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MEETING ABSTRACT

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Anidulafungin concentrations in human tissues

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Background: Echinocandins such as anidulafungin (ANI) are recommended for the treatment of invasive candidiasis in critically ill patients. Data on target-site penetration in human tissues are sparse. Therefore, we assessed ANI concentrations in liver, lung, spleen, kidney, pancreas, myocardium and muscle tissue.
Methods: Human tissue samples were taken at routine autopsies of patients who had been treated with standard doses of ANI. ANI was measured by high-pressure liquid chromatography (HPLC) and UV detection. Sample preparation was performed by protein precipitation via acetonitrile and methanol, followed by mechanical homogenysation (Precelly's homogenizer) and centrifugation. For establishment and validation of the method and for preparation of HPLC standards, porcine and bovine tissues spiked with ANI were used. The lower limit of quantification (LLOQ) was 0.05 µg/g.
Results: The method fulfilled the requirements of the European Medicine Agency (EMA). Samples were obtained from four autopsy cases. Highest concentrations were found in the liver (13.5–56.2 µg/g) followed by the spleen (3.2–28.3 µg/g) and the lung (1.3–18.6 µg/g). Concentrations in pancreas (1.4–13.5 µg/g), kidney (0.0–11.4 µg/g), myocardium (0.3–4.1 µg/g) and muscle (0.5–8.2 µg/g) where lower. Duration of treatment ranged from 6 to 17 days, thus all patients were at steady state. Cumulative dose ranged from 700 to 1,800 mg. Time from last ANI infusion to death was 11.5–299 hours.
Discussion: ANI concentrations were highly variable, even within the same tissue. In most of the samples, ANI tissue concentrations exceeded the minimal inhibitory concentrations (MICs) reported for *Candida albicans* (0.008 to 2.0 µg/ml) and *C. glabrata* (0.015 to 4.0 µg/ml). ANI could be measured in the liver, in the lung, in the spleen, in the pancreas, in myocardium and in muscle tissue, even 11 days after the last infusion.
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Keywords: antifungals – invasive candidiasis – invasive fungal disease – tissue distribution – target-site pharmacokinetics

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