Review 1: "Safety and efficacy of the ChAdOx1 nCoV-19 (AZD1222) Covid-19 vaccine against the B.1.351 variant in South Africa"

Alfonso J. Rodriguez-Morales¹

¹Faculty and Senior Researcher, Fundacion Universitaria Autonoma de las Americas, Faculty of Medicine, Colombia

Published on: Apr 20, 2021

License: [Creative Commons Attribution 4.0 International License \(CC-BY 4.0\)](https://creativecommons.org/licenses/by/4.0/)

RR:C19 Evidence Scale rating by reviewer:

- **Reliable.** The main study claims are generally justified by its methods and data. The results and conclusions are likely to be similar to the hypothetical ideal study. There are some minor caveats or limitations, but they would/do not change the major claims of the study. The study provides sufficient strength of evidence on its own that its main claims should be considered actionable, with some room for future revision.

Review:

This is a very interesting study raising concerns over the efficacy of the ChAdOx1 nCoV-19 (AZD1222) Covid-19 vaccine in the emerging scenario of the circulation of one of the new variants of concern (VOC), the B.1.351 in South Africa.

The efficacy against the B.1.351 variant was only 10.4% (95%CI: -76.8; 54.8), but this was analyzed as a secondary objective. Therefore, other studies would be necessary to confirm these findings and to have that objective be the primary endpoint.

Interestingly, the authors provided information about pseudotyped (PSVNA) and live virus (LVNA) neutralization assays performed, showing that there is a reduced or abrogated vaccine-induced antibody neutralization against the B.1.351 variant. As expected, and suggested by the authors, the evolution of other SARS-CoV-2 lineages that include similar mutations needs further evaluation.

The paper lacks a detailed discussion of the scenarios where the vaccine can be used, despite the circulation of the B.1.351 variant. For example, even in Africa, in areas where genomic surveillance can demonstrate that this variant is not present, this vaccine may be employed. This is really important considering the lack of available vaccines, as it has implications for vaccine coverage despite the emergence of different variants.

As has been emphasized by the World Health Organization (WHO), indirect evidence suggests that there is protection against severe COVID-19; however, this remains to be demonstrated in ongoing clinical trials and post-implementation evaluations (https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-2021.1). In view of this, WHO currently recommends the use of AZD1222 vaccine according to the Prioritization Roadmap (4) even if

variants are present in a country. Countries should conduct a benefit-risk assessment according to the local epidemiological situation including the extent of circulating virus variants. These preliminary findings highlight the urgent need for a coordinated approach for surveillance and evaluation of variants and their potential impact on vaccine effectiveness.

In view of these results, the efficacy of the ChAdOx1 nCoV-19 (AZD1222) Covid-19 vaccine should be assessed in other epidemiological scenarios where other VOCs are circulating, as is the case especially in countries such as the United Kingdom or Brazil, as well as many others.

In further clinical trials, coupling the molecular diagnosis with sequencing and phylogenetic analyses will be necessary to prospectively assess the impact of the new variants of concern of the SARS-CoV-2. The introduction and increased spread of new SARS-CoV-2 variants first identified in the United Kingdom (B.1.1.7), South Africa (B.1.351), and Brazil (P.1) have raised concerns. And recently the European CDC has also emphasized that, due to the increased transmissibility, the evidence of increased severity, the potential for the existing licensed COVID-19 vaccines to be partially or significantly less effective against a variant of concern (VOC), and the high probability that the proportion of SARS-CoV-2 cases due to B.1.1.7 (and possibly also B.1.351 and P.1) will increase, the risk assessment of the further spread of the SARS-CoV-2 VOCs in the European Union and other regions of the world is high to very high for the overall population and very high for vulnerable individuals.

Therefore, more studies are necessary (<https://www.ecdc.europa.eu/en/publications-data/covid-19-risk-assessment-variants-vaccine-fourteenth-update-february-2021>).