The presence of \textit{ermB} in \textit{Streptococcus pneumoniae} has no influence on AZD2563 MIC values

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Sir,

The treatment of \textit{Streptococcus pneumoniae} infections is increasingly threatened by the emergence of penicillin- and macrolide-resistant strains. Macrolide-resistant or not fully susceptible \textit{S. pneumoniae} isolates often contain either \textit{ermB}, \textit{mefE} or both determinants. In some cases a mutant ribosomal protein has been detected. Methylation of ribosomal RNA by the \textit{ermB}-encoded methylase prevents the action of macrolides. The \textit{mefE} gene encodes a macrolide efflux system. \textit{ermB}-carrying isolates often have, for unexplained reasons, higher MIC values for macrolides than \textit{mefE}-containing isolates, and cross-resistance for \textit{ermB}-harbouring isolates is also higher.\footnote{1} This would potentially limit the therapeutic usefulness of these antibiotic compounds.

AZD2563 is a new oxazolidinone with activity against Gram-positive bacteria. It acts by interfering with ribosome function and thus protein synthesis,\footnote{2} as do macrolides. Therefore, the MICs of AZD2563 were determined for \textit{ermB}-containing isolates.

\textit{S. pneumoniae} isolates were collected from across Europe. Only one isolate per patient was allowed. The isolates were identified at the source and when deemed clinically significant by local criteria, and sent to the Eijkman–Winkler Center using Amies Charcoal Medium transport swabs (Difco, Chicago, IL, USA). Isolates were cultured on blood agar and stored at \(-70^\circ\text{C}\) using Microbank (Oxoid, Basingstoke, UK) until further testing. Isolate identity was confirmed using optochin discs (Oxoid). Nearly all isolates were obtained from blood culture, sputa, bronchoalveolar lavage and throat swabs. The MICs of erythromycin, clindamycin and AZD2563 were determined using a broth microdilution (Trek Diagnostic Systems, Westlake, OH, USA) method and standard methods defined by the NCCLS.\footnote{3} The erythromycin-resistant isolates were tested by \textit{ermB}-specific PCR as described by Sutcliffe \textit{et al}.\footnote{4}

A total of 77 \textit{S. pneumoniae} isolates were erythromycin resistant and \textit{ermB} positive. These isolates came from Belgium ($n = 2$), Denmark ($n = 1$), France ($n = 12$), Italy ($n = 5$), Luxembourg ($n = 21$), The Netherlands ($n = 5$), Poland ($n = 3$), Portugal ($n = 1$), Spain ($n = 3$), Switzerland ($n = 4$) and Turkey ($n = 20$). All isolates except six were also clindamycin resistant.

The MICs of AZD2563 for these isolates ranged from 0.12 to 2 mg/L (Table 1). Only one isolate had an MIC of 2 mg/L. Both the MIC\textsubscript{50} and MIC\textsubscript{90} values for all \textit{ermB}-positive isolates were 0.5 mg/L. In a surveillance study with a collection of \textit{S. pneumoniae} isolates with similar origins, the MIC\textsubscript{50} and MIC\textsubscript{90} values were 0.5 and 1 mg/L, respectively.\footnote{5}

The presence of the \textit{ermB} determinant in macrolide-resistant \textit{S. pneumoniae} does not influence the MICs of AZD2563. Therefore, AZD2563 might be a treatment option for infections with macrolide-resistant \textit{S. pneumoniae}.

\textit{Acknowledgements}


\textit{References}

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to macrolides, tetracycline, quinolones, or trimethoprim/sulfamethoxazole. European Journal of Clinical Microbiology and Infectious Diseases 20, 827–9.


