Project Brief: TB Champ

Full Title of Study/Programme	A phase III cluster randomised placebo-controlled trial to assess the efficacy of preventive therapy in child contacts of multidrug-resistant (MDR) tuberculosis (TB)
Technical Focus Area	Research (Paediatrics and Maternal)
Rationale	This trial specifically targets children less than five years for two reasons. First, children less than five years are at the highest risk of progressing to TB disease following infection. Second, concordance of drug susceptibility is high between adults with MDR-TB and young child household contacts. This group is therefore most likely to be benefit from MDR-TB preventive therapy. In addition, global policy and national guidelines in South Africa advocate preventive therapy only for HIV-negative child contacts less than five years following exposure to a drug-susceptible TB index case, enhancing the programmatic relevance of our proposed trial. Furthermore, this trial will target children (HIV-infected and uninfected) under 5 years of age, regardless of tuberculin skin test (TST) status, to ensure programmatic relevance, since WHO and the South African National TB Programme (SA NTP) do not mandate tests of TB infection prior to initiating TB preventive therapy.
Primary Objectives	To determine whether LFX, the intervention arm, given daily for 24 weeks, is efficacious in preventing MDR-TB in high-risk child household contacts (HHC) of confirmed adult MDR-TB cases.
Secondary Objectives	1. Does LFX have acceptable toxicity and tolerability in children? 2. Is mortality (non-traumatic death) similar in children on the 2 study arms? 3. What is the adherence to 24 weeks of daily MDR-TB prevention? 4. Are there differences in LFX resistance between study arms in children developing incident TB? 5. Is LFX cost-effective and acceptable to both families and to the TB programme in preventing MDR-TB in child household contacts?
Primary Endpoint/Outcome	Incident TB disease (probable or confirmed) including TB death, by 48 weeks post-randomisation
Secondary Endpoint/Outcome	• Mortality (all cause, non-traumatic, and TB related) • Adverse events ≥ grade 3 (at least possibly associated) during 24 weeks of treatment • Percentage of levofloxacin or levofloxacin-placebo doses ingested and retained over 24 weeks • TB disease over 96 weeks • Incidence of levofloxacin resistant TB disease
Study Design	Phase III cluster randomised placebo-controlled trial
Study Population	HIV-infected and -uninfected child (< 5 years) household contacts of adult MDR-TB index cases

Study Sample Size	778 households (1556 children) of adult MDR-TB index case (with on average 2 children aged 0-5 years per household)
Follow-up/Duration	96 weeks in total, including treatment for 24 weeks and post-treatment follow-up of 72 weeks
Study/Programme Sites	• Wits RHI Shandukani Research Centre (SRC) • Tygerberg, Cape Town • Pietermaritzburg • Klerksdorp
Study/Programme Duration	January 2017 – June 2021
Investigators	• Dr Lee Fairlie, Principal Investigator • Dr Masebole Masenya, Sub Investigator • Dr Faeezah Patel, Sub Investigator • Dr Elizea Horne • Dr Mishal Bawa
Other Partners & Collaborators	Desmond Tutu TB Centre (DTTC) (Prof Anneke Hesseling)
Sponsors/Donors	Joint Global Health Trials Scheme of the Department for International Development, UK (DFID), the Wellcome Trust and the Medical Research Council (MRC UK), Grant number MR/M007340/1 and the South African Medical Research Council (SA MRC). Trial drugs will be supplied by McCleods, India.
Publications/Key Presentations to Date	None as yet
Progress Update as at Jan 2019	Submitted to MCC and HREC, approval received July 2017, first enrolment Nov 2017. Currently 46 enrolled and 5 LTFU (1 relocated, 1 withdrew consent and 3 LTFU)
Frequency of Donor Narrative Report	Monthly
Overall Study/Project Contact	Dr Hermien Gous (hgous@wrhi.ac.za), Janet Grab (jgrab@wrhi.ac.za)
Briefing Owner and Date	Dr Lee Fairlie, Nov 2016, updated January 2019