

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.

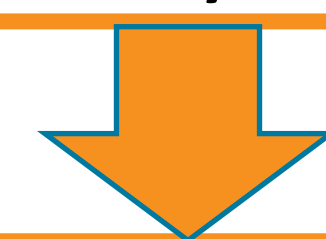
FURI DESIGN

VVC Evaluation

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



Test-of-Cure (ToC) Visit
Day 17

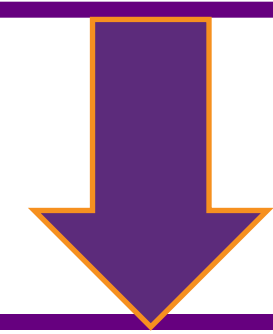


Follow-Up Visit
Day 32

- 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



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



End of Treatment
(Final dose of IBX)
180 Days



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
<i>C. albicans</i> (n=32)	19 (59%)	7 (22%)	4 (13%)	2 (6%)
<i>C. glabrata</i> (n=19) [#]	10 (53%)	6 (60%)	1 (5%)	2 (11%) [#]
<i>C. krusei</i> (n=6)	2 (33%)	2 (33%)	1 (17%)	1 (17%)
<i>Candida</i> spp (n=4)	2 (50%)	2 (100%)	0	0
<i>C. parapsilosis</i> (n=2)	2 (100%)	0	0	0
<i>C. tropicalis</i> (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.