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Real-time data are necessary to plan effective control measures should this outbreak grow further. The work builds on infrastructure developed for epidemic control and pandemic preparedness and was used for the COVID-19 pandemic.<sup>7</sup> Global efforts are needed to ensure similar efforts to rapidly harmonise and publish detailed epidemiological data are supported during future outbreaks of emerging and re-emerging pathogens. This example will be a learning pathway to build better surveillance systems globally.

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## Neutralisation sensitivity of SARS-CoV-2 omicron subvariants to therapeutic monoclonal antibodies

During the current pandemic, SARS-CoV-2 has considerably diversified. The omicron variant (B.1.1.529) was identified at the end of November, 2021, and rapidly spread worldwide. As of May, 2022, the omicron BA.2 subvariant is the most dominant variant in the world. Other omicron subvariants have since emerged and some of them have begun to outcompete BA.2 in multiple countries. For instance, omicron BA.2.11 subvariant is spreading in France, and the BA.2.12.1 and BA.4/5 subvariants are becoming dominant in the USA and South Africa, respectively (appendix pp 4–5).

Newly emerging SARS-CoV-2 variants need to be carefully monitored for a potential increase in transmission rate, pathogenicity, and resistance to immune responses. The resistance of variants to vaccines

and therapeutic antibodies can be attributed to a variety of mutations in the viral spike protein. Although the spike proteins of new omicron subvariants (BA.2.11, BA.2.12.1, and BA.4/5) are derived from the BA.2 spike protein, the majority of them additionally bear the following mutations in the spike: BA.2.11, L452R; BA.2.12.1, L452Q and S704L; and BA.4/5, L452R, HV69-70del, F486V, and R493Q (appendix pp 4–5). In particular, the L452R and L452Q substitutions were detected in the delta (B.1.617.2) and lambda (C.37) variants, respectively, and we demonstrated that the L452R/Q substitution affects sensitivity to vaccine-induced neutralising antibodies.<sup>1,2</sup> Therefore, it is reasonable to assume that these new omicron subvariants have reduced sensitivity to therapeutic monoclonal antibodies. To address this possibility, we generated pseudoviruses harbouring the spike proteins of these omicron subvariants and derivatives and prepared eight therapeutic monoclonal antibodies (appendix pp 2–3). Consistent with previous studies,<sup>3–5</sup> bamlanivimab, casirivimab, etesevimab, imdevimab, and tixagevimab were less functional against BA.2 than the parental virus (table). These five antibodies were also less functional against new omicron subvariants, whereas the BA.2 spike bearing the R493Q substitution was partially sensitive to casirivimab and tixagevimab (table; appendix pp 4–5). Bebtelovimab was approximately 2-fold more effective against BA.2 and all omicron subvariants tested than the parental virus (table). Although sotrovimab was roughly 20-fold less effective against BA.2 than the parental virus, the omicron subvariants bearing the L452R substitution, including BA.2.11 and BA.4/5, were more sensitive to sotrovimab than BA.2 (table). Evusheld (cilgavimab and tixagevimab), particularly cilgavimab, was effective against BA.2, whereas

See Online for appendix

	Bamlanivimab	Bebtelovimab	Casirivimab	Cilgavimab	Etesevimab	Imdevimab	Sotrovimab	Tixagevimab	Casirivimab plus imdevimab (Ronapreve)	Etesevimab plus bamlanivimab	Cilgavimab plus tixagevimab (Evusheld)
B.1.1 (parental)	12.8	8.1	9.9	21	12	79	94	6.7	6.2	6.7	4.1
BA.2	>3700	3.8	>50 417	19	>6050	>50 000	2190	>2750	>2400	>3700	33
BA.2.11	>3700	2.3	>50 417	71	>6050	>50 000	540	>2750	>2400	>3700	154
BA.2.12.1	>3700	5.5	>50 417	75	>6050	>50 000	629	>2750	>2400	>3700	135
BA.4/5	>3700	6.3	>50 417	443	>6050	>50 000	1261	>2750	>2400	>3700	609
BA.2 L452Q	>3700	5.0	>50 417	26	>6050	>50 000	2443	>2750	>2400	>3700	82
BA.2 S704L	>3700	1.1	>50 417	28	>6050	>50 000	1213	>2750	>2400	>3700	27
BA.2 HV69-70del	>3700	2.2	>50 417	19	>6050	>50 000	774	>2750	>2400	>3700	34
BA.2 F486V	>3700	1.1	>50 417	18	>6050	>50 000	1575	>2750	>2400	>3700	23
BA.2 R493Q	>3700	4.2	3697	22	>6050	>50 000	1791	101	431	>3700	31

Representative neutralisation curves are shown in appendix pp 4-5.

**Table: 50% neutralisation concentration (ng/mL)**

the L452R/Q substitution rendered approximately 2–5-fold resistance. Notably, BA.4/5 exhibited about 20-fold more resistance to cilgavimab and Evusheld than BA.2 (table). Recently, Cao and colleagues showed that the neutralising activity of cilgavimab against BA.4/5 is approximately 4-fold lower than that against BA.2.<sup>6</sup> Here, we used lentivirus-based pseudoviruses, whereas Cao and colleagues used vesicular stomatitis virus-based pseudoviruses.<sup>6</sup> Therefore, the disparity between our results and those of Cao and colleagues might be due to the difference in the type of pseudoviruses used in the neutralisation assay.

Since mutations are accumulated in the spike proteins of newly emerging SARS-CoV-2 variants, we suggest the importance of rapid evaluation of the efficiency of therapeutic monoclonal antibodies against novel SARS-CoV-2 variants.

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## Immune responses after omicron infection in triple-vaccinated health-care workers with and without previous SARS-CoV-2 infection



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The SARS-CoV-2 omicron variant (B.1.1.529) is less sensitive to neutralising antibody responses induced by vaccination and prior infection than previous variants.<sup>1,2</sup> Less is known regarding omicron-induced serological and T-cell responses after breakthrough infection of vaccinated individuals with and without prior infection.

In this prospective cohort study, we analysed serological and T-cell responses following omicron infection in 56 triple-vaccinated health-care workers in Sweden with and without prior SARS-CoV-2 infection. A surrogate virus neutralisation test (sVNT) was used to assess neutralisation of SARS-CoV-2 variants. Immune responses of all participants had been