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ePoster Viewing
Antimicrobials: antibiotic usage

Efficacy and safety of ceftazidime-avibactam and best available therapy in the treatment of ceftazidime-resistant infections – results from a Phase III study

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Objectives: REPRISE was a prospective, open-label study (NCT01644643) investigating the efficacy and safety of ceftazidime-avibactam and best available therapy (BAT) in patients with selected serious infections caused by ceftazidime-resistant Gram-negative pathogens.

Methods: Adults (aged 18-90 years) with complicated intra-abdominal (cIAI) or complicated urinary tract infections (cUTI) caused by ceftazidime-resistant Gram-negative pathogens, isolated from an appropriate culture within 5 days prior to study entry, were randomised. Ceftazidime-resistant *Enterobacteriaceae* and *Pseudomonas aeruginosa* were defined as having ceftazidime MICs ≥8 mg/L and ≥16 mg/L, respectively. For 5-21 days, patients received IV ceftazidime-avibactam 2000-500 mg (2-h infusion) every 8 hours (q8h) or BAT as determined by the investigator based on standard care, following label recommendations, and documented prior to randomisation. In patients with cIAI, IV metronidazole 500 mg (60-min infusion) was administered q8h for patients randomised to ceftazidime-avibactam for anaerobe coverage. The primary endpoint was assessment of clinical response to ceftazidime-avibactam or BAT at test-of-cure visit (TOC) 7-10 days after last infusion in the microbiologically modified intent-to-treat population (mMITT). Secondary endpoints included per-patient microbiological response in the mMITT population. Safety was assessed by monitoring adverse events (AEs) and laboratory parameters.

Results: This abstract includes results from the first data cut-off, comprising 126 patients enrolled from June 2012-December 2013 of the 333 patients randomised. In total, 64 patients (cUTI: n=58; cIAI: n=6) were randomised to ceftazidime-avibactam and 62 to BAT (cUTI: n=56; cIAI: n=6) from 13 countries worldwide. Patients in the BAT group received a carbapenem antibiotic as monotherapy or in combination with a second antibiotic. Overall clinical cure rates at TOC in the mMITT population were 55/59 (93.2%; 95% CI, 84.7, 97.7) and 47/52 (90.4%; 95% CI, 80.2, 96.2) in the ceftazidime-avibactam and BAT groups, respectively. In patients with cIAI, 3/4 and 1/4 in the ceftazidime-avibactam and BAT groups, respectively, had an outcome of clinical cure. In patients with cUTI, clinical cure rates were similar between treatment groups (ceftazidime-avibactam: 52/55 [94.5%; 95% CI, 86.2, 98.4]; BAT: 46/48 [95.8%; 95% CI 87.3, 99.1]), however, per-patient microbiological response rates were higher with ceftazidime-avibactam (43/55 [78.2%; 95% CI, 66.0, 87.5]) than with BAT (24/48 [50.0%; 95% CI, 36.2, 63.8]). By the last follow-up visit (28-35 days

post-randomisation), 18/64 patients (28.1%) in the ceftazidime-avibactam group and 31/62 (50%) in the BAT group had experienced AEs, with serious AEs in 4.7% and 6.5%, respectively. Gastrointestinal disorders were the most frequently reported AEs in both groups. Final study results will be presented.

Conclusion: Based on results from the first data cut-off, treatment of selected serious ceftazidime-resistant Gram-negative infections with ceftazidime-avibactam results in similar clinical cure rates to treatment with BAT, and higher favourable per-patient microbiological response rates. The safety and tolerability profile of ceftazidime-avibactam is broadly similar to ceftazidime alone.