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Authors' response

The author of the letter has stated that the doses used in the viral challenge studies are not uniform, which might explain the variation in data obtained from these studies. We agree that the inoculum dose for the virus challenge studies has not been uniform in the studies considered for the systematic review.

Sub-genomic RNA (sgRNA) has been considered as a marker of active replication of virus, but other factors such as virus clearance from tissues, IgG antibody titres post-vaccination, neutralizing antibody response, humoural- and cell-mediated immunity response, histopathology and immunohistochemistry response are also important factors in overall assessment of the immunogenicity and efficacy of vaccine candidates in non-human primates (NHP) studies. These factors have been brought out in our article. Since there are no standardized norms to the effect as to the volume of inoculum of virus to be used for SARS-CoV-2 challenge studies in NHP as per our knowledge and the investigators of the various pre-clinical trials mentioned in the review used doses as per their understanding, sgRNA cannot be considered as the only marker of immunogenicity and efficacy assessment of vaccine candidates.

The author has also commented on the lack of details of bronchoscopy in the review article and the lobes of lungs accessed during the procedure. Since no details about the bronchoscopy, volume of saline instilled before collection of bronchoalveolar lavage (BAL) fluid and the lobes of lungs accessed to collect the BAL fluid were mentioned in the NHP challenge studies, we did not include these factors in our review article. As highlighted earlier, we used the other factors to compare the immunogenicity and efficacy assessment of vaccine candidates. Again, we would like to state that in the absence of any standardized norms as to bronchoscopy and BAL fluid collection details in NHP challenge studies, these factors were not considered in our review article. The NHP challenge studies for the vaccine candidates ChAdOx1 nCoV-19[1] and BBV152[2] have done BAL fluid aspiration from multiple lung lobes (four lobes out of total of seven lobes) and have demonstrated the immunogenicity and efficacy. The access to all the lobes of lungs of NHP is not feasible due to the anatomical orientation of the bronchus and technical difficulties to access these lobes during bronchoscopy. Furthermore, the objective of the systematic review was to compare the protective efficacy of the vaccine candidates in NHP. Virus clearance from BAL fluid was not studied for four vaccine candidates that conducted virus challenge studies in NHPs: PiCoVacc[3], BBIBP-CorV[4], S-Trimer[5] and GX-19[6].

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References

1. van Doremalen N, Lambe T, Spencer A, Belij-Rammerstorfer S, Purushotham JN, Port JR, *et al*. ChAdOx1 nCoV-19 vaccination prevents SARS-CoV-2 pneumonia in rhesus macaques. *bioRxiv* 2020. doi: 10.1101/2020.05.13.093195.
2. Yadav P, Kumar S, Patil D, Mohandas S, Shete A, Bhati G, *et al*. Remarkable immunogenicity and protective efficacy of BBV152, an inactivated SARS-CoV-2 vaccine in Rhesus macaques. Available from: *https://www.researchsquare.com/article/rs-65715/v1*, accessed on October 29, 2020.
3. Gao Q, Bao L, Mao H, Wang L, Xu K, Yang M, *et al*. Development of an inactivated vaccine candidate for SARS- CoV-2. *Science* 2020; *369* : 77-81.
4. Wang H, Zhang Y, Huang B, Deng W, Quan Y, Wang W, *et al.* Development of an inactivated vaccine candidate, BBIBP-corV, with potent protection against SARS-CoV-2. *Cell* 2020; *182* : 713-21.
5. Liang JG, Su D, Song TZ, Zeng Y, Huang W, Wu J, *et al*. S-Trimer, a COVID-19 subunit vaccine candidate, induces protective immunity in nonhuman primates. *bioRxiv* 2020. doi: 10.1101/2020.09.24.311027.
6. Seo YB, Suh YS, Ryu JI, Jang H, Oh H, Koo BS, *et al*. Soluble spike DNA vaccine provides long-term protective immunity against SARS-CoV-2 in mice and nonhuman primates. *bioRxiv* 2020. doi: 10.1101/2020.10.09.334136.