

Optimising ART

June 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 Celicia Serenata before the 1st Wednesday of every month.

This month we are excited to have our first input from a study looking at optimised ART outside of the USAID-funded OPTIMIZE consortium. This comes from NAMSAL, funded through Unitaid. We hope to include inputs from other studies in future.

The OPTIMIZE consortium had a very successful 3-day Technical Steering Committee meeting. CHAI participated on day 1 and 2, and Unitaid was able to participate in the entire meeting. The meeting was instrumental in providing guidance on priorities for the 3rd year of funding, including discussions on clinical studies that are required to answer outstanding questions on both 1st and 2nd line ART.



Team Photo taken at the Technical Steering Committee Meeting, Rosebank, Johannesburg, 24 May 2017

Major Achievements from May 2017

LOW-DOSE DARUNAVIR STUDY, Wits RHI

- As of end May, there were 350 participants screened and 298 enrolled in the low-dose DRV (WRHI052) study. We expect to close enrolment end of week 9th June with the last 2 participants to be enrolled. Participants in the lopinavir/ritonavir arm that have completed 48 weeks in the study have already begun with exit visits. Many of these participants may be enrolled in an 052 rollover switch study, if funding can be secured. If this study is not funded, then post-trial access will be provided for those participants in the darunavir/ritonavir arm. The participants in the



Upcoming Events

13-15 June, SA AIDS Conference,
Durban, www.saaid.com

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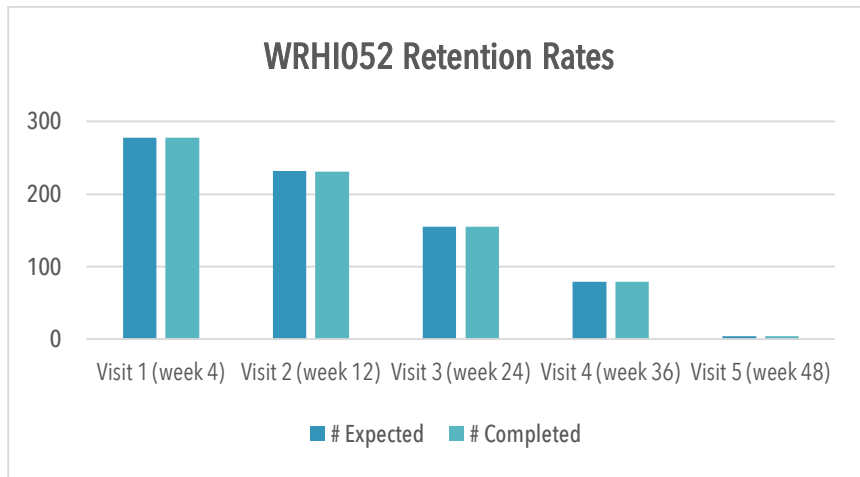
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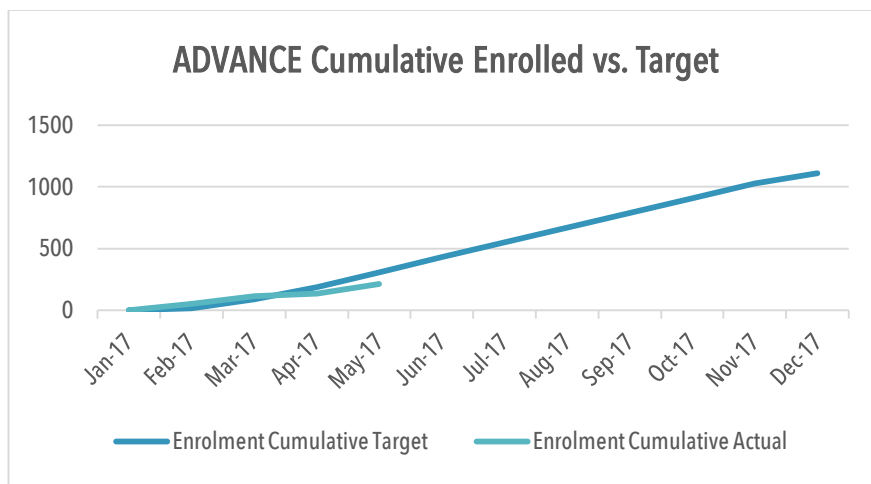
lopinavir/ritonavir arm will be transitioned back to the public sector.

- Retention graph:



ADVANCE STUDY, Wits RHI

- As 2 June, 323 participants had been screened, 288 were eligible for enrolment, and 229 enrolled in total. The enrolled participants include 6 adolescents. As seen below, the number of people enrolled is below target. As such Wits RHI is looking at short- and medium-term solutions to increase enrolment. The assistance from TAC has already made a significant impact in increasing enrollments.



