# OPTIMIZE

*This is a monthly update shared with all members involved in Project OPTIMIZE, 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.*

***Please note that some of the information in this update are confidential, so please do not share outside of OPTIMIZE.***

## Major Achievements from November 2016

### *GENERAL*

- The UNITAID Board approved the grant that complements the USAID funded activities, and importantly will fund several PK studies to generate evidence for the use of TAF and DTG in patients on rifampicin. The UNITAID grant also funds a significant mobilisation and uptake effort with health workers and community members through the TAC, Southern African HIV Clinicians Society (SAHCS) and HIV i-Base. In 2017 we will include updates from these additional partners. The important next step is to finalise contracting.
- The Technical Working Group on the 2018 South African ARV Tender had further deliberations in November, including a consultation with clinicians to get broader clinical input into what should be included in the 2018 tender, as well as guideline revisions. The final recommendations will be provided to the Department of Health in December. CHAI and Wits RHI will also hold a briefing with manufacturers, as per the request from the DOH.
- The first PAC for 2016 was held on 9-10 November in Washington, DC. The meeting was very successful, with very engaged participation, and it has made some excellent recommendations that are now being considered by all the members and participants.
- CHAI, St. Stephen's AIDS Trust and Wits RHI participate in a monthly call for updates on the SSAT PK studies. As the results from these studies will inform the design of the PK studies to be conducted in South Africa, this is an important coordination platform.

### Upcoming Events

None

Liverpool and Wits RHI close between Christmas and New Year. Last day in office is 23 December, and first day back is 3 January.

### Important Contacts

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

- As of 30 November, 178 participants have been screened, and 139 have been enrolled in the study.
- Recruitment strategies continue to be reviewed and amended where necessary to improve participant numbers.
- In terms of retention, 115 of 116 participants have completed their first follow-up visit (99%), and 65/67 completed their 2nd follow-up visit (97%).

## *ADVANCE STUDY, Wits RHI*

- Wits RHI finalised the contractual negotiations with ViiV and Gilead, and both agreements were signed in November. Originally we had hoped for drug delivery by 25 November, but at this stage neither have shipped their drugs.
- Version 2 of the protocol has been finalised, and has been submitted to the MCC and Ethics Committee. We hope to get approval for the revised protocol before the year ends, which will allow us to start enrolment in January.

## *MARKET ACCESS AND PRODUCT INTRODUCTION, ICAP*

*Country-level Activities:*

- ICAP finalized the South Africa needs assessment results after discussions with partners about how to frame results in the context of the rapidly changing ARV environment in South Africa.
- USAID DC, ICAP NY, and ICAP Kenya had a call with USAID Kenya to introduce the project to the USAID Mission.
- ICAP Mozambique met with the USAID Mission in Mozambique to introduce the project there.
- ICAP developed a first draft of a Country Operational Plan (COP) introduction to OPTIMIZE, which will be shared with USAID Country Missions to consider inclusion of OPTIMIZE in their next round of COP funding.

*Documents and Tools Development*

- All WS3 partners shared feedback on the Impact Overview document, which ICAP integrated into a final draft.
- ICAP engaged Blue Raster, a web-development firm, to finalize the administrative aspects of the work to develop a website to host ICAP's materials as well as an online country-level impact calculator.
- ICAP initiated the development of a market shaping strategy based on summaries of past market-shaping discussions and conversations at the PAC to develop a single strategy for market shaping interventions among the multiple partners in the consortium to enhance ARV markets both at the global and country levels.

*Collaborations*

- ICAP and Results4Development, who are conducting a landscape analysis on manufacturing and distribution components of ARV optimization, held a call to discuss OPTIMIZE and introduce the various workstreams and partners.
- ICAP virtually attended a CHAI/UNITAID meeting in Geneva to discuss a DTG pilot in Kenya,

Uganda and Nigeria. Since then, ICAP has had follow-up calls with CHAI to learn more about the planned pilot, specifically in Kenya. ICAP may be able to contribute to implementation science research overlaying the DTG pilot.

- CHAI, ICAP, UNITAID, USAID, and WHRI met to discuss the collaboration between OPTIMIZE and Project Optimal in countries where the two projects overlap. ICAP and CHAI will be collaborating on product introduction activities in Kenya and have scheduled follow-up conversations to map out how this joint effort should play out.

*Implementation Science*

- ICAP developed two proposals for implementation science research studies – one on the DTG pilot in Kenya and one using existing WHO tools to monitor pregnancy and birth outcomes in Botswana – which will be presented to OGAC by USAID.

