**Objectives:** Invasive fungal diseases (IFDs) caused by mould pathogens, in particular azole-resistant fungi, are a significant cause of treatment-related mortality and morbidity in pediatric hemato-oncology patients. Olorofim (F901318), a novel oral antifungal agent belonging to the orotomide class, is being developed for complicated and/or azole-resistant IFDs in adults. No published data regarding the use of olorofim in children are available. We describe the use of olorofim in a case series of pediatric cancer patients with IFDs.

**Materials & Methods:** Data from patients treated with olorofim were retrospectively collected from two hospitals (Princess Maxima Center for Pediatric Oncology, NL and Great Ormond Street Hospital, UK). Access to olorofim was allowed for children with IFDs above 6 years of age under compassionate use. All pediatric patients received bodyweight-dependent doses of oral olorofim with a loading dose of 60, 120, or 150 mg twice daily (bd) for 1 day followed by maintenance doses of 30, 60, or 90 mg bd (target exposure of ≥0.1 mg/L). Pre-dose plasma concentrations of olorofim were measured by validated LC-MS/MS analysis to safeguard concentrations being within range. Olorofim-related adverse events (AE) were assessed during the entire period of olorofim treatment according to the Common Terminology Criteria for Adverse Events (CTCAE).

**Results:** Five pediatric patients with a total of six treatment episodes with olorofim were included (Table 1). All patients had hemato-oncological disease and two patients underwent allogenic stem cell transplantation (SCT). According to EORTC/MSG criteria, three patients had probable pulmonary aspergillosis, one had proven central nervous system (CNS) aspergillosis, and one had proven CNS *Scedosporium apiospermum* infection. Olorofim was provided on compassionate use for overlapping reasons: proven azole-resistance, failure to improve under azole and/or liposomal amphotericin B (L-AMB) or intolerance to L-AMB. Plasma levels of olorofim determined after at least 7 days of dosing exceeded the threshold needed for efficacy in all patients for whom plasma levels were assessed (N=4). Mean duration of olorofim treatment was 150 days (range 91-210 days). Olorofim was well tolerated with no treatment discontinuation or dose adjustments due to adverse events. Mild to moderate nausea occurred in all patients during olorofim treatment. One patient developed grade 3 hepatotoxicity (increase in alanine transaminase (ALT) levels) two months after starting olorofim, possibly related to concomitant use of sorafenib (kinase inhibitor) and cotrimoxazole. Two patients developed grade 1 hepatotoxicity (increase in ALT levels). Bilirubin levels were not significantly altered in any of the patients during olorofim treatment. In five out of six episodes, clinical and radiological improvement was observed after the start of olorofim. Death occurred in one out of six episodes during a second course of olorofim, most likely due to severe bronchiectasis and chronic pulmonary graft-versus-host disease after SCT.

**Conclusions:** Olorofim given using a bodyweight-based dosing algorithm is feasible, has acceptable tolerance, and provides an oral alternative for complicated and/or azole-resistant mould infections of the lungs and CNS in pediatric cancer patients. The safety profile was similar to that seen in adults.