Review 3: "Neutralization against B.1.351 and B.1.617.2 with sera of COVID-19 recovered cases and vaccinees of BBV152"

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RR:C19 Evidence Scale rating by reviewer:

Strong. The main study claims are very well-justified by the data and analytic methods used. There is little room for doubt that the study produced has very similar results and conclusions as compared with the hypothetical ideal study. The study's main claims should be considered conclusive and actionable without reservation.

Review:

This is a very relevant work about the Bharat Biotech COVID19 vaccine BBV152 (Covaxin®) against two variants of concern (VOC). One VOC is the Delta variant which has become dominant worldwide these past months. The authors confirm the well-known finding that the South African strain of SARS-CoV-2 (a.k.a. WHO beta variant of concern or B.1.351 in PANGOLIN phylogeny) is less sensitive to neutralization by convalescent plasma (collected during former waves) and vaccines. Such data is not a premiere for BBV152. The reduction in neutralization (3 folds lower) is in line with what has been shown for both mRNA vaccines (BNT162b2 and mRNA-1273) and adenoviral vector vaccines. A former preprint reported no reduction in neutralization against B.1.351 from BBV152-elicited sera [1].

Most importantly, the authors show that BBV152 has reduced neutralization against B.1.617.2, the major subclade of the Delta variant, by 2.7-folds. A more recent preprint has confirmed reduced neutralization by BBV152-elicited sera, albeit with smaller reduction [2], against B.1.671.2 and AY.1 subclades of the Delta variant, while a former preprint reported unchanged efficacy [3]. Accordingly, in clinical trials, BBV152 efficacy at preventing infection from the Delta variant has been suboptimal at about 65% [4].

The manuscript is relevant since viral neutralization assays employ authentic viral isolates (as opposed to surrogate Spike pseudoviruses), and sera are collected weeks after full-course (2 doses) BBV152 vaccinations.

At the top of this reviewer's head, BBV152 efficacy data is missing for alpha and gamma VOCs, but the data is available for P.2 (zeta VOI) [5]. Since BBV152 is the main COVID-19 vaccine for more than a billion people, fast-track publication of efficacy data against SARS-CoV-2 variants is both relevant and urgent.

1. Sapkal GN, Yadav P, Ella R, Deshpande G, Sahay R, Gupta N, et al. Neutralization of UK-variant VUI-202012/01 with COVAXIN vaccinated human serum. 2021:2021.01.26.426986. doi: 10.1101/2021.01.26.426986 %J bioRxiv.
2. Yadav PD, Sahay RR, Sapkal G, Nyayanit D, Shete A, Deshpande G, et al. Comparable neutralization of SARS-CoV-2 Delta AY.1 and Delta in individuals sera vaccinated with BBV152. 2021:2021.07.30.454511. doi: 10.1101/2021.07.30.454511 %J bioRxiv.
3. Yadav P, Sapkal GN, Abraham P, Ella R, Deshpande G, Patil DY, et al. Neutralization of variant under investigation B.1.617 with sera of BBV152 vaccinees. 2021:2021.04.23.441101. doi: 10.1101/2021.04.23.441101 %J bioRxiv.
4. Ella R, Vadrevu KM, Jogdand H, Prasad S, Reddy S, Sarangi V, et al. Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBV152: a double-blind, randomised, phase 1 trial. *The Lancet Infectious Diseases*. 2021;21(5):637-46. doi: 10.1016/S1473-3099(20)30942-7.
5. Sapkal G, Yadav PD, Ella R, Abraham P, Patil DY, Gupta N, et al. Neutralization of B.1.1.28 P2 variant with sera of natural SARS-CoV-2 infection and recipients of BBV152 vaccine. 2021:2021.04.30.441559. doi: 10.1101/2021.04.30.441559 %J bioRxiv.