

P858

Abstract (poster session)

**Posaconazole plasma concentrations and invasive mould infection in patients with haematologic malignancies: a cohort study**

M. Hoenigl\*, R. Raggam, T. Valentin, H. Salzer, A. Valentin, A. Woelfler, K. Seeber, A. Strohmeier, I. Zollner-Schwetz, A. Grisold, H. Sill, R. Krause (Graz, AT)

**Objectives:** Posaconazole is a new triazole antifungal agent that has broad activity against pathogenic fungi and is increasingly used for prophylaxis and treatment of invasive mould infections (IMI). Posaconazole is available only as oral formulation with varying absorption from the gastro-intestinal tract. Reports correlating posaconazole plasma concentrations (PPCs) with breakthrough IMI, however, are rare. **Methods:** We analyzed posaconazole plasma concentrations (PPCs) in a prospective observational single-centre study in 2010 and evaluated correlation of PPCs with breakthrough IMI in patients with hematological malignancies. We further evaluated risk factors associated with low PPCs. **Results:** A total of 109 PPCs were measured in 34 patients receiving posaconazole prophylaxis (n=31) or treatment (n=3). Insufficient levels were detected in 24/34 (70%) of patients; in 15 of these 24 patients concentrations were found under the limit of detection (<0.20 µg/ml). Insufficient PPCs yielded either way in a modification of intake procedures, discontinuation of PPIs or switch of antifungal therapy. In 12 of these 24 cases with insufficient PPC, modification of intake - i.e. with a high fat meal - led to sufficient PPCs. As discontinuation of PPIs led to an improvement of PPC levels in only 1/24 cases, antifungal therapy had to be switched due to insufficient PPCs in another 5 cases. In three patients with insufficient PPCs, antifungal therapy had to be changed from posaconazole prophylaxis to echinocandin empiric treatment due to development of febrile neutropenia, these patients did not fulfil IFI criteria. Three patients on posaconazole prophylaxis met the criteria of breakthrough infection. Prior to development of invasive fungal infection (IFI), however, PPCs were insufficient in all three patients. Details are depicted in table 1. Associated risk factors for insufficient PPCs varied from previous reports. **Conclusion:** These data demonstrate that therapeutic drug monitoring (TDM) of posaconazole is mandatory in all patients with hematological malignancies as low PPCs are common and may be associated with development of IFI.

Table 2: IMI under Posaconazole prophylaxis

Fungal species	Posaconazole MIC (mg/L)	Patient's age years/ sex	Specimen of fungal detection	Days of posaconazole prophylaxis before breakthrough infection	Last posaconazole plasma level before diagnosis of IMI (days before diagnosis)	Antifungal therapy after IMI diagnosis	Outcome
<i>Aspergillus fumigatus</i>	0.032	58/f	BAL	8	0.28 µg/ml (1)	Voriconazole	Died
<i>Aspergillus</i> spp.	n.a.	20/m	BAL / Serum	23	<0.20 µg/ml (4)	Voriconazole	Survived
<i>Geosmithia argillacea</i>	0.25	52/m	BAL / Blood culture	>60	0.31 µg/ml (7)	Voriconazole, Lip.Amph B	Died

Abbreviation: f, female; m, male; BAL, Bronchoalveolar-lavage fluid; n.a., not available.