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

UK

- The site initiation visit occurred on 29 September. This visit resulted in a request for several amendments. Protocol v4.0 and PIS/ICF v4.0 was approved by the REC, MHRA, HRA and R&D (R&D approval received on 16 November 2016).
- 2 patients have completed screening. Cohort 1's baseline visit was scheduled for 5 December; 1 subject scheduled.
- 5 screening visits have been booked for 9 January (Cohort 2). An estimated 8 subjects will be included in this cohort.
- As previously indicated, recruitment for this study is challenging – estimated to only enrol 2 participants per month
- Preliminary UK data will be analysed in April 2017 – this analysis will include all data available at the time

Uganda

- Protocol v2.0 and PIS/ICF (v2.0 and PG v1.0) was presented to the site's Scientific Review Committee (SRC). The presentation to SRC was successful. Several items were recommended and are now under internal review:
    - Add a schematic diagram to protocol appendix to summarise the key aspects of the two-step study
    - Tone down the language level in the current version of the consent form (English)
    - Translate the consent to a local language
- A summary of the approval process in Uganda is:
    - Present the submission to the SCR IDI committee
    - Once the IDI committee provides approval, submit to the Ethics Committee (EC) and National Drug Authority (EC process can take 1-3 months as the committee reviews protocols in batches of three, i.e., they wait to receive three protocols before conducting a review)
    - The National Drug Authority will release its approval only after the EC approval (process can take up to 3 months from start of review, in parallel to the EC review)

- Once the EC and NDA have provided approval, it is submitted to the UNCST (this process takes approximately 2 weeks to 1 month. UNSCT will work with the Presidential Office to obtain approval).

### *EFAVIRENZ 400mg PREGNANCY PK STUDY (SSAT063), Mylan (St. Stephen's AIDS Trust)*[1]

UK

- 6 women have been enrolled; three of which have finalised results. Two are due for follow-up in the next 2 weeks, and one is ongoing.
- The first Trial Steering Committee meeting was held on 4 October. The members present during the meeting had no concerns regarding the study and were happy for the study to continue. The 2nd meeting is scheduled once 15 participants have completed week 4 (this included participants from Uganda). A meeting will be held next week with the CI in order to discuss this further and establish a date.
- It is anticipated that the UK site will meet its recruitment target of 7 participants
- In Q1 2017 it is anticipated that preliminary data will be provided on 6/7 participants

### *NANOTECHNOLOGY, University of Liverpool*

- Three different formulations of DRV have been identified during laboratory testing as potentially beneficial. These formulations are either DRV alone, or DRV/r in varying ratios. Now laboratory testing is complete for these formulations, and they can further be developed for use in *in vivo* testing. One of these formulations will be tested *in vivo* in the coming weeks.
- Chemistry has received radiolabelled ATV, allowing UoL to develop new formulations of ATV ready for laboratory analysis using cell lines.

## Major Plans for December 2016

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

- Continue to enrol participants

### *ADVANCE, Wits RHI*

- Receive study drugs from ViiV and Gilead – the ViiV drugs will require additional labelling, as the drugs will be from their non-commercial stock. The Gilead re-labelling is simpler, as we will be receiving commercial stock. Delivery is expected the week of 12 December.
- Plan the Site Initiation Visit with the CRO early in January 2017.

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

*Country-level activities*

- Disseminate findings from South Africa needs assessment with WS3 partners. Initiate planning for Kenya and Mozambique needs assessments

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

- Hold discussions with USG partners to introduce the project in Kenya and Mozambique; initiate introductions of the project to MOHs.
- Introduce the project to ICAP's Swaziland team.
- Finalize the project summary document for product introduction at a country-level; disseminate the document across USAID Missions for COP planning.

*Documents and Tools Development*

- Format final version of the Impact Overview and an accompanying PowerPoint presentation with a graphic designer.
- Meet with web developers to agree on a phased workplan for the development of a dynamic country-level impact calculator for the introduction of optimized ARVs.
- Finalize market shaping strategy document and share with partners for feedback and to initiate a workplan going forward.

*Collaborations*

- Continue regular conversations with CHAI regarding the coordination of product introduction activities in Kenya.
- Further develop ideas for implementation science and/or enhanced monitoring as early adopter research in collaboration with CHAI.

*Implementation Science*

- Based on the outcomes of a meeting between USAID and OGAC, ICAP will further refine the concepts for the Implementation Science studies.

### *NANOTECHNOLOGY, University of Liverpool*

- Planning for ATV formulations to be generated so that *in vitro* analysis of ATV can start in January.
- Planning for remaining 2 DRV *in vivo* experiments to be completed in January. Completion of DRV *in vivo* experiments will allow UoL to potentially further optimise one or more formulations.

## Staffing Changes

- Ellisha (Elle) Maharaj, the Wits RHI Programme Manager, to work alongside Celicia (Deputy Chief of Party for OPTIMIZE) will start on 1 December 2016.
- Vusi Sibeko, the Programme Manager seconded to the TAC, will start on 3 January 2017.
- ICAP is hiring a Product Introduction Coordinator. The link to the job description is here.

## Outputs

*List any articles, manuscripts submitted for review; abstracts submitted; presentations given. (Also provide electronic version of such products for the Dropbox)*

- Francois Venter, 29 November 2016: *ART: Do or Die*, at 14th Prestigious Research Lecture, Wits Medical School (see http://www.timeslive.co.za/thetimes/2016/11/29/New-HIV-drug-a-wonder)

- Francois Venter, 18 November 2016: Open the Right to Care conference, during which he profiled ADVANCE and other studies
- Francois Venter – briefed the Aspen Senior Executive, Stavros Nicolaou, on ADVANCE.