

## **New hplc–uv validated method for therapeutic drug monitoring of antifungal agents in acute myeloid leukemia.**

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Voriconazole (VRC) and posaconazole (PSC) are two antifungal drugs widely used in routine clinical practice for the treatment of invasive fungal infections. Aim of our work was to develop and validate, according Food and Drug Administration guidelines (FDA, 2001), an HPLC-UV method for the quantification of plasma concentrations of VRC and PSC. After specific extraction of analytes from plasma, chromatographic separation was achieved on C18 reverse phase column, the eluate was monitored at 250 nm wavelength and each run ended in 10 minutes. Method validation was conducted on three separate days. Range for calibration curves, based on the data available in the literature, was set at 0.125-8 mg/ml, while limits of quantification for VRC and PSC were, respectively, 0.100 and 0.030 mg/ml and limits of method sensitivity 0.050 and 0.020 mg/ml. For VRC we obtained a mean variability intra- and inter-day of 4.77 and 6.31%, a mean accuracy intra- and inter-day of 8.52 and 8.60% and a mean extraction recovery of 111.94%. For PSC we obtained a mean variability intra- and inter-day of 5.76 and 6.67%, a mean accuracy intra- and inter-day of 11.34 and 10.91% and a mean extraction recovery of 118.73%. Methodology developed and validated was used for the analysis of plasma samples of acute myeloid leukemia patients in therapy with VRC or PSC for treatment of fungal infections, in order to perform therapeutic monitoring of antifungal agents levels. We observed that drugs circulating levels found in patients were within the therapeutic range defined in the literature for VRC and PSC (Myrianthefs, 2010; Jang, 2010). Our developed validated method, therefore, easily applicable and reproducible, could be an useful tool in clinical routine in order to improve patients management for antifungal therapy.

FDA guidelines (2001). *Guidance for Industry Bioanalytical Method Validation*.

Myrianthefs (2010). *Int J Antimicrob Agents*. 35, 468-472.

Jang (2010). *Clin Pharmacol Ther*. 88, 115-119.