Oral Ibrexafungerp Outcomes by Fungal Disease in Patients from an Interim Analysis of a Phase 3 Open-label Study (FURI)

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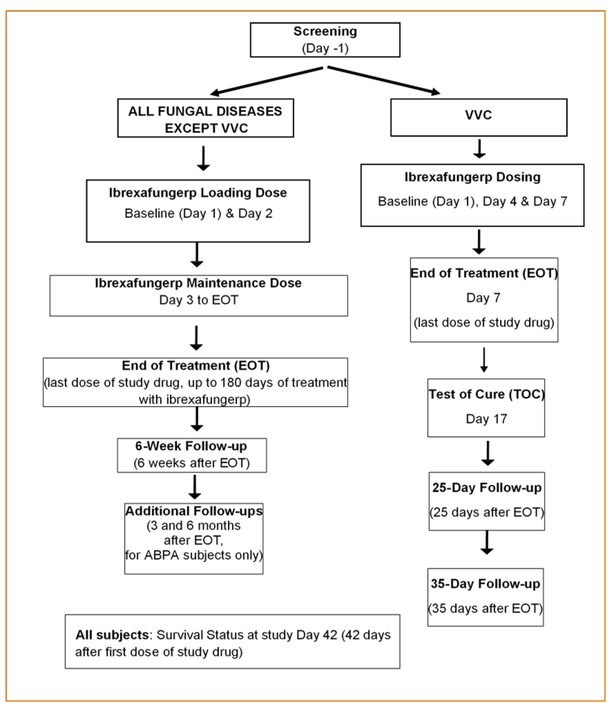
BACKGROUND

- 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 is an investigational broad-spectrum orally-dosed 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; NCT03059992) is ongoing for the treatment of patients who were intolerant of, or with fungal disease refractory to standard antifungal therapy.

METHODS

- FURI subjects from global sites were eligible for enrollment if they had proven or probable refractory or intolerance to standard treatment:
  - mucocutaneous candidiasis,
  - invasive candidiasis,
  - invasive aspergillosis, or other fungal diseases.
- The data reported here are from patients who completed therapy by October 2021 and who had received an assessment by the Data Review Committee (DRC).
- The FURI study design is summarized in Figure 1 (below).
- Enrolled patients received oral ibrexafungerp 750 mg BID for 2 days, followed by oral ibrexafungerp 750 mg QD
- Up to 180 days of treatment were permitted
- All patients were assessed annually by a Data Review Committee (DRC) comprising 3 infectious disease experts
- DRC assessment included clinical, microbiological response, and global response per MSG/EORTC 2008 criteria
- End of treatment (EoT) was occurred at Day 180 after start of treatment.



- This interim report provides data on the FURI Study Cohorts 1-4, who had a DRC assessment before October 2021.
- Subjects (N=113) in Cohorts 1 through 4 were enrolled in FURI from 27 centers located in North America, Europe, Africa, and Asia.
- The focus of this report is on all-cause mortality through 30 days post end of treatment for patients who entered FURI with a diagnosis of candidemia or invasive candidiasis.
- Baseline fungal diseases are summarized by categories and specific diseases in **Table 1**.

Table 1. Baseline Fungal Disease

Category	Baseline Fungal Disease	Number of patients n=113 (%)
Invasive Candidiasis and Candidemia n=56 (49.6%)	Intra-abdominal infections	41 (36.3)
	Candidemia	15 (13.2)
Mucocutaneous Candidiasis n=46 (40.7%)	Non-vulvovaginal cases	32 (28.3)
	Vulvovaginal cases	14 (12.4)
Aspergillosis n=11 (9.7%)	Invasive pulmonary aspergillosis	10 (8.8%)
	Chronic pulmonary aspergillosis	1 (0.8%)

