

# Optimising ART

## April 2018



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*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 before the 1<sup>st</sup> Wednesday of every month.*

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OPTIMIZE was featured in USAID's Center for Innovation and Impact (CII) 2018 Impact Brief (pages 5 and 34). [Go to <https://www.usaid.gov/cii>, and click on 2018 Impact Brief.] The CII Impact Brief has reached nearly 27,000 people through the CII newsletter and social media outreach, and the audience includes partners, other external groups, and internal USAID teams.

We are also sharing in the newsletter an outline of a study on DTG conducted by University Hospital, Geneva.

In South Africa Wits RHI and CHAI is assisting the National Department of Health with the transition to TLD. Wits RHI will co-ordinate a national TL Transition Task Team. The transition planning has recently suffered a setback in that the generic TLD fixed-dose combinations have not been registered by SAHPRA, citing the lack of clinical evidence – evidence being generated through NAMSAL and ADVANCE. Wits RHI and CHAI is assisting the National Department of Health in crafting a response to SAHPRA in this regard.

### Achievements from March 2018

#### **ADVANCE, Wits RHI**

- The pressure to recruit the last 80 participants to close enrolment continued during the month of March, as the challenge to find participants who met the study inclusion criteria persisted. Many of the people identified as potential study participants are found out to be “defaulters” who have prior ARV exposure or are females who are unable to commit to not conceiving over the study duration, with a minority being infected with TB.
- 1024 participants have been enrolled as at end of March 2018 (14 are adolescents).
- Monthly recruitment progress illustrated in the graph below:-

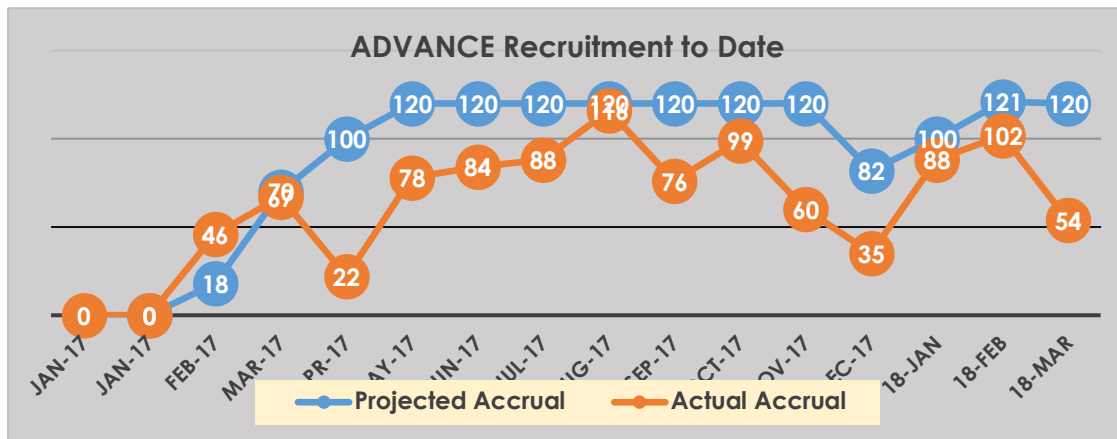
### Upcoming Events

- 16 Apr: Year 3 semi-annual progress report (SAPR) due to Wits RHI
- 24 Apr: WS 1 call with USAID
- 25 Apr: WS 2 call with USAID
- 30 Apr: WS 3 call with USAID; DSMB meeting (ADVANCE safety data)
- 30 Apr: Year 3 SAPR submitted to USAID

