

IMPALA NEWS



IMPROVING HIV OUTCOMES IN AFRICA WITH LONG ACTING ANTIRETROVIRALS



Welcome to the 4th edition of the IMPALA trial newsletter!



A huge shoutout to the entire team for your continued dedication and excellent work. You have truly kept the momentum going, and it shows!

Since our last update, there's been a flurry of exciting progress. Retention remains outstanding, data quality is excellent, and we have begun the successful exit of participants. More than half of the participants have already completed follow-up. The social science component is thriving too, with some of our investigators recently interviewed as key informants by Dominic who leads this component. Keep those insights coming!

But let's be honest, the most exciting development was Dr Fiona Cresswell's presentation of our primary safety and efficacy data at the IAS 2025 Conference in Kigali, and in the co-chair's session, no less! The data confirmed that long-acting rilpivirine and cabotegravir is not only safe and effective but also preferred by individuals who struggle with daily pill adherence. This is a major step forward in improving outcomes for high-risk populations, and it supports expanding long-acting options in HIV programmes.

Dr Ubaldo Bahemuka also delivered a key oral presentation reporting that there were no clinically detectable reactivations of hepatitis B virus, but people on long-acting regimens are at risk of de novo hepatitis B infection if they are not vaccinated. Hepatitis B vaccination efforts must be strengthened ready for the roll out of injectable treatment.

As if that wasn't enough, we had two engaging poster presentations: one by Dominic Bukenya on the acceptability of long-acting ART in Uganda and South Africa, and another by Violent Ankunda exploring why people choose oral lead-in vs. direct-to-injection when starting long-acting therapy in East and Southern Africa. These all coincided beautifully with the WHO's inclusion of 2-monthly long-acting rilpivirine and cabotegravir in the treatment guidelines for virally suppressed individuals, a timely and exciting boost!

So, what's next? We will continue wrapping up participant exits and shift gears toward our next major milestone: publishing the primary analysis paper. Stay tuned!

Congratulations once again to everyone for the incredible progress. Enjoy this edition, and as always, thank you for making the IMPALA trial a success to be proud of!

Dr Eugene Ruzagira, Coordinating Principal Investigator

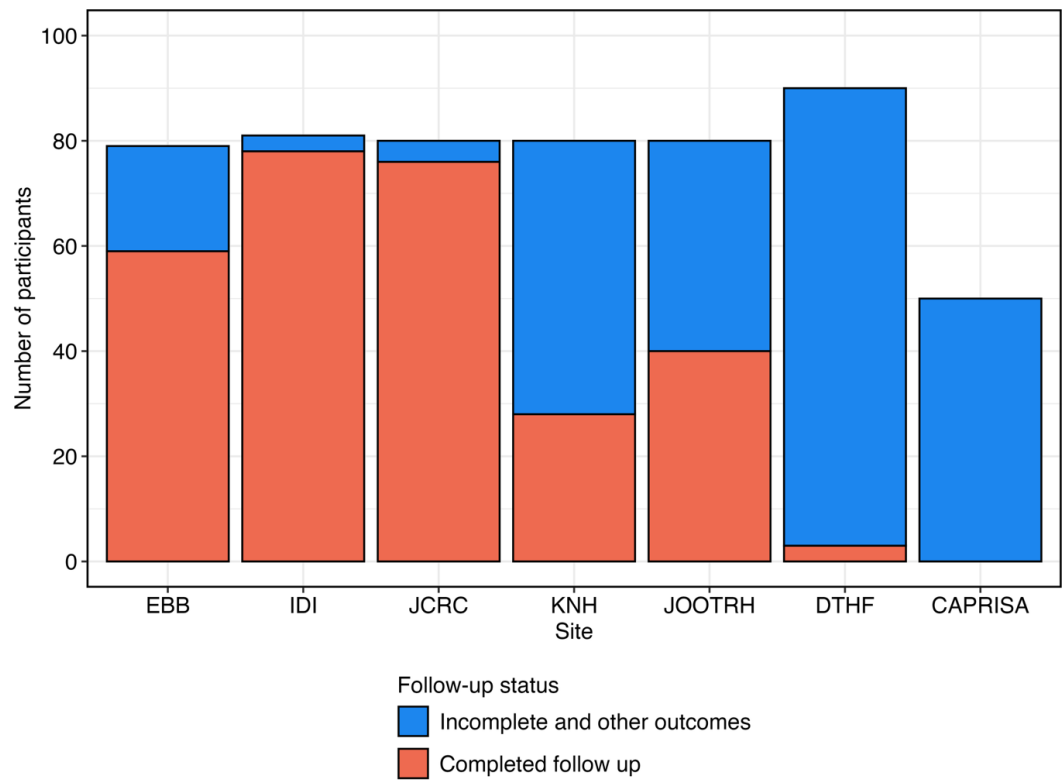
STUDY PROGRESS UPDATE

We’re excited to share a key update on the progress of our clinical trial. Thanks to the dedication of our collaborators and the commitment of the participants, follow-up visits are progressing smoothly, and we are pleased to report that over half of the 540 participants have now completed their final study visit.

