

2121. Isavuconazole (ISAV) as Primary Anti-Fungal Prophylaxis (PAP) in Patients with Acute Myeloid Leukemia (AML) or Myelodysplastic Syndrome (MDS): An Open-Label, Prospective Study

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Background. Mold-active antifungal prophylaxis (ppx) is recommended in neutropenic patients with newly diagnosed AML or MDS. ISAV is an extended spectrum triazole with superior tolerability, reliability of absorption, fewer drug-drug interactions, lack of QT prolongation or need for therapeutic drug monitoring, approved for the treatment of invasive aspergillosis (IA) and mucormycosis. NCT03019939 is an investigator-initiated, phase 2 trial of PAP with ISAV in patients with AML/MDS.

Methods. Treatment-naïve adult patients with AML or MDS initiating remission-induction chemotherapy (RIC) received ISAV per the dosing recommendations in the United States label until recovery from neutropenia (neutrophils (ANC) $\geq 0.5 \times 10^9/L$) and attainment of complete remission (CR), occurrence of proven or probable invasive fungal infection (IFI, EORTC/MSG criteria), or for a maximum of 12 weeks. The primary endpoint was incidence of proven/probable IFI during the study period (up to 30 days from the last dose of ISAV).

Results. 67 patients were enrolled (April 28, 2017 to February 14, 2019) and 60 patients were eligible for assessment (median age 67 years, 57 patients with AML, median ANC on enrollment was 660). Reasons for study completion were achievement of CR with ANC recovery ($n = 35$), completion of 12 weeks of PAP ($n = 9$), possible IFI ($n = 7$), investigator decision ($n = 3$), death ($n = 2$, 1 disease progression, 1 cardiac arrest), proven/probable IFI ($n = 3$), and mild transaminitis, possibly ISAV-related ($n = 2$). The median durations of neutropenia and ISAV ppx were 33 (7–86) and 31 (7–86) days, respectively. One microbiologically-proven (gluteal abscess due to *Candida glabrata*) and 2 cases of probable breakthrough IFIs (probable IA with positive galactomannan) occurred (IFI incidence 5%). ISAV trough serum concentrations were available in 31 patients on both day 8 (median 3.74 $\mu\text{g/mL}$, 2.03–7.65) and day 15 (median 4.10 $\mu\text{g/mL}$, 2.17–9.25), and were not significantly different.

Conclusion. ISAV is a safe and effective alternative for PAP in patients with newly diagnosed AML/MDS undergoing RIC, with a breakthrough (proven/probable) IFI rate of 5%. ISAV serum levels were adequate in patients with AML/MDS undergoing RIC. Pharmacological features make ISAV attractive for PAP in the era of recently approved or emerging small-molecule AML therapies.

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2122. Isavuconazonium for Invasive Fungal Therapy: Single-Center Pediatric Experience

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Background. Isavuconazole (ISZ), dosed as the pre-drug isavuconazonium (ISM), is active against a wide variety of clinically important fungal pathogens. ISM is approved for the treatment of invasive aspergillosis and mucormycosis in adults ≥ 18 years of age. We present our experience with ISM to treat proven or to prevent fungal infection in pediatric patients.

Methods. In a retrospective review of patients who received ISM at our institution between April 2016 and April 2019, we abstracted demographic information, primary diagnosis, indication for ISM therapy, ISZ serum concentrations if available, and outcomes.

Results. Of 16 patients who received ISM, 12 were < 18 years of age (range 6–17 years). Underlying conditions included leukemia ($n = 8$), lymphoma ($n = 1$), post BMT ($n = 1$), diabetes ($n = 1$), and cardiac transplant ($n = 1$). Nine (75%) had proven invasive fungal infection with aspergillosis ($n = 2$), zygomycosis ($n = 3$), mixed aspergillosis and zygomycosis ($n = 2$), mixed Rhizopus and Scedosporium ($n = 1$), and pathology only ($n = 1$). Five of these 9 patients received combination ISM and liposomal amphotericin initially, followed by monotherapy with ISM in 4 patients after a mean of 26 days (range 6–63), and continued dual therapy in the fifth. The other 4 received liposomal amphotericin with or without other azoles prior to changing to ISM monotherapy. ISM dosing was 10 mg/kg q8h on days 1 and 2, followed by q24 thereafter, up to a maximum of 372 mg/dose. There were 19 measured ISZ serum concentrations obtained from 8 patients after > 1 week of verified inpatient dosing, ranging from 1.0 to 7.5 mg/L, above the MIC in all cases when known. Five (42%) patients died of underlying non-mycological causes, 1 (8%) died of progressive scedosporiosis, and 6 (50%) improved. The two patients receiving ISM prophylaxis did not suffer a

