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Tigecycline

A Viewpoint by Mark H. Wilcox

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Tigecycline represents a new class of antibiotics, the glycylcyclines, which have many of the advantages of tetracyclines, such as good tissue penetration. Additionally, it has expanded broad spectrum activity that includes antimicrobial-resistant pathogens, e.g. methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci, multidrug-resistant *Streptococcus pneumoniae*, extended-spectrum β-lactamase-producing Gram-negative bacteria, *Acinetobacter baumannii*, and bacteria with tetracycline resistance determinants. Tigecycline is not, however, active against some bacteria, such as *Proteus*, *Providencia* and *Pseudomonas* species.

The lack of an oral formulation of tigecycline partly limits its clinical utility. However, this may be advantageous with respect to the selective pressure favouring the emergence of resistance (which needs surveying) being reduced relative to community-based and/or prolonged antimicrobial therapy. The novel mechanism of action of tigecycline is also potentially beneficial in terms of the (reduced) likelihood of cross-resistance to other agents. Modest plasma concentrations of tigecycline are achieved. However, breakthrough bacteraemia (a theoretical concern) was not seen in clinical studies; widespread tissue distribution of the drug is expected to reduce the likelihood of such occurrences. A standard dosage regimen is used, with no adjustment required for age, gender, race, weight, renal function or mild-to-moderate hepatic insufficiency. Clinical trial experience with tigecycline has been primarily with the treatment of community-acquired infections. Phase III clinical trials showed the drug was equivalent to the combination of vancomycin and aztreonam for the treatment of complicated skin and skin structure infections (cSSSIs).

Tigecycline provides the clinician with an option for monotherapy of cSSSIs, including the increasing proportion of patients at risk of MRSA infection. Although nausea and vomiting were relatively common in the phase III studies, these symptoms were generally mild and did not lead to treatment discontinuation more often than the comparator treatment. Thus, tigecycline is potentially useful as a monotherapy for cSSSIs, which may be of polymicrobial aetiology, or, increasingly, caused by multidrug-resistant bacteria, notably MRSA. ▲