

Optimising ART

August 2017



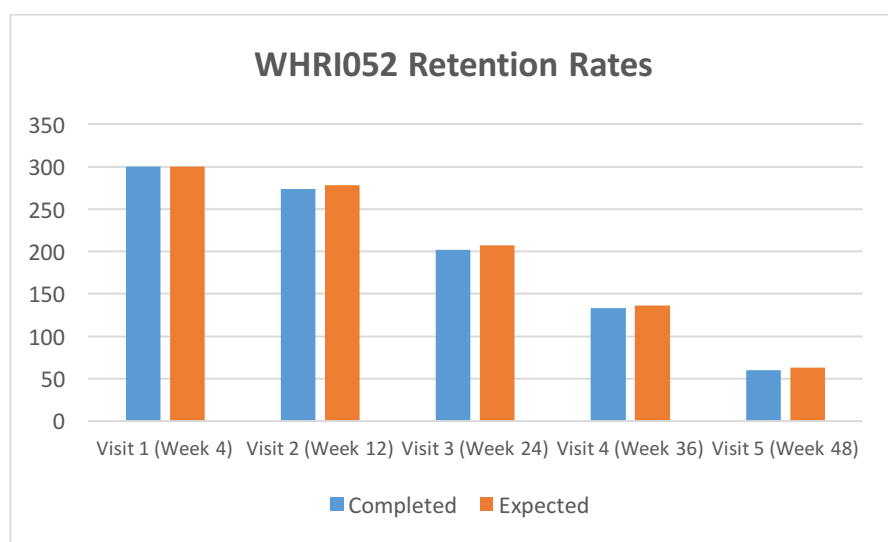
This is a monthly update shared with all members involved in projects aimed at optimising ART, and is meant to provide a short update of major achievements, challenges, and plans for the future. Please submit any inputs to Celia Serenata by the 1st Wednesday of every month.

Several collaborators and partners participated in IAS 2017 in Paris, including an investigator meeting convened by WHO/Unitaid post-IAS. There were several ART optimisation presentations at IAS, and much of the findings of these were covered by multiple publications. A summary of some of the key findings were presented at the Investigators Meeting, and can be found on the DropBox link.

Major Achievements from July 2017

LOW-DOSE DARUNAVIR STUDY, Wits RHI

- Retention rates are being successfully managed and maintained at 99% average as study visits increase with the close of enrolment last month.



- Site had a 3-day monitoring visit from 11 – 13 July. There were no significant findings.

Upcoming Events

17 August: USAID Year 3 workplans due to Wits RHI

25 August: Unitaid Semi-Annual progress reports due to Wits RHI

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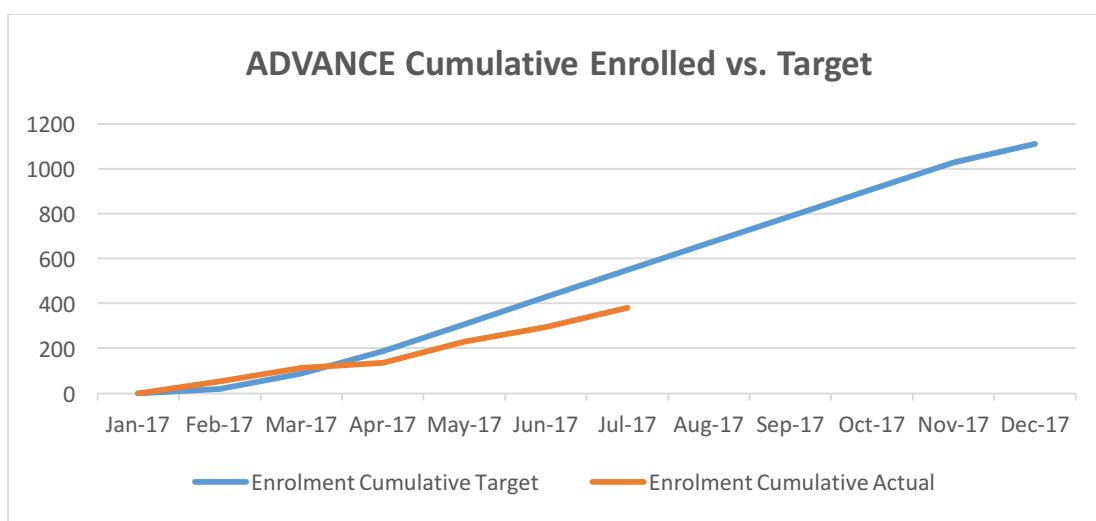
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ADVANCE STUDY, Wits RHI

- As of 31 July, 555 participants screened, 57 are in the pipeline for eligibility assessment, and 382 enrolled in total.
- The ADVANCE poster received regulatory approval on 18 July and has and has been distributed.
- The team is still experiencing dire challenges with recruitment of adolescents. Wits RHI submitted a letter to the Ministry of Health asking for a waiver from parental consent for those participants between the ages of 15 and 18. We have found this to be a key factor in the difficulty recruiting this age group. The regulatory authorities denied a similar request in April, indicating that only the Minister of Health could grant a waiver.
- Protocol amendment 3 has been worked on extensively with target of submitting the amendment for regulatory approval by mid-August.



