NEWSLETTER #2

18 DECEMBER 2023

# IMPALA NEWS

IMPROVING HIV OUTCOMES IN AFRICA WITH LONG ACTING ANTIRETROVIRALS

## FOREWORD FROM COORDINATING CENTRE

Welcome to the second edition of the IMPALA newsletter, what an action-packed year we have had! We thank you for your efforts and expertise, and wish you a very merry and peaceful festive period.

By way of a brief reminder, IMPALA (IMProving HIV control in Africa with Long-acting Antiretrovirals) is a phase 3, randomised, open-label clinical trial testing the effectiveness of the 2-monthly injectable long-acting (LA) antiretroviral therapy (cabotegravir LA 600 mg plus rilpivirine LA 900 mg by intramuscular injection) compared to continuation of daily oral dolutegravir-based antiretroviral therapy in people with a history of sub-optimal HIV control in sub-Saharan Africa.

All collaborating partners have received approval from their regulatory committees and are now busy undertaking study activities. So far, the three Ugandan sites have completed enrolment and are monitoring participants in the 2 year follow-up period. Kenyan sites are nearing completion of enrolment and South African sites are working hard to complete enrolment in Q1 2024.

**Dr Fiona Cresswell**
Chief Investigator

Academic Clinical Lecturer & Honorary Research Fellow

**Dr Eugene Ruzagira**
Principal Investigator

Head of HIV Interventions Programme

**Victoria Babirye Tumusiime**

Trial Manager

# ACTIVITY AND RECRUITMENT UPDATES

MRC/UVRI and LSHTM Uganda Research Unit

**SIV**: 29th Nov 2022
**FPFV:** 8th Dec 2022
**1st IN:** 6th Jan 2023
**Screened:** 124
**Randomised:** 60

JCRC Joint Clinical Research Centre

**SIV**: 7th Feb 2023
**FPFV:** 2nd March 2023
**1st IN:** 16th March 2023
**Screened:** 101
**Randomised:** 80

IDI Infectious Diseases Institute

**SIV**: 9th Dec 2022
**FPFV:** 23rd Feb 2023
**1st IN:** 20th March 2023
**Screened:** 108
**Randomised:** 81

DESMOND TUTU HEALTH FOUNDATION

**SIV**: 6th June 2023
**FPFV:** 25th July 2023
**1st IN:** 24th August 2023
**Screened:** 46
**Randomised:** 30/70

CAPRISA
CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

**SIV**: 8th June 2023
**FPFV:** August 2023
**1st IN:** 13th September 2023
**Screened:** 36
**Randomised:** 20/90

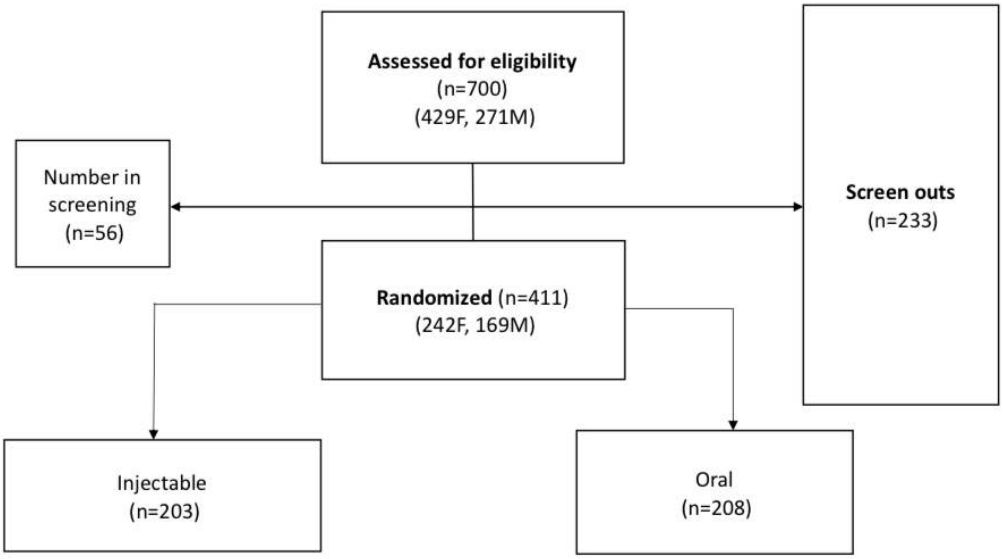
UNIVERSITY OF NAIROBI

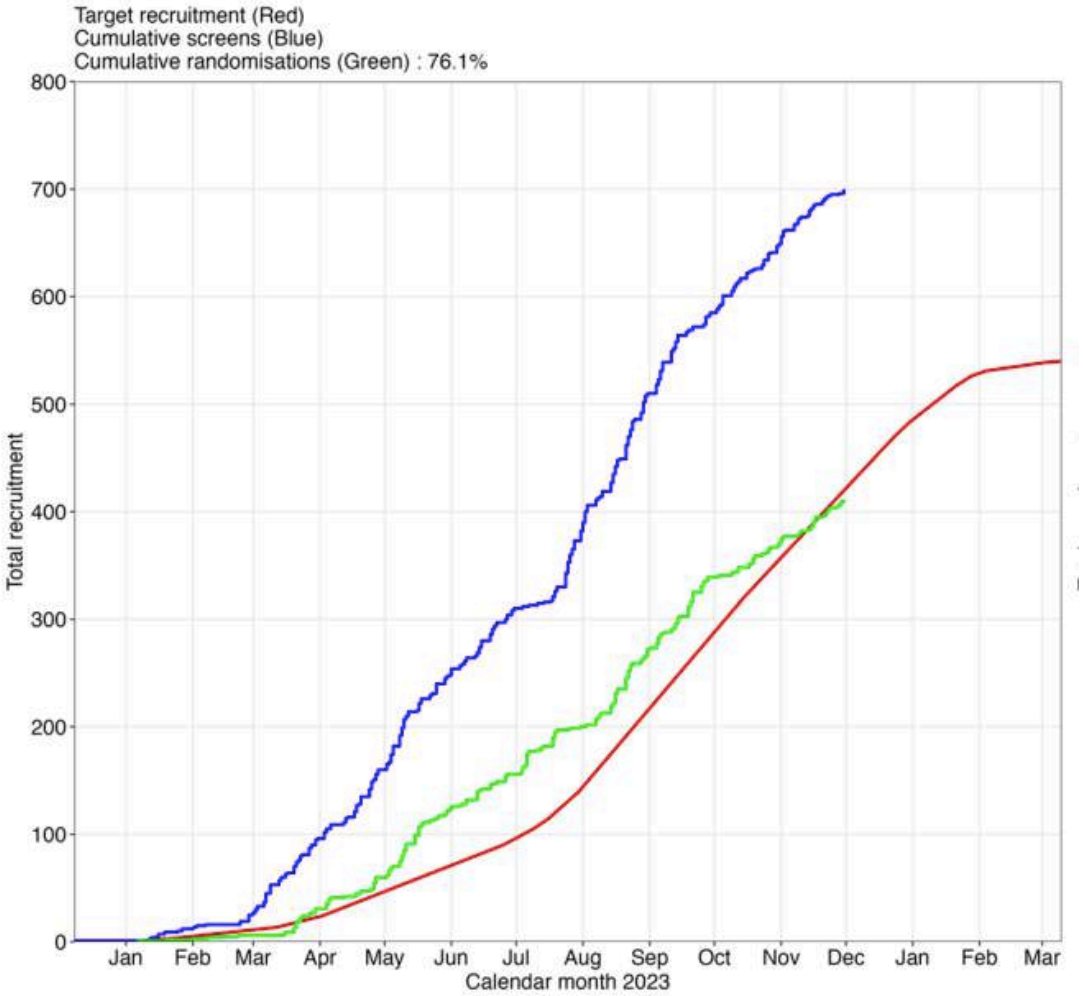
**Kenyatta National Hospital**
**SIV**: 7th July 2023
**FPFV:** 24th July 2023
**1st IN:** 15th Aug 2023
**Screened:** 117
**Randomised:** 78/80

