



CORRELATION OF EARLY TROUGH LEVELS (DAY 4) WITH STEADY-STATE POSACONAZOLE PLASMA CONCENTRATIONS - A COHORT STUDY

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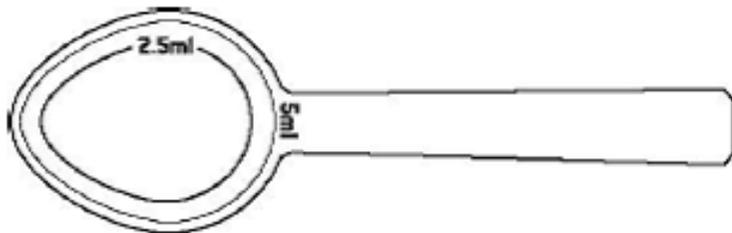
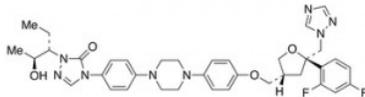
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Introduction

Low posaconazole plasma concentrations (PPCs) may be associated with breakthrough invasive mould infections (IMI) among patients with hematological malignancies. Generally it is considered that steady-state plasma concentrations of posaconazole are achieved after 6 to 10 days. The purpose of this study was to correlate PPCs measured early (day 4 of prophylaxis) with those obtained during steady state.

Materials and Methods

The study was conducted at the Division of Hematology, Medical University of Graz, Austria between June 2012 and May 2013. Hematologic patients receiving posaconazole with initial trough PPCs obtained on day 4 of prophylaxis and then subsequent PPCs obtained between day 7 and 8 (defined as 'early steady state') as well as between days 10 and 14 (defined as 'late steady state') were included. The two steady state time points were always compared to concentrations of day 4. PPCs above the target of 0.5 mg/L were defined as satisfactory and those below the target as low PPCs.



Results

A total of 37 patients with PPCs obtained at all 3 time points were included. 8 patients (22%) had PPCs below 0.2 on day 4. PPCs remained unchanged in all patients at early steady state, while at late steady state 1/8 had a satisfactory PPC and 3/8 had PPCs between 0.2 and 0.5. 11 patients (30%) had PPCs between 0.2 and 0.5 at day 4. At early steady state 2 of those 11 patients had satisfactory levels and one a PPC <0.20, while PPCs remained unchanged in 8/11 patients. At late steady state PPCs had decreased in 2 pts to <0.2 and increased in 3 pts to >0.5, while they remained unchanged in 6/11 patients. The majority of included patients (n=18; 49%) had satisfactory PPCs on day 4. PPCs decreased below 0.5 in 4/18 patients at early and 3/18 patients at late steady state (each compared to day 4). Concentrations remained satisfactory in 14/18 patients at early steady state and 15/18 patients at late steady state, although accumulating to twice or more of the initial day 4 PPC in 4 patients at early and 6 at late steady state.

Conclusions

A positive correlation was found between PPCs obtained on day 4 and those on days 7/8 and 10-14. In patients with insufficient PPCs on day 4 only 4/19 had satisfactory PPCs at late steady-state. In patients with PPCs >0.5 on day 4 concentrations remained satisfactory in nearly 80% at both steady-state time points. Bigger studies are needed to evaluate potential benefits of early PPC measurements and early intervention (e.g. modification of intake procedure and dosage).



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