JOURNAL CLUB

Linezolid for XDR-TB

This randomised phase 2a trial in South Korea recruited 41 patients with sputum culture-positive pulmonary extensively drug-resistant tuberculosis (XDR-TB), who had failed to respond to 6 months of available treatment. Daily dosage of 600 mg linezolid was added either immediately or after a delay of two months. After four months of linezolid, or two consecutive negative sputum smears, patients continued either 300 mg or 600 mg daily for another 18 months.

After 4 months, the primary outcome of sputum culture conversion was achieved in 15 of the 19 immediately treated patients, and in 7 of 20 in the delayed treatment group. Eighty-seven per cent of all linezolid-treated patients had negative sputum cultures after 6 months. Significant adverse events including myelosupression, peripheral neuropathy, ocular toxicity and rhabdomyolysis occurred in 82%. The majority resolved, but linezolid was consequently withdrawn in three patients.

The lower dose of the drug was associated with fewer adverse events, but trough linezolid blood levels in the 300 mg group were lower than the mean minimum inhibitory concentration in nine patients including two who developed drug resistance. Resistance was also seen in two patients in the 600 mg group. Only 13 patients had completed 18 months of linezolid on protocol which was ongoing at the time of reporting.

Linezolid is effective in chronic XDR-TB at the cost of frequent adverse events. The optimum dose and duration of therapy, as well as its exact place in an XDR-TB treatment regimen, remain unclear. Linezolid should be used only under experienced supervision.

▶ Lee M, Lee J, Carroll MW, *et al*. Linezolid for treatment of chronic extensively drug-resistant tuberculosis. *N Engl J Med* 2012;367:1508–18.

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