**JOOTRH, Kisumu**
**SIV**: 5th July 2023
**FPFV:** 18th July 2023
**1st IN:** 14th Aug 2023
**Screened:** 117
**Randomised:** 79/80

# TRIAL PROGRESS

**2.1 Screening, enrolment and Randomization profile of study participants**



# NEW TCC MEMBERS

**Jane Nabbuto** is the Trial Manager (laboratory operations) for IMPALA study. She's a biomedical scientist by training and an experienced clinical research professional with over ten years' experience in clinical quality/compliance. Jane has worked on several vaccine and drug trials in different therapeutic areas including medical devices. She has been a GCP/GCLP Auditor on several trials and has a strength in conducting laboratory audits. Jane is a GCLP/GCP/LQMS trainer; a certified CRA and a member of Association for Clinical Research Professionals.

**Violet Ankunda - TCC Statistician** Violet is a statistician with a core focus on applying statistical methods to biological and medical data especially SARS-Cov-2 and HIV. Violet is also involved in machine learning and data science that uses statistical techniques to develop and train algorithms that enable to make predictions and data driven decisions.

**Dominic Bukenya - Social Scientist**

Dominic has been engaged in biomedical research for 19 years as a social science researcher. He has worked in Rakai, Kyamulibwa and Masaka on studies that aim to improve HIV care. He is currently a PhD student with the IMPALA project and in charge of executing the qualitative sub-study of the trial. -The qualitative sub study aims to explore the experience of taking the 2 different treatments in the clinical trial and the potential barriers and facilitators to widespread implementation of injectables long-acting antiretrovirals in the different country settings. We are glad that he has joined the team.

**Dr Jonathan Kitonsa** will be joining the team in January as study co-lead. He will be overseeing data and supporting day to day running of the study. Claire will continue to focus on clinical matters and safety as the medical monitor. Jonathan has several years of clinical vaccine trial experience as well as epidemiological studies. Jonathan is keen to explore the metabolic aspects of long-acting drugs compared with oral ART.

# SOCIAL SCIENCES STUDY

The IMPALA qualitative sub study has begun at two sites, IDI Uganda and CAPRISA in South Africa. Recruitment for the qualitative sub-study has been completed at IDI, with19 participants completing in-depth interviews in the study. At CAPRISA the sub-study has very recently commenced, with two participants interviewed to date. The target for the CAPRISA site will be 20 participants. Participants are interviewed at baseline, Month 6, Month 12, and Month 18 visits. The advantage of this approach is the ability to look in-depth at change in perceptions, experiences and stigma over two years on LA ART.

# 50% MILESTONE ACHEIVED

At the beginning of September 2023, we were excited to achieve the milestone of 50% enrolment and a card was shared by email to all our collaborators. Looking forward to the next milestone of 100% participants.

# INDEPENDENT DATA MONITORING COMMITTEE MEETING

The Independent Data Monitoring Committee meeting took place virtually on the 27th of June and 1st December 2023. The sessions commenced with an open session to review study progress with members of the Trial Management Group and was followed by a closed session between the IDMC members and the Trial Statistician. The IDMC congratulated the team for the recruitment progressing well. They had no major safety concerns and were happy with the study to continue as per the current protocol. The main suggestion was to ensure continued rapid HIV RNA result turnaround time, as well as thorough review of any available prior resistance data for each participant in screening.

# TRIAL STEERING COMMITTEE MEETING

The first TSC meeting took place in December 2022 and the next meeting will take place on 22nd January 2024. The TSC plays an essential oversight role in supporting the effective and ethical implementation of the trial.

# INVESTIGATOR MEETING

The first IMPALA investigator meeting took place on the 19th & 20th September 2023 at The Lake Victoria Hotel in Entebbe. We were joined by teams from collaborators from Infectious Disease Institute Kampala, Joint Clinical Research Center Lubowa & Fort Portal, University of Nairobi, CAPRISA Durban, Desmond Tutu Health Foundation Cape Town, London School of Hygiene and Tropical Medicine and Johnson & Johnson Global Health. There were also notable online presentations on health economics from Massachusetts General Hospital, Harvard USA and on real world implementation from Prof Chloe Orkin from SHARE collaborative at Queen Mary University of London, UK.

