CAPRISA
CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

Newsletter

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Pharmacokinetics and safety of dolutegravir in children receiving rifampicin tuberculosis treatment in South Africa

Children with HIV are at higher risk of acquiring tuberculosis and tend to experience more rapid disease progression and severity compared with children without HIV. Data on the safety and pharmacokinetics of the first line WHO recommended antiretroviral drug dolutegravir in children with HIV and tuberculosis is scarce. The CAPRISA 258 ORCHID study aimed to determine the safety and pharmacokinetics of dolutegravir 50 mg twice daily in children receiving rifampicin, and to use innovative pharmacokinetic modelling and simulations to predict exposures for once daily dolutegravir with rifampicin.

The findings of the ORCHID trial provide empiric pharmacokinetic, safety, and efficacy data for dolutegravir 50 mg film-coated tablet in children (aged <18 years) weighing 20–35 kg (where no pharmacokinetic data currently exist), demonstrating that dolutegravir dosed twice daily in this group achieves high levels of virological suppression, target drug exposures in plasma (similar to or higher than those seen in adults), and is well tolerated.

ORCHID also provides the first estimates based on population pharmacokinetic modelling to suggest that once-daily dolutegravir dosing in children with tuberculosis mirrors exposures seen in a similar population of adults in the RADIANT-TB trial and should be investigated further in clinical studies as an alternative option in children.

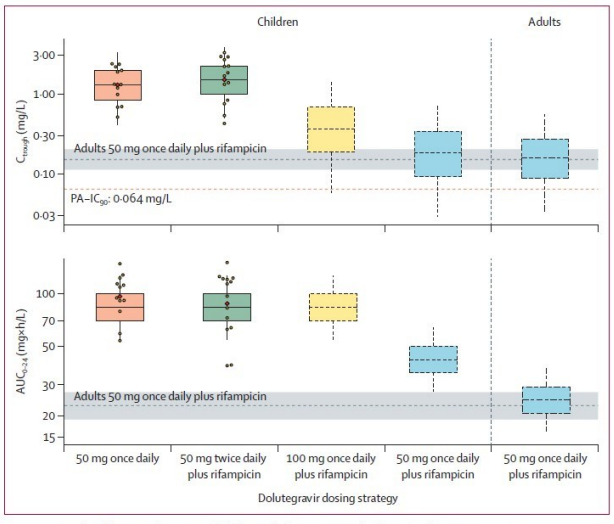

Figure 1: Simulated C_{trough} and AUC_{0-24} of different dolutegravir and rifampicin dosing strategies

In conclusion, the ORCHID study provides additional supportive evidence for the international and local guidelines recommending twice daily dolutegravir dosing in children with HIV-associated tuberculosis on rifampicin and modelling data that suggest once-daily dosing in children is adequate.

For further reading see: Naidoo A, Waalewijn H, Naidoo K, *et al*. Pharmacokinetics and safety of dolutegravir in children receiving rifampicin tuberculosis treatment in South Africa (ORCHID): A prospective cohort study. *Lancet HIV*. 2025 Apr 1;12(4):e273–82. *https://doi.org/10.1016/s2352-3018(24)00312-6*

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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
@CAPRISAOfficial
@caprisaofficial

“We can do excellent science in Africa and, for the benefit of all.” - Professor Quarraisha Abdool Karim, FRS

CAPRISA Associate Scientific Director Professor Quarraisha Abdool Karim, FRS joins the ranks of Stephen Hawking, Isaac Newton, Charles Darwin and Albert Einstein, following her election to the Fellowship of the Royal Society. Formed in 1660, the Royal Society is a fellowship of the world's most eminent scientists. Abdool Karim joins 6 other South Africans who have previously received this honour – Wits Vice-Chancellor and physicist Professor Zeblon Vilakazi, tuberculosis researcher Professor Valerie Mizrahi, epidemiologist Professor Salim Abdool Karim, chemist Professor Tebello Nyokong, physicist Professor Bernie Fanaroff and theoretical physicist Professor George Ellis.

Prof. Quarraisha Abdool Karim has played a leading role in shaping the global HIV prevention field, especially in developing prevention technologies for adolescent girls and young women. Her landmark research has demonstrated that antiretrovirals can prevent the sexual transmission of HIV, providing proof of concept for pre-exposure prophylaxis (PrEP). Speaking to the link between her 40-year research career and social justice, Abdool Karim said, “Who bears the greatest burden of AIDS? It is the poorest of the poor where we face a multiplicity of challenges. The burden of infectious diseases and social inequality go hand-in-hand.”

