# 論 文 要 旨

Pharmacokinetic/pharmacodynamic evaluation of sulbactam against *Acinetobacter baumannii* in *in vitro* and murine thigh and lung infection models

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*Acinetobacter baumannii* is a pathogen that has become globally associated with nosocomial infections. Sulbactam, a potent inhibitor of β-lactamases, was previously shown to be active against *A. baumannii* strains *in vitro* and effective against *A. baumannii* infections. However, a pharmacokinetic/pharmacodynamic (PK/PD) analysis of sulbactam against *A. baumannii* infections has not yet been performed. This is necessary because optimisation of dosing regimens should be based on PK/PD analysis. Therefore, *in vitro* and *in vivo* PK/PD analyses of sulbactam were performed using murine thigh and lung infection models of *A. baumannii* to evaluate the pharmacokinetics and pharmacodynamics of sulbactam. Sulbactam showed time-dependent bactericidal activity *in vitro* against *A. baumannii*. The PK/PD index that best correlated with its *in vivo* effects was the time that the free drug concentration remained above the minimum inhibitory concentration (*f*T>MIC) both in the thigh ($R^2 = 0.95$) and lung ($R^2 = 0.96$) infection models. Values of *f*T>MIC for a static effect and 1, 2 and 3 $\log_{10}$ kill, respectively, were 21.0%, 32.9%, 43.6% and 57.3% in the thigh infection model and 20.4%, 24.5%, 29.3% and 37.3% in the lung infection model. Here we report the *in vitro* and *in vivo* time-dependent activities of sulbactam against *A. baumannii* infection and demonstrate that sulbactam was sufficiently bactericidal when an *f*T>MIC of >60% against *A. baumannii* thigh infection and >40% against *A. baumannii* lung infection was achieved.