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Therapeutic drug monitoring of posaconazole oral suspension in pediatric patients younger than 13 years of age: a retrospective analysis and literature review

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Abstract

What is Known and Objective—Posaconazole is an extended-spectrum triazole antifungal with activity against a variety of clinically significant yeasts and molds. Posaconazole is not currently approved by the U.S. Food and Drug Administration for use in children younger than 13 years of age. Our primary objective was to describe the dosing and observed trough concentrations with posaconazole oral suspension in pediatric patients at the National Institutes of Health Clinical Center (Bethesda, MD).

Methods—This retrospective single-center study reviewed pediatric patients younger than 13 years of age initiated on posaconazole oral suspension. Patients were included if they were initiated on posaconazole for prophylaxis or treatment of fungal infections from September 2006

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

Online Appendix/Supplemental Digital Content 1.

Table which describes the identified publications (pdf)

through March 2013 with at least one trough concentration collected after at least 7 days of therapy.

Results and Discussion—A total of 20 male patients were included, of whom 15 (75%) had chronic granulomatous disease. The median age of patients was 6.5 years (range: 2.8 – 10.7). A total of 79 posaconazole trough concentrations were measured in patients receiving posaconazole as prophylaxis (n=8) or treatment (n=12). Posaconazole dose referenced to total body weight ranged from 10.0 – 49.2 mg/kg/day. Posaconazole trough concentrations ranged from undetectable (<50 ng/mL) up to 3620 ng/mL and were 500, 700, and 1250 ng/mL in 95, 60, and 25% of patients, respectively.

What is New and Conclusions—Patients younger than 13 years of age had highly variable trough concentrations and recommendations for the appropriate dosing of posaconazole oral suspension remain challenging. Until studies are conducted to determine the appropriate dosing of posaconazole in this patient population, therapeutic drug monitoring should be considered to ensure adequate posaconazole exposure.

Keywords

posaconazole; pediatric; therapeutic drug monitoring; pharmacokinetics

WHAT IS KNOWN AND OBJECTIVE

Posaconazole is an extended-spectrum triazole antifungal with potent *in vitro* activity against pathogenic yeasts and molds.¹ In the United States, the oral suspension, delayed-release tablet, and intravenous formulation of posaconazole are indicated for the prophylaxis of invasive *Aspergillus* and *Candida* infections in high-risk patients. In addition, the oral suspension is indicated for the treatment of oropharyngeal candidiasis including cases refractory to itraconazole or fluconazole. Posaconazole oral suspension and the delayed-release tablet are approved for patients 13 years of age and older; however, the intravenous formulation is only approved for patients 18 years of age and older.² As such, clinical experience and pharmacokinetic data are limited in pediatric patients younger than 13 years of age; nonetheless, posaconazole is an attractive agent for this population because of its extended-spectrum of activity and favorable adverse event and drug interaction profile compared to itraconazole and voriconazole.

The use of posaconazole oral suspension can be limited by its variable oral bioavailability, even when used as approved by the U.S. Food and Drug Administration for patients 13 years of age and older. Factors that can potentially reduce the systemic exposure of posaconazole oral suspension include drug-drug interactions, increase in gastric pH, increase in gastric motility, administration in a fasted state, administration via nasogastric tube, mucositis, and diarrhea.^{2–5} In adults, posaconazole oral suspension exhibits linear pharmacokinetics between doses of 50 – 800 mg; however, saturable absorption occurs when single doses exceed 800 mg.⁶ In addition to the inter- and inpatient variability shown by posaconazole oral suspension, defining accurate target concentrations for posaconazole remains challenging. Target posaconazole concentrations greater than or equal to 700 ng/mL for prophylaxis and greater than or equal to 1000 ng/mL for treatment have been suggested.^{7–9}

The primary objective of this retrospective analysis was to describe posaconazole dosing and observed trough concentrations in pediatric patients enrolled in various study protocols of the National Institute of Allergy and Infectious Diseases (NIAID) at the National Institutes of Health Clinical Center (Bethesda, MD).

