

Report of the 4th South African HIV Drug Resistance and Treatment Monitoring Workshop

REPORT/SUMMARY OF WORKSHOP:

The 4th South African HIV Drug Resistance and Treatment Monitoring Workshop took place at the Faculty of Medicine at the University of the Free State, Bloemfontein. In total 134 participants from over 60 institutes/hospitals/NGOs attended the event. The great majority of the participants were medical doctors (MDs), who are involved in the treatment of HIV patients with antiretroviral (ARV) therapy in Southern Africa.

The two-day workshop program included international and local experts on HIV ARV treatment. The workshop was opened by Prof. Gert van Zyl, Dean, Faculty of Health Sciences, University of the Free State. Prof. van Zyl delivered a very instructive presentation based on a series of six recent manuscripts in *Lancet* that summarize the state of Health in South Africa. This was followed by the first keynote presentation by Prof. Amilcar Tanuri (URFJ, Brazil) who presented an overview of the interactions between ARV drugs and HIV proteins. Prof. Tanuri also explained how drug resistance appears by the accumulation of mutations (resistance mutations), which alter binding properties of ARV drugs to HIV proteins.

His talk was followed by Prof. Wendy Stevens (Wits, South Africa), who gave an instructive talk on the cost of HIV drug resistance genotyping in the private and public sector in South Africa. Prof. Stevens demonstrated by modelling that it is cost effective to include HIV drug resistance genotyping as part of ARV treatment in South Africa. HIV drug resistance genotyping helped the clinician to avoid changing first line ARV regimen to a more expensive second line ARV regimen (which includes a boosted protease inhibitor such as LPV/r).

Dr. Chris Seebregts (MRC, South Africa) presented the Free State Initiative on Resistance, Surveillance and Treatment (FIRST). This project is funded by the European Union and supports the development of a centre of excellence in Bloemfontein, where specialized clinicians manage HIV ARV treatment failure cases with the aid of HIV drug resistance genotyping technology. His presentation was followed by a tea break.

The second section was focused on the clinical use and technical aspects of HIV drug resistance genotyping technique. Three hypothetical clinical cases were presented and discussed with the audience by Dr. Richard Lessells (Africa Centre, South Africa). This was followed by Dr. Tulio de Oliveira's (Africa Centre, South Africa) presentation on a pilot implementation of the RegaDB HIV drug resistance database in South Africa. RegaDB is used to collate and analyze drug resistance mutations in local HIV genotypes produced by a network of researchers, the South African Treatment Research Network (SATuRN). This section was finalized with a presentation by Dr. Bertus Cruywagen on the TruGene resistance genotyping system.

The third section, which started after lunch, was based on the discussion and presentation of strategies for affordable HIV resistance testing for the public sector in South Africa. Dr. Dominique Goedhals (UFS/NHLS, South Africa) presented the genotypic results of the FIRST

project in Bloemfontein. This was followed by a presentation from Mr. Glenn Malherbe (UP, South Africa) on the development of a low cost screening assay (OLA) at Pretoria University. This section was finalized with a half-an-hour panel discussion led by Prof. Wendy Stevens on developing low cost assays for HIV genotyping in Africa. The panel was composed of the presenters, Dr. Visva Pillay (Roche, South Africa) and Dr. Carole Wallis (WITS, South Africa).

The last section of the first day was chaired by Prof. Amilcar Tanuri and was focused on the presentation of two clinical cases of HIV drug resistance and on the methodology used to interpret it. Dr. Cloete van Vuuren (one of the main workshop's organizer from the UFS, South Africa) presented a very interesting case of ARV treatment management where a patient has been in treatment for 10 years with cardiovascular complications. That was followed by Dr. Theresa Rossouw's (Pretoria Univ, South Africa) presentation of a second case of a South African patient on ARV treatment for over 20 years. This section, and the first workshop day, was finalized by Dr. Michele Gordon (UKZN, South Africa), who presented a number of resistance algorithms developed by the Stanford HIV Drug resistance database.

The second day of the workshop was focused on clinical cases and programmatic approaches for the expansion of successful HIV ARV treatment in Africa. It was opened by Prof. Mollentze (Head of the Department of Internal Medicine of the Medical School UFS, South Africa), who gave an interesting presentation on the importance of good governance. The first keynote speaker of the second day was Prof. Jeff Klausner (Chief of the ARV treatment branch of the PEPFAR/CDC program in South Africa). Prof. Klausner presented the impact of the PEPFAR/CDC program in South Africa as well as the plans for the next few years, which will contribute in 2009 alone, 500 million dollars (around 4.5 billion rands) to the ARV treatment in South Africa. The Department of Health are funding the treatment programme with additional support from CDC/PEPFAR and other donors with somewhere around 800,000 patients on ARV treatment in South Africa.

Prof. Amilcar Tanuri, the second keynote speaker of this section, presented on HIV ARV drug resistance in non-B subtypes. Prof. Tanuri gave a convincing presentation showing that non-B subtypes (which are found in the majority of developing nations) are as susceptible to ARVs as B subtypes, which are found in the USA and Europe and were used for ARVs validation. Moreover, published results from Prof. Tanuri's laboratory have shown that subtype C (which is present in southern Brazil and dominates the Southern African HIV/AIDS epidemic) accumulates drug resistance mutations slower than subtype B.

