USAID FROM THE AMERICAN PEOPLE

Supporting, Mobilizing, and Accelerating Research for Tuberculosis Elimination

SMART4TB Consortium

SMILE-TB Trial

Shortened Regimen for Drug-Susceptible TB in Children

BACKGROUND

Though preventable and curable, tuberculosis (TB) remains a top 10 cause of mortality for children under five years old; over one million children developed TB and 214,000 children died of TB in 2022 (WHO, 2023). While drug-susceptible TB currently requires four to six months of treatment, most children may be able to be cured with a shorter treatment of more powerful drugs. Shorter treatment may be easier for children to tolerate and finish, as well as ease caregiver strain from managing treatment side effects and supporting children over many months. It may also help TB programs be more efficient in addressing childhood TB and end this deadly neglected disease.

STUDY GOAL

To evaluate if two months of TB treatment is as safe and effective as four to six months in children with drug-susceptible TB disease. The study is testing a new regimen that replaces rifampicin and ethambutol with two powerful antibiotics, rifapentine and moxifloxacin.

STUDY LEADERS

SMILE-TB is led by **Nicole Salazar-Austin** at Johns Hopkins University, in partnership with the University of California, San Francisco; KNCV Tuberculosis Foundation; Treatment Action Group; the Elizabeth Glaser Pediatric AIDS Foundation; and local community and research partners.

STUDY POPULATION

Children under 10 years with newly diagnosed TB disease, presumed to be drug-susceptible, in the lungs and/or lymph nodes. Participants can be living with or without HIV.

STUDY LOCATIONS

India, Indonesia, Mozambique, South Africa, Uganda, and Zambia

STUDY DESIGN (ClinicalTrials.gov NCT06253715)

SMILE-TB is a Phase III, **open-label**, **randomized**, **controlled**, **non-inferiority** trial enrolling 860 participants. The main objectives are to find out:

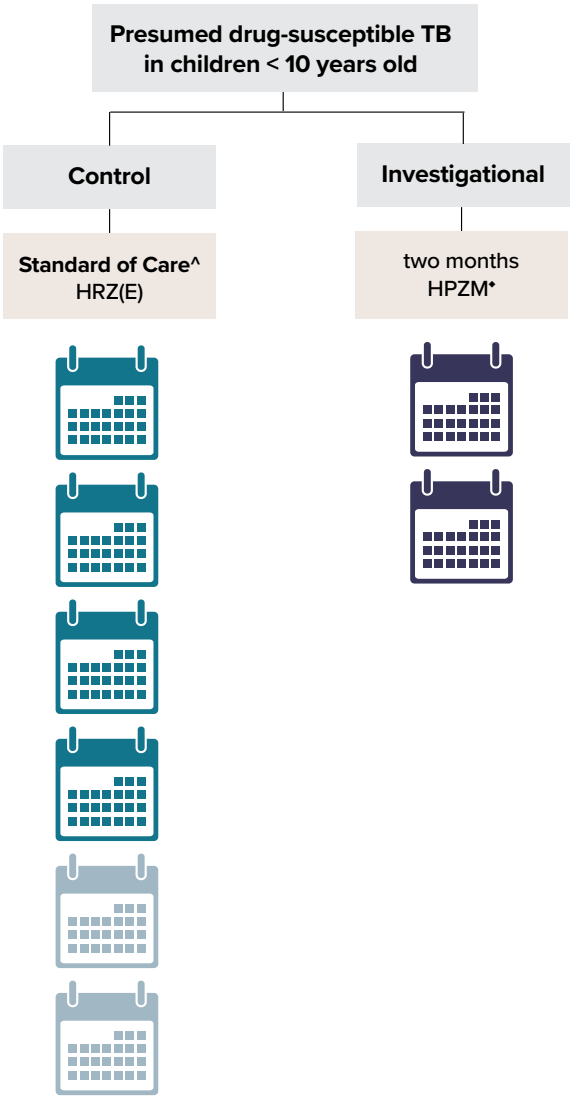
- If a two-month regimen (isoniazid, rifapentine, pyrazinamide, moxifloxacin) regimen is safe and non-inferior to the current standard of care (4-6 months of isoniazid, rifampicin, pyrazinamide with or without ethambutol).
- What the best dose is for rifapentine and moxifloxacin in children of different weight bands in the new regimen.
- How both study regimens affect the levels of the HIV medication, dolutegravir, in the body.
- What children and caregivers think and how they feel about taking TB medicines.
- Which children, based on variables such nutritional and HIV status, can benefit from a two-month regimen.

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

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

Noninferiority trials test if the treatment being studied is not worse than standard treatment.

STUDY DESIGN, CONTINUED



^ 4-6 months of isoniazid, rifampicin, and pyrazinamide with or without ethambutol
• H=isoniazid P=rifapentine, Z=pyrazinamide M=moxifloxacin

ABOUT SMART4TB

The SMART4TB Consortium brings together experts in TB tools development, implementation science, capacity strengthening, civil society engagement and policy translation. Led by Johns Hopkins University, consortium members include University of California, San Francisco; the Elizabeth Glaser Pediatric AIDS Foundation; KNCV Tuberculosis Foundation; Treatment Action Group; and local community and research partners.

This overview 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