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## Sotrovimab drives SARS-CoV-2 omicron variant evolution in immunocompromised patients

Sotrovimab is a monoclonal antibody used as monotherapy in outpatients at risk of developing severe COVID-19 disease. Indications include patients with respiratory, cardiac, metabolic, and immunosuppression comorbidities. Rockett and colleagues[1] have shown that, among 100 patients infected with the delta (B.1.617.2) variant and treated with sotrovimab monotherapy, four were immunocompromised and rapidly developed resistant mutations in the spike protein at positions 337 or 340, or both. These mutations are associated with prolonged excretion and in-vitro resistance.[1,2] Given that sotrovimab is one of the few monoclonal antibodies that retains efficacy against the widely circulating omicron BA.1 sublineage, monitoring the prevalence of these mutations is crucial.[3] As part of routine genomic surveillance at the French National Reference Center for respiratory Viruses at the Hospices Civils de Lyon (Lyon, France) from December, 2021, to March, 2022,[4] we detected mutations in the spike protein at positions 340 and 337 in 24 (0·13%) of 18 882 omicron BA.1 lineages and in one (0·02%) of 4025 omicron BA.2 lineages. These 25 samples corresponded to 18 patients infected with SARS-CoV-2 variants carrying either P337 or E340 mutations (appendix p 5). Clinical data were available for eight patients, all of whom were immunocompromised and had been treated with sotrovimab at 0–10 days after symptoms onset (appendix pp 6–7). For six patients with a follow-up, mutations at positions 337 and 340 were absent before sotrovimab infusion and were detected at low relative frequency or high relative frequency (6–100%) at 5–18 days after sotrovimab infusion. Selection of resistant viral escape variants was associated with persistent SARS-CoV-2 excretion for up to 43 days, except for one patient who cleared their infection after convalescent plasma infusion at day 24 (appendix p 4). These results suggest that sotrovimab can rapidly select mutations at positions 337 and 340 in BA.1 and BA.2 sublineages (although in-vitro findings suggest that neutralisation is not effective against the BA.2 sublineage[3]). These mutations rarely emerge in the omicron variant (2756 [0·03%] of all 10 042 757 omicron sequences reported on the GISAID database; appendix p 8). Notably, these mutations have been exclusively reported after sotrovimab treatment in immunocompromised patients (by Rockett and colleagues[1] and in this Correspondence). As previously reported for patients treated with bamlanivimab,[5] we urge to consider monoclonal antibody as monotherapy in immunocompromised patients as a risk for escape mutant selection that might hamper viral clearance. Immunocompromised patients treated with monoclonal antibodies should benefit from a reinforced virological follow-up, including viral sequencing and viral load assessment.

GD, AB, and BS contributed equally. We declare no competing interests.



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See **Online** for appendix