Outcomes of Oral Ibrexafungerp in Refractory Patients with *Candida* from an Interim Analysis of a Phase 3 Open-Label Study (FURI)

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BACKGROUND

- There are limited oral treatment options available for patients with fungal infections who fail currently available antifungals or who have an infection caused by resistant organisms.
- Ibrexafungerp (IBX) is an investigational broad-spectrum glucan synthase inhibitor antifungal with activity against *Candida* and *Aspergillus* species, including azole- and echinocandin-resistant strains.
- A Phase 3, open-label, single-arm study of ibrexafungerp (FURI; NCT3059992) is ongoing for the treatment of patients who are intolerant of or who have fungal disease refractory to standard antifungal therapy.
- FURI subjects were eligible for enrollment if: they had proven or probable:
  - severe mucocutaneous candidiasis, invasive candidiasis, invasive aspergillosis, or other fungal diseases, or
  - 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.
- **We present a subset of patients with *Candida* infections from the FURI study who were refractory to therapy as determined by the investigator.**

FURI DESIGN

VVC Evaluation

Baseline- Day 1, Day 4
End of Treatment- Day 7

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Test-of-Cure (ToC) Visit
Day 17

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Follow-Up Visit
Day 32

- Enrolled subjects were evaluated annually by an independent Data Review Committee (DRC) each year.
- VVC Subjects were evaluated for **Clinical Improvement (resolution of signs and symptoms (total VSS score ≤1)** without the need for additional antifungal, at Test of Cure (ToC) visit on study Day 17 (EoT +10 days).
- VVC and non-VVC Case outcomes were evaluated for **Complete or Partial Response, Stable Response, or Progression.**

Non-VVC Evaluation

Ibrexafungerp Loading Dose
Baseline: Day 1 and Day 2

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Ibrexafungerp Maintenance Dosing
Daily from Day 3 to EOT
(up to 180 Days)

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End of Treatment
(Final dose of IBX)
180 Days

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6 Week Follow-Up
(6 Weeks After EOT)

- Subjects were continually monitored for safety throughout their participation in FURI.
- **Stable Response (recorded in one VVC patient and 16 non-VVC patients)** was defined as **survival and minor/no improvement in fungal disease, but no evidence of progression.**

RESULTS

- There were 113 patients enrolled in the FURI study from 2016-2021 from centers in US, UK and EU.
- Of those 113, 64 subjects were enrolled with fungal disease that was considered refractory to standard of care antifungal therapy.
- The mean age of enrolled participants in FURI who had refractory *Candida* infection was 54.9 years.
- Sex: 40 subjects were female; 24 were male.
- The mean duration of treatment on ibrexafungerp for this population was 45.2 days at the time of data analysis.

Baseline Fungal Disease, number of cases	Clinical Improvement (VSS Score ≤1 at EoT)	Stable Response	No Clinical Improvement (VSS >1 at EoT)	Indeterminate
Vulvovaginal Candidiasis (VVC), n=14	10 (71%)	1 (7%)	2 (14%)	1 (7%)
	Complete/Partial Response	**Stable Response**	**Disease Progression**	**Indeterminate**
Esophageal/Oropharyngeal, n=26*	13 (50%)	9 (35%)	3 (16%)	1* (4%)
Intraabdominal, n=10	6 (60%)	4 (40%)	0	0
Bone, n=4	2 (50%)	1 (25%)	0	1 (25%)
Disseminated Candidiasis, n=3	1 (33%)	1 (33%)	0	1 (33%)
Bladder, n=2	2 (100%)	0	0	0
Candidemia, n=2	1 (50%)	0	0	1 (50%)
Paraspinal abscess, n=1	0	0	1 (100%)	0
Paronychia, n=1	0	1 (100%)	0	0
Wound, unspecified, n=1	1 (100%)	0	0	0
Total (n=64)*	**36 (56%)**	**17 (27%)**	**6 (9%)**	**5 (8%)**

*Includes one death due to underlying disease.

Predominant organism isolated	Clinical Improvement* or Complete/Partial Response	Stable Response	No Clinical Improvement* or Progression	Indeterminate
***C. albicans* (n=32)**	19 (59%)	7 (22%)	4 (13%)	2 (6%)
***C. glabrata* (n=19)#**	10 (53%)	6 (60%)	1 (5%)	2 (11%)#
***C. krusei* (n=6)**	2 (33%)	2 (33%)	1 (17%)	1 (17%)
***Candida* spp (n=4)**	2 (50%)	2 (100%)	0	0
***C. parapsilosis* (n=2)**	2 (100%)	0	0	0
***C. tropicalis* (n=1)**	1 (100%)	0	0	0
Total (n=64)#	**36 (56%)**	**17 (27%)**	**6 (9%)**	**5 (8%)**

*Clinical Improvement for VVC cases only (resolution of signs and symptoms [total VSS score ≤1]).
#Includes one death due to underlying disease.

- For VVC, 71% pf patients had clinical improvement.
- For non-VVC, 56% had positive clinical response.
- The organisms isolated in patients in the Candidemia category were *C. parapsilosis* and *C. albicans.*
- Adverse events were consistent with those associated with IBX and were primarily gastrointestinal in nature.

CONCLUSIONS

Analysis of refractory patients from the FURI study indicates that oral ibrexafungerp provides a favorable therapeutic response in patients who have failed other therapies with difficult to treat fungal infections.

For additional information contact SCYNEXIS at info@scynexis.com