# GEOGRAPHIC AND INDIVIDUAL RISK FACTORS FOR TB OR DEATH IN THE BRIEF-TB TRIAL (A5279)

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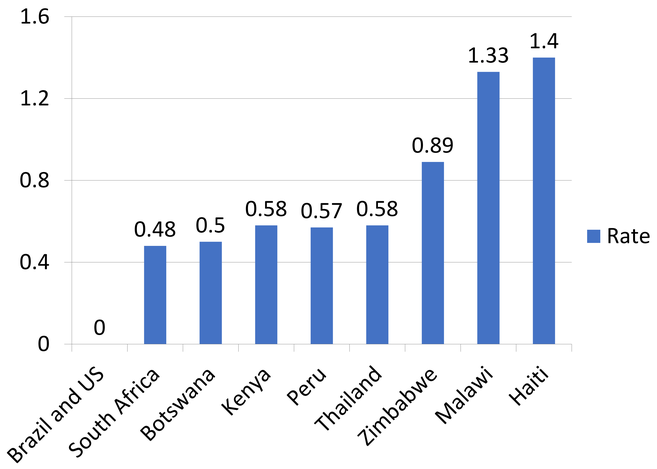
## BACKGROUND

The BRIEF TB trial (A5279, NCT01404312) demonstrated non-inferiority of one-month of isoniazid and rifapentine (1HP) versus nine months of isoniazid (9H) for TB prevention in people with HIV. We explored differences in rates of the primary outcome by demographic, clinical, and geographic factors in a pre-planned secondary analysis.

## METHODS

BRIEF TB enrolled 3000 adults and adolescents with HIV infection in 10 countries who were followed for at least 3 years. The primary endpoints were TB or death from TB or an unknown cause. We analyzed risk of reaching an endpoint by baseline factors, including sex, race, tuberculin skin test (TST)/interferon-gamma release assay (IGRA) status, CD4 count, country of residence, and time-dependent receipt of antiretroviral therapy (ART). We performed a multivariate Cox proportional hazards analyses of factors associated with experiencing a primary endpoint and tested two-way interactions between each factor and treatment.

**Incidence rate of TB or Death from TB per 100 persons year**




**Graph 1: TB and death incidence rates**

**Rates of TB or death from TB or an unknown cause varied in PLWH by country, reflecting local TB dynamics. CD4 count, BMI, and a positive test for latent TB (TST or IGRA) were associated with TB risk, regardless of regimen. 1HP was non-inferior to 9H for all participants, including those with a positive TST/IGRA.**

## RESULTS

Primary endpoint rates were higher in individuals with lower CD4 counts, who were not on ART, and who had a positive TST or IGRA at baseline. In the Cox proportional hazards analysis (Table), reaching an endpoint was significantly associated with baseline CD4 count, TST/IGRA positivity, and BMI, but not with time dependent ART status, age, sex, or treatment assignment. For TST/IGRA positive individuals, 1HP met non-inferiority criteria. There remained unexplained heterogeneity between countries when added to the model (not shown) but estimates of other covariates were similar in both models.

| Covariate | Hazard Ratio | Lower 95% Wald Confidence Limit | Upper 95% Wald Confidence Limit |
|---|---|---|---|
| Time-Dependent ART: Started ART vs. Not Started ART | 0.562 | 0.288 | 1.096 |
| Treatment: 9H vs. 1HP | 1.119 | 0.680 | 1.844 |
| Age: Per 1 Year Increase | 1.009 | 0.986 | 1.034 |
| Sex: Female vs. Male | 1.580 | 0.946 | 2.641 |
| CD4 count: Per 10 Cell Increase | 0.978 | 0.965 | 0.991 |
| BMI: Per 1 Unit Increase | 0.934 | 0.881 | 0.991 |
| IGRA/TST: Not Positive vs. Positive at Entry | 0.513 | 0.298 | 0.884 |

**Table 1: Cox proportional hazards analysis**

| Arm | No. PPD+ or IGRA+ | Endpoints/PY Follow Up | Rate Per 100 PY | Difference |
|---|---|---|---|---|
| 1HP | 342 | 10/1110 | 0.90 | -0.07 (95% CI -0.87-0.73) |
| 9H | 351 | 11/1137 | 0.97 | |

**Table 2: Study endpoint rates per arm**

## CONCLUSIONS

- TB risk was greater for those with lower CD4 counts, lower BMI, and a positive TST/IGRA test at baseline.
- 1HP met criteria for non-inferiority in all patients and in the subgroup with a positive TST/IGRA at baseline.
- There was considerable heterogeneity by country of residence, indicating that local TB transmission patterns likely affect TB risk.
- 1HP represents an exciting new strategy for preventing TB in people living with HIV.

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