



CAPRISA

CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

Newsletter

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No improvement in the treatment of recurrent TB using Moxifloxacin

In this Issue

Our feature story this month focuses on a trial, published in the *Journal of Clinical Infectious Diseases*, which shows no improvement of recurrent TB in patients treated with moxifloxacin.

On page 2 we report on the NIH-funded manuscript writing workshop, CAPRISA FLAIR fellow's visit to the Royal Society in the UK and on the presentations of bNabs by Penny Moore and colleagues at the SA Immunology conference.

We congratulate Ken Bridbord as the first recipient of the inaugural HPTN Leadership award on page 3

On page 4 we feature highlights of CAPRISA's participation at the 9th SA AIDS conference.

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An open label randomised controlled study showed that replacement of ethambutol with moxifloxacin for treatment of recurrent TB did not improve culture conversion rates at the end of 8 weeks or treatment success compared with the standard regimen.

The results of the trial (CAPRISA 011), published in the *Journal of Clinical Infectious Diseases* showed that moxifloxacin was associated with a shorter time to culture conversion but a higher incidence of adverse events.

This trial demonstrated that high levels of treatment success are achievable with the current first-line anti-tuberculosis regimen and highlighted the potential role of a fluoroquinolone-containing regimen to improve time to culture conversion and possibly reduce overall treatment duration.

The researchers conducted a randomised controlled trial to compare a fluoroquinolone-containing anti-TB treatment regimen (where ethambutol was substituted for moxifloxacin), with the current standard

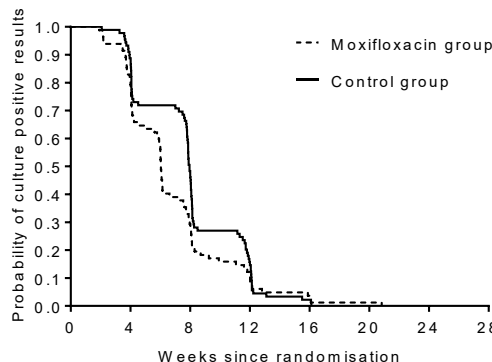
first-line regimen. A total of 96 participants; 70% male, and 70% co-infected with HIV, were enrolled.

The study found no significant difference in 8-week culture conversion rates, [83.0% (Moxifloxacin arm) vs 78.5% (Control arm), $p=0.463$].

The median time to culture conversion was significantly shorter in the moxifloxacin group compared to the control group (6.0 vs 7.9 weeks, $p=0.018$).

Favourable end-of-treatment outcomes were reported in 87.8% (86/98) of participants in the moxifloxacin group and in 94.9% of participants (93/98) in the control group. Furthermore, the researchers found significantly higher rates of grade 3 and 4 adverse events [43.9% (43/98) vs 25.5% (25/98), $p=0.011$] and serious adverse events [27.6% (27/98) vs 12.2% (12/98), $p=0.012$] in the moxifloxacin group.

Recurrent TB remains a challenge in low- and middle-income countries where up to a third of patients present with previously treated TB.



For further reading:

Perumal P, Padayatchi N, et al. A moxifloxacin-based regimen for the treatment of recurrent drug-sensitive pulmonary tuberculosis: An open-label randomised controlled trial. *Clinical Infectious Diseases*. 2019. doi: 10.1093/cid/ciz152. [Epub ahead of print]. <https://www.ncbi.nlm.nih.gov/pubmed/?term=30809633>

Figure 1. Kaplan–Meier estimates of time to culture conversion among participants with a favourable outcome. Wilcoxon test p -value = 0.005

	culture conversions/ at risk							
Moxifloxacin	0/86	16/66	58/24	73/9	79/3	81/1	82/0	82/0
Control	0/93	10/79	46/43	75/14	87/2	89/0	89/0	89/0



Capacity building in Vulindlela through NIH manuscript writing workshop



Several staff and research fellows from the CAPRISA Vulindlela Clinic attended a NIH-funded manuscript writing course at Calderwood Lodge on the 27 June. The workshop, which was facilitated by CAPRISA's Research Associate Dr Cheryl Baxter, is part of the NIH-funded CAPRISA Research Administration and Management Training Program. To date, eight

grant administration / grant writing workshops have been held.

"We are hoping to expand the number of young investigators applying for research grants but to do this they need to show a track record in publishing their research. We hope the manuscript writing workshops will demystify the publication process and encourage young students and investigators to publish their research." said Baxter.

