common side effect of this tetracycline. The plasma concentration of minocycline, determined by HPLC, was 2.1 mg/L.

The serum and respective plasma concentrations were determined 5 weeks after onset of treatment and 14 h after the last medication.

The PCR for T. whipplei in the CSF was negative, both 12 and 24 months later. The patient has been asymptomatic now for more than 9 years after the initial examination and treatment.

Obviously, this new treatment option, found to be efficacious in a single patient, should be evaluated in a prospective trial. The regimen is attractive as the combination of minocycline and chloroquine can be given orally. However, vestibular side effects (occurring in >70% of women taking 100 mg of minocycline every 12 h)13 will render any study difficult. Our male patient had to reduce the dose of minocycline for several days.

The observation in this patient indicates that host factors and not necessarily in vitro antimicrobial susceptibilities may determine success or failure of antimicrobial treatment in cerebrospinal infection of Whipple’s disease. The host factors in this patient are unknown.

Our experience may be useful for other cases of refractory cerebrospinal infection with T. whipplei.

Acknowledgements
The plasma concentration of minocycline was kindly determined by C. Dilger (AAI Pharma Deutschland GmbH, Ulm, Germany). The serum concentration of chloroquine was kindly determined by the MVZ für Laboratoriumsmedizin Koblenz-Mittelrhein.

Funding
Funded by the 5th Framework Program of the European Commission.

Transparency declarations
No financial conflicts to declare.

References
isiatic pressure sore. No other comorbidities were present. Culture of the ulcer biopsy specimens grew methicillin-resistant *Staphylococcus aureus*, multidrug-resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. The patient started antibiotic treatment with 15 mg/kg amikacin daily intravenously and 100 mg of tigecycline intravenously, as initial dose, followed by 50 mg twice daily as a maintenance dose. The renal and liver functions were normal. The patient initially tolerated the antibiotics without complaint of nausea and vomiting or other adverse effects. During the second week of antibiotic therapy, the patient underwent surgery including ulcerectomy, partial ischiectomy, and coverage with the gluteal muscle flap and V-Y advancement flap. On the first post-operative day, the patient suddenly developed nausea, vomiting and acute severe upper abdominal pain. Blood tests showed increased amylase (312 U/L), lipase (382 U/L), white blood cells (42 770/μL) and C-reactive protein (131 mg/L). The abdominal CT scan showed inflammation of the pancreas and peripancreatic fat, necrosis of 40% of the pancreatic gland, peripancreatic stranding, and fluid collection (Balthazar CT severity index 7). No other common causes of acute pancreatitis, such as alcoholism, stones, total parenteral nutrition, endoscopic retrograde cholangiopancreatography, trauma, hypertriglyceridaemia and hypercalcemia, were identified. Drug-induced pancreatitis was suspected and tigecycline immediately discontinued. Owing to the critical condition (APACHE II score 14), the patient was treated in the intensive care unit with aggressive fluid resuscitation, pain management, proton-pump inhibitors, total parenteral nutrition and antimicrobial prophylaxis with imipenem/cliastatin. The symptoms resolved and pancreatic enzymes normalized within 10 days. Interestingly, the patient developed acute necrotizing pancreatitis on day 12 of tigecycline treatment and 8 h after receiving a single dose of propofol for the induction of general anesthesia. Propofol was the only other medication in the patient’s regimen that could possibly induce pancreatitis. Cases of propofol-related pancreatitis, even after a single dose, have been reported. In some cases, propofol has been implicated in causing pancreatitis by increasing the level of triglycerides. However, the pathogenesis is unknown and the causal relationship remains to be established. In our patient, the level of triglycerides remained normal; moreover, the patient had received propofol on two previous occasions for general anesthesia without developing pancreatitis. It is possible that propofol could have a role as a cofactor triggering acute pancreatitis in a previously tigecycline-sensitized pancreas. The concomitant administration of tigecycline and propofol led to the more severe pancreatic injury observed in this case.

The reported mortality rates of <1% in patients with interstitial pancreatitis dramatically increase to 10%–23% in patients with necrotizing pancreatitis. Clinicians should be aware of this potentially life-threatening side effect of tigecycline. Close monitoring of gastrointestinal symptoms and serum amylase, especially after the first week of treatment, have been advocated previously.

Based on our experience presented herein, we suggest that special caution should be exercised when administering tigecycline in association with propofol.

The patient gave informed consent to the publication of this article.

Funding
This study was carried out as a part of our routine work.

Transparency declarations
None to declare.

References

Blood and CSF monitoring of cefepime-induced neurotoxicity: nine case reports

Charlotte Durand-Maugard1,2*, Anne-Sophie Lemaire-Hurteul1, Valérie Gras-Champeil1, Lionel Hary1, Julien Maizel2,3, Aurore Prud’homme-Bernardy1, Claire Andréjak4 and Michel Andréjak1,2

1Department of Clinical Pharmacology, Amiens Picardie University Hospital, Amiens, France; 2INSERM U1088, Jules Verne University of Picardie, Amiens, France; 3Medical Intensive Care Unit, Amiens Picardie University Hospital, Amiens, France; *Respiratory Intensive Care Unit, Amiens Picardie University Hospital, Amiens, France

*Corresponding author. Laboratoire de Pharmacologie et Toxicologie, Service de Pharmacologie Clinique, CHU AMIENS Sud, Avenue René Laennec, F-80054 Amiens cedex, France. Tel: +33-322-455788; Fax: +33-322-455660; E-mail: durand-maugard.charlotte@chu-amiens.fr

Keywords: trough concentrations, CSF concentrations, renal failure

Sir, Cefepime is a parenteral fourth-generation cephalosporin commonly used as a first-line empirical treatment for severe