

Dial down the rhetoric over COVID-19 vaccines

The SAMJ editorial^[1] entitled 'South Africa should be using all the COVID-19 vaccines available to it – urgently' implies, *inter alia*, that the reasons for the suspension of the AstraZeneca (AZ) roll-out have been shrouded in secrecy by the Ministerial Advisory Committee on Vaccines (VMAC). It is regrettable that there has been a lag in publicising these advisories on the Department of Health website. Nevertheless, the reasons have received fairly wide publicity in the media.^[2] Alternatively, I could simply have been approached for a response. I was not.

Allow me to again briefly summarise the science behind the decision. First, and fundamentally, there is currently no evidence that the AZ vaccine will effectively prevent severe COVID-19 disease caused by the dominant B.1.351 (501Y.V2) variant in South Africa (SA). The only clinical trial of its protective efficacy against B.1.351 was, regrettably, not designed to assess the most relevant clinical endpoint – that of severe disease and hospitalisation (obviously most unlikely, given that the cohort selected for the trial consisted of healthy individuals aged 18 - 65 years).^[3]

Second, that trial showed a dramatic drop in the only clinical efficacy endpoint, mild to moderate disease, from 70% and 79% in the UK and USA, down to 22% in SA and even lower to 10.4% in a subset enriched with B.1.351.^[3]

Third, it has been shown that the baseline level of neutralising antibody production by AZ vaccination is only fairly modest, and several times lower than that of other vaccines, e.g. the Pfizer vaccine.^[4,5]

Fourth, corresponding to these findings, AZ-induced antibodies had little or no neutralising activity against B.1.351 using various neutralisation assays.^[6]

Against this background, the editorial still exhorts us to try out AZ, despite no evidence of its efficacy, and despite some signals rather worryingly suggesting ineffectiveness against B.1.351. Presumably, this is on the speculation that there may possibly be some hitherto undiscovered mechanisms, biological or immunological, that may result in some effectiveness against B.1.351 severe disease. Perhaps T-cell immunity or non-neutralising blocking antibodies may play that critical role. This of course may well be true, even though there is currently no evidence for it. So, why not at least give it a try?

There are five main reasons for not 'giving it a try'.

First, rolling out this vaccine to healthcare workers, as has been proposed, where there would be a real risk of multiple failures, would clearly seriously damage the worryingly fragile public trust and fuel vaccine hesitancy.

Second, the risk of a false sense of security from a very suboptimal vaccine could be a serious public health danger.

Third, diverting precious resources, such as human vaccinator resources and global syringe shortages, to a vaccine of unproven efficacy would hardly be justifiable.

Fourth, vaccinating a fairly sizeable cohort with a vaccine of poor immunogenicity would be a recipe for the selection of even further escape variants.

Fifth, the implementation of any medical intervention, drugs or vaccines, must be guided by scientific evidence of efficacy – no less for a COVID vaccine than it was for ivermectin, a drug with a plausible biological mechanism, but failure to prove efficacy.^[7]

Fundamentally, the editorial ignores the centrality of the B.1.351 virus in the context of vaccines for SA. For example, using AZ vaccine efficacy against the B.1.1.7 variant in the UK to suggest similarities to B.1.351 in SA is simply wrong. Minimal B.1.1.7 immune escape

cannot be compared to B.1.351 immune escape. It is therefore hardly reassuring that there have been few breakthroughs due to variants in the UK following the widespread use of AZ.

Despite a rather impressive list of references, a number are misused. For example, reference 6 is used to support the contention that immunised animals are fully protected against the variants.^[8] However, this reference makes no mention of variants, nor could it have, given it was published on 13 May 2020, some 4 months before the first serious variants were first described – erroneously given as 13 May 2021 in the reference list.

