



CAPRISA

CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

Newsletter

April/May2023 Volume 22 Issue 5

Results of a study of long-acting anti-HIV bNabs - CAP256V2LS & VRC07I523LS in women in South Africa

In this Issue

On page 1 we feature the results of the (CAPRISA 012B): a phase 1, dose-escalation, randomised controlled trial published in *The Lancet HIV*—the first trial to evaluate CAP256V2LS as a PrEP concept.

On page 2 we announce Professor Nigel Garrett's appointment as the eThekweni Clinical Research Site Leader and report on Dr Sharana Mahomed's participation in the prestigious NAM's Emerging Leaders Forum held in the US.

We congratulate our new graduates on page 3 on their outstanding results and feature the study "Implementation and outcomes of dolutegravir-based first-line antiretroviral therapy for people with HIV in South Africa" published in *The Lancet HIV*, with a translated version of the abstract in isiZulu.

On page 4 we feature our teams' recognition for a successful SA-PHRA GCP compliance inspection. & the visit of colleagues from UKZN.

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In this phase 1 dose-escalation, randomised controlled trial clinical trial, Mahomed et al evaluated the safety and pharmacokinetic profile of the broadly neutralising monoclonal antibody CAP256V2LS alone and in combination with VRC07-523LS in young HIV-negative women in Durban, South Africa.

The results of the CAPRISA 012B trial found that CAP256V2LS and VRC07-523LS with or without ENHANZE, a recombinant human hyaluronidase, was safe and well tolerated, with detectable antibody concentrations 6 months after product administration.

The trial published in the journal *The Lancet HIV* was the first trial to evaluate the engineered CAP256V2LS as a PrEP concept. This trial also evaluated for the first time the use of ENHANZE with a bNab as a concept for HIV prevention, potentially allowing for increased volumes of bNabs to be administered subcutaneously.

The study design consisted of three groups. Groups 1 and 2 were open label with CAP256V2LS administered at 5 mg/kg and 10 mg/kg intravenously and 5 mg/kg, 10 mg/kg, and 20 mg/kg subcutaneously. In group 3, participants were randomly allocated to receive a combination of CAP256V2LS and VRC07-523LS at 10 mg/kg and 20 mg/kg subcutaneously co-mixed with ENHANZE.

From July 13, 2020, to Jan 13, 2021, 42 HIV-negative women, aged 18–45 years, were enrolled and completed the trial. There were no serious adverse events or dose-limiting toxicities. Data from this trial supports further assessment of CAP256V2LS and VRC07-523LS as a long-acting 6-monthly administered PrEP agent in larger clinical studies.

For further reading see:

Mahomed S, et al. (CAPRISA 012B): a phase 1, dose-escalation, randomised controlled trial.

Lancet HIV. 2023 Apr;10(4): e230–e243.:

doi: [https://doi.org/10.1016/S2352-3018\(23\)00003-6](https://doi.org/10.1016/S2352-3018(23)00003-6)

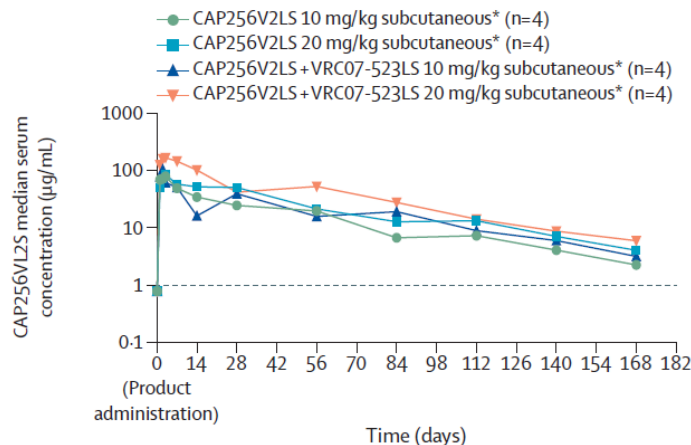


Figure 1:

Median concentrations of the study drug per study group



Prof Nigel Garrett appointed Leader of the CAPRISA eThekweni Research Site



Professor Nigel Garrett, Head of the CAPRISA HIV Pathogenesis and Vaccine Research Programme has been appointed Leader of the CAPRISA eThekweni Research Site (ECRS). Garrett brings a wealth of experience as a specialist physician in HIV and Sexual Health and has conducted more than 20 randomized clinical trials and large cohort studies related to HIV prevention and COVID-19 vaccines. He is the CAPRISA Lead to the HIV Vaccine Trials Network (HVTN). Professors Salim and Quarraisha Abdool Karim congratulated Garrett on his appointment and wished him ‘every success in this new role’.

Garrett is a Technical Expert Consultant of the South African National Strategic Plan (NSP) for HIV, TB and STIs 2023 – 2028 and provides input on objectives and interventions on reducing STIs, cervical cancer and hepatitis that draws on his extensive experience in evaluating point of care diagnostics and STI interventions.

