



CAPRISA

CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

Newsletter

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Study shows low rifampicin levels in critically ill TB patients in ICU

In this Issue

On page 1 we feature the results from a CAPRISA randomised sequential pharmacokinetic study, published in the *International Journal of Infectious Diseases*.

On page 2 we report on the launch of the Eastern and Southern Africa Commission on Drugs (ESACD); and on Dr Sharana Mahomed's invitation to the 2023 National Academy of Medicine's Emerging Leaders Forum in the US.

CAPRISA's participation at CROI in Seattle features on page 3, as well as our community engagement with students to raise awareness on STI's.

On page 4 we report on our international visitors from Gilead Sciences & the Institute of Human Virology (IHV), in Nigeria & on the University of KwaZulu Natal's recognition of eminent alumni.

CONTACT DETAILS

CAPRISA
Doris Duke Medical
Research Institute (DDMRI)
2nd Floor
University of KwaZulu-Natal
Private Bag X7, Congella 4013
South Africa

T: +27-31-260 4555
F: +27-31-260 4566

E-mail: caprisa@caprisa.org

www.caprisa.org.za



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The study on *The impact of enteral feeding and therapeutic monitoring of Rifampicin with dose escalation in critically ill patients with tuberculosis*, demonstrated low rifampicin concentrations in most of the critically ill patients receiving standard treatment, irrespective of feeding status at the time of drug administration.

Results from a randomised sequential pharmacokinetic study, led by CAPRISA researchers to determine the frequency of low plasma concentrations of rifampicin in critically ill patients with TB, the effect of feeding on drug exposure, and the effect of dose-escalation (TDM) on pharmacokinetic target attainment, was published in the *International Journal of Infectious Diseases*.

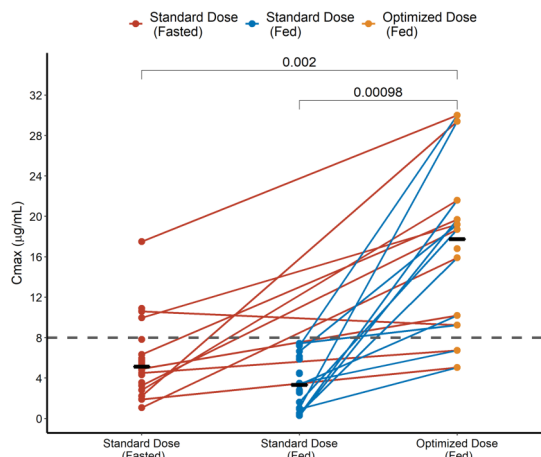
TB drug concentrations are frequently below the recommended therapeutic concentrations in critically ill patients with active TB. The study involved two intensive sessions of pharmacokinetic sampling on consecutive days in adult patients on drug-susceptible TB treatment.

Among 20 critically ill patients (40% HIV-infected), median rifampicin C_{max} (maximum serum concentration) in the fasted and fed states were 5.1 $\mu\text{g}/\text{mL}$ versus 3.3 $\mu\text{g}/\text{mL}$, respectively [$p < 0.0001$; geometric-mean-ratio (GMR) 1.95; 90% CI 1.46-2.60].

The proportion of patients with low rifampicin concentrations in the fasted and fed states was 80% versus 100% ($p=0.1336$). Optimized dosing led to a per-patient median rifampicin dosing of 24.6 mg/kg, and median C_{max} increase from 2.4 $\mu\text{g}/\text{mL}$ to 17.8 $\mu\text{g}/\text{mL}$ ($p=0.0005$; GMR 8.29; 90%CI 3.88-17.74).

TDM-guided dose-escalation increased the proportion of patients achieving the suggested target rifampicin concentration compared to standard dosing (83% versus 0%, $p=0.004$).

The researchers concluded a higher starting dose and the use of TDM may significantly improve the pharmacokinetic - pharmacodynamic profiles and treatment outcomes in critically ill patients.



For further reading see: Perumal R, et al. *Int J Infect Dis.* 2023. doi: 10.1016/j.ijid.2022.11.033. <https://pubmed.ncbi.nlm.nih.gov/36462574/>

Figure: Comparison of maximum rifampicin concentrations on standard dosing (fed and fasted) and optimised dosing. Standard dosing in the fed state (blue), standard dosing in the fasted state (red), optimised dosing (orange). Dashed horizontal line represents the minimum concentration threshold: 8 $\mu\text{g}/\text{mL}$. Solid horizontal lines represent median values.



