CAPRISA
CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA
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Hyaluronidase-enhanced subcutaneous delivery of broadly neutralizing antibodies

Broadly neutralizing antibodies (bNAbs) are a promising strategy for HIV prevention, offering targeted protection against diverse viral strains. However, their delivery has been constrained by the challenges of intravenous administration and the need for large subcutaneous (SC) injection volumes. In the recently published *Nature Communications* article, researchers from CAPRISA and collaborators report on the use of a novel hyaluronidase-based technology to enhance SC delivery of HIV bNAbs.

This phase 1 randomized trial, conducted at the CAPRISA eThekwini Clinical Research Site, evaluated the impact of the ENHANZE™ drug product (EDP), which contains recombinant human hyaluronidase (rHuPH20). Fifty-seven HIV-negative South African women were enrolled, with a predefined sub-analysis comparing 20 mg/kg doses of the bNAbs CAP256V2LS and VRC07-523LS administered with and without EDP.

The study demonstrated that co-administration with EDP markedly improved feasibility and pharmacokinetics of SC bNAb delivery. Median administration time was reduced from nearly 50 minutes to 10 minutes, and injections per dose decreased from three to one. Importantly, serum concentrations of both bNAbs were significantly higher at 24 weeks in the EDP group, with CAP256V2LS exposure increased by 40%. Although peak concentrations were modestly reduced, overall bioavailability was substantially enhanced. Safety analyses confirmed that EDP was well tolerated, with no serious adverse events or anti-drug antibodies detected.

Population pharmacokinetic modeling further highlighted the advantages of EDP, showing consistently greater antibody exposure across all dosing scenarios compared with SC administration without hyaluronidase. These results suggest that hyaluronidase-enabled SC delivery could provide an efficient, scalable, and patient-friendly approach for long-acting HIV prevention, particularly in high-burden, resource-limited settings.

This trial represents the first evaluation of hyaluronidase-enhanced SC administration of HIV bNAbs and supports the broader development of combination antibody regimens that may overcome viral resistance while simplifying delivery. These findings bring us closer to achieving practical, long-acting HIV prevention interventions for populations most at risk. - Dr. Sharana Mahomed

For further reading: Mahomed S, Osman F, Beliveau M et al. Hyaluronidase-enhanced subcutaneous delivery of bNAbs: a phase 1 randomized controlled clinical trial in HIV uninfected women. *Nature Communications*. https://doi.org/10.1038/s41467-025-63051-8

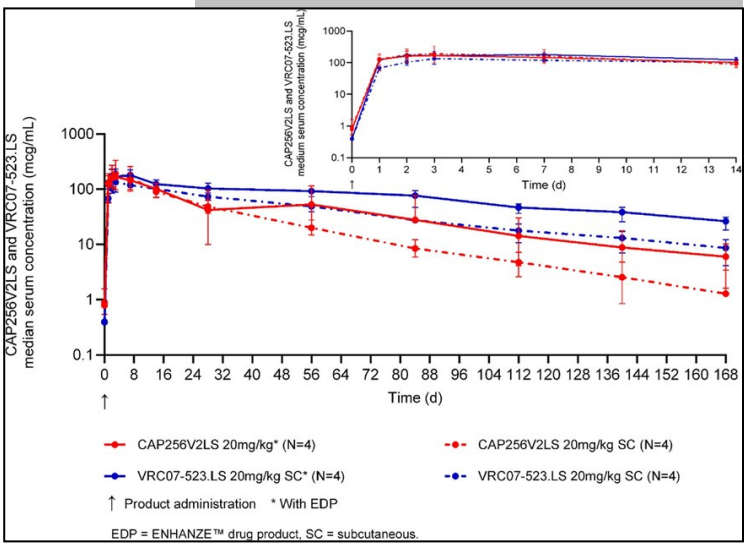

Figure 1 illustrates the serum concentrations of CAP256V2LS and VRC07-523LS with and without EDP following a single subcutaneous dose

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"Science that unites and not divides"

...Professor Quarraisha Abdool Karim

Professor Quarraisha Abdool Karim, FRS has been honored with the Virchow Prize 2025 alongside her fellow laureate, global child health expert Doctor Zulfiqar Ahmed Bhutta, at Rotes Rathaus, Berlin City Hall in Germany. President of the non-profit Virchow Foundation and the Berlin-Brandenburg Academy of Sciences and Humanities (BBAW) Christoph Markschies said, "Though their paths are distinct, both laureates have helped redefine the global health architecture by focusing on those historically excluded from mainstream health systems and scientific discourse."

In awarding Abdool Karim the prize, the Jury noted the following, "In line with Virchow's vision, Abdool Karim positions health as a manifestation of social determinants and power structures, challenging the persistent gendered neglect in global health research and development. She has consistently underscored the intersection of biology and structural violence, showing that empowerment and prevention must go hand-in-hand to curb epidemics and sustain health gains.

Delivering the Virchow Prize Lecture, Professor Abdool Karim referred to the context of the moment of the awards and the convergence of many challenges, saying, "It demands of all of us to give our very best to ensure we tackle these complex challenges. There are no easy solutions. There are no quick solutions. But science is forward looking at it brings hope and it is that hope as privileged members of society that in these times we have to hold high. It's the hope that bring through science, science that unites and not divides. Science that fosters peace, not wars and conflicts and science that ensures we have a sustainable future for generations to come."

Watch the Virchow Prize Lecture 2025

Who was Rudolf Virchow?