The participants will receive ongoing mentorship to support them through the process of writing up their research.

The workshop was very beneficial said Pharmacist, Michele Upfold. "Cheryl Baxter's knowledge in grant writing was impressive and knowing that we have support for future publications is encouraging and makes the process much less daunting."

Meeting of the Minds for FLAIR Fellow

CAPRISA mucosal immunology scientist and FLAIR Fellow, Dr Lenine Liebenberg, attended a three-day programme of training and networking held at the Royal Society and the Academy of Medical Sciences in London where she met with UK based research collaborators.

The programme is part of her FLAIR (Future Leaders - African Independent Researchers) fellowship and is facilitated by the Royal Society and the African Academy of Sciences.

The workshops focused on scientific communication and media reporting, the benefits and pitfalls of mentorship, and

successful grant management. Liebenberg attended the prestigious annual Meeting of the Minds, where she interacted with over 200 Royal Society Research Fellows.

A highlight of her visit was her discussion with HRH The Duke of York, over tea at St James's Palace, on the genital immune response associated with unprotected sex. In his closing remarks the Duke urged the Royal Society Research Fellows in attendance "to communicate their research to younger generations and encourage excitement in scientific research."

Lenine Liebenberg at the lectern at which many revered scientists have spoken.



Broadly neutralising antibodies in the spotlight

The National Institute for Communicable Diseases (NICD) HIV Virology Section was strongly represented at the annual meeting of the South African Immunology Society, held in Durban from 18-20 June. Prof Penny Moore (in photo), CAPRISA Senior Honorary Scientist, presented a comparison of broadly neutralizing antibodies in HIV infected adults and children, highlighting the exceptional bNABs that develop in many slow-progressing children.

Dr Cathrine Scheepers showed how isotype switching in antibodies represents an alternative to conventional affinity maturation in countering HIV viral escape, with implications for adjuvants in vaccine regimens. Dr

Charissa Mynhardt described the isolation and characterisation of HIV-1 V2-directed vaccine-elicited antibodies.

Lastly, Vincent Hlatshwayo, a PhD student supervised by Moore and Scheepers, described his work using next generation antibody sequencing to define the development of bNABs in CAPRISA donor CAP248. Vincent was awarded second prize for the best oral presentation.





HPTN honours Ken Bridbord's distinguished leadership in global health



The photo above was from a dinner graciously and generously hosted by Peter and Nicha Kilmarx at their home in Bethesda in honour of Ken Bridbord being the recipient of the inaugural HPTN Leadership Award earlier that day and James Hakim from the University of Zimbabwe School of Medicine recognised as the fourth recipient of the Ward Cates Spirit award. Both awards were made at the HPTN Annual Meeting in Washington DC in June 2019. Photo: Back row from L-R): Sten Vermund, Catherine Hankins, Peter Kilmarx, James Hakim, Tim Mastro, Roger Glass; (front row from L-R): Ken Mayer, Maureen Goodenow, Quarraisha Abdool Karim, Ken Bridbord, Maryanne Lachat, Flora Katz, and Kevin DeCock.

Inset: Quarraisha Abdool Karim presents the inaugural HPTN Leadership award to Ken Bridbord (L) with Kevin DeCock on her right at the HPTN Annual meeting on 4 June. In her citation Abdool Karim said that Bridbord is widely recognised for his contributions to disease prevention and global health. Highlights in his career that spanned nearly five decades in the US government included enhancing the global and country level responses to HIV/AIDS, said Abdool Karim.

Empowering young girl learners on scientific careers

CAPRISA hosted 21 enthusiastic young girl learners and 3 teachers from rural schools on 30th May to gain insight into a scientific research organisation as part of the annual Cell C Take a Girl Child to Work initiative.

Hosted by CAPRISA's HR department, the learners had an informative tour of the eThekweni Research Clinic. At the CAPRISA headquarters associate Scientific Director, Professor Quarraisha Abdool Karim gave the learners an overview of CAPRISA and the HIV prevalence amongst young females.

Dr Nonhlanhla Yende-Zuma, Head of Statistics and Data Management led a robust discussion on women in the workshop together with Ms Khosi Mdladla, Research Assistant at CAPRISA Vulindlela Research Clinic and Dr Nolwazi Mncwabe, Research Clinician at eThekweni Research Clinic who shared their personal experiences in the workplace.