- The tracking database designed to retain participant details and aid as a tool for scheduling of participant visits has been rolled out. Sites 1 & 2 have completed entering all of the currently enrolled participants into the database; and will actively use the database to prompt an automated approach to scheduling of upcoming visits. In past experience this has aided as an efficient tool to sustaining good retention rates.

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

UK

- Recruitment is ongoing and was not completed by 30 May 2017 as originally completed, and is likely only to be completed by around end June. Although recruitment has been a priority for this study, the Easter break in April resulted in slower than expected recruitment.
- 17 participants are ongoing or completed in the study (19 enrolled; 3 withdrawn, of which 2 will be replaced; 4 participants have now completed the study).
- 4 participants have been screened and are awaiting confirmation of their baseline visit dates.
- Protocol version 5.0 and PIS/ICF v5.0 have been fully approved in the UK – the changes redefined eligibility criteria to allow for an expanded subject pool.

Uganda

- The initial ethics submission was sent on 19 May 2017.
- The NDA (National Drug Authority) is currently understaffed and the expected review timeline is between 3-4 months. However, the submission was performed in line with the planned Uganda FPFV, and approval is still expected by September 2017.

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

- 11 participants were enrolled on 1st June.
- Working on bringing the data in-house over the next few months.
- PK samples/data will be sent to JHU in Baltimore for analysis early August with preliminary results available early September.

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

- The funding agreement between SSAT and Wits RHI has been finalised.
- SSAT is preparing the submission package for the regulatory/ethics authorities.

ANRS 12313 (NAMSAL), IBB/IRD/ANRS

[NAMSAL/ANRS 12313 is a phase 3 trial with two support studies that primarily intends to demonstrate that DTG is non-inferior or superior to EFV 400mg when both combined with TDF/3TC in first-line HIV treatment for ART-naïve patients 18 years or older. The trial takes place at trial sites in Cameroon.]

- As of 22nd May, there were 653 participants screened, and 442 enrolled in the ANRS 12313 NAMSAL trial
- The protocol clarification memo (amendment) #3 submitted for regulatory approval to the CNERSH (Comité National d'éthique de la Recherche pour la Santé Humaine)

¹ Funded by Gilead

received approval on 5 May. This amendment describes the follow-up procedures after week 48 (post-trial follow).

- Aurobindo generic DTG and the Mylan FDC TDF/3TC/EFV400 were ordered for post-trial access.

NANOTECHNOLOGY, University of Liverpool

- Completed a multi-dose DRV/r 8:1 formulation study, showing good results.
- Completed two ATV formulation experiments in vivo.
- ATV/r formulations being generated.

MARKET ACCESS AND PRODUCT INTRODUCTION, ICAP

Country-level activities:

- Mozambique:
 - Attended a 3-day technical consultation to discuss ARV optimisation:
 - Strong interest in adopting TLD as first-line when a fixed-dose combination becomes available in 2018, initially as an "alternative" adult 1L until more data is available in pregnant women.
 - ATV/r for 2L PI also supported with the option for LPV/r for patients with TB and on 2L.
 - Strong support for PI-based 1L in pediatric patients with RAL in 2L until DTG-based pediatric regimens are available.
 - Though the 2016 guidelines have been published, changes may be made through issuing of circulars/communiqués. ICAP contributed to the presentation on pediatric ART optimisation as well as communicated with the MoH and other stakeholders in planning for LPV/r oral pellet introduction.
 - ICAP shared Kenya's experience in introduction of DTG into the Kenyan ART guidelines and the current plans for phasing in DTG.
 - Needs assessment drafted and internally reviewed; currently with USAID for review. Plans made to finalize the needs assessment in June and disseminate to the Mozambique MoH and stakeholders in early July.
- Kenya:
 - Stakeholders meeting held in Kenya where the immediate ART optimisation plans were agreed for all PLHIV in Kenya as:
 - Use of TDF/3TC/EFV as the preferred first-line; use of TLE400 recommended as the preferred first-line for ART naïve patients
 - DTG recommended as the alternative first-line for: PLHIV with neuropsychiatric manifestations related to EFV, PWID
 - A total of 155,000 packs of DTG were delivered in Kenya, made possible through CHAI support.
 - Concept note on the national ARV phase-in plan for ARV optimization developed and submitted to NASCOP for review.
 - Communiqué and service provider training materials for ARV optimisation drafted and submitted to NASCOP for review.