Effectiveness and Safety of Tenofovir Gel, an Antiretroviral Microbicide, for the Prevention of HIV Infection in Women

Quarraisha Abdool Karim,[1,2]*† Salim S. Abdool Karim,[1,2,3]* Janet A. Frohlich,[1] Anneke C. Grobler,[1] Cheryl Baxter,[1] Leila E. Mansoor,[1] Ayesha B. M. Kharsany,[1] Sengeziwe Sibeko,[1] Koleka P. Mlisana,[1] Zaheen Omar,[1] Tanuja N. Gengiah,[1] Silvia Maarsch[1] Lynn Morris,[4] Douglas Taylor,[5] on behalf of the CA

The Centre for the AIDS Program of Research in Sou effectiveness and safety of a 1% vaginal gel formula inhibitor, for the prevention of HIV acquisition in wo was conducted comparing tenofovir gel (*n* = 445 wo active, HIV-uninfected 18- to 40-year-old women in HIV serostatus, safety, sexual behavior, and gel and c for 30 months. HIV incidence in the tenofovir gel ar study observation) (38 out of 680.6 women-years) c 660.7 women-years) in the placebo gel arm (incident (gel adherence > 80%), HIV incidence was 54% low intermediate adherers (gel adherence 50 to 80%) a incidence reduction was 38 and 28%, respectively. estimated 39% overall, and by 54% in women with adverse event rates was observed. There were no cha seroconverters. Tenofovir gel could potentially fill an women unable to successfully negotiate mutual mon

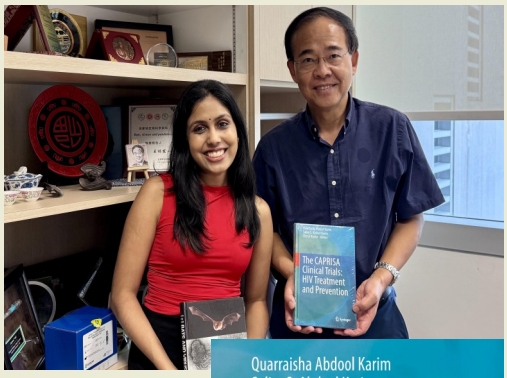
Knowledge sharing at home and away

Chinese Consul General of Durban Li Zhigong held discussions with Director Professor Salim Abdool Karim and his team on strengthening AIDS research and prevention, as well as promoting community health. Li and Deputy Consul General Sun Anlin also visited the eThekweni Clinical Research Site where they met with Senior Scientist Dr Leila Mansoor, Head of Vaccine Research, Dr Nivashnee Naicker, Head of HIV Pathogenesis Dr Sharana Mahomed and site manager Floyd Gobey.

Photos: (Consul General of Durban Li Zhigong meets Professors Salim and Quarraisha Abdool Karim, Prof Kogie Naidoo and the team at CAPRISA. Together with the Deputy Consul General Sun Anlin, he also visited CAPRISA's eThekwini Clinical Research Site where he was briefed by the Head of HIV Pathogenesis Dr. Sharana Mahomed, Senior Scientist Leila Mansoor and Head of HIV Vaccines Dr. Nivashnee Naicker and Research clinician, Dr. Busisiwe Ntsalaze

Nǐ hǎo Singapore!

Research associate at CAPRISA Dr. Jivanka Mohan was invited by renowned virologist Professor Linfa Wang to visit the Emerging Infectious Diseases (EID) Department at Duke-NUS Medical School in Singapore. As part of the programme, Jivanka delivered a presentation on CAPRISA's groundbreaking work in HIV prevention and treatment. Her talk emphasised the organization's community-based approach and its contributions to the global HIV response, sparking valuable dialogue on common challenges in infectious disease control.



The core focus of her visit was to explore bat immunology, particularly how bats tolerate viruses without developing disease. These mechanisms offer insights that could inform human therapies. Working closely with Dr Matae Ahn and his team, Dr Mohan gained hands-on experience with advanced immunological assays and techniques. This knowledge will support her new research into inflammasome activity in HIV-infected individuals in South Africa. The visit also helped lay the foundation for potential research collaborations between CAPRISA and global institutions tackling emerging infectious diseases and immune regulation.

