Review 2: "SARS-CoV-2 variant B.1.617 is resistant to Bamlanivimab and evades antibodies induced by infection and vaccination"

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Published on: Sep 15, 2021

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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:

The article addresses the potential evasion of monoclonal antibodies and the vaccine (BNT162b2) by the newly emerging SARS-CoV-2 variant B.1.617, detected in the UK and India. There are three sub-lineages viz. B.1.617.1, B.1.617.2, and B.1.617.3. Based on the further emerging evidence, WHO has classified B.1.617.2 as the Delta variant and a Variant of Concern (VOC). In the light of this changed classification, the data needs to be reanalyzed to understand the degree of evasion of immunity for the VOC, B.1.617.2, to get a clearer understanding.

The data presented for resistance against the neutralizing monoclonal antibodies, approved for COVID-19 therapy, demonstrates that Casirivimab and Bamlanivimab monotherapy may not be effective against the B.1.617.2 variant. Although this is an important finding, this needs to be corroborated with data for the VOC B.1.617.2. The authors have proposed that the increased spread of variant B.1.617 in India might be due to increased evasion to the pre-existing immune responses against SARS-CoV-2. However, the studies cited for the seroprevalence in India have no data regarding the prevailing strain when these serosurveys were conducted. Moreover, there have been no reports/studies from these sites included in the serosurvey of increased cases of reinfection demonstrating the escape of immunity. Thus, the authors' claim that increased cases in resource-poor communities by the variant B.1.617 is not supported by epidemiological/reinfection data. The authors have mentioned that antibody evasion is most prominent by variant B.1.351, but the manuscript is unclear whether variants can arise with increased or complete neutralization resistance. Multiple studies have been published demonstrating increased neutralizing resistance of individuals who have been vaccinated and/or are recovered patients of COVID-19. In the introduction subsection, the authors have mentioned that the emergence of COVID19 is associated with a record number of cases and deaths. To clarify the data, we advise the authors to

mention the exact number of cases and deaths at a definite timepoint. The authors have mentioned the availability of efficient mRNA and vector-based vaccines. However, other vaccines like inactivated viruses and DNA vaccines need to be mentioned to complete the spectrum of the available vaccines rolled out in different countries worldwide. The authors have demonstrated variant B.1.351 in the results and presented it in the figures. However, no significant mention of these findings has been brought out in the discussion.

Conclusion: The article is relevant given the emerging variants and their effect on the ongoing immunization drive in the world. However, because of the revised nomenclature of variants and declaration of B.1.617.2 as VOC by WHO, the article needs a major revision with additional experiments against B.1.617.2 if feasible to address the protective efficacy of BNT162b2/monoclonal antibodies.