Daptomycin is not active against rapidly growing mycobacteria

Rapidly growing mycobacteria, formerly referred to as 'Group IV' in the Runyon classification, are being increasingly described as causative agents of infectious diseases, mainly respiratory diseases in cystic fibrosis patients (*Mycobacterium abscessus*) and either community-acquired (*Mycobacterium fortuitum*) or health-care-associated (*Mycobacterium chelonae*) cutaneous infections. The number of antibiotics available to treat infections caused by these organisms is very limited and most of them are poorly active. Treatment usually relies on antibiotic combinations given intravenously for several months. Consequently, new drugs are urgently needed to treat infections due to rapidly growing mycobacteria. Recently, tigecycline and to a less extent linezolid have been shown to have some *in vitro* activity against rapidly growing mycobacteria (Brown-Elliott *et al.*, 2003; Martin-de-Hijas *et al.*, 2008).

Daptomycin, the first in a class of agents known as lipopeptides, is a novel antimicrobial agent used for the treatment of Gram-positive infections (Hawkey, 2008). The compound has a distinctive mechanism of action in that it exerts its bactericidal activity by disrupting plasma membrane function without penetrating into the cytoplasm. Daptomycin is active against multidrug-resistant, Gram-positive bacteria such as meticillin-resistant *Staphylococcus aureus*, vancomycin-

resistant enterococci, and glycopeptide-intermediate and -resistant *S. aureus*. To our knowledge, daptomycin has not been evaluated against mycobacteria.

We prospectively evaluated the *in vitro* activity of daptomycin against rapidly growing mycobacteria received at the National Reference Center for Mycobacteria (NRC) for susceptibility testing. We included in the study 40 strains involved in pulmonary ($n=32$), skin and soft tissue ($n=5$) or other ($n=3$) infection. All the strains were identified by sequencing the heat-shock protein 65 gene. Mycobacteria were identified as *M. abscessus* (22), *M. chelonae* (7), *M. fortuitum* (5), *Mycobacterium massiliense* (4) and *Mycobacterium bolletii* (2). The MIC of daptomycin was measured by E-test on Mueller–Hinton medium. Readings were taken after 3–7 days of incubation at 30 °C depending on growth of the organism.

MICs are presented in Table 1. Daptomycin MICs were $>64 \text{ mg l}^{-1}$ for 33 of the 40 mycobacteria tested. The MIC was $>256 \text{ mg l}^{-1}$ for *M. chelonae*, *M. massiliense* and *M. bolletii*. MICs were lower (48 mg l^{-1}) against 3 of the 22 strains of *M. abscessus*, and *M. fortuitum* showed the most sensitive pattern with the MIC being $\leq 64 \text{ mg l}^{-1}$.

According to the European Committee on Antimicrobial Susceptibility Testing, the

MICs of daptomycin against staphylococci and streptococci considered susceptible to this drug were below 1 mg l^{-1} (EUCAST, 2008). Taking into account this breakpoint, daptomycin should be considered as inactive against rapidly growing mycobacteria. However, considering that an MIC below the peak serum level of the drug can be predictive of some *in vivo* activity, daptomycin could have some activity *in vivo*. Indeed, the peak serum level generated by the usual dosing 4 mg kg^{-1} ranges from 57 to 77 mg l^{-1} (Hawkey, 2008). Thus, according to the MIC measured in this experiment, daptomycin could have some activity against a small fraction of the strains of *M. abscessus* and against the species *M. fortuitum*, which is the most sensitive of the five tested species. However, this activity is likely to be weak.

Even considering that MICs measured by E-test are often a little higher than those measured by the microdilution method, daptomycin will not be an antibiotic of first choice for treating infection due to rapidly growing mycobacteria (Woods *et al.*, 2000).

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Table 1. MIC of daptomycin against clinical strains of *M. abscessus*, *M. massiliense*, *M. chelonae*, *M. bolletii* and *M. fortuitum* received at the NRC

	MIC (mg l ⁻¹)							Total
	32	48	64	96	128	256	>256	
<i>M. abscessus</i>		3			1	1	17	22
<i>M. massiliense</i>				1			3	4
<i>M. chelonae</i>							7	7
<i>M. bolletii</i>							2	2
<i>M. fortuitum</i>	1	1	2				1	5
Total	1	4	2	1	1	1	30	40

activity of linezolid against slowly growing nontuberculous mycobacteria. *Antimicrob Agents Chemother* **47**, 1736–1738.

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