Photo: Dr. Jivanka Mohan and Prof. Linfa Wang from the Emerging Infectious Diseases (EID) Department at Duke-NUS Medical School in Singapore

Professor Penny Moore elected to prestigious NAS

Professor Penny Moore- CAPRISA Honorary Senior Scientist in Virus-Host Dynamics- has been elected as a member of the National Academy of Sciences (NAS), one of the world's most prestigious science academies. Scientists are elected to the NAS as a way of honouring their significant and ongoing contributions to original research. Prof. Moore is the South African Research Chair of Virus-Host Dynamics and a Research Professor at Wits University and at the NICD. She is also Director of the Antibody Immunity Research Unit, an extramural unit of the SAMRC and a Research Fellow at the IDORI. The NAS currently has over 2 and a half thousand members of which 556 are based outside the USA and only 5 in South Africa.

"This was a huge surprise, and I feel overwhelmed and humbled by the recognition of the work that we have all done together over the last 20 years."- Professor Penny Moore

HIV data analysis in KZN taking SHAPE

Honorary Research Scientist Dr Jienchi Dorward from CAPRISA's SHAPE programme presented a webinar titled, "Fake trials? Emulating target trials in observational data." Using examples from SHAPE analyses of HIV data in KwaZulu-Natal, the SHAPE Team described what emulated target trials are, the reasons for using them, and the potential pitfalls.

Photo (Front): Lara Lewis, Kwena Tlhaku, Lisanthini Naidu, Dr. Sharana Mahomed, Sanele Mbeje. Photo (Back): Dr. Johan van der Molen, Dr. Jienchi Dorward

SHAPE
Strengthening Health systems through Audit & Programmatic data Evaluation

SisterLove at 36: Fighting for equitable access to HIV services for women

CAPRISA was honored to welcome a dynamic delegation from SisterLove. This pioneering United States based organization works towards advancing women's HIV, sexual and reproductive justice. The visit was led by Dr. Dazon Diallo, founder of SisterLove. She was joined by her South African colleagues Busi Ndlovu and Thabsile Mungwe, along with international team member Jiang Sizun.

SisterLove's South African chapter is actively driving change through impactful initiatives like the Healthy Love Party, POWaR Focus group discussions, and Screen-Identify-Link to Care. These programmes are aimed at empowering women and girls with the knowledge and tools to safeguard their sexual health.

The visit marked a powerful exchange of ideas and commitment to advancing women's health and rights across borders.

Photo (Front): Dr. Dazon Diallo, Prof. Quarraisha Abdool Karim. Photo (Back): Dr. Tanuja Gengiah. Dr. Sharana Mahomed, Siphelele Gabokhutle, Jiang Sizun and Patrick Mdletshe

Community check-ins at eThekwini and Umlazi

The CAPRISA Umlazi Clinical Research Site hosted a stakeholder engagement at the Umlazi V Hall. All CAPRISA partners were invited and representatives from about 32 organizations attended. Study updates from the Umlazi site were presented by Dr. Evette Moodley. Head of the Community Programme Patrick Mdletshe spoke on 'The Last Mile to 2030: Community mobilisation to end AIDS.' Mduduzi Ngubane from the SAMRC discussed HIV vaccine studies and Welcome Mbokazi from AHRI presented an overview of their studies.

Photos: Stakeholders at the eThekwini CRSG meeting

Sibusiso Mngadi receives Octavio Valente Jr Service Award

CAPRISA Global Community Advisory Board member Sibusiso Mngadi has received the Octavio Valente Jr Service Award from the HIV Vaccine Trials Networks. The award is given to a Community Advisory Board (CAB) member who has demonstrated exemplary leadership and dedication in the HVTN. Octavio Valente, Jr. was a dedicated CAB member who passed away in 2006. He played several roles in the HVTN and in the HIV prevention community in Brazil.

Mngadi has served on the global CAB as a full member since 2015. Currently, he represents the community in the Concept Working Group and is a member of the Protocol Team of HVTN 305. Mngadi has participated in several studies and outreach programmes that includes HIV prevention and ATI where research literacy is promoted.

"This award does not belong to me alone. It represents all the dedicated men and women I have worked with over the years"- Sibusiso Mngadi

A selection of scientific papers published in 2025

1 Schmidt AC, Fairlie L, Hellström E, Luabeya Kany Kany A, Middelkoop K, **Naidoo K**, Nair G, Gela A, Nemes E, Scriba TJ, Cinar A, Frahm N, Mogg R, Kaufman D, Dunne MW, Hatherill M; BCG REVAX Study Team. BCG Revaccination for the Prevention of Mycobacterium tuberculosis Infection. *N Engl J Med*. 2025 May 8;392(18):1789-1800. doi: 10.1056/NEJMoa2412381.