- German physician, pathologist and politician
- He is often referred to as "The father of modern pathology"
- His work focused on cell pathology, pathophysiology and the modern histopathology of tumors
- Socially, Virchow lent on his medical background to fight for social justice. In describing the latter, the Virchow Foundation said, "There is consensus that the relationship between medical, political, economic and social determinants must be addressed directly and jointly in order to achieve sustainable and universal improvement of health."

Left to right: Member of the Virchow Prize Committee and Executive Director of UNAIDS, Winnie Byanyima delivers the laudation speech for Professor Quarraisha Abdool Karim. Prof. Abdool Karim and Dr. Zulfiqar A. Bhutta with the Virchow Award and the Virchow Prize Lecture 2025. All pics courtesy of The Virchow Foundation.

Young people call for the science to be relevant

Young students in Durban have shared their lived experience on transactional sex, unplanned teenage pregnancies and the very real social factors that are contributing to the high HIV rate among young women in Africa. CAPRSIA's Community Outreach team and Fellows hosted a frank and engaging fishbowl session, where tertiary students studying in Durban, sounded the call for HIV prevention interventions to meet them where they are at. The age disparity that is seeing older men having sex with young women is fuelled by the challenges of peer pressure, substance abuse, gender based violence and unemployment among others. Concerningly candid conversations emerged about the drivers behind transactional sex, from sugar daddies and the blesser phenomenon to sex for power as a status symbol. In light of this, the social pressures facing young women continues to be a driving factor behind the high HIV rate in this vulnerable group.

Among the recommendations are calls for such open conversations at a school level, an awareness of the dangers of social media, empowering young women with information and education not only to make informed decisions but to seek out financial independence and the decriminalisation of sex work.
- Contributions by Nonsikelelo Ndlela, Senamile Ngema, Kwena Tlhaku

Celebrating excellence

The eThekwini Clinical Research Site's Treatment Team together with colleagues from the Pharmacy, Laboratory and QA units, have been commended for excellence following a SAHPRA Good Clinical Practice (GCP) inspection for the BNT 164-02 trial. It was through the team's collective diligence, professionalism, and commitment to the highest standards in clinical research that the audit report reflected exceptional site performance, with no critical or major findings.

These efforts were recognized and commended by the sponsor, CRO, and several senior ICON and BNT team members for the high level of quality and excellence demonstrated. This achievement reflects the strength of teamwork and dedication. The Achievement Awards were presented to the team in recognition of this outstanding accomplishment.

Above: CAPRISA Deputy Director Professor Kogie Naidoo and the awardees

Honing in on Latent Class Analysis

CAPRISA hosted a workshop on latent class analysis (LCA), presented by the Associate Professor of Medicine and Epidemiology in the Department of Epidemiology at Columbia University Medical Centre in New York, Max O'Donnell, and pulmonologist at the Columbia University Medical Centre, Doctor Kevin Guzman. The workshop was attended by researchers from CAPRISA, the Africa Health Research Institute and the South African Medical Research Council. LCA is used in clinical research to identify hidden subgroups within a patient population based on observed characteristics.

The workshop began with an introduction to LCA, followed by discussions on the structure of LCA models, how to run an analysis, and how to evaluate and interpret the results. Assumptions and limitations of the method were also addressed. The method was illustrated using a real dataset to enhance understanding and demonstrate implementation in R. Participants found the workshop useful and informative, engaging in discussions about applying LCA to their own research questions and datasets. - Mahboubeh Akbari-Lakeh

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Professor Norbert Ndjeka, Chief Director of TB Control and Management at the National Department of Health and Honorary Associate Professor of Medicine at the University of Cape Town, has been awarded a PhD in Public Health Medicine from the University of KwaZulu-Natal (UKZN). His thesis, titled “Analysis of Determinants of Rifampicin-Resistant Tuberculosis Treatment Outcomes in South Africa (2011–2021)”, was supervised by CAPRISA Deputy Director, Prof Kogie Naidoo with mentorship from CAPRISA’s Head of TB, Prof. Rubeshan Perumal. Prof Ndjeka has been a key figure in strengthening the country’s response to TB, with a particular focus on drug-resistant strains. Pof. Naidoo said, “His stewardship of the National TB Control Program has seen a significant reduction in TB associated mortality, reduction in TB incidence, improved patient outcomes and introduction novel drugs and diagnostics. His commitment to the fight against TB has significantly advanced research, policy development, and translation of evidence-based interventions into programme implementation.”

Left: Prof Kogie Naidoo, Prof Norbert Ndjeka and Prof Rubeshan Perumal

In conversation this month, we meet 31-year-old Estcourt born Doctor Nomusa Zondo, one of our intrepid post-doctoral research fellows working in the HIV prevention space.

She joined CAPRISA in 2020 in the middle of the COVID-19 pandemic to undertake her PhD in Virology, investigating three biological factors impacting the efficacy of pre-exposure prophylaxis (PrEP) in African women from an HIV endemic area in KwaZulu-Natal over a prolonged time. Zondo is currently part of the team that is investigating broadly neutralizing antibodies as a prophylaxis and the biological factors that impact this. In the first episode of *The Unconventional Scientist*, Nomusa shares her thoughts on how young people view HIV, her passion for mentorship and the lessons she has learned from working alongside inspired women scientists breaking barriers in the HIV and TB space.

The Unconventional Scientist uncovers what makes our scientists tick and challenges them on some of the burning questions facing science. Available on our website and social media platforms.

A selection of scientific papers published in 2025

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*Continued from previous newsletter

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

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