Launch of the Eastern and Southern Africa Commission on Drugs (ESACD)

Professor Quarraisha Abdool Karim joined former South African president Kgalema Motlanthe, ex-Mozambican president Joaquim Chissano, former New Zealand prime minister Helen Clark, and Michel Sidibe, a former executive director of UNAIDS, at the launch of the Eastern and Southern Africa Commission on Drugs (ESACD) held in Cape Town from 10 - 11 February, to facilitate cooperation and coordination among the member states in drug trafficking and abuse in the region.



Photo: At the press briefing: (from left) Former South African president Kgalema Motlanthe, Former Mozambican president Joaquim Chissano, Professor Quarraisha Abdool Karim, Former New Zealand prime minister Helen Clark, and Dr Michel Sidibe, a former executive director of UNAIDS, at the launch of the Eastern and Southern Africa Commission on Drugs in Cape Town.

The ESACD was established in 2012 to address the serious and multifaceted drug problem facing parts of Eastern and Southern Africa. The four current commissioners, Kgalema Motlanthe, Joaquim Chissano of Mozambique, Cassam Uteem of Mauritius and Quarraisha Abdool Karim aim to provide evidence-based high level and authoritative recommendations for drug policy reform and engage in high level strategic outreach and advocacy.

The commission has identified four priority areas for its work: strengthening drug law enforcement and interdiction efforts, improving drug treatment and rehabilitation services, enhancing regional cooperation and information sharing, and mainstreaming drug control into national policies and strategies. Listen to the media briefing here: <https://bit.ly/3ksCOxP>

Sharana Mahomed invited to US National Academy of Medicine Emerging Leaders Forum in Washington, DC

Dr Sharana Mahomed, CAPRISA Research clinician and principal investigator will participate in the 2023 National Academy of Medicine (NAM) Emerging Leaders Forum. It is an invitation-only event to connect emerging science leaders with NAM members from various fields of medicine.

The Forum is a key gathering of the Emerging Leaders in Health and Medicine Program (ELHM), 'which aims to increase the NAM's engagement with exceptional, interdisciplinary early- to mid-career professionals working in biomedical science, population health, health care, health policy, and related fields.



The ELHM Forum provides a platform to identify novel approaches to shared challenges in health and medicine and spark transformative change across fields.' "I am honoured to attend this forum that creates collaborative opportunities for emerging science leaders. African scientists are crucial for Africa's advancement. However, the challenges faced such as lack of equipment and infrastructure remain barriers to success," said Mahomed. "This Forum is an opportunity to share these challenges and to be a role model in promoting young African women in science." The National Academy of Medicine (NAM) is one of three academies that make up the National Academies of Sciences, Engineering, and Medicine in the United States.



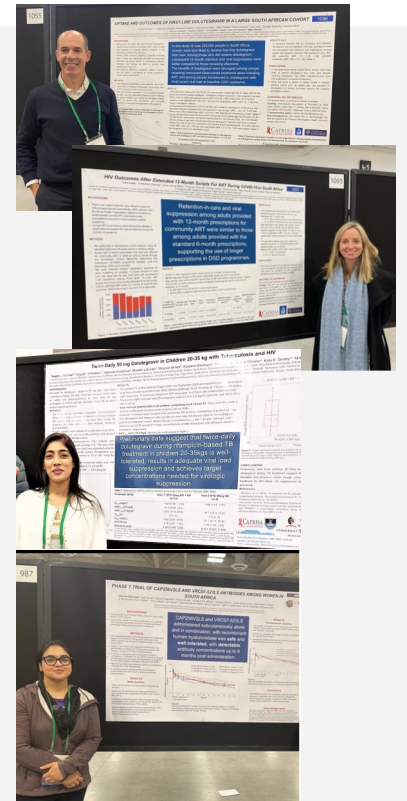
'CROI is back on track' – CAPRISA Researchers present at the CROI conference in Seattle

CAPRISA's Prof Nigel Garrett, Dr Sharana Mahomed, Dr Anushka Naidoo and Ms Lara Lewis attended and presented at the 30th Conference on Retroviruses and Opportunistic Infections (CROI) from 19-22 February in Seattle, Washington. "CROI is back" was the catch phrase of the conference as it was the first in-person CROI since the start of the COVID-19 pandemic. The in-person conference featured innovative interactive sessions, informative poster sessions, and networking opportunities. The CAPRISA team collectively presented seven posters.

