Outcomes of Oral Ibrexafungerp by Pathogen from Two Open-label Studies of Patients with Serious Fungal Infections (FURI and CARES)

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OBJECTIVES

- *Candida* and *Aspergillus* infections resistant to currently available antifungals are an emerging global threat.
- Ibrexafungerp is an investigational broad-spectrum glucan synthase inhibitor antifungal with activity against *Candida* and *Aspergillus* species, including azole- and echinocandin-resistant strains.
- Two ongoing Phase 3 open-label, single-arm studies of oral ibrexafungerp for the treatment of patients (>18 years) are underway:
- FURI (Clinicaltrials.gov NCT03059992) with fungal diseases that are refractory to or intolerant of standard antifungal therapies, and
- CARES (Clinicaltrials.gov NCT03363841) for adult patients with *Candida auris* infections.

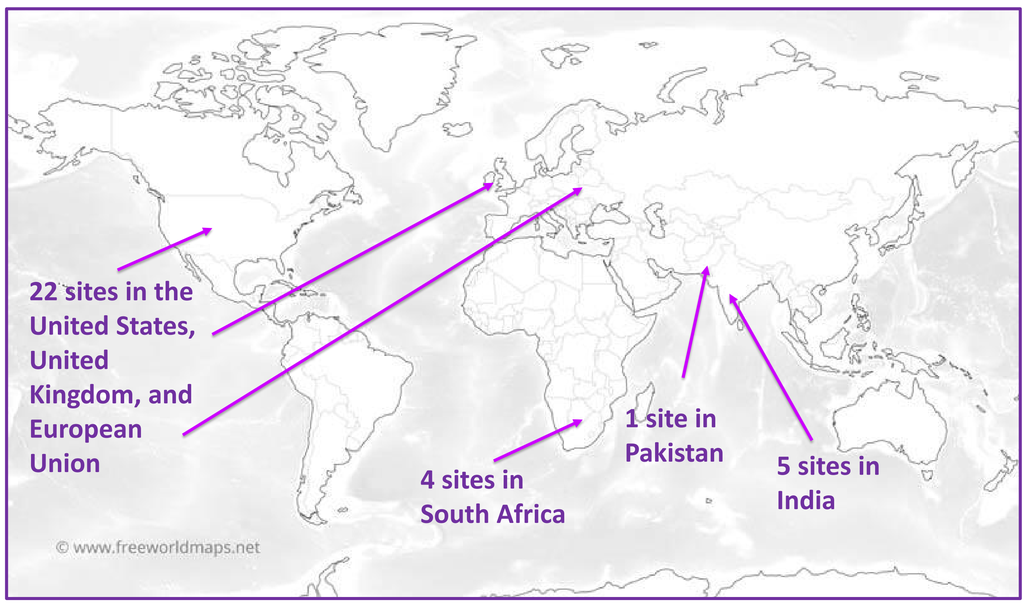
METHODS

- FURI subjects were eligible for enrollment if they had proven or probable:
  - severe mucocutaneous candidiasis,
  - invasive candidiasis,
  - invasive aspergillosis, or other fungal diseases
- Evidence of treatment failure, intolerance, or toxicity related to a currently approved standard-of-care antifungal treatment was required, or
- If patients were unable to receive an approved oral antifungal option (e.g., susceptibility of the organism) and a continued IV antifungal therapy was clinically undesirable or unfeasible.
- CARES patients were eligible for enrollment if they had proven or probable *Candida auris* infection.

RESULTS

- There were 74 patients enrolled in the FURI study from 22 centers in US, UK and EU. An additional 10 patients were enrolled in the CARES study from 4 centers in South Africa, Pakistan, and India for a total of 84 ibrexafungerp-treated patients.
- All enrolled patients were treated with ibrexafungerp for invasive and severe mucocutaneous fungal infections.
- In the two studies, the predominant fungal disease diagnoses at baseline included:
  - candidemia,
  - intra-abdominal candidiasis,
  - bone/joint candidiasis,
  - oropharyngeal candidiasis,
  - esophageal candidiasis,
  - vulvovaginal candidiasis,
  - other *Candida* infections,
  - and invasive pulmonary aspergillosis.
- Combining outcomes from the two studies, the percent of patients who were determined to have:
  - a complete response (CR), partial response (PR) and clinical improvement (CI) was 64.3%;
  - stable disease (SD) was 21.4%;
  - patients with progression of disease 6.0%;
  - and 4 patients were indeterminate.
- Additionally, there was 1 death in the CARES study; 1 patient with a pathogen not identified and 1 death in the FURI study. The deaths were determined to be not related to fungal disease.