Updates and experiences in operationalising the IMPALA study were shared by all collaborating study sites. We enjoyed an array of excellent presentations with interesting discussions on topics such as pregnancy, alternative oral bridging, virology, cost effectiveness, and translating evidence into policy. We also reviewed the first outline of the publication plan.

It was agreed that quarterly study-wide meetings would take place to share experiences and keep everyone abreast of progress. The evening was lively with a band and lots of dancing, the award winning dancers were Dr Nigel Garrett (CAPRISA) and Provia Ainembabazi (IDI).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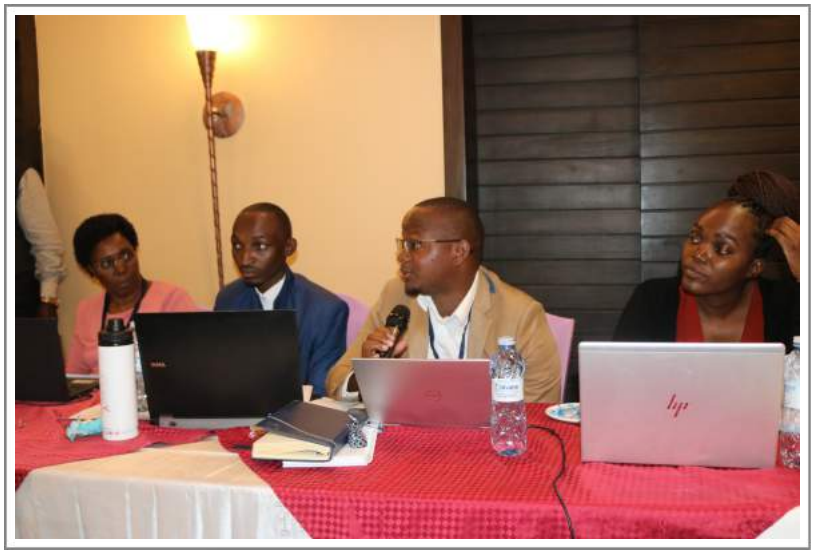


IMPALA


Introduction
Global HIV related morbidity and mortality
since 2004 and 2010


WELCOME TO THE 2023 IMPALA
INVESTIGATOR MEETING


PLEASE
REPAIR


IMPALA


Trial Operational Updates

# PLANNED AMENDMENTS

A number of minor amendments to some study documents and tools are planned. These will be shared with collaborating partners to ensure that everyone is content with the changes prior to regulatory submissions. The aim is for the amendments to be submitted together, as a single submission in the new year after approval from the TSC.

## Protocol

The key proposed changes in the protocol are:

- inclusion of alternative oral bridging (with tenofovir/lamivudine/dolutegravir) as this is likely to be what is used in real-world delivery and is easier to operationalize.
- There is also a reduction in the number of adverse events of special interest and we have corrected some minor inconsistencies.
- To provide useful data on the safety of LA ART in people with prior hepatitis B exposure, hepatitis b surface antigen at month 12 and 24 has been added to exclude reactivation.
- Baseline HIV VL does not contribute to definition of confirmed virological failure in the LA arm as it is pre-intervention.

## Informed Consent Forms

Individual ethics committees in different settings have made different recommendations for changes to the informed consent forms when initially submitted. However, it is preferred that a clinical trial of this scale has a master template, where only situation-specific information is changed for individual sites, such as contact details and remuneration details. As such, changes suggested by all the ethics committees have been incorporated into a new master template (v2.0) for the Main Consent and the Sample Storage ICFs. Once this is approved participants will need to be reconsented on the new harmonized informed consent forms.

## eCRF amendments

Several minor changes will be made to clarify certain elements of the database and further guide those entering data on what is expected. This includes re-phrasing of some questions and answer options, as well as additions of banners to guide on potential further actions/interventions.

