

# Optimising ART September 2017

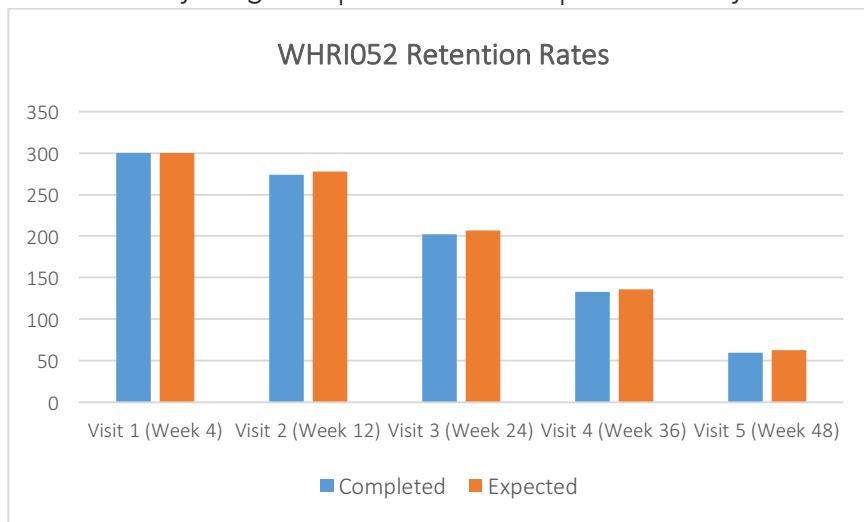
This is a monthly update shared with all members involved in projects aimed at optimising ART, and is meant to provide a short update of major achievements, challenges, and plans for the future. Please submit any inputs to Celicia Serenata before the 1<sup>st</sup> Wednesday of every month.

Several Wits RHI staff participated in a one-day meeting convened by the Department of Health, with assistance from CHAI, to finalise guideline recommendations for paediatric ART. This is similar to the meetings held in 2016 and 2017 with adult HIV clinicians on revising the national treatment guidelines and introducing optimised ARVs, especially DTG.

## Major Achievements from August 2017

### LOW-DOSE DARUNAVIR STUDY, Wits RHI

- Follow-up study visits are successfully progressing, with average retention rate being maintained at 98%. All of the enrolled participants have completed Visit 1 as illustrated below, with no deaths or participants lost to follow-up reported since study inception.
- Orders have been placed with Hetero for the delivery of the next batch of study drugs – expected in late September/early October.



## Upcoming Events

8 Sep: Unitaid Semi-Annual Report submitted

25 Sep: Please note that this is a public holiday (Heritage Day) in South Africa

28 Sep: Final USAID Y3 Work plan submitted

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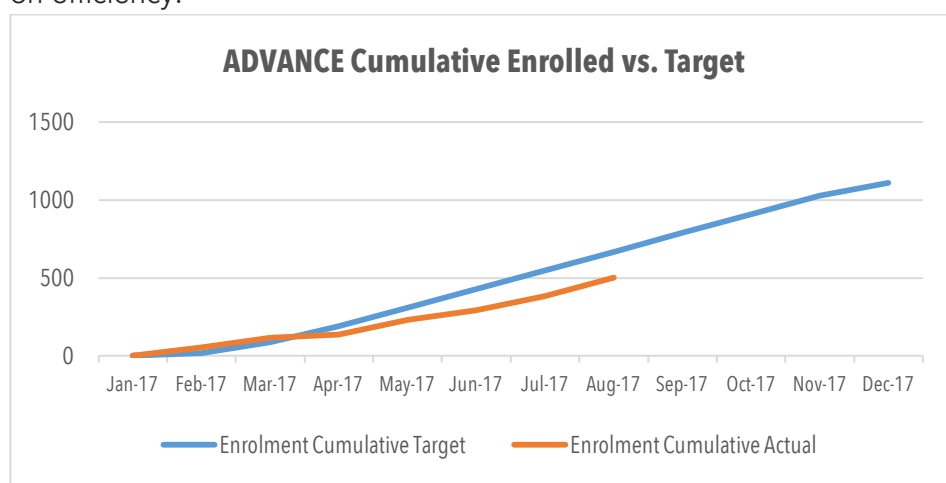
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## ADVANCE STUDY, Wits RHI

- As of 31 August 2017, 502 participants enrolled with August reflecting the highest number of enrolments (116) since the start of the study. 67 participants are still to undergo eligibility assessment.
- Recruitment of adolescents is an ongoing challenge. Aside from issues with disclosure, many of the adolescents who are identified as HIV positive are also pregnant, which excludes them from study participation. Wits RHI has liaised with several organisations working with adolescents, and one such organisation, Shout it Out Now, has been instrumental in providing adolescent referrals and the Shandukani team have been fervently pursuing these potential participants.
- In collaboration with TAC, a testing event was held in Soweto (Region D) from 30 August – 01 September 2017 to aid recruitment. These efforts were somewhat hampered by a shortage of test kits in the public sector clinic.
- Protocol amendment#3 has been through the first panel of reviews and is close to finalisation for submission for regulatory approvals.
- The Yeoville site has implemented additional QA/QC measures and the installation of a dedicated printer at which lab reports will be automatically scheduled to print, improving on efficiency.



