Online-Only Abstract: Population-based burden of bloodstream infections in Finland

The role of pharmacokinetics/pharmacodynamics in setting clinical MIC breakpoints: the EUCAST approach


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Abstract

Clinical breakpoints are used in clinical microbiology laboratories to categorize microorganisms as clinically susceptible (S), intermediate (I) or resistant (R) dependent on the quantitative antimicrobial susceptibility as indicated by the MIC value determined in a well-defined standard test system. The laboratory report, with the designations of S, I or R for each antimicrobial agent, provides guidance to clinicians with respect to the potential use of agents in the treatment of patients, and clinical breakpoints should therefore distinguish between patients that are likely or unlikely to respond to antimicrobial treatment. In Europe, clinical breakpoints are set by the European Committee on Antimicrobial Susceptibility Testing (EUCAST), following a defined procedure. This includes evaluation of efficacy in experimental settings and clinical studies to derive pharmacodynamic targets such as the fAUC/MIC ratio or %T > MIC required for efficacy, the pharmacokinetic properties of the agent, Monte Carlo simulations to estimate exposures of the antimicrobial agent in the target patient population and commonly used dosing regimens. The probability of target attainment is subsequently determined for a range of pharmacodynamic targets and the results from the Monte Carlo simulations. The breakpoints derived are subsequently evaluated with respect to the wild-type population of the target microorganisms, specific resistance mechanisms and other relevant data. In this paper, we provide an overview of the EUCAST process and considerations for setting pharmacokinetic/pharmacodynamic breakpoints. These are the breakpoints that in the EUCAST breakpoint tables are referred to as ‘non-species-related breakpoints’.