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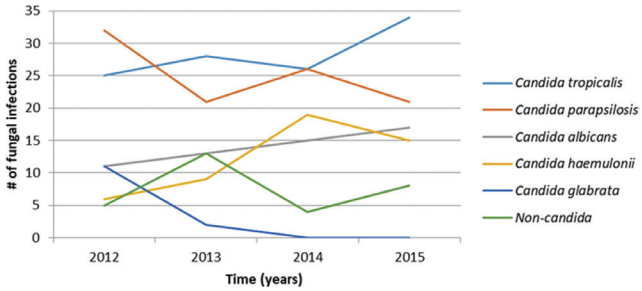
***Background.*** Despite a significant increase in fungal blood stream (BSI) infections in India, there is paucity of data on regional prevalence of major fungal species, and risk factors for this infection. We describe the epidemiology and predictors of fungal BSI in a tertiary care center in Kerala, India with a novel antimicrobial stewardship program in place.

***Methods.*** Data on adult inpatients who had at least one positive fungal culture from blood samples were collected from electronic medical records over a period of 48 months (January 2012 and December 2015). Year wise epidemiology and risk factor characterization of fungal BSI were done using $\chi^2$ method.

***Results.*** A total of 219 fungal BSI were identified with incidence of 1.08 cases/1,000 patients and there was a 15% decrease over the 4-year period. There was a 300% increase in fungal BSI in patients older than 80 years. *Candida* was the most common cause of fungal BSI (92%), with a 100% increase in incidence of *C. glabrata* and *C. haemolunii*, and a 45% decrease in *C. parapsilosis* seen over the 4-year period. Community-acquired fungal BSI increased by 700% while hospital-associated infections dropped by 29%. Twenty-three percent decrease in inappropriate antifungal treatment was observed from 2012 to 2015. Isolates reflected a 71% increase in resistance to amphotericin B and a 114% increase in fluconazole resistance. Thirty-one percent reduction in all-cause mortality was seen in the cohort over the study period. Among the risk factors for fungal BSI, ICU stay, use of urinary catheter, surgery, neutropenia, and diabetes decreased while prior antibiotic use and steroid use significantly increased over the years ($P < 0.05$). Predictors of mortality included male gender, prior use of antibiotics, ICU stay, use of ventilator, chemotherapy, chronic liver disease, hypertension, presence of *Candida parapsilosis*, and inappropriate therapy ($P < 0.05$).

***Conclusion.*** A significant shift in fungal BSI epidemiology was observed in our center with increase in overall antifungal resistance. Antimicrobial stewardship and infection control programs may have contributed to reduced mortality and reduced hospital-associated infections.




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

**410. Impact of Pediatric Antifungal Adverse Drug Reactions on Prescribing Practices**

Jennifer Goldman, MD, MS[1]; Jason Newland, MD, MEd, FPIDS[2]; Diana Yu, PharmD, BCPS-AQ ID[3]; Karisma Patel, PharmD, BCPPS[4]; Alaina Burns, PharmD[1]; Ann Wirtz, PharmD[1] and Brian R. Lee, MPH, PhD[5,6]; [1]Children's Mercy Kansas City, Kansas City, Missouri, [2]Washington University S, Kansas City, Missouri, [3]Doernbecher Children's Hospital, Portland, Oregon, [4]Children's Health, Dallas, Texas, [5]Health Outcomes, Children's Mercy Kansas City and University of Missouri-Kansas City SOM, Kansas City, Missouri, [6]Children's Mercy Hospital, Kansas City, Missouri

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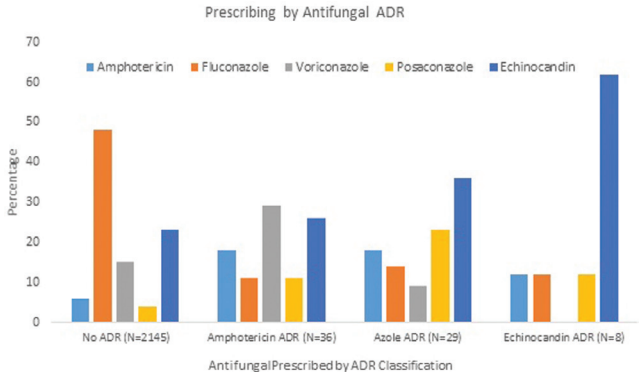
***Background.*** While antibiotics frequently cause adverse drug reactions (ADR), the rate of antifungal (AF) ADR is unknown. The mechanisms of AF ADR and cross-reactivity among a drug class (i.e., azoles) are poorly understood. Given the use of AF therapy is on the rise, it is important to better understand the prevalence of AF ADR and how these reactions influence prescribing.

