SUMMARY OF ONGOING AND PLANNED CLINICAL RESEARCH ON TUBERCULOSIS DRUGS IN CHILDREN AND PREGNANT WOMEN

Protocol name/number Trial registration	Phase	Design	Study type	Primary objective	Indication	Special populations/ considerations	Funder, sponsor, principal investigator	Network/CTU Countries	Status
Paediatric studies									
P4v9 Trial NCT00170209	III	Randomized open label positive-controlled multicenter trial	Prevention	Safety and tolerability of 4 months rifampicin and 9 months Isoniazid for treatment of LTBI in children	DS-TB	Children, adolescents Children with LTBI at high risk of TB	Canadian Institutes of Health Research (CIHR) Menzies dick.menzies@mcgill.ca	N/A Canada, Australia, Benin, Guinee, Indonesia	Enrolling
ACTG 5279 NCT01404312	III	Randomized, open-label multicenter trial	Prevention	Evaluate the efficacy of an ultra short rifapentine-based regimen in adults and adolescents	DS-TB	Adolescents, adults HIV+ Drug drug interactions	NIAID Chaisson/Swindells rchaiss@jhmi.edu	ACTG; IMPAACT co-endorsed Thailand, Africa	Enrolling
Otsuka 232 and 233 NCT01856634/ NCT01859923	I II	Open-label, single arm dose finding study of delaminid in HIV-negative children with MDR-TB	Treatment	Evaluate the PK, safety, tolerability and anti-mycobacterial activity of Delaminid in combination with MDR-TB therapy for HIV-uninfected and HIV-infected children and adolescents		Children, infants, adolescents HIV- Pop PK modeling Age de-escalation	Otsuka Jeffrey.Hafkin@otsuka-us.com	N/A Phillippines, South Africa	Enrolling
Delamanid DDI	I/II	Open-label, single arm dose finding study	Treatment	Evaluate the PK, safety, tolerability and anti-mycobacterial activity of Delaminid in combination with MDR-TB therapy for infected children and adolescents		Children, infants, adolescents HIV+ Pop PK modeling	NIAID kdooley1@jhmi.edu	IMPAACT	Planned
DAtiC NICHD-069175	I	Intensive PK sampling, firstline TB drugs	Treatment	Evaluate the PK of first line antituberculosis drugs using 2010 WHO guidelines across paediatric populations	DS-TB	Children, infants HIV+/HIV- Malnutrition Drug-drug interactions Pop PK modeling	NICHD R01 McIlleron University of Cape Town, South Africa	N/A South Africa, Malawi	Enrolling

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NCT01637558							helen.mcilleron@uct.ac.za		
DNDi: RTV Superbooster for HIV/TB co-infection	I/II	Develop a stand-alone ritonavir (RTV) booster formulation to be added to the optimized LPV/r-based paediatric ARV regimen	Treatment	PK ARV and TB drugs	DS-TB	Children, infants HIV+	AFD, MSF, AECID Spain; SDC Lallemant Switzerland mlallemant@dndi.org	DNDi South Africa, Thailand; France	Ongoing
PK-PTB HIV01 NCT01687504 NCT01699633 NCT01704144	IV	Open-label steady state PK of first-line TB drugs and ARV	Treatment	Evaluate the pharmacokinetics and safety of the WHO recommended increased dosages of the first-line anti-TB medications in children with TB and HIV/TB co-infection	DS-TB	Children, infants HIV+/- Drug-drug interaction studies	NICHD R01 Awewura The Miriam Hospital, Rhode Island, USA AKwara@Lifespan.orgKwara	NA Ghana	Enrolling
MDR-PK study NICHD-069169	I	Intensive PK sampling, routine 2ndline TB drugs	Treatment	Evaluate the PK and safety of secondline antituberculosis drugs in HIV-infected and uninfected children	DR-TB	Children, infants, adolescents HIV+/HIV- Drug-drug interactions	NICHD R01 Hesseling Stellenbosch University, South Africa annekeh@sun.ac.za	N/A South Africa	Enrolling
IMPAACT 1108: Bedaquiline	I/II	Open-label, single arm dose finding and safety study	Treatment	Evaluate the PK, safety, tolerability and anti-mycobacterial activity of Bedaquiline in combination with MDR-		Children, infants, adolescents HIV+/- Pop PK modeling Age de-escalation	NIAID Hesseling annekeh@sun.ac.za	IMPAACT South Africa	Opening 2015

