Pharmacokinetics/Pharmacodynamics and Phase 3 Dose Projection For the Novel β-lactamase Inhibitor ETX2514 in Combination with Sublactam Against Acinetobacter baumannii-calcoaceticus Complex (ABC)

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Abstract

ETX2514 is a novel β-lactamase inhibitor with broad spectrum activity against several classes of ABC. ETX2514 and sulbactam (SUL) are being developed as a combination to treat ABC infections. ETX2514 is a novel β-lactamase inhibitor currently in Phase 3 clinical development for the treatment of infections caused by β-lactamase-producing bacteria. The combination of ETX2514 and SUL was determined in healthy subjects to achieve >90% probability of target attainment against isolates with AUC/MIC = 10. ETX2514 and SUL were 0.36 and 0.5 in healthy subjects. Accounting for ELF penetration, Monte Carlo simulation suggests >90% probability of target attainment against isolates with AUC/MIC > 30.

Background

The algorithm-based probability of target attainment (PTA) strategy is a tool used to establish PK/PD targets in preclinical and clinical studies. The PTA for a 1-log kill across renal categories considering sulbactam MICs probability of target attainment: The PTA across renal categories for a 1-log kill with sulbactam and ETX2514 is being developed to treat serious ABC infections. The combination of sulbactam and ETX2514 (ETX2514SUL) is being developed to treat serious ABC infections. The combination of sulbactam and ETX2514 (ETX2514SUL) is being developed to treat serious ABC infections. The combination of sulbactam and ETX2514 (ETX2514SUL) is being developed to treat serious ABC infections. The combination of sulbactam and ETX2514 (ETX2514SUL) is being developed to treat serious ABC infections. The combination of sulbactam and ETX2514 (ETX2514SUL) is being developed to treat serious ABC infections. The combination of sulbactam and ETX2514 (ETX2514SUL) is being developed to treat serious ABC infections. The combination of sulbactam and ETX2514 (ETX2514SUL) is being developed to treat serious ABC infections. The combination of sulbactam and ETX2514 (ETX2514SUL) is being developed to treat serious ABC infections. The combination of sulbactam and ETX2514 (ETX2514SUL) is being developed to treat serious ABC infections. The combination of sulbactam and ETX2514 (ETX2514SUL) is being developed to treat serious ABC infections. The combination of sulbactam and ETX2514 (ETX2514SUL) is being developed to treat serious ABC infections.