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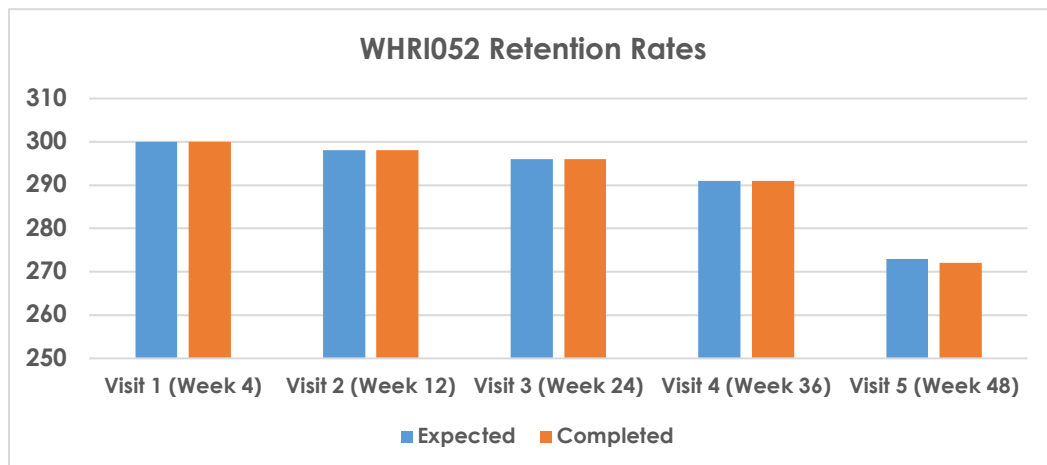
### Queries can be directed to:

Celia Serenata, Wits RHI,  
[cserenata@wrhi.ac.za](mailto:cserenata@wrhi.ac.za)



### LOW-DOSE DARUNAVIR (WRHI052), Wits RHI

- Study retention continued to progress successfully with current retention rate of 100%, with about 9% of participants still due to complete their Week 48 visit. The last participant last visit is scheduled for late May (with the window for the last visit in mid-June).



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

- Recruitment has been completed in Uganda for Stage 2 of the study (last participant enrolled on 6<sup>th</sup> March) with 9 patients now having completed their Day 28 PK visits.

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

- Monitoring close-out visit took place and the database was locked on 1 March 2018.
- Study abstract submitted to the 19<sup>th</sup> PK Workshop (Baltimore May 2018) for acceptance.

### NANOTECHNOLOGY, University of Liverpool

- Non-GMP stability testing of DRV/r formulations is underway, and formulations are tested monthly.
- Mass spec methods are under development for DRV, ATV and RTV for analysis of *in vivo* samples.

- Juniper started manufacture of EFV for the clinical trial, and the process should be complete within 6 weeks.
- SSAT have started to screen patients for the stage 2 EFV study.
- *In vivo* confirmation experiments are undergoing planning for spray dried formulations of DRV/r.
- ATV experiments are continuing at a steady state.

## HEALTH WORKER ENGAGEMENT, SAHCS

- Viral Load training (in the form of PowerPoint slides) was developed by Dr. Jeremy Nel for doctors and nurses, in accordance with the objectives of the Unitaid grant for 2018, and this will be rolled out across all provinces to nurses. The first workshop was held on 23 March in Polokwane. The sessions was well attended, with 61 participants ranging from HIV/AIDS, STI and TB (HAST) district managers, facility coordinators, wellness nurses from universities and Correctional Services, and PHC nurses from various clinics in the Capricorn district.
- The VL training went extremely well. Participants were fully engaged with the trainer and shared their experiences of working in resource-limited environments, as well as illiterate communities.
- The provincial Regional Training Centre manager Joyce Khota attended the training, and request the Society to conduct another training for those districts that could not attend on 23 March. Such a training would be for ±150 participants. The Society agreed, and is in the process of planning for this.
- ART optimisation training for doctors took place on Saturday 17 February in Pretoria, and was attend by 53 people, with good engagement between attendees and the speakers. The next ART optimisation training is planned for May in Cape Town, and will include the viral load component.

## COMMUNITY ENGAGEMENT, TAC

### Training

- The training of trainers (TOT) took place from 19-23 March in Johannesburg. During this, the TAC trainers and district organisers were updated on the latest developments with regards to HIV treatment, treatment optimisation, HIV self-screening, and additional training on cancer, and mental health. Sixteen (16) people were trained, and they have been tasked with cascading the information to their respective provinces and districts through the provincial TOTs planned for April and May. Assistance was provided by Polly Clayden (HIV i-Base) and Michelle Moorhouse (Wits RHI).
- The provincial TOTs with confirmed training dates are Limpopo (4-6 April), Free State (21-23 April), and Western Cape (16-19 April).
- Branch training has been taking place in the provinces as usual, and 1443 people were trained in March.

