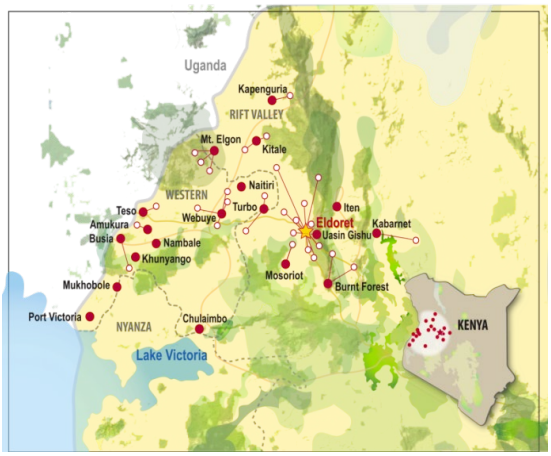
Moi University Clinical Research Centre Provides Resources Needed for Clinical Trials



The Moi University Clinical Research Centre (MUCRC) is located at the Chandaria Cancer and Chronic Diseases Centre at Moi Teaching and Referral Hospital (MTRH) in Eldoret, Kenya. MUCRC was established as a Clinical Research Site (CRS) for the AIDS Clinical Trials Group (ACTG) Network by the Division of AIDS (DAIDS), National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH) of the United States' Department of Health and Human Services. In December 2008, MUCRC became a CRS for the United States Military HIV Research Program (US MHRP). MUCRC operates in partnership with the Academic Model Providing Access to Healthcare (AMPATH). The AMPATH partnership is a collaboration between Moi University School of Medicine (MUSoM), MTRH and the AMPATH Consortium, a global collaboration academic medical centers led by Indiana University. AMPATH research projects are active at clinic sites throughout the catchment area as well as in the communities served by AMPATH clinics. MTRH is one of the two national referral hospitals in Kenya. MTRH serves a population of approximately 24 million from western Kenya and neighboring countries. The MTRH campus includes the AMPATH Centre and other several specialty care buildings including Chandaria Cancer and Chronic Diseases Centre, Shoe4Africa Children's Hospital, Riley Mother and Baby Hospital, Rafiki Center for Excellence in Adolescent Health and Majaliwa surgical theaters. MTRH has an emergency department, general and special outpatient clinics and inpatient services for all areas of medical care. The hospital has specialists in various fields of medicine, pediatrics, obstetrics and gynecology, surgery, psychiatry and medical research. MTRH, in collaboration with MUSOM and other AMPATH partners, has established centers of excellence in diabetes, hematology/oncology, pulmonary, cardiology, psychiatry and medical informatics.

Physical Infrastructure: The MUCRC occupies 5,424 square feet on the 3rd floor of the MTRH Chandaria Cancer and Chronic Diseases Centre at and meets all AIDS Clinical Trials Group (ACTG) physical and staffing requirements for an active clinical trials unit. The centre recently expanded to an annex site in the Moi University Daima pension towers.

The site has three sinks along the corridors each with running water, a soap dispenser and hand dryer. MUCRC also has washrooms for both staff and participants. Electrical power supply from the main grid

is backed up by a generator during power blackouts. There is reliable 24-hour security including bomb detectors and the CCCDC building has the hospital patrol base manned by armed security personnel. Double locking system is in place in every room within the MUCRC. The facility has a vehicle for transportation of study samples to back-up labs as well as recruitment and retention activities. The site also has access to transport from the AMPATH program.

Staffing

MUCRC has nine investigators, one pharmacist, one backup associate pharmacist, three backup pharmacy technologist; one site manager; two study coordinators; one regulatory affairs officer; two Quality Assurance/Quality Control officers; two medical officers; six clinical officers, one data manager; three assistant data managers and three data officers; one phlebotomist; one laboratory manager; four study nurses and eight recruitment officers.

Community Advisory Board (CAB)

The MCTU-CAB was constituted in 2004 when establishing the site as part of the ACTG. The MCTU-CAB's initial mission was to integrate community involvement into the AIDS Clinical Trials Unit (ACTU) to advance HIV/AIDS research. As the unit has expanded to include studies funded through other sources, including local investigator-initiated studies, the CAB's role has expanded. The MCTU-CAB has six members who meet twice per month: one represents teachers, three represent the patients (two adult and one youth), one represents a community-based organization focused on human rights, and one represents women's issues. They review protocols utilizing project-developed summary sheets and provide feedback early in the protocol development and initiation stage. They are responsible for community sensitization and dissemination of results to the community. They also act as a conduit for community concerns about research and as educators of the community about HIV and research.