A highlight for the learners was the interaction with two 2018 Take a Girl Child alumni who are currently 1st year medical students, on life at varsity. The learners left CAPRISA with their attendance certificates equipped with new knowledge on STEM careers in medical research.



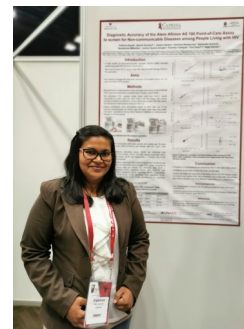
'No time for Complacency' resonates at the 9th SA AIDS conference

In the opening plenary session on 11th June titled, Where are we: Statistics, Successes, Failures and Challenges, Professor Salim Abdool Karim, CAPRISA's Director reminded over 3 000 delegates at the 9th SA AIDS conference that globally there are 5 000 new HIV infections each day in his presentation entitled: *No Time for Complacency*. On 12th June Abdool Karim participated in the Bhekisisa Health Journalism forum on the effect of blessers and blessed on HIV transmission.

CAPRISA's Senior Scientist, Professor Ayesha Kharsany, co-chaired track one: Clinical Science and Biomedical Innovation: Technologies and Responses. She contextualised the status of the HIV epidemic in her presentation: *Putting HIV into Context*. Professor Kogie Naidoo, Head of HIV-TB treatment, participated in the ASSAf panel discussion "The Nexus between Science Policy and Society in the HIV AIDS perspective".

CAPRISA colleagues, Mr Lindani Msimango, DST-NRF Research Fellow, presented the results of his qualitative study on acceptability of point-of-care HIV viral load testing as part of the STREAM trial, and Dr Nigel Garrett, Head of Vaccines and Pathogenesis presented the results of the STREAM study and Study Co-ordinator, Ms Fathima Sayed, presented her poster on point-of-care testing for non-communicable diseases amongst people living with HIV in Durban, South Africa.

In her presentation, Study Co-ordinator, Nonzwakazi Ntombela described the *Progress of UNAIDS 90-90-90 targets among pregnant women in rural KwaZulu-Natal, South Africa*. Research Clinician, Dr Rochelle Adams, showed in her poster presentation the *Strengthening of Advanced Clinical Care of Complicated HIV and HIV-TB through Case-based Learning Workshops* and Ms Thandeka Nkosi presented a poster on, *A Rapid Screening tool to assess HIV risk in pregnant women utilising PHC clinics in the public sector in KwaZulu-Natal, South Africa: Potential for targeted PrEP provision to pregnant women*



Photos: from the top (First row) (L-R): Salim Abdool Karim; Conference Chair Refilwe Nancy Phaswana; Minister of Health Zweli Mkhize & Ayesha Kharsany; (Second row) Rochelle Adams and Fathima Sayed with their posters and Nonzwakazi Ntombela; (Third row): Jienchi Dorward, Lindani Msimango, Fathima Sayed & Nigel Garrett and Kogie Naidoo with ASSAf's Tebogo Mabotha, Keymanthri Moodley & Stanley Maphosa; (Fourth row): Bhekisisa's Health Journalism Forum: Salim Abdool Karim Director, (CAPRISA); Natsayi Chimbindi, Post-doctoral Senior Researcher, (AHRI); Helen Rees, Executive Director, Wits Reproductive Health and HIV Institute (Wits RHI); Mia Malan, Executive Director and editor-in-chief, Bhekisisa Centre for Health Journalism; Yogan Pillay, Deputy Director-General, South African National Department of Health; Lerato Mofokeng, Deputy Chairperson, South African National Aids Council's (SANAC) civil society youth sector; Mandisa Dlamini, Founder and Director, The Gugu Dlamini Foundation.



Scientific papers published in 2019

35* **Naidoo A**, Chirehwa M, **Ramsuran V**, McIllleran H, **Naidoo K**, **Yende-Zuma N**, Singh R, **Ncgapu S**, Adamson J, Govender K, Denti P, **Padayatchi N**. Effects of genetic variability on rifampicin and isoniazid pharmacokinetics in South African patients with recurrent tuberculosis. *Pharmacogenomics* 2019; 20(4):225-240.

