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Supporting, Mobilizing, and Accelerating Research for Tuberculosis Elimination

SMART4TB Consortium

The BREACH-TB Trial

Bedaquiline Roll-out Evidence in Contacts and People Living with HIV to Prevent TB

BACKGROUND

Tuberculosis (TB) is a leading infectious killer globally, causing an estimated 1.3 million deaths in 2022 (WHO, 2023). While we lack a broadly effective vaccine, preventive therapy is crucial to prevent TB disease, especially in those who are at higher risk and have complex considerations including children, people with HIV, and pregnant people. Short-course regimens, which are more easily accepted and completed, have been available for several years for preventing drug-susceptible TB, but have not been tested in all these populations, and are not effective against the most common forms of drug-resistant TB. Bedaquiline, a powerful and safe medicine to treat TB disease, offers potential for universal short-course TB preventive therapy.

STUDY GOAL

To test a four-week regimen of bedaquiline as preventive therapy for people at high risk for developing either drug-resistant or drug-susceptible TB, including populations normally excluded from clinical trials.

STUDY LEADERS

BREACH-TB is led by **Eric Nuermberger** and **Sonya Krishnan** at Johns Hopkins University in partnership with University of California, San Francisco, KNCV Tuberculosis Foundation, Treatment Action Group, and the Elizabeth Glaser Pediatric AIDS Foundation.

STUDY POPULATION

See study design below for key included populations.

STUDY LOCATIONS

South Africa

STUDY DESIGN

BREACH-TB is a Phase III, **open-label**, **multicenter**, **randomized**, **controlled**, **non-inferiority** trial, enrolling approximately 2,530 people. The main objectives are to find out if one month of daily, oral bedaquiline is safe and effective at preventing TB in people who are at high risk of developing TB, including:

- people living with HIV and people of all ages, including lactating adults, who are at high risk of developing TB and have had close contact with someone with drug-susceptible TB. The comparator will be either one month of daily isoniazid and rifapentine, or three months of once-weekly isoniazid and rifapentine.
- those who have had close contact with someone with drug-resistant TB. The comparator will be six months of daily levofloxacin.

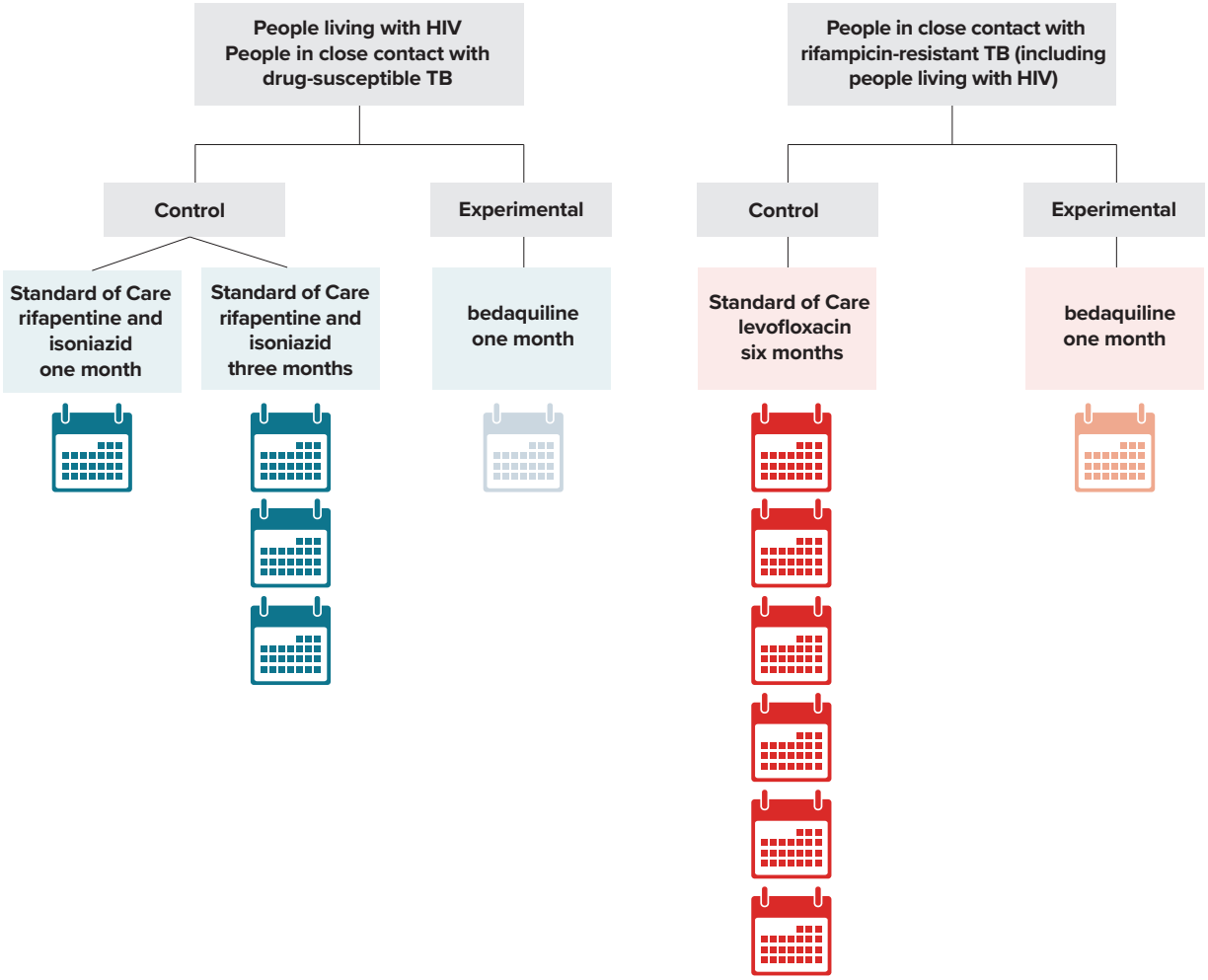
Open-label means the researcher and participant know the drug that is being used.

Multicenter means the trial is conducted at many sites, offering more diversity in participants, results relevant to more settings, and more efficiency in recruiting participants and sharing resources.

A **randomized controlled** trial assigns participants to the study intervention (in this case, the one-month bedaquiline regimen) or the control (the standard of care) at random, to balance participant characteristics with a goal of minimizing bias.

Non-inferiority trials test that the experiemental treatment being studied is not worse than standard treatment.

STUDY DESIGN, CONTINUED



KEY POPULATIONS

	Drug-Susceptible TB Prevention with BDQ		Rifampicin-Resistant TB Prevention with BDQ	
Demographic	Living with HIV	Living without HIV	Living with HIV	Living without HIV
Adults and adolescents, including lactating people	Included	Included +TBI test	Included	Included +TBI test
Pregnant adults and adolescents	Excluded	Included +TBI test	Included +TBI test	Included +TBI test
Children 5 to < 15 years	Excluded	Included +TBI test	Included	Included +TBI test
Children < 5 years	Excluded	Included	Included	Included

Included +TBI test = participants in these groups must test positive for TB infection to be eligible, per WHO guidelines

Children and pregnant people living with HIV are excluded from the drug-susceptible arm until data on the use of rifapentine and dolutegravir together in these populations are available, per WHO guidelines

ABOUT SMART4TB

This report is made possible by the support of the American people through the United States Agency for International Development (USAID). The contents are the sole responsibility of SMART4TB and do not necessarily reflect the views of USAID or the United States Government or consortium collaborators or members.

If you have any questions, please contact us at: smart4tbinfo@jh.edu