CAPRISA
CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

Newsletter

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Study assesses the subcutaneously administration of monoclonal antibodies VRC07-523LS and PGT121

The results of the CAPRISA 012A trial showed that monoclonal antibodies VRC07-523LS and PGT121 administered subcutaneously individually and in combination at high doses were safe and well tolerated.

The study, *Safety and Pharmacokinetics of Monoclonal Antibodies VRC07-523LS and PGT121 Administered Subcutaneously for Human Immunodeficiency Virus Prevention,* was published in the *Journal of Infectious Diseases.*

The study a randomised, double-blinded, placebo-controlled, dose-escalation phase 1 trial, assessed the safety, tolerability, pharmacokinetics, neutralization activity and anti-drug antibody levels of monoclonal antibodies VRC07-523LS and PGT121 in 45 HIV-negative women enrolled at the CAPRISA eThekwini Research clinic in Durban South Africa.

Pharmacokinetic modelling was conducted to predict steady-state concentrations for 16- and 24-weekly dosing intervals. Most common reactogenicity events were injection site tenderness and headaches. Nine product-related adverse events were mild and transient. Median VRC07-523LS concentrations following 20mg/kg doses were 9.65µg/ml and 3.86µg/ml at 16 and 24 weeks.
The median week 8 concentration following the 10mg/kg PGT121 dose was 8.26µg/ml. Modelling of PGT121 at 20mg/kg showed median concentrations of 1.37µg/ml and 0.22µg/ml at 16 and 24 weeks (Figure 1). Half-lives of VRC07-523LS and PGT121 were 29 and 20 days. The antibodies retained neutralizing activity post administration and no anti-drug antibodies were detected.

It showed that 24-week dosing of VRC07-523LS SC produced drug levels above the target concentration, while more frequent dosing is needed for PGT121.

Thanks to the VRC, IAVI and Dan Barouch for their collaboration in this study.

For further reading see: *Mahomed S, et al. JID 2022. doi: 10.1093/infdis/jiac041.* https://pubmed.ncbi.nlm.nih.gov/35134995/

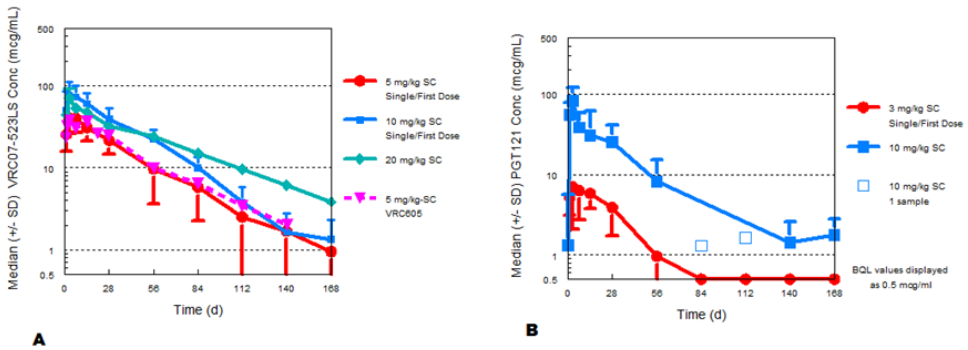

Figure 1: *A) Observed median VRC07-523LS concentrations following 5, 10 and 20mg/kg subcutaneous administrations in the CAPRISA 012A trial and median concentrations following 5mg/kg subcutaneous administration in the VRC605 clinical trial. B) Observed median PGT121 concentrations following 3 and 10mg/kg subcutaneous administrations in the CAPRISA 012A trial.*

In this Issue

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Rhodes University confers Quarraisha Abdool Karim with an honorary doctorate

Prof Quarraisha Abdool Karim CAPRISA's Associate Scientific Director was awarded an honorary degree, Doctor of Science (DSc) (honoris causa) by Rhodes University (RU) at its graduation ceremony held on 8th April.

RU bestowed the honour in recognition of Abdool Karim's research on HIV prevention in adolescent girls and young women and for her seminal study, the CAP 004 trial, which demonstrated for the first time that antiretrovirals could prevent HIV infection.