## 2<sup>ND</sup> LINE ADHERENCE STUDY, Wits RHI

- This study received HREC approval, and data analysis has commenced.

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

- Recruitment and monitoring are ongoing.
- A response to the Uganda IRB has been submitted, and full approval is pending.
- The protocol has been updated as a non-substantial amendment to v6.0 (following the IRB request for updates), and implemented at the UK site on 18 August.

### **TAF-RIF TB PK STUDY (RIFT), St. Stephen's AIDS Trust<sup>1</sup>**

- Enrolment is ongoing with 3 more participants required due to 2 participants who dropped-out.

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

- MHRA approval was granted on 1 August 2017.

### **NAMSAL Trial, ANRS 12313, IBB/IRD/ANRS**

- As of 22 August, there were 820 participants screened, and 616 were enrolled and randomised in the ANRS12313 NAMSAL trial. The target has been reached, and recruitment is now closed.
- 8 participants are currently pregnant.
- A total of 21 participants were/are TB co-infected, and all but one received/are receiving rifampicin during the trial follow-up, with protocol-defined ART dose adjustments.
- 70 participants have completed their week 48 visit, and have started the post-trial follow-up. These participants have been switched to new formulations of the study drugs: Aurobindo generic formulation of DTG and Mylan FDC TDF/3TC/EFV400 for DTG and EFV 400mg-based regimens, respectively.
- Below a picture with some members of the NAMSAL team.



### **NANOTECHNOLOGY, University of Liverpool**

- Initial mass spectrometry work has begun, tailoring analytical methods for optimisation.
- University of Liverpool and MPP held a call with PSM, and plans to meet face-to-face at the PAC in November 2017.
- EFV SDN work progressing.

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<sup>1</sup> Funded by Gilead

## MARKET ACCESS AND PRODUCT INTRODUCTION, CHAI

- Through CHAI's OPTIMAL grant, CHAI's HIV Access Program launched two new resources to support product introduction at the country level: the HIV New Product Introduction Toolkit website, and the HIV New Product Introduction Guide.
- The HIV New Product Introduction Toolkit (<https://www.newhivdrugs.org/>) is a website that provides the tools and resources needed to introduce and scale new ARVs in-country, spanning the entire product introduction process, including product adoption, forecasting, procurement, facility phase-in, and supply planning and monitoring.
- Accompanying the website resource is a downloadable HIV New Product Introduction Guide (<https://clintonhealth.app.box.com/s/lkshjlcxrss8l37g7onpf4jj5te1dcxc>) which provides an in-depth overview of the key considerations when adopting and rolling out new ARVs.

## MARKET ACCESS AND PRODUCT INTRODUCTION, ICAP

- Global Activities:
  - ICAP finalized the framework for the new product implementation toolkit.
  - ICAP reworked the anchor case study on first-line transitions to align with the country product introduction framework and incorporated feedback from Wits RHI and USAID.
  - ICAP finalized the mapping exercise on national drug regulatory processes, focusing on four phase one OPTIMIZE focus countries.
  - ICAP hosted a team from USAID to review and finalize draft of Year 3 workplan.
  - ICAP finalized the draft of a market shaping intervention report for circulation and feedback.

Version 1 of the ICAP "Optimized ARV Uptake Toolkit" is in the final stage of development and will be made available in Q4 of 2017. The toolkit provides country programs with the resources necessary to support the successful introduction of new, optimized ARVs in LMIC with a particular focus on the need for interdisciplinary collaboration and strong communication plans at both the national and local level. ICAP is actively working with CHAI to ensure synergy with the newly launched CHAI New Product Introduction Guide and will be working with both CHAI and other partners on the ground / in-country to test the resources and tools in the Optimize toolkit over the course of the next year to ensure that the toolkit addresses the needs of the HIV care and treatment community. The toolkit highlights resources available to support the introduction of new ARVs across functions and levels of the health care system, but puts particular emphasis on the real-world implementation needs at the patient / facility / service delivery level. In particular, it will include a number of new tools and resources to support providers and other healthcare workers with the information needed to drive rapid, yet rational, product uptake at the facility level.

