



**In this Issue**



# CAPRISA

CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

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## Impact of rifampicin and efavirenz on moxifloxacin concentrations in TB patients

Our feature story this month focuses on the study that provides insight on the possible reasons for sub-optimal TB treatment outcomes among patients administered a moxifloxacin containing TB treatment regimen and ART.

On page 2 we highlight an ethics symposium co-hosted by CAPRISA on the inclusion of adolescents and pregnant women in HIV prevention research. The inaugural meeting of the WHO STAC held in Geneva and visit of Kenneth Cole, UNAIDS International Goodwill Ambassador is provided on page 3.

On page 4, we pay tribute to our great friend and struggle icon, Ahmed Kathrada. We report on the visit of DAIDS new bureau chief, the publication of the CAPRISA book on Clinical Trials and we congratulate Dr Lyle Mckinnon on his award for excellence in research on page 5.

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**A** study conducted by the HIV-TB Treatment Research Programme was recently published in the *Journal of Antimicrobial Chemotherapy*. The study sheds new light on reasons for sub-optimal TB treatment outcomes among patients administered a moxifloxacin containing TB treatment regimen and ART.

The study conducted within the CAPRISA 011 Improving Retreatment Success Clinical (IMPRESS) trial, compared the pharmacokinetics of moxifloxacin during co-treatment with rifampicin or when dosed alone in patients with drug susceptible, recurrent tuberculosis (TB), the majority of whom were HIV co-infected and on efavirenz-based ART.

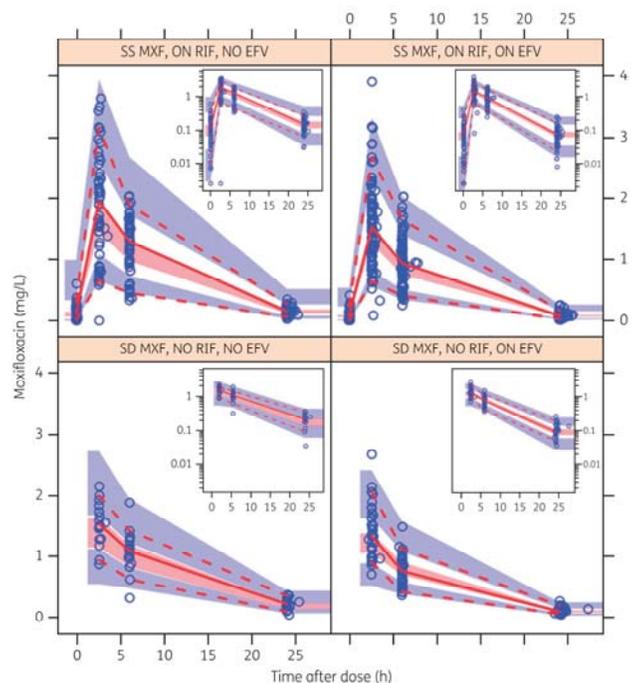
Fifty-eight patients were included in the study; 42(72.4%) were HIV co-infected and 40 (95%) on an efavirenz-based ART. Moxifloxacin clearance was high and plasma concentrations low in patients overall. Clearance of moxifloxacin during rifampicin-based TB treatment was 7.8% lower than when a single dose of moxifloxacin was given alone after TB treatment completion. Among the HIV co-infected patients taking efavirenz-based ART, clearance of moxifloxacin was increased by 42.4% resulting in a further 30% reduction in blood concentration of moxifloxacin (Figure).

The significant drug interaction found between moxifloxacin and efavirenz-based ART in HIV co-infected patients has not been previously described. Although this finding needs validation in other studies, it remains concerning, given the high HIV-TB co-

infection rates in many TB endemic settings where the ART backbone remains efavirenz.

These findings have direct implications for studies evaluating novel drug regimens containing moxifloxacin and for current national and international guidelines that advocate moxifloxacin use in non-standard treatment regimens for both drug-susceptible and drug resistant TB.

For more information see: Naidoo A, et al. Effect of rifampicin and efavirenz on moxifloxacin concentrations when co-administered in patients with drug-susceptible TB. *Journal of Antimicrobial Chemotherapy* 2017 February. doi: 10.1093/jac/dkx004.



