# Poster abstract submission

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**Poster title**

Dealing with the myth of 40% T>MIC for amoxicillin clavulanate: a hollow-fiber study using clinically relevant concentrations

**Poster abstract**

Time above the minimum inhibitory concentration (T>MIC) has been shown to correlate with the clinical efficacy of β-lactams. Optimization of treatment performance with amoxicillin/clavulanate (AMC) requires therefore regimens that potentially extend the T>MIC and consequently increase the probability of bacterial eradication and clinical cure. Currently, the AMC 14:1 (90 mg/6.4 mg, Augmentin ES®) is a frontline antibiotic for community-acquired bacterial infections, including community-acquired pneumonia and bacterial rhinosinusitis. In light of these premises, the objectives of this work were to establish the T>MIC associated with bacterial eradication following exposure of S. pneumoniae to AMC 14:1, and to

characterize the antibacterial activity and probability of target attainment (PTA) for different dosing regimens.
In that sense, an in vitro study using the hollow-fiber system (HFS) was conducted to characterize the effect of variable T>MIC for AMC 14:1 against S. pneumonia. Growth dynamics of S. pneumoniae were evaluated against a range of thresholds for T>MIC (0, 30, 40, 60%) over 24 hours, including strains with different susceptibility to AMC (MICAMC = 2 µg/ml and 4 µg/ml) for 10 days. Subsequently, the concentration-effect relationship of AMC 14:1 was evaluated against varying inocula of this pathogen. Serial bacterial counts were performed up to day 10 and AMC concentrations were analysed. Simulations were then implemented based on a population PK model to determine AMC 14:1 doses/regimens that maximize the PTA.
Growth dynamics results showed that S. pneumoniae demonstrated an increasing probability of eradication with increasing T>MIC of AMC. For the susceptible strain (MICAMC = 2 µg/ml), eradication required greater T>MIC (40%), regardless of inocula. For the less susceptible strain (MICAMC = 4 µg/ml), bacterial eradication was achieved only with 60% T>MIC, also regardless of inocula. Simulations demonstrated that higher PTA is achieved with higher doses and more frequent dosing.
In summary, HFS provides a valuable tool for the characterization of the implications of varying inocula, AMC concentrations and MIC thresholds for Augmentin ES® against different strains of S. pneumoniae. Besides, given the evolving bacterial resistance, simulations show that increased PTA is warranted for higher, more frequent doses of AMC.

**Research topic**

PK/PD