In this real-world study in patients with Staphylococcal osteomyelitis and joint infection, DAL resulted in high rates of clinical and microbiological success.

**Disclosures.** Jennifer McGregor, RPh, AbbVie (Employee) Anathakrishnan Ramani, MD, FACP, AAHIVS, CIC, Allergan (prior to its acquisition by AbbVie) (Speaker’s Bureau) John Lock, PharmD, BCPS, A-Q-ID, AbbVie (Employee) Pedro Gonzalez, MD, MT, AbbVie (Employee).

1248. Efficacy and Safety of Oral Ibrexafungerp in 41 Patients with Refractory Fungal Diseases, Interim Analysis of a Phase 3 Open-label Study (FURI) Barbara D. Alexander, MD, MHS; Oliver Cornely, Prof.; Peter Pappas, MD; Rachel Miller, MD; Jose A. Vazquez, MD, FIDSA; Luis Ostrosky-Zeichner, MD; Andrej Spec, MD; Riina Rauteamaa-Richardson, DDS, PhD, FRCPath; Robert Krause, MD; George R. Thompson III, MD; Carolyn Morse, MD; John W. Sanders, III, MD; David Andes, MD, PhD; George Lyon, MD; Francisco M. Marty, MD; Emily Silverman, BS; Marisa H. Miceli, MD, FIDSA, MD; Thomas F. Patterson, MD; Martin Hoeningl, MD, PhD; Necchi Azzi, MD, PhD; David A. Angulo, MD, PhD; Duke University, Durham, NC; University of Cologne, Faculty of Medicine and University Hospital Cologne, Cologne, Nordrhein-Westfalen, Germany; University of Alabama at Birmingham, Birmingham, Alabama; Medical College of Georgia at Augusta University, Augusta, Georgia; University of Texas Health Science Center, Houston, Houston, Texas; Washington University, St. Louis, St. Louis, Missouri; University of Manchester, Manchester, England; United Kingdom; Medical University, Graz, Graz, Steiermark, Austria; UC-Davis, Sacramento, California; Wake Forest Baptist Hospital, Winston-Salem, North Carolina; Wake Forest School of Medicine, Winston-Salem, NC; University of Wisconsin, Madison, Wisconsin; Emory Health, Atlanta, Georgia; Bringham and Women’s Hospital Hospital, Boston, Massachusetts; Dana Farber Cancer Institute, Boston, Massachusetts; University of Michigan, Ann Arbor, Michigan; University of Texas Health San Antonio, San Antonio, TX; University of California, San Diego, San Diego, CA; SCYNEXIS, Inc., Jersey City, New Jersey.

**Session:** P-58. Novel Agents

**Background.** Candida infections resistant to currently available antifungals are an emerging global threat. Ibrexafungerp 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 oral ibrexafungerp (FURI) (Clinicaltrials.gov NCT03059992) is ongoing for the treatment of patients (≥18 years) with fungal diseases who are intolerant or of reluctance to standard antifungal therapies.

**Methods.** An independent Data Review Committee (DRC) provided an assessment of treatment response for 41 patients. Patients were enrolled in 22 centers from 6 countries. Patients were eligible for enrollment if they had proven or probable, invasive candidiasis or mucocutaneous candidiasis and documented evidence of failure of, intolerance to, or toxicity related to a currently approved standard-of-care antifungal treatment or could not receive approved oral antifungal options (e.g., susceptibility of the organism) and a continued IV antifungal therapy was undesirable or contraindicated. Ibrexafungerp was well-tolerated with the most common treatment-related adverse events being of gastrointestinal origin. No deaths due to progression of fungal disease were reported.

**Conclusion.** Preliminary analysis of these 41 cases indicates that oral ibrexafungerp provides a favorable therapeutic response in the majority of patients with difficult-to-treat Candida spp. infections, including those caused by non-albicans Candida species.

