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Supporting, Mobilizing, and Accelerating Research for Tuberculosis Elimination

SMART4TB Consortium

The PRISM-TB Trial

Program for Rifampicin-resistant disease with Stratified Medicine for TB

BACKGROUND

Drug-resistant TB– TB that can't be cured by standard first-line antibiotics—is more difficult and expensive to treat. According to the World Health Organization (WHO), 410,000 people a year fall ill with drug-resistant TB. Recent advances have improved treatment for drug-resistant TB using a combination of more powerful, safer medicines: bedaquiline, pretomanid, linezolid, and moxifloxacin. But the current WHO-recommended regimen still takes six months of treatment. People receive the same length of treatment, regardless of their individual risk factors for unfavorable treatment outcomes.

STUDY GOAL

To evaluate whether shorter treatment—three or four months, depending on individual risk factors for treatment failure or relapse, is effective at curing drug-resistant TB in adults and adolescents.

STUDY LEADER

PRISM-TB is led by Dr. Gustavo Velásquez at the University of California, San Francisco (UCSF) and the clinical trials unit at the UCSF Center for Tuberculosis in partnership with Johns Hopkins University, KNCV Tuberculosis Foundation, Treatment Action Group, and the Elizabeth Glaser Pediatric AIDS Foundation.

STUDY POPULATION

Adults and adolescents aged ≥14 years with confirmed TB of the lungs that is resistant to the first-line antibiotic rifampicin.

SAMPLE SIZE

The study will include 690 participants.

STUDY DESIGN

PRISM-TB is a **multi-arm multi-stage**, **randomized**, **controlled**, **noninferiority** Phase 3 trial. The main objectives are to find out:

- Whether shorter treatment strategies have as good efficacy as standard treatment as measured by TB-related unfavorable outcomes (death, **relapse**, or **treatment failure**) at 18 months after treatment. The treatment strategies being tested are

  Four months for all participants and

  Three months for easier-to-treat TB, six months for harder-to-treat TB
- Whether shorter treatment strategies are as safe as the control, by looking at the proportion of participants who experience adverse events that are serious or of special interest.

Multi-arm multi-stage (MAMS) trials allow comparing several regimens, with prespecified decision-making for which regimen(s) can advance to the next stage and are more efficient than multiple separate studies.

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

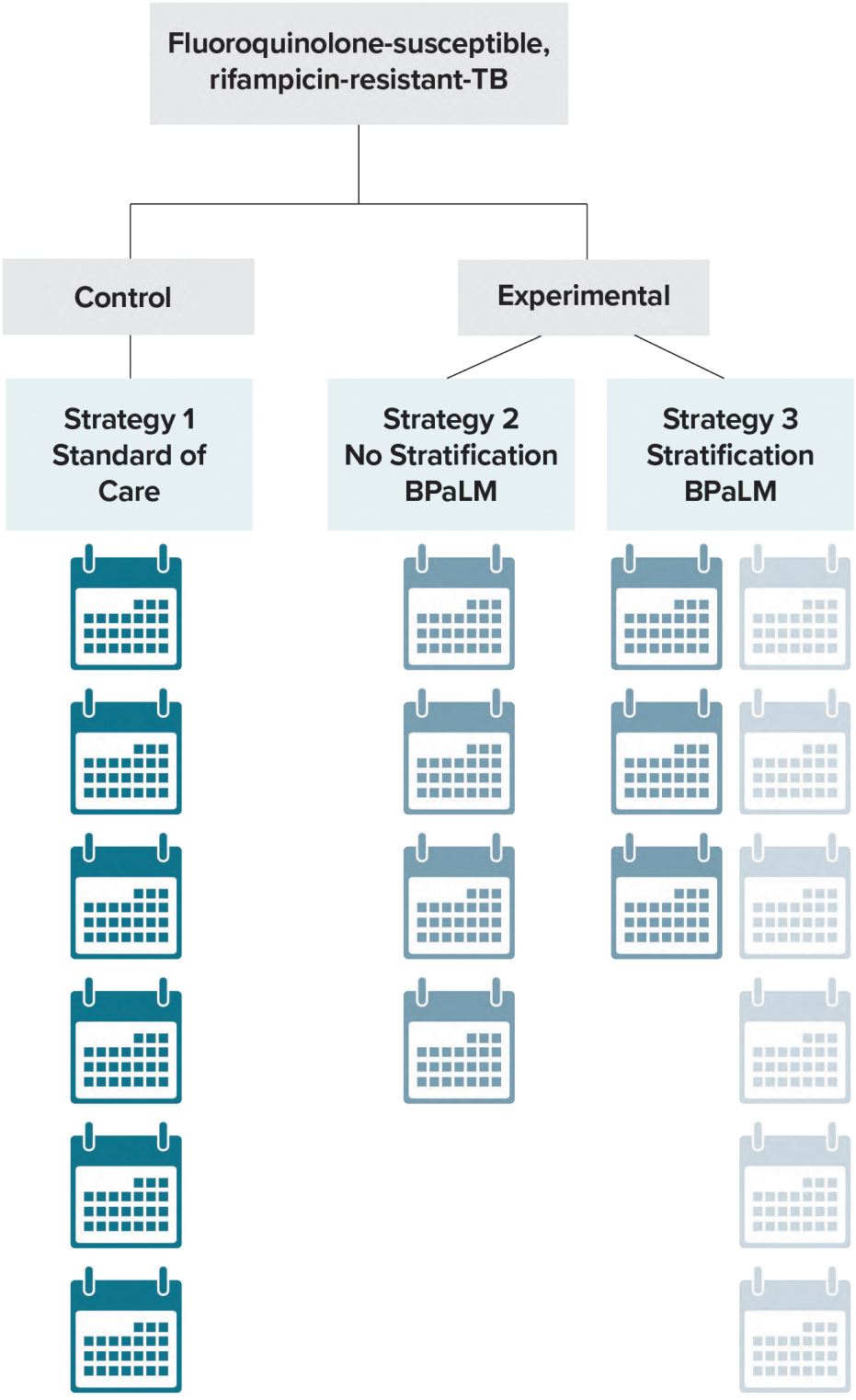
Noninferiority trials test that the treatment being studied is not worse than standard treatment.

Relapse is a return of TB disease following a period of partial improvement.

Treatment failure is when the treatment fails to cure TB.

Adverse event is any unfavorable and unintended sign (including laboratory test results), symptom or diagnosis that occurs in a study participant during the study.

STUDY DESIGN, CONTINUED



B=bedaquiline, Pa=pretomanid, L=linezolid, M= moxifloxacin

ABOUT SMART4TB

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