Garrett, who is Head of Vaccines and Pathogenesis research, shared findings from the SHERPA and Ubuntu studies, assessing the safety of mRNA COVID-19 booster vaccinations in South Africa. He also presented an analysis by Dr Jienchi Dorward, Honorary Associate Scientist and the SHAPE team on the roll-out of Dolutegravir and its impact on clinical outcomes in KwaZulu-Natal.

Ms Lara Lewis, Senior Statistician presented results from an analysis of community ART usage patterns and the impact of extending ART prescriptions in community ART programmes from 6 to 12 months.

Dr Sharana Mahomed, Research Clinician and Principal Investigator shared findings from the CAPRISA 012B study which demonstrated that both VRC07-523LS and PGT121 administered subcutaneously individually and in combination at high doses were safe and well tolerated. Dr Anushka Naidoo Research Fellow & Principal Investigator shared findings on a study on Dolutegravir in Children coinfecting with HIV and TB.



Photos (top—bottom) Presenting at CROI : Prof Nigel Garrett, Ms Lara Lewis, Dr Anushka Naidoo & Dr Sharana Mahomed
Photo (left): (L-R) Prof Nigel Garrett, Dr Anthony Fauci, Dr Sharana Mahomed & Ms Lara Lewis at CROI



Highlights from the conference included a presentation of the results from the Doxy-PEP studies for STI prevention, research being undertaken for HIV cure and an opening plenary by Dr Anthony Fauci chronicling the 30 years of CROI.

Patrick Mdletshe addresses students on HIV & STIs



Patrick Mdletshe, CAPRISA Head of Community Programmes emphasized the importance of using condoms and having one sexual partner for HIV prevention and protection against STIs.

He addressed students at the Durban University of Technology (DUT) on 22 February at an event aimed at raising awareness about safe sex practices among students and members of the community and to break down the stigma of STIs. Addressing students Mdletshe said "taking control of your sexual health is essential in preventing STIs and HIV."



University of KwaZulu-Natal's Medical School Wall of Fame



Photo left: Top Row—Prof Salim Abdool Karim fourth from the left. Second row: Prof Quarraisha Abdool Karim second from the left

Professors Salim and Quarraisha Abdool Karim have been recognised by the University of KwaZulu-Natal for their leadership, innovation and science to feature on a designated “Medical School Legends Wall of Fame.”

“Alumni and other individuals who have contributed tremendously to the University and the health space through their humanitarian work, innovation, science, leadership, research contribution, outreach projects, and contribution to the Department of Health and Government do not get acknowledged,” said Prof Ncoza Dlova, Dean of UKZN’s School of Clinical Medicine.

“I felt it is about time that we put them on a pedestal for all to see and additionally get the youth and junior alumni to be inspired by their contribution and hopefully this will rub off and create great mentorship and role modelling,” she said.

Collaboration with international partners

In February, CAPRISA hosted delegates from Gilead Sciences in the US and the Institute of Human Virology (IHV) Nigeria aimed at exploring potential collaboration opportunities in the future and establishing research collaborations. Dr James Rooney, Vice President of Medical Affairs, Gilead Sciences, met with Professor Salim Abdool Karim and senior scientists during his visit on 1 February to gain insights into CAPRISA’s current research.

Dr Evaezi Okpokoro, from IHVN has been the project director for the CAPRISA 094 TRiAD study in Nigeria since 2020. He was hosted by Prof Kogie Naidoo CAPRISA’s Deputy Director and the TRiAD study Principal Investigator as well as other CAPRISA TRiAD team members.

Nigeria has enrolled over 100 participants in the study, making it the top study recruiting site. Okpokoro expressed an interest in further research collaborations and joint projects.



Photo (L-R): Dr James Rooney, Vice President Medical Affairs, Gilead Sciences with Prof Salim Abdool Karim at CAPRISA’s headquarters



Photo bottom (L-R) Ms Resha Boodhram, Study Co-ordinator; Dr Letitia Shunmugam, Postdoc Research Fellow; Dr Evaezi Okpokoro, Project Director for the TRiAD study in Nigeria; Prof Kogie Naidoo, TRiAD National Lead Investigator for the TRiAD study; Mrs Natasha Samsunder, Director Laboratories and Mr Khodani Ramakulukusha, Data Manager.

Project director for the TRiAD study in Nigeria, meets with CAPRISA’s Deputy Director and National PI of TRiAD and CAPRISA TRiAD team.



