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Background. Blastomycosis is an endemic dimorphic fungal infection caused by *Blastomyces dermatitidis*. The risk factors associated with severe presentation are not well defined.

Methods. Retrospective study of patients treated for blastomycosis at the University of Kentucky Hospital from 2004-2019. Statistical analyses were performed with STATA version 12.0 (College Station, Texas). Logistic regression was used to identify variables associated with severe infections.

Results. Among 82 patients, median age was 48 years old (range: 16 - 89); 66 (80.5%) were male and 71 (92.2%) were white, 25/77 (32.4%) were obese, 24 (29.2%) were diabetic, 21 (25.6%) had COPD, 26 (31.7%) had at least one immunosuppressive condition. The median duration of illness was 86 (3-365) days. 37 (45.1%) had cough and 35 (42.6%) had dyspnea 19 (23.1%) patients were treated in the ICU, 42 (51.3%) in non-ICU inpatient wards, and 21 (25.6%) in an outpatient setting. Cultures were obtained in 69 cases, 59 (85.5%) reported as positive, KOH stain positive in 30/61 (49.1%). Histopathology was positive in 48/66 (72.7%) samples. Urine *Histoplasma or Blastomyces* antigen was positive in 41/58 (70.6%), and Serum *Histoplasma or Blastomyces* antigen was positive in 22/34 (64.7%). Among 64 (78.0%) patients with pulmonary blastomycosis, acute and chronic pneumonia were 16 (25.0%) and 12 (18.7%) cases respectively, and nodular lung lesions were reported in 36 (56.2%). Initial antifungal treatment was amphotericin B liposomal in 38/80 (47.5%), overall mortality was 11 (13.4%). A multivariable analysis was performed to find predictors of severe blastomycosis infection, no association was seen with factors as male sex (IRR 1.96; 95%CI 0.84 – 4.55), and was confirmed that significant independent associated risk factors for severe infection were age older than 50 (IRR 3.5; 95%CI 1.42-8.83), obesity (IRR 3.1; 95% CI 1.41-6.87), diabetes (IRR 2.5; 95% CI 1.16-5.50), leukocytosis (IRR 1.03; 95%CI 1.00-1.07) and anemia (IRR 3.0; 95% CI 1.55-5.85).

Conclusion. Pulmonary Blastomycosis is the most common presentation. Culture and histopathology are more sensitive than antigen assay. Independent factors associated to severe disease were older age, obesity, diabetes, and anemia at admission.

Disclosures. **All Authors**: No reported disclosures

1157. Clinical Safety, Efficacy, and Pharmacokinetics of Fosmanogepix, a Novel First-in-class Antifungal, in Patients with Renal Insufficiency: Subset Analysis from a Phase 2 Candidemia Trial

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Background. Fosmanogepix (FMGX) is a first-in-class antifungal agent, with a unique MOA targeting the fungal enzyme Gwt1, and broad-spectrum activity against yeasts and molds, including fungi resistant to other antifungal agents. Patients with candidemia often have underlying renal insufficiency or are receiving medications that affect renal function. This analysis evaluated outcomes in patients with varying degrees of renal insufficiency.

Methods. This global, multicenter, open-label, non-comparative study evaluated the safety and efficacy of FMGX for first-line treatment of candidemia. Patients with a recent diagnosis of candidemia defined as positive blood culture for *Candida* spp within 96 hrs prior to study entry with ≤ 2 days of prior antifungal treatment were eligible, including those with renal insufficiency. Patients with neutropenia, *C. krusei* infection, deep-seated *Candida* infections or receiving hemodialysis were excluded. Subjects were treated with FMGX for up to 14 days: 1000 mg IV BID for 1 day, then 600 mg IV QD for at least 2 days, followed by either 600 mg IV QD or 700 mg PO QD. Patients requiring antifungal treatment beyond 14 days received fluconazole. The primary efficacy endpoint was outcome at end of study treatment (EOST) as determined by an independent data review committee. Successful outcome was defined as survival with clearance of *Candida* from blood cultures with no additional antifungal treatment.

Results. 14/21 (66%) subjects had some degree of renal insufficiency: 7 had mild renal insufficiency (GFR:60-89), 5 had moderate renal insufficiency (GFR:30-59), and 2 had severe renal insufficiency (GFR:15-29). 12/14 (86%) completed study treatment, and treatment was successful at EOST in 12/14 (86%) subjects. Decline in renal function was not observed at EOST. 4 had worsening of renal function during the follow-up period; none required dialysis. Renal impairment did not increase exposure of FMGX. There were no treatment-related adverse events.

Conclusion. FMGX demonstrated high level treatment success with no evidence of drug-related nephrotoxicity, with no dose adjustments required. These preliminary data support the continued evaluation of FMGX in patients with candidemia and renal dysfunction as an alternative to potentially nephrotoxic antifungal agents.

