CAPRISA
CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA
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Implications of new SARS-CoV-2 variants – next generation vaccines a priority

In a letter published recently in the *New England Journal of Medicine,* Professors Salim S. Abdool Karim, Director, CAPRISA and Tulio de Oliveira, Director, KRISP describe the clinical, public health and vaccine implications of three new SARS-CoV-2 variants identified during the period 14th December 2020 to 12th January 2021 and their effects on viral transmissibility, disease severity, reinfection rates and vaccine effectiveness.

The B.1.1.7 variant was first described in the United Kingdom on 14 December 2020, the 501Y.V2 variant was initially reported in South Africa on 18 December 2020 while the P.1 variant was reported on 12 January 2021 from Brazil. According to reports by the third week in February 2021, the B.1.1.7, 501Y.V2 and P.1 variants were reported in 93, 45 and 21 countries, respectively.

The transmissibility of the 501Y.V2 variant found in South Africa showed a 50% faster rate of infection in one province in the second wave compared to the first wave. With the B.1.1.7 variant, the UK reported higher death rates perhaps due to the patient overload, limitations of care and over burden resources.

Of concern was the impact of the variants on natural - and vaccine-induced immunity which showed an overall decrease in neutralising activities raising concern of the efficacy of vaccines to the 501Y.V2 variant in South Africa (Table 1).

In conclusion the authors believe the development of the next generation of vaccines that elicit broadly neutralizing activity against current and future variants is a priority. Equally, the importance of genomic surveillance for early detection of dominant future SARS-CoV-2 variants is highlighted.

For further reading: *Abdool Karim SS, de Oliveira T. New SARS-CoV-2 Variants - Clinical, Public Health, and Vaccine Implications. N Engl J Med. 2021. doi: 10.1056/NEJMc2100362. https://www.nejm.org/doi/full/10.1056/NEJMc2100362*

Table 1: Summary results on SARS-CoV-2 vaccine trial efficacy and viral neutralisation of the B.1.1.7, P.1 and 501Y.V2 variants compared to pre-existing variants

	Pre-existing variants			Neutralisation by pseudovirion or live viral plaque assay			
Vaccine (Company)	Sample size	Efficacy for preventing clinical Covid-19 (vaccine vs placebo endpoints)	Efficacy for preventing severe Covid-19 (vaccine vs placebo endpoints)	P.1 variant	B.1.1.7 variant	501Y.V2 variant	Efficacy in settings with 501Y.V2 variant
Ad26.COV2-S (Johnson & Johnson)	43,783	66% (n/a)	85% NA	NA	NA	NA	57%† 85%‡
BNT162 (Pfizer)	34,922	95% (8 vs 162)	90% (1 vs 9)	Decrease by 6.7X	Decrease by 2X	Decrease by <6.5X	NA
mRNA-1273 (Moderna)	28,207	94% (11 vs 185)	100% (0 vs 30)	Decrease by 4.5X	Decrease by 1.8X	Decrease by <8.6X	NA
Sputnik V rAd5, rAd26 (Gamaleya)	19,866	92% (16 vs 62)	100% (0 vs 20)	NA	NA	NA	NA
AZD1222 (AstraZeneca)	17,177	67% (84 vs 248)	100% (0 vs 3)	NA	NA	Decrease by <86X to complete escape	22% §
NVX-CoV2373 (Novavax)	15,000	89% (6 vs 56)	100% (0 vs 1)	NA	Decrease by 1.8X	NA	49% §
CoronaVac (Sinovac) ¶							
Brazil	12,396	51% (NA)	100% (NA)	NA	NA	NA	NA
Turkey	7,371	91 (3 vs 26)	NA	NA	NA	NA	NA
BBIBP-CorV (Sinopharm)	n/a	79% (NA)	NA	NA	NA	Decrease by 1.6X	NA

* Data were available up to March 18, 2021. The definitions of mild, moderate, and severe coronavirus disease 2019 (Covid-19) vary across the vaccine trials. A list of references associated with these vaccines is provided in the Supplementary Appendix, available with the full text of this letter at NEJM.org. NA denotes not available, and SARS-CoV-2 severe acute respiratory syndrome coronavirus 2.; † Shown is the efficacy of the vaccine, as compared with placebo, against moderate-to-severe Covid-19.; ‡ Shown is efficacy of the vaccine, as compared with placebo, against severe Covid-19 and hospitalization.; § Shown is efficacy of the vaccine, as compared with placebo, against symptomatic Covid-19.; ¶ Data are shown separately for the trial sites in Brazil and Turkey.

In this Issue

Our feature story this month focuses on the clinical, public health and vaccine implications of the new SARS-CoV-2 variants.

On page 2 we report on the hybrid event held at CAPRISA at which the French Ambassador to South Africa presented the Diploma and Medallion of the Christophe Mérieux, to Prof Quarraisha Abdool Karim.