METHODS

This study was conducted under protocol number 09-I-N145 and was approved by the NIAID Institutional Review Board. This single-center retrospective study included pediatric patients younger than 13 years of age initiated on posaconazole oral suspension from September 2006 through March 2013. Posaconazole trough concentrations were collected within 2 hours prior to the first daily dose and after at least 7 days of therapy to ensure achievement of steady-state concentrations. Posaconazole serum concentrations were determined using a validated assay by liquid chromatography-tandem mass spectrometry assay at Mayo Medical Laboratories (Rochester, MN), or by high performance liquid chromatography at the Fungus Testing Laboratory (San Antonio, TX). Definitions for posaconazole indication were taken from the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group.¹⁰

Demographic variables assessed included the following: age, race, sex, weight, underlying diagnosis, presence/absence of gastrointestinal (GI) disease (e.g., chronic granulomatous disease [CGD] colitis), and use of proton pump inhibitors (PPIs) or histamine H₂-receptor antagonists (H₂RAs). Patient weight, daily posaconazole dose and trough posaconazole concentration were recorded so that the dose per weight (mg/kg/day) and concentration per dose (ng/mL/mg) could be normalized. We examined the potential association with patient characteristics and the within-person average concentration. Univariate associations were examined with Wilcoxon rank-sum test for dichotomous variables and linear regression for the continuous variables of age and weight. All tests were two-sided and a p-value <0.05 was considered significant. Analyses were performed using SAS 9.3 (Cary, NC) and R v2.15 (Vienna, Austria).

RESULTS

A total of 20 male patients meeting inclusion criteria were evaluated for the study. Patient demographics, underlying diagnosis, and posaconazole doses and trough concentrations are included in Table 1. There were 13 White, 5 Black, and 2 Hispanic subjects. At the time of posaconazole initiation, the most common underlying diagnosis was CGD (75%) and the median age was 6.5 years (range: 2.8 – 10.7). Posaconazole was used as primary prophylaxis in 3 patients, secondary prophylaxis in 5 patients, and treatment of probable or proven invasive fungal diseases in 12 patients. All patients received posaconazole via oral administration, 7 patients were taking a concomitant PPI, 2 patients were taking a concomitant H₂RA, and 8 patients had CGD colitis. Posaconazole was generally well tolerated and was not discontinued in any patient because of a suspected adverse event.

Posaconazole was dosed 2 to 4 times daily and the dose referenced to total body weight ranged from 10 – 49.2 mg/kg/day. A total of 79 posaconazole trough concentrations were measured as described above. Three patients had a single concentration measured and 17 patients had multiple concentrations measured, with a median of 3 concentrations per patient (range: 2 – 12). Posaconazole trough concentrations ranged from undetectable (< 50 ng/mL) up to 3620 ng/mL, and were 500, 700, and 1250 ng/mL in 95, 60, and 25% of patients, respectively.

The covariates assessed for an association with normalized posaconazole concentration included indication (prophylaxis/treatment), GI disease (yes/no), use of PPI/H2RA, race (White or non-White), weight, and age. Only indication and age were found to be significant. An individual's average normalized concentration (ng/mL/mg), is expected to decrease by 0.23 (95% CI: 0.04 – 0.43) ng/mL/mg for every year increase in age ($p=0.02$). Median within-person average concentration for those taking posaconazole as prophylaxis was 2.34 ng/mL/mg (range: 1.09 – 4.77) compared to 0.89 ng/mL/mg (range: 0.56 – 2.70) for those taking posaconazole for treatment of a probable or proven fungal infection ($p=0.01$). A similar analysis of the non-normalized concentration revealed no significant associations, though indication trended towards significance with a median concentration of 1114 ng/mL (range: 610 – 2386) in the treatment group versus 686 ng/mL (range: 444 – 2160) in the prophylaxis group ($p=0.07$).