breakthrough fungal infection. ISM was well tolerated with no dose-limiting, drug-related toxicities noted.

Conclusion. ISM is a well-tolerated therapeutic option in pediatric patients at risk for or with invasive mycosis. Only 1 of our 12 patients died from progressive fungal disease.

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2123. Rapid Phenotypic Detection of Gram-Negative Bacilli-Resistant to Oximinocephalosporins and Carbapenems in Positive Blood Cultures Using a Novel Protocol

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Background. Early and adequate antibiotic treatment are the cornerstones to improve clinical outcomes in patients with Bloodstream infections (BSI). Delays in appropriate antimicrobial therapy have catastrophic consequences for patients with BSI. Microbiological characterization of multi-drug-resistant pathogens (MDRP) allow clinicians to provide appropriate treatments. Current available microbiologic techniques may take-up to 96 hours to identify causative pathogens and its resistant patterns. Therefore, there is an important need to develop rapid diagnostic strategies for MDRP. However, rapid detection techniques are costly and are not widely available. We tested a modified protocol designed to detect Gram-negative bacilli (GNB) resistant to oximinocephalosporins and carbapenems from positive blood cultures.

Methods. This is a prospective, cohort study of consecutive patients with bacteremia. We developed a modified protocol using HB&L* system to detect MDRP. We then attempted to determine accuracy, concordance and reduction of identification time of this novel method in a reference hospital. Descriptive statistics and logistical regressions were used.

Results. Ninety-six patients with BSI were included in the study. A total of 161 positive blood cultures were analyzed. *Escherichia coli* (50%, 81/161) was the most frequently identified pathogen followed by *Klebsiella pneumoniae* (15%, 24/161) and *Pseudomonas aeruginosa* (8%, 13/161). 32% of isolations had usual resistance patterns. However, in 29/161 (18%) of identified pathogens were producer of carbapenemases and 21/161 (13%) of extended-spectrum β -lactamases. Concordance among our HB&L* modified protocol and traditional method was 99% (159/161). Finally, identification times were significantly shorter using our HB&L* modified protocol than traditional methods (Mean, hours [SD], 20.8 [6.22] vs. 62.8 [6.22], $P < 0.001$).

Conclusion. Here we provided novel evidence that using our HB&L* modified protocol is an effective strategy to reduce the time to MDRP detection/identification; with a great concordance rate when compared with the gold standard. Further studies are needed to confirm these findings and to determine whether this method may improve clinical outcomes.

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2124. The Epidemiology, Demographics, and Geographical Distribution of Human Non-Tuberculosis Mycobacteria (NTM) Disease in the Endemic Central Florida Region

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Background. Of the $> 100,000$ people in the United States infected yearly with non-tuberculosis mycobacteria (NTM), Florida has the highest yearly incidence and prevalence of NTM disease. However, little has been documented on the epidemiology and distribution of NTM disease within Central Florida.

Methods. A retrospective case review study was conducted from January, 2011 to December, 2017 at a large tertiary acute care medical center in Tampa, Florida to identify all NTM infection cases. Demographics (age, sex at birth, ethnicity), comorbidities, HIV testing status, residential zip code, NTM species, and specimen sources were collected.

Results. Of the 507 isolates, *Mycobacterium abscessus* group was the most common (45.4%; $n = 230$), and contained *M. abscessus* spp. abscessus (34.5%; $n = 175$), *M. abscessus* spp. massilense (8.7%; $n = 44$), and *M. abscessus* spp. bolletii (1.18%; $n = 6$). Other rapid growers were *M. fortuitum* species (6.9%; $n = 35$) and *M. chelonae*