

O503

Abstract (oral session)

**Voriconazole therapeutic drug monitoring in haematological and intensive care unit (ICU) patients: a cohort study**

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Objectives: Studies have shown that voriconazole plasma concentrations (VPCs) vary widely. The objective of this cohort study was to evaluate VPCs among ICU and hematological patients. Methods: The study was conducted from August 2011 to September 2012 at the Medical University Hospital Graz, Austria. All trough VPCs measured during that time in patients with hematological malignancies or at ICU were included. The primary goal in this real life setting was to identify risk factors for insufficient VPCs. VPCs were analyzed with high performance liquid chromatography, the target range was defined from 1.5 to 5.5mg/L. Statistical analysis including multivariate logistic regression analysis was performed using SPSS. Results: A total of 221 trough VPCs were analyzed in 61 patients receiving voriconazole (144 VPCs in 40 hematology; 77 VPCs in 21 ICU patients). Twenty hematological patients received prophylaxis, all other patients voriconazole therapy. 124 of 221 VPCs (56%) were found under the targeted range. VPCs were significantly higher among patients that received therapeutic ( $p < 0.001$ ) and intravenous formulation ( $p = 0.018$ ), that experienced a side effect ( $p < 0.001$ ), that survived at 6 weeks ( $p = 0.03$ ) and that did not receive concomitant ppi ( $p = 0.015$ ). No significant difference was found for other variables (e.g. corticosteroids or rifampicin, sex, diarrhea) as well as between hematologic and ICU patients with therapeutic voriconazole. Body-mass index was significantly higher among patients with VPCs  $> 1.5$  ( $p < 0.001$ ) as was age ( $p < 0.001$ ). Multivariate analysis revealed that VPCs  $> 1.5$  were associated with clinical response ( $p = 0.015$ ; OR 2.922, 95% CI 1.228-6.954), therapeutic usage ( $p < 0.001$ ; OR 11.172, 95% CI 4.386-28.461), older age ( $p = 0.003$ ; OR 1.046, 95% CI 1.016-1.077 per year) and occurrence of side effects ( $p = 0.031$ ; OR 10.727, 95% CI 1.235-93.142), while not reaching sufficient levels was associated with use of proton-pump inhibitors ( $p < 0.001$ ; OR 0.190, 95% CI 0.071-0.504). The target was reached by 79/221 (36%) of samples. In 18 samples potentially toxic levels were measured. Concerning toxicity neurological side effects occurred in 6 (associated with VPCs of 3.0, 4.5, 4.7, 4.9, 5.1, and 5.9) and cholestatic hepatopathy in 5 patients. Conclusion: VPCs below target were frequently found in hematology and ICU patients. Multivariate analysis identified younger age, prophylaxis, absence of clinical response and side effects and concomitant ppi as risk factors for insufficient levels.