Laboratory Capacity

MUCRC utilizes The AMPATH Reference Laboratory (ARL) which is an International Organization of Standardization (ISO) 15189-2012 accredited Good Clinical Laboratory Practice (GCLP) certified and Division of Acquired Immune Diseases (DAIDs) approved laboratory to analyze DAIDS sponsored protocols. ARL has a robust quality management system with all assays participating in an approved external quality assurance panel (College of American Pathologists-CAP; United Kingdom National External Quality Assurance Services-UKNEQAS; One World accuracy, Virology Quality Assurance-VQA Gap and in-country inter laboratory assessments. It also undergoes periodic audits by the study specific auditors, ISO surveillance and study specific monitoring. It has within it five sections:

1. **Immunology** (single platform flow cytometry) for (Cluster of Differentiation) CD3, CD4, CD8 and Lymphocyte Counts (absolute and %) and leukemia lymphoma diagnosis; using FACS calibur from Becton and Dickson and cytoflex from Beckman Ccoulter
2. **Molecular Biology** for HIV DNA, Viral Loads for HIV (real time and end point polymerase chain reaction-PCR), gonorrhea and chlamydia PCR, chlamydia PCR, tuberculosis PCR, HIV Genotyping (currently under discussion with Abbott) SARs COV2 real time PCR, hepatitis B virus DNA, human papillomavirus-HPV; **Automated SP/RT m2000 Abbott analyzer, quant studio bios real time PCR, and GeneXpert.**
3. **Serology** for Hepatitis B surface antigen (rapid test), HIV Enzyme Linked Immuno Sorbent Assay (ELISA), Herpes Simplex Virus ELISA, Pregnancy testing (urinary hCG), Syphilis testing by RPR (Rapid Plasma Reagin) and Treponema pallidum hemagglutination assay, toxoplasma antibody, cryptococcal antigen, streptococcal antigen, histoplasma antigen, and anti-histoplasma antibody, SARs COV 2 rapid antibody test and ELISA test. The site participates in approved external quality assurance panel for all its test, PPR, Rapid Antibody tests and Antibody ELISA
4. **Biochemistry** (automated, colorimetric and ion sensitive electrode) for Albumin, Alanine Aminotransferase Alkaline Phosphatase, Amylase, Aspartate Aminotransferase, Bicarbonate, Bilirubin, Chloride, Cholesterol, Creatine Kinase, Creatinine, Glucose, High Density and Low Density Lipoproteins – HDL/LDL cholesterol, Lactic Acid, Lipase, Potassium, Sodium, Total Protein, Triglycerides, Blood Urea Nitrogen HBA1C; Hematology (automated, impedance/laser, 22 parameters) for White Blood Cells (total and differential counts for neutrophils, lymphocytes, monocytes, eosinophils and basophils), Red Blood Cell Count, Hemoglobin, Hematocrit, Mean Cell Volume, Mean Cell Hemoglobin and Mean Cell Hemoglobin Concentration, Red Cell Distribution Width, Platelet Count, Mean Platelet Volume, Platelet Concentration, and Platelet Distribution Width. cytogenetics, using Flourescent InSitu Hybridization (FISH) technology for diagnosing, breakpoint cluster region/Abelson (BCR/ABL) positive chronic myeloid leukemia (CML), acute lymphocytic leukemia (ALL), marker for Burkitts lymphoma (Myc).
5. **Histopathology** for Hematoxylin/Eosin, Giemsa, and modified Ziehl Nielsen stains; immunohistochemistry and flow cytometry.

Backup Laboratories

For tests that cannot be conducted at the site or for which protocol approval has not been granted by the sponsor, MUCRC utilizes the services of,

1. Kenya Medical Research Institute/ Walter Reed Project Clinical Research Center, Laboratory, Kericho.
2. Kenya Medical Research Institute/Center for Disease Control (KEMRI/CDC) TB Research Laboratory, Kisumu.

