

**O1067 Population pharmacokinetics and pharmacodynamics of anidulafungin against *Candida albicans* in a cohort of critically ill patients**

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**Background:** Anidulafungin is commonly used for the treatment of *Candida* spp. infections in critically ill patients but limited pharmacokinetic data are available in this population. The objective was to assess the population pharmacokinetics (popPK) of anidulafungin in ICU patients.

**Materials/methods:** Twenty-three patients with a proven/suspected fungal infection were included (10 (43.5%) male; median (range): age 65 (28-81 years), total body weight (TBW): 75(54-168) kg; APACHE 21(10-48). All patients received a loading dose 200 mg followed by 100 mg/day. A of 106 blood samples were collected at different times of the dosing interval and anidulafungin concentrations were determined using HPLC. Median  $C_{min}$ ,  $C_{max}$  and  $AUC_{0-24h}$  were 2.9 (0.7-5.3) mg/L, 6.3 (3.9-11.8) mg/L and 77.9 (40.9-136.1) mg\*h/L, respectively.

One and two-compartment models were fitted with the Nonparametric Adaptive Grid (NPAG) algorithm (Pmetrics). Elimination from the central compartment and intercompartmental distribution were modeled as first-order processes. Patient' age, gender, TBW, APACHE and liver cirrhosis were evaluated as covariates. Models were assessed by comparison of the -2 log likelihood (-2LL), observed predicted values and visual predictive checks. A probability of target attainment (PTA) against *Candida albicans* was calculated using a free AUC/MIC target of 20 against different MIC values (0.002-16 mg/L) and patients' TBW (50,100 and 150 kg).

**Results:** A two-compartment linear model best described anidulafungin concentrations. TBW was associated with clearance (CL) and described using a power function ( $CL = CL_1 * (TBW/70)^{0.75}$ ). Table 1 shows the popPK estimates for anidulafungin.

	<b>Median</b>	<b>Mean</b>	<b>SD</b>
CL1 (L/h)	0.873	0.821	0.224
V (L)	9.966	12.219	9.434
K <sub>cp</sub> (h <sup>-1</sup> )	2.261	6.655	7.131
K <sub>pc</sub> (h <sup>-1</sup> )	0.791	1.359	1.417

A ≥ 90% PTA could be achieved for *C.albicans* isolates with MIC values ≤ 0.032 mg/L in patients with TBW ≤100 kg and with MIC values ≤ 0.016 mg/L for patients with TBW of 150 kg.

**Conclusions:** This is the largest population PK study of anidulafungin in ICU patients. The wild type population of *C.albicans* (ECOFF value 0.03 mg/L) could be covered with standard doses of anidulafungin in patients up to 100 kg. However, heavier patients may require higher doses of this antifungal to avoid potential clinical failures.

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