**Disclosures.** Barbara D. Alexander, MD, MHS, SCYNEXIS, Inc. (Employee, Scientific Research Study Investigator, Research Grant or Support) Oliver Cornely, Prof., Actelion (Consultant, Research Grant or Support); Allovir (Consultant, Scientific Research Study Investigator, Research Grant or Support); Merck (Consultant, Other Financial or Material Support, Personal fees) Pfizer (Consultant, Scientific Research Study Investigator); Alleece Therapeutics (Other Financial or Material Support, Personal fees) Gilead Sciences, Inc. (Grants/Research Support) Ninebotica (Grants/Research Support) Astellas (Grant/Research Support, Member of Advisory Panel) Roche Diagnostics (Grants/Research Support, Member of Advisory Panel)

Table 1: Ibrexafungerp Outcomes by Pathogen

| Pathogen          | Complete or Partial Response | Stable Disease | Progression of Disease |
|-------------------|-----------------------------|----------------|------------------------|
| C. glabrata       | 9                           | 5              | 3                      |
| C. albicans       | 5                           | 2              | 2                      |
| C. krusei         | 2                           | 3              | 3                      |
| C. parapsilosis   | 2                           | 3              | 3                      |
| C. glabrata / C. albicans | 2                           | 2              | 2                      |
| C. krusei / C. albicans | 1                           | 1              | 1                      |
| C. tropicalis / C. albicans | 1                           | 1              | 1                      |

One patient outcome indeterminate. One patient organism not identified.

**Conclusion.** Preliminary analysis of these 41 cases indicates that oral ibrexafungerp provides a favorable therapeutic response in the majority of patients with difficult-to-treat Candida spp. infections, including those caused by non-albicans Candida species.

**Disclosures.** Barbara D. Alexander, MD, MHS, SCYNEXIS, Inc. (Employee, Scientific Research Study Investigator, Research Grant or Support) Oliver Cornely, Prof., Actelion (Consultant, Research Grant or Support); Allovir (Consultant, Scientific Research Study Investigator, Research Grant or Support); Merck (Consultant, Other Financial or Material Support, Personal fees) Pfizer (Consultant, Scientific Research Study Investigator); Alleece Therapeutics (Other Financial or Material Support, Personal fees) Gilead Sciences, Inc. (Grants/Research Support) Ninebotica (Grants/Research Support) Astellas (Grant/Research Support, Member of Advisory Panel) Roche Diagnostics (Grants/Research Support, Member of Advisory Panel)
the microbiological activity of this novel compound against SBL- and MBL-producing E. coli (Table 1).

Table 1. IC₅₀ values and in vitro activity results for s08033 against selected SBLs and MBLs.

| Antibiotic (AB) | S08033 | CFDC | GEP | OFID |
|----------------|--------|------|-----|------|
| CFDC           | 1.00   | 0.005| 0.005| 0.005|
| GEP            | 0.50   | 0.005| 0.005| 0.005|
| OFID           | 0.50   | 0.005| 0.005| 0.005|

Conclusion. Addition of a free-thiol group to the BATSIs scaffold increases the range of these compounds resulting in a broad-spectrum inhibitor toward clinically important carbapenemases and cephalosporinases.

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1251. Prevention of Pneumocystis Pneumonia by Ibrexafungerp in a Murine Prophylaxis Model
Katyna Borroto-Esoda, PhD; Nkechi Azie, MD; Alan Ashbaugh, PhD; Melanie Cushion, PhD; David A. Angelo, MD, D1; SCYNEXIS, Inc., Jersey City, NJ; 2University of Cincinnati, Cincinnati, Ohio

Session: P-58. Novel Agents

Background. Pneumocystis pneumonia (PCP) is an opportunistic fungal infection that affects immunocompromised patients. Ibrexafungerp (IBX) is an oral and intravenous antifungal from a novel class of glucan synthase inhibitors, tripterpenoids, and has shown activity against Candida, Aspergillus, and PCP in a murine therapy model. We evaluated the ability of IBX to prevent PCP in a prophylaxis model of murine PCP.

