

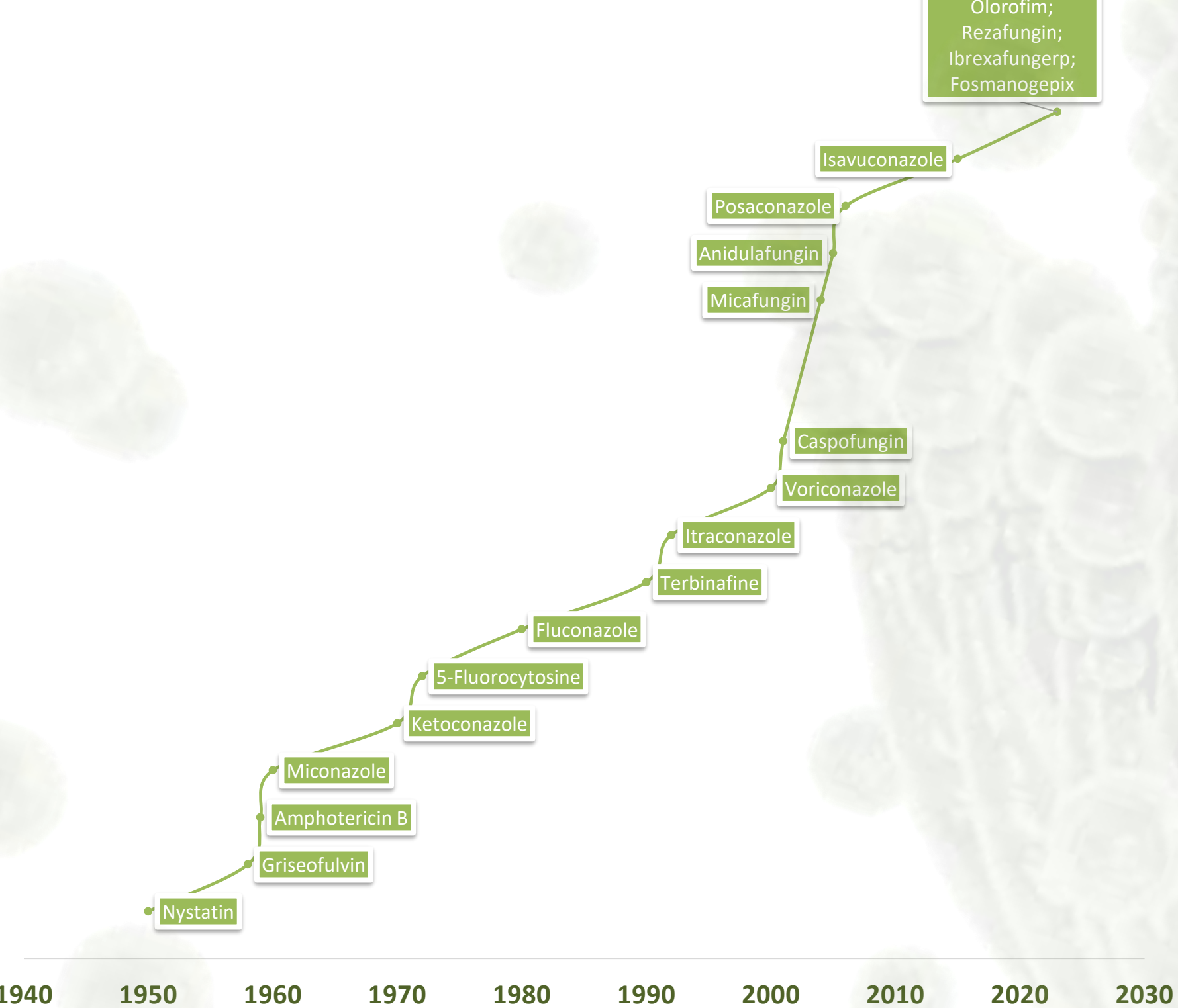


Introduction

Invasive fungal infections caused by cryptic *Aspergillus* species and *Lomentospora prolificans* pose a serious threat to immunocompromised patients, significantly complicating treatment due to intrinsic or acquired resistance to currently available antifungal agents. Of particular concern are *Aspergillus lentulus* and *Aspergillus fumigatiaffinis*, which are morphologically similar to *A. fumigatus* but exhibit distinct susceptibility profiles, often leading to suboptimal therapy. An even greater challenge is represented by *Lomentospora prolificans*, known for its multidrug resistance and high mortality associated with the infections it causes.

