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2-hour Oral Session

New antibacterial agents - phase 2 and phase 3 clinical trials

A Phase III trial of ceftaroline fosamil 600 mg q8h versus vancomycin plus aztreonam in patients with cSSTI with systemic inflammatory response or underlying comorbidities

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Objectives: Ceftaroline fosamil (CPT-F) 600 mg administered every 8 h (q8h), as compared with the currently approved 600 mg q12h dosage regimen, may be useful in selected patients and versus selected pathogens. This Phase III trial compared the efficacy and safety of CPT-F 600 mg q8h with vancomycin (VAN) plus aztreonam (AZT) for patients with complicated skin and soft tissue infections (cSSTI) and evidence of systemic inflammatory response or underlying comorbidities.

Methods: In this Phase III, multicentre, randomised, double-blind trial (NCT01499277), 772 adult patients with cSSTI with evidence of systemic inflammatory response or underlying comorbidities (e.g. diabetes, HIV infection or malignancy), were randomised 2:1 across 113 sites in Asia, Europe, North and South America to receive CPT-F 600 mg 120-min intravenous (IV) infusion q8h (n=514) or vancomycin 15 mg/kg q12h plus aztreonam 1g q8h (n=258) for 5–14 days. Clinical cure was assessed at the test-of-cure (TOC) visit (8–15 days after the final dose) in the modified intent-to-treat (MITT) and clinically evaluable (CE) populations. Non-inferiority was defined as a lower limit of the 95% CI >–10% for the between-group difference. Safety was evaluated as a secondary objective.

Results: Baseline patient characteristics were balanced across groups; approximately 40% had systemic inflammatory response syndrome (SIRS) or bacteraemia, and 64% had C-reactive protein >50 mg/L. Median (range) durations of treatment were 7.6 (0.07–13.8) days and 7.7 (0.01–13.8) days for CPT-F and VAN+AZT, respectively. Respective clinical cure rates at TOC were 396/506 (78.3%) and 202/255 (79.2%) in the MITT population, and 342/395 (86.6%) and 180/211 (85.3%) in the CE population. Between-group differences (95% CI) for the MITT and CE populations were –0.95% (–6.90, 5.41) and 1.27% (–4.32, 7.48) respectively, demonstrating the non-inferiority of CPT-F 600 mg q8h versus VAN+AZT. Cure rates between treatment arms were comparable across demographic subgroups, geographic regions, baseline disease characteristics and diagnoses. The most common isolate was Staphylococcus aureus (54/222 [24.3%] MRSA). The MIC of >95% pathogens was at or below the CPT-F breakpoint. Microbiological responses in the mMITT and ME populations were consistent with clinical response. CPT-F was well tolerated: 232/506 (45.6%) and 116/255 (45.5%) patients treated with CPT-F and VAN+AZT, respectively, experienced ≥1 adverse event. In the CPT-F arm, the frequency of rash in non-Asian patients was similar to VAN+AZT, and to that observed in prior Phase III cSSTI trials. However, late (Day 7–10) rash occurred more frequently in Asian patients on CPT-F.

Conclusions: CPT-F 600 mg q8h 120-min IV infusion was effective and well-tolerated for patients with cSSTI with evidence of SIRS or underlying comorbidities. The qualitative safety profile of CPT-F 600 mg q8h was similar to previous trials with 600 mg q12h dosing, with no new safety signals identified.