**Figure.** Visual predictive check (VPC) stratified by co-administration with rifampicin and/or efavirenz. The dashed and solid lines are the 5th percentile, median and 95th percentile of the observed concentrations, while the shaded regions represent the corresponding 95% CIs for the same percentiles.



## CAPRISA/NIH/SARETI/UKZN Ethics Symposium: Inclusion of adolescents and pregnant women in HIV prevention research

On the 16<sup>th</sup> of March CAPRISA co-hosted an ethics symposium on the inclusion of adolescents and pregnant women in HIV prevention research in partnership with the National Institutes of Health (NIH) and the South African Research Ethics Training Initiative (SARETI) and the University of KwaZulu-Natal. The workshop was co-chaired by Professors Quarraisha Abdool Karim, Doug Wassenaar and Daya Moodley.

Professor Abdool Karim started the day by painting a detailed picture of the HIV epidemic in sub-Saharan Africa, highlighting the vulnerability of adolescent girls, young women and pregnant women and the urgent need for all these groups of women to be included in HIV prevention research. She underscored that adolescent girls and young women can be pregnant or not and the ethics of delays in access to products need to be considered.

The morning session was devoted to adolescents and the first presenter was Dr Christine Grady who discussed the ethics of inclusion of adolescents in research from an international perspective stressing that exclusion from research can be harmful, she furthermore advocated for a need to justify exclusion rather than motivate for inclusion. An additional important point she highlighted was the need to balance protectionism with reducing vulnerability. The revised Council for International Organisations of Medical Sciences (CIOMS) guidelines in fact ask for a justification if adolescents are excluded from research.

Local perspectives on the ethical and legal considerations of adolescent inclusion in research were provided by Cathy Slack and Ann Strode. They highlighted the possible tensions between the intricacies of the South African legal system and ethical considerations. They also indicated the possible conflicts between parental consent and adolescent privacy.

The afternoon sessions were chaired by Professor Daya Moodley. The challenges of including or excluding pregnant women in research and balancing the vulnerability of pregnant women vs minimising risk to the unborn foetus. Professor Joseph Millum challenged the notion of pregnant women as vulnerable populations in the traditional sense and stressed the fact that 'sick women get pregnant and pregnant women get sick' and in both cases there needs to be safe, efficacious treatment made available. However, the exclusion of pregnant women in research had less to do with the mother and everything to do with potential harm to the foetus.

Lively discussions followed, highlighting the relevance of this conversation and reminding panellists that although they are rarely included in clinical research trials, adolescents and pregnant women receive treatments that, for the most part, have not been tested specifically for them. The discussions also underscored the other factors that impact decisions to exclude this population including regulatory authorities; pharmaceutical companies reducing risk of litigation; package insert labelling.



*Presenters and delegates at the workshop. Front Row seated (L-R) – Viren Rambiritch, Ann Strode, Joe Millum, Daya Moodley, Doug Wassenaar, Christine Grady, Reidar Lie, Quarraisha Abdool Karim, second row (L-R): Catherine Slack, Mariana Kruger, Hilton Humphries, Gugulethu Mzobe, Palesa Xulu, Nivedhna Singh, Wendy Mkhize, Neetha Morar, Zaynar Essack, Gethwana Mahlase, Back row (L-R): Ayesha Kharsany, Nicola Barsdorf, Wendy Mphatswe, Eliza Govender, Nonzwakazi Ntombela, Samukelisiwe Chiliza, Thobile Mthembu, Heidi Matisonn, Tshidi Sebitloane*



## WHO STAC meets to address HIV and viral hepatitis agenda

The first meeting of the newly constituted WHO Strategic and Technical Advisory Committee on HIV and Viral Hepatitis (STAC) was held in Geneva on 13<sup>th</sup> March. Co-chaired by Professor Salim Abdool Karim Director CAPRISA, and Professor Margaret Hellard, Head of the Centre for Population Health and Head of Hepatitis Services Infectious Diseases Unit, Burnet Institute in Melbourne, Australia, STAC brings together a diverse group of experts to formulate recommendations on how best to support countries to achieve HIV and hepatitis targets.



The committee developed comprehensive recommendations aimed to guide work in HIV and

hepatitis over the next few years. Its Report will be tabled with the Director-General of the WHO.