In this context, the search for new antifungal compounds with broad-spectrum activity and novel mechanisms of action is of critical importance. One promising candidate is SCY-247, an experimental antifungal agent for intravenous and oral administration, currently under investigation.

Chronology of Available Systemic Antifungal Agents



Methodology

Clinical Fungal Isolates

- Aspergillus spp.* (cryptic species)
- Lomentospora prolificans*

Susceptibility Testing Guidelines

- EUCAST E.Def 9.4
- CLSI M38-A2

Antifungal Agents

- SCY-247
- Amphotericin B
- Voriconazole
- Anidulafungin

Assessment Parameters

- MIC (for AMB, VCZ)
- MEC (for AND, SCY-247)
- Incubation: 35°C, 48 h

Calculations:

- MIC/MEC₅₀
- MIC/MEC₉₀
- Geometric mean
- Range of values

In vitro activity of SCY-247 and comparators against clinical isolates of *Aspergillus spp.* and *Lomentospora prolificans*

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Aim

This study aims to evaluate the **in vitro** activity of SCY-247 compared to amphotericin B, voriconazole, and anidulafungin against clinical isolates of cryptic *Aspergillus spp.* and *Lomentospora prolificans*, using standardized EUCAST and CLSI methodologies. The results aim to provide new data on the potential of SCY-247 as an alternative antifungal treatment for infections caused by resistant filamentous fungi.

Results

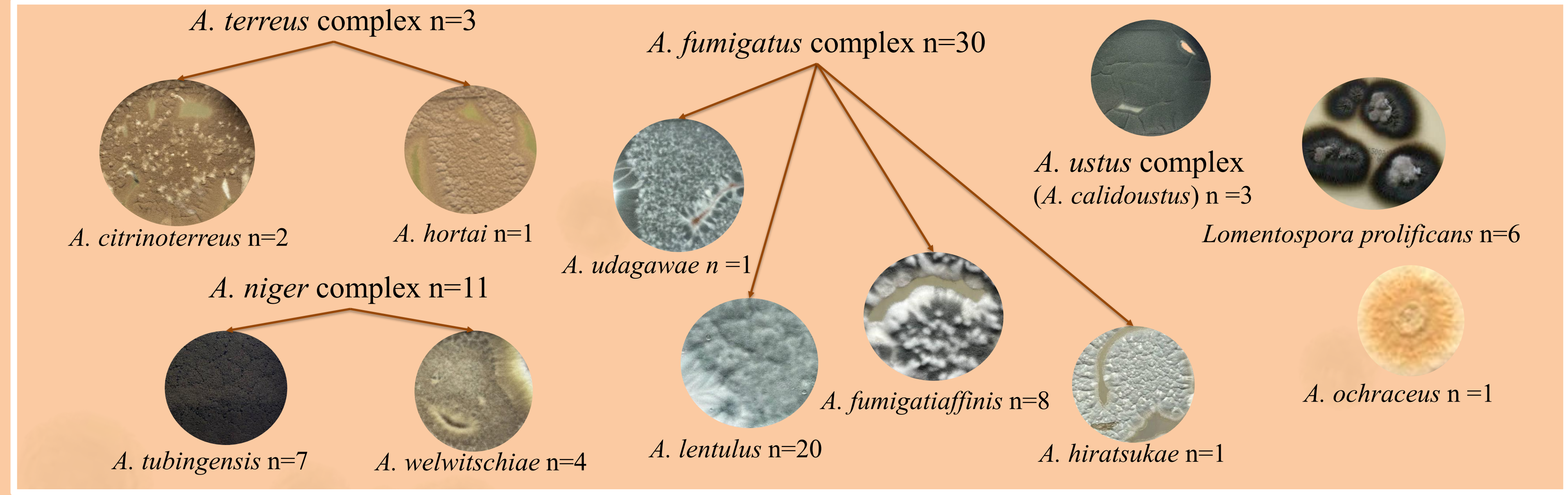


Figure 1. Number of complex, cryptic *Aspergillus* species and *Lomentospora prolificans* included in the study

Table 1 Geometric Mean (GM), MIC₅₀ (MIC that inhibits 50% of the isolates), MIC₉₀ (MIC that inhibits 90% of the isolates) and range for the antifungals tested to *Aspergillus spp.* and *Lomentospora prolificans*.

