Comment on: Daily 300 mg dose of linezolid for the treatment of intractable multidrug-resistant and extensively drug-resistant tuberculosis

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Sir,

Koh et al.1 reported the use of 300 mg of linezolid daily for the treatment of intractable drug-resistant tuberculosis. While it is certainly beneficial to reduce the dosage of linezolid and minimize undesirable adverse drug reactions, there are a number of concomitant concerns.

Although the proportion of reported patients with consecutive negative sputum culture taken at least 4 weeks apart appeared high (92%), the actual cure rate would be likely to be much lower,1 as suggested by a previous report.2 Even if there were cures, it might be difficult to attribute them to treatment with 300 mg of linezolid daily. Important confounders included accompanying drugs used, alongside their dosages and scheduling (especially for moxifloxacin/levofloxacin), as well as recourse to surgical resection. Furthermore, the peak serum levels of linezolid did not appear to correlate well with the reported outcomes.1 While linezolid can achieve a good concentration in epithelial lining fluid in human volunteers,3 this might not be so in the presence of sequestered pulmonary tuberculosis with sizeable thick-walled cavities.

Resistance to linezolid among Mycobacterium tuberculosis isolates is emerging in various parts of the world.4,5 It is indeed a pressing issue to delineate the optimal dosage and scheduling of linezolid in the treatment of difficult drug-resistant tuberculosis, through balancing efficacy, suppression of drug resistance, tolerance and toxicity of the oxazolidinone.6 It would be very important to follow-up on the susceptibility of the M. tuberculosis isolates harboured by those patients reported by Koh et al.1 who failed to achieve cure after antituberculosis chemotherapy.

Transparency declarations

None to declare.

References


We agree that linezolid, like other second-line drugs, may not have good access to the destroyed parenchymal lesions, such as thick-walled cavities. However, although we do not know the exact reasons why linezolid is so potent at eradicating drug-resistant Mycobacterium tuberculosis, a previous study showed that PNU-100480, another oxazolidinone now in Phase I clinical trials, also had dramatic anti-TB activity.\textsuperscript{10} Finally, we also agree with the concern of Yew \textit{et al.}\textsuperscript{1} that low-dose linezolid is likely to increase the possibility of developing linezolid-resistant TB. In our study, the MIC\textsubscript{99} for serial isolates of \textit{M. tuberculosis} during linezolid treatment in one patient who failed culture conversion was consistently 0.25–0.5 mg/L. A follow-up study on the susceptibility of \textit{M. tuberculosis} isolates in patients who fail culture conversion is needed.

\textbf{Transparency declarations}

None to declare.

\textbf{References}


