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 October 2016

CONSORTIUM MANAGEMENT & OTHER INITIATIVES

- The first Scientific Advisory Committee call took place on 3 October. The call discussed updated on current clinical studies, as well as ideas for future potential studies
- The Year 2 USAID workplan and budget was finalised following the USAID technical review
- Under the leadership of the National Department of Health, CHAI and Wits RHI collaborated on setting up a Technical Working Group on the 2017 South African ARV Tender. The terms of reference concern primarily considering the clinical and programmatic benefits associated with the introduction of new 1st and 2nd line products; considering timelines for product availability; and present different introduction scenarios in the context of the national tender schedule. This TWG will aim to complete its recommendations in November.
- Wits RHI expects to get feedback from the UNITAID Board decision on its grant application in the first week of November

LOW-DOSE DARUNAVIR STUDY, Wits RHI

- Recruiting for this study is ongoing, though at a slower rate than initially anticipated. However, recruitment is now consistent, and timelines have only been pushed back by 3 weeks.
- First termination of a participant from the study due to DRV

Upcoming Events

1 November: DSMB meeting in Washington, DC. Francois Venter will update on ADVANCE and WRHI052 (low-dose DRV)

3 November: Francois Venter presenting a Boston University, on *HIV: Succeeding at Treatment, Failing at Prevention*

9-10 November: First PAC meeting in Washington, DC

29 November: Francois Venter to profile OPTIMIZE at the Wits University 14th Prestigious Research Lecture, entitled *ART: Do or Die*.

Important Contacts

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liver toxicity.
- 20 of the 108 patients have completed visit 1

ADVANCE STUDY, Wits RHI

- The ADVANCE study was presented to the Wits RHI Community Advisory Board (CAB) meeting
- Wits RHI met with the selected CRO for the ADVANCE study, Triclinium Clinical Development (TCD). Contractual issues will be finalised and signed in early November.
- Wits RHI finalised the contractual negotiations with ViiV and Gilead, and hope to be signing the final contracts for the donation of study drug in the first week of November.
- Version 2 of the protocol has been finalised, and is being submitted to the MCC and Ethics Committee in the first week of November
- The South African Medical Journal (SAMJ) accepted an advocacy paper on ADVANCE. This paper was co-written with people in USAID, UNITAID, the Department of Health, and a variety of clinicians and other collaborators. We are awaiting news on the publication date.

MARKET ACCESS AND PRODUCT INTRODUCTION, ICAP

- ICAP shared preliminary results from the South Africa needs assessment with OPTIMIZE Workstream 3 partners; discussions followed on how to frame results in the context of the rapidly changing ARV environment in South Africa
- The Impact Overview document was disseminated to all Workstream 3 partners who shared comprehensive feedback, which ICAP is currently integrating into a final draft.
- CHAI, ICAP, and CII discussed past work on modeling the impact (cost and health outcomes) of optimized ARVs at a country-level, including an overview of CHAI's Guidelines Costing Tool. ICAP initiated the development of a web-based Country-Level Impact Overview tool to simulate potential impact of various ARV introduction scenarios.
- USAID CII and GHSC-PSM organized a call with ICAP to discuss potential interventions as identified in the landscape analysis, variation in procedures for revising national treatment guidelines, and demand forecasts.
- Workstream #3 held a bi-monthly workstream call on which the plan for introducing the project to USAID Missions, findings from a multi-month prescribing survey, and registration processes were discussed.
- ICAP held a conference call to introduce project OPTIMIZE to the ICAP Mozambique country team, including the Country Director and Technical Director.
- Materials were developed to introduce the project and Workstream 3 scope to USAID Missions.
- In an effort to disseminate key findings from the landscape analysis more broadly, ICAP initiated a synthesis of the landscape analysis as part of the preparation for the PAC meeting.
- ICAP and CII determined a way forward for developing a market shaping strategy, which includes both global and country-level activities and engages all partners.
- ICAP engaged with R4D, funded by Gates, to schedule a call to discuss each organization's work on mapping the ARV landscape.

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

UK

- The Site Initiation Visit (SIV) occurred on 29 September. During the SIV, errors pertaining to the protocol were identified, including whether the EFV dose to be ingested at the baseline visit was to be witnessed by the research team or not. During the meeting, it was determined that a protocol amendment would be required. This amendment has been submitted to the UK authorities and is pending approval. The latest possible approval date is 21 November.
- The site has been given the green light to commence recruitment. Screening of the first group of participants will commence 7 November
- During the SIV, Dr Boffito mentioned that recruitment will be challenging – the aim is to recruit at a rate of 2 participants per month
- Anticipated preliminary data will be available by April 2017 (recruitment dependent)

Uganda

- The study was presented to the site's Scientific Review Committee (SRC). The presentation to SRC was successful
- The SRC requested a few edits to the protocol, and to tone down language in the consent form
- SSAT plans to submit to the IRB in 3 weeks

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

UK

- 6 women have been enrolled, three of which have finalised results
- The 1st Trial Steering Committee meeting was held on 4 October. The viral loads and EFV levels for 5 participants during the first 4 weeks were reviewed. Members present during the meeting had no concerns regarding the study and were happy for the study to continue.
- It is anticipated that the UK will meet their recruitment target of 7 participants
- Preliminary data anticipated for 6/7 women by Q1 2017

Uganda

- The site was given the green light to screen on 3 October
- The site screened their first patient on 13 October; 5 patients have now been screened

NANOTECHNOLOGY, University of Liverpool

- Continuous cell lines grown and maintained
- A number of DRV formulations have been through in vitro processing
- Leading formulations will be taken through in vivo testing in rats shortly
- ATV formulations have been generated and are awaiting radiolabelling ready for in vitro processing

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

- DTG formulations are being generated in Chemistry

Major Plans for November 2016

LOW-DOSE DARUNAVIR STUDY, Wits RHI

- Continue to enrol participants

ADVANCE, Wits RHI

- As per above, finalise contracts with ViiV, Gilead, the CRO, as well as Bliss Pharmaceuticals (for the ADVANCE drugs) in early November
- 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
- Finalise recruitment for ADVANCE study staff now that the start date is more imminent

MARKET ACCESS AND PRODUCT INTRODUCTION, ICAP

- Introduce the project to the USAID Missions in Kenya and Mozambique.
- Complete compilation of findings from the South Africa Country Needs Assessment and share more broadly.
- Finalize the Impact Overview, including visuals and graphics, and develop an accompanying PowerPoint presentation.
- Refine and finalize the ARV optimization country introduction note and package of ARV optimization materials to share with ICAP country teams.
- Continue to synthesize Landscape Analysis into shorter publication and appropriate fora (journals and/or advocacy meetings)
- Refine approach to market-shaping strategy development, and continue to summarize information to date.

NANOTECHNOLOGY, University of Liverpool

- Generate in vivo rat results for DRV formulations
- Generate in vitro results for ATV formulations

Staffing Changes

- Ellisha Maharaj, the Wits RHI Programme Manager, to work alongside Celicia (Deputy Chief of Party for OPTIMIZE) will start on 1 December 2016.
- Deepa Rajamani started as the Market Access Coordinator at ICAP on October 10th. Welcome, Deepa!
- 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, 6 October 2016: *Challenges to Test and Treat, and ART Optimization*, at Annual Workshop on Advanced Clinical Care – HIV (AWACC), Durban, South Africa