Disclosures. **Pierre Bulpa, MD**, **Amplyx Pharmaceuticals** (Scientific Research Study Investigator) **Galia Rahav, MD**, **AstraZeneca** (Scientific Research Study Investigator) **Mickaël Aoun, MD**, **Amplyx Pharmaceuticals** (Scientific Research Study Investigator) **Peter Pappas, MD**, **SCYNEXIS, Inc.** (Consultant, Advisor or Review Panel member, Research Grant or Support) **Bart Jan Kullberg, MD, FRCP, FIDSA**, **Amplyx** (Advisor or Review Panel member) **Sara Barbat, BSN, RN**, **Amplyx Pharmaceuticals** (Employee) **Pamela Wedel, BSc**, **Amplyx Pharmaceuticals** (Employee) **Haran T. Schlamm, MD**, **Amplyx** (Consultant) **Michael Hodges, BSc. MD**, **Amplyx Pharmaceuticals Inc.** (Employee)

1158. D-index as a Novel Index to Predict Invasive Fungal Disease in High-Risk Neutropenic Pediatric Cancer Patients and Hematopoietic Stem Cell Transplantation

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Background. Prolonged and profound neutropenia are risk factors for invasive fungal disease (IFD) during febrile neutropenia (FN) episodes. The D-index combines both depth and duration of neutropenia in a single assessment and has been proposed as a useful tool to exclude or predict IFD in high-risk adult patients. We assessed the D-index as a predictor of IFD in pediatric cancer patients.

Methods. We conducted a retrospective study of pediatric oncology patients with FN at UCM Comer Children's Hospitals. IFD was stratified as possible, probable, and proven according EORTC/MSG criteria. Patients considered high risk of IFD were receiving intensive chemotherapy with expected prolonged neutropenia >7 days, including, but not limited to, AML, high-risk acute ALL, and hematopoietic stem cell transplantation (HSCT). The D1-index was equal to $2t_1 + 3t_2$, where t_1 and t_2 are the number of days from the first day of neutropenia < 500mm^3 and < 100/ mm^3 respectively, until the development of IFD. The D2-index approximates the area over the neutrophil curve during neutropenia. A cumulative D-index (c-D-index) was also calculated using the first day of neutropenia until the date of the first clinical manifestation of IFD. We compared duration of neutropenia vs D-index vs c-D-index as a predictor of IFD using receiver operating characteristic curve (ROC)/ AUC analysis.

Figure 1

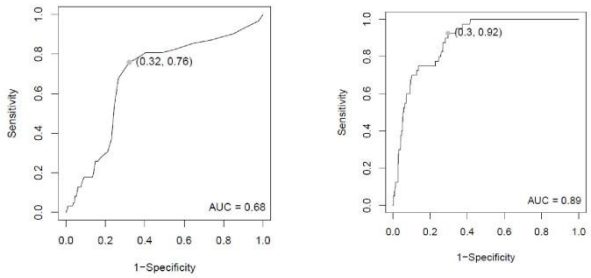

Figure 1. A Receiver operating characteristic curves comparing D-index with the days of neutropenia (<500 mm3), from fever onset through first clinical manifestation of IFD. A)AUC/D-index 0.89, sensitivity 92%, specificity 70%, NPV 98%. B) AUC/duration of neutropenia 0.68, sensitivity 76%, specificity 68%, NPV 80%.

Figure 2

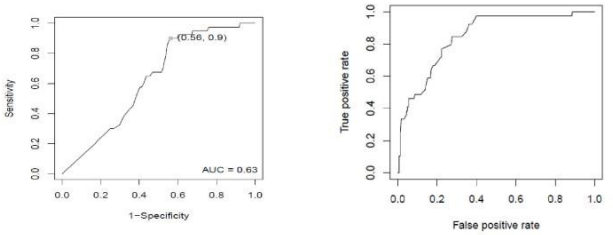

Figure 2. A Receiver operating characteristic curves comparing cD-index with the cumulative days of neutropenia (<500 mm3) from onset neutropenia before fever through first clinical manifestation of IFD. A)AUC/cD-index 0.82, sensitivity 82%, specificity 70%, NPV 92%. B) AUC/duration of neutropenia 0.63, sensitivity 90%, specificity 56%, NPV 81%.

Results. We identified 455 FN episodes in 203 high-risk patients. 53/455 (11.6%) had IFD, 12 (2.6%) proven, 23 (5%) probable, and 18 (4%) possible. The median of D1, D2 indexes and c-D-index were significantly higher in patients developing IFD (38, 5225, 7352) compared to the non-IFD group (26, 3857, 5169) (P=.001, P=.001, and P=.01) respectively. The ROC curve of D-index and c-D-index (figure 1,2,3) showed better performance (AUC of 0.85,0.89, 0.81) respectively compared to the duration of neutropenia alone. The ROC was highest when D-index was combined with prolonged fever >5 days (AUC 0.94)