

Optimising ART

July 2018



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 share an update on one of the ADVANCE sub-studies. The last month has been very occupied with dealing with some of the fallout of the safety signal from Botswana relating to neural tube defects (NTDs) in babies exposed to DTG during conception. For ADVANCE that meant revising the informed consent for women, reconsenting women of childbearing potential, and edits to the national algorithm proposed for a tender that potentially includes TLD introduction as of April 2019.

The USAID-funded OPTIMIZE consortium held a successful 2-day Technical Steering Committee meeting on 4-5 June in Johannesburg. All consortium partners were able to attend. The meeting focused on the priorities for the consortium over the next 12 months. The draft report of the meeting has been shared with the consortium.

Achievements from June 2018

ADVANCE, Wits RHI

- The site investigator meeting #2 was held from 06 – 08 June 2018. This meeting was a platform to provide training and to discuss implementation aspects of Protocol Amendment #3. Protocol Amendment #3 was implemented effective 20 June 2018.
- Given the recent safety signal on the increased risk of infant NTDs in women on DTG, more evidence is needed urgently on the impact of DTG on folate concentrations in the periconception period. An evaluation of folate concentrations in a sub-cohort of female participants is well placed within the ADVANCE study and will allow us to evaluate whether concerns regarding DTG-associated folate deficiencies are more common, compared to those women receiving EFV-based regimens. Analysis of serum from stored plasma samples of female participants enrolled in the ADVANCE is currently underway with results expected in September, 2018.
- The study informed consent forms (ICF) which were revised to address the safety signal of DTG in pregnancy (neural tube defects) received ethics approval on 11 June 2018. Participants are being reconsented based on the revised ICFs.
- The participant reimbursement rate increase received ethics approval on 29 June 2018. This change was effected as per the recommendation from the South African Health Products Regulatory Authority (SAHPRA).
- The pain and activity sub-study of ADVANCE is a collaboration with the Wits School of Physiology. The study is looking at the effects of HIV stigma on pain and activity over a 1-year period (at three time-points: 0, 6 and 12 months). Participants provide 2 weeks of accelerometry data at each visit. To date the team has recruited 97 of 150 participants, and 48 participants have completed their 6-month follow-up.

Upcoming Events

23-27 Jul: IAS Amsterdam

27 Jul: WHO/Unitaid ART Optimisation Annual Implementers Meeting, Amsterdam

30 Jul: Workstream 1 – Quarterly JPPM Call

31 Jul: Workstream 2 – Quarterly JPPM Call

LOW-DOSE DARUNAVIR (WRH1052), Wits RHI

- A study close-out visit was successfully conducted on 25 June 2018.
- The final study dataset was submitted for statistical review on 29 June 2018.
- The oral abstract "Non-inferior efficacy for darunavir/ritonavir 400/100 mg once daily versus lopinavir/ritonavir for patients with HIV RNA below 50 copies/mL at screening" was accepted for IAS 2018.

DaRiFi (PK study of adjusted doses of darunavir/ritonavir with Rifampicin in HIV-infected volunteers), University of Cape Town

- Enrolment of cohort 1 was successfully completed with 5 participants enrolled.

NANOTECHNOLOGY, University of Liverpool

- Both single and multiple spray-dried dose finding studies have been completed, with analysis of the studies ongoing.
- Juniper started feasibility studies for DRV/r SDN.
- SSAT stage 2 first-in-human study samples due at UoL at end of study.

COMMUNITY ENGAGEMENT, TAC

- 1184 people were trained at TAC branches and within communities.
- *HIV in our Lives* has been distributed to all trainers.

COUNTRY INTRODUCTION AND UPTAKE, ICAP

Global Activities

- Finalised the Country Readiness Assessment. The tool is available on the ICAP/OPTIMIZE website at <https://optimize.icap.columbia.edu/resource/country-readiness-assessment/>
- Updated the implementation considerations document with new information and considerations for introduction of TLD in women of childbearing age.
- Provided remote TA to Swaziland MOH to consider options for rollout of DTG in women of childbearing age in light of new evidence about the potential risk of increased neural tube defects.
- Developed and led an internal ICAP web-based discussion for technical staff on country considerations for use of TLD in women of childbearing age and oriented staff to OPTIMIZE website and new OPTIMIZE resources.
- Reviewed Toxicity Monitoring training module with WHO TDR team and provided materials for pilot HCW training on pharmacovigilance in Botswana.

