

CORRESPONDENCE

Serum Neutralizing Activity Elicited by mRNA-1273 Vaccine — Preliminary Report

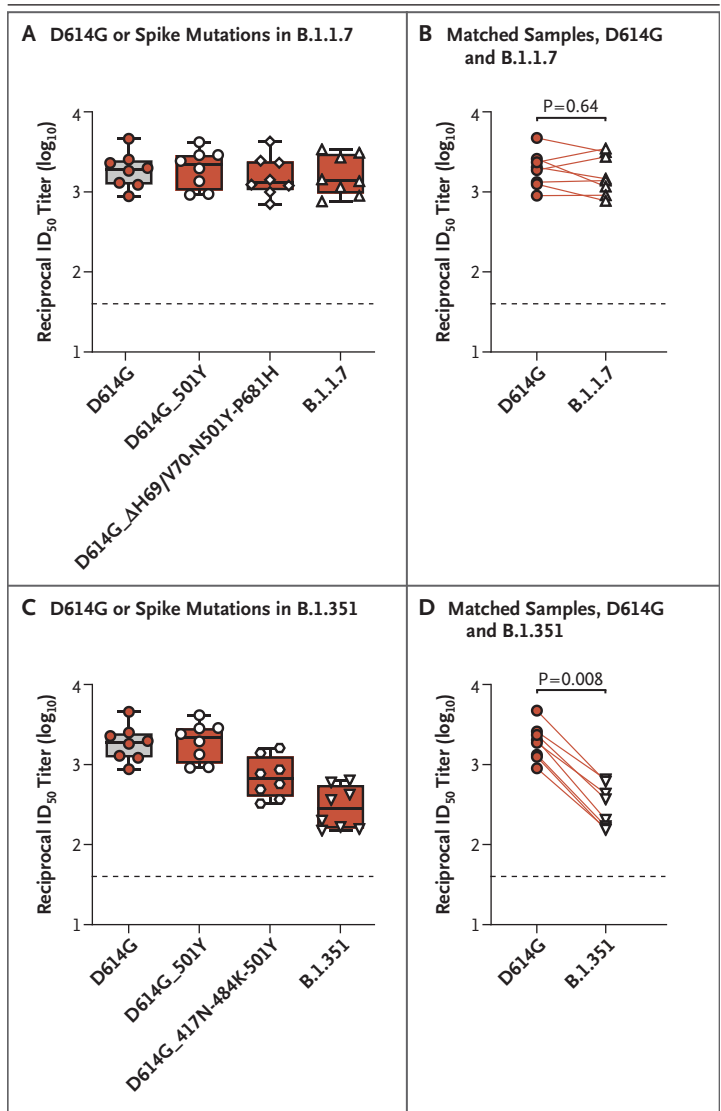
TO THE EDITOR: The mRNA-1273 vaccine against SARS-CoV-2 elicited high neutralizing-antibody titers in phase 1 trial participants^{1,2} and has been shown to be highly efficacious in preventing symptomatic Covid-19 disease and severe disease.³ The recent emergence of SARS-CoV-2 variants in the United Kingdom (the B.1.1.7 lineage) and in South Africa (the B.1.351 lineage) has led to concerns about increased transmission and the potential of these variants to circumvent immunity elicited by natural infection or vaccination.

We assayed the serum neutralizing activity against recombinant vesicular stomatitis virus (rVSV)-based SARS-CoV-2 (a pseudovirus-based

model) in specimens obtained from participants in the phase 1 trial of the mRNA-1273 vaccine. We tested pseudoviruses bearing the spike protein from the original Wuhan-Hu-1 isolate, the D614G variant, the B.1.1.7 and B.1.351 variants, and other variants (20E [EU1], 20A.EU2, N439K-

Figure 1. Neutralization of B.1.1.7 and B.1.351 SARS-CoV-2 Pseudoviruses in Serum Samples.