CLINICAL OUTCOMES

- Of the 113 patients treated with ibrexafungerp for various fungal infections:
  - 94 (83.2%) enrolled with disease refractory to antifungal therapy; and
  - 12 (10.6%) due to intolerance or toxicity to prior antifungal therapy
  - 7 (6.2%) enrolled due to continued IV antifungal therapy undesirable/unfeasible
- For invasive candidiasis and candidemia, 35/56 (62.5%) subjects had a complete or partial clinical response; 13 (23.2%) had stable disease, 4 (7.1%) showed disease progression, and 4 were indeterminate.
- For mucocutaneous candidiasis, 17/32 (53%) subjects had complete or partial response, 11 (34.3%) had stable disease, 3 (9.4%) were indeterminate, and one death occurred due to underlying disease.
- For vulvovaginal candidiasis, 10/14 (71.4%) showed clinical improvement, 1 (7.1%) had stable disease, and 2 (14.3%) did not show clinical improvement.
- For chronic and invasive pulmonary aspergillosis, 4/11 patients had complete response, 2 had stable disease, 4 had progression of disease, and 1 outcome was indeterminate.
- Most patients had *Candida glabrata* and *Candida albicans*, other organisms implicated in fungal disease from FURI included *Candida krusei, Candida tropicalis,* and *Aspergillus fumigatus*.
- Outcomes by fungal isolate are listed in **Table 2**.

Table 2. Outcomes by Fungal Isolates

Baseline Fungal Pathogen Isolated	Complete Response or Clinical Improvement	Stable Response	Disease Progression/ no Clinical Improvement	Indeterminate	Death
Candida glabrata **(n=34)**	24	7	1	1	1
Candida albicans **(n=32)**	20	6	4	2	0
Candida krusei **(n=7)**	2	3	1	1	0
Candida **spp (NOS) (n=4)**	3	1	0	0	0
Candida parapsilosis **(n=5)**	3	1	1	0	0
Candida metapsilosis **(n=1)**	0	0	0	1	0
Candida tropicalis **(n=1)**	1	0	0	0	0
Candida albicans/glabrata **(n=7)**	2	4	1	0	0
Candida albicans/tropicalis **(n=3)**	3	0	0	0	0
Candida glabrata/tropicalis **(n=1)**	1	0	0	0	0
Candida glabrata/krusei **(n=1)**	1	0	0	0	0
Candida glabrata/dubliniensis **(n=1)**	0	0	1	0	0
Positive 1,3-ß-D-glucan test (n=3)	0	3	0	0	0
Yeast identified by no ID (n=2)	2	0	0	0	0
Candida **totals (n=102)**	**62 (60.7%)**	**25 (24.5%)**	**9 (8.8%)**	**5 (4.9%)**	**1**
Aspergillus fumigatus **(n=6)**	2	1	3	0	0
Aspergillus **spp (NOS) (n=2)**	1	1	0	0	0
Positive galactomannan (n=3)	1	0	1	1	0
Totals (n=113)	**66 (58.4%)**	**27 (23.9%)**	**13 (11.5%)**	**6 (5.3%)**	**1**

EFFICACY SUMMARY

- Of the 113 patients treated with ibrexafungerp for various fungal infections:
  - The predominant organisms isolated were *Candida albicans* and *Candida glabrata* alone or with another species of *Candida*
  - Most patients had complete or partial response, or clinical improvement (66/113 or 58.4%).
  - Smaller percentages showed stable disease (23.9%) or disease progression or no complete response (11.5%).
- The majority of patients with infections with *Candida glabrata* or *Candida albicans* had a positive response to treatment with ibrexafungerp.
- Results of patients with chronic or invasive pulmonary aspergillosis were mixed, with 4/11 patients showing complete response, 2 stable disease, and 4 with disease progression (and one indeterminate).
- There was a single death in the study not attributed to ibrexafungerp.

CONCLUSIONS

- This is an ongoing study.
- In this population with difficult to treat fungal infections with limited treatment options, ibrexafungerp treatment led to favorable responses in 58% of patients.
- Treatment responses to ibrexafungerp in patients with *Candida albicans* or *Candida glabrata* were generally positive.
- Ibrexafungerp is a promising oral antifungal agent for *Candida* infections.