All-Cause Mortality in Patients with Invasive Candidiasis or Candidemia from an Interim Analysis of a Phase 3 Ibrexafungerp Open-label Study (FURI)

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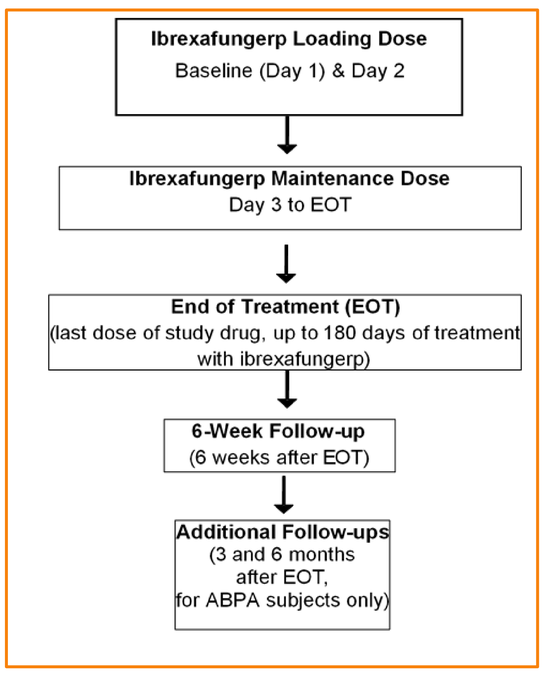
BACKGROUND

- 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 had candidiasis or invasive candidemia and 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.



- 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 the 56 patients who entered FURI with a diagnosis of candidemia (n=15/113) or invasive candidiasis (n=41/113).
- Fungal diseases (invasive candidiasis and candidemia) are summarized in **Table 1**.

Table 1. Baseline Fungal Disease

Disease description	Number of patients
Candidemia	15 (26.8%)
Invasive Candidiasis	41 (73.2%)
Intra-abdominal infection	13
Bone: spondylodiscitis, articular knee, tibia, zygomatic arch, NOS	10
Hepatosplenic	3
Mediastinum	3
Disseminated	3
Bladder	2
Wound, not otherwise specified	2
AV fistula	1
Pancreas	1
Paraspinal abscess	1
Empyema/Pleural	1
Endocarditis	1
TOTAL Candidemia and Invasive Candidiasis	**56**

RESULTS

Clinical Outcomes	Invasive Candidiasis n=41	Candidemia n=15	Totals N=56
Complete or Partial Response	22	13	35 (62.5%)
Stable Disease	12	1	13 (23.2%)
Progression of Disease	4	0	4 (7.1%)
Indeterminate	3	1	4 (6.7%)
Deaths Within 30 days Post-treatment With Ibrexafungerp	**2/41**	**1/15**	**3/56**
Survival	**39/41 (95.1%)**	**14/15 (93.3%)**	**53/56 (94.6%)**

- Most patients had isolated *Candida glabrata* and *Candida albicans*, *Candida krusei, Candida tropicalis,* and *Candida parapsilosis*.
- Overall survival within 30 days after completion of treatment with ibrexafungerp in this population of patients with a baseline fungal disease diagnosis of invasive candidemia or candidiasis was 94.6% (3 deaths out of 56 treated patients). Three additional patients died 31, 50, and 56 days after completion of therapy, respectively.
- The mean time on treatment with ibrexafungerp for these patients was 15.7 days.
- The mean time to death post-treatment in this group of patients was 27 days (median 21 days).
- In 5 of 6 deceased patients, their deaths were determined by the investigator to be not related to the underlying fungal disease. For the remaining case, the cause was not disclosed.

FUNGAL ISOLATES FROM DECEASED PATIENTS

Fungal Disease (source)	Previous Treatments	Organism Isolated	Susceptibility Testing (µg/mL)	Days on IBX	Day Elapsed from IBX EoT to Death
Intra-abdominal (fluid) Hepatic abscess	Oral fluconazole, micafungin	*C glabrata*	Amphotericin B = 1; Fluconazole = 4; Micafungin ≤ 0.25; Posaconazole = 0.03; Ibrexafungerp = 1; Voriconazole = 0.03	45	21
Intra-abdominal (fluid) Hepatic abscess	Micafungin, fluconazole, ampho B, flucytosine	*C glabrata*	Amphotericin B = 2; Fluconazole = 2; Micafungin = 0.12; Posaconazole = 0.12; Ibrexafungerp = 0.5; Voriconazole = 0.016	4	1
Candidemia (blood)	IV Micafungin	*C glabrata*	Amphotericin B = 2; Fluconazole = 2; Micafungin ≤ 0.016; Posaconazole = 0.06; Ibrexafungerp = 0.5; Voriconazole = 0.016	7	1
Candidemia (blood)	Oral Fluconazole, IV fluconazole, posaconazole	*C parapsilosis*	Amphotericin B = 0.5; Fluconazole = 0.25; Micafungin = 0.5; Posaconazole ≤ .008; Ibrexafungerp = 0.25; Voriconazole ≤ .016	8	31
Candidemia (blood)	IV micafungin, IV fluconazole	*C parapsilosis*	Amphotericin B = 1.0; Fluconazole = 2.0; Micafungin = 1.0; Posaconazole ≤ .016; Ibrexafungerp = 0.25; Voriconazole = .06	10	50
Candidemia (blood)	Micafungin	*C parapsilosis*	Not available	19	56

- Results of antifungal susceptibility testing showed a broad range of MICs in these isolates. For ibrexafungerp, MICs measured in two isolates of *Candida parapsilosis* were 0.25 µg/mL; ibrexafungerp MICs for 3 isolates of *Candida glabrata* were 0.5 µg/mL, 0.5 µg/mL, and 1.0 µg/mL.

CONCLUSIONS

- This is an ongoing study.
- In this population with difficult to treat fungal infections with limited treatment options, overall survival at 30 days after treatment with ibrexafungerp was 94%.
- Treatment responses to ibrexafungerp in patients with *Candida albicans* or *Candida glabrata* were generally positive.