## UNAIDS international goodwill ambassador visits CAPRISA



UNAIDS International Goodwill Ambassador Mr Kenneth Cole met with CAPRISA scientists to gain a deeper understanding of HIV and TB prevention and control in South Africa and globally, during his visit to Durban South Africa, on 7<sup>th</sup>- 8<sup>th</sup> March. At a special dinner to mark the occasion, he met with Dr Sibongiseni Dhlomo MEC for Health in Kwa-Zulu-Natal and Ms Frances Chisholm US Consul General Durban. On 8<sup>th</sup> April Mr Cole paid a visit to the King DinuZulu Hospital, the largest TB referral hospital in the province and a CAPRISA XDR-TB research study site. Mr Cole has been vocal about the global response to AIDS for more than 30 years and is a champion for people living with HIV. Mr Cole has been chairman of amfAR, the American Foundation for AIDS Research, since 2005.

Professors Salim and Quarraisha Abdool Karim hosted a dinner at their residence. Front Row (L-R): Prof Quarraisha Abdool Karim, Dr Bonginkosi Mafuze, Prof Koleka Mlisana, Catie Cole. Second Row (L-R): Mr Kenneth Cole, Dr Nesri Padayatchi, Dr Sibongiseni Dhlomo, Jennifer Moore. Back Row (L-R): Prof Salim Abdool Karim, Ms Francis Chisholm and Dr Alasdair Reid of UNAIDS.



## In memory of Ahmed Kathrada

South Africa's anti-apartheid stalwart, Ahmed Kathrada, passed away on 28th March following a short illness. He was 87 years old. His courage, humility, fortitude and principled actions will always be remembered said Quarraisha Abdool Karim, Associate Scientific Director CAPRISA.

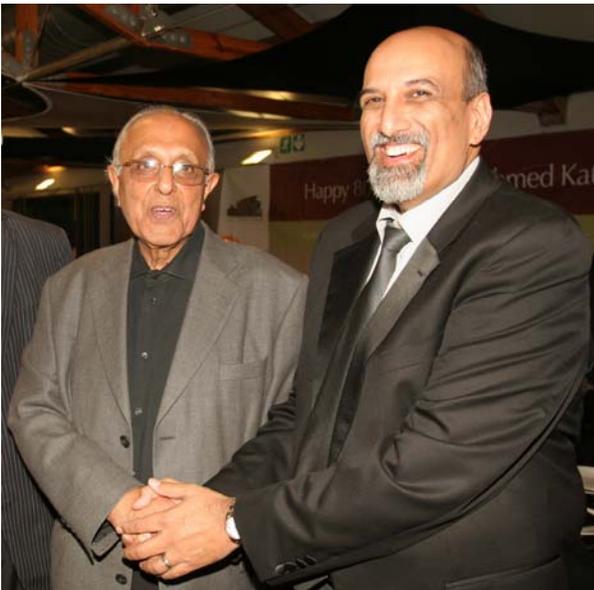
For over seven decades Ahmed Kathrada dedicated his life to a free and just South Africa. He played a central role in South Africa's democratic dispensation at great personal sacrifice. Together with Nelson Mandela he was incarcerated and imprisoned for 26 years for his fight against the apartheid system in South Africa. While in prison he pursued his studies and obtained four university degrees.

Kathrada was an inspiration to the youth of South Africa urging them to contribute to the country and society. Through the Kathrada Foundation he promoted youth leadership, and development, human rights and the ideals enshrined in South Africa's democratic Constitution. The fight against HIV and AIDS was close to his heart and on 31st October 2014, UKZN and CAPRISA hosted a lecture delivered by Ahmed Kathrada at the Nelson R Mandela School of Medicine where he addressed medical students, scientists and academics.

In his lecture he urged the youth to embrace the many opportunities of education and skills development and to

contribute to society. Professor Abdool Karim said, "Uncle Kathy, as he was fondly known to us in CAPRISA, was a leader among leaders – a man of great integrity with profound humility and dedication to the poor and downtrodden. He showed South Africans what compassion and love for fellow countrymen, regardless of race, was about. He saw the good in everyone and he brought out the best in all of us. He always put others first. His departure at this troubled time in our country when so many of our leaders are self-serving and bereft of morality, leaves us poorer as a nation. Kathy was vocal on the need to ensure leaders served the nation, first by being true to their oath to uphold the country's constitution. As an exemplary leader himself, he had given his entire life to serving humanity, never once expecting anything in return. His was a life of selflessness and greatness – he will be sadly missed by us all."