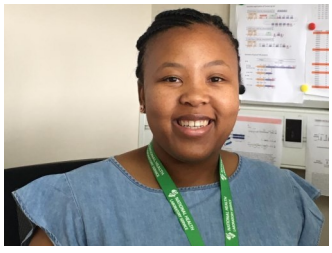
"Our nation is singularly privileged and distinctly honoured to have a scientist of her calibre and stature who is expanding the frontiers of knowledge in a manner that makes real, tangible and meaningful change in the lives of ordinary people of our country, "said Rhodes University Vice-Chancellor, Professor Sizwe Mabizela.

Photo (L-R): RU Chancellor, Honourable Justice Lex Mpati; Prof Quarraisha Abdool Karim; and RU Vice-Chancellor, Dr Sizwe Mabizela.

Professor Abdool Karim's scientific contributions in highlighting the vulnerability of young women, the need for women-initiated technologies and the integration of HIV prevention efforts into sexual reproductive health services have been recognised by more than forty local and international prestigious awards.

"We all owe Professor Abdool Karim an unpayable debt of gratitude and appreciation," said Mabizela, "for her immense and sustained contribution to the work that has saved many lives and has significantly improved the quality of life for those infected and affected by HIV in our country and beyond."

NICD/Wits PhD student in Gates seminar series on Pandemic Prevention



Boitumelo Motsoeneng *(left)* a PhD student supervised by Prof. Penny Moore *(right in the photo)* and Dr. Simone Richardson at the NICD and University of the Witwatersrand attended a Gates Notes Deep Dive virtual discussion series, held on 22 April 2022. She was one of 33 high-performing graduate students selected globally because her experience in researching infectious diseases and global health.

The learning session was chaired by Dr. Alaa Murabit, who serves as the Director of Program Advocacy and Communications, Health at the Bill & Melinda Gates Foundation. Experts delivered presentations on key areas needed for prevention.

Epidemiologist, Dr. Sofonias Tessema explained the crucial role of disease monitoring through genomic surveillance. Dr. Padmini Srikantiah, a respiratory disease expert, reviewed the lessons learned from COVID -19 vaccines.

Global health expert, Dr. Nancy Messonnier presented on building a global-to-local pandemic prevention system, to respond efficiently to threats of emerging diseases.

Following a panel discussion students had the rare opportunity to engage in a Q&A session with Mr. Bill Gates. Students highlighted concerns regarding health systems, vaccine production capacity, the sustainability of the prevention plans and how to go about establishing the global response teams.

Congratulations to CAPRISA's new graduates!

Congratulations to CAPRISA's staff (3) and fellows (11) who have successfully completed their degrees. Two have graduated from UCT and one will graduate at UNISA. Eleven will graduate at the University of KwaZulu-Natal's graduation ceremony this month (May). Two have obtained PhDs, 4 Masters and 8 honours degrees. CAPRISA Fellow, Mr Mali Mlaba completed his Honours in Medical Microbiology (*cum laude*).

Photo: Top Row (L-R): Dr Nireshni Mitchev, Fellow (PhD); Mr Nzuzo Magini, CAPRISA Medical Technologist (Master of Science in Medical Microbiology); Dr Santhana Gengiah, Fellow (PhD).
Second Row (L-R): Ms Sherishka Dhindayal, Research Pharmacist (Master of Pharmacy in Pharmacy Practice); Ms Senamile Ngema, Fellow (Master of Medical Science in Medical Microbiology) and Ms Ntombenhle Mntambo, Fellow (Master of Science in Biochemistry).

Photo bottom: Top Row (L-R): Ms Pinky Kunene, Quality Assurance Officer (BA Honours Social Behavioural Studies in HIV-AIDS); Ms Slindile Ngubane, Fellow (BMedSci Honours in Medical Microbiology); Ms Kirsten Welp, Fellow (BSc Honours in Infectious Diseases and Immunology); and Ms Rovanya Pillay, Fellow (BMedSci Honours in Medical Microbiology).
Second Row (L-R): Mr Mali Mlaba Fellow (Honours Medical Microbiology - *cum laude*); Ms Nosipho Ndlovu, Fellow (Honours Medical Science in Microbiology); Ms Mandisa Mazibuko, Fellow (BMedSci Honours in Medical Microbiology); and Ms Hannah Livingstone, Fellow (BSc Honours in Infectious Diseases and Immunology).

