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EXPERIENCE IN THE PHARMACOKINETIC MONITORING OF POSACONAZOLE IN ORAL SUSPENSION AS PROPHYLAXIS IN IMMUNOCOMPROMISED PEDIATRIC PATIENTS

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BACKGROUND AND IMPORTANCE

The Pediatric Antimicrobial Stewardship Program promotes rational antifungal use and monitoring of antifungals.

AIM AND OBJECTIVES

To describe the experience with **pharmacokinetic monitoring of posaconazole suspension** in immunocompromised pediatric patients, **and to evaluate its effectiveness and safety.**

MATERIALS AND METHODS

- Single-center **retrospective** study (January 2017– December 2023)
- **Immunocompromised pediatric patients** (< 18 years) receiving **posaconazole suspension prophylaxis** with at least one plasma concentration (Cp) determination (obtained at least 5-7 days after initiation to ensure steady-state).
- **Therapeutic range** considered was **0.7–2.5 µg/ml.**
- Demographic, clinical, and pharmacological variables were collected.
- *Quantitative variables were expressed as median ± interquartile range (IQR), and qualitative variables as number (%). Statistical analysis was performed using SAS® software.*

Initial dosing posaconazole suspension:

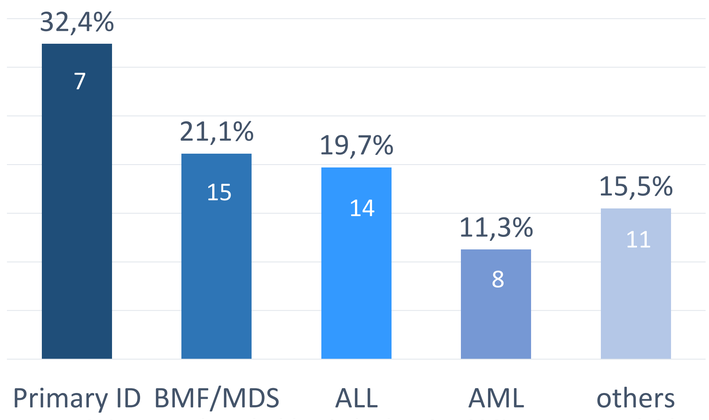
- 4mg/kg/8h if weight <34 kg.
- 200 mg/8h if weight >34 kg.
- in chronic granulomatous disease, dosing was every 12h (Welzen et al. 2011)

RESULTS

Cohort Characteristics

- **71 patients (67.6% male).**
- Median age: **4.8** (IQR 2.4–8.9) **years.**

Distribution of underlying condition



ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; BMF, bone marrow failure; MDS, mielodysplastic sindrom; ID, inmunodeficiencies.

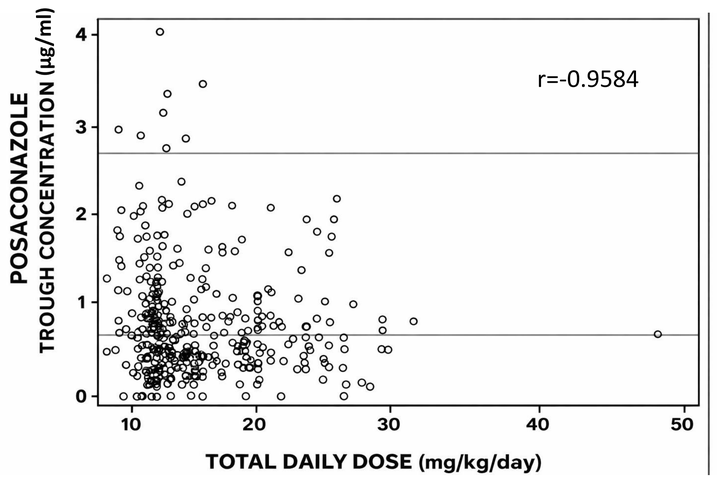
Pharmacokinetic Monitoring

•**373 posaconazole Cp** were analyzed:

Cp	Number (%)
Therapeutic	**178 (47.8%)**
Subtherapeutic	**187 (50.1%)**
Supratherapeutic	**8 (2.1%)**

•Median daily dose: **13.4** (IQR 12–18.4) **mg/kg/day.**
•Median duration of prophylaxis: **209** (IQR 91–444) **days.**

Relation between Cp and daily dose



- **no differences in dose were found between therapeutic and supratherapeutic Cp (p=0.0614).**

Breakthrough invasive fungal infection (IFI)

- 6 (8.5%) patients **developed IFI** (3 proven,3 probable).
- Median time to IFI was 78.6 (IQR 51–140) days.

Patients	Cp subterapheutic	p
IFI (n=6)	11/16 (68.7%)	p=0.128
No IFI (n=65)	176/357 (49.2%)	

- Patients with IFI presented a higher proportion of subtherapeutic Cp than the rest of the cohort, although without achieving statistical significance.

Safety of posaconazole suspension

Prophylaxis was **discontinued in 4 (5.6%).**

Adverse events:

- transaminase elevation (2/4).
- gastrointestinal disorders (2/4).
- skin reactions (2/4).

CONCLUSIONS

- **Therapeutic drug monitoring (TDM) of posaconazole suspension is essential** in immunocompromised pediatric patients receiving antifungal prophylaxis.
- The **standard prophylactic dose may be insufficient**, as reflected by the high proportion of **subtherapeutic plasma concentrations.**
- Despite frequent subtherapeutic levels, **posaconazole was generally well tolerated**, with a low rate of treatment discontinuation due to adverse events.