Research Portfolio

MUCRC has implemented several ACTG (DAIDS-funded) randomized clinical trials as well as non-DAIDS-funded protocols from the pharmaceutical industry, the European and Developing Countries Clinical Trials Partnership (EDCTP), the UK Medical Research Council (MRC) and the President's Emergency Plan for AIDS Relief (PEPFAR) Public Health Evaluation (PHE) among others. (Appendix 1).

Some of these trials have been landmark clinical trials that have changed clinical practice. For example:

A5208- The OCTANE clinical trial : (Optimal Combination Therapy after Nevirapine Exposure) – informed the use of Nevirapine among pregnant women. The findings of this trial also informed the choice of HAART among women and children exposed to Nevirapine as part of prevention of mother to child transmission.

The EARNEST trial was a randomized controlled trial to evaluate options for second-line therapy in patients failing a first-line 2NRTI+ NNRTI regimen in Africa. This trial informed the choice of second line HAART therapy among people living with HIV (PLWH).

A5279: Phase III Clinical Trial of Ultra-Short-Course Rifapentine/Isoniazid for the Prevention of Active TB in HIV-Infected Individuals with Latent TB Infection. This trial informed the current TB preventive therapy among PLWH.

The NADIA trial ,“A randomised controlled trial of darunavir versus dolutegravir and tenofovir versus zidovudine in second-line antiretroviral therapy regimens for the public health approach in sub-Saharan Africa” – informed the use of dolutegravir and is currently the WHO recommended first line HAART therapy.

Appendices

Appendix 1 Previous Studies conducted at MUCRC

PREVIOUS STUDIES				
Protocol Name	**Sponsor**	**Enrollment Goal**	**Enrollment**	**Status of study**
A5208-OCTANE: Optimal Combination Therapy after Nevirapine Exposure	ACTG	64	64	Completed
A5221-STRIDE: A Strategy Study of Immediate Versus Deferred Initiation of Antiretroviral Therapy for HIV Infected Persons Treated for TB with CD4 <200 cells/mm3	ACTG	75	61	Completed
A5225-HiFLAC: A Phase I/II Dose-Finding Study of High-Dose Fluconazole Treatment in AIDS-Associated Cryptococcal Meningitis	ACTG	30	26	Completed
A5264-REACT-KS: A Randomized Evaluation of ART Alone or with Delayed Chemotherapy versus ART with Immediate Adjunctive Chemotherapy for Treatment of Limited Stage AIDS-KS in Resource-Limited Settings	ACTG	70	17	Completed
A5265-GIVEN: A Phase III, Open-Label, Randomized, Assessment-Blinded Clinical Trial to Compare the Safety and Efficacy of Topical Gentian Violet to that of Nystatin Oral Suspension for the Treatment of Oropharyngeal Candidiasis in HIV-1 Infected Participants in Non-U.S. Settings	ACTG	80	15	Completed. Study closed to accrual early following DSMB recommendation
A5274- REMEMBER: Reducing Early Mortality and Early Morbidity by Empiric TB Treatment	ACTG	100	70	Completed
A5273- SELECT: Multicenter Study of Options for Second-Line Effective Combination Therapy	ACTG	100	48	Completed

A5278 AMC 074: Pharmacology Substudies of A5263 and A5264	ACTG	15	3	Completed
A5279: Phase III Clinical Trial of Ultra-Short-Course Rifapentine/Isoniazid for the Prevention of Active TB in HIV-Infected Individuals with Latent TB Infection	ACTG	300	52	Completed
A5290: A Randomized, Phase 2b Study of Double-Dose Lopinavir/Ritonavir-Based ART with Rifampin-Based TB Treatment versus Standard-Dose Lopinavir/Ritonavir-Based ART with Rifabutin-Based TB Treatment with or without Raltegravir in HIV-1-Infected Persons Requiring Treatment for Active TB and HIV	ACTG	50	9	Completed
A5297: An Open-Label, Proof of Concept, Randomized Trial Comparing a LPV/r-Based to an nNRTI-Based Antiretroviral Therapy Regimen for Clearance of Plasmodium falciparum Subclinical Parasitemia in HIV-infected Adults with CD4+ Counts >200 and <350 cells/mm3	ACTG	20	3	Completed
EARNEST: A randomized controlled trial to evaluate options for second-line therapy in patients failing a first-line 2NRTI+ NNRTI regimen in Africa	EDCTP; UK MRC	70	52	Completed
A5263/AMC 066 “A Randomized Comparison of Three Regimens of Chemotherapy with Compatible ART for Treatment of Advanced AIDS-KS in Resource-Limited Settings”	ACTG	100	28	Completed. Study closed to accrual early following DSMB recommendation
A5288- MULTI-OCTAVE “Management Using the Latest Technologies in Resource-limited Settings to Optimize Combination Therapy After Viral Failure	ACTG	60	23	Completed
A5349/TBTC S31 “Rifapentine-containing treatment shortening regimens for pulmonary tuberculosis: A randomized, open-label, controlled phase 3 clinical trial”	TBTC/ACTG	300	28	Completed
NADIA “A randomised controlled trial of darunavir versus dolutegravir and tenofovir versus zidovudine in second-line	Janssen	200	51	Closed to accrual. Follow up ongoing