- Kenya:
  - ICAP finalized the protocol for enhanced monitoring activities.
  - ICAP met with Palladium to discuss the next steps for enhanced monitoring activities, including site selection, proposed indicators, etc.
  - ICAP finalized the hiring of the HMIS Technical Advisor position to work with in-country partners around enhanced monitoring activities.

- ICAP conducted preparatory activities for the Kenya situational analysis to be carried out in September.
- ICAP attended an Ad Hoc Clinical TWG meeting and revised training materials based on feedback received during the meeting.
- Zimbabwe:
  - ICAP presented the Zimbabwe Needs Assessment to the HIV/TB unit of the Ministry of Health, which was well received. Feedback obtained during the discussion has been incorporated into the final document that will be disseminated in-country and online once final formatting is complete.
  - ICAP hosted a small community meeting to brainstorm with members from AfroCab, Zimbabwe AIDS Network and ITECH on pediatric advocacy opportunities.
  - ICAP began a series of facility visits to gather feedback on the initial stages of TLE400 introduction in conjunction with representatives from the AIDS/TB and Logistics unit. Facility visits are to be completed in early September and a report will be finalized with observations and recommendations for ongoing phase-in activities.
- Mozambique:
  - The ICAP Mozambique country team liaised with the USAID mission to share the Needs Assessment and begin planning for a larger dissemination meeting with the MoH.

### **DEMAND CREATION AND COMMUNITY ENGAGEMENT, HIV i-Base**

- Working on ART information for communities in LMICs transitioning to DTG, which will be distributed on the HIV i-Base website. This will also provide content for the TAC materials.

### **COMMUNITY ENGAGEMENT, TAC**

- 703 people reached with patient treatment literacy (PTL) and treatment optimisation information in branch workshops in conducted in August. The people reached with this information as in all the previous activities done since the beginning of 2017 are receiving the information well and are very excited about the new innovations with regards to the treatment of HIV, and are anticipating the rollout of dolutegravir in South Africa in 2018.

### **CLINICIAN/HEALTH WORKER ENGAGEMENT, Southern African HIV Clinicians Society**

- Optimisation CMEs were held in Bloemfontein (Free State) on 5<sup>th</sup> August for 26 doctors, and in Kimberley (Northern Cape) on 25<sup>th</sup> August for 34 doctors.
- 12 TAC branch trainers attended optimisation training and information workshops on stockouts in Soweto on 11<sup>th</sup> August.

## **Major Plans for September 2017**

### **LOW-DOSE DARUNAVIR STUDY, Wits RHI**

- Receipt of study drugs to continue with the study and to be able to provide post-trial access for those participants that are scheduled for last on-study visit.

## **ADVANCE, Wits RHI**

- Finalise submission of Protocol Amendment #3 for regulatory approvals.
- Receipt of formal City of Johannesburg (COJ) district approval.
- Receipt of Ekurhuleni Research Committee approval to expand the catchment area for recruitment.
- Conduct an ADVANCE recruitment drive and testing event in Region E (Alexandra) using the Wits RHI mobile unit, once approval.

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

- Expected IRB approval in Uganda.
- Submission of a CTA (NDA) in Uganda for study approval. The package is currently being reviewed prior to submission.
- Completion of recruitment in the UK (stage 1). Two additional patients are left to be enrolled, following an additional withdrawn patient prior to their Day 42/43 visit.
- Substantial amendment to the protocol to update the criteria for the Trial Steering Committee to allow recruitment in Uganda to start within the expected timelines. The current criteria requires 25 completed patients' data to be reviewed prior to Uganda starting.

## **TAF-RIF TB PK STUDY (RIFT), St. Stephen's AIDS Trust<sup>2</sup>**

- Analysis of first 11 patients to be reported.

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

- Response to Ethics provisional opinion was sent on 1 September 2017.
- Site set-up to continue throughout September with a view to open the study at the beginning of October.

## **NANOTECHNOLOGY, University of Liverpool**

- Multiple dose ATV model *in vivo* arranged.
- Newly generated ATV/r formulations tested *in vitro* in the Transwell system.

