United States of America

SMART4TB Consortium

SMILE-TB Trial

Shortened Regimen for Drug-Susceptible TB in Children

BACKGROUND

The U.S. government invests in and promotes American health innovation globally, with TB pediatric research a vital component of these efforts. 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 174,000 children and young adolescents died of TB in 2024 (Global TB Report 2025). 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

Nicole Salazar-Austin at Johns Hopkins University, **Eric Woubudeya** at MU-JHU **Chishala Chibala** and **Bwendo Nduna** at University of Zambia Teaching Hospital, **Rovina Ruslami** at Research Center for Care and Control of Infectious Disease, **Celso Khosa** at Instituto Nacional de Saúde, **Aishwarya Venkataraman** at National Institutes of Research in TB, **Shailaja Mane** at DY Patil, **Mutsa Bwakura** and **Lynda Stranix Chibanda** at Harare Health and Research Consortium

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
Uganda
Zambia
Zimbabwe

STUDY DESIGN ClinicalTrials.gov NCT06253715

SMILE-TB is a Phase 3, **open-label**, **randomized**, **controlled**, **non-inferiority** trial enrolling 860 participants. The main objectives are to find out:

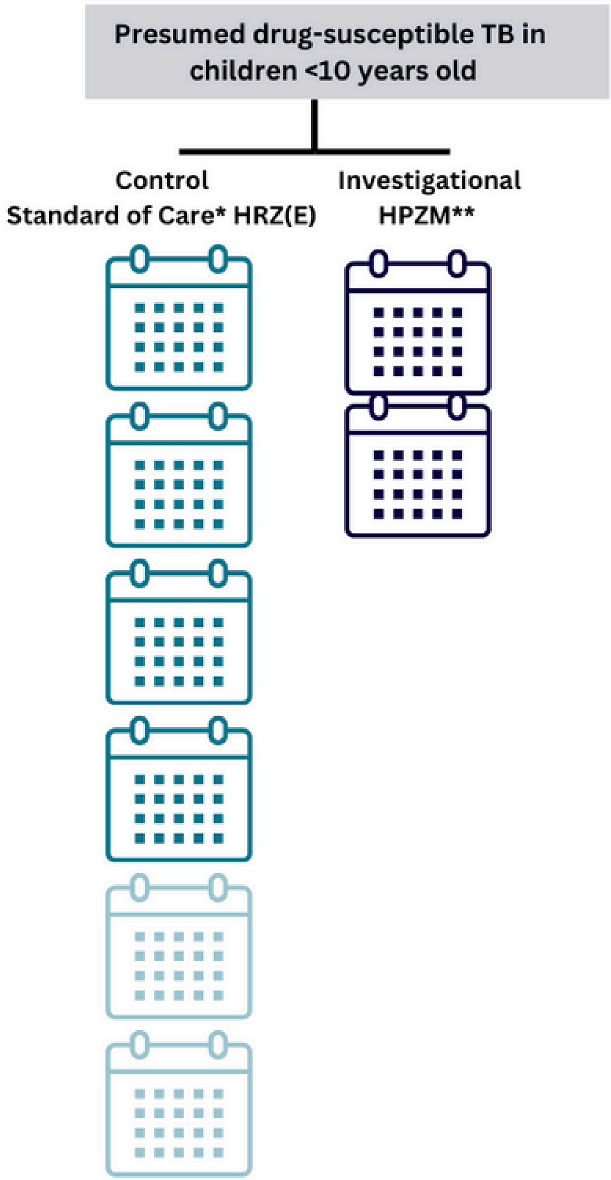
- If a two-month regimen (isoniazid, rifapentine, pyrazinamide, moxifloxacin) regimen is safe and non-inferior to the current standard of care (4-6 months of isoniazid, rifampicin, pyrazinamide with or without ethambutol).
- What the best dose is for rifapentine and moxifloxacin in children of different 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.

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.

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

STUDY DESIGN, CONTINUED



*4-6 months of isoniazid, rifampicin (R), and pyrazinamide with or without ethambutol

**H=isoniazid P=rifapentine Z= pyrazinamide M=moxifloxacin

If you have any questions, please contact smart4tbcomms@jh.edu

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