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Lung alert

Diarylquinoline TMC207 as potential new therapy for multidrug-resistant tuberculosis

TMC207 is an investigational diarylquinoline which inhibits mycobacterial ATP synthase in drug-sensitive and drug-resistant *Mycobacterium tuberculosis* in vitro. It is bactericidal to dormant tubercle bacilli, therefore offering a new mechanism for the treatment of multidrug-resistant tuberculosis.

This study is the first stage of a phase 2 randomised controlled trial. Conducted in South Africa, newly diagnosed patients with pulmonary tuberculosis resistant to both isoniazid and rifampin were randomly assigned to TMC207 or placebo in a double-blind manner in combination with a standard five-drug second-line antituberculosis regime and given over an 8-week period. The primary end point was the conversion of sputum cultures from positive to negative; the study also collected further pharmacokinetic, safety and adverse event data.

Of the initial 47 patients (predominantly HIV-negative black men with a median age of 33 years), 41 completed the 8-week course. The addition of TMC207 to the standard drug regime resulted in a quicker conversion to negative sputum culture, with 48% of the patients receiving TMC207 having a negative culture at 8 weeks compared with 9% of those given placebo (hazard ratio 11.8, 95% confidence interval 2.3 to 61.3; $p = 0.003$). Similar proportions of patients completed both courses with a similar side effects profile consistent with antituberculosis therapy; only nausea occurred significantly more frequently in the TMC207 group.

This study shows quicker conversion of sputum cultures in patients on the TMC207 regimen, highlighting its potential as antituberculous treatment in multidrug-resistant tuberculosis.

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