## **MARKET ACCESS AND PRODUCT INTRODUCTION, ICAP**

- Global:
  - Finalize new product implementation toolkit;
  - Finalize content for the training package;
  - Collaborate with USAID around supply chain issues and on manuscript for peer-reviewed publication on ARV transitions;

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<sup>1</sup> Funded by Gilead

- Complete various tools to support transition to optimal ARVs, including clinical considerations on transition to DTG-containing regimens.
- Kenya:
  - Share the finalized protocol for enhanced monitoring activities with NASCOP, Palladium and USAID for review and feedback;
  - 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 finalized training materials;
  - Conduct Kenya situation analysis;
  - Develop facility assessment tool to be used as part of the enhanced monitoring activities.
- Mozambique:
  - Hold dissemination meeting for the needs assessment and develop an initial Optimize workplan for 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.
- Zimbabwe: Complete facility visits and share draft report with phase-in recommendations with MoHCC. Begin interviews for supply chain management case study to be completed in Year 3.

### **COMMUNITY ENGAGEMENT, TAC**

- Training of trainers is scheduled to take place in Johannesburg from 18 – 22 September 2017. This will be an advanced/refresher training for the 7 trainers and 8 District organisers who in turn will go back to their respective provinces and do provincial training of trainers who will assist in cascading the information to branches and communities.
- Trainers to continue with their branch trainings as not all the branches have been covered as yet, and treatment optimisation will continue being incorporated into all capacity building activities at branch and provincial level.

### **CLINICIAN/HEALTH WORKER ENGAGEMENT, Southern African HIV Clinicians Society**

- The next CME scheduled for 30 September 2017 in Port Elizabeth.
- Planning underway for a TAC TOT for provincial and branch trainers on treatment optimisation and stockouts (2 – 3 further trainings for the remainder of 2017).
- Materials development: HIV i-Base Fit for Purpose – meeting planned with Polly Clayden on 14 September in South Africa to discuss distribution of materials.
- Lauren Jankelowitz is attending the AWACC conference from 7-8 September 2017 to distribute the Society's new Adult ARV Guidelines. There are also 2 OPTIMIZE presentations at AWACC: Dr Michelle Moorhouse presenting on "Better First-Line ART" and Dr Munira Khan presenting on "Optimisation in TB".
- The Rural Health Conference being held in Taung from 22 – 25 September 2017 will include a treatment optimisation session delivered by Dr Trevor Majoro (<http://www.hst.org.za/events/rural-health-conference-2017>)

- Mylan Academic HIV Meeting in Limpopo on 16 September 2017 – treatment optimisation session by Prof Remco Peters.
- The HIV Nursing Matters print run has been delayed and will be distributed beginning of October 2017 as a bumper issue.
- Planning continues for the International HIV-Drug Resistance Workshop, November 2017 (<http://www.hivresistance2017.co.za/>)
- Planning continues for the SA HIV Clinicians Society conference in 2018 (<http://www.sahivsoc2018.co.za/>)

## Staffing Changes

- None

## 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>)

Also, to assist with all communication, branding and marketing opportunities, please find relevant guidance and documents in the Dropbox at: <https://www.dropbox.com/home/OPTIMIZE%20TechnicalSteeringCommittee/Communications+Branding+Marketing>

### Papers published

- None

### Online Posts

- None

## Media Coverage

- 7 August: Mylan receives FDA tentative approval for TLD: <http://www.prnewswire.com/news-releases/mylan-receives-tentative-approval-for-tld-under-pepfar-300500233.html>
- 8 August: MPP statement on the Mylan TLD approval from FDA: <http://www.medicinespatentpool.org/statement-the-medicines-patent-pool-welcomes-first-generic-dolutegravir-combination-to-receive-tentative-approval-from-u-s-food-and-drug-administration/>
- 21 August: Aurobindo Pharma HIV drug gets USFDA approval under PEPFAR: <https://ultra.news/s-k/32772/aurobindo-pharma-hiv-drug-gets-usfda-approval-pepfar>

## 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)

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## 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](http://www.rudasa.org.za/conference/about-the-conference)
- AWACC, Durban, 7-8 September 2017, [www.awacc.org/2014](http://www.awacc.org/2014) - speakers are being allocated
- Mylan – Academic HIV Meeting, Limpopo 16<sup>th</sup> September, 2017 – Treatment Optimisation session by Prof Remco Peters
- 24-27 October 2018: 4<sup>th</sup> Southern African HIV Clinicians Society Conference, Gallagher Convention Centre, Midrand. [www.sahivsoc2018.co.za](http://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](http://www.usaid.gov)

Unitaid finds new and better ways to prevent, test and treat HIV, tuberculosis and malaria quickly and more affordably. It takes game-changing ideas and turns those into practical solutions that can help accelerate the end of the three diseases. Established in 2006 by Brazil, Chile, France, Norway and the United Kingdom, Unitaid plays an important part in the global effort to defeat HIV, tuberculosis and malaria. For more information, please visit: [www.unitaid.org](http://www.unitaid.org)