Garrett says, he is looking forward to lead one of the flagship clinical research sites at CAPRISA and engage with all stakeholders to continue to strive for clinical excellence.

Dr Sharana Mahomed attends the US National Academy of Medicine’s Emerging Leaders Forum

Dr Sharana Mahomed, CAPRISA Research Clinician and Site Principal Investigator of CAP 012C attended the 2023 National Academy of Medicine (NAM) Emerging Leaders Forum, an invitation-only event held in Washington, D.C., on April 18-19.

The NAM Emerging Leaders Forum gathers interdisciplinary professionals working in health care, biomedical science, population health, health policy and other related fields. The Forum also allows for collaboration between scholars and NAM members to identify innovative approaches to health care.

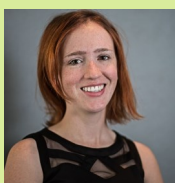
The program consisted of a selection of interactive breakout sessions that addressed health and human behaviour, intersection of cardiovascular disease and diabetes, retroviruses and infectious diseases, artificial intelligence, digital health and modelling, healthcare delivery to reduce disparities and the application of CRISPR in Human Diseases. NAM Mem-

bers engaged in interactive plenary discussions on “moving scientific research into the policy realm, fostering career transitions from research to policy, and advice on how researchers can effectively engage with policy makers.”

Strategies for more effective communication while addressing polarizing issues in society and healthcare were also discussed. Mahomed said it was an honour to participate in the forum and foster collaborations and friendships with other emerging leader scholars. “The opportunity to engage in open discussions with highly respected NAM members was a privilege, and I look forward to the continuous mentorship and engagement that the program provides.”



NICD scientist receives award for her omicron research



Dr Simone Richardson was awarded the 2022 Faculty of Health Science’s Research Prize from the University of the Witwatersrand for her paper entitled: “SARS-CoV-2 Omicron triggers cross-reactive neutralization and Fc effector functions in previously vaccinated, but not unvaccinated, individuals” at the Wits Faculty Honours Celebration which took place on 7 March 2023. In this paper, published in *Cell Host & Microbe*, Richardson et al. showed that SARS-CoV-2 Omicron infection in unvaccinated individuals triggers potent antibody responses; however, cross-reactivity against variants of concern is poor. In contrast,

Omicron BA.1 breakthrough infection in vaccinated individuals elicits high titer cross-reactive antibodies. Omicron-based vaccines are thus unlikely to be superior immunogens in SARS-COV-2-naive individuals.



Congratulations to our new graduates!

Congratulations to CAPRISA's staff (3) and fellows (1) who have successfully completed their degrees and will graduate from the University of KwaZulu-Natal. Dr Rubeshan Perumal, pulmonologist and CAPRISA senior scientist; and Dr Sharana Mahomed Research Clinician have obtained PhDs; Fellow Ms Nonsikelelo Ndlela her master's degree *cum laude* and Ms Silindile Myeza (left) a post-graduate Diploma in Finance, Banking and Investment Management.



Dr Perumal's PhD, titled "Optimising the pharmacological treatment of drug-susceptible pulmonary tuberculosis" was supervised by Prof Kogie Naidoo (Deputy Director) and Prof Nesri Padayatchi (Senior Scientist).

"Congratulations on a spectacular set of research projects which display an incredible volume of work, a variety of study designs and statistical analysis techniques," commented an examiner. "This is a very impressive body of work - well structured, comprehensive, detailed and with some valuable results that are likely to have impact in the TB field. I believe the requirements for a PhD have been fulfilled a few times over."



Dr Mahomed's PhD, titled "Assessing the safety and pharmacokinetics of the broadly neutralising monoclonal antibodies VRC07-523LS, PGT121 and CAP256V2LS in young women in Africa" was supervised by CAPRISA's Director, Prof Salim Abdool Karim. An

examiner's comment read: "Ms. Sharana Mahomed has demonstrated to be a distinguished expert in the fields of broadly neutralizing antibodies targeting HIV-1 and in their evaluation by performing clinical trials. The work is of highest quality and I recommend to accept this exceptional thesis."



Ms Nonsikelelo Ndlela, master's degree in medical microbiology titled: 'The Impact of Point-of-care Testing and Treatment of Sexually Transmitted Infections and Bacterial Vaginitis on the Genital Epithelial Barrier Integrity' was supervised by senior scientist, Professor Lenine Liebenberg.

"Her research has contributed significantly to our understanding of the impact of point-of-care treatment for STIs and BV," said Liebenberg. "We are confident that she will continue to make important contributions to the field."

