P402

Successful Treatment of a Patient with Retroperitoneal Abscess caused by *Candida krusei* with the Investigational Agent, Ibrexafungerp (formerly SCY-078): A Case Report from the FURI Study

George R. Thompson III[1], David Angulo[2],

[1]University of California, Davis Medical Center, [2]SCYNEXIS, Inc. USA

BACKGROUND

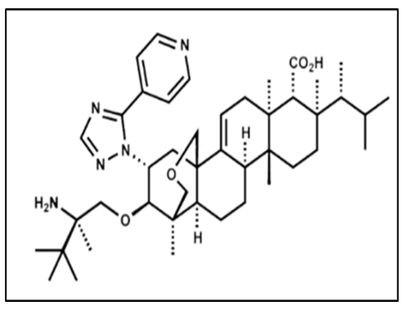


Figure 1. Ibrexafungerp, a novel triterpenoid

Intraabdominal candidiasis is the second most common *Candida* infection after candidemia. *Candida albicans* is the predominant cause of these infections, with non-*albicans Candida* becoming more frequently observed in this clinical setting. Echinocandins are the recommended treatment for intraabdominal *Candida* infections but have varied clinical response. This is postulated to be based on poor drug levels in tissue and abscesses. Ibrexafungerp (formerly SCY-078),(Figure 1) is a novel IV/oral glucan synthase inhibitor (triterpenoid) antifungal with activity against *Candida*, *Aspergillus* and *Pneumocystis.* Perlin et al., presented data (ASM Microbe 2019) on an intraabdominal infection mouse model comparing ibrexafungerp (IBX) versus micafungin (MFG). Ibrexafungerp penetrated into and accumulated within intra-abdominal abscesses highly efficiently, resulting in superior drug levels and antifungal efficacy compared to micafungin (Figure 2).[1] This data is supportive of additional research in the treatment of intraabdominal infections caused by *Candida* spp.

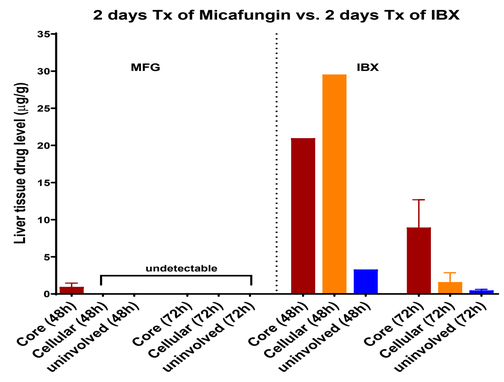


Figure 2: Drug accumulation comparison in infected liver compartments between repeated doses of MFG and IBX. Drug concentration was measured in lesions (necrotic core, cellular rim) and uninvolved areas dissected from liver sections collected at 48 and 72h after the last dose of two days treatment of MFG (IP) at 5mg/kg q.d. or IBX (PO) at 15mg/kg b.i.d.

A Phase 3 open-label, single-arm study of oral ibrexafungerp (FURI; NCT03059992) is ongoing for the treatment of patients intolerant of or with fungal disease refractory to standard antifungal therapy. An interim analysis of 20 patients from the FURI study was performed in late 2018. Of the 20 patients there were 5 patients with intraabdominal candidiasis infections. We present a patient case of retroperitoneal abscess caused by *Candida krusei* from the ongoing FURI study.

METHODS

SCYNEXIS initiated an open-label study to evaluate the efficacy and safety of oral ibrexafungerp in patients with invasive fungal infections that are refractory to or intolerant of standard antifungal treatment (FURI) (Clinicaltrials.gov NCT03059992), including mucocutaneous and invasive candidiasis. The primary objective of the FURI study is to evaluate the efficacy of oral ibrexafungerp as determined by a Data Monitoring Committee (DMC) by assessing Global Success (composite assessment of clinical, microbiological, serological and/or radiological responses) at End of Treatment (EoT) and to evaluate the safety of oral ibrexafungerp. Patients are eligible for enrollment if they have acute or chronic invasive candidiasis including candidemia and/or acute or chronic severe mucocutaneous candidiasis that is refractory to or intolerant of, or has toxicities associated with at least one approved standard of care (SoC) antifungal treatment and/or long -term IV antifungal therapy is not feasible or desirable due to clinical or logistical circumstances or if other oral antifungal alternatives are not appropriate. Patients were allowed treatment with ibrexafungerp for 90 days. We present a patient with intra-abdominal candidiasis who was successfully treated with ibrexafungerp.

A 71 year old white male with ischemic stroke, pulmonary edema, and tracheostomy was being treated for a retroperitoneal abscess, a complication of a perforated duodenal ulcer. *Candida krusei* was isolated in peri-duodenal aspirate of the abscess and the patient was initiated on micafungin therapy for 21 days. During micafungin therapy, cultures from the peri-duodenal drain on three occasions remained positive for *Candida krusei* despite a micafungin MIC of 0.25 µg/mL and placement of a drain. The patient underwent additional drain placement and was enrolled into the FURI study due to micafungin treatment failure and was treated with oral ibrexafungerp 750mg BID for two days followed by 750mg daily.

RESULTS

The patient was treated with oral ibrexafungerp therapy for 21 days and improvement was observed during therapy. Following the initiation of ibrexafungerp the patient rapidly defervesced over the following three days, his symptoms of malaise and fever resolved, and radiographic improvement was noted over the next 11 days. Radiographic improvement as indicated in figures 3, 4 and 5, showed continued improvement during therapy with ibrexafungerp and resolution of the fluid collection on day 15. At End of Treatment visit, the clinical signs and symptoms of fungal disease were considered by the investigator to be resolved and the physical exam noted minimal discharge from the patient's retroperitoneal drain. As of the 6-week follow-up visit, clinical signs and symptoms of infection were still resolved and the drain was no longer in place. No drug-related adverse events were reported.