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				TB therapy for HIV--infected and uninfected children and adolescents					
"SHINE" (Shorter treatment for mINimal TB in childrEn)	III	Randomised, non-inferiority, open label efficacy trial	Treatment	Evaluate the efficacy of 4 vs. 6 months treatment for minimal TB in children with new WHO-recommended first-line TB doses	DS-TB	Children, adolescents, infants HIV+/HIV- Nested PK studies Drug-drug interactions	BMRC/DFID/Wellcome Trust BMRC CTU at University College London (UCL) Gibb diana.gibb@ucl.ac.uk	MRC CTU Endorsed by IMPAACT India, Uganda, Zambia, South Africa	Opening 2015
Treat infant TB	I	Intensive PK sampling, first line TB drugs, single drug formulation	Treatment	Evaluate the PK and safety of first line antituberculosis drugs using 2010 WHO dosing in infants < 12 months	DS-TB	Infants HIV+/-	Unitaid, Step-TB Project Hesseling/Bekker Stellenbosch University, South Africa annekeh@sun.ac.za	TB Alliance South Africa	Enrolling
IMPAACT P1106	I	PK characteristics of cART and TB therapy in premature and LBW infants	Treatment	Evaluate the PK of ARV and first and secondline TB drugs in low birth weight infants	DS-TB DR-TB	Infants HIV+/- Low birth weight, premature	NIAID Mirochnik/Cotton Mark.Mirochnick@bmc.org	IMPAACT	Opening 2014
"TB-CHAMP" (TuBerculosis CHild and Adolescent Multidrug-resistant Preventive therapy trial)	III	Randomized double blind placebo-controlled, superiority multicenter trial	Prevention	Evaluate the efficacy of levofloxacin vs. placebo for the prevention of MDR-TB in child and adolescent household contacts	DR-TB	Children, adolescents, infants HIV+/HIV- Household randomization	BMRC/DFID/Wellcome Trust Hesseling/Seddon/Schaaf annekeh@sun.ac.za	BMRC CTU South Africa	Opening 2015
PHOENIX	III	Randomized open label, superiority multicenter trial	Prevention	Evaluate the efficacy of levofloxacin vs. INH for the prevention of MDR-TB in adult, child and	DR-TB	Children, adolescents, infants, adults HIV+/HIV-	NIAID Churchyard	ACTG/IMPAACT	Planned

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				adolescent household contacts		Household randomization	GChurchyard@aurumininstitute.org Gupta agupta25@jhmi.edu		
TBTC Study 35	I/II	PK and safety study of RFPT/INH co-formulation in children for prevention of TB	Prevention	Determine the optimal dose and assess PK and safety of rifapentine, given in combination with INH, in children with LTBI	DS-TB	Children, infants HIV- Age de-escalation Pop PK modeling	TBTC, in collaboration with Sanofi Hesseling/MacKenzie annekeh@sun.ac.za	TBTC USA, South Africa	Planned
Rifabutin PK trial	IV	PK and safety of rifabutin in adults and children	Treatment	PK and safety of rifabutin in adults and children	DS-TB	Adults Children HIV-	ICMR, NACO Swaminathan National Institute for Research in Tuberculosis (NIRT), Chennai, India doctorsoumya@yahoo.com	Pending India	Planned
"PATCH": Innovative PK/PD approaches to optimize TB meningitis treatment in children	II	Intensive PK, pop PK modeling	Treatment	Evalute the efficacy and safety of levofloxacin and rifampicin for the treatment of TB meningitis in children	DS-TB	Children, infants HIV+/-	R01 Dooley/Gupta/Swaminathan Johns Hopkins University Kdooley1@jhmi.edu	N/A	Planned; funded
Pregnancy studies (including infants)									
IMPAACT P1026S NCT00042289	IV	Drug-drug interactions in management of TB/HIV in pregnancy	Treatment	Peripartum and postpartum PK of first line TB drugs in women with and without ART	DS-TB	Pregnant women HIV+	NIAID Mirochnik Mark.Mirochnick@bmc.org.	IMPAACT	Enrolling

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								USA, Brazil, Botswana, Uganda, South Africa	
TSHEPISO Study: The effect of TB and its treatment on HIV-infected pregnant women and their infants. R01HD064354-04	IV	Study the impact of TB/HIV co-infection in pregnancy on maternal and infant outcomes; characterize the impact of TB treatment using rifampin on the PK and PD of NNRTIs used for PMTCT.	Treatment	Nested PK studies in pregnant women and infants	DS-TB	Pregnant women HIV+/- Nested PK studies Drug-drug interactions	NAID RO1 Johns Hopkins University Chaisson rchaiss@jhmi.edu	N/A South Africa	Enrolling
IMPAACT P1078 "TB Apprise" NCT01494038	IV	Randomized double blind placebo-controlled multicenter trial	Prevention	Evaluate the safety of antepartum vs. post-partum INH in HIV-infected pregnant women	DS-TB	Pregnant women HIV+	NIAID Gupta; agupta25@jhmi.edu JHU	IMPAACT India, South Africa, Uganda, Botswana, Malawi, Zimbabwe	Opening 2014
IMPAACT P1101 Raltegravir PK NCT01751568	I/II	Dose-finding, safety, tolerability, drug-drug interaction and PK study of RAL- naïve children who have received ≥ 1 week and ≤ 20 weeks of rRIF-based TB therapy prior to initiation of ARV therapy	Treatment	To determine the pk and appropriate dose of RAL when administered with a RIF-containing anti-TB therapy in HIV/TB co-infected children		ARV naïve HIV/TB co-infected children ≥ 3 to < 12 years old	NICHD MIAID Meyers tammy@myers.net	IMPAACT South Africa	Opening 2014

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IMPAACT P2001 Rifapentine in pregnant women	I/II	PK and safety of rifapentine and INH in HIV-infected pregnant women	Prevention	Evaluate the PK and safety of rifapentine and INH given as part of an LTBI regimen in HIV-infected and uninfected women and their infants.	DS-TB	Pregnant women Infants	NIAID Mathad jsm9009@med.cornell.edu	IMPAACT	Opening 2015
Evaluation of PK between Depo-medroxyprogesteroneacetate (DMPA), Rifampicin, and Efavirenz in HIV and TB co-infected women	I/II	Estimate optimal dosing frequency of DMPA for TB/HIV+ women on RIF/EFV. Determine whether MPA levels will be adequate to suppress ovulation through 12 weeks in these women	Treatment	Nested PK studies	DS-TB	Pregnant women HIV+ Nested PK studies	NIAID Mngqibisa University KwaZulu Natal mngqibisa@ukzn.ac.za	ACTG	Planned