

OPTIMIZE, May 2017

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

MAJOR ACHIEVEMENTS FROM APRIL 2017

LOW-DOSE DARUNAVIR STUDY, Wits RHI

- As of end April, there were 334 participants screened and 278 enrolled in the low-dose DRV (WRHI052) study. This means that we only have to recruit 22 participants in May to reach full enrolment.
- Retention to date:
 - Visit 1 (week 04) = 261 expected/ 258 completed (99%)
 - Visit 2 (week 12) = 204 expected/ 204 completed (100%)
 - Visit 3 (week 24) = 129 expected/ 128 completed (99%)
 - Visit 4 (week 36) = 61 expected/ 61 completed (100%)
- The study was presented to the DSMB on 26 April, including the first interim analysis (presented by Prof. Andy Hill). The DSMB feedback was very positive. It asked for some additional information at the next meeting (in November 2017), including:
 - A statistical analysis plan describing how the arm will be compared
 - Show the percentage with HIV RNA <50 copies/mL in each arm, with associated 95% confidence intervals
- One of the lab processes to be potentially amended following the DSMB is to re-test any HIV RNA results in the 50-200 copies/mL range

ADVANCE STUDY, Wits RHI

- As at the end of April, 196 participants had been screened, 178 eligible for enrolment, and 136 enrolled. The enrolled participants include 5 under the age of 19.
- Due to the many public holidays in April, enrolment in April was very low. The team is exploring strategies to increase enrolment in May to make up for the shortfall.
- The Protocol Clarification Memo #2 submitted for regulatory approval in March received ethics (HREC) approval on 6 April.
- Wits RHI also received approval for one additional sub-investigator for both WRHI052 and WRHI060 in April – this boosts our number of doctors that can see study participants.



Upcoming Events

8 May, ADVANCE Clinical Endpoints Committee teleconference

16-19 May, INTEREST Workshop, Malawi, Lilongwe (<http://interestworkshop.org/>)

14 May, pre-INTEREST meeting with treatment activists on HIV self-testing; 15 May, treatment optimisation

22-24 May, OPTIMIZE Technical Steering Committee meeting (USAID consortium), Johannesburg

27 May, Prof Francois Venter speaking at the Mylan masterclass, "Debating the future: DTG vs. EFV", Johannesburg

Important Contacts

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- One drawback this month is that HREC did not approve the waiver request submitted to allow for adolescents between the ages of 16-18 to consent to study participation without requiring a guardian's approval.
- The ADVANCE study update was also presented at the DSMB. The main feedback included:
 - Consider changing the two interim analyses to just one interim 48-week analysis. Prof Andy Hill suggested this be done once the first 400 participants have completed 48-weeks.
 - Provide more details on the interim and final analyses

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

- The study has recruited over half of all study participants: 15 ongoing or completed (17 enrolled, 3 withdrawn, of which 2 will be replaced. One can be evaluated as withdrawn after PK on day 42/43). All of these are in the UK.
- Preliminary data and a revised protocol will be submitted to the Uganda authorities, with regulatory approval expected by September 2017.

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

- Site clearance for this study has been provided, and screening will now commence. The baseline visit for the first 10 subjects is planned for 1 June.

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

- Study set-up is currently ongoing. Submission to the UK ethics and regulatory authorities is expected this month with a view to open to recruitment in August 2017.

EFAVIRENZ 400mg PREGNANCY PK STUDY (SSAT063), Mylan (St. Stephen's AIDS Trust)²

- 23 participants have been enrolled in the study – 15 in Uganda and 8 in the UK. Recruitment is now officially closed in the UK. Currently screening additional women in Uganda to reach the target of 25.
- A late-breaker abstract is being planned for IAS in July 2017, with preliminary data on 21 women.

NANOTECHNOLOGY, University of Liverpool

- The in vivo work on atazanavir has started, and darunavir is being further optimised in vivo.

MARKET ACCESS AND PRODUCT INTRODUCTION, ICAP

Country-level activities:

- South Africa country needs assessment: Wits RHI will share this with South Africa contributors and other partners

¹ Funded by Gilead, not OPTIMIZE

² This study is not funded through OPTIMIZE, but is included here as a point of interest

- Mozambique: Needs assessment complete; currently under review internally. ICAP will host a meeting with stakeholders in Mozambique to review the findings and how they should inform the work of OPTIMIZE going forward.
- Kenya:
 - ICAP is developing a concept note, requested by NASCOP, which will outline the phase-in plans for DTG and other optimized ARVs in Kenya.
 - ICAP has drafted a communique, which NASCOP will share with health facilities on the phase-in plan. ICAP is also developing provider training materials for the phase-in.
 - A protocol and questionnaire have been developed for the needs assessment, which will be submitted to KEMRI to obtain IRB approval.
 - ICAP completed a protocol for an enhanced data system for monitoring DTG. The protocol has been reviewed internally and a meeting has been scheduled to review with NASCOP.
 - A meeting has been planned by ICAP to discuss the progress on the DTG introduction and plans for monitoring adverse drug reactions to DTG with CHAI and NASCOP while the WHO HQ treatment focal officers are in the Kenya.
- Zimbabwe: Arrangements were made to conduct interviews for the needs assessment in May. Candidates were interviewed for the Program Coordinator role.

MARKET ACCESS, Mylan

- Mylan will file its TAF/FTC/DTG formulation with the FDA in May 2017 once the necessary waiver has been received from the innovators. The TAF/3TC/DTG filing is expected between October and December 2017.
- The Mylan DRV/r/DTG formulation that was to be filed later this year will now only be filed in early 2018. The delay is in order to ensure a successful bioequivalence result.
- The Mylan DRV/r filing is also imminent.