***Methods.*** Thirty-two hospitals participated in a quarterly pediatric point prevalence survey that documented details on all admitted patients 0–17 years receiving any systemic antimicrobials, including drug, dose, and documented history of an antimicrobial ADR between June 2016 and December 2017. Patients who were recorded as receiving at least one systemic AF were included. A comparison of AF prescribing practices between those with and without an AF ADR was performed.

***Results.*** Among 13,179 total patients, 2,213 AF were prescribed to 2,101 unique patients. The most common indications for AF included prophylaxis (64%), fever with neutropenia (4%), neonatal sepsis (3%), and catheter-related bloodstream infection (3%). The prevalence of patients with any documented AF ADR was 2.9%. Amphotericin was most commonly associated with an ADR. Fluconazole was the most commonly prescribed AF in those with no ADR (49%) when compared with those with an AF ADR (13%; $P < .05$). Patients with an amphotericin ADR were more likely to receive voriconazole (29%) when compared with those without (15%; $P < .05$). Interestingly, posaconazole use was highest in those with an azole ADR (22%) when compared with those with no azole ADR (4%; $P < .05$). Echinocandin ADR were infrequent, and those with a reported ADR still received an echinocandin 62% of the time.

***Conclusion.*** Significant differences in antifungal prescribing exists based on ADR status. More work is needed to be able to effectively classify AF ADR, determine safe prescribing practices in those with an AF ADR, and evaluate outcomes associated with AF ADR status.




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

**411. Tolerability of Isavuconazole After Posaconazole Toxicity in Leukemia Patients**

Adam J. DiPippo, PharmD[1], Caitlin R. Rausch, PharmD[2] and Dimitrios P. Kontoyiannis, MD, ScD, PhD (Hon), FACP, FIDSA, FECMM, FAAM[3]; [1]Division of Pharmacy, The University of Texas MD Anderson Cancer Center, Houston, Texas, [2]Pharmacy, University of Texas MD Anderson Cancer Center, Houston, Texas and [3]Department of Infectious Diseases Infection Control and Employee Health, The University of Texas MD Anderson Cancer Center, Houston, Texas

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***Background.*** Oral posaconazole (PCZ) is widely used for both prophylaxis and treatment of invasive fungal infections (IFIs) in adult leukemia patients due to its broad antifungal spectrum. However, issues with PCZ tolerability can result in treatment interruption or discontinuation, and the need for alternative oral options with comparable antifungal coverage. Isavuconazole (ISA) is the newest triazole antifungal with a similar spectrum of activity to PCZ and is increasingly used in leukemia patients. Real-world data regarding the tolerability of ISA after PCZ toxicity are lacking.

***Methods.*** We retrospectively assessed safety and tolerability of ISA utilization after PCZ toxicity in adult (age > 18 years) leukemia patients from March 2015 to December 2016. We included all patients who received ≥7 days of oral or intravenous ISA 372 mg immediately after receiving at least one dose of oral PCZ. Demographic and clinical data were recorded including age, sex, underlying disease and disease status, and prior allogeneic stem-cell transplantation (alloSCT). Relevant toxicity markers were collected at three time points: prior to PCZ initiation, at switch to ISA therapy, and after ISA therapy was completed.

***Results.*** We identified 8 such patients, all with acute myeloid leukemia. No patient had prior alloSCT and all except one patient had relapsed or refractory disease (88%). Five patients were neutropenic at the time of ISA initiation. PCZ was administered as prophylaxis in one and as treatment in seven patients. Increased liver function tests (LFTs) or total bilirubin was noted in seven patients on PCZ, while two patients had confirmed Grade 3/4 QTc prolongation. No patient discontinued subsequent ISA due to toxicity. Overall, Grade 3/4 elevations in LFTs were decreased after changing to ISA (25% after PCZ vs. 0% after ISA). The two patients who experienced Grade 3/4 QTc prolongation with PCZ returned to normal EKG findings after changing to ISA.

***Conclusion.*** Overall, we found ISA to be well tolerated in patients requiring discontinuation of PCZ due to toxicity, with no patients discontinuing ISA due to toxicity. ISA was found to be a safe alternative choice in the setting of PCZ toxicity in heavily immunocompromised patients.

***Disclosures.*** **D. P. Kontoyiannis**, Merck: Consultant, Research support and Speaker honorarium. Pfizer: Consultant, Research support. Astellas: Consultant, Research support and Speaker honorarium. Gilead: Speaker's Bureau, Speaker honorarium. F2G Inc.: Speaker's Bureau, Speaker honorarium. Cidara Inc.: Speaker's Bureau, Speaker honorarium. Jazz Pharmaceuticals: Speaker's Bureau, Speaker honorarium.

**412. Clinical and Pharmacoeconomic Evaluation of Antifungal Prophylaxis With Continuous Micafungin Compared to Posaconazole With Micafungin Bridging in Patients Undergoing Allogeneic Stem Cell Transplantation: A 6-Year Cohort Analysis**

Sebastian M. Heimann, PhD[1]; Maria J.G.T. Vehreschild, MD[2]; Bernd Franke, Database Development[3]; Oliver Cornely, MD, FACP, FIDSA, FAAM[3]; Axel Hamprecht, MD[4]; Ellen Piepenbrock, MD[5]; Christoph Scheid, MD[3] and Janne Vehreschild, Prof. Dr. Med.[6]; [1]Department I of Internal Medicine, University Hospital of Cologne, Cologne, Germany, [2]University Hospital of Cologne and German Centre for Infection Research, Partner Site Bonn-Cologne, Cologne, Germany, [3]University Hospital of Cologne, Cologne, Germany, [4]Institute for Medical Microbiology, Immunology and Hygiene, University Hospital of Cologne, Cologne, Germany, [5]University Hospital Cologne, Cologne, Germany, [6]German Center for Infection Research, Cologne-Bonn, Cologne, Germany

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***Background.*** Patients undergoing allogeneic stem-cell transplantation (aSCT) are at high risk of invasive fungal disease (IFD). Optimization of antifungal prophylaxis strategies may further improve patient outcomes and reduce treatment costs.

***Methods.*** We performed a retrospective single-center pharmacoeconomic evaluation comparing patients who received either posaconazole oral solution plus micafungin as intravenous bridging as required (POS-MIC) to patients who received only micafungin (MIC) as antifungal prophylaxis after aSCT at the University Hospital of Cologne. Epidemiological, clinical, and direct treatment cost data extracted from the Cologne Cohort of Neutropenic Patients (CoCoNut) were analyzed. Revised 2008 EORTC/MSG criteria were used for classification of IFD.

***Results.*** During the observation period from January 2010 to December 2015, 313 patients (97 patients in the POS-MIC and 216 patients in the MIC group) fulfilled inclusion criteria. Most patients were male ($n$ = 174; 56%) and median age was 52 years (range: 18–75 years). Acute myeloid leukemia was the most common underlying disease ($n$ = 146; 47%). In the POS-MIC and MIC group, median overall length of stay (LOS) was 42 days (IQR: 35–52 days) vs. 40 days (IQR: 35–49 days; $P$ = 0.296), resulting in median overall direct treatment costs of €42,964 (IQR: 35,040 - €56,348) vs. €43,291 (IQR: €37,281 vs. €51,848; $P$ = 0.993), respectively. In both groups, possible IFD occurred in six patients (6%) vs. 16 patients (7%; $P$ = 0.696) and probable/proven IFD occurred in five patients (5%) vs. threepatients (1%; $P$ = 0.051). Overall in-hospital mortality rates in the POS-MIC and MIC group were 10% ($n$ = 10) and 4% ($n$ = 9; $P$ = 0.035). Kaplan–Meier analysis showed improved outcome of patients who received MIC at day 100 ($P$ = 0.037) and at day 365 ($P$ < 0.001) following aSCT. Multivariable cox-regression model demonstrated treatment on ICU as the most important independent covariate for mortality at day 100 (HR: 8.08; $P$ < 0.001) and at day 365 (HR: 4.70; $P$ < 0.001).

***Conclusion.*** We observed a higher mortality in patients receiving POS-MIC instead of MIC, which was not explained by breakthrough IFDs. The higher drug acquisition costs of micafungin compared with posaconazole oral solution did not translate into higher overall direct treatment costs.

***Disclosures.*** **S. M. Heimann**, Astellas: Grant Investigator and Lecture honoraria, Research grant and Speaker honorarium. **M. J. G. T. Vehreschild**, Astellas: Grant Investigator and Speaker's Bureau, Research grant. **O. Cornely**, Astellas: Consultant, Grant Investigator and Lecture honoraria, Consulting fee, Research grant and Speaker honorarium. **J. Vehreschild**, Astellas: Grant Investigator and Speaker's Bureau, Research grant and Speaker honorarium.

### 413. Intravenous and Tablet Formulation of Posaconazole in Antifungal Therapy and Prophylaxis: A Retrospective, Non-Interventional, Multicenter Analysis of Patients Treated in German Tertiary-Care Hospitals

Sebastian M. Heimann, PhD[1]; Olaf Penack, Professor of Medicine[2]; Werner J. Heinz, MD[3]; Tobias Rachow, MD[4]; Gerlinde Egerer, MD[5]; Johanna Kessel, MD[6]; Annika Löhnert, MD[7] and Janne Vehreschild, Prof. Dr. Med.[7]; [1]Department I of Internal Medicine, University Hospital of Cologne, Cologne, Germany, [2]Charité University Hospitals, Berlin, Germany, [3]University of Würzburg Medical Center, Würzburg, Germany, [4]University Hospital of Jena, Jena, Germany, [5]University Hospital of Heidelberg, Heidelberg, Germany, [6]Department II of Internal Medicine, Infectiology, University Hospital of Frankfurt, Frankfurt/Main, Germany, [7]University Hospital of Cologne, Cologne, Germany

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***Background.*** Novel formulations (gastro-resistant tablet and intravenous solution) of posaconazole (POS) have been approved in prophylaxis and therapy of invasive fungal diseases (IFDs). The aim of this multicenter noninterventional study was to analyze treatment strategies and clinical effectiveness of these new options.

***Methods.*** We set up a web-based registry on the science platform *www.ClinicalSurveys.net* and members of the Infectious Diseases Working Party of the German Society of Hematology and Medical Oncology (AGIHO) were invited to provide clinical data on patients who received novel POS formulations. Data analysis was split into two groups of patients who received novel POS formulations for antifungal prophylaxis (posaconazole prophylaxis group) and antifungal therapy (posaconazole therapy group), respectively.

***Results.*** One hundred eighty hospitalized patients (151 in the posaconazole prophylaxis group and 29 in the posaconazole therapy group) from six German tertiary care centers treated between July 2014 and March 2016 were included into our analysis. Seventy-six patients were female (42%) and median age was 58 years (range: 19 – 77 years). Most patients ($n$ = 111; 62%) had an acute myeloid leukemia as primary underlying disease. In the posaconazole prophylaxis group and posaconazole therapy group, mean POS serum levels at steady-state were 1,154 µg/L ($n$ = 40; 95% CI: 911 – 1,396 µg/L) and 1,097 µg/L ($n$ = 19; 95% CI: 817 – 1,378 µg/L), respectively ($P$ = 0.776). In the posaconazole prophylaxis group, nine (6%) probable/proven fungal breakthroughs were reported. In the posaconazole therapy group, 17 and 12 patients received POS as first-line therapy and salvage therapy, respectively. Most frequent indications were possible ($n$ = 9) and probable ($n$ = 7) aspergillosis and proven ($n$ = 7) mucormycosis. The median overall duration of POS therapy was 18 days (IQR: 7–23 days). Thirteen patients (45%) had progressive IFD under treatment with novel POS formulations.

***Conclusion.*** Our study demonstrates clinical effectiveness of antifungal prophylaxis with novel POS formulations. In patients treated for possible/probable/proven IFD, the observed tolerability and overall mortality was comparable to previous studies with other antifungals in similar patient population.

***Disclosures.*** **S. M. Heimann**, MSD: Consultant, Grant Investigator and Lecture honoraria, Research grant and Speaker honorarium. **W. J. Heinz**, MSD: Grant Investigator and Speaker's Bureau, Research grant and Speaker honorarium. **J. Vehreschild**, MSD: Grant Investigator and Speaker's Bureau, Research grant and Speaker honorarium.

### 414. Diagnostic Usefulness of Differential Time to Positivity (DTP) in Neutropenic Cancer Patients With Suspected Catheter-Related Candidemia (CRC)

Kyeong Min Jo, M.D[1]; Hae-In Kim, MD[1]; Sungim Choi, M.D[1]; Kyung Hwa Jung, MD[1]; Jung Wan Park, MD[1]; Ji Hyun Yun, MD[1]; Min Jae Kim, MD[1]; Yong Pil Chong, MD, PhD[1]; Sang-Oh Lee, MD, PhD[1]; Sang-Ho Choi, MD, PhD[1]; Yang Soo Kim, MD, PhD[1]; Jun Hee Woo, MD[1]; Jung-Hee Lee, MD, PhD[2]; Je-Hwan Lee, MD, PhD[2]; Kyoo-Hyung Lee, MD, PhD[2] and Sung-Han Kim, MD, PhD[1]; [1]Department of Infectious Diseases, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Republic of (South), [2]Department of Hematology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Republic of (South)

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***Background.*** The decision of catheter removal in neutropenic patients with candidemia is difficult because they usually have surgically implanted catheter, and CRC are less frequent than in non-neutropenic patients. However, there are limited data on distinguishing CRC from non-CRC before catheter removal. We thus evaluated the diagnostic performances of DTP to diagnose CRC in neutropenic cancer patients with suspected CRC.