Species (N° isolates)		EUCAST				CLSI			
		AMB	VCZ	AND	SCY	AMB	VCZ	AND	SCY
<i>A. lentulus</i> (20)	GM	8	8	0.03	0.25	1	8	0.008	0.03
	MIC/MEC ₅₀	8	8	0.03	0.25	1	8	0.008	0.06
	MIC/MEC ₉₀	16	16	0.06	0.5	2	8	0.008	0.25
	RANGE	0.5 – 16	0.5 – 16	0.008 – 0.125	0.025 – 2	0.25 – 2	1 – 8	0.008 – 0.008	0.03 – 0.25
<i>A. fumigatiaffinis</i> (8)	GM	16	8	0.03	0.25	2	8	0.008	0.03
	MIC/MEC ₅₀	8	8	0,03	0,25	1	8	0,008	0,06
	MIC/MEC ₉₀	32	8	0.06	1	2	8	0.008	0.25
	RANGE	0.5 – 32	0.5 – 8	0.008 – 0.06	0.025 – 1	0.25 – 2	1 – 8	0.008 – 0.008	0.03 – 0.25
<i>A. tubingensis</i> (7)	GM	0.5	1	0.03	0.25	0.25	1	0.008	0.06
	MIC/MEC ₅₀	0.5	1	0.03	0.5	0.125	1	0.008	0.06
	MIC/MEC ₉₀	0.5	1	0.03	0.5	0.25	8	0.008	0.25
	RANGE	0.125 – 0.5	1 – 1	0.008 – 0.03	0.25 – 1	0.06 – 0.25	0.125 – 8	0.008 – 0.008	0.03 – 0.25
<i>Lomentospora prolificans</i> (6)	GM	32	16	8	4	16	16	8	4
	MIC/MEC ₅₀	32	16	8	4	16	16	8	4
	MIC/MEC ₉₀	32	16	8	8	32	16	8	8
	RANGE	4 – 32	16 – 16	0,03 – 8	1 – 8	4 – 32	16 – 16	4 – 8	2 – 8
<i>A. welwitschiae</i> (4)	GM	32	16	8	4	16	16	8	4
	MIC/MEC ₅₀	NA	NA	NA	NA	NA	NA	NA	NA
	MIC/MEC ₉₀	NA	NA	NA	NA	NA	NA	NA	NA
	RANGE	0.5	1	0.03	2	0.5	8	0.008	0.25
<i>A. calidoustus</i> (3)	GM	1	8	0.016	2	1	8	0.25	8
	MIC/MEC ₅₀	NA	NA	NA	NA	NA	NA	NA	NA
	MIC/MEC ₉₀	NA	NA	NA	NA	NA	NA	NA	NA
	RANGE	0.5 – 1	8 – 8	0.016 – 0.5	2 – 4	0.25 – 1	1 – 8	0.25 – 0.5	8 – 8
<i>A. citrinoterreus</i> (2)	GM	4	1	0.06	0.125	1	1	0.008	0.03
	MIC/MEC ₅₀	NA	NA	NA	NA	NA	NA	NA	NA
	MIC/MEC ₉₀	NA	NA	NA	NA	NA	NA	NA	NA
	RANGE	0.25 – 0.5	0.5 – 1	0.008 – 0.03	0.25 – 2	0.06 – 0.5	1 – 8	0.008 – 0.008	0.03 – 0.25

MICs/MECs are expressed in mg/L
NA: Not applicable. MIC₅₀ and MIC₉₀ were only calculated when more than five isolates were tested.

Conclusion

- SCY-247 exhibited low MECs against cryptic *Aspergillus species* using both EUCAST and CLSI methodologies.
- Aspergillus lentulus* and *Aspergillus fumigatiaffinis* showed high MICs to amphotericin B and voriconazole but lower MECs to anidulafungin and SCY-247.
- Lomentospora prolificans* demonstrated high MICs/MECs to all antifungals including SCY-247.

Logo



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Photo presenting author and the team