Methods. Experiment 1: Balb/c mice (10 mice/group) were infected intranasally with Pneumocystis murina, immune-suppressed with dexamethasone in an acidic diet. Mice were treated with IBX (15 mg/kg daily) for 7 days, with or without 3 days of antibiotic prophylaxis with trimethoprim/sulfamethoxazole (TMP/SMX). After 6 weeks, mice were sacrificed, and the infection was determined by organism burdens (asci and total nuclei).

Experiment 2: Balb/c mice were immune-suppressed and infected as in Exp. 1. Treatment groups included: 1) 30 mg/kg BID x 6wk; 2) 30 mg/kg/BID x 6wk followed by cessation of treatment with IBX but with immune-suppression for 3 additional weeks; 3) 15 mg/kg BID 1 week prior and 6 wks after infection and immune suppression; 4) 15 mg/kg BID for 6 wks then IBX was discontinued but with immune-suppression; 5) 15 mg/kg BID for 6 wks then IBX was discontinued but with immune suppression; 6) untreated, vehicle control.

Results. Experiment 1: No P. murina nuclei or ascii were observed after 6 weeks of treatment at a dose of 30 mg/kg/BID in the prophylaxis mouse model of PCP, similar to positive control, TMP/SMX. Some nuclei and ascii were observed in the lower dose IBX groups.

Experiment 2: To investigate whether any P. murina remained after different regimens of prophylaxis, treatment of IBX was withdrawn at both doses for an additional 3 wks of immune suppression to provoke the growth of any remaining fungi. Group 1 showed reduction in total nuclei and asci to undetectable. Group 2 did not result in any recrudescence of infection. Group 3 and 4 showed similar reduction in organism burden. Group 5 was similar to untreated control.

Conclusion. These results demonstrate that 30 mg/kg BID IBX prevented PCP in a murine model. We suggest that IBX could be a viable option for preventing PCP in immunocompromised patients.

Disclosures. Katyna Borroto-Esoda, PhD, SCYNEXIS, Inc. (Employee, Shareholder) Nkechi Azie, MD, SCYNEXIS, Inc. (Employee, Shareholder) Alan Ashbaugh, PhD, SCYNEXIS, Inc. (Grant/Research Support) Melanie Cushion, PhD, SCYNEXIS, Inc. (Grant/Research Support) David A. Angelo, MD, SCYNEXIS, Inc. (Employee, Shareholder)

1252. In Vitro Activity of Cefiderocol Against Metallo-β-Lactamase-Producing Gram-Negative Bacteria Collected in North America and Europe Between 2014 and 2017: SIDERO-WT-2014-2016 Studies
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Session: P-58. Novel Agents

Background. Metallo-β-lactamases (MBLs; eg, NDM, VIM, and IMP) can inactivate almost completely used β-lactam antibiotics, including carbapenems. Infections caused by MBL-producing bacteria are difficult to treat due to their resistance to many antibiotics. Cefiderocol (CFDC) is a siderophore cephalosporin antibiotic approved in the USA in 2019, with potent activity against carbapenem-resistant Gram-negative bacteria (GNB), including both serine- and metallo-carbapenemase positive strains. We evaluated the in vitro activity of CFDC and comparator agents against MBL-producing strains of GNB from North America and Europe in 3 years of consecutive surveillance studies (SIDERO-WT-2014-2016).

Methods. Susceptibility testing for CFDC, ceftazidime-avibactam (CZA), cefotaxime-tazobactam (C/T), meropenem (MEM), cefepime (FEP), ciprofloxacin (CIP), and aztreonam (AZT) was performed by the broth microdilution method according to CLSI guidelines. CFDC was tested in iron-depleted medium. A total of 275 MBL-producing strains, consisting of 120 Enterobacteriaceae (45 NDM; 75 VIM), 5 NDM-producing Acinetobacter baumannii, and 150 Pseudomonas aeruginosa (134 VIM; 16 IMP), identified among...