Project Brief: HPTN 084

Full Title of Study/Programme	HPTN 084: A Phase 3 Double Blind Safety and Efficacy Study of Long-Acting Injectable Cabotegravir Compared to Daily Oral TDF/FTC for Pre-Exposure Prophylaxis in HIV-Uninfected Women
Technical Focus Area/Key Words	HIV Prevention, Long acting Injectable, Cabotegravir tenofovir/emtricitabine (trade name: Truvada®)
Rationale	PrEP may only reach its full potential for HIV prevention with agents that do not depend on daily or near-daily pill-taking. The development of alternative agents for PrEP, and/or more adherence-friendly schedules for currently available agents, could increase prevention choices and increase acceptability. Long-acting injectable agents have the potential to prevent HIV acquisition without relying on adherence to a daily oral regimen.
Primary Objectives	Efficacy: To evaluate the relative efficacy of oral CAB/CAB LA (oral run-in and injections, Steps 1 and 2) vs. daily oral TDF/FTC for HIV prevention (Steps 1 and 2). Safety: To evaluate the relative safety of oral CAB/CAB LA (oral run-in and injections, Steps 1 and 2) vs. daily oral TDF/FTC for HIV prevention (Steps 1 and 2).
Primary Endpoint/Outcome	Number of documented incident HIV infections in Steps 1 and 2
Study Design	Multi-site, double blind, two-arm, randomized (1:1), controlled superiority trial of the safety and efficacy of CAB LA compared to daily oral TDF/FTC for HIV prevention.
Study arms	Step 1 - Oral Run-in Phase (Blinded daily oral tablet) Participants will be randomized 1:1 to one of two study arms: Arm A: CAB 30 mg tablet, one tablet orally daily for five weeks and placebo for TDF/FTC tablet. Arm B: TDF/FTC 300 mg/200 mg fixed dose combination tablet and placebo for CAB tablet. Step 2 – Injection Phase (Blinded injections and blinded daily oral tablet) Arm A: CAB LA 600 mg administered as one 3 mL (600 mg) IM injection and placebo for TDF/FTC tablet. Arm B: TDF/FTC 300 mg/200 mg fixed done tablet orally daily, with or without food and placebo for CAB LA (Intralipid 20% fat emulsion infusion) administered as one 3mL IM injection. Step 3 – Follow-up Phase All participants, including those who permanently discontinue receiving injections before their Step 2 participation in the study ends, will receive open-label TDF/FTC 300 mg/200 mg fixed dose combination tablet, one tablet orally daily for up to 48 weeks.
Study population	HIV-uninfected women at risk for acquiring HIV, 18 to 45 years old.
Study sample size	3,224 HIV-uninfected women from Sub Saharan Africa
Follow up/duration	Between 1.6 years (for the last enrolling participants) to approximately 3.6 years (for the earliest enrolling participants)
Study/Programme sites	Baylor Uganda CRS Kampala Uganda Blantyre CRS Blantyre Malawi Botha's Hill CRS Botha's Hill South Africa Desmond Tutu TB Centre - Stellenbosch University CRS Cape Town South Africa Emavundleni CRS Cape Town South Africa

	Gaborone CRS Gaborone Botswana Isipingo CRS Durban South Africa Kisumu CRS Kisumu Kenya Malawi CRS Lilongwe Malawi MU-JHU Research Collaboration CRS Kampala Uganda Parirenyatwa CRS Harare Zimbabwe Seke South CRS Chitungwiza Zimbabwe Soweto HPTN CRS Soweto South Africa Spilhaus CRS Harare Zimbabwe St Mary's CRS Chitungwiza Zimbabwe Swaziland Prevention Center Mbabane Swaziland UVRI-IAVI Entebbe Uganda Verulam CRS Verulam South Africa Ward 21 Johannesburg South Africa Zengeza CRS Chitungwiza Zimbabwe
Study/Programme duration	Approximately 4.6 years total, with individual participants being followed on randomized study product: between 1.6 years (for the last enrolling participants) to approximately 3.6 years (for the earliest enrolling participants), and on oral TDF/ FTC for an additional 48 weeks. Accrual will require approximately 2 years
Intervention	CAB (oral and LA injectable, TDF/FTC oral study product)
Investigators	IOR: Dr Carrie-Anne Mathew Sub Investigators: Prof Sinead Delany-Moretlwe, Dr Elizabeth Roos, Dr Kim Helen Comline, Dr Jeanne Omony, Dr Nicole Poovan
Other Partners & Collaborators	ViiV Healthcare. Gilead Sciences, Inc.
Sponsors/Donors	Division of AIDS (DAIDS), United States (US) National Institute of Allergy and Infectious Disease (NIAID), US National Institute of Mental Health (NIMH) and US National Institute of Health (NIH).
Linked Sub Studies and post grad projects	HPTN 084-01: Safety, Tolerability and Acceptability of Long-Acting Cabotegravir (CAB LA) for the Prevention of HIV among Adolescent Females – A Sub-study of HPTN 084. HPTN 084 Contraception Substudy
Publications/key presentations to date	None
Progress Update as at 08 March 2021	Screened: 268 Enrolled: 206 Withdrawals: 5 Product Hold: 13 Product Discontinuation: 16 Transition to step 3/Open Label: 11
Frequency of donor narrative report	Annual
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Briefing owner and date	Dr Carrie- Anne Mathew cmathew@wrhi.ac.za 08 March 2021