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Supporting, Mobilizing, and Accelerating Research for Tuberculosis Elimination

SMART4TB Consortium

PRISM Kids

Program for Rifampicin-Resistant Disease with Stratified Medicine for Tuberculosis in Children

BACKGROUND

Children with rifampicin-resistant tuberculosis (RR-TB) often face long, toxic, non-child-friendly treatment regimens, despite having fewer TB bacteria, which generally requires less intensive treatment. Treatment of drug-susceptible TB in children can be as short as four months. A six-month oral regimen of bedaquiline, delamanid, linezolid, and levofloxacin **is now recommended by the World Health Organization** for children with RR-TB. Some children may benefit from even shorter RR-TB treatment.

STUDY GOAL

To evaluate whether an approach that stratifies participants to receive shorter treatment (four months) or standard treatment (six months) depending on risk factors for a less favorable treatment outcome, is effective at curing RR-TB in children under 14 years old.

STUDY LEADERS

PRISM Kids is led by **Ethel Weld** and **Nicole Salazar-Austin** at the 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 aged 0 to <14 years with confirmed or probable pulmonary RR-TB and/or selected forms of extrapulmonary TB, with or without HIV.

STUDY LOCATIONS

Under active discussion

STUDY DESIGN

PRISM Kids is a **randomized, controlled** Phase IIc trial enrolling 120-200 children. The main objective is to find out if a four-month or six-month regimen with optimized drug dosing (with length determined by the extent and severity of the child's TB) is safe and effective at treating RR-TB in children. The study will also look at acceptability and **pharmacokinetics**. Participants will be randomized to either receive a stratified medicine approach:

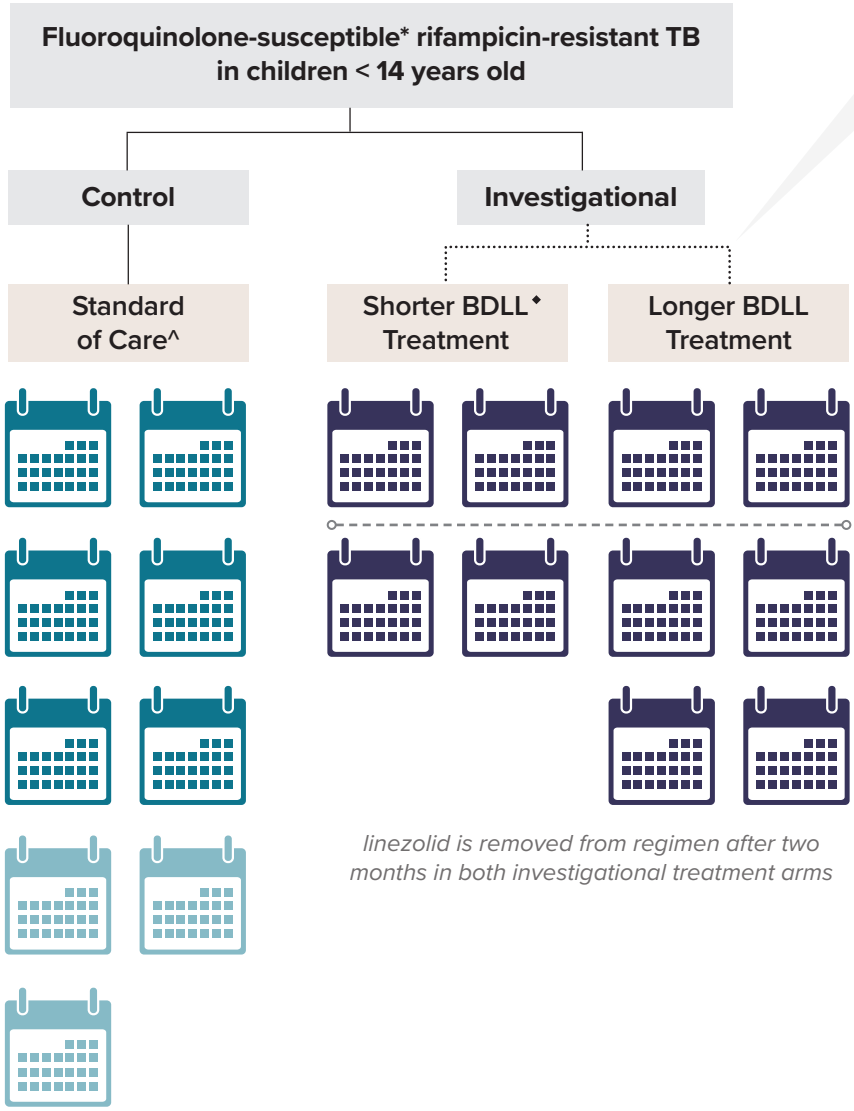
- *Shorter treatment arm:* four months of bedaquiline, delamanid, levofloxacin with two months of linezolid
- *Longer treatment arm:* six months of bedaquiline, delamanid, levofloxacin with two months of linezolid

OR to receive a local standard of care regimen, which must include all-oral medicines and be no longer than nine months.

A **randomized controlled** trial assigns participants to the study intervention (the stratified approach of four versus six months bedaquiline, delamanid, levofloxacin with two months of linezolid, depending on how extensive their TB is) or the control (the local standard of care), to balance participant characteristics with a goal of minimizing bias.

Pharmacokinetics means how the drug moves through the body or how its concentration in the body changes over time, which determines the drug's effect and informs dosing.

STUDY DESIGN, CONTINUED



linezolid is removed from regimen after two months in both investigational treatment arms

Stratification Approach

PRISM Kids uses an algorithm to assign a participant to shorter or longer treatment. This algorithm is based on a combination of factors demonstrated to be associated with treatment outcomes in children. These factors include:

- Presence of at least one **cavity** in the lung
- **Smear positivity** (TB bacteria that stain positive in a sputum sample, meaning that there are many of them present)
- **Where the TB is in the body** (e.g., lungs, abdomen, peripheral lymph node only, or lymph nodes in the thorax with significant airway obstruction)
- Complex or complicated **pleural effusion** (fluid around the lungs)
- **Miliary pattern** (widespread infection, with tiny, seed-like lesions throughout affected organs like lung, liver, or spleen)

** Known or suspected*
^ Standard of care may be any of several all-oral six- or nine-month regimens
◆ B=bedaquiline D=delamanid L=levofloxacin L=linezolid

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.

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