## Study operations manual

A number of study forms have been updated to consider feedback from investigators and monitoring visits. The laboratory section was removed and made into a standalone document. Information has been updated to correct minor inconsistencies with other documents, such as the Safety Management Plan and Data Management Plan and to reflect Trial Memos

# SAFETY

Please remember to follow up on adverse events until resolution. Concurrent medications should also be should be reviewed at each visit and stopped dates entered in the eCRF where appropriate.

Timely action for abnormal laboratory results is important for participant safety. It is also critical to keep viral load result turnaround times as short as possible so that viral rebound can be promptly recognised.

It is important that adverse events are actively (not passively) elicited at all study visits i.e. the study nurse or doctor asks about *any* interim symptoms and considers whether the reported symptoms warrant an adverse event being recorded. A telephone call 2 weeks post injection is suggested to allow accurate recall of ISRs.

# MONITORING UPDATES

Dr Geofrey, Charles and Miriam have now conducted early monitoring visits at all sites and second visits in Uganda. Reports have been shared with site Principal Investigators and Coordinators. Early monitoring visits took place in Kenya in October and in South Africa in November. Paddy and Claire continue to do regular remote monitoring via REDCap. A key finding across all sites relates to minimising the time from receipt of results to entry into REDCap.

| Sites | Monitoring visits | Inspections |
|---|---|---|
| **Entebbe, Ug** | MV01, MV02 | UVRI REC |
| **IDI Kampala** | MV01 | UNCST |
| **JCRC Fort Portal** | MV01, MV02 | |
| **KNH, Nairobi** | MV01 | |
| **JOOTRH, Kisumu** | MV01 | |
| **DTHF, SA** | MV01 | |
| **CAPRISA, SA** | MV01 | |

# STUDY-WIDE MEMOS

To date three study-wide memos have been shared with all collaborators. There are all available on Sharepoint:

Clarification Memo #1
- Definition of first-line patients in the study setting

Clarification Memo #2
- Adherence to oral ART during the oral pre-injection phase

Clarification Memo # 3
- Management of hyperglycemia

# POLITE NOTICES AND REMINDERS

**Sample storage – cover split storage of samples.**

PBMC and plasma samples should be collected in the right tubes at at the correct time points as indicated on the sample collection schedule and lab analytical plan. Aliquots should be split and placed in two cryoboxes and stored in different freezers or tanks and the storage temperature should be checked regularly and documented. This minimizes the risk of all aliquots from one sample being spoiled or lost.

**Upload SOPs to SharePoint**
All IMPALA collaborating partners are required to upload their SOPs on the shared folder as a regulatory requirement. In addition frequent updates of the Investigator site binder are important.

**Query Resolution**
The Data resolution workflow module in REDCap is used to ensure quality of data for the IMPALA Trial. This module enables the Data Managers and the Monitors to raise queries for clarification to individuals at the specific sites directly through the system. Once raised, the overall target for response and closure of queries on the study database is 7 calendar days. Please stick to this and make Paddy happy.

On a weekly basis, a query report is generated by the Coordinating Data Manager, with the main aim of enforcing sites to follow up on any pending issues that need clarity as required. This report includes numbers on open queries, closed queries, most common queries, time to query response, most outstanding query, and the time to query resolution.

**Laboratory results entry** Please ensure timely result entry. Kind reminder to inform TCC when there are problems affecting results lack of reagents/broken analysers etc.

**The protocol manuscript**
In line with open science principles, we are preparing a protocol paper that summarizes the key aspects of the IMPALA study

**The SOM** version 3 was shared in November; key changes are listed on page 9.

MRC/UVRI and LSHTM Uganda Research Unit

# CONTACTS

TCC communications: impala@lists.lshtm.ac.uk

Safety: impala_safety@lists.lshtm.ac.uk

## HELPFUL LINKS

https://clinicaltrials.gov/ct2/show/NCT05546242

https://www.lshtm.ac.uk/research/centres-projects-groups/impala