Summary of the follow up status by site:

Site Name	Completed Follow-up	Expected Completion Date
EBB	-	21 January 2026
IDI	24 July 2025	-
JCRC	29 July 2025	-
KNH	-	30 October 2025
JOOTRH	-	22 October 2025
DTHF	-	27 March 2026
CAPRISA	-	09 March 2026

This marks an important step as we move closer to completing data collection and preparing for analysis.



We are continuing to monitor data quality and participant safety closely through both onsite visits and remote review processes.

SAFETY OVERSIGHT AND MONITORING



Safety monitoring remains a top priority:

- **Onsite monitoring** is ongoing as per the monitoring plan.
- Our remote **data management and safety teams** are actively reviewing the arising trial data.
- The **Independent Data Monitoring Committee (IDMC)** continues to review accumulating safety data in accordance with the approved charter. The last IDMC meeting was held on the 3rd of February 2025 and the next IDMC meeting will take place later this year.
- The **Trial Steering Committee (TSC)** continues to oversee the IMPALA study conduct and our last TSC meeting was held on 3rd February 2025 and the next TSC meeting will take place later this year.
- The **Trial Safety Group** regularly assesses adverse event data and trial safety reports.

FEWER PROTOCOL DEVIATIONS

Protocol deviations have reduced during this phase of the trial. Most deviations observed have been minor and primarily due to participant-related constraints; such as scheduling conflicts, travel limitations, or other personal challenges impacting visit attendance. Delayed shipment of medication over the Christmas break and a temperature excursion have resulted in delayed injections. However, this has been resolved.

This improvement reflects:

- Enhanced site engagement and communication,
- Proactive scheduling and follow-up efforts, and
- Ongoing support provided to participants throughout the follow-up period.

We thank all site teams for their continued vigilance in identifying, documenting, and addressing deviations promptly. Maintaining high protocol compliance remains key to ensuring the quality and reliability of our study data.

DATA MANAGEMENT

With many participants completing their final visits, we are now entering a critical phase of the trial - data cleaning. This process ensures that all collected data is complete, accurate, and ready for analysis.

Our data management team is working closely with site staff to:

- Address outstanding queries
- Reconcile any discrepancies
- Validate database entries
- Lock clean datasets in preparation for final analysis.

This is a major step toward unlocking the insights from our study, and we appreciate the ongoing attention to detail and responsiveness from all sites. Your efforts are instrumental in ensuring the integrity of our trial results.

• Primary Analysis Progress

This year we will prepare a manuscript reporting the results of the 48 week primary data analysis. This publication will represent a major milestone and will be shared as soon as it's ready for review by respective site Principal Investigators and co-authors.

• Key Informant Interviews kick off

The social sciences team has already contacted key staff members from Uganda and South African sites except DTHF. In Uganda the KIIs are physical while those with participants from South Africa will be online. A link is shared once individuals confirm their willingness to participate. Consent forms are available at every site for the key informant and in-depth interviews, and every participant is expected to sign one prior to commencement of the interview.

PRIMARY RESULTS MEETING

April highlights

In April, we held a primary results meeting at K Hotel in Entebbe, bringing together Principal Investigators and Trial Coordinating Centre (TCC) members for an important milestone in the study.

Key activities included:

- Confidential presentation of primary results: The team reviewed key findings from the primary analysis in preparation for the International AIDS Society conference.
- Manuscript planning: we discussed and agreed on structure and key points for the primary manuscript and the supplementary appendix.
- Late-breaker abstract: a late-breaking abstract was drafted for submission to IAS conference. Key findings remained confidential until presented at the conference.



Beyond the scientific discussions, the meeting also offered time to connect and recharge:

- A walk through the botanical gardens provided a welcome breath of fresh air and informal networking.
- The day concluded with a team dinner, where we celebrated progress and shared goals.