The last keynote speaker from this section was Prof. Ian Sanne (WITS, South Africa). Prof. Sanne delivered an exciting and lively presentation on the use of Therapy Edge™, a biomedical informatics system that is used in the Johannesburg area to manage patients on ARV therapy in the public and private sector. Prof. Sanne also presented studies conducted in pooled treatment data which showed that this medical informatics system delivers better care to patients on ARVs.

The second section of the day was focused on case presentations. In this section a panel of experts was formed by Dr. Ashraf Grimwood (ARK, National AIDS Council, South Africa), Dr. Willi Sieling (private physician, South Africa), Dr. Diana Dickenson (private physician, Botswana), and Dr. Theresa Rossouw (UP, South Africa). The panel was chaired by Prof. Amilcar Tanuri and clinical cases were presented by Dr. Cloete van Vuuren and Dr. Gert van Zyl (NHLS Tygerberg and Stellenbosh, South Africa). Two adult treatment cases were

presented and discussed and followed by three pediatric cases. The case discussion sessions attracted intense interest and debate between participants, presenters and panel members.

The following session presented after lunch was also very lively and interactive. This session, the seventh in the workshop, was focused on Southern African country experiences on the scale up of ARV treatment. The first presenter was Dr. Diana Dickinson (private physician, Botswana) who received applause several times from the participants during her presentation on the success of the expansion of the Botswana HIV ARV program. Dr. Dickinson showed that life expectancy has already reversed the decrease trend in the recent past and that most of the HIV infected patients in Botswana were alive and well after 8 years of the start of their treatment program. Her presentation was followed by Dr. Richard Lessells (Africa Centre, South Africa) who showed the expansion of the ARV treatment in rural KwaZulu-Natal and the challenges faced in this process.

The last session presented was chaired by Dr. Dewald Steyn (UFS and main organizer of the workshop, South Africa). In this section, a clinical case of multiple ARV's resistance in a South Africa patient was presented by Dr. Theresa Rossouw (UP, South Africa). This case was debated by the expert panel and participants of the workshop. The workshop was closed by Dr. Cloete van Vuuren and Dr. Tulio de Oliveira. All sponsors, presenters, representative of the DoH and participants were acknowledged in the closing remarks.

The 4th South African HIV Drug Resistance and Treatment Monitoring Workshop was funded by the European Union (EU), the Centre for Disease Control (CDC), the President's Emergency Plan for AIDS Relief (PEPFAR), the South African Medical Research Council (MRC), Merck (MSD, Pty) and the International Development Research Centre (IDRC). The workshop was organized as a network of academic institutions in South Africa, including the Free State Initiative on Resistance, Surveillance, and Treatment (FIRST) Study, Faculty of Medicine at the University of the Free State (UFS), The University of the Western Cape (UWC), the South African National Bioinformatics Institute (SANBI), the Africa Centre for Health and Population Studies, University of KwaZulu-Natal and the South African Medical Research Council (MRC).

The program of the workshop, presentation handouts (6 slides per page in PDF format) and this report of the workshop are available at the bioafrica.net website (<http://www.bioafrica.net/workshops/4thresitanceworkshop.html>).

Workshop Presenters.

Prof Gert van Zyl (Dean Faculty of Health Sciences, University of the Free State).

Prof. Amilcar Tanuri (URFJ/Columbia, Brazil/USA)

Prof. Wendy Stevens (Wits, South Africa)

Dr. Chris Seebregts (MRC, South Africa)

Dr. Richard Lessells (Africa Centre, South Africa)

Dr. Tulio de Oliveira (Africa Centre, South Africa)

Dr. Bertus Cruywagen (TruGene, Siemens)

Dr. Dominique Goedhals (UFS/NHLS, South Africa)

Mr. Glenn Malherbe (UP, South Africa)

Dr. Visva Pillay (Roche, South Africa)

Dr. Carole Wallis (WITS, South Africa)
Dr. Cloete van Vuuren (UFS, South Africa)
Dr. Theresa Rossouw (Pretoria Univ, South Africa)
Dr. Michele Gordon (UKZN, South Africa)
Prof. Mollentze (Head of Department of Internal Medicine of the Medical School UFS, South Africa)
Prof. Jeff Klausner (Chief of the ARV treatment branch of the PEPFAR/CDC program in South Africa)
Prof. Ian Sanne (WITS, South Africa)
Dr. Ashraf Grimwood (ARK, National AIDS Council, South Africa)
Dr. Willi Sieling (Private physician, South Africa)
Dr. Diana Dickenson (Private physician, Botswana)
Dr Gert van Zyl (Stellenboh, South Africa)
Dr. Dewald Steyn (UFS, South Africa).

Workshop Organizers Team:

Dr. Cloete van Vuuren (University of the Free State, South Africa)
Dr. Tulio de Oliveira (Africa Centre for Health and Population Studies, UKZN, South Africa)
Dr. Chris Seebregts (MRC, South Africa)
Dr. Dominique Goedhals (University of the Free State/NHLS, South Africa)
Dr. Dewald Steyn (University of the Free State, South Africa)
Mrs. Anthea van Blerk (MRC, South Africa)
Mrs. Janet Geyer (MRC, South Africa)
Mrs. Tamlin Peterson (University of the Western Cape, South Africa)