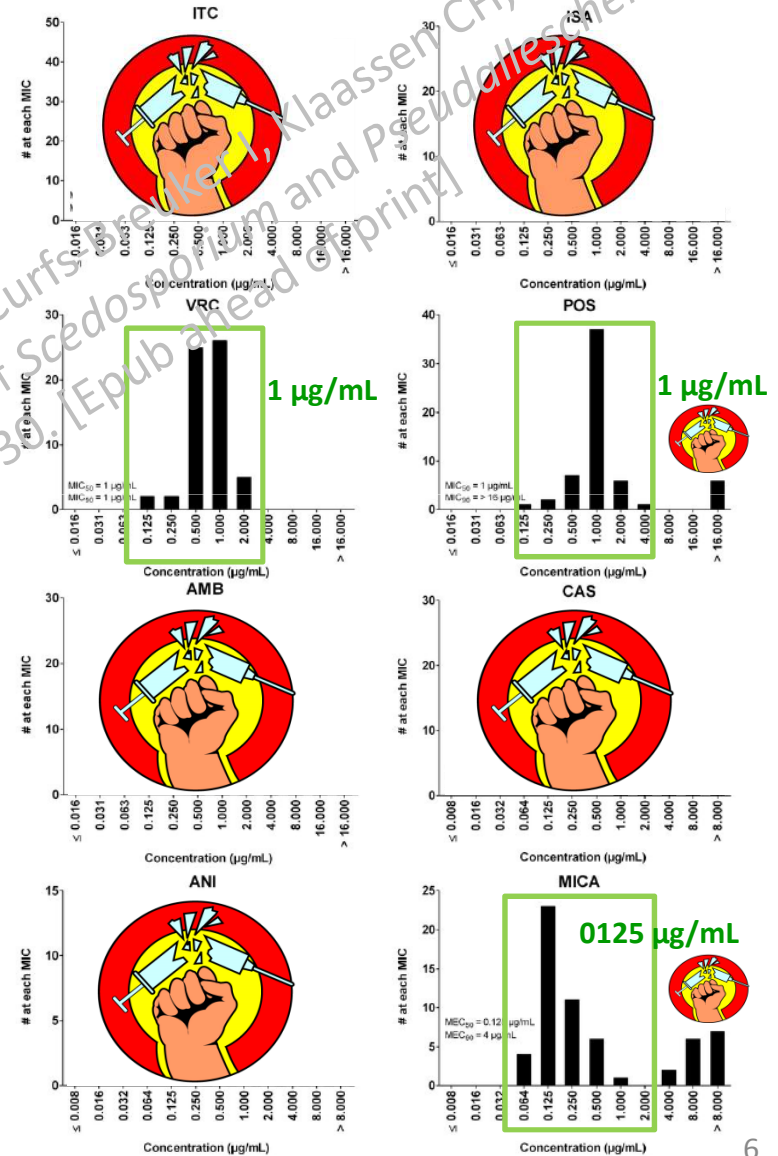| Azoles	ITC	VRC	POS	ISA		Echinocandins	CAS	ANI	MICA
ITC	1	0.64*	0.58*	0.63*	CAS	1	0.86*	0.86*
VRC		1	0.67*	0.77*	ANI		1	0.90*
POS			1	0.72*	MICA			1
ISA				1				

*p < 0.0001

Cross resistances were observed for all substances of the same drug classes.

BUT, no cross resistances between echinocandins and azoles !

Lackner M, de Hoog GS, Verweij PE, Najafzadeh MJ, Curfs-Breuker I, Klaassen CH, Meis JF. Species-specific antifungal susceptibility patterns of Scedosporium and Pseudallescheria species. *Antimicrob Agents Chemother.* 2012 Jan 30. [Epub ahead of print]

Clinical *versus* Environmental

	n	AMB				CAS				ANI				MICA			
		Range	MIC_{50}	MIC_{90}	GM	Range	MEC_{50}	MEC_{90}	GM	Range	MEC_{50}	MEC_{90}	GM	Range	MEC_{50}	MEC_{90}	GM
P. apiosperma [cl]	124	0.5 - >16	8	>16	6.5	0.5 - >8	1	8	1.6	0.125 - >8	0.5	8	0.9	0.006 - >8	0.125	4	*0.2
P. apiosperma [en]	29	1 - >16	16	>16	9.0	1 - >8	1	2	1.2	0.125 - 8	0.5	4	0.6	0.031 - >0.5	0.125	0.5	*0.1
P. boydii [cl]	44	0.5 - >16	16	>16	11.3	1 - >8	2	8	2.1	0.25 - >8	1	4	0.4	0.062 - >8	0.25	8	0.4
P. boydii [en]	14	2 - >16	16	>16	13.1	1 - >8	2	>8	3.1	0.5 - >8	2	8	1.8	0.062 - >8	0.25	>8	1.2

	n	ITC				VRC				POS				ISA			
		Range	MIC_{50}	MIC_{90}	GM	Range	MIC_{50}	MIC_{90}	GM	Range	MIC_{50}	MIC_{90}	GM	Range	MIC_{50}	MIC_{90}	GM
P. apiosperma [cl]	124	0.25 - >16	>16	>16	15.3	0.25 - >8	2	2	0.9	0.25 - >16	1	>16	*2.0	1 - >16	8	16	7.1
P. apiosperma [en]	29	0.5 - >16	>16	>16	20.3	1 - 2	1	2	1.0	0.25 - >16	2	>16	*5.1	1.00 - >16	8	16	9.0
P. boydii [cl]	44	0.125 - >16	>16	>16	11.8	0.125 - 2	0.5	2	0.7	0.125 - >16	1	>16	1.5	0.50 - >16	8	16	5.8
P. boydii [en]	14	4.0 - >16	>16	>16	27.6	0.5 - 1	1	1	0.8	0.5 - 2	1	2	1.1	2 - 16	8	8	5.9

n[cl],number of strains from clinical specimens; n[en], number of strains from environmental samples; n[-]/unknown, number of unknown origin/source;*MIC/MEC distribution statistically significant difference (p ≤ 0.05);

P. apiosperma strains from clinical sources had statistically significant higher MEC values for MICA and significant lower values for POS.

No correlation with origin!

http://www.health-qna.com/

8

Summary

P. apiosperma and P. boydii

VRC*:	$MIC_{50} = 1$ µg/mL	$MIC_{90} = 2$ µg/mL (*P. boydii* 1 µg/mL)
POS:	$MIC_{50} = 1$ µg/mL	$MIC_{90} = 16$ µg/mL
MICA:	$MIC_{50} = 0.125$ **µg/mL**	$MIC_{90} = 4$ µg/mL

S. prolificans multi-resistant, single isolates susceptible against MICA, ANI.

S. aurantiacum only susceptible against VRC ($MIC_{50} = 0.5$ µg/mL; $MIC_{90} = 1$ µg/mL).

Only for VRC populations are normal distributed, POS resistant population, MICA divided population.

Cross resistances between azoles as well as echinocandins, no correlation between echinocandin and azole resistance

→ **combination therapy of VRC and MICA/POS and MICA.**

* VRC only registered drug for the treatment of
Scedosporium infections, all other drugs are off label use.

Acknowledgements

Cooperation partners
Jacques Meis (CWZ)
Corné Klaassen (CWZ
Sybren de Hoog (CBS)
Cornelia Lass-Flörl (HMM)
Paul E. Verweij (Radboud University)

Techical assistance
Erik Geertsen (CWZ)
MJ Najafzadeh (CBS)
Ilse Curfs-Breuker (CWZ)
Corina Bens (CWZ)