- The situation analysis protocol in support of product introduction activities has been submitted to NASCOP for review.
- Enhanced monitoring protocol under review by NASCOP.
- Zimbabwe:
 - Needs assessment interviews completed with various stakeholders, including MOHCC, National AIDS Council, CHAI, MSF, Zimbabwe National Network for PLWH, and others. Key findings include:
 - TLE400 has been procured by the government (~1 million packs) and is available in Zimbabwe. This stock will be used for adolescents and patients currently experiencing toxicity on TLE600. It has not yet been distributed to sites but site selection is underway by the MoH.
 - Two generic suppliers have applied for the registration of TLD in the country. There is an expedited pathway that allows Zimbabwe to complete registration in 6 months.
 - MSF plans to conduct a demonstration project for DTG (protocol currently awaiting approval). Early discussions with MSF to harmonize data collection to allow for comparison of patient outcomes.
- Global activities
 - ICAP has drafted a case study on past transitions to adult 1st line ART regimens, which is currently undergoing internal review.
 - Presented on Pediatric Optimization opportunities at a community meeting during the INTEREST workshop in Lilongwe, Malawi.

DEMAND CREATION AND COMMUNITY ENGAGEMENT, HIV i-Base

- Continued working on the TAC treatment literacy materials (to be launched at the SA AIDS conference in June).
- 1-day ART Optimisation Community meeting held at the 11th INTEREST Workshop in May 2017 with AfroCAB and TAC, funded by USAID. CHAI, Unitaid, Wits RHI, ICAP, the Southern African HIV Clinicians Society and Stop Stockouts Project also attended as presenters and/or observers. Community members participated in the INTEREST workshop including in a session entitled, "Treatment optimisation: the community perspective".
- Held a 1-day meeting with Unitaid to discuss community engagement in Unitaid programmes and introduce the HIV self-testing programme.

COMMUNITY ENGAGEMENT, TAC

- The TAC provincial trainers are continuing with their branch training, and in May they reached 918 people with treatment literacy information, with a focus on ARVs and treatment optimisation.
- The TAC Task Team is assisting Wits RHI with recruitment for ADVANCE in Gauteng. Information about the study has been shared with 831 people.
- The material development and updating of treatment literacy materials have been delayed as quotes are being sought for design, layout and printing.

CLINICIAN/HEALTH WORKER ENGAGEMENT, Southern African HIV Clinicians Society

- *HIV Nursing Matters* printed with treatment optimisation and new drugs articles, written by Wits RHI staff involved in ART optimisation work.
- Attended INTEREST 2017: networked, strengthened relationships, made AfroCAB connections in the region, connected with TAC provincial trainers for upcoming healthcare worker treatment optimization CMEs (as feedback is that they are educating the HCWs, so we've asked them to refer them into our training also), made stockouts app connection with AfroCAB, made self-testing connections.
- Polokwane treatment optimization CME held with 55 attendees, and one in Cape Town with 76 attendees. This attendance has been some of the largest turnouts the Society has had in years. It shows the real interest in HIV self-testing and treatment optimisation. [The Cape Town CME was professionally filmed, and will be used for further training such as e-learning modules for the Advanced Management of HIV Course which runs twice a year for approximately 50 doctors, and is a precursor to the HIV Diploma at the Colleges of Medicine]. The next CME is planned for 24 June in Rustenburg.
- The 2-week Advanced Clinical Management of HIV course is complete – 20 doctors registered and completed the course, which included components of treatment optimisation in the learning material.
- New Southern African HIV Clinicians Society Adult Treatment Guidelines have been finalised and is ready for distribution (with new drugs and new regimens, and advocating treatment optimisation). SAHCS and CHAI have also had several meetings on guideline development broadly.
- HTB-South distribution:
 - 1 copy of HTB-South sent to all members who received a Society journal.
 - 1 copy of HTB-South inserted with the *HIV Nursing Matters* magazines.
 - In total, 3300 HTB-South magazines distributed, with a remaining 700 to be handed out at CMEs and conferences in June and July.
- *HIV Nursing Matters* distribution:
 - Sent to 1300 clinics and 900 active members who elected to receive *HIV Nursing Matters* – 2200 sent in total.
 - There are 1800 magazines left, for distribution primarily at the 8th SA AIDS Conference in June.

Major Plans for June 2017

Low-Dose Darunavir Study, Wits RHI

- Proceed with procurement of the next batch of study drugs (darunavir 400mg/ritonavir 100mg). This has been possible now that the manufacturer, Hetero, has received USAID approval for procurement as of May 2017.
- Prepare for close-out of enrolment phase of the study, and an external monitoring visit in July 2017 which will include a review of the last enrolment visits.

