Outcomes of Oral Ibrexafungerp in the Treatment of 18 Patients with *Candida auris* Infections, from the CARES Study

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RS Siebert[1], D Juneja[2], O Singh[2], B Tarai[2], C Ross[3], RC Reuben[3], J Breedt[4], N Yaddanapudi[5], M Conradie[6], F Mahmood[7], **S Sanchez[8]**, TR King[8], NE Azie[8], DA Angulo[8]

1. Life Groenkloof Hospital, Pretoria, South Africa 2. Max Super Specialty Hospital, New Delhi, India, 3. St. Johns Medical College Hospital, Bangalore, India, 4. Jakaranda Hospital, Pretoria, South Africa, 5. Postgraduate Institute of Medical Education and Research, Chandigarh, India, 6. Unitas Hospital, Gauteng, South Africa, 7. Aha Khan University Hospital, Karachi, Pakistan, 8. SCYNEXIS, Inc., Jersey City, NJ

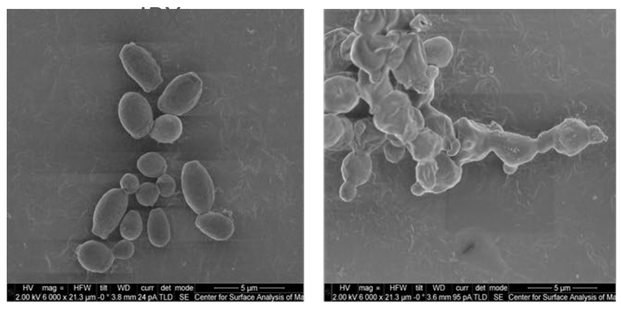
BACKGROUND

- *Candida auris* is a multi-drug resistant fungus associated with high mortality, has been implicated in healthcare setting outbreaks, and subsequently was added as an Urgent Threat Pathogen to the CDC Antimicrobial Resistance Threat Report 2019.
- Ibrexafungerp is an IV/oral, first-in-class triterpenoid, broad-spectrum fungicidal β-D-glucan synthase inhibitor (similar to the echinocandins).
- Ibrexafungerp has activity against *Candida*, *Aspergillus*, *Mucor*, *Pneumocystis* spp. and dimorphic fungi, including azole- and echinocandin-resistant strains.
- Ibrexafungerp also has high tissue penetration into organ and tissue compartments commonly associated with invasive fungal infections and is in development for life-threatening infections due to these pathogens.

Ibrexafungerp is fungicidal against *Candida* spp.

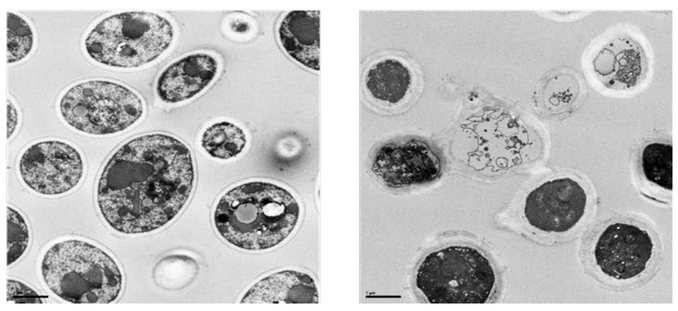
Scanning electron microscopy

Before IBX | After IBX



Transmission electron microscopy

Before IBX | After IBX



- Fungicidal action of ibrexafungerp (IBX) against cells of *Candida auris* (SEM and TEM images)
  - abnormalities in cell division (fused cells),
  - thickening of the cell wall with disappearance of the cell membrane,
  - leakage of cytoplasmic matrix, and
  - destruction of cytoplasmic organelles. (Images from Larkin, et al, AAC 2017.)

PATIENT CHARACTERISTICS/DEMOGRAPHICS

Baseline Fungal Disease	Number of patients	Mean Patient Age	% Female	Mean days on Ibrexafungerp
Candidemia	12	59	25	14
Lower Urinary Tract	5	62	60	27
Intra-abdominal	1	64	0	1
OVERALL	**18**	**60**	**33%**	**18**

- Of the 18 enrolled patients, 11 had received prior antifungal therapy for their infection, and 7 were treatment-naïve.

