Rapid Reviews COVID-19

Review 1: "Neutralization of N501Y mutant SARS-CoV-2 by BNT162b2 vaccine-elicited sera"

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Published on: Feb 07, 2021

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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:

The emergence of the new lineages of SARS-CoV-2 such as the B.1.1.7 in the UK and South Africa is a cause of serious concern primarily due to their increased infection rate compared to the parental strain. Another key concern with these lineages is the possibility of a loss in the efficacy of the currently available vaccines, especially those that target the spike protein, which mediates the interaction of the virus with ACE2 receptor on host cell membrane. The reason for this that a number of mutations in these lineages localize to the S1 subunit of the spike protein (S1 spike protein) including a mutation in the residue N501 (N501Y) which is involved in the interaction between the S1 spike protein and ACE2 receptor. Therefore, the authors in the current preprint article entitled "Neutralization of N501Y mutant SARS-CoV-2 by BNT162b2 vaccine-elicited sera" have tested the ability of the nucleoside-modified RNA vaccine, BNT162b2, in neutralizing the virus expressing the N501Y mutant S1 spike protein. Specifically, the authors have determined the efficacy of patient sera obtained after either the first or the second dose of the BNT162b2 vaccine in inhibiting plaque formation by the N501Y mutant virus in comparison to the parental virus. Based on the results, the authors suggest that the BNT162b2 vaccine-elicited sera is similarly effective against SARS-CoV-2 expressing the N501Y mutant S1 spike protein. Thus, the preprint article is of paramount importance. Addressing the following points may further increase the impact of the article:

1. Sera from 50% (10 out of 20) of the patients showed higher values for the PRNT50 (50% plaque reduction neutralization assay) ratio of the mutant Y501 and the parental N501 virus (ranging from 2 – 4) while the rest showed similar values (Supporting media-1, Table 1). Does this reflect a differential efficacy of BNT162b2 vaccine-elicited patient sera?
2. The number of patient samples appear to be lower than those used in the initial studies describing vaccine efficacy (cited in the article). Inclusion of additional samples may increase the confidence in the results.
3. It is apparent that the N501Y mutant spike protein has an increased affinity for ACE2 receptor, and perhaps plays a significant role in the increased rate of infection of the novel SARS-CoV-2 lineages

reported from UK and South Africa. However, these variants also have several other mutations in the S1 spike protein, in addition to the N501Y mutation.

These include deletion mutations Δ H69V70 and Δ Y144, and missense mutations A570D, P681H, T716I, S982A and D1118H in the B.1.1.7 lineage, for instance. Therefore, it would be ideal to determine the efficacy of vaccinated patient sera in inhibiting plaque formation by virus expressing S1 spike protein with all mutations in order to make the suggestion that the BNT162b2 vaccine is effective against the novel SARS-CoV-2 lineages.