**Objectives**:   
In 2023, isavuconazole, a triazole antifungal, was registered for paediatric patients. Isavuconazole is described to have a favourable safety profile, less drug-drug interactions, predictable pharmacokinetics, and large spectrum of action. We aimed to assess the real-world usage and exposure of isavuconazole in paediatric patients.

**Materials & Methods:** This cohort study describes the experience with isavuconazole in paediatric oncology patients between 2018-2023 in the Princess Máxima Center, the Netherlands. Standard starting intravenous dose was 5.4 mg/kg/day after a loading dose of three times daily 5.4 mg/kg/dose for 2 days) or a bodyweight dependent dose with 100 mg increments. TDM was performed using a target Ctrough of 2-4 mg/L, or higher if clinically indicated. Clinical data were extracted from patient records. Laboratory toxicity data were classified following the Common Terminology Criteria for Adverse Events. Drug concentrations were used to calculate isavuconazole exposure by *post hoc* estimation using non-linear mixed-effects modelling1. Exposure was expressed as average 24-hours area under-the-concentration-time curve during the first week of treatment (AUC24), using the adult average exposure of 60-233 mg·h/L2 as target exposure.

**Results**:   
Isavuconazole was administered to 77 patients (median age 8.0 (range, 0.6-18.0) years) during 92 episodes. 72/77 patients had a haematological malignancy and 34/77 underwent an HSCT. Isavuconazole was prescribed as therapy (56.5%), therapy and secondary prophylaxis (16.3%), secondary prophylaxis (20.7%), primary prophylaxis and therapy (1.1%), and primary prophylaxis (5.4%). Isavuconazole was mainly (78.2%) deployed as second-line treatment. Primary reasons to start isavuconazole were persistent suboptimal concentrations of alternative azoles (40.2%), toxicity of alternatives (29.3%), its broad antifungal spectrum and cerebral penetration (22.8%). The median episode duration was 75 (IQR, 44-115) days. The main site of infection was pulmonary (97.8%), in 31.1% with cerebral involvement. 68.9% of infections were probable/proven3. Treatment was completed in all patients without discontinuation due to definite drug-related toxicity. Observed laboratory toxicity (grade 3/4 toxicity) were: hepatoxicity (59.8%), electrolyte disbalance (48.3%), and nephrotoxicity (3.4%). Toxicity was mainly due to the existing underlying disease, and unlikely related to isavuconazole.   
958 isavuconazole plasma concentrations were available, of which 746 Ctrough (figure 1). The median Ctrough was 3.2 (range, 0.04-12.6) mg/L, 46.1% of all measurements were between 2.0-4.0 mg/L. The intra-patient variation expressed as coefficient of variation, was 31.7% (IQR 21.2%-42.3%). The median model predicted AUC24 was 79.2 (range, 35.2-95.8) mg·h/L, expressed as daily average during the first week of treatment, and >60 mg·h/L in 81.8% of patients (figure 2). Adequate AUC24 was reached after median 3.0 (range 2.0-19.0) days, and in 70.1% directly after loading dose. Despite a Ctrough <2.0 mg/L in the first week of treatment, 67.7% had an adequate average AUC24 of above 60 mg·h/L.

**Conclusions**:   
We describe, to our knowledge, the largest cohort of paediatric patients receiving isavuconazole. Isavuconazole was generally well tolerated within this population where laboratory toxicity was most likely caused by extensive co-medication. Overall, adequate exposure was reached albeit at the lower boundary of the adult equivalent exposure. Substantial inter- and intra-patient variability in exposure highlights the need for TDM in this population.

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