Serum samples obtained from participants who received the mRNA-1273 vaccine in a phase 1 trial were collected on day 36 (7 days after the participants received the second dose of the vaccine). Neutralization was measured with the use of a recombinant vesicular stomatitis virus (rVSV)-based pseudovirus neutralization assay that incorporated D614G or the indicated spike mutations present in the B.1.1.7 variant (Panels A and B) or the B.1.351 variant (Panels C and D). The red dots indicate the results from serum samples of the individual participants, the white dots, white diamonds, and white triangles the same samples tested against the variants shown on the x axis, and the horizontal dashed lines the lower limit of quantification. The reciprocal neutralizing titers on the pseudovirus neutralization assay at a 50% inhibitory dilution (ID_{50}) are shown. In Panels A and C, boxes and horizontal bars denote the interquartile range (IQR) and the median neutralizing titer, respectively. Whisker end points are equal to the maximum and minimum values below or above the median at 1.5 times the IQR. In Panels B and D, the lines connect the D614G and variant neutralization titers in matched samples. We detected reductions by a factor of 1.2 in titers of neutralizing antibodies against the B.1.1.7 variant (Panel B) and by a factor of 6.4 against the B.1.351 variant (Panel D). Statistical analysis of matched pairs was performed with the use of the Wilcoxon signed-rank test.



D614G, and the mink cluster 5 variant that was first identified in Denmark).

Both the full panel of mutations in S and a subset of mutations affecting the receptor-binding domain (RBD) region of the B.1.1.7 variant had no significant effect on neutralization by serum obtained from participants who had received the mRNA-1273 vaccine in the phase 1 trial (Fig. 1A and 1B). In contrast, we observed a decrease in titers of neutralizing antibodies against the B.1.351 variant and a subset of its mutations affecting the RBD. In serum samples obtained 1 week after the participants received the second dose of vaccine, we detected reductions by a factor of 2.7 in titers of neutralizing antibodies against the partial panel of mutations and by a factor of 6.4 against the full panel of mutations (Fig. 1C and 1D). However, in serum samples obtained from eight participants in the phase 1 trial, the geometric mean neutralizing titer against B.1.351 was 1:290, and all the serum samples neutralized the rVSV pseudovirus, albeit at relatively low dilutions (Fig. S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org). With the use of both rVSV and lentiviral neutralization assays, we observed a similar trend in serum samples obtained from macaque monkeys (Figs. S2 and S3).

We used an rVSV-based pseudovirus neutralization assay to assess the neutralizing activity of serum obtained from participants who had received the mRNA-1273 vaccine in the phase 1 trial against the full-length spike protein of the dominant strain in 2020 (D614G), as well as against 20E (EU1), 20A.EU2, N439K-D614G, and mink cluster 5 variants (Table S1). We observed levels of neutralization against these variants that were similar to those against the Wuhan-Hu-1 (D614) isolate (Fig. S4).

Protection against the B.1.351 variant conferred by the mRNA-1273 vaccine remains to be determined. Our findings underscore the importance of continued viral surveillance and evaluation of vaccine efficacy against new viral variants and may help to facilitate the establishment of correlates of protection in both nonhuman primates and humans.

Kai Wu, Ph.D.

Moderna
Cambridge, MA

Anne P. Werner, B.S.

National Institute of Allergy and Infectious Diseases
Bethesda, MD

Matthew Koch, B.S.

Angela Choi, Ph.D.

Elisabeth Narayanan, Ph.D.

Guillaume B.E. Stewart-Jones, Ph.D.

Tonya Colpitts, Ph.D.

Hamilton Bennett, M.S.

Moderna
Cambridge, MA

Seyhan Boyoglu-Barnum, Ph.D.

Wei Shi, Ph.D.

Juan I. Moliva, Ph.D.

Nancy J. Sullivan, Ph.D.

Barney S. Graham, M.D.

National Institute of Allergy and Infectious Diseases
Bethesda, MD

Andrea Carfi, Ph.D.

Moderna
Cambridge, MA

Kizzmekia S. Corbett, Ph.D.

Robert A. Seder, M.D.

National Institute of Allergy and Infectious Diseases
Bethesda, MD

Darin K. Edwards, Ph.D.

Moderna
Cambridge, MA
darin.edwards@modernatx.com

Dr. Wu and Ms. Werner and Drs. Seder and Edwards contributed equally to this letter.

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