Figure 3: CT Scan: -Day 0

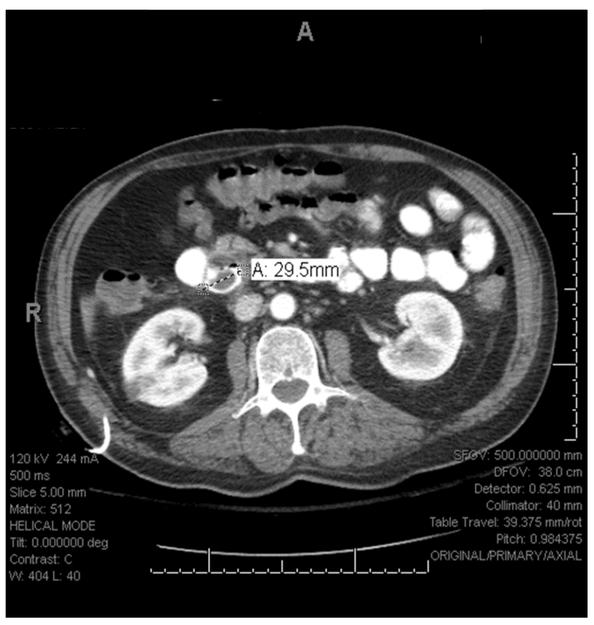


Figure 4: CT Scan: -Day 11

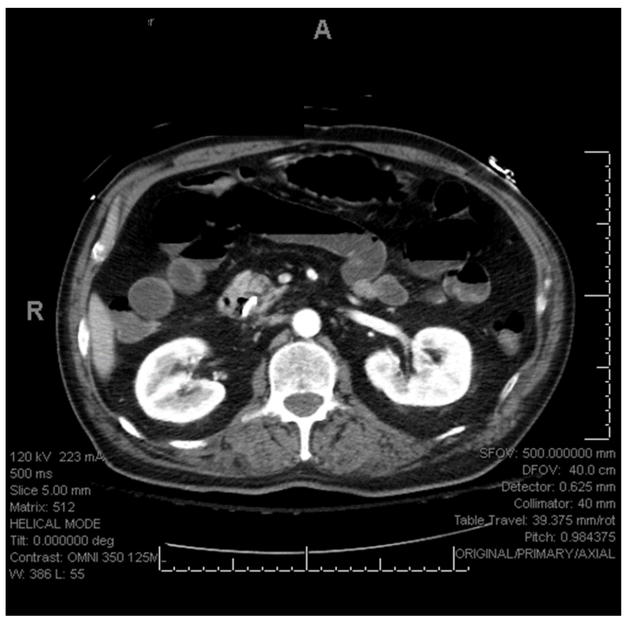
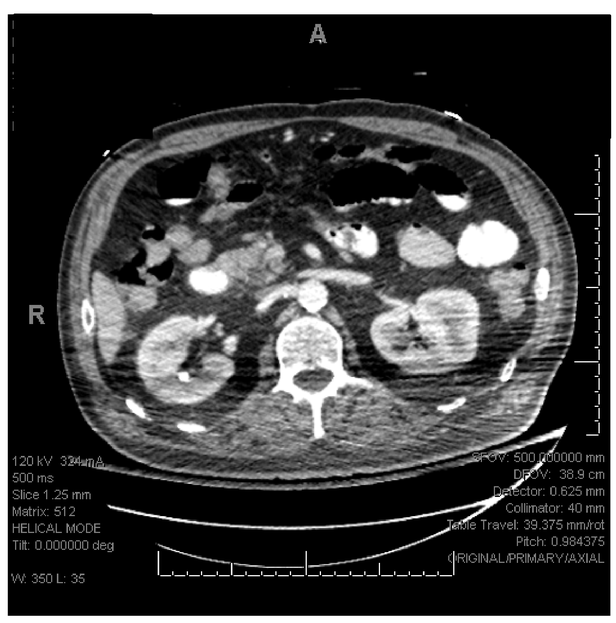


Figure 5: CT Scan: -Day 15



FURI Study Outcomes

An independent Data Monitoring Committee (DMC) provided an assessment of treatment response for 20 patients who completed therapy in the FURI study at the end of 2018. Patients were enrolled in 14 centers from 4 countries. Of the 20 patients assessed, 5 patients enrolled had intraabdominal candidiasis. The global outcome for the 20 patients, along with 5 patients intraabdominal candidiasis, analyzed in the FURI study by the DMC is shown below (Table 1.)

Table 1: FURI Study- Global outcome for the 20 patient analysis, including 5 patients with intraabdominal candidiasis

	Complete/Partial Response	Stable Disease	Progression of Disease	Indeterminate
All Patients (20)	11 (55%)	6 (30%)	2 (10%)	1
Intraabdominal Candidiasis (5)	2 (40%)	1 (20%)	1 (20%)	1 (20%)

Within the interim analysis of the 20 patients, oral ibrexafungerp was well-tolerated with the most common treatment related adverse events being gastrointestinal. No deaths due to progressive fungal disease were reported. No safety signals warranting changes in the study were observed.

CONCLUSION

This case report shows the potential of oral ibrexafungerp to treat intraabdominal infections caused by *Candida krusei*. Continued enrollment in the FURI study is warranted and investigation of other sequestered sites of infection and resistant antifungal species is indicated.