Anti-tuberculosis Activity of Radezolid

Joseph DeVito, Andrea Marra, Eric Burak and Erin Duffy
 Rib-X Pharmaceuticals, Inc., New Haven, CT, USA

ABSTRACT

Background. Radezolid (RX-1294) is a novel thiazolidinedione antibiotic that has potent activity against M. tuberculosis, M. chelonae, and M. abscessus. In vivo efficacy studies in a mouse model of pulmonary tuberculosis demonstrated that radezolid has efficacy comparable to that of rifampicin and isoniazid, the first-line drugs for treatment of tuberculosis (TB).

Methods. A strain of drug-resistant M. tuberculosis that is sensitive to ethambutol and isoniazid but resistant to rifampicin was used in this study. The MIC of radezolid against this strain was determined using the broth microdilution method. The minimum bactericidal concentration (MBC) was determined by serial dilution in broth cultures. The time-kill experiment was performed by adding various concentrations of radezolid to stationary-phase cultures of the drug-resistant M. tuberculosis strain. The bacterial growth was monitored by staining with a LIVE/DEAD BacLight kit (Invitrogen).

Results. The MIC of radezolid against the strain of drug-resistant M. tuberculosis was 0.25 \( \mu \text{g/mL} \). The MBC was 0.5 \( \mu \text{g/mL} \). In the time-kill experiment, a concentration of 0.5 \( \mu \text{g/mL} \) of radezolid completely inhibited growth of the drug-resistant M. tuberculosis strain. After 6 hours of incubation, all of the bacteria were killed. No bacterial growth was detected after 24 hours of incubation.

Introduction

Radezolid is a novel thiazolidinedione antibacterial agent that has potent activity against M. tuberculosis, M. chelonae, and M. abscessus. In vivo efficacy studies in a mouse model of pulmonary tuberculosis demonstrated that radezolid has efficacy comparable to that of rifampicin and isoniazid, the first-line drugs for treatment of tuberculosis (TB).

METHODS

Background. Radezolid (RX-1294) is a novel thiazolidinedione antibiotic that has potent activity against M. tuberculosis, M. chelonae, and M. abscessus. In vivo efficacy studies in a mouse model of pulmonary tuberculosis demonstrated that radezolid has efficacy comparable to that of rifampicin and isoniazid, the first-line drugs for treatment of tuberculosis (TB).

Methods. A strain of drug-resistant M. tuberculosis that is sensitive to ethambutol and isoniazid but resistant to rifampicin was used in this study. The MIC of radezolid against this strain was determined using the broth microdilution method. The minimum bactericidal concentration (MBC) was determined by serial dilution in broth cultures. The time-kill experiment was performed by adding various concentrations of radezolid to stationary-phase cultures of the drug-resistant M. tuberculosis strain. The bacterial growth was monitored by staining with a LIVE/DEAD BacLight kit (Invitrogen).

Results. The MIC of radezolid against the strain of drug-resistant M. tuberculosis was 0.25 \( \mu \text{g/mL} \). The MBC was 0.5 \( \mu \text{g/mL} \). In the time-kill experiment, a concentration of 0.5 \( \mu \text{g/mL} \) of radezolid completely inhibited growth of the drug-resistant M. tuberculosis strain. After 6 hours of incubation, all of the bacteria were killed. No bacterial growth was detected after 24 hours of incubation.

Conclusions

Radezolid is highly active in vitro against drug-resistant M. tuberculosis, achieving the inhibition of bacterial replication as a measure of antitubercular potency. In fact, radezolid activity is superior to rifampicin that can be the first line of therapy for tuberculosis patients (e.g., HIV-infected, smear+.).

Reduced to the bottom line...