EFAVIRENZ 400mg TB PK STUDY (SSAT062), Mylan (St. Stephen's AIDS Trust)

- Ongoing recruitment and monitoring activities continue.
- Half of the patients in the UK (Stage 1) have now completed up to Day 98/99 of the study.
- The IRB in Uganda provided feedback, resulting in a minor update to the protocol and Uganda informed consent form.

TAF-RIF TB PK STUDY (RIFT), St. Stephen's AIDS Trust¹

- 19 of the 20 participants have been enrolled.
- Preliminary analysis of the first 11 subjects will be completed by early September.

DTG-RIF TB PK STUDY (RADIO), St. Stephen's AIDS Trust

- Submissions have been made to the HRA/REC and MHRA.
- An initial HRA assessment has allowed the site to initiate document setup.

¹ Funded by Gilead

NANOTECHNOLOGY, University of Liverpool

- DRV/r multiple dose studies have been completed *in vivo* and show promising results for choosing a candidate to take forward.
- Spray drying preparation completed.
- Method obtained for mass spec of PIs.
- MHRA approval of our Investigational Medicinal Product Dossier (IMPD) for our existing EFV SDN solution.
- The FDA is in agreement with the approach of filing 505(b)(2) NDA, meaning Liverpool can translate SDNs based on PK without the need for efficacy studies.
- A call was held between UoL, MPP, USAID and the Global Health Supply Chain-Procurement and Supply Chain Management (GHSC-PSM) project to see if PSM can support current processes.

MARKET ACCESS AND PRODUCT INTRODUCTION, ICAP

Global activities

- Dr. Elaine Abrams joined the panel at the WHO, Unitaaid and MPP symposium at the IAS 2017 conference in Paris, *Accelerating Access to New HIV Medicines in Low and Middle Income Countries*, to discuss Project OPTIMIZE and its role in helping to introduce new optimal ARVs to countries.
- Dr. Nandita Sugandhi presented on Clinical Considerations for the Introduction of Dolutegravir at the satellite session *Accelerating Access to Dolutegravir and Other Optimal ARVs* hosted by CHAI and Unitaaid. The talk included the evidence that programs should consider when introducing DTG-containing regimens for specific populations including new data presented at IAS 2017 on use of DTG in pregnancy and as 2nd line.
- A mapping exercise was conducted to identify countries that are considering or have adopted recommendations for TLE400 and DTG among care and treatment programs in 17 countries in sub-Saharan Africa, Central and Southeast Asia, and Eastern Europe. Though the majority are not formerly included under the OPTIMIZE project, ICAP care and treatment teams will be prepared with up-to-date information and resources related to optimal ARVs introduction.
- ICAP collaborated with PAWG members to finalize and submit an invited article on ARV dosing in neonates to the journal *Expert Review of Clinical Pharmacology*.
- Held a monthly call with WITS to on-board the new Program Manager and ensure smooth transition with Averie Gachuhi's departure.

Kenya

- Finalized a training package (PowerPoint slides and FAQs) for healthcare providers on the transition to DTG that will now be used for training ToT and HCW nationally.
- Revised the concept note for the enhanced data system for monitoring optimized ARVs following the system re-designed in collaboration with Palladium.
- Attended a NASCOP optimization meeting to review the current ARV pipeline information and update the national transition plan for ARV optimization timelines.
- Worked on the development of the Adverse Event clinical assessment tool.

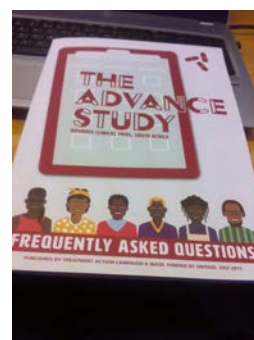
- ICAP in collaboration with Palladium held four planning meetings to: 1) conduct joint interviews to identify a suitable candidate for the HMIS Technical Advisor position; 2) support the development of the interoperability layer for the enhanced data system; and 3) discuss the adverse event clinical assessment tool to be included in the EMR.