2 Omole TE, Nguyen HM, Marcinow A, Oo MM, Jahan N, Ssemaganda A, Severini G, Thomas KK, Celum C, Mugo N, Mujugira A, Kublin J, Corey L, **Sivro A**, Lingappa JR, Gray G, **McKinnon LR**. Pre-Human Immunodeficiency Virus (HIV) α4β7hi CD4+ T Cells and HIV Risk Among Heterosexual Individuals in Africa. *J Infect Dis*. 2025 Apr 15;231(4):e770-e780. doi: 10.1093/infdis/jiae638

3 **Mahomed S, Pillay K, Hassan-Moosa R**, Galvão BPGV, Burgers WA, **Moore PL, Rose-Abrahams M, Williamson C, Garrett N**. Clinical trials of broadly neutralizing monoclonal antibodies in people living with HIV - a review. *AIDS Res Ther*. 2025 Apr 6;22(1):44. doi: 10.1186/s12981-025-00734-8.

4 **Naidoo K, Lessells RJ, Dorward J**, Moosa MYS, Sookrajh Y, Moodley P, Drain PK, **Garrett N**. Rapid emergence of dolutegravir resistance on second-line dolutegravir-based ART. *South Afr J HIV Med*. 2025 Apr 23;26(1):1701. doi: 10.4102/sajhivmed.v26i1.1701

5 van Zyl DJ, Dunaiski M, Tegally H, **Baxter C, de Oliveira T**, Xavier JS; INFORM Africa research study group. Alignment-free viral sequence classification at scale. *BMC Genomics*. 2025 Apr 18;26(1):389. doi: 10.1186/s12864-025-11554-5.

6 Pillay K, Coetzer T, Connolly C, Pillay B, Chiliza T, **Naidoo K**, Sutherland J, Ndung'u T, Mayanja-Kizza H, Pillay M. IgG antibody response to Mycobacterium tuberculosis curli pili (MTP) in people from different geographical regions in Sub-Saharan Africa. *Tuberculosis (Edinb)*. 2025 May;152:102634. doi: 10.1016/j.tube.2025.102634.

7 Harris V, Holmes J, Gbinigie-Thompson O, Rahman NM, Richards DB, Hayward G, **Dorward J**, Lowe DM, Standing JF, Breuer J, Khoo S, Petrou S, Hood K, Ahmed H, Carson-Stevens A, Nguyen-Van-Tam JS, Patel MG, Saville BR, Francis N, Thomas NPB, Evans P, Dobson M, Png ME, Lown M, van Hecke O, Jani BD, Hart ND, Butler D, Cureton L, Patil M, Andersson M, Coates M, Bateman C, Davies JC, Raymundo-Wood I, Ustianowski A, Yu LM, Hobbs FDR, Little P, Butler CC; PANORAMIC Trial Collaborative Group. Health outcomes 3 months and 6 months after molnupiravir treatment for COVID-19 for people at higher risk in the community (PANORAMIC): a randomised controlled trial. Lancet Infect Dis. 2025;25(1):68-79. doi: 10.1016/S1473-3099(24)00431-6.

8 Beesham I, Beksinska M, Milford C, **Mansoor LE**. Disclosure of oral pre-exposure prophylaxis use for HIV prevention among women enrolled in a contraceptive study: qualitative findings from Durban, South Africa. *Front Glob Womens Health*. 2025 Jan 7;5:1505643. doi: 10.3389/fgwh.2024.1505643.

9 Ndembi N, Folayan MO, Komakech A, Mercy K, Tessema S, Mbala-Kingebeni P, Ngandu C, Ngongo N, Kaseya J, **Abdool Karim SS**. Evolving Epidemiology of Mpox in Africa in 2024. *N Engl J Med*. 2025 Feb 13;392(7):666-676. doi: 10.1056/NEJMoa2411368. PMID: 39887004.

For the complete list of publications see here: https://www.caprisa.org/Publication/1/1

CAPRISA hosts a DSI-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

Partner Institutions: University of KwaZulu-Natal, Inyuvesi YaKwaZulu-Natali; Columbia University Mailman School of Public Health; National Institute for Communicable Diseases; University of Cape Town, iYunivesithi yaseKapa • Universiteit van Kaapstad

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