antiretroviral therapy regimens for the public health approach in sub-Saharan Africa"				

Appendix 2: Ongoing studies at MUCRC

Protocol Name	**Sponsor**	**Enrollment Goal**	**Enrollment**	**Status of study**
A5381 "Observational Cohort to Assess Therapeutic Efficacy and Emergence of HIV Drug Resistance Following Initiation of Tenofovir-Lamivudine-Dolutegravir (TLD) for First- or Second-Line ART or with Rifampicin-Containing TB Treatment"	ACTG	170	124	Completed
A5300B/I2003B "Protecting Households on Exposure to Newly Diagnosed Index Multidrug-Resistant Tuberculosis Patients (PHOENIx MDR-TB)"	ACTG	350	18	Enrollment ongoing
CoVPN 3008 (Ubuntu)" Multi-Center, Randomized, Efficacy Study of COVID-19 mRNA Vaccine in Regions with SARS-CoV-2 Variants of Concern"	CoVPN	500	252	Ongoing
CoVPN 3005 VAT00008 "A parallel-group, Phase III, multi-stage, modified double-blind, multi-armed study to assess the efficacy, safety, and immunogenicity of two SARS-CoV-2 Adjuvanted Recombinant Protein Vaccines (monovalent and bivalent) for prevention against COVID-19 in adults 18 years of age and older"	CoVPN	100	765	Ongoing
CARES" Cabotegravir and Rilpivirine: Efficacy and Safety Study (CARES)"	JCRC	100	50	Ongoing
BREATHER Plus "A randomized open-label 2-arm, 96-week trial evaluating the efficacy, safety and acceptability of short cycle (five days on, two days off) dolutegravir/tenofovir-based triple antiretroviral therapy (ART) compared to daily dolutegravir/tenofovir-based triple ART in virologically suppressed HIV-infected adolescents aged 12 to 19 years of age in sub-Saharan Africa"	EDCTP	80	Pending	Enrollment ongoing

LATA "Long-Acting Treatment in Adolescents (LATA) A randomized open-label 2-arm 96-week trial in virologically suppressed HIV-1-positive adolescents aged 12-19 years of age in Sub-Saharan Africa"	EDCTP	80	Pending	Submitted to IRB: IREC
A5384 "A Phase II, Randomized, Open-Label Trial of a Six-Month Regimen of High-Dose Rifampicin, High-Dose Isoniazid, Linezolid, and Pyrazinamide versus a Standard Nine-Month Regimen for the Treatment of Adults and Adolescents with Tuberculous Meningitis: Improved Management with Antimicrobial Agents Isoniazid Rifampicin LinEzolid for TBM (IMAGINE-TBM)"	ACTG	50	Pending	Submitted to ECCT
A5356 "A Phase II, Prospective, Randomized, Multicenter Trial to Evaluate the Efficacy and Safety/Tolerability of Two Linezolid Dosing Strategies in Combination with a Short Course Regimen for the Treatment of Drug-Resistant Pulmonary Tuberculosis"	ACTG	30	Pending	Submitted to ECCT
A5407 "A Phase 3, multicenter, randomized, double-blind, 24-week study of the clinical and antiviral effect of S-217622 compared with placebo in non-hospitalized participants with COVID-19"	ACTG	200	Pending	Pending Activation