DISCUSSION

To date, only a small number of studies and case reports in patients younger than 13 years of age include both the posaconazole dose and observed concentration. A recent literature review summarized studies of posaconazole in pediatric patients 12 years of age and younger through December 2013.¹¹ To identify additional patients, we conducted an updated literature review of posaconazole oral suspension in pediatric patients younger than 13 years of age (see Table, Online Appendix/Supplemental Digital Content, which describes the identified publications). In our review of the literature, 10 publications were identified.^{12–21} For the indication of treatment, one prospective cohort study¹², four case reports^{13–16}, and one retrospective cohort study¹⁷ described the use of posaconazole in 29 patients younger than 13 years of age using doses of 9 – 70 mg/kg/day. Reported posaconazole concentrations ranged from 85 – 2160 ng/mL.^{12–17} For the indication of prophylaxis, two prospective cohort studies^{18,21} and two retrospective cohort studies^{19,20} described the use of posaconazole in 53 patients younger than 13 years of age using doses of 10 – 21.2 mg/kg/day. Reported posaconazole trough concentrations ranged from 104 – 3285 ng/mL in three studies^{18–20}, and the fourth study²¹ reported a mean trough concentration of 850 ng/mL (range not reported). Many of the published reports included small numbers of patients and did not contain details regarding concomitant medications or the amount or type of foods administered with each dose. Two additional publications, which described patients who received posaconazole oral suspension via feeding tube, were not included in our literature review because this route of administration has been shown to reduce posaconazole exposure.^{2,5} The first case report described two pediatric patients with *Rhizopus* spp. infections after allogeneic bone marrow transplants who received high-dose posaconazole oral suspension (120 – 300 mg/kg/day) via nasogastric and jejunostomy tube. The first

patient was a 10-year-old male (weight: 19.1 kg) on concomitant phenytoin, and the second patient was a 19-month-old male (weight: 11.6 kg). Even with high-dose therapy using divided doses, continuous administration, use of enteral nutrition, and limited use of gastric acid-blocking agents, posaconazole concentrations in both patients were less than 1000 ng/mL.²² The second case report described a 2-year-old male (weight: 13 kg) with rhino-cerebral-orbital zygomycosis receiving posaconazole oral suspension by gastrostomy tube. To obtain posaconazole concentrations >1250 ng/mL, the posaconazole dose was increased from 100 mg/dose every 6 hours to 200 mg/dose every 6 hours (61.5 mg/kg/day).²³ If posaconazole oral suspension must be administered via a feeding tube, it is recommended to closely monitor patients for breakthrough fungal infections because reduced exposure may be associated with an increased risk of treatment failure.² Therapeutic drug monitoring is also recommended to ensure adequate posaconazole exposure.

In the current investigation, posaconazole trough concentrations ranged from undetectable up to 3620 ng/mL, and the weight-normalized dose ranged from 10.0 – 49.2 mg/kg/day. An argument could be made that the variability in posaconazole concentrations would be expected with such a wide range of doses; however, variable oral bioavailability has been established with posaconazole oral suspension.^{4,7} In addition, three of the cohort studies identified in the pediatric literature review reported significant variability in posaconazole concentrations when using a standardized posaconazole dose based on body weight or body surface area.^{19–21}

Posaconazole oral suspension should always be given with, or immediately after food or a nutritional supplement to maximize oral bioavailability. If concentrations are found to be subtherapeutic, a review of the patient's dietary intake should be performed and high-fat items could be used. Other strategies that can be used include further dividing the daily dose or administration with an acidic beverage.^{24,25} Although PPIs and H2RAs did not significantly decrease posaconazole concentrations in our study, when administered with concomitant posaconazole oral suspension, these two classes of medications have been shown to lower posaconazole exposure.^{2,24,25} Therefore, avoidance of these agents in the setting of suboptimal posaconazole concentrations is still recommended.

Potential limitations to our study include its retrospective nature and relatively small sample size which consisted primarily of male CGD patients; therefore, our results cannot necessarily be extrapolated to other patient populations. In addition, adherence for outpatients and timing of posaconazole administration with regards to meals was not recorded. Outcomes were not reported because many of our patients receive care at other institutions and full histories are not always available. In addition, interpreting the exact role of posaconazole in patient outcomes is limited by concurrent or sequential treatment with other antifungal agents, and in some patients, adjunctive surgical debridement or granulocyte transfusion. Moreover, there may be additional variables, not identified in this investigation, which may have influenced posaconazole disposition and subsequent concentrations. Nevertheless, our data reflect the use of posaconazole oral suspension in a unique patient population.

