Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

sublineages. Geometric mean titres against BA.2.75 after the BA.1 and BA.2 infection wave were more than 7 times those of sera sampled before the wave of infections (appendix p 6), probably reflecting a combined contribution of BA.1 and BA.2 infections, as well as third-dose booster vaccine rollout, with coverage in Stockholm expanding among people aged 18 years or older from 5% during Nov 8–14, 2021, to 59% during April 11–17, 2022 (appendix p 3). During April 11–17, 2022, titres against BA.2.75 were slightly but significantly lower than those against BA.2, and similar to those against BA.5. The relative sensitivity of BA.2.75 in these cohorts of blood donors is largely concordant with those seen in vaccinated individuals (CoronaVac; Sinovac Life Sciences, Beijing, China) with and without BA.1 or BA.2 breakthrough infection.[7]

See Online for appendix

As infection histories become more complex, and a large proportion of infections go undetected, monitoring of population-level immunity from random samples is increasingly crucial for understanding and contextualising the immune evasion properties of new SARS-CoV-2 variants. Here we show that the emerging sublineage, BA.2.75, does not show greater antibody evasion than the currently dominating BA.5 variant in a set of random samples from Stockholm. BA.2.75 largely maintains sensitivity to bebtelovimab despite a slight reduction in potency, and exhibits moderate susceptibility to tixagevimab and cilgavimab.

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Neutralisation sensitivity of the SARS-CoV-2 omicron BA.2.75 sublineage

After its first identification in a sample collected at the end of May, 2022, genomic surveillance revealed a rapid increase of the omicron BA.2.75 sublineage to more than 30% of sequenced SARS-CoV-2 infections in India by mid-July, 2022.[1] Moreover, cases of BA.2.75 infections have been reported in numerous countries globally.[1] Accordingly, on July 15, 2022, the European Centre for Disease Prevention and Control elevated the BA.2.75 sublineage to a variant of interest. Compared with the parental BA.2 lineage of SARS-CoV-2, the spike protein of BA.2.75 differs in nine amino acid residues in the N-terminal domain (K147E, W152R, F157L, I210V, and G257S) and the receptor binding domain (D339H, G446S, N460K, and R493Q; appendix p 2). By affecting crucial epitopes, mutations in these domains can confer a growth advantage through reduced susceptibility to SARS-CoV-2 neutralising antibodies.[2] To investigate antibody sensitivity of BA.2.75 in comparison with prevalent omicron sublineages, we performed neutralisation assays using pseudoviruses expressing the B.1 (D614G), BA.2, BA.4/5, BA.2.12.1, or BA.2.75 spike proteins.

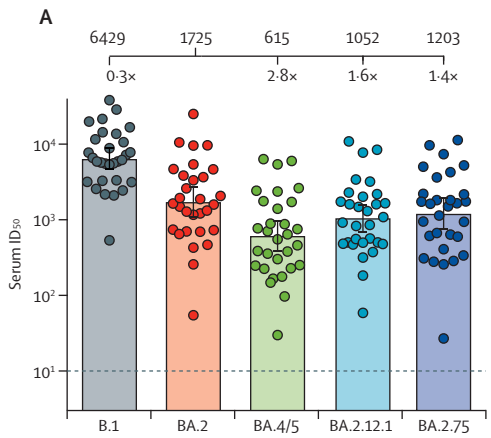
First, we determined 50% inhibitory dilutions (ID_{50}) in serum samples collected 4 weeks after administration of a BNT162b2 vaccine booster dose in a cohort of 30 health-care workers and older individuals (aged >70 years; appendix pp 5–6). All individuals had received three BNT162b2 doses, and no intermittent SARS-CoV-2 infections were reported. Although the neutralising activity against omicron sublineages was considerably lower than that against B.1, the differences between individual omicron sublineages were more subtle (figure A; appendix p 3). Serum activity against BA.2.75 was significantly lower than that against BA.2 (p=0·0145) but higher than the serum activity against BA.4/5 (p=0·0329; appendix p 3).