A selection of scientific papers published in 2023

- 1 **Perumal R, Naidoo K, Naidoo A**, Letsoalo MP, Esmail A, Joubert I, Denti P, Wiesner L, **Padayatchi N**, Maartens G, Dheda K. The impact of enteral feeding and therapeutic monitoring of rifampicin *with dose-escalation in critically ill patients with tuberculosis*. *International Journal of Infectious Diseases* 2023;126:174-180. doi: 10.1016/j.ijid.2022.11.033.
- 2 Collins C, Isbell MT, **Abdool Karim Q**, Sohn AH, Beyrer C, Maleche A. Leveraging the HIV response to strengthen pandemic preparedness. *PLoS Global Public Health* 2023; 3(1): e0001511. doi: 10.1371/journal.pgph.0001511
- 3 Lazarus JV, **Abdool Karim SS**, Batista C, Rabin K, El-Mohandes A. Vaccine inequity and hesitancy persist—we must tackle both. *BMJ* 2023; 380:8. doi: 10.1136/bmj.p8.
- 4 Nevrekar N, Butler K, Shapiro DE, Atuhaire P, Taha TE, Makanani B, Chinula L, Owor M, **Moodley D**, et.al. Self-Reported Antiretroviral Adherence: Association with Maternal Viral Load Suppression in Postpartum Women Living with HIV-1 from Promoting Maternal and Infant Survival Everywhere (PROMISE), a Randomized Controlled Trial in Sub-Saharan Africa and India. *JAIDS* 2023; 92(1):76-83. doi: 10.1097/QAI.0000000000003102.
- 5 **Perumal R**, Nimmo C, O'Donnell M. Regimens for Drug-Resistant Tuberculosis. *New England Journal of Medicine* 2023; 388(2):189. doi: 10.1056/NEJMc2213970.
- 6 **Naidoo K**, Montgomery ET, Katz AW, Morgan G, Krishnaveni R, Lydia ST, Sarita N, **Mansoor L**. Efficacy and Action of the Dapivirine Vaginal Ring as Understood by Women Participating in an Open Label Extension Study. *AIDS and Behavior* 2023; 27(1):75-81. doi: 10.1007/s10461-022-03745-y.
- 7 Morar NS, **Mansoor LE, Naidoo K**, Katz AW, Garcia M, Duma C, **Precious Myeni NB**, Tshabalala T, Naidoo S, Montgomery ET. Male partner opinions of the dapivirine vaginal ring used during an open-label extension HIV prevention trial in KwaZulu-Natal, South Africa. *JAIDS* 2023; 92(2):127-133. doi: 10.1097/QAI.0000000000003119.
- 8 Pooley N, **Abdool Karim SS**, Combadière B, Ooi EE, Harris RC, El Guerche Seblain C, Kisomi M, Shaikh N. Durability of Vaccine-Induced and Natural Immunity Against COVID-19: A Narrative Review. *Infectious Diseases and Therapy* 2023; 12(2):367-387. doi: 10.1007/s40121-022-00753-2.
- 9 Bhiman JN, Richardson SI, Lambson BE, Kgagudi P, Mzindle N, Kaldine H, Crowther C, Gray G, Bekker LG; Novavax trial clinical lead author group; Shinde V, Bennett C, Glenn GM, Madhi SA, **Moore PL**. Novavax NVX-COV2373 triggers neutralization of Omicron sub-lineages. *Scientific Reports* 2023;13(1):1222. doi: 10.1038/s41598-023-27698-x.
- 10 Shvartsman E, Perciani CT, Richmond MEI, Russell JNH, Tough RH, Vancuren SJ, Hill JE, Kavi-Icr, Jaoko W, **McKinnon LR**, et.al. Gardnerella subgroup dominant microbiomes are associated with divergent cervicovaginal immune responses in a longitudinal cohort of Kenyan women. *Frontiers in Immunology* 2023;13:974195. doi: 10.3389/fimmu.2022.974195.
- 11 Voutouri C, Hardin CC, **Naranbhai V**, Nikmaneshi MR, Khandekar MJ, Gainor JF, Stylianopoulos T, Munn LL, Jain RK. Mechanistic model for booster doses effectiveness in healthy, cancer, and immunosuppressed patients infected with SARS-CoV-2. *PNAS* 2023; 120(3):e221132120. doi: 10.1073/pnas.221132120.

For the complete list of publications see here: <http://bit.ly/3IRvjZd>



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