WHAT IS NEW AND CONCLUSION

In conclusion, we found a wide range of dosing and high inter- and inpatient variability in posaconazole concentrations which make it difficult to determine the optimal dose and frequency in patients younger than 13 years of age. Based on our findings and the published literature, there may not be a predictable approach for a dose-concentration correlation. Before implementing therapy with posaconazole oral suspension in pediatric patients, the following factors should be reviewed: (1) route of administration, (2) patient's ability to take the drug with meals, liquid nutritional supplement, or an acidic carbonated beverage, (3) number of daily posaconazole doses, and (4) concomitant medications that can decrease posaconazole exposure. Therapeutic drug monitoring can be used to assess posaconazole adherence and verify adequate drug exposure; this approach serves to maximize the potential for therapeutic success, particularly in the treatment of invasive fungal diseases.

Further pharmacokinetic studies of posaconazole in diverse patient populations are needed to optimize its use, especially in pediatric patients younger than 13 years of age. Compared to the oral suspension, the posaconazole delayed-release tablet has an improved pharmacokinetic profile including greater oral bioavailability and less frequent dosing.^{2,3} Unfortunately, the posaconazole delayed-release tablet is not approved for use in children younger than 13 years of age. Age notwithstanding, some patients may have difficulty swallowing the delayed-release tablet, which is an important consideration, as they cannot be crushed or divided.² In addition, alternative dosing strategies in pediatric patients using body surface area or a new formulation of posaconazole oral suspension with improved oral bioavailability similar to the delayed-release tablet should be considered.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Sabatelli F, Patel R, Mann PA, et al. In vitro activities of posaconazole, fluconazole, itraconazole, voriconazole, and amphotericin B against a large collection of clinically important molds and yeasts. *Antimicrob Agents Chemother.* 2006; 50:2009–15. [PubMed: 16723559]
2. Noxafil (posaconazole) [package insert]. Whitehouse Station, NJ: Merck & Co., Inc; 2015.
3. Krishna G, Ma L, Martinho M, et al. Single-dose phase I study to evaluate the pharmacokinetics of posaconazole in new tablet and capsule formulations relative to oral suspension. *Antimicrob Agents Chemother.* 2012; 56:4196–201. [PubMed: 22615291]
4. Dolton MJ, Brüggemann RJ, Burger DM, et al. Understanding variability in posaconazole exposure using an integrated population pharmacokinetic analysis. *Antimicrob Agents Chemother.* 2014; 58:6879–85. [PubMed: 25199779]
5. Dodds Ashley ES, Varkey JB, Krishna G, et al. Pharmacokinetics of posaconazole administered orally or by nasogastric tube in healthy volunteers. *Antimicrob Agents Chemother.* 2009; 53:2960–4. [PubMed: 19433558]