Zimbabwe

- Circulated for external review and received feedback on the Zimbabwe Needs Assessment.
- Initiated plans for a dissemination meeting to present and discuss findings from the Needs Assessment to the MOHCC.
- Developed a concept note for the Zimbabwe Baseline Assessment and mapped proposed indicators against data fields in current and previous versions of Zimbabwe's "green booklet" (released in 2016 and 2012, respectively).

DEMAND CREATION AND COMMUNITY ENGAGEMENT, HIV i-Base

- The updated *Fit for Purpose* was distributed at IAS, as well as online (<http://i-base.info/htb/31974>)
- ADVANCE FAQs booklets were distributed at IAS. These documents were available at the IAS stand at IAS.



COMMUNITY ENGAGEMENT, TAC

- Provincial trainers trained 1180 people at branch and community level on HIV and treatment optimisation.
- ADVANCE FAQs completed with 1000 printed for the initial round (760 copies distributed at branch and community levels, and 300 copies at IAS 2017).

CLINICIAN/HEALTH WORKER ENGAGEMENT, Southern African HIV Clinicians Society

- An Optimisation CME was held in Durban, attended by 147 doctors.
- Lauren Jankelowitz (CEO) attended sessions on: "DAWNING" – results were presented amongst other studies; CHAI symposium on Treatment Optimisation and; session on mono & dual therapy where treatment interruption option studies were debated at IAS, Paris 23rd to 25th July 2017.
- Conversation post-IAS with the executive committee of Adult Guidelines (Graeme Meintjes, Gary Maartens, Francois Venter) about the implications of "DAWNING" – the decision is not to change our guidelines until published evidence is available.
- Planning continues for the Linked Treatment Optimisation and Stop Stock Outs project.
- Videos from OPTIMIZE CMEs and podcasts from Wits RHI training built into the Treatment Optimisation learning module of the Advanced HIV Management Course.
- Nurses Clinical Tips sent out weekly via SMS to approximately 2800 nurses.

Major Plans for August 2017

Low-Dose Darunavir Study, Wits RHI

- Resolve all minor monitoring findings and implement corrective actions were necessary to close out the external monitoring report.

ADVANCE, Wits RHI

- Finalise a Facebook advertisement that may appeal to adolescents who may not be keen to access healthcare via the traditional clinic option, which is still associated with levels of stigma.
- Expect feedback from the MOH regarding the request to grant a waiver for parental consent for those adolescents aged 15-18 years.
- Submit protocol amendment 3 for regulatory approval.

EFAVIRENZ 400mg TB PK STUDY (SSAT062), Mylan (St. Stephen's AIDS Trust)

- Completion of the UK recruitment (Stage 1). The study only has to enrol one additional participant, following a participant withdrawal prior to their Day 42 visit.
- Submission of response to the Uganda IRB.
- Submission to Uganda NDA for study approval. First Participant First Visit planned for October 2017.
- Set-up of the next Trial Steering Committee meeting to evaluate the study data in Stage 1.

DTG-RIF TB PK STUDY (RADIO), St. Stephen's AIDS Trust

- Attend the ethics review meeting and secure REC/HRA approval for the study.
- Secure MHRA approval for the study.

NANOTECHNOLOGY, University of Liverpool

- Planning for multiple dose ATV studies *in vivo*.
- Initial spray drying testing of appropriate formulations.
- Mass spec work to begin.
- EFV SDN preparation work to progress.
- Follow-up call with GHSC-PSM to explore collaboration.

MARKET ACCESS AND PRODUCT INTRODUCTION, ICAP

- Mozambique: Hold a dissemination meeting for the needs assessment and develop an initial OPTIMIZE workplan for the introduction of optimized ARVs in-country in collaboration with USAID, MOH, and other key stakeholders; continue to share the most up-to-date evidence and experiences about DTG, including planning a post-IAS update meeting.
- Kenya: Share a concept note for enhanced monitoring activities for external review; finalize the protocol for enhanced monitoring activities; finalize the hiring of the HMIS Technical Advisor position to work with in-country partners around enhanced monitoring activities;

receive feedback on the Kenya situational analysis from all required ethics committees; conduct trainings on transition to DTG using the recently finalized training materials.

