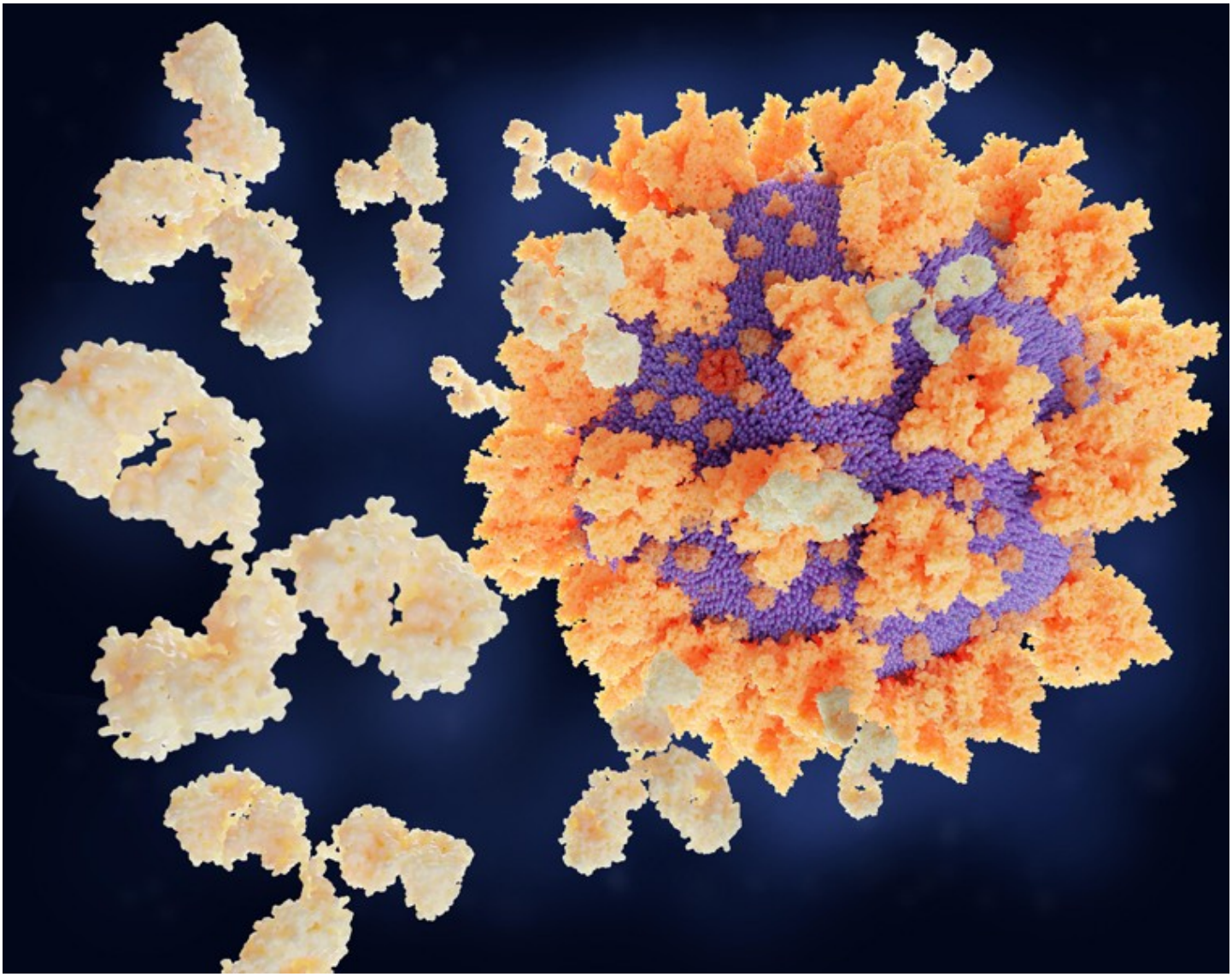
NEWS · 12 MARCH 2021

COVID antibody treatments show promise for preventing severe disease

But uptake by patients and physicians has been low in the United States, where some therapies have been authorized for months.

Heidi Ledford



Antibodies attacking a coronavirus particle (illustration). Credit: Juan Gaertner/SPL/Alamy

Two clinical trials suggest that specific antibody treatments can prevent deaths and hospitalizations among people with mild or moderate COVID-19 — particularly those who are at high risk of developing severe disease.