6. Courtney R, Pai S, Laughlin M, et al. Pharmacokinetics, safety, and tolerability of oral posaconazole administered in single and multiple doses in healthy adults. *Antimicrob Agents Chemother.* 2003; 47:2788–95. [PubMed: 12936975]
7. Jang SH, Colangelo PM, Gobburu JV. Exposure-response of posaconazole used for prophylaxis against invasive fungal infections: evaluating the need to adjust doses based on drug concentrations in plasma. *Clin Pharmacol Ther.* 2010; 88:115–19. [PubMed: 20505665]
8. Walsh TJ, Raad I, Patterson TF, et al. Treatment of invasive aspergillosis with posaconazole in patients monitoring who are refractory to or intolerant of conventional therapy: an externally controlled trial. *Clin Infect Dis.* 2007; 44:2–12. [PubMed: 17143808]
9. Ashbee HR, Barnes RA, Johnson EM, et al. Therapeutic drug monitoring (TDM) of antifungal agents: guidelines from the British Society for Medical Mycology. *J Antimicrob Chemother.* 2014; 69:1162–76. [PubMed: 24379304]
10. De Pauw B, Walsh TJ, Donnelly JP, et al. Revised definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group. *Clin Infect Dis.* 2008; 46:1813–21. [PubMed: 18462102]
11. Gwee A, Cranswick N, Curtis N. Posaconazole: promising but problematic in practice in pediatric patients. *Pediatr Infect Dis J.* 2015; 34:604–6. [PubMed: 25973938]
12. Krishna G, Sansone-Parsons A, Martinho M, et al. Posaconazole plasma concentrations in juvenile patients with invasive fungal infection. *Antimicrob Agents Chemother.* 2007; 51:812–8. [PubMed: 17210771]
13. Sedlacek P, Vavra V, Masova I, et al. Successful therapy with ABLC, surgery and posaconazole for *Rhizopus microsporus* var. *rhizopodiformis* liver eumycetoma in a child with acute leukaemia. *Mycoses.* 2009; 52:276–9. [PubMed: 18643916]
14. Srinivasan A, Wickes BL, Romanelli AM, et al. Cutaneous infection caused by *Macrosporum phaseolina* in a child with acute myeloid leukemia. *J Clin Microbiol.* 2009; 47:1969–72. [PubMed: 19386841]
15. Lür S, Berger S, Diepold M, et al. Treatment of intestinal and hepatic mucormycosis in an immunocompromized child. *Pediatr Blood Cancer.* 2009; 52:872–4. [PubMed: 19127570]
16. Wildenbeest JG, Oomen MW, Brüggemann RJ, et al. *Rhizopus oryzae* skin infection treated with posaconazole in a boy with chronic granulomatous disease. *Pediatr Infect Dis J.* 2010; 29:578.
17. Bernardo VA, Cross SJ, Crews KR, et al. Posaconazole therapeutic drug monitoring in pediatric patients and young adults with cancer. *Ann Pharmacother.* 2013; 47:976–83. [PubMed: 23737511]
18. Welzen ME, Brüggemann RJ, Van Den Berg JM, et al. A twice daily posaconazole dosing algorithm for children with chronic granulomatous disease. *Pediatr Infect Dis J.* 2011; 30:794–7. [PubMed: 21772229]
19. Döring M, Müller C, Johann PD, et al. Analysis of posaconazole as oral antifungal prophylaxis in pediatric patients under 12 years of age following allogeneic stem cell transplantation. *BMC Infect Dis.* 2012; 12:263. [PubMed: 23082876]
20. Heinz WJ, Cabanillas Stanchi KM, Klinker H, et al. Posaconazole plasma concentration in pediatric patients receiving antifungal prophylaxis after allogeneic hematopoietic stem cell transplantation. *Med Mycol.* 2016; 54:128–37. [PubMed: 26483433]
21. Vanstraelen K, Colita A, Bica AM, et al. Pharmacokinetics of posaconazole oral suspension in children dosed according to body surface area. *Pediatr Infect Dis J.* 2016; 35:183–8. [PubMed: 26544987]
22. Matthias KR, Nix DE, Peloquin CA, et al. Poor absorption of high-dose posaconazole in pediatric bone marrow transplant patients. *Ann Pharmacother.* 2012; 46:e22. [PubMed: 22872751]
23. Egelund EF, Egelund TA, Ng JS, et al. Posaconazole pharmacokinetics in a 2-year-old boy with rhino-cerebral-orbital zygomycosis. *Pharmacotherapy.* 2013; 33:e1–8. [PubMed: 23307552]
24. Walravens J, Brouwers J, Spriet I, et al. Effect of pH and comedication on gastrointestinal absorption of posaconazole: monitoring of intraluminal and plasma drug concentrations. *Clin Pharmacokinet.* 2011; 50:725–34. [PubMed: 21973269]

25. Krishna G, Moton A, Ma L, et al. Pharmacokinetics and absorption of posaconazole oral suspension under various gastric conditions in healthy volunteers. *Antimicrob Agents Chemother.* 2009; 53:958–66. [PubMed: 19075045]

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TABLE 1
Demographics and Characteristics of Pediatric Patients (<13 years of age) Receiving Posaconazole Oral Suspension