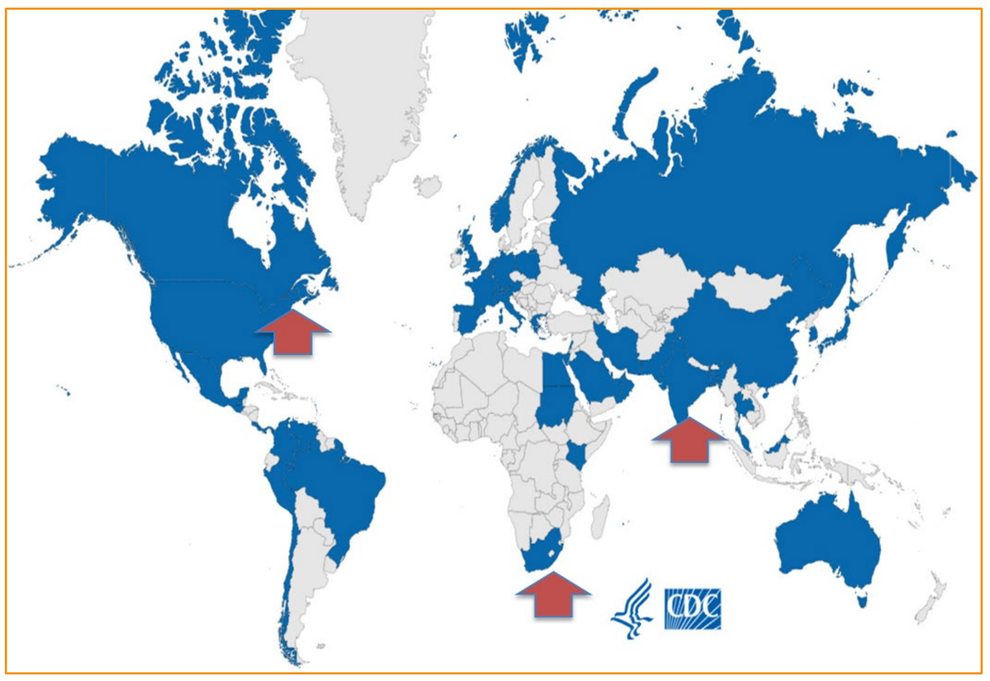
TREATMENT OUTCOMES

	(n=18 patients)
Complete or Partial Response	14
Stable Response	2
Disease Progression	0
Death	1
Indeterminate	1

TREATMENT OUTCOMES BY SITE OF DISEASE

	Candidemia	Lower Urinary	Intraabdominal
Complete or Partial Response (n=14)	8	5	1
Stable Response (n=2)	2	0	0
Disease Progression	0	0	0
Death (n=1)	1	0	0
Indeterminate (n=1)	1	0	0

CARES Patient Locations



CARES METHODS

- CARES is currently in recruitment (for this cohort, see patient locations in map above).
- Eligible patients have a documented *Candida auris* infection and receive a loading dose of oral ibrexafungerp 750 mg BID the first 2 days, then subsequent oral ibrexafungerp 750 mg QD up to 90 days and are followed for 6-weeks post-therapy.
- An independent Data Review Committee (DRC) provided an assessment of treatment response for 18 patients who enrolled and completed therapy by October 2021.
- Outcome data from DRC assessments are reported here.

RESULTS SUMMARY

- As of the latest interim data analysis (October 2021), CARES has enrolled 18 patients from areas where *Candida auris* outbreaks have occurred: South Africa, South Asia, and North America.
- Eighteen patients (mean age 58.3 years, 11 males and 7 females) were determined to have invasive candidiasis (n=6) or candidemia (n=12) due to *Candida auris*.
- Of the 18 patients treated with oral ibrexafungerp, 14 (78%) showed complete or partial response, 2 (11%) had stable disease, 1 died of other causes, and 1 outcome was indeterminate.
- Ibrexafungerp median duration of therapy was 18 days.
- The most frequent treatment-related adverse event were gastrointestinal in nature including diarrhea, nausea and abdominal pain.

CONCLUSION

- These cases provide continued evidence of the potential clinical utility of ibrexafungerp in the treatment of invasive candidiasis and candidemia caused by *Candida auris*.