Next, we investigated the activity of 17 monoclonal antibodies conditionally authorised for use against COVID-19 or in advanced stages of clinical investigation by determining their 50% inhibitory concentrations (IC_{50}). Most antibodies did not neutralise BA.2, BA.4/5, or BA.2.12.1 (IC_{50} >10 μg/mL). However, several of these antibodies showed appreciable activity against BA.2.75 (figure B; appendix p 4). For example, tixagevimab and regdanvimab, authorised for COVID-19 prevention

and treatment (in South Korea), showed no or only poor activity against any of the other tested omicron sublineages but potently neutralised BA.2.75 (IC_{50} ≤0·04 µg/mL). Similar to the activity shown for all other omicron sublineages, bebtelovimab also showed high BA.2.75 neutralising potency (IC_{50} 0·007 µg/mL; figure B), although this activity was lower than that against the other variants (appendix p 4). Although only 29–35% of the tested antibodies neutralised BA.2, BA.4/5, or BA.2.12.1, activity against BA.2.75 was detected for 59% of antibodies.

Variants of SARS-CoV-2 with reduced sensitivity to neutralising antibodies can pose a challenge to immunity induced by vaccination or infection and can render therapeutic monoclonal antibodies ineffective.[3–6] Our results suggest that the mutations in the spike protein of the BA.2.75 sublineage decrease susceptibility to vaccine-induced neutralising activity compared with BA.2, albeit to a lesser extent than the mutations present in BA.4/5. Moreover, BA.2.75 showed an overall higher sensitivity to SARS-CoV-2 neutralising monoclonal antibodies in advanced development, including antibodies currently in clinical use. Although our analysis of vaccinee sera was limited to a single post-booster timepoint, our results and those of others suggest that antibody escape is an overall less pronounced characteristic of BA.2.75 compared with BA.4/5.[7–9] Thus, additional features favouring viral expansion beyond vaccine escape might be required for BA.2.75 to gain a growth advantage over BA.4/5.

HG, KV, and FKl are listed as inventors on patent applications on SARS-CoV-2 neutralising antibodies filed by the University of Cologne (Cologne, Germany). HG and FKl received payments from the University of Cologne for licensed antibodies. All other authors declare no competing interests.



B

Antibody	IC_{50} (µg/ml)				
	B.1	BA.2	BA.4/5	BA.2.12.1	BA.2.75
Bamlanivimab	<0·005	>10	>10	>10	>10
Etesevimab	0·030	>10	>10	>10	>10
Bebtelovimab*	0·001	0·001	0·001	0·001	0·007
Imdevimab	<0·005	2·001	2·438	4·484	>10
Casirivimab	<0·005	>10	>10	>10	1·167
Sotrovimab	0·028	2·118	4·309	4·671	0·655
Tixagevimab*	<0·005	>10	>10	8·612	0·017
Cilgavimab*	<0·005	0·008	0·094	0·017	0·095
Regdanvimab*	<0·005	>10	>10	>10	0·040
DZIF-10c	<0·005	0·016	>10	0·133	0·017
BRII-196*	0·009	>10	1·160	3·610	4·323
COV2-2381*	0·008	>10	>10	>10	1·181
MAD0004J08*	<0·005	>10	>10	>10	0·336
ADG-2*	<0·005	>10	>10	>10	>10
C135*	<0·005	>10	>10	>10	>10
C144*	<0·005	>10	>10	>10	>10
BD-368-2*	<0·005	>10	>10	>10	>10

* Fc-unmodified IgG1 antibody

Figure: **Neutralisation sensitivity of the BA.2.75 sublineage**
(A) ID_{50} against SARS-CoV-2 variants in serum samples collected 4 weeks after a BNT162b2 booster, determined in a lentivirus-based pseudovirus neutralisation assay. Circles indicate mean ID_{50} of two experiments for each variant and individual participant. Bars and upper numbers indicate geometric mean ID_{50}, and lower numbers indicate geometric mean ID_{50} fold-difference relative to BA.2. Solid lines show 95% CIs and the dashed line shows the lower limit of quantification. Statistical analyses are detailed in the appendix (p 3). (B) IC_{50} of monoclonal antibodies against SARS-CoV-2 variants, determined in a lentivirus-based pseudovirus neutralisation assay (mean IC_{50} of two experiments for each variant). IC_{50}=50% inhibitory concentration. ID_{50}=50% inhibitory dilution.

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