GLOBAL STUDY SITES



RESPONSE TO TREATMENT

	FURI n=74 (%)	CARES n=10 (%)	Aggregate (FURI+CARES) n=84 (%)
Complete, Partial Response or Clinical Improvement	46 (62.1)	8 (80.0)	54 (64.3)
Stable Disease	18 (24.3)	0 (0.0)	18 (21.4)
Progression of Disease or No Clinical Improvement	5 (6.8)	0 (0.0)	5 (6.0)
Death While on Tx*	1 (1.4)	1 (10.0)	2 (2.4)
Unable to Determine	4 (5.4)	1 (10.0)	5 (6.0)

*Deaths due to underlying condition and deemed unrelated to study drug or fungal disease

BASELINE FUNGAL DISEASE

	Baseline Fungal Disease	Number of patients n=84 (%)
Invasive Candidiasis (58.3%)	Candidemia	18 (21.4)
	Intra-abdominal infections	13 (15.5)
	Bone / Joint infection	8 (9.5)
	Urinary tract infection	3 (3.6)
	Subcutaneous wound infection	2 (2.4)
	Chronic disseminated candidiasis	2 (2.4)
	Mediastinitis (1), empyema (1), endocarditis (1)	3 (3.6)
Mucocutaneous Candidiasis (38.1%)	Oropharyngeal candidiasis	14 (16.7)
	Esophageal candidiasis	10 (11.9)
	Vulvovaginal candidiasis	7 (8.3)
	Chronic mucocutaneous candidiasis-skin	1 (1.2)
Aspergillosis (3.6%)	Invasive pulmonary infection	3 (3.6)

- Baseline disease diagnosis at baseline for both the FURI and CARES studies. Ten patients from CARES were diagnosed with candidemia (7), urinary tract infections (2) and intra-abdominal infection (1) are included in the table.

RESPONSE BY PATHOGEN

	Positive Response* N (%)	Stable Response N (%)	Progression of Disease N (%)	Indeterminate N (%)	Death N(%)
C. auris (10)	8 (80)			1 (10)	1 (10)
C. glabrata (26)	18 (69.2)	4 (16)	2 (8)	1 (4)	1 (4)
C. albicans (24)	17 (70.8)	5 (20.8)		2 (8.3)	
C. krusei (6)	2 (33.3)	3 (50)		1 (16.7)	
C. parapsilosis (4)	3 (75)	1 (25)			
C. tropicalis (1)	1 (100)				
C. glabrata/C. albicans (5)	2 (40)	1 (20)	2 (40)		
C. glabrata/C. dubliniensis (2)		1 (50)	1 (50)		
C. glabrata/C. tropicalis (1)	1 (100)				
C. albicans / C. tropicalis (1)		1 (100)			
Aspergillus spp (3)	2 (66.7)	1 (33.3)			

- "Positive Response" denotes Complete or Partial Response or Clinical Improvement.

RESPONSE BY DISEASE

	Positive Response* N (%)	Stable Response N (%)	Progression of Disease N (%)	Indeterminate N (%)	Death N(%)
Invasive Candidiasis (n=49)	25	7	3	3	1
Mucocutaneous Candidiasis (n=32)	20	9	1	1	0
Aspergillosis (n=3)	2	1	0	0	0

- "Positive Response" denotes Complete or Partial Response or Clinical Improvement.

CONCLUSION

- Preliminary analysis of these 84 cases from the FURI and CARES studies indicate that oral ibrexafungerp provides a favorable and similar therapeutic response in patients with fungal infections caused by Candida, regardless of species.

For additional information, contact info@scynexis.com