Implementation and outcomes of the dolutegravir rollout in South Africa

Original article in Lancet HIV accompanied by an abstract in isiZulu

According to a collaborative team of researchers at CAPRISA, the eThekweni Municipality, the National Department of Health Informatics Directorate and the University of Oxford, the rollout of dolutegravir initially favoured men but did lead to improved retention in care and viral suppression in KwaZulu-Natal, South Africa. The study "Implementation and outcomes of dolutegravir-based first-line antiretroviral therapy for people with HIV in South Africa: a retrospective cohort study", was published in *The Lancet HIV*, along with a translated version of the abstract in isiZulu.

Using routine, de-identified data from 220,000 people with HIV in South African primary care, the researchers found that early in the rollout, women were less likely to receive dolutegravir. This was likely because of initial safety concerns around dolutegravir use in pregnancy, and once guidelines were updated to re-

flect new data confirming safety, the disparity between men and women disappeared.

Among people receiving dolutegravir, subsequent 12-month retention and viral suppression were better compared to those receiving the older drug, efavirenz. The benefits of dolutegravir were strongest among people receiving concurrent tuberculosis treatment when initiating ART, and among people transitioned to dolutegravir with most recent viral load at baseline ≥ 200 copies/mL. The analysis was part of the SHAPE project, which is led by Dr Jienchi Dorward CAPRISA Honorary Associate and lead author on the study and Prof Nigel Garrett.

For further reading see: Dorward J, et al. Implementation and outcomes of dolutegravir-based first-line antiretroviral therapy for people with HIV in South Africa: a retrospective cohort study. *Lancet HIV* 2023 doi: [https://doi.org/10.1016/S2352-3018\(23\)00047-4](https://doi.org/10.1016/S2352-3018(23)00047-4)



Teams do well in a SAHPRA GCP inspection

The Springfield Research (KDH) Site Team and Quality Assurance (QA) Team were recently awarded a Certificate of Recognition for their contribution to the successful results of a South African Health Products Regulatory Authority (SAHPRA) Good Clinical Practice (GCP) compliance inspection. The achievement was due to their hard work, dedication, and commitment to ensuring that the INSIGHT clinical trial was conducted in accordance with the highest standards of GCP. The SAHPRA GCP compliance inspection is a rigorous process that ensures that clinical trials are conducted in compliance with ethical and regulatory requirements, and that the safety and well-being of study participants are protected. The KDH Site Team and QA Team's contributions have not only led to the successful completion of the INSIGHT clinical trial audit but also to the advancement of research in TB and HIV and best practices for patient care. Their achievement is a remarkable accomplishment and sets an example for other clinical trial teams to follow.



Dr Anushka Naidoo, Senior Scientist, congratulates the Quality Assurance and Springfield Research Site teams for their outstanding contributions. Photo left: Quality Assurance team (L-R): Dr Anushka Naidoo, Ms Pinky Kunene, Ms Nokukhanya Khuzwayo, Ms Nokuthula Zungu and Dr Leila Mansoor

Photo right: Springfield Research Site team (L-R): Ms Anokhee Leela, Ms Nompumelelo Zungu, Ms Khanyisile Vilakazi, Ms Lungile Maphumulo, Dr Gillian Dorse, Ms Resha Boodhram, Ms Nokwanda Depargo, Ms Bhavna Maharaj, Ms Emmanuella Chinonso Osuala, Ms Marlene Venter, Ms Adejumoke Abiose, Dr Anushka Naidoo and Ms Magashree Govender

UKZN School of Chemistry visit



Seated (L-R): Prof Yin-Zhe Ma, Prof Quarraisha Abdool, Prof Salim Abdool Karim and Prof Neil Koorbanally the Dean of Research in the College.

UKZN's School of Chemistry and Physics visited CAPRISA to meet with Profs Salim and Quarraisha Abdool Karim and personally congratulate Professor Quarraisha Abdool Karim on her election to serve as the seventh President of The World Academy of Sciences (TWAS). The UKZN delegation led by astrophysicist Professor Yin-Zhe Ma, gained insight into CAPRISA's core research programmes and found the visit on 6 April inspiring and motivating as young scientists. Ma "praised the persistence of academic interests and passion for research that he observed among the CAPRISA researchers and staff."

Scientist participates in IPVC 2023

Dr Nivashnee Naicker, CAPRISA Research Clinician and HVTN/COVPN site PI at the CAPRISA eThekweni Clinical Research



Site attended and participated in the 35th International Papillomavirus Conference, IPVC 2023, held in Washington DC from 17-21 April 23.

Naicker was invited to speak at the Cepheid symposium on the real-world implementation of Xpert® HPV in high risk populations. Her presentation on 'A novel cervical cancer screening approach using GeneXpert technology for WLHIV, South Africa', preliminary data from the STREAM HIV trial, was well received.