Patient no.	Age* (years)	Sex	Underlying Disease	Indication	Weight [†] (kg)	Posaconazole Dose and Frequency	Posaconazole Weight-Normalized Dose [‡] (mg/kg/day)	Posaconazole Concentrations (ng/mL) Concentration or Median [‡] (range)	PPI/H2RA*
1	2.8	M	CGD (gp91)	Primary Prophylaxis Liver enzyme elevation with itraconazole	17.0	200 mg BID	23.5	495 (133 – 1060)	PPI
2	2.9	M	CGD (gp91)	Primary Prophylaxis Liver enzyme elevation with itraconazole	15.9	300 mg BID	37.7	752	
3	4.1	M	CGD (gp91)	Secondary Prophylaxis <i>Aspergillus</i> spp.	15.8	200 mg TID	40.0	1340 (1230 – 1660)	None
4	4.6	M	CGD (gp91)	Probable IFD, Lung Organism not identified	14.4	200 mg BID	27.8	1075 (869 – 1280)	None
5	5.0	M	CGD (p67)	Probable IFD, Lung Organism not identified	19.4	200 mg QID	41.2	587 (573 – 630)	None
6	5.4	M	CGD (gp91)	Probable IFD, Lung Organism not identified	20.5	400 mg BID	39.0	582 (354 – 721)	
7	5.7	M	HIES (STAT3)	Secondary Prophylaxis <i>Aspergillus</i> spp.	15.3	200 mg TID	39.2	473 (226 – 1030)	PPI
8	5.9	M	CGD (gp91)	Proven IFD, Lung and Bone <i>Aspergillus nidulans</i>	20.0	100 mg BID	10.0	596	None
9	6.3	M	CGD (gp91)	Secondary Prophylaxis <i>Aspergillus</i> spp.	20.5	200 mg BID	19.5	674	
10	6.4	M	CGD (gp91)	Proven IFD, Lung <i>Inocutis/Inonotus/Phellinus</i> group	16.2	200 mg TID	37.0	890 (774 – 1510)	PPI
11	6.7	M	CGD (gp91)	Primary Prophylaxis	20.4	200 mg TID	29.4	2480 (849 – 3620)	H2RA
					16.7	200 mg QID	47.9	408 (<50 – 936)	PPI
					19.7	200 mg QID	40.6	1110	None
					19.5	280 mg TID	43.1	3190	

Patient no.	Age* (years)	Sex	Underlying Disease	Indication	Weight [†] (kg)	Posaconazole Dose and Frequency	Posaconazole Weight-Normalized Dose [‡] (mg/kg/day)	Posaconazole Concentrations (ng/mL) Concentration or Median [‡] (range)	PPI/H2RA*
12	7.4	M	CGD (gp91)	Secondary Prophylaxis <i>Candida</i> spp., <i>Aspergillus</i> spp.	20.4	300 mg TID	44.1	1435 (201 – 1820)	H2RA
13	7.6	M	CGD (gp91)	Proven IFD, Lung and Bone <i>A. nidulans</i>	19.1	200 mg QID	41.9	707 (342 – 1040)	None
14	8.1	M	HIES (STAT3)	Probable IFD, Lung Organism not identified	43.2	200 mg QID	18.5	2160	None
15	9.7	M	HIES (STAT3)	Proven IFD, Lung <i>Aspergillus fumigatus</i> , <i>Aspergillus viridinutans</i>	23.5	260 mg TID	33.2	530	None
16	9.8	M	CGD (gp91)	Proven IFD, Lung <i>Rhizomonia argillacea</i> (formerly <i>Geosmithia argillacea</i>)	23.6 24.3	300 mg TID 250 mg QID	38.1 41.2	1270 772 (691 – 852)	None
17	9.9	M	CGD (gp91)	Proven IFD, Lung <i>A. fumigatus</i> , <i>Phoma</i> spp.	27.8 26.6	300 mg BID 300 mg TID	21.6 33.8	230 665 (650 – 680)	PPI
18	10.0	M	CGD (gp91)	Secondary Prophylaxis <i>Aspergillus</i> spp.	29.8	400 mg BID	26.8	906 (497 – 1210)	PPI
19	10.1	M	ABPA	Treatment <i>A. fumigatus</i>	25.4	400 mg BID	31.5	874	PPI
20	10.7	M	Unknown Immuno-deficiency	Proven IFD, Lung <i>Scedosporium apiospermum</i>	26.2	240 mg TID	27.5	710 (590 – 830)	None

Abbreviations: ABPA, allergic bronchopulmonary aspergillosis; BID, twice daily; CGD, chronic granulomatous disease; H2RA, H2-receptor antagonist; HIES, hyper-IgE syndrome; IFD, invasive fungal disease; M, male; PPI, proton pump inhibitor; QID, four times daily; STAT3, signal transducer and activator of transcription 3; TID, three times daily

* At the time of posaconazole initiation

Mean weight calculated using the weights recorded with or around each serum concentration

For any concentration below the lowest limit of quantitation (50 ng/mL), 25 ng/mL was used to calculate the median