## Publications

- Posters: In the national TOT the trainers had a brainstorming session with Polly Clayden for the development of posters introducing TLD. These will only be finalised once the South African ART guidelines and timelines for TLD transition are confirmed.
- *HIV in Our Lives*: The publication is at the last stages of design draft 3). TAC and the designer are working well within the set timelines for feedback and inputs. The finalisation of this publication is imminent.

## COMMUNITY ENGAGEMENT, HIV i-Base

- The *HTB South* 2018 bumper edition was distributed with the Southern African Journal of HIV Medicine. It can be found online at <http://i-base.info/htb-south/3131>
- HIV i-Base completed the *Modern ART for Africa* and *Modern ART for South Africa* booklets and slide sets to support transition to TLD. This will be posted to the HIV i-Base website in April 2018.
- HIV i-Base supported the TAC training in Johannesburg from 19-23 March 2018, including new materials and ideas for posters and booklets to support the transition to TLD in South Africa.
- The *Fit for Purpose* revision is underway, and will be published in April 2018 – this will include developments from CADO3 and PADO4, as well as CROI 2018 and the WHO Think Tank meeting.
- Planning for the ART optimisation community meetings at INTEREST 2018 (Kigali) and IAS 2018 (Amsterdam) is underway.

## COUNTRY INTRODUCTION & UPTAKE, ICAP

### Global Activities

- ICAP/OPTIMIZE's new *Checklist to Guide Optimal ARV Introduction* has been launched online. The document can be accessed [here](#).
- ICAP hosted a two-part webinar series in February in coordination with the Antiretroviral Procurement Working Group (APWG) on the introduction of optimal new ARVs, and considerations for country programs.
- A completed draft of the TLD training for healthcare workers was piloted in Swaziland and feedback will be incorporated as the training package is finalised.

### Kenya

- ICAP has been a leading partner in providing technical assistance to the revision of the national ARV guidelines. Draft guidelines were shared with stakeholders, including the ICAP OPTIMIZE New York team for formal review, with feedback incorporated into the finalisation of the national guidelines.
- ICAP conducted 10 ARV optimisation trainings for clinicians and pharmacists/pharmacy technicians from ARV ordering sites. A total of 421 participants from 123 ARV ordering sites drawn from 7 counties that participated.
- Enhanced Data System (EDS) development:

- ICAP received IRB approval from Columbia University for the EDS protocol to analyse and disseminate data generated through the EDS.
- ICAP analysed data on adverse events from the EDS in one facility (JOOTRH) to ascertain the functionality of the EDS prior to its scale-up. ICAP supported the installation of the IL system at Siaya County Referral Hospital, currently undergoing testing to ensure functionality of the system.

## Plans for April 2018

### *ADVANCE, Wits RHI*

- Ongoing monitoring activities with close review of QC processes and annual review of SOPs.
- Data cleaning and data review activities in preparation for DSMB at end of April.

### *LOW-DOSE DARUNAVIR (WRHI052), Wits RHI*

- Ongoing data cleaning and data review activities as the study approaches close-out with LPLV in June 2018.
- Discussions and preparation to begin on the draft manuscript. Manuscript will be submitted to HIV Drug Therapy which takes places in Glasgow at the end of October 2018.

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

- Final participant follow-up visits for Uganda cohort with LPLV expected by mid-April 2018.
- PK results expected following sample shipment to the UK from Uganda. Data to be submitted to IAS as part of a late-breaker submission in May.
- Monitoring and data cleaning activities ongoing in Uganda.
- Close-out monitoring visit at the UK site.

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

- Study close-out activities.

### *NANOTECHNOLOGY, University of Liverpool*

- Juniper are due to complete the GMP manufacturing process and will send material to SSAT in April.
- SSAT will start the stage 2 EFV trial in April.
- Planning and executing of further *in vivo* experiments for DRV/r and ATV formulations.
- Continuation of non-GMP stability testing.

