

## P0292 Population pharmacokinetic analysis of anidulafungin in critically ill patients

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**Background:** Anidulafungin is used for the treatment of invasive candidiasis in critically ill patients. Physiological and pathological changes in those patients may result in variable pharmacokinetics. The objective of our study was to develop a model to describe the population pharmacokinetics of anidulafungin in critically ill patients and identify covariates which explain the significant variability mentioned by previous studies.

**Materials/methods:** A total of 192 plasma concentrations of Anidulafungin were collected from 13 patients at the ICUs of Attikon and Ippokrateion General Hospitals of Athens. A 100mg dose of Anidulafungin was administered as a short-time intravenous infusion once a day, while 9 patients out of 13 received a loading dose of 200 mg on the first day. Plasma sample collection followed a dense sample strategy, which included a pre-dose sample and 5 to 7 samples in a 24 hr time interval after the start of infusion. Anidulafungin concentrations were measured with a validated HPLC-fluorescence plasma assay method. The population PK analysis was performed using non-linear mixed effects modelling in NONMEM® (version 7.3). Covariates including body weight, height, and age, in addition to ICU specific covariates as the SOFA Score and APACHE II score were examined and the final model was validated based on the likelihood ratio test, diagnostic plots, and visual predictive checks.

**Results:** A two-compartment model, with first-order elimination and proportional residual error, best describes the time course of plasma Anidulafungin concentrations. The estimates of the PK parameters (inter-individual variability measured as CV%) were: Clearance (CL)= 0.868 L/h (49.7%), central volume of distribution (V1)=14.1 L (58.9%) , peripheral volume of distribution (V2)= 19.1 L/h (19.2%) , and inter-compartmental clearance (Q)= 4.67 L/h. A significant inter-occasion variability was estimated for Clearance and Central Volume to be 27.1 (%CV) and 38.1 (%CV) respectively. No statistically significant covariates were detected among those examined.

**Conclusions:** A model was developed for anidulafungin PK in ICU patients, based on dense data. The significant inter-occasion variability observed, challenges the need of dose optimization of anidulafungin. Further analysis, could examine the influence of time-varying covariates on PK parameters and explain the significant inter-occasion variability.