A selection of scientific papers published in 2023

- *22 **Mahomed S, Garrett N, Capparelli EV, Osman F, Mkhize NN, Harkoo I, Gengiah TN, Mansoor LE, Baxter C, Archary D, Yende-Zuma N, Samsunder N, Carlton K, Narpala S, McDermott AB, Doria-Rose NA, Moore PL, Morris L, Abdool Karim Q, Mascola JR, Abdool Karim SS.** Safety and pharmacokinetics of escalating doses of neutralising monoclonal antibody CAP256V2LS administered with and without VRC07-523LS in HIV-negative women in South Africa (CAPRISA 012B): a phase 1, dose-escalation, randomised controlled trial. *Lancet HIV*. 2023;10(4):e230-e243. doi: 10.1016/S2352-3018(23)00003-6
- 23 **Perumal R, Naidoo K, Naidoo A, Padayatchi N.** Clinical impact of plasma concentrations of first-line antituberculosis drugs. *SAMJ: South African Medical Journal*. 2023;113(3):148-53. doi: 10.7196/SAMJ.2023.v113i3.16761
- 24 **Beesham I, Milford C, Joseph Davey DL, Smit J, Mansoor LE, Beksinska M.** Key stakeholders' perspectives on providing oral pre-exposure prophylaxis as HIV-prevention standard of care in clinical trials in South Africa. *African Journal of AIDS Research*. 2023;1-9. doi: 10.2989/16085906.2023.2169177
- 25 **Bristow CC, Mortimer TD, Morris S, Grad YH, Soge OO, Wakatake E, Pascual R, Murphy SM, Fryling KE, Adamson PC, Dillon JA, Parmar NR, Le HHL, Van Le H, Ovalles Urefia RM, Mitchev N, Mlisana K, Wi T, Dickson SP, Klausner JD.** Whole-Genome Sequencing to Predict Antimicrobial Susceptibility Profiles in *Neisseria gonorrhoeae*. *J Infectious Diseases*. 2023;227(7):917-925. doi: 10.1093/infdis/jiad027.
- 26 **Jassat W, Abdool Karim SS, Ozougwu L, Welch R, Mudara C, Masha M, Rousseau P, Wolmarans M, Selikow A, Govender N, Walaza S, von Gottberg A, Wolter N, Terrence Pisa P, Sanne I, Govender S, Blumberg L, Cohen C, Groome MJ; DATCOV Author Group.** Trends in Cases, Hospitalizations, and Mortality Related to the Omicron BA.4/BA.5 Subvariants in South Africa. *Clinical Infectious Diseases*. 2023;76(8):1468-1475. doi: 10.1093/cid/ciac921.
- 27 **Taylor-Robinson AW, Liebenberg L. et al.** Research training experience of Vietnamese health sciences undergraduates visiting the Centre for the AIDS Programme of Research in South Africa. *Pan African Medical Journal*. 2023;44(109). doi: 10.11604/pamj.2023.44.109.39039
- 28 **Garcia M, Roberts ST, Mayo AJ, Scheckter R, Mansoor LE, Palanee-Phillips T, Reddy K, Naidoo Y, Akello CA, Gaffoo Z, Siva S.** Integrating gender-based violence screening and support into the research clinic setting: experiences from an HIV prevention open-label extension trial in Sub-Saharan Africa. *AIDS and Behaviour*. 2023;27(4):1277-86. doi: 10.1007/s10461-022-03864-6
- 29 **Mvelase NR, Cele LP, Singh R, Naidoo Y, Giandhari J, Wilkinson E, de Oliveira T, Swe-Han KS, Mlisana KP.** Consequences of rpoB mutations missed by the GenoType MTBDRplus assay in a programmatic setting in South Africa. *Afr J Lab Med*. 2023;12(1):1975. doi: 10.4102/ajlm.v12i1.1975.
- 30 **Happel AU, Balle C, Havyarimana E, Brown B, Maust BS, Feng C, Yi BH, Gill K, Bekker LG, Passmore JS, Jaspán HB, Varsani A.** Cervicovaginal Human Papillomavirus Genomes, Microbiota Composition and Cytokine Concentrations in South African Adolescents. *Viruses*. 2023;15(3):758. doi: 10.3390/v15030758.
- 31 **Abdelatif N, Naidoo I, Dunn S, Mazinu M, Essack Z, Groenewald C, Maharaj P, Msomi N, Reddy T, Roberts B, Zuma K.** Heterogeneity in COVID-19 infection among older persons in South Africa: Evidence from national surveillance data. *Front Public Health*. 2023;11:1009309. doi: 10.3389/fpubh.2023.1009309.
- 32 **Gokul A, Arumugam T, Ramsuran V.** Genetic Ethnic Differences in Human 2'-5'-Oligoadenylate Synthetase and Disease Associations: A Systematic Review. *Genes (Basel)*. 2023;14(2):527. doi: 10.3390/genes14020527. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9956131/>

* continuation from previous newsletter

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



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