DEMAND CREATION AND COMMUNITY ENGAGEMENT, HIV i-Base

- Finalising plans for ART optimisation community meetings in Malawi in May
- Planning community meeting at IAS
- Working on the texts for TAC's ART optimisation and treatment literacy materials

COMMUNITY ENGAGEMENT, TAC

Train the trainer (treatment literacy)

- The provincial trainings were successfully completed in 4 provinces (Free State, Limpopo, KwaZulu-Natal, and Mpumalanga). The Gauteng and Eastern Cape trainings are to be scheduled.
- The train the trainer (TOT) sessions targeted TAC district organisers, community advocates and branch educators, whose task it is to assist with the training of TAC branches, communities and other stakeholders.
- TAC has created both a manual and electronic filing system to capture training activities.

Developing briefing documents (treatment literacy)

- The *HIV in our Lives* manual was reviewed, and changes have been sent to HIV i-Base for further review. The only outstanding section relates to updating or obtaining new stories / testimonies.

Demand creation for ADVANCE recruitment

- A good working relationship with targeted clinics in region F was established to allow TAC to assist Wits RHI with recruiting for ADVANCE. The Wits RHI Health Systems Strengthening team facilitated the linkage.

CLINICIAN/HEALTH WORKER ENGAGEMENT, Southern African HIV Clinicians Society

- Continuous medical education (CME) training on “ART Optimisation – New Drugs, New Guidelines” took place on 8 April 2017 in Johannesburg, with 110 doctors attending. Prof. Francois Venter presented on ART optimisation.
- The next two trainings are taking place in Polokwane (20 May) and Cape Town (3 June)
- Dr. Michelle Moorhouse from Wits RHI trained Society staff on treatment optimisation on 31 March 2017.
- Booked a Treatment Optimisation skills building workshop at the following conferences:
 - SA AIDS Conference, 13-15 June 2017, Durban
 - Rural Health Conference, September 2017, Taung
 - Annual Workshop on Advanced Clinical Care – AIDS (AWACC), September 2017, Durban
- Two articles finalised for the Society publication *HIV Nursing Matters on Treatment Optimisation* (written by Wits RHI staff). It is undergoing final edit and will be printed in May 2017
- The HTB-South magazine sent to doctors and nurses that are members of the Society – around 4000 in total
- ART optimisation information being distributed weekly via SMS to designated groups of healthcare workers, nurses, technical and clinical staff, amongst other

MAJOR PLANS FOR MAY 2017

LOW-DOSE DARUNAVIR STUDY, Wits RHI

- Complete enrolment of all participants
- Develop plans for responding to DSMB recommendations
- Finalisation of procurement for next batch of study drugs for participant visits, as well as post-trial access

ADVANCE, Wits RHI

- Scale up recruitment efforts to make up shortfall from April
- Develop plans for responding to DSMB recommendations, including amending the statistical analysis plan

- Have first meeting of the Clinical Endpoint Committee (CEC) to review the safety data generated from the first 3 months of the ADVANCE study participants. This committee meets quarterly.

NANOTECHNOLOGY, University of Liverpool

- Continue the in vivo work on ATV and DRV

MARKET ACCESS AND PRODUCT INTRODUCTION, ICAP

Country-level activities

- Mozambique: ICAP will share the needs assessment with key MOH personnel and the USAID Mission for review. Then ICAP will schedule a meeting with all stakeholders to discuss how the assessment should inform activities for introducing optimized ARVs moving forward.
- Kenya: ICAP will continue to develop the concept note, communicate, and training materials for DTG phase-in. We will also submit the protocol to KEMRI for the situation analysis and develop the second version of the enhanced data monitoring system protocol after review from NASCOP.
- Zimbabwe: ICAP will conduct the needs assessment and hire a program coordinator if possible. ICAP NY will visit Zimbabwe to meet with the MOHCC and the ICAP country team.

COMMUNITY ENGAGEMENT, TAC

Train the trainer: Treatment literacy

- The Gauteng and Eastern Cape training will be finalised.
- The master trainers are expected to develop a training plan for branch trainings. Some of these have already commenced.

Develop briefing documents: Treatment literacy

- Finalise reviewing the treatment literacy content to begin the design work of the treatment optimisation brochure (with HIV i-Base)

Demand creation for ADVANCE recruitment

- The TAC Task Team will be re-introduced to the targeted facilities by the Wits RHI team, after which TAC will assist with recruitment.

COMMUNITY ENGAGEMENT, HIV i-Base

- ART optimisation meetings at INTEREST
- Attending the OPTIMIZE Technical Steering Committee meeting in Johannesburg
- Planning community meeting at IAS
- Finalising TAC ART optimisation and treatment literacy materials

STAFFING CHANGES

- Dr. Nandita Sugandhi has been hired as the Product Introduction Coordinator. She can be reached at: nss14@cumc.columbia.edu.
- ICAP is hiring a Market Access Officer. Please share the job description, which can be found here: <http://icap.columbia.edu/jobs/detail/market-access-officer-optimize2>

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%20TechnicalSteeringCommittee/Calendar+Events>)

- Finalised the infographic on the nanotechnology work. This will be shared with the consortium, and used of different electronic media (e.g. University of Liverpool website, USAID website)

Papers in process

- C Serenata, H Gous, J Grab, M Moorhouse, E Maharaj. Optimising ART in the 21st Century. HIV Nursing Matters. Publication in May 2017.
- FOA Nabeemeeah, T Masemola, MA Moorhouse. Dolutegravir: The game changer? HIV Nursing Matters. Publication in May 2017.
- 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.

MEDIA COVERAGE

- None since the last update

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)