CAPRISA scientists present on Covid-19 at the 2022 AIDS Society of India Conference

CAPRISA's senior scientist and pulmonologist Dr Rubeshan Perumal and honorary associate scientist Dr Jienchi Dorward were invited plenary speakers at the 13th National Conference of AIDS Society of India (ASICON), a hybrid event held in Hyderabad, India from 3rd – 5th April, themed: *'Confronting Pandemics with Proficiency, Precision and Persistance'.*

Perumal was invited by Dr Ishwar Gilada, President of the AIDS Society of India. He delivered his presentation titled: *Long COVID – what we know so far,* alongside Dr Nagalingeswaran Kumarasamy, Chief Director of the Chennai Antiviral Research and Treatment Unit. Dr Jyoti Dhar, HIV Physician from Leicester in the UK chaired this session.

Dr Dorward's talk titled, "*Rapid HIV viral load testing at the clinical point-of-care to improve treatment outcomes in South Africa*", outlined the point-of-care research conducted by CAPRISA and its influence on WHO HIV guidelines. CAPRISA is a long-standing academic partner of ASICON which is the official National HIV meeting of the AIDS Society of India.

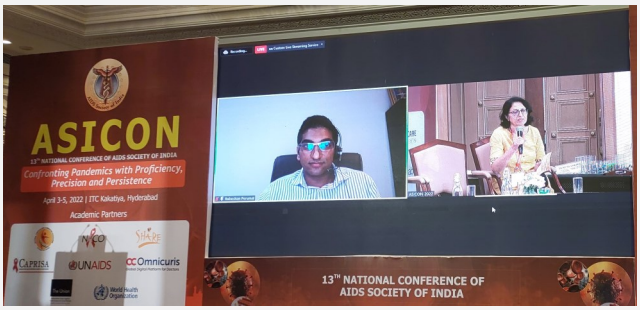


Photo top: (L) Dr Rubeshan Perumal delivers his talk chaired by Dr Jyoti Dhar(R)

Photo: (L) Dr Jienchi Dorward CAPRISA; Dr K.S. Gururaja, Organising Committee; Dr V.H.T. Swamy, Organising Committee

SARS-CoV-2 Omicron triggers cross-reactive neutralization and Fc effector functions in previously vaccinated, but not unvaccinated individuals

Dr. Simone Richardson and colleagues at the NICD published a study entitled:" SARS-CoV-2 Omicron triggers cross-reactive neutralization and Fc effector functions in previously vaccinated, but not unvaccinated individuals" in Cell Host and Microbe.

Richardson 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.

Click here: https://www.sciencedirect.com/science/article/pii/S1931312822001597

Senior Data Manager Precious Radebe recognised for excellence

CAPRISA Senior Data Manager, Precious Radebe was recognized for her service excellence for managing a multi-country study PROMOTE and maintained a complete and high-quality database throughout the 5 years concurrently with other CAPRISA studies while providing training and guidance to the data management team. *Photo: Prof Salim Abdool Karim CAPRISA Director presents the award to Ms Precious Radebe. Right: Dr Nonhlanhla Yende Zuma, Head of Statistics and Data Management.*

CAPRISA engages with traditional leadership

iNkosi Zondi, newly appointed head of the Inadi ward of Vulindlela, in KwaZulu Natal visited CAPRISA Vulindlela Research Clinic on 8 April to gain insight on various key research studies conducted at the Site.

Mr Patrick Mdletshe, CAPRISA Head of Community Programme led the proceedings. In his welcome address, he thanked the Inadi Tribal Authority Leadership for their support and participation in CAPRISA's research and highlighted the importance of working together with the community - taking science to the community and involving the community in research. Dr Disebo Potloane, Vulindlela Research Clinic Site Director, Drs Jansen van Vuuren and Mlungisi Khanyile Research Clinicians at the Site provided an overview of CAPRISA's scientific research programmes.

"aMakhosi have a very important role to play in the development of society and CAPRISA is honoured by your presence Ndabezitha (Great One)", Mdletshe said.

INkosi Zondi was accompanied by iziNduna, iziNyosi (Poets), members and amaNadi Royal House. "I would like to congratulate CAPRISA on what the have done for this community and hope that the research is successful and changes lives of many people around the world, "he said.

*Photo: **Front row**(L-R): Nduna Magwaza; Dr Disebo Potloane, Vulindlela Research Clinic Site Director; Nkosi Zondi, Head of the Inadi ward of Vulindlela; Dr Mlungisi Khanyile, CAPRISA Research Clinician; Mr Patrick Mdletshe, CAPRISA Head of Community Programme; Nduna Hadebe; and Mr Nkosana Zondi **Back row** (L-R): Undunankulu Magubane; Nduna Mkhize; and Nduna Zuma*

The Traditional leaders also engaged with researchers on HIV Prevention studies that are underway at the research clinic in Vulindlela.