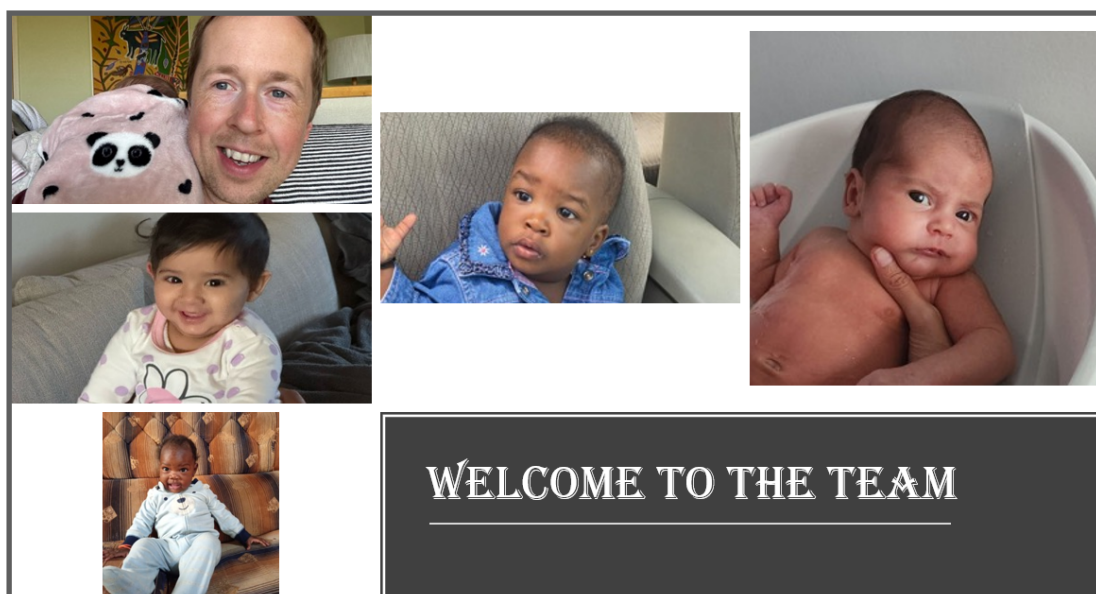


Reflecting on two years of change and growth in the IMPALA team

Over the past two years, the IMPALA study team has undergone a remarkable journey marked not just by the milestones in our work, but by the transitions and personal moments that have shaped our team along the way.

We've said heartfelt goodbyes to some incredible colleagues who've moved on to new paths, leaving behind a legacy of dedication and impact. At the same time, we've welcomed new colleagues and celebrated joyful beginnings, as several team members welcomed new life into the world.

Through all the changes, the IMPALA have remained steady in its purpose, stronger in its bonds, and full of gratitude for the people past and present, who have made our work meaningful.



IMPALA AT IAS 2025: Advocating for equity and innovation in HIV response

The IMPALA team had a strong presence at the recently concluded IAS 2025 Conference, with team members from MRC/UVRI-LSHTM Uganda Research Unit, the Infectious Diseases Institute, University of Nairobi, Joint Clinical Research Centre, CAPRISA and Desmond Tutu Desmond Tutu Health Foundation in attendance. It was also wonderful to see four members of the trial steering committee – Prof Di Gibb, Dr Mina Ssali, Dr Cissy Kityo and Prof Chloe Orkin – in attendance. The conference was held from 13th to 17th July at the Kigali Convention Center in Rwanda. Two oral presentations and two e-posters were presented; the IMPALA results contributed meaningfully to global discussions on the opportunities and challenges of long-acting HIV treatment in African HIV programmes. The conference was marked by a blend of urgency and innovation, drawing experts, policymakers, researchers, and advocates from around the world. Among the many important discussions, two major themes stood out:

► A call to action on funding cuts

A key concern resonating throughout the sessions was the impending funding cuts by the United States Government, a major financier of global HIV programmes. Several Ministry of Health officials from low- and middle-income countries shared how these reductions are already affecting HIV prevention efforts and HIV service delivery. The cuts threaten to reverse gains in prevention, treatment, and care—especially in regions with high HIV burdens. Speakers across various sessions emphasised the need for global solidarity and coordinated action. Civil society organisations, donors, governments, and development partners were urged to advocate for the protection of HIV Programme funding and to explore alternative financing mechanisms to bridge the emerging gaps.