## COUNTRY INTRODUCTION & UPTAKE, ICAP

### Global Activities

- ICAP/OPTIMIZE to host a webinar with the APWG on the introduction of optimal new ARVs and considerations for country programs. This new webinar will be a consolidated 90-minute version with the aim of reaching a country-level audience.
- ICAP will participate (remotely) in the APWG Annual Meeting, and lead a discussion on optimising treatment and 2018 priorities.
- Finalise the comprehensive training package for healthcare workers to support transition to TLD.
- Finalise the Country Readiness Assessment tool and make it publically available through the ICAP/OPTIMIZE website.

### Kenya:

- Continue providing support to NASCOP towards the revision of the national ARV guidelines.
- Support NASCOP in finalising the DTG uptake data and discuss the gaps identified during the optimisation process with NASCOP in order to determine strategies to mitigate against the identified challenges, including addressing the low DTG uptake.
- Facilitate a dissemination meeting to share findings from the Situational Analysis.
- Finalise the visualisation dashboards for the Enhanced Data System.

## Staffing Changes

- Wits RHI: Natasha Arulappan, the Project Manager for ADVANCE, is leaving Wits RHI on 4 May. She is relocating to Sweden. Natasha has been the driving force in overseeing both ADVANCE and WRHI052, and her loss to the programme is immense.
- TAC: Portia Serote, the Gauteng Trainer, has resigned. The position has already been advertised, and a replacement will be appointed soon.

## Additional Studies (not funded by USAID and Unitaid)

The University Hospital in Geneva is conducting a randomised controlled trial, within the framework of the Swiss HIV Cohort Study, with a factorial design assessing (a) the efficacy of dual therapy of DTG-FTC in switch, and (2) the effect of simplified, patient-centred monitoring.

The study, titled *Evaluation of a Simplified Strategy for the Long-Term Management of HIV Infection (Simpl'HIV)*, is fully funded through academic funding, and will enrol 184 participants, followed for 48 weeks. The purpose of this study is to evaluate whether maintenance antiretroviral therapy could be simplified to DTG + FTC dual therapy and/or patient-centred monitoring once virological suppression is achieved. Using a factorial design, the study aims to assess the efficacy of DTG + FTC dual therapy to maintain virological suppression through 48 weeks of follow-up as well as the costs of a patient-centred ART laboratory monitoring.

The primary outcomes are:

- Proportion of patients maintaining HIV-RNA <100 copies/ml throughout 48 weeks
- Direct costs of the two study arms from the healthcare system perspective at week 48

More details at:

<https://clinicaltrials.gov/ct2/show/NCT03160105?recrs=a&rslt=Without&type=Intr&cond=HIV+Infections&titles=SIMPL%27HIV&rank=1>

The principal investigator is Alexandra Calmy ([Alexandra.calmy@hcuge.ch](mailto:Alexandra.calmy@hcuge.ch)).

## Outputs

*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 relevant guidance and documents in the Dropbox at:*

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

### Papers published

- None

### Talks Given

- None

### Presentations

- None

### Resources

- ICAP's *Checklist to Guide Optimal ARV Introduction*. Available online at <https://optimize.icap.columbia.edu/resource/checklist-to-guide-optimal-arv-introduction/>
- HIV i-Base's *HTB South*, January 2018: Volume 11 Number 1. Available online at <http://i-base.info/htb-south/3131>

## Media Coverage

- 16 March 2018, Andrew Owen and Steve Rannard interviewed about nanotechnology on BBC Radio Merseyside (Tony Snell in the morning). <http://www.bbc.co.uk/programmes/p05y49pw> (click on the link, then go to 1:53 in the programme).

Other articles/news stories that could be of interest:

- The cost-effectiveness and budgetary impact of a dolutegravir-based regimen as first-line treatment of HIV infection in India. JIAS.  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5878415/>
- 27 March 2018: £3 million boost for Liverpool advances materials and healthcare research. [https://www.eurekalert.org/pub\\_releases/2018-03/uol-bf032718.php](https://www.eurekalert.org/pub_releases/2018-03/uol-bf032718.php)

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## 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)
- ICAP website for its OPTIMIZE activities: <https://optimize.icap.columbia.edu/>

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## Future Conferences/Trainings

- 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)