But perhaps the most egregious of these misused references was that used to support a distasteful accusation that the SA authorities behaved unethically in selling its stock of AZ vaccine to African countries because the 'B.1.351 variant has been detected throughout Africa and may be responsible for the devastating second wave many countries have just experienced'. There is undoubted evidence of the spread and penetration of B.1.351 into several southern African countries, and in a few neighbouring countries it appears to be the major virus strain. However, reference 19 mentions only one country, Zambia,^[9] and in reference 20, the PANGA list of countries,^[10] B.1.351 has been found in eight countries in southern Africa and five others – a total of 13 of the 48 countries of continental Africa. In some of these, few B.1.351 isolates were found. Hardly 'the dominant variant ... circulating in much of Africa'. This assertion is not only loathsome, but also totally wrong. On the contrary, it would actually have been highly unethical for SA to have rolled out one million doses of a vaccine of unproven efficacy when it could have been of great value to economically disadvantaged African countries struggling to acquire sufficient vaccine, where B.1.351 is either undetectable or relatively unimportant.

Finally, I must appeal to our colleagues to please bring to an end this obsession with media in order to disparage the Department and VMAC. It serves only one purpose, damaging the fragile trust of the public.^[11] Science certainly encourages various interpretations and enquiry from diverse standpoints, and these importantly need to be discussed. However, especially in the COVID-19 era, discussions must be in a respectful and professional manner. These avenues are wide open and available, and presentations to the VMAC are most welcome. I hope this will be the end of this distasteful, uncalled-for, and damaging activity.

Declarations of interest. None.

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1. Venter WDF, Mahdi SA, Nel J, Mendelson M, van den Heever A, Moshabela M. South Africa should be using all the COVID-19 vaccines available to it – urgently. *S Afr Med J* 2021 (epub 25 March 2021). <https://doi.org/10.7196/SAMJ.2021.v111i5.1571>
2. Schoub BD. The ABC of AstraZeneca vaccine and the B.1.351 link. *News24*, 23 March 2021. <https://www.news24.com/news24/analysis/barry-schoub-the-abc-of-astrazeneca-vaccine-and-the-b1351-variant-20210323> (accessed 2 April 2021).
3. Madhi SA, Baillie V, Cutland CL, et al. Efficacy of the ChAdOx1 nCoV-19 Covid-19 vaccine against the B.1.351 variant. *N Engl J Med* 2021 (epub 16 March 2021). <https://doi.org/10.1056/NEJMoa2102214>
4. Ramasamy MN, Minassian AM, Ewer KJ, et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): A single-blind, randomised, controlled, phase 2/3 trial. *Lancet* 2020;396(10267):1979-1993. [https://doi.org/10.1016/S0140-6736\(20\)32466-1](https://doi.org/10.1016/S0140-6736(20)32466-1)
5. Mulligan MJ, Lyke KE, Kitchin N, et al. Phase I/II study of COVID-19 RNA vaccine BNT162b1 in adults. *Nature* 2020;586:589-593. <https://doi.org/10.1038/s41586-020-2639-4>

6. Karim SSA, de Oliveira T. New SARS-CoV-2 variants – clinical, public health, and vaccine implications. *N Engl J Med* 2021 (epub 24 March 2021). <https://doi.org/10.1056/NEJMc2100362>
7. Pandey S, Pathak SK, Pandey A, et al. Ivermectin in COVID-19: What do we know? *Diabetes Metab Syndr Clin Res Rev* 2020;14(6):1921-1922. <https://doi.org/10.1016/j.dsx.2020.09.027>
8. Van Doremalen N, Lambe T, Spencer A, et al. ChAdOx1 nCoV-19 vaccination prevents SARS-CoV-2 pneumonia in rhesus macaques. *bioRxiv* 2020 (epub 13 May 2021). <https://doi.org/10.1101/2020.05.13.093195>
9. Mwenda M, Saasa N, Sinyange N, et al. Detection of B.1.351 SARS-CoV-2 variant strain – Zambia, December 2020. *MMWR Morb Mortal Wkly Rep* 2021;70(8):280-282. <https://doi.org/10.15585/mmwr.mm7008e2>
10. Pango. Pango lineages: A dynamic nomenclature proposal for SARS-CoV-2 lineages to assist genomic epidemiology. 2021. https://cov-lineages.org/global_report_B.1.351.html (accessed 24 March 2021).
11. Editorial. Politicians must dial down the rhetoric over COVID vaccines. *Nature* 2021;591:502. <https://doi.org/10.1038/d41586-021-00769-7>

S Afr Med J 2021;111(6):522-523. <https://doi.org/10.7196/SAMJ.2021.v111i6.15740>