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TRUNCATE-TB: an innovative trial design for drug-sensitive tuberculosis

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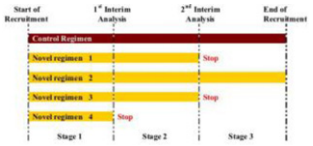
Background: The number of potential regimens of drug treatment for TB is vast, meaning that evaluating each new treatment against a control in separate two-arm trials requires a huge amount of resources. There is, therefore, a need for innovative trial designs that can evaluate drug regimens simultaneously.

Methods & Materials: TRUNCATE-TB (two-month regimens using novel combinations to augment treatment effectiveness for drug-sensitive tuberculosis) is a randomised, open-label, multi-arm, multi-stage (MAMS), parallel group strategy trial. The MAMS design has been applied successfuly in a trial of multiple regimens for prostate cancer, and more recently in a TB trial. In the MAMS design, the trial starts with multiple arms, and, as it progresses, recruitment to those arms that do not show sufficient promise on an early interim outcome measure are discontinued, whilst recruitment to the control arm and remaining promising novel boosted arms continues until sufficient numbers of patients have been enrolled to assess the outcome on the defined primary outcome. Recommendations about stopping or continuing arms are made by an Independent Data Monitoring Committee on the basis of safety and efficacy data.



Results: Up to 1080 adult patients with pulmonary TB (diagnosed using sputum GeneXpert) will be randomised at equal probability to receive 6-months standard treatment as a control, or to one of a number of boosted regimens (these regimens are combinations of standard drugs with new or repurposed drugs including: high-dose rifampicin, linezolid, clofazimine, bedaquiline, delamanid, rifapentine or levofloxacin.

Conclusion: The primary aim of the trial is to determine whether a strategy of treating drug-sensitive TB for 2 months with one of a number of novel combination regimens and re-treating relapse with a 6-month course of standard treatment will be non-inferior to the standard WHO-recommended 6-month treatment/8-month re-treatment approach in terms of TB sputum culture status at 2 years after randomisation. The secondary aims are to assess the possible advantages of the TRUNCATE-TB management strategy compared to the standard management strategy from the patient perspective (including acceptability, quality of life and clinical adverse events) and the programme perspective (including treatment adherence, default, new drug resistance and community transmission) as well as cost-effectiveness.

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