One study found that an antibody against the coronavirus developed by Vir Biotechnology in San Francisco, California, and GSK, headquartered in London, reduced the chances of hospitalization or death among participants by 85%. In another trial, a cocktail of two antibodies — bamlanivimab and etesevimab, both made by Eli Lilly of Indianapolis, Indiana — cut the risk of hospitalization and death by 87%.

The study results, both announced on 10 March, come from randomized, placebo-controlled, double-blind clinical trials, but have not yet been published. They add to a growing body of evidence that the treatments can help fend off severe disease when administered early, says Derek Angus, an intensive-care physician at the University of Pittsburgh in Pennsylvania.

The antibodies “appear to be incredibly effective”, he says. “I’m very excited about the results of these trials.”

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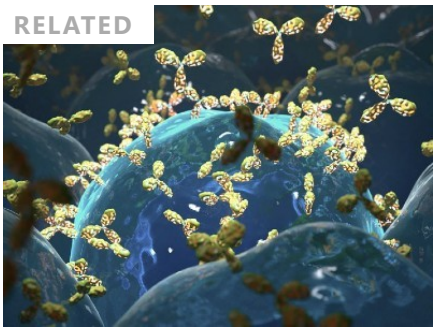

Antibody therapies could be a bridge to a coronavirus vaccine — but will the world benefit?

The body’s natural response to viral infection is to generate a variety of antibodies, some of which are able to directly interfere with the virus’s ability to replicate. In the early days of the pandemic, researchers raced to identify the antibodies that are most effective against the coronavirus and to produce them in bulk. The resulting ‘monoclonal antibodies’ have since been tested in a variety of settings as treatments for COVID-19.

Vir and GSK’s antibody, called VIR-7831, was first isolated in 2003 from someone recovering from severe acute respiratory syndrome (SARS), which is caused by a similar coronavirus. The antibody was later found to bind to the SARS-CoV-2 ‘spike’ protein, too.

The companies also announced that in laboratory studies[1], VIR-7831 bound to SARS-CoV-2 variants — including the fast-spreading 501Y.V2 variant (also called B.1.351) first identified in South Africa. They attributed the resilience of the antibody to its target: a particular region of the spike protein that does not tend to accumulate mutations.

Low uptake

VIR-7831 joins a list of monoclonal antibodies that have been tested against COVID-19, some of which — including Lilly’s combination — have already been authorized for use in the United States and elsewhere. But there has been relatively little uptake by US physicians and their patients, says Angus.

One problem, he says, is that although results have been press released and submitted to the US Food and Drug Administration, companies have yet to publish data from key clinical trials in peer-reviewed journals. The drugs are also expensive and must be administered by infusion in a specialized facility, such as a hospital or outpatient-treatment centre — a difficult task when medical resources have already been stretched by a surge in cases.

Another challenge has been mixed messaging. Earlier in the pandemic, some key clinical trials involving people who had been hospitalized with COVID-19 found no benefit from monoclonal antibodies. Many researchers had anticipated that result: monoclonal-antibody therapy is expected to work best early in disease, and the late-stage symptoms of severe COVID-19 are sometimes driven more by the immune system itself than by the virus.

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Even so, those clinical-trial failures created a narrative that competed with positive results in studies of milder infections, says Angus, fuelling scepticism. “People would say, ‘But I thought it didn’t work,’” he says. “It’s totally getting in the way.”

And although studies in mild infections have shown promise, they are too small to allow researchers to draw definitive conclusions, says Saye Khoo, a pharmacologist at the University of Liverpool, UK, who is leading the UK AGILE Coronavirus Drug Testing Initiative. Only a small fraction of people with mild COVID-19 will progress to severe disease, meaning that although the trials have enrolled hundreds of participants, the number of those who were hospitalized or died was low.

But it will be a long wait until everyone is vaccinated, and monoclonal antibodies could provide an important bridge between vaccines and the treatments that have been found for people who are hospitalized, says Jens Lundgren, an infectious-disease physician at the University of Copenhagen and Rigshospitalet. “It is not a replacement for vaccines, but it is a plan B,” he says, adding that the drugs could be particularly important for those who cannot mount an immune response to vaccination.

The speed with which these monoclonal antibodies were developed holds a lesson for future pandemics, says Khoo. “These compounds are without a doubt exciting,” he says. “We shouldn’t forget this, because there will be other pandemics coming to us. This has been a real lesson in how to be prepared.”

doi: https://doi.org/10.1038/d41586-021-00650-7

References

1. Cathcart, A. L. *et al.* Preprint at bioRxiv https://doi.org/10.1101/2021.03.09.434607 (2021).

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Nature | ISSN 1476-4687 (online)