Tigecycline: an antibiotic for the twenty-first century

Matthew Dryden*

Department of Microbiology, Hampshire Hospitals Foundation Trust, Winchester SO22 5DG, UK

*Tel: +44-1962-824451; Fax: +44-1962-825431; E-mail: matthew.dryden@hhft.nhs.uk

This Supplement in the Journal of Antimicrobial Chemotherapy comprises a series of papers reporting on ‘real-life’ clinical experience with tigecycline. The data reported are derived from five European observational studies on the use of tigecycline, either as monotherapy or in combination with other antibiotics, for the treatment of complicated skin and soft-tissue infections or complicated intra-abdominal infections. Taken together, this collection of articles gives clinical insight into the use of tigecycline for the treatment of complicated infections.

Keywords: tetracyclines, antibiotics, anti-infective development

Modern medicine may be running out of antibiotics.1,2 These drugs have supported the development of highly technical medical interventions such as transplantation, cancer chemotherapy and complex surgery, all of which benefit patients, but have as a downside the fact that they predispose to opportunistic infections. Without the availability of antibiotics to prevent or treat such infections, the whole infrastructure of medicine as we have come to know it could collapse. This is a sobering thought. This situation has arisen through three main factors. The first is overuse of antibiotics in human and veterinary medicine and in livestock rearing, which has provided the selection pressure for the emergence and spread of antibiotic resistance. The second problem has been the uncontrollable transmission of resistant microbes by poor public health sanitation in the community and infection control in healthcare. The third factor is that few new antibiotics are coming into clinical use; there have been almost no new classes of antibiotics since the main classes were developed between the 1940s and the 1960s. A brief renaissance in the past decade with the development of oxazolidinones, lipopeptide antibiotics and glycyclines in response to the threat of methicillin-resistant Staphylococcus aureus has largely come to a halt in the present decade.

Tigecycline is a glycycline antibiotic3,4 given FDA fast-track review and approval in the USA in June 2005. Tigecycline was subsequently licensed in 2006 in Europe for the treatment of patients with complicated skin and soft-tissue infections and complicated intra-abdominal infections. It was developed in response to the growing prevalence of antibiotic resistance in bacteria such as S. aureus, Enterobacteriaceae and Acinetobacter baumannii. Multidrug-resistant Enterobacteriaceae, including those producing carbapenemases, such as the New Delhi metallo-β-lactamase, have also shown in vitro susceptibility to tigecycline.5 In this Supplement of the Journal of Antimicrobial Chemotherapy, a series of articles provides an overview of the use of tigecycline in ‘real-life’ clinical settings. Bassetti et al.6 describe prescribing practices for tigecycline and Heizmann et al.7 give an overview of the problem of antimicrobial resistance in Europe and outline the few remaining treatment options.

The registration process for new antibiotics requires randomized blinded studies comparing the new agent with standard treatment (so-called Phase III studies), which are generally powered statistically to demonstrate non-inferiority. All aspects of such trials have become increasingly complex, supervised by independent clinical trial organizations with absolute attention to detail so that every aspect of the data can be source verified and audited by regulatory authorities. While this is doubtless a very good thing for the data, it is not ideal for the patient. Patients by and large do not fit into protocols. Many patients are excluded from Phase III studies due to size, age, comorbidities and often downright contrariness. They do not want to stay in hospital for the trial duration and if they do stay, they do not want their drug infusion at that time, they want to have breakfast or they do not want more blood taken—and who can blame them! Hence, Phase III trials represent a very narrow study of clinical use. They certainly do not represent day-to-day clinical practice.

This Supplement presents observational clinical data by practising physicians across Europe using tigecycline to treat often serious infections of skin and soft tissue (Montravers et al.8) and intra-abdominal infections (Eckmann et al.9). The reported observational studies include large numbers of patients from several sites across Europe. They include a wide range of clinical conditions and a wide range of illness severity. They certainly do not represent day-to-day clinical practice.

*Tel: +44-1962-824451; Fax: +44-1962-825431; E-mail: matthew.dryden@hhft.nhs.uk

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In Europe, the benefit/risk evaluation of the EMA’s Committee for Medicinal Products for Human Use (CHMP) concluded that the benefits of tigecycline continue to outweigh its risks, but recommended changes to the product information to ensure that it is used appropriately by making prescribers aware that the medicine has been associated with an increased mortality in clinical studies. This Supplement provides a valuable collection of observational clinical data in the use of tigecycline across Europe. Controlled and careful antibiotic use is required to maintain the efficacy of anti-infective treatment. We also need a greater diversity of agents to reduce selection pressure. Tigecycline clearly has a role to play as a valuable option in antimicrobial treatment in the twenty-first century.

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References