O230a
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A PHASE 3 RANDOMIZED, DOUBLE-BLIND TRIAL EVALUATING ISAVUCONAZOLE VS. VORICONAZOLE FOR THE PRIMARY TREATMENT OF INVASIVE FUNGAL DISEASE CAUSED BY ASPERGILLUS SPP. OR OTHER FILAMENTOUS FUNGI (SECURE)

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OBJECTIVES: Isavuconazole (ISA) is a novel triazole with broad spectrum antifungal activity *in-vitro* and is offered in an intravenous and bioequivalent oral formulation. The objectives of this randomized, double-blind, multi-national study were to assess efficacy and safety of ISA versus voriconazole (VRC) in patients with invasive fungal disease (IFD) caused by *Aspergillus spp.* or other filamentous fungi.

METHODS: Patients meeting the EORTC criteria for proven/probable/possible disease were randomized 1:1 to ISA or VRC. ISA patients received 200mg IV-TID for two days, followed by 200mg QD (either IV or oral). VRC patients received 6mg/kg IV-BID on day one, then 4mg/kg IV-BID on day two, then either 4mg/kg IV-BID or 200mg PO-BID. Study-drug could be administered for up to 84 days. The primary efficacy endpoint was non-inferiority for day 42 All-Cause-Mortality (ACM) in the ITT population based on a pre-specified non-inferiority margin (NIM) of 10%. The key secondary efficacy endpoint was Overall Response at end-of-treatment (EOT) as determined by an independent blinded data-review committee (DRC) in the mITT population. The mITT population included patients with proven or probable disease as determined by the DRC.

RESULTS: 527 patients were randomized, 516 (258 per group) received at least one dose of study drug and comprised the ITT population. The mITT population included 143 ISA and 129 VRC patients (85% aspergillosis). Baseline characteristics were balanced between treatment groups; 92% pulmonary involvement, 84% hematologic malignancies, 65% neutropenic and 20% allogeneic haemotopoetic stem-cell transplantion. ACM through day 42 for the ITT population was 18.6% (ISA) and 20.2% (VRC). The primary objective was achieved since the upper bound of the 95% CI (-7.8, 5.7) for the adjusted treatment difference was lower than the NIM of 10%. ACM through day 42 in the mITT population was 19.6% (ISA) and 23.3% (VRC). ACM through day 84 in the ITT population was 29.1% (ISA) and 31.0% (VRC) and in the mITT population was 30.1% (ISA) and 37.2% (VRC). Overall Response rates at EOT in the mITT population were 35.0% (ISA) and 36.4% (VRC). Treatment-emergent adverse events (AE) were reported in 96.1% (ISA) and 98.5% (VRC) of patients. The most common AEs (i.e. nausea, vomiting, pyrexia, diarrhea) were reported at similar rates between treatment groups. Drug related AEs were reported in 42.4% (ISA) and 59.8% (VRC) of patients. Fewer ($p<0.05$) AEs were reported in the ISA treatment group in the System Organ Classes (SOC) of Skin (33.5% v 43.5%), Eye (15.2% v 26.6%) and Hepatobiliary Disorders (8.9% v 16.2%).

CONCLUSION: ISA is effective for the primary treatment of invasive fungal disease caused by *Aspergillus* species or other filamentous fungi. ISA was well tolerated relative to VRC, with fewer study drug related AEs and AEs of the Skin, Eye and Hepatobiliary system.