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Omicron overpowers key COVID antibody treatments in early tests

Nearly all of the monoclonal antibodies used to prevent severe disease fail to stand up to the new variant, laboratory assays show.

Max Kozlov

A nurse in Boston, Massachusetts, gives a dose of the monoclonal antibody bamlanivimab to a man with COVID-19. Credit: Craig F. Walker/The Boston Globe/Getty

Strained hospitals bracing for a COVID-19 surge caused by the quickly spreading Omicron variant could face another grim possibility: preliminary experiments

suggest that most of the antibody treatments for the disease are powerless against Omicron[1,2,3,4].

Doctors use artificial versions of natural antibodies to stave off severe COVID-19 in high-risk people who are infected with the coronavirus. But a slew of publications posted on preprint servers report laboratory evidence that Omicron is totally or partially resistant to all currently available treatments based on these monoclonal antibodies. The publications have not yet been peer reviewed, but some of the companies that manufacture antibody therapies already concede that their products have lower potency against Omicron than against other variants.

The preprints report that only two antibodies show strong evidence of retaining some ability to thwart the variant: sotrovimab, developed by Vir Biotechnology in San Francisco, California, and GSK, headquartered in London; and DXP-604, which is undergoing clinical trials in China and was developed by BeiGene and Singlomics, both based in Beijing.

These findings are already affecting health-care policy. US health officials have said they will ration sotrovimab, allotting it to states on the basis of numbers of infections and hospitalizations and the prevalence of Omicron. But many countries either can't meet the impending demand for sotrovimab or can't access it at all, which will increase the burden for an "already stressed health-care system", says Rajesh Gandhi, an infectious-disease physician at Massachusetts General Hospital in Boston.

A last defence

Some monoclonal-antibody treatments for COVID-19 consist of a single antibody; others of a cocktail of several. The details differ, but all of the monoclonal antibodies against SARS-CoV-2 bind to the virus's spike protein, preventing the virus from infecting human cells. The treatments reduce the risk of severe COVID-19 by up to 85%.

But when virologists saw that Omicron has a multitude of mutations concentrated on its spike protein, they feared what it would mean for these treatments. The outcome was even worse than they anticipated, says Olivier Schwartz, a virologist at the Pasteur Institute in Paris and a co-author of one of the preprints[3]. "We didn't expect to see such a shift in the antibodies' effectiveness," he says.

To test the treatments' powers against Omicron, researchers combined either live SARS-CoV-2 or artificial 'pseudoviruses' that have traits of the actual pathogen with varying concentrations of each antibody treatment. They then pitted the antibody–virus combination against cells that express ACE2, the receptor that the virus uses to gain entry to human cells.

Researchers then identified the concentration of each treatment that would cut viral replication in half, as measured by the number of infected cells. Most of the drugs couldn't reach that threshold, even at an extremely high concentration. The antibodies made by Regeneron Pharmaceuticals in Tarrytown, New York, for example, "have diminished potency against Omicron", the company conceded in a 16 December statement.

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Sotrovimab is the best of the lot. Even so, the concentration required to halve viral replication was roughly three times higher for Omicron than for other coronavirus variants. Although sotrovimab's drop in potency against the new variant is significant, says Stuart Turville, a virologist at the Kirby Institute in Sydney, Australia, and a co-author of one of the preprints[2], "it's nothing like what we saw for the others". That might be because sotrovimab targets a part of the spike protein that is unchanged across many related coronaviruses.

Some of the studies found that two antibodies developed by AstraZeneca in Cambridge, UK, retained some neutralization power — although it was significantly

diminished[2,3,4]. Schwartz adds that it's important to complement the neutralization data with actual clinical data to confirm the findings.

Beyond antibodies

Scientists are racing to determine exactly how severe Omicron infections are, compared with infections caused by other variants, such as Delta. But if the antibody arsenal is wiped out, physicians will be without a key tool to prevent severe disease. "If Omicron bites hard, it'll be a recipe for disaster," says Turville.

Gandhi says that this calls for an expedited review and production of oral antiviral drugs such as Paxlovid (nirmatrelvir and ritonavir) and molnupiravir, which are expected to be effective against Omicron because of their mechanism of action, and which are cheaper than antibody treatments. Paxlovid manufacturer Pfizer, based in New York City, reported on 14 December that the antiviral was 89% effective at preventing hospitalization and death in high-risk patients when administered soon after symptoms began.

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Another challenge will be to discern whether an individual is infected with Delta or Omicron, says Gandhi, because that will determine which treatments are most likely to be effective. Ideally, physicians would have access to a quick test to identify the variant. But without such a tool, he says, they will have to rely on Omicron's prevalence in their local community to make that decision.

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