Prof Kogie Naidoo calls for urgent intervention to increase testing and treatment programmes and research showing that SARS-CoV-2 501Y.V2 escapes neutralization is featured on page 3. We also congratulate Ms Zanele Gwamanda on her appointment to a ACTG subcommittee.

On page 4 we highlight the Sisonke study which reached a milestone after 8 weeks since the initiation of the programme & CAPRISA's Clinical Research Placement who published a book on his personal experience at medical school.

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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French Ambassador bestows prestigious 2020 Christophe Mérieux Prize to Quarraisha Abdool Karim

Infectious diseases epidemiologist and associate Scientific Director, Professor Quarraisha Abdool Karim, was awarded the 2020 prestigious Christophe Mérieux Prize, in the field of infectious diseases in developing countries in a special and momentous hybrid ceremony held at CAPRISA on Tuesday 30th March. His Excellency Mr Aurélien Lechevallier, Ambassador of France to South Africa, on behalf of the Fondation Christophe et Rodolphe Mérieux-Institut de France and the French Academy of Sciences, bestowed the certificate and medallion to Abdool Karim in recognition of her pioneering research work 'resulting from the use of antiretroviral drugs to prevent the sexual transmission of HIV infection in women'.

The award presentation was preceded by citations from an eminent panel of speakers that include : Professor Pascale Cossart, the Permanent Secretary of the French Academy of Sciences; Mr Alain Mérieux, President of the Institut Mérieux Family Foundation; Professor Françoise Barré-Sinoussi, 2008 Nobel Laureate in Physiology/Medicine and Chair of the CAPRISA Scientific advisory Board; and *Professor Valerie Mizrahi, the 2013 recipient of the Christophe Merieux Award and UCT Emeritus Professor in TB biology.*

In her citation, Cossart recognized Abdool Karim as only 'the sixth woman scientist to receive the biggest prize of the French Academy of Sciences'. In his citation Mérieux, highlighted that the 'fight against infectious diseases continues to be a world-wide problem' and this annual award from the Christophe and Rudolphe Merieux Family Foundation is to encourage research in addressing this challenge. Barré-Sinoussi in her citation highlighted that Abdool Karim is 'one of the examples of successful women scientists in the world, with an immense international reputation in women's health'. "I am very impressed by the achievements of CAPRISA and in particular of Quarraisha," she said.
Mizrahi said what resonated with her was 'Quarraisha's selfless determination to build research capacity in southern Africa' and underscored the importance of 'the several hundreds of scientists that she has trained through the Columbia University-Southern African Fogarty AIDS training Programme and the numerous young investigators she has lifted and inspired'.

Photo: (L-R) His Excellency Mr Aurélien Lechevallier, Ambassador presents the Christophe Mérieux Prize *certificate and medallion to Professor Quarraisha Abdool Karim. Below: the hybrid event held at CAPRISA.*

"It is a great honour for the HIV research in young women in Africa undertaken by the CAPRISA team to be recognized by this pre-eminent award from the Christophe Mérieux Foundation and the French Academy of Sciences ," said Abdool Karim. She paid tribute to the CAPRISA team of scientists and researchers, students and collaborators across the globe and research participants for their important and invaluable contributions to this research. She said it was important to use new scientific knowledge to impact policies and programming and to get to those who will benefit from this knowledge. The Covid-19 pandemic has shown us that we have the 'ability to pivot globally as rapidly as we were able to which comes from decades of investment in responding to other pandemics such as HIV, TB, Malaria and Ebola that remain ongoing challenges and global threats – but when we work together, we can achieve so much more'.

Stronger advocacy aimed at strengthening demand for TB testing and treatment services needed

The theme for World TB Day 2021, *The Clock is Ticking*, highlights the urgency in delivering on commitments to end TB by 2035.

According to Prof Kogie Naidoo, Deputy Director and Head of HIV and TB Treatment at CAPRISA, despite great strides achieved in TB prevention, diagnosis and treatment, each year approximately 10 million people fall ill and 1.4 million die from TB globally, with an estimated 4000 TB-related deaths each day. "In South Africa, 'approximately 400,000 new TB cases, and 58,000 TB deaths were recorded in 2019 alone," said Naidoo.

She cautioned that over the past 15 months, the COVID-19 pandemic disruption to health services has negatively impacted gains made toward global TB control. A recent WHO report indicated a 20% decline in TB diagnosis globally over the last year. "SA among the worst affected countries, shows a TB testing decline of 41%, largely due to re-prioritization of routine health services for COVID-19 and restricted patient access to TB diagnosis and treatment services, " said Naidoo.