Kenya

- Product introduction
 - Supported and participated in the urgent development of the national guidance on the use of DTG in women of reproductive age following the release of WHO and other global advisories in May 2018.
 - Supported NASCOP in developing the following materials:
 - Communication packages for healthcare providers and patients on use of DTG in women of reproductive age

- Rapid assessment guide to assess the current status at 24 enhanced monitoring facilities
 - National protocol development to evaluate outcomes including birth outcomes among women of reproductive age on DTG
- Participated in the rapid assessment of use of DTG in women of reproductive age at 24 enhanced monitoring facilities in Kenya.
- Co-facilitated presentation on transition of eligible populations on first-line ART to TLD and strengthening of pharmacovigilance in Nairobi County (County Health Management Team, implementing partners and healthcare providers).
- Enhanced Data System (EDS)
 - Re-submitted the EDS protocol to guide review of data produced through the EDS to KEMRI SERU in response to queries from KEMRI.
 - Finalized revisions of the site assessment toolkit ahead of additional interoperability layer and EDS installation.

Plans for July 2018

ADVANCE, Wits RHI

- Focus on resolution of database queries and cleaning of data in preparation for the interim analysis.
- Prof Venter to present interim data on folate levels within ADVANCE at the 2 July IAS/WHO meeting on “Preconception exposure to dolutegravir: Reviewing the data”.

DaRiFi (PK study of adjusted doses of darunavir/ritonavir with Rifampicin in HIV-infected volunteers), University of Cape Town

- Ongoing study activities with last participant last visit (phase 1) expected on 27 July 2018.

PK study of associations between Darunavir plasma concentrations and virological suppression, lipids and glucose, University of Cape Town and Wits RHI

- Shipment of stored plasma specimens from participants enrolled on the Darunavir arm of the WRHI 052 study.

NANOTECHNOLOGY, University of Liverpool

- Analysis of continued bioanalysis.
- Juniper work continues into stability studies.
- Analysis of SSAT first-in-human study samples.

COMMUNITY ENGAGEMENT, TAC

- 3 TAC trainers and the training coordinator will be attending IAS Amsterdam, including a community meeting post-IAS.

COUNTRY INTRODUCTION AND UPTAKE, ICAP

Global Activities

- Light touch engagement in Cote d'Ivoire and Mozambique in preparation for COP activities to start this month.
- Finalize comprehensive training package for healthcare workers to support transition to TLD with updates to incorporate new evidence and guidance for use of TLD in women of childbearing age.
- Finalize training modules on pregnancy and toxicity monitoring incorporating feedback from WHO TDR pilot training on pharmacovigilance.

Kenya

- Product introduction
 - Finalize the rapid assessment of use of DTG in women of reproductive age at the 24 enhanced monitoring facilities.
 - Continue providing support to NASCOP towards revision of the national ARV guidelines.
 - Finalize the addendum to the situational analysis report in line with the recent advisory on use of DTG in women of reproductive age.
- Enhanced Data System (EDS)
 - Conduct site assessments and upgrade the facility electronic health information systems in preparation for IL and EDS installation.
 - Develop standard operating procedures for data cleaning of unmerged patient records across the EDS systems in preparation for IL and EDS installation.
 - Link the EDS data and dashboards to the national data warehouse.

Staffing Changes

- Welcome to Drs Melissa Tibbatts and Dale Africa who have joined ADVANCE, and will be supporting the Yeoville site.

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/OPTIMIZE Technical Steering Committee/Calendar+Events](https://www.dropbox.com/home/OPTIMIZE%20Technical%20Steering%20Committee/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 Technical Steering Committee/Communications+Branding+Marketing](https://www.dropbox.com/home/OPTIMIZE%20Technical%20Steering%20Committee/Communications+Branding+Marketing)

Talks Given

- 30 Jun 2018: Dr Michelle Moorhouse gave a talk on DTG – focusing on safety. The talk was hosted in Johannesburg as part of a national, academic multidisciplinary meeting sponsored by Mylan and was attended by doctors from around the country.

Resources

- ICAP's Country Readiness Assessment tool <https://optimize.icap.columbia.edu/resource/country-readiness-assessment/>

Media Coverage

- (Will be updated in the next newsletter).

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/>

Future Conferences/Trainings

- 24-27 October 2018: 4th Southern African HIV Clinicians Society Conference, Gallagher Convention Centre, Midrand. www.sahivsoc2018.co.za

Acknowledgements

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