► Long-acting innovations

Despite financial uncertainties, the conference also highlighted significant advancements in long-acting HIV prevention and treatment options. Sessions spotlighted the promise of lenacapavir, a long-acting antiretroviral that could reshape HIV prevention with just two injections annually. Importantly, the WHO announced the inclusion of

long acting cabotegravir and rilpivirine in their treatment guidelines for use in virally suppressed individuals. In an essential step towards access, the [Medicines Patent Pool announced that ViiV Healthcare](#) had agreed to expand the voluntary licensing agreement for cabotegravir LA to enable its use in long-acting treatment. Rilpivirine LA will be off patent within two years and generic companies have already started the process to produce a generic version. This is a huge step forward, although it will take 2-3 years for the generic versions to be available for use in treatment programmes. Nonetheless, it is important to begin laying the foundations for how LA treatment services could be delivered.

Attention was also drawn to emerging LA options like MK-8527, an investigational once-month oral pill for HIV prevention, which is currently under investigation. These long-acting tools offer hope for improving adherence and easing the burden of daily medication, but only if made accessible and equitably distributed.

Importantly, there was a strong call to include pregnant and breastfeeding individuals in trials and programming of these innovations. Experts emphasised the right of women to make informed health decisions based on a clear understanding of the benefits, risks, and available options.

The IMPALA consortium remains committed to contributing to global research, advocacy, and policy that prioritize equity, sustainability, and innovation in the HIV response. The insights gained from IAS 2025 will continue to inform our work and strengthen our resolve.

Some members of our team shared key insights from the trial at the recently concluded International AIDS Society (IAS) Conference:

In-person presentations:

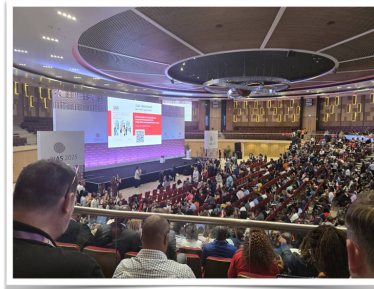
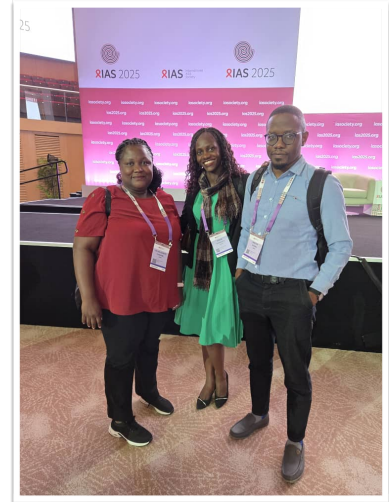
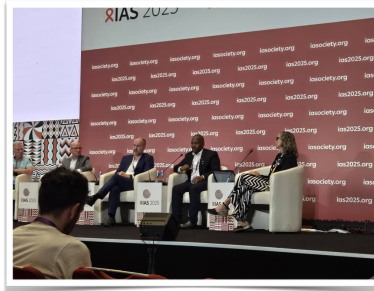


LA cabotegravir and rilpivirine in adults with suboptimal HIV control in sub-Saharan Africa: the IMPALA trial 48-week results (presenting author: Fiona Cresswell)



Is LA-ART safe in countries with high hepatitis B prevalence? Insights from the IMPALA study (presenting author: Ubaldo Bahemuka).

Highlights from the IAS 2025 conference in Kigali, Rwanda



Publications

We're proud to share recent and upcoming milestones in the dissemination of our study findings:

- **Protocol Paper Published**

The trial protocol paper has been published in the *Wellcome Open Research* journal, providing a detailed overview of our study design and methodology. The paper is titled: *Efficacy and Safety of Long-acting Injectable cabotegravir and rilpivirine in Improving HIV-1 Control in sub-Saharan Africa: Protocol for a Phase 3b Open-Label Randomized Controlled Trial (IMPALA)*; <https://wellcomeopenresearch.org/articles/10-166>).

- Our week 48 paper is in progress with the aim of sharing a first draft in Q4.
- We compiled and shared a draft list of manuscripts and abstracts developed so far, including the recently published protocol paper which we made with your valuable input. The publication list has two sections.
- **List 1** features papers and abstracts directly tied to the study objectives.
- **List 2** captures ideas proposed by trial team members and more ideas are welcome.

What's next?

As more participants reach their final visits, our focus will shift increasingly toward final data cleaning and preparation for analysis. We'll continue to keep you updated as the study moves toward its next major milestones. We hope to hold an investigator meeting in South Africa in 2026.

MRC/UVRI and LSHTM Uganda Research Unit



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UNIVERSITY OF NAIROBI



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HYGIENE
& TROPICAL
MEDICINE



CONTACTS

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

Safety: impala_safety@lists.lshtm.ac.uk

HELPFUL LINKS

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