Naidoo explained that in addition to the worldwide decline in TB diagnosis and treatment, 'data from South Africa show that people co-infected with TB and COVID-19 have three times higher mortality than people infected with TB alone, supporting calls for contact tracing, case finding and bi-directional TB and COVID-19 testing and treatment services. "Every effort must be made for greater public awareness and stronger TB advocacy aimed at strengthening demand for TB testing and treatment services," she said.

SARS-CoV-2 501Y.V2 escapes neutralization by South African COVID-19 donor plasma

Kurt Wibmer (left in the photo), Jinal Bhiman, Penny Moore and colleagues from the HIV Virology Section of the NICD showed, in a paper published in *Nature Medicine,* that SARS-CoV-2 501Y.V2 escapes neutralization by South African COVID-19 donor plasma. The 501Y.V2 lineage, which was identified in South Africa, contains substitutions in two immunodominant domains of the spike protein.

Wibmer showed that pseudoviruses expressing the 501Y.V2 spike protein completely escape three classes of therapeutically relevant antibodies directed at epitopes in the receptor binding domain and the N-terminal domain. Furthermore, 501Y.V2 exhibits substantial to complete escape from neutralization by convalescent plasma, with 48% of donors (n=44) unable to neutralize this novel lineage.

These data highlighted the prospect of reinfection with antigenically distinct variants and provided a mechanism for the reduced efficacy of spike-based vaccines that has since been described.

CAPRISA CLO elected to serve on the ACTG's PDISC

We congratulate Ms Zanele Gwamanda, CAPRISA Community Liaison Officer, on her election to serve on the ACTG's Protocol Development and Implementation Subcommittee (PDISC) as an appointee to the Outreach, Recruitment, and Retention Working Group (ORRWG).

Gwamanda will serve a two-year term from March 1, 2021 to November 30, 2022.

She continues to play an integral role in recruiting and tracking study participants at the CAPRISA eThekiwini Research Clinic and expressed her gratitude to Professor Kogie Naidoo for 'giving me opportunities to grow my experience'.

Sisonke study successfully vaccinates more than 250 000 health workers

On the 30th March, the Sisonke study had vaccinated 251,707 health workers marking its halfway point as it continues to move forward towards its target of vaccinating half a million of the country's health workers. This unique effort, spearheaded by the South African Medical Research Council in partnership with the National Department of Health, Desmond Tutu Health Foundation, CAPRISA, Janssen and Johnson & Johnson, has used research to bridge the delay posed by the need to reconsider first-line vaccine choice in the context of the 501Y.V2 variant dominant in South Africa.

'We are proud of our colleagues and collaborators who have made an important contribution to providing COVID-19 vaccine access to health care workers in South Africa over the past eight weeks. We are looking forward to delivering another 250 000 doses by the end of April.' – Dr Nigel Garrett, National Co-PI Sisonke Programme & CAPRISA's Head of Vaccines and Pathogenesis Research.

The Sisonke study commenced on the 17th of February in 18 sites in urban areas. Since then it has expanded well beyond urban centres reaching 85 sites across the country, with research staff spending many hours on the road to ensure the vaccine is distributed as equitably as is possible.

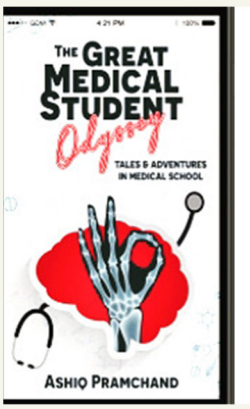
This open label, single-arm Phase 3b vaccine clinical trial of the investigational single-dose Janssen COVID-19 vaccine candidate aims to monitor the effectiveness of the investigational single-dose Janssen vaccine candidate at preventing severe COVID-19, hospitalizations and deaths among healthcare workers as compared to the general unvaccinated population in South Africa. (https://www.samrc.ac.za/media-release/sisonke-study-successfully-vaccinates-more-250-000-health-workers-third-wave).

CAPRISA research placement explores the great odyssey of the medical student in his new book

Mr Ashiq Pramchand, a final year medical student at the University of KwaZulu-Natal (UKZN) and a CAPRISA Research placement, has published a book, *The Great Medical Student Odyssey: Tales and Adventures in Medical School,* that traces his incredible journey as a medical student and explores the great odyssey of the medical student.

Pramchand's passion for writing was encouraged during his research placement years at CAPRISA from 2017 – 2021, under the mentorship of Dr Lenine Liebenberg, Senior Scientist in the CAPRISA Mucosal Immunology Laboratory. He has published work in three publications – two Pulse Magazine articles, the Albert Einstein College of Medicine and one with the Harvard Medical Student Review-Journal.

