This is the first report of maraviroc plasma concentrations when the drug is given as 150 mg once daily with lopinavir/ritonavir. It is noteworthy that the current recommended minimum effective values of the trough concentration (50 ng/mL) and average concentration (100 ng/mL) were derived from a sub-study of the MOTIVATE trial, where patients were administered 150 mg of maraviroc once daily or twice daily: these cut-off values are most likely applicable to multi-experienced subjects. A subsequent analysis of the MERIT trial, in fact, showed lower pharmacological requirements in treatment-naive patients. All patients in our study were treatment naive and showed average concentrations >75 ng/mL for near maximal virological efficacy according to exposure–response analysis of the MERIT study. Furthermore, the post hoc analysis of the MOTIVATE trial did not confirm the relationship between the efficacy and plasma concentration of maraviroc administered with protease inhibitors, further supporting the evaluation of maraviroc at reduced dosing when associated with the latter. Interestingly, maraviroc exposure in our patients is comparable to the PK of the same dose in association with atazanavir/ritonavir (AUC 4330 ng·h/mL and C_{ave} 180 ng/mL) and darunavir/ritonavir (C_{group}, 43 ng/mL). Moreover, lopinavir and ritonavir exposure did not seem to be affected by the coadministration of maraviroc, as all PK parameters were comparable to what was previously reported.

In conclusion, our study suggests that once-daily 150 mg dosing of maraviroc appears to be pharmacologically adequate in association with lopinavir/ritonavir in treatment-naive subjects. The potential impact in terms of regimen simplification and cost savings, coupled with the promising immunovirological results of the VEMAN study, deserves further clinical evaluation.

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**Transparency declarations**

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**Successful use of fidaxomicin in recurrent Clostridium difficile infection in a child**

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Sir, 

Clostridium difficile infection (CDI) is a disease with an increasing incidence in the paediatric population, increasing from 7.24 to 12.80/10000 hospitalizations from 1997 to 2006 in the USA.1 The explanation for this increase has not yet been determined,
and a reporting bias due to increased hospitalizations for rotavirus-associated infections cannot be excluded. Recurrence rates in the paediatric population are around 25%, and mortality rates are low, with one death seen among 82 patients with CDI in one study. We report a case of recurrent CDI in a 10-year-old child who was successfully treated with fidaxomycin, a newly approved macrocyclic antibiotic.

A 10-year-old patient presented with a history of five previous instances of CDI over 1 year, related to multiple use of antimicrobial therapy for recurrent pneumonia. He presented with a history of several days’ diarrhoea, lethargy and reduced intake. Physical exam findings were significant for dry skin with cold extremities and a soft, mildly distended abdomen upon palpation. On admission he had a fever of 101.3°F and a white blood cell count of 16 × 10⁹/L with an elevated neutrophil count of 78%. His mother had initiated oral vancomycin therapy 2 days prior to admission with no significant improvement. He had a known history of chromosomal disorder, microcephaly, seizures and gastric tube (G tube) feeding. It is to be noted that G tube feeding can also contribute to diarrhoea. His previous episode of CDI was more than 10 weeks ago and he had finished his tapering 6 week course of oral vancomycin 2 weeks prior to his admission. His workup on admission showed positive faecal leukocytes, and a stool specimen was positive by PCR for C. difficile toxin. The stool specimen gave negative culture and test results for other bacterial pathogens, ova and parasites; blood cultures were also negative.

Owing to multiple recurrences of CDI following therapy with vancomycin he was started on 200 mg fidaxomycin twice daily, the tablet being crushed, mixed with water and given through a G tube. The patient’s diarrhoea improved within 24 h and he was discharged on the third day. He finished the 10 day course of fidaxomycin while at home and remained symptom free at his 1 month follow-up appointment. A few months later the patient developed pneumonia, which was treated with clarithromycin, and he subsequently developed another episode of CDI with a similar presentation to that seen in the prior episode. The patient was treated with fidaxomycin again and his symptoms resolved in 24 h.

Treatment of recurrent CDI in the paediatric population is often difficult owing to limited approved therapeutic options. Current options include metronidazole and vancomycin, which are associated with a similar recurrence rate (27.1% and 24.0%, respectively), while metronidazole has a higher rate of treatment failure (22.4% versus 14.2%). However, an alternative to vancomycin and metronidazole is now available in the form of fidaxomycin, a novel macrocyclic antibiotic approved in the USA in 2011 for use in adults. Fidaxomycin works by inhibiting DNA-dependent RNA polymerase and thus RNA synthesis. It has a t½ of 11.7 h and an MIC range of 0.03–0.25 mg/L. Compared with vancomycin, fidaxomycin has a post-antibiotic effect of >24 h and has poor activity against normal Gram-negative and Gram-positive flora in the gut. Fidaxomycin also results in lower spore counts after treatment than vancomycin and is associated with less recurrence. The current disadvantage of fidaxomycin is its cost of use, although due to recent legislation, effective on 1 October 2012, Medicare set the maximum hospital add-on payment at $868, which covers half of the average cost. The current recommended dose for adults is 200 mg twice daily and our patient was started on this regimen, despite his young age, in view of his past history of recurrence of CDI. The route of administration was via a G tube in view of negligible gastrointestinal absorption.

We believe this is the first reported case of the use of fidaxomycin for the treatment of CDI in a child in the literature.

We have obtained verbal consent for this case report from the patient’s guardian.

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Elevated serum procalcitonin in anaphylaxis
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