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A Phase I Single Site Open Label Clinical Trial for the Development of a Human BCG Challenge Model to Assess TB Drugs and Vaccines

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Background: Tuberculosis (TB) remains a leading cause of death from an infectious disease worldwide. The only approved and available vaccine is Mycobacterium bovis Bacillus Calmette–Guérin (BCG), which has suboptimal efficacy in the prevention of pulmonary TB. A human challenge model would simplify testing new vaccines and treatments.

Methods: This was a phase I clinical trial (NCT05592223) intended to develop a human BCG challenge model. Ten participants were enrolled and received intradermal BCG on Day 0. Participants were randomized to receive rifampin 600 mg days 4-10 post-BCG vs. placebo. Skin biopsies were collected: two on Day 3, two on Day 15, and an optional fifth on Day 28. Participants were monitored for safety and tolerability. Skin biopsy samples were homogenized for BCG measurement by conventional culture with colony forming units (CFU) and molecular viability testing (MVT) by pre-rRNA PCR.

Results: Ten participants were enrolled with a median age of 33.5. All participants experienced erythema and induration at the vaccination site, with two participants experiencing grade 3 erythema. One participant experienced a sustained local granulomatous response lasting 9 months that was potentially exacerbated by skin biopsies. Participants receiving rifampin had significantly lower CFU in culture on Day 15 compared to placebo (p=0.010). The CFU in the rifampin group was higher at Day 3, but this was not statistically significant (p=0.067). MVT showed no significant difference between groups at Day 15 (p=0.22).

Conclusions: This study demonstrated acceptable safety and tolerability of intradermal BCG. Rifampin did have an impact on the presence of viable BCG by culture, although differences did not reach statistical significance by MVT. The demonstration of an appropriate response to anti-TB therapy is promising for the use of BCG challenge models to evaluate novel treatments for TB.

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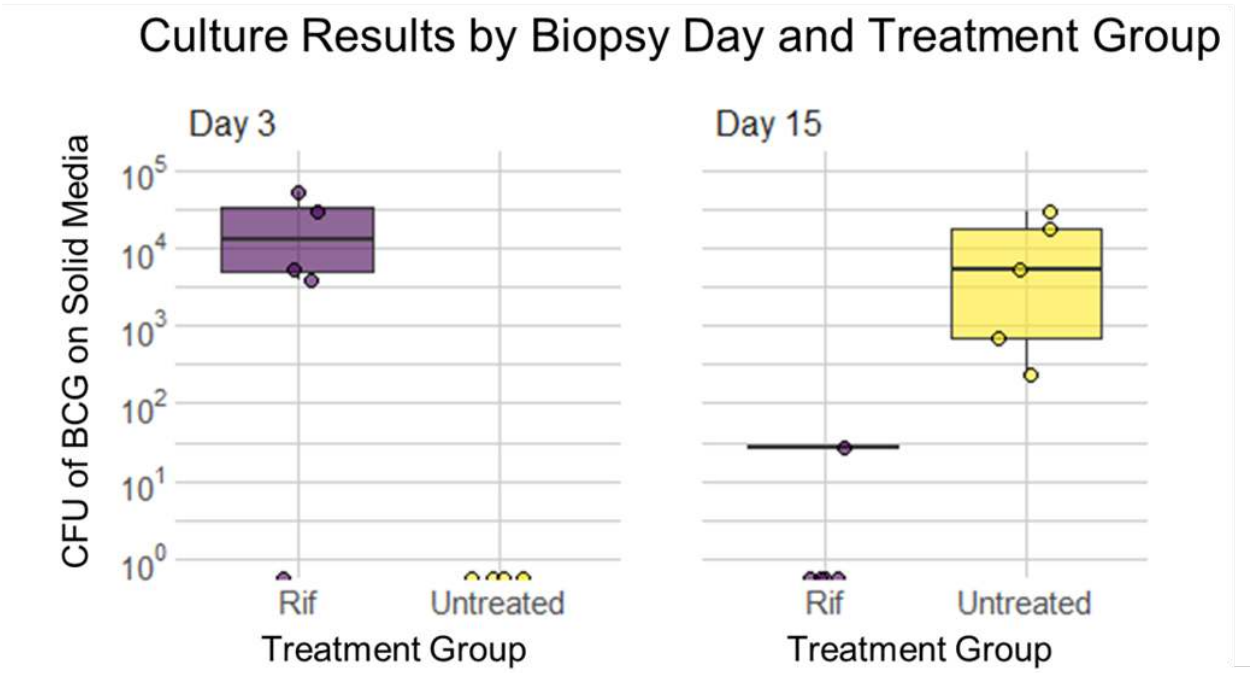
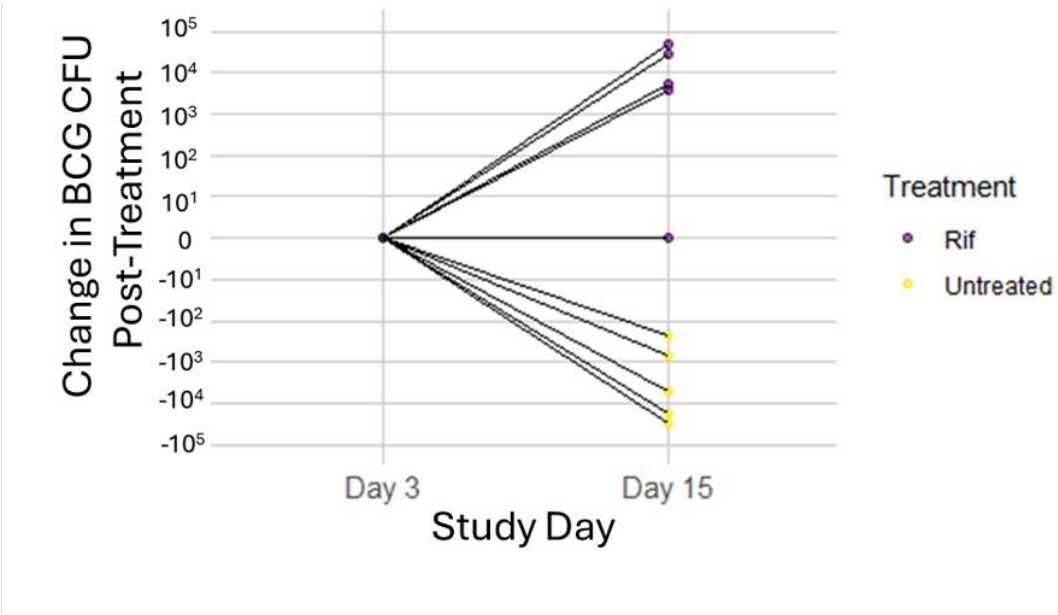
Conflicts of Interest
None


Culture Results by Biopsy Day and Treatment Group
Day 3
Day 15
CFU of BCG on Solid Media
10^5
10^4
10^3
10^2
10^1
10^0
Rif
Untreated
Treatment Group


Change in BCG CFU Post-Treatment
10^5
10^4
10^3
10^2
10^1
0
-10^1
-10^2
-10^3
-10^4
-10^5
Day 3
Day 15
Study Day
Treatment
Rif
Untreated