The Great Medical Student Odyssey: Tales and Adventures in Medical School is a 194-page book that documents his life-changing moments as a medical student, life-changing moments with patients and researching life-threatening diseases. "One experiences a myriad of emotions during the different undergraduate clinical rotations-joy, heartbreak, anger towards a harsh consultant...the list goes on. These rotations, which can last anywhere from 6 weeks to 12 weeks, change you as a person… These places are autoclaves for the soul, where pressure, high patient caseloads, and low resources purify us-they force us to abandon or challenge our vices, to help others.



These experiences are life- changing and profound. In my anecdotes, I try to capture this profoundness...the clinical years is where the real adventure begins…"reflects Pramchand.

The book is available on Amazon and in bookstores worldwide.

Scientific papers published in 2021

11	**Mtshali A, Ngcapu S, Osman F, Garrett N,** Singh R, Rompalo A, **Mindel A**, **Liebenberg LJP**. Genital HSV-1 DNA detection is associated with a low inflammatory profile in HIV-uninfected South African women. *Sex Transm Infect.* 2021;97(1):33-37.
12	WHO Ad Hoc Expert Group on the Next Steps for Covid-19 Vaccine Evaluation, Krause PR, Fleming TR, Longini IM, Peto R, Beral V, Bhargava B, Cravioto A, Cramer J, Ellenberg SS, Figueroa JP, Halloran E, Henao-Restrepo AM, Ryan MJ, Levine MM, Nason M, Nohynek HM, Plotkin S, Rees H, **Singh JA**, Swaminathan S. Placebo-controlled trials of Covid-19 vaccines - why we still need them. *New England Journal of Medicine* 2021;384(2):e2. doi: 10.1056/NEJMp2033538.
13	Stranix-Chibanda L, Tierney C, Sebikari D, Aizire J, Dadabhai S, Zanga A, Mukwasi-Kahari C, Vhembo T, Violari A, Theron G, **Moodley D**, George K, Fan B, Sommer MJ, Browning R, Mofenson LM, Shepherd J, Nelson B, Fowler MG, Siberry GK; PROMISE P1084s study team. Impact of postpartum tenofovir-based antiretroviral therapy on bone mineral density in breastfeeding women with HIV enrolled in a randomized clinical trial. *PLoS One* 2021; 16(2):e0246272. doi: 10.1371/journal.pone.0246272.
14	Balán IC, Giguere R, Lentz C, Kutner BA, Kajura-Manyindo C, Byogero R, Asiimwe FB, Makala Y, Jambaya J, Khanyile N, **Chetty D**, Soto-Torres L, Mayo A, Mgodi NM, Palanee-Phillips T, Baeten JM. Client-Centered Adherence Counseling with Adherence Measurement Feedback to Support Use of the Dapivirine Ring in MTN-025 (The HOPE Study). *AIDS Behavior* 2021; 25(2):447-458.
15	WHO Solidarity Trial Consortium, Pan H, Peto R, Henao-Restrepo AM, Preziosi MP, Sathiyamoorthy V, **Abdool Karim Q**, Alejandria MM, Hernández García C, Kieny MP, Malekzadeh R, et al. Repurposed Antiviral Drugs for Covid-19 - Interim WHO Solidarity Trial Results. *New England Journal of Medicine* 2021; 384(6):497-511.
16	**Mahomed S, Garrett N, Baxter C, Abdool Karim Q, Abdool Karim SS**. Clinical trials of broadly neutralizing monoclonal antibodies for HIV Prevention: A Review. *Journal of Infectious Diseases* 2021; 223(3):370-380.
17	Mbichila T, Kumwenda G, Yola N, **Abdool Karim Q**, Tchelidze T, Lau J, Buchholz S, Lehnert R, Molina JM, Mayer K, Miller V. Commentary Title: COVID-19 Research, Africa, and Global Health. *Journal of Virus Eradication* 2021; 7(1):100030. doi: 10.1016/j.jve.2021.100030.
18	Seneviratne HK, Hamlin AN, Li S, Grinsztejn B, **Dawood H**, Liu AY, Kuo I, Hosseinipour MC, Panchia R, Cottle L, Chau G. Identification of Novel UGT1A1 Variants Including UGT1A1 454C> A through the Genotyping of Healthy Participants of the HPTN 077 Study. *ACS Pharmacology and Translational Science* 2021; 4(1): 226–239.
19	**Abdool Karim SS,** de Oliveira T, Loots G. Appropriate names for COVID-19 variants. ***Science*** 2021 March; 371(6535):1215. doi: 10.1126/science.abh0836.
20	Misra N, **Padayatchi N**, Naidoo P. Dose-related treatment outcomes in South African patients prescribed clofazimine for drug-resistant tuberculosis. South African Medical Journal 2021;111(1):61-67.
21	**Abdool Karim SS,** de Oliveira T. New SARS-CoV-2 Variants — Clinical, Public Health, and Vaccine Implications. *New England Journal of Medicine* 2021; DOI: 10.1056/NEJMc2100362

**continuation from previous newsletter*

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