ADVANCE, Wits RHI

- Finalisation of the design of a poster which will be circulated at local clinics, hospitals, and general practitioner rooms as an aid to boost recruitment.
- Release of an advertisement in the local newspaper to generate interest in local communities amongst people who could qualify for enrolment onto the study.
- Meeting with TAC to discuss the way forward of better integrating TAC task members to assist with meeting recruitment demands and achievement of monthly enrolment targets.

ANRS 12313 (NAMSAL), IBB/IRD/ANRS

- Reach the target of 500 patients by end of June.
- UNITAID project team visit to Cameroon, 20-21 June.

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

- Submit the study to the UK regulatory/ethics authorities by mid-June.
- Start site set-up in parallel to the approval processes.

NANOTECHNOLOGY, University of Liverpool

- Complete ATV formulation experiments and collate results.
- Complete a second multi-dose study for DRV/r to investigate lowering dose.

MARKET ACCESS AND PRODUCT INTRODUCTION, ICAP

Country-level activities

- Mozambique:
 - Hold dissemination meeting for needs assessment and develop initial OPTIMIZE workplan for introduction of optimised ARVs in-country in collaboration with USAID, MOH, and other key stakeholders. Support quantification and country-level decision-making on introduction of LPV/r oral pellets. Support development of training materials for introduction of ATV/r in 2nd line ART.
- Kenya:
 - Enhanced monitoring work is currently on hold due to funding restrictions. Submit protocol for situation analysis to KEMRI. Finalise training slides for national training of trainers (TOT) for DTG introduction. Meet with Pharmacy and Poisons Board to review AE reporting and include in training materials. NASCOP to send communiqué on immediate DTG phase-in plans to all counties. Facilitate training of county TOTs to support DTG use in Kenya.
- Zimbabwe:
 - Review and finalise the country needs assessment internally and with partners; plan for needs assessment dissemination meeting. Conduct initial baseline analysis of current situation using routinely collected electronic data. Engage with MOHCC to support plans for introduction of EFV400. Initiate conceptualisation of EFV400 demonstration project, including mechanisms for strengthening documentation of

processes to inform future TLD rollout. Liaise with community groups to plan for dissemination of information on new optimal ARVs for adults and children.

- Global:
 - Coordination call with CHAI scheduled for early June to discuss webinars, IAS satellite planning, and country-level coordination activities. Finalise case study on past transitions and disseminate to partners for review. Create outline/initial draft of toolkit for optimised product introduction. Support the development of an IAS satellite on country experiences with DTG introduction. Begin developing webinar for APWG to disseminate supply information on optimised new regimens.

COMMUNITY ENGAGEMENT, HIV i-Base

- Developing July 2017 Fit for Purpose to be distributed at IAS 2017.
- Developing TAC treatment literacy materials. First booklet to be distributed at IAS 2017.
- Planning follow-up AfroCAB and TAC community meeting – to take place after IAS 2017 in July.

CLINICIAN/HEALTH WORKER ENGAGEMENT, Southern African HIV Clinicians Society

- SAHCS is conducting a treatment optimisation session at the SA AIDS conference, as a skills building satellite.
- Durban and Restenburg CMEs on treatment optimisation.

Staffing Changes

- Welcome to Dr. Innocent Hove who has been hired as the ICAP Country Program Officer for OPTIMIZE in Zimbabwe.
- Advertisement has been placed for Post-Doctoral Research Associate vacancy at UoL.

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/OPTIMIZE/TechnicalSteeringCommittee/Calendar+Events](https://www.dropbox.com/home/OPTIMIZE%20TechnicalSteeringCommittee/Calendar+Events))

- Presentations from the Technical Steering Committee meeting held 22-24 May 2017 can be found on the Dropbox

Papers in process

- WDF Venter, P Clayden, C Serenata. The ADVANCE Study: A Groundbreaking Trial to Evaluate a Candidate Universal Antiretroviral Regimen. Current Opinion in HIV and AIDS. Publication in June/July 2017.

Papers published

- C Serenata, H Gous, J Grab, M Moorhouse, E Maharaj. Optimising ART in the 21st Century. HIV Nursing Matters. Publication in May 2017.
(<http://www.sahivsoc.org/Files/Nursing%20matters%20May%202017.pdf>)
- FOA Nabeemeeah, T Masemola, MA Moorhouse. Dolutegravir: The game changer? HIV Nursing Matters. Publication in May 2017.
(<http://www.sahivsoc.org/Files/Nursing%20matters%20May%202017.pdf>)

Media Coverage

- University of Liverpool podcast on nanotechnology:
https://www.blubrry.com/universityofliverpool_podcast/22528167/episode-3-nano-medicine-shrinks-the-cost-of-hiv-treatment/

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)