Below are some photos from his visit to CAPRISA in 2014



## NIH-funded STREAM study underway

The STREAM Study (CAPRISA 087) led by Co-PIs Dr Nigel Garrett from CAPRISA and Dr Paul Drain from the University of Washington started at the end of February, and has so far enrolled 41 participants with a target of 390 participants. STREAM (Simplified Treatment and Management of HIV) is a randomized controlled trial assessing the effect of point-of-care (POC) viral load (VL) monitoring on treatment outcomes for patients on antiretroviral therapy. The participants will be recruited from the Prince Cyril Zulu Communicable Diseases Clinic and randomized to

receive laboratory-based VL monitoring or POC VL monitoring using the Xpert HIV-1 VL assay. This assay runs on the GeneXpert platform that is commonly used for TB diagnosis and, more recently, has been introduced for STI diagnosis at CAPRISA. Results are available 2 hours after blood draw, meaning patients can receive results and management on the same day. The primary outcome of the study is retention in care and virological suppression after 12 months in the study. STREAM is funded by the NIH.



## DAIDS Pharmaceutical Branch Chief impressed with CAPRISA Pharmacy operations

**D**r Ruth Ebiasah Chief, Pharmaceutical Affairs Branch and Dr Bijal Patel Protocol pharmacist, from the Pharmacy Affairs Branch (PAB), Office of Clinical Site Oversight (OCSO), Division of AIDS (DAIDS), US National Institutes of Health recently visited the CAPRISA Clinical Trials Unit. Dr Ebiasah who was recently appointed branch chief was introduced to the site pharmacists, explained Dr Tanuja Gengiah head of Pharmacy, and together with Dr Patel visited the research pharmacies at the CAPRISA eThekweni and Umlazi clinics. The visit began at the CAPRISA headquarters where the PAB team met with Dr Tanuja Gengiah, Prof Salim Abdool Karim (CTU, Co PI), Dr Nesri Padayatchi (eThekweni CRS leader) and Ms Natasha Samsunder, laboratory Director. Dr Ebiasah thanked each of the pharmacy teams at the sites and said that they “were very impressed with the organization and level of engagement of the site leadership and staff, as well as with many aspects of the clinic and



(L-R) Dr Tanuja Gengiah, Dr Nesri Padayatchi, Dr Ruth Ebiasah, Prof Salim Abdool Karim, Dr Bijal Patel and Ms Natasha Samsunder

pharmacy operations.” She reiterated her support and looked forward to continuing to work with the CAPRISA pharmacy team on the “very important protocols being conducted as part of DAIDS clinical trial networks.”

## Excellence in research award

**C**APRISA Research associate Dr Lyle McKinnon has been awarded the prestigious 2017 CAHR-CANFAR Excellence in Research Award in the Basic Sciences track for his ‘dedication to the field of HIV research’. The award will be made at the 26<sup>th</sup> Annual Canadian Conference on HIV/AIDS

Research during the first week in April, in Montreal. An immunologist with a specific interest in mucosal immune systems Dr McKinnon’s main research focuses on correlates of HIV acquisition in high-risk populations including young women in sub-Saharan Africa.



Dr Lyle McKinnon

## Book provides valuable insights on clinical trials

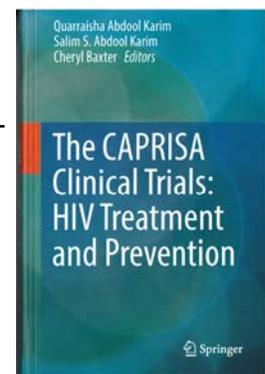
**T**he *CAPRISA Clinical Trials: HIV Treatment and Prevention* was recently published. The book is intended as a resource for undergraduate and postgraduate students, health care providers, doctors, decision-makers and researchers who are seeking guidance and insights on clinical trials – their creation, conduct and impact.

Since its inception 14 years ago, CAPRISA has conducted numerous clinical studies that have influenced international TB-HIV treatment guidelines as well as HIV prevention through innovations in the microbicide and vaccine fields. This book provides a historical account of how each of CAPRISA’s high impact studies was created, developed, implemented, analysed and communicated. In doing so, the reader is taken on a journey that provides glimpses into the genesis of research ideas and how this ultimately leads to a range of HIV prevention and treatment studies that have impacted the global response

to the HIV and TB epidemics.

