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LETTER TO THE EDITOR

Retrospective survey on the off-label use of posaconazole in pediatric hematology patients

S. Cesaro · G. M. Milano · F. Aversa

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Sir,

Lehrnbecher et al. recently reported the off-label use of posaconazole in 15 pediatric hematology patients affected by invasive fungal infections. They concluded that posaconazole is safe and well-tolerated in pediatric patients, although pharmacokinetic studies are needed to optimize its use in this age group [1]. We assessed retrospectively the patients treated off-label at our centers with posaconazole from 1 March 2008 to 30 May 2009. Over a 15-month period we collected 15 patients, median age of 10 years, range 3–17, affected by acute lymphoblastic leukemia (5), acute myeloid leukemia/myelodysplasia (7), severe aplastic anemia (1), hemophagocytic lymphohystiocytosis (1), and Ewing's sarcoma (1), who received posaconazole. Nine of the patients had undergone allogeneic stem cell transplantation (SCT) with different stem cell donor sources: two haploidentical donors, three cord blood, three unrelated donors, and one sibling donor, while six were neutropenic patients on treatment for acute myeloid leukemia/myelodysplasia. Lung involvement was present in 12 patients and classified as proven aspergillosis in one patient, probable aspergillosis in ten patients, and possible mycosis in one patient; the remaining three patients received posaconazole as primary (2 patients) or secondary (1 patient) prophylaxis for high-risk situations such as acute graft versus host disease treated with steroids (2 patients) and haploidentical SCT (1 patient). The dose used was 3 x 200 mg/day in 12 patients, 2 x 400 mg/day in two patients, and 3 x 100 mg/day in one patient. No therapeutic drug monitoring was performed. For the 12 patients with lung infections, nine were treated with posaconazole as rescue therapy after one course (1 patient), two courses (5 patients) or three courses (3 patients) of antifungal therapy while three patients received posaconazole as secondary prophylaxis. The antifungal drugs used alone or in combination before starting posaconazole were liposomal amphotericin B in 11 patients, voriconazole in six patients, and caspofungin in four patients. As of August 30, 2009, these patients had been treated with posaconazole for a median of 273 days, range 150–665 days. The assessment of efficacy after 90 days of posaconazole showed a significant clinical-radiological improvement in nine patients. After a median follow-up of 12 months from the beginning of infection, 11 of 12 patients were alive, with a complete response in nine and a partial response in two. One patient with Ewing's sarcoma died during treatment due to progression of the disease but in complete response from posaconazole. None of the three patients treated as primary or secondary prophylaxis developed or had a relapse of mycoses. These patients were treated for 124, 158 and 332 days, respectively. Posaconazole was well-tolerated and no patient was withdrawn from treatment for adverse events related to its use. Posaconazole is a broad-spectrum triazole licensed for adult patients as antifungal prophylaxis in acute myeloid leukemia, myelodysplastic

S. Cesaro
Pediatric Hematology Oncology, Department of Pediatrics,
University of Padova,
Padova, Italy

G. M. Milano · F. Aversa
Pediatric Hematology, Ospedale Santa Maria della Misericordia,
Azienda Ospedaliera,
Perugia, Italy

Present Address:
S. Cesaro (✉)
Pediatric Hematology Oncology, Policlinico G.B. Rossi,
Azienda Ospedaliera Universitaria Integrata,
Piazzale LA Scuro 10,
37134 Verona, Italy
e-mail: simone.cesaro@ospedaleuniverona.it

syndrome, allogeneic transplant patients during treatment for acute graft versus host disease and as salvage treatment for aspergillosis and other mould infections [2]. Pharmacokinetic data for pediatric patients are limited as well as data on efficacy [1, 3]. Given the paucity of data available so far, we submit this further evidence that posaconazole may represent an alternative choice for the therapy and prophylaxis of fungal infections in pediatric patients, although we recognize that more studies are needed to optimize the posaconazole dosage.

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