36 van Diepen MT, Chapman R, Douglass N, Galant S, **Moore PL**, Margolin E, Margolin E, Ximba P, **Morris L**, Rybicki EP, Williamson AL. Prime-boost immunizations with DNA, Modified Vaccinia Virus Ankara, and protein-based vaccines elicit robust HIV-1 Tier 2 neutralizing antibodies against the CAP256 superinfecting virus. *Journal of Virology* 2019; 93(8):e02155-18.

37 **Loveday M**, Reuter A, Furin J, Seddon JA, Cox H. The STREAM trial: missed opportunities and lessons for future clinical trials. *Lancet Infectious Diseases* 2019; 19(4):351-353.

38 **Dabee S**, Barnabas SL, Lennard KS, **Jaumdally SZ**, Gamielien H, Balle C, **Happel AU**, Murugan BD, Williamson AL, Mkhize N, Dietrich J, Lewis DA, Chiodi F, Hope TJ, Shattock R, Gray G, Bekker LG, Jaspan HB, **Passmore JS**. Defining characteristics of genital health in South African adolescent girls and young women at high risk for HIV infection. *PLoS One* 2019; 14(4):e0213975.

39 O'Brien SP, Swanstrom AE, Pegu A, Ko SY, Immonen TT, Del Prete GQ, Fennessey CM, Gorman J, Foulds KE, Schmidt SD, Doria-Rose N, **Williamson C**, Hatzioannou T, Bieniasz PD, Li H, Shaw GM, Mascola JR, Koup RA, Kwong PD, Lifson JD, Roederer M, Keele BF. Rational design and in vivo selection of SHIVs encoding transmitted/founder subtype C HIV-1 envelopes. *PLoS Pathogens* 2019; 15(4):e1007632.

40 Frank DJ, Horne DJ, Dutta NK, Shaku MT, Madensein R, Hawn TR, Steyn AJC, Karakousis PC, **Kana BD**, Meintjes G, Laughon B, Tanvir Z. Remembering the Host in Tuberculosis Drug Development. *Journal of Infectious Diseases* 2019; 219(10):1518-1524.

41 Mvelase NR, Pillay M, Sibanda W, Ngozo JN, Brust JCM, **Mlisana KP**. rpoB Mutations Causing Discordant Rifampicin Susceptibility in Mycobacterium tuberculosis: Retrospective Analysis of Prevalence, Phenotypic, Genotypic, and Treatment Outcomes. *Open Forum Infect Dis* 2019 ; 6(4):ofz065.

42 **Chimukangara B**, **Lessells RJ**, Rhee S-Y, Giandhari J, **Kharsany ABM**, **Naidoo K**, **Lewis L**, Cawood C, Khanyile D, Ayalew KA, Diallo K, Samuel R, Hunt G, Vandormael A, Stray-Pedersen B, Gordon M, Makadzange T, Kiepiela P, Ramjee G, Ledwaba J, Kalimashe M, **Morris L**, Parikh UM, Mellors JW, Shafer RW, Katzenstein D, Moodley P, Gupta RK, Pillay D, **Abdool Karim SS**, **de Oliveira T**. Trends in pretreatment HIV-1 drug resistance in antiretroviral therapy-naive adults in South Africa, 2000–2016: a pooled sequence analysis. *EClinicalMedicine* 2019; 9:26-34.

43 **Perumal P**, **Padayatchi N**, **Yende-Zuma N**, **Naidoo A**, **Govender D**, **Naidoo K**. A moxifloxacin-based regimen for the treatment of recurrent drug-sensitive pulmonary tuberculosis: An open-label randomised controlled trial. *Clinical Infectious Diseases* 2019; pii: ciz152. <https://doi.org/10.1093/cid/ciz152> [Epub ahead of print].

*continuation from previous newsletter

CAPRISA Achievement Awards



Research Pharmacists at the CAPRISA Vulindlela Research clinic, Sherishka Dhindoyal (L) and Michele Upfold (R), received the CAPRISA Achievement awards in recognition of the high standards of pharmacy practice at the Vulindlela Pharmacy that received praise from the South African Pharmacy Council.

Head of Pharmacy, Dr Tanuja Gengiah (centre) presented the awards to Dhindoyal and Upfold. Congratulations!



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



CAPRISA is the UNAIDS Collaborating Centre for HIV Research and Policy



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



CAPRISA hosts a DoH-MRC Special Initiative for HIV Prevention Technology

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