A selection of scientific papers published in 2022

23* **Mahomed S, Garrett N,** Capparelli EV, **Osman F, Harkoo I, Yende-Zuma N, Gengiah TN, Archary D, Samsunder N, Baxter C,** Mkhize NN, Modise T, Carlton K, McDermott A, **Moore PL, Abdool Karim Q,** Barouch DH, Fast PE, Mascola JR, Ledgerwood JE, **Morris L, Abdool Karim SS**. Safety and pharmacokinetics of monoclonal antibodies VRC07-523LS and PGT121 administered subcutaneously for HIV prevention. *Journal of Infectious Diseases* 2022. doi: 10.1093/infdis/jiac041.

24 **Abdool Karim SS, Baxter C.** Impact of SARS-CoV-2 variants of concern on Covid-19 epidemic in South Africa. *Transactions of the Royal Society of South Africa* 2022; 77(1):101–104.

25 **Naidoo K, Dookie N.** Can the GeneXpert MTB/XDR deliver on the promise of expanded, near-patient tuberculosis drug-susceptibility testing? *Lancet Infectious Diseases* 2022 April; 22(4):e121-e127.

26 Lazarus JV, **Abdool Karim SS,** van Selm L, Doran J, Batista C, Ben Amor Y, Hellard M, Kim B, Kopka CJ, Yadav P. COVID-19 vaccine wastage in the midst of vaccine inequity: causes, types and practical steps. *BMJ Global Health* 2022; 7(4):e009010. doi: 10.1136/bmjgh-2022-009010.

27 **Dookie N, Khan A, Padayatchi N, Naidoo K.** Application of Next Generation Sequencing for Diagnosis and Clinical Management of Drug-Resistant Tuberculosis: Updates on Recent Developments in the Field. *Frontiers in Immunology* 2022; 13:775030. doi: 10.3389/fmicb.2022.775030.

28 **Abdool Karim Q, Baxter C.** COVID-19: Impact on the HIV and Tuberculosis Response, Service Delivery, and Research in South Africa. *Current HIV/AIDS Reports* 2022; 19(1):46-53.

29 Bekker LG**, Garrett N,** Goga A, Fairall L, Reddy T, Yende-Zuma N, Kassanjee R, Collie S, Sanne I, Boulle A, Seocharan I. Effectiveness of the Ad26.COV2.S vaccine in health-care workers in South Africa (the Sisonke study): results from a single-arm, open-label, phase 3B, implementation study. *Lancet 2022*; 399(10330):1141-53.

30 Hunter DJ, **Abdool Karim SS**, Baden LR, Farrar JJ, Hamel MB, Longo DL, Morrissey S, Rubin EJ. Addressing Vaccine Inequity - Covid-19 Vaccines as a Global Public Good. *New England Journal of Medicine* 2022; 386(12):1176-1179.

31 **Naranbhai V,** Nathan A, Kaseke C, Berrios C, Khatri A, Choi S, Getz MA, Tano-Menka R, Ofoman O, Gayton A, Senjobe F, Zhao Z, St Denis KJ, Lam EC, Carrington M, Garcia-Beltran WF, Balazs AB, Walker BD, Iafrate AJ, Gaiha GD. T cell reactivity to the SARS-CoV-2 Omicron variant is preserved in most but not all individuals. *Cell* 2022; 185(6):1041-1051.

32 Card CM, Abrenica B, **McKinnon LR**, Ball TB, Su RC. Endothelial cells promote productive HIV infection of resting CD4+ T cells by an integrin-mediated cell adhesion-dependent mechanism. *AIDS Research and Human Retroviruses* 2022; 38(2):111-126.

33 **Abdool Karim SS, Baxter C, Abdool Karim Q.** Advancing HIV prevention using tenofovir-based pre-exposure prophylaxis. *Antiviral Therapy* 2022; 27(2):13596535211067589. doi: 10.1177/13596535211067589.

34 **Moore PL**, Baden LR. Omicron - Decoupling Infection from Severe Disease. *New England Journal of Medicine* 2022; 386:1361-1362.