Rapid Reviews COVID-19 •

Review 1: "Infectivity and immune escape of the new SARS-CoV-2 variant of interest Lambda"

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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 claims are strong given the data and the methods used. In this short manuscript, the authors test the escape of the Lambda SARS-CoV-2 variant from neutralization with plasma from healthcare workers vaccinated with two doses of the CoronaVac inactivated virus vaccine in Santiago, Chile. The authors make two claims: the mutations on the spike glycoprotein of the Lambda variant make it more infectious, and the spike mutations (and one deletion) mediate escape from CoronaVac-elicited neutralization.

These claims are based on a pseudo-neutralization assay (PNA) study design, where the authors made several observations. In the absence of vaccinated plasma, there is a greater luminescence signal per well of pseudovirus-infected cells, indicating more viruses entering each cell. In the presence of plasma, the Lambda variant is more poorly neutralized—about a 3-fold drop in neutralization capacity relative to their reference pseudovirus—with no spike mutations and more than the Gamma variant in their assay. A major strength of the work is that it is of immediate relevance—infections with Lambda are ramping up in South America and it is important to know why.

The higher infectivity data seems preliminary and should be verified using other systems (like live viruses). The fold-change for Gamma also seems to be low and may indicate low sensitivity in the assay due to technical factors. The Beta variant, which mediates strong neutralization escape, is most often used as a benchmark and would have provided a better comparison. Nevertheless, given the higher escape of the Lambda variant relative to Gamma in their system, the conclusion of the paper that this variant is effective at escaping vaccine-elicited neutralization is most likely correct.

As a side note, one of the mutations of Lambda, F490S, [was previously observed in a patient with advanced HIV](#) who had a prolonged SARS-CoV-2 infection—showing possible convergent evolution.