

Pathology as read-out for efficacy testing of the benzothiazinone BTZ-043 against *Mycobacterium tuberculosis* in a guinea pig (*Cavia porcellus*) model

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Background and objectives: Tuberculosis (TB) is the leading bacterial cause of human death worldwide. The proportion of antibiotic resistant *Mycobacterium tuberculosis* (Mtb) strains is increasing. The aim of this study was to analyze the effect of an orally administered anti-TB drug candidate - benzothiazinone (BTZ) - 043 on Mtb induced granulomas.

Material and Methods: Eighteen guinea pigs were infected s.c. with 1×10^3 Mtb H37Rv. Starting 14 d after infection, subgroups (n=6, each) were orally treated with BTZ-043, isoniazid, and vehicle, respectively, daily for 28 d. On day 42 after infection, animals were euthanized and a complete autopsy with macroscopic assessment of lesions was conducted. Fixed (4 % formaldehyde) tissue samples and granulomas were processed by histochemical and immunohistochemical methods. Stained tissue sections were scanned as whole-slide images to allow quantification and statistical testing of lesion parameters.

Results: The extent of subcutaneous granulomas and the proportion of necrosis were significantly reduced in BTZ-043-treated guinea pigs compared to vehicle controls. Systemic spread with granuloma genesis in other organs did not occur in this group. A highly significant reduction in mycobacterial load in subcutaneous granulomas, draining lymph nodes and spleen was demonstrated.

Conclusions: BTZ-043 is a promising antibiotic and showed significant efficacy in the guinea pig model of TB after only 28 days of oral administration.

Keywords

BTZ-043, guinea pig, *Mycobacterium tuberculosis*, MDR-TB, treatment, new antibiotics

Registration-ID code

450

Professional Status of the Speaker

Postdoc

Junior Scientist Status

No, I am not a Junior Scientist.

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