- Zimbabwe: Finalize the Zimbabwe Needs Assessment and send to designers for formatting; conduct an initial baseline analysis of the current situation using routinely collected electronic data; plan to monitor the uptake of TLE 400 in Zimbabwe through site visits and commodity data review meetings at the end of the month; share findings from the needs assessment with the MoHCC; conduct facility visits to collect feedback on the experience and use of TLE400; participate in the national quantification meeting.
- Global: Finalize the New Product Introduction toolkit and case study on past transitions using feedback received from external review; develop the outline for a case study on “positive deviance”; begin development of the Optimal ARV training package; host in-person meeting with USAID partners to finalize the Year 3 workplan; finalize market shaping intervention report.

COMMUNITY ENGAGEMENT, TAC

- Finalisation and selection of designer/printer for the *HIV in our Lives* hardcopy, challenges still being experienced in trying to ascertain an alternative service provider.
- Provinces to continue with branch trainings, community engagement, and demand creation activities.

CLINICIAN/HEALTH WORKER ENGAGEMENT, Southern African HIV Clinicians Society

- Next CME is scheduled for Saturday 5 August in Bloemfontein, Free State, and Saturday 26 August in Kimberley, Northern Cape.
- 3 trainings in 3 different provinces for the TAC TOT-Team and Branch Trainers on Treatment Optimisation including the development of the material (original curriculum developed for doctors); Clinicians Society will be using clinicians and lay trainers to deliver training; in conjunction with Stock outs workshops hosted by Stop Stock outs Project.
- HIV i-Base *Fit for Purpose* – Antiretroviral treatment optimisation for adults and children obtained in Paris, IAS 2017. Will order further copies for distribution at CMEs, AWACC, FIDSSA and Rural Health Conference.
- Planning continues for the International HIV-Drug Resistance Workshop in November 2017 (<http://www.hivresistance2017.co.za>)
- Planning continues for SA HIV Clinicians Society conference in 2018 (<http://www.sahivsoc2018.co.za>)
- There is a private practitioner guidelines meeting scheduled for the week of 7 August to ensure that our guidelines speak to the needs in the private sector and will be adapted accordingly (e.g. pull out algorithms and may write something specifically for medical aids).

Staffing Changes

- Dr. Pooja Balani has been appointed as Medical Technical Advisor at SAHCS, it's been a challenge to get this position filled, so we welcome her.

Outputs

List any articles, manuscripts submitted for review; abstracts submitted; presentations given. (Also provide electronic version of such products for the Dropbox – see

<https://www.dropbox.com/home/OPTIMIZETechnicalSteeringCommittee/Calendar+Events>)

Also, to assist with all communication, branding and marketing opportunities, please find it in the Dropbox at:

<https://www.dropbox.com/home/OPTIMIZETechnicalSteeringCommittee/Communications+Branding+Marketing>

Papers published

- None.

Online posts:

- 26 July 2017: HIV i-Base posting regarding DTG pregnancy outcomes reported at IAS: <http://i-base.info/htb/32182>
- USAID blog relating to the CHAI session at IAS 2017 on optimising ART: <https://www.usaid.gov/what-we-do/global-health/hiv-and-aids/information-center/hiv-and-aids-research-corner/highlights-ias2017>

Media Coverage

- None.

Useful Websites

USAID page on ART optimisation: <https://www.usaid.gov/what-we-do/global-health/hiv-and-aids/technical-areas/antiretroviral-therapy-optimization>

UNITAID page on ART optimisation: <https://www.unitaid.eu/project/safer-robust-less-expensive-first-line-antiretroviral-therapy-advance-trial/> (for the grant with Wits RHI, see associated grants below that)

Future Conferences/Trainings

- Rural Health Conference, Taung, 22-25 September 2017: Dr Trevor Majoro confirmed to deliver training on treatment optimisation. www.rudasa.org.za/conference/about-the-conference
- AWACC, Durban, 7-8 September 2017, www.awacc.org/2014 - speakers are being allocated
- 24-27 October 2018: 4th Southern African HIV Clinicians Society Conference, Gallagher Convention Centre, Midrand. www.sahivsoc2018.co.za

Acknowledgements

The U.S. Agency for International Development (USAID) is a proud supporter of OPTIMIZE. OPTIMIZE is led by the Wits Reproductive Health and HIV Institute (Wits RHI) and founding members include ICAP at Columbia University, Mylan Laboratories, the University of Liverpool, and the UNITAID-funded Medicines Patent Pool. As an expanding partnership aimed at harnessing multiple stakeholders' collective efforts, OPTIMIZE also includes the University of Cape Town (UCT) and contributions from private sector partners. USAID is a key implementing agency of the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) and is responsible for over half of all PEPFAR programs with activities focused in 35 priority countries and regions, mainly in sub-Saharan Africa and Asia. For more information, please visit: www.usaid.gov

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