The five sections in the book deal with the : HIV epidemic in South Africa; CAPRISA’s clinical trials on HIV and HSV-2 prevention; CAPRISA’s research on the treatment of HIV and TB co-infection; a review of the major scientific findings from the CAPRISA studies on acute infection and genital mucosal immunology, and essential support activities for the conduct of clinical trials. *The CAPRISA Clinical Trials: HIV Treatment and Prevention* edited by Quarraisha Abdool Karim, Salim Abdool Karim and Cheryl Baxter is published by Springer.

The book is available from: <http://www.springer.com/gp/book/9783319475172>





# Scientific papers published in 2017

- 15\* **Abdool Karim SS.** Assessing progress with HIV incidence in national cohorts. *Lancet HIV* 2017 Feb;4(2):e56-e58. doi: 10.1016/S2352-3018(16)30187-4.
- 16 **Ramsuran V,** Hernandez-Sanchez PG, O'HUigin C, Sharma G, Spence N, Augusto DG, Gao X, Garcia-Sepulveda CA, Kaur G, Mehra NK, Carrington M. Sequence and Phylogenetic Analysis of the Untranslated Promoter Regions for HLA Class I Genes. *Journal of Immunology* 2017 2017 March; 198 (6):2320-2329.
- 17 **Moore PL,** Gorman J, Doria-Rose NA, **Morris L.** Ontogeny-based immunogens for the induction of V2-directed HIV broadly neutralizing antibodies. *Immunological Reviews* 2017 January; 275(1):217-229.
- 18 Haffejee F, Naicker T, Singh M, **Kharsany AB,** Adhikari M, Singh R, Maharaj N, Moodley J. Placental leptin mRNA expression and serum leptin levels in pre-eclampsia associated with HIV infection. *J Obstet Gynaecology* 2017 January;37(1):48-52.
- 19 Gregson J, Kaleebu P, Marconi VC, van Vuuren C, Ndembi N, Hamers RL, Kanki P, Hoffmann CJ, Lockman S, Pillay D, **de Oliveira T,** Clumeck N, Hunt G, Kerschberger B, Shafer RW, Yang C, Raizes E, Kantor R, Gupta RK. Occult HIV-1 drug resistance to thymidine analogues following failure of first-line tenofovir combined with a cytosine analogue and nevirapine or efavirenz in Sub-Saharan Africa: a retrospective multi-centre cohort study. *Lancet Infectious Diseases* 2017 March; 17(3):296-304
- 20 **Singh JA, Abdool Karim SS.** Trump's "global gag rule": implications for human rights and global health. *The Lancet Global Health* 2017 April; 5(4): e387–e389.
- 21 **Naidoo A,** Chirehwa M, McIlleron H, **Naidoo K,** Essack S, **Yende-Zuma N,** Kimba-Phongi E, Adamson J, Govender K, **Padayatchi N,** Denti P. Effect of rifampicin and efavirenz on moxifloxacin concentrations when co-administered in patients with drug-susceptible TB. *Journal of Antimicrobial Chemotherapy* 2017 February. doi: 10.1093/jac/dkx004.

\*continuation from previous newsletter

## Scientific Reviews

Abstracts submitted for review		Manuscripts submitted for review		Ancillary studies submitted for review	
Total#	Cumulative^	Total#	Cumulative^	Total#	Cumulative^
1	383	0	212	1	75

# for month, ^ since committee initiation

**12<sup>TH</sup> INTERNATIONAL WORKSHOP ON**

# HIV TRANSMISSION

**PRINCIPLES OF INTERVENTION**

**PARIS, FRANCE • 21-22 JULY 2017**



Don't miss the opportunity to attend the 12<sup>th</sup> International Workshop of HIV Transmission, which is scheduled to take place on July 21 and 22, 2017 in Paris, France, prior to IAS 2017. Should you wish to attend, please contact Cheryl Baxter [cheryl.baxter@caprisa.org](mailto:cheryl.baxter@caprisa.org)



CAPRISA hosts a DST-NRF Centre of Excellence in HIV Prevention



UNAIDS  
Collaborating Centre for HIV Research and Policy

CAPRISA is the UNAIDS Collaborating Centre for HIV Research and Policy



CAPRISA hosts a MRC HIV-TB Pathogenesis and Treatment Research Unit

Partner institutions:

