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.

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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

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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.

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

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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.

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

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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.