***Methods.*** All adult neutropenic cancer patients with candidemia were enrolled in a tertiary care hospital from July 2012 to December 2016. Definite CRC was defined if ≥15 CFU of *Candida* spp. in a removed catheter tip. Probable CRC was defined if (1) one to 14 CFU in catheter tip, and clinical improvement within 48 hours after catheter removal with antifungal agent therapy or (2) the infection was refractory to antifungal therapy alone but improved within 48 hours after catheter removal. Non-CRC was defined if any of the following conditions were satisfied: (1) catheter tip cultures were negative and a noncatheter source of candidemia was found by culture, (2) the catheter tip cultures within 24 h before the start of antifungal therapy were negative, or (3) the clinical improvement before or without catheter removal. If the above conditions are not met, they were grouped into indeterminate, and were excluded from the final analysis. We defined the DTP as the difference in the time to positivity between blood cultures drawn simultaneously from the central vein and a peripheral vein.

***Results.*** A total of 35 neutropenic patients with candidemia were enrolled. Of these, 15 patients (43%) with CRC (6 definite and nine probable) and 17 (48.5%) with non-CRC were finally analyzed, excluding threeindeterminate candidemia. On the basis of the receiver operating characteristics (ROC) curve, the optimal cut-off was ≥1.45 hours and the area under the ROC curve was 0.89 (95% CI, 76 to 100) in diagnosing CRC. Of the 15 patients with CRC, 11 (73%) revealed positive DTP, whereas none of the 17 patients with non-CRC exhibits positive DTP. The sensitivity and specificity of DTP for the diagnosis of CRC were 73% (95% CI, 58 to 94) and 100% (95% CI, 71 to 100), respectively.

***Conclusion.*** DTP appears to be useful to rule in CRC and DTP ≥ 1.45 hours to be the optimal cut-off for CRC in neutropenic cancer patients.

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

### 415. Breakthrough Invasive Fungal Infections in Adult Hematologic Malignancy Patients Receiving Isavuconazole Prophylaxis

Catherine DeVoe, MD[1]; Monica Fung, MD, MPH[2]; Brian Schwartz, MD[2]; Sarah B. Doernberg, MD[2]; Mimi Lo, PharmD[3]; Larissa Graff, PharmD[3]; Marisela Tan, PharmD[3]; Aaron Logan, MD, PhD[4]; Jennifer Babik, MD, PhD[5] and Peter Chin-Hong, MD[2]; [1]Division of Hospital Medicine, University of California, San Francisco, San Francisco, California, [2]Division of Infectious Diseases, University of California, San Francisco, San Francisco, California, [3]University of California, San Francisco, San Francisco, California, [4]Hematology Oncology, University of California, San Francisco, San Francisco, California, [5]Department of Medicine, Division of Infectious Diseases, University of California, San Francisco, San Francisco, California

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***Background.*** Isavuconazole (ISA) is a novel triazole antifungal approved for treating invasive aspergillosis and mucormycosis. While ISA is increasingly used for prophylaxis in hematologic malignancy patients when other azoles are contraindicated, there are currently limited data on breakthrough invasive fungal infection (IFI) rates in this context.

***Methods.*** We retrospectively reviewed inpatient and outpatient pharmacy records from March 2015 to April 2018 to identify adult patients with hematologic malignancy who received at least 7 days of ISA for prophylaxis. Breakthrough IFI was defined by EORTC-MSG criteria.

***Results.*** We identified 73 hematologic malignancy patients who received ISA; 29 received at least 7 days ISA for prophylaxis in 33 separate episodes. Of these patients, 52% had acute myeloid leukemia, 14% had acute promyelocytic leukemia, 10% had myelodysplastic syndrome, and 21% had another malignancy. Eighty-six percent of patients were neutropenic (median duration 24 days; range 2–213). Median duration of ISA prophylaxis was 61 days (range 8–635). The most common reason for choosing ISA over other antifungal agents was QTc prolongation (45%), followed by intolerance of other antifungals (27%) and drug-drug interactions with other azoles (21%). Four patients (12%) developed proven or probable breakthrough IFI (Table 1). Among patients with breakthrough IFI, mortality was 50% at 12 weeks.