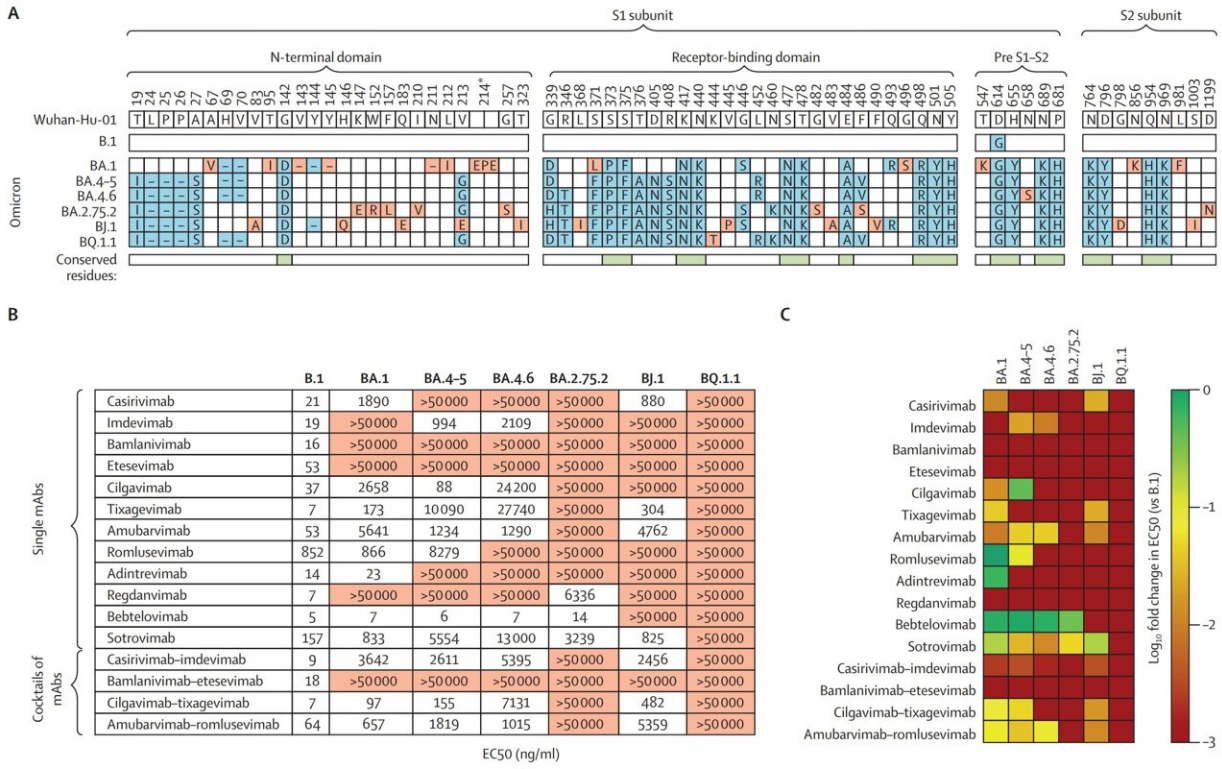
Omicron variant BQ.1.1 found to be resistant to all monoclonal antibody treatments

November 22 2022, by Bob Yirka



Extensive resistance of Omicron sublineage B.Q.1.1 to neutralization by mAbs (A) Location of mutations (blue and red) in the spike proteins of SARS-CoV-2 lineages B.1, BA.1, and BA.4–5 (which are identical at the amino acid level), BA.4.6, BA.2.75.2, BJ.1, and BQ.1.1 (numbered according to the spike protein of SARS-CoV-2 Wuhan-Hu-01). Mutations that are unique to only one of the Omicron sublineages are highlighted in red and conserved mutations among Omicron sublineages are indicated beneath the sequences in green. (B) Pseudovirus particles carrying the indicated S proteins were preincubated with different concentrations of single mAbs or cocktails of mAbs, before being

inoculated onto Vero cells. Pseudovirus entry was analyzed at 16–18 h post-inoculation, by measuring firefly luciferase activity in cell lysates, and was normalized against samples without any antibodies (0% inhibition). The EC50 was calculated by use of a non-linear regression model. Data represent the mean of three biological replicates (performed with four technical replicates). For additional information see the appendix (p 12). (C) Heatmap indicating the fold change in EC50 compared with B.1 pseudovirus particles. EC50=the concentration required for 50% of maximum inhibition. mAbs=monoclonal antibodies. Pre S1–S2=the domain between the receptor-binding domain and the S1–S2 cleavage site. S=spike. *The BA.1 spike protein contains a unique insertion at position 214 (EPE). Credit: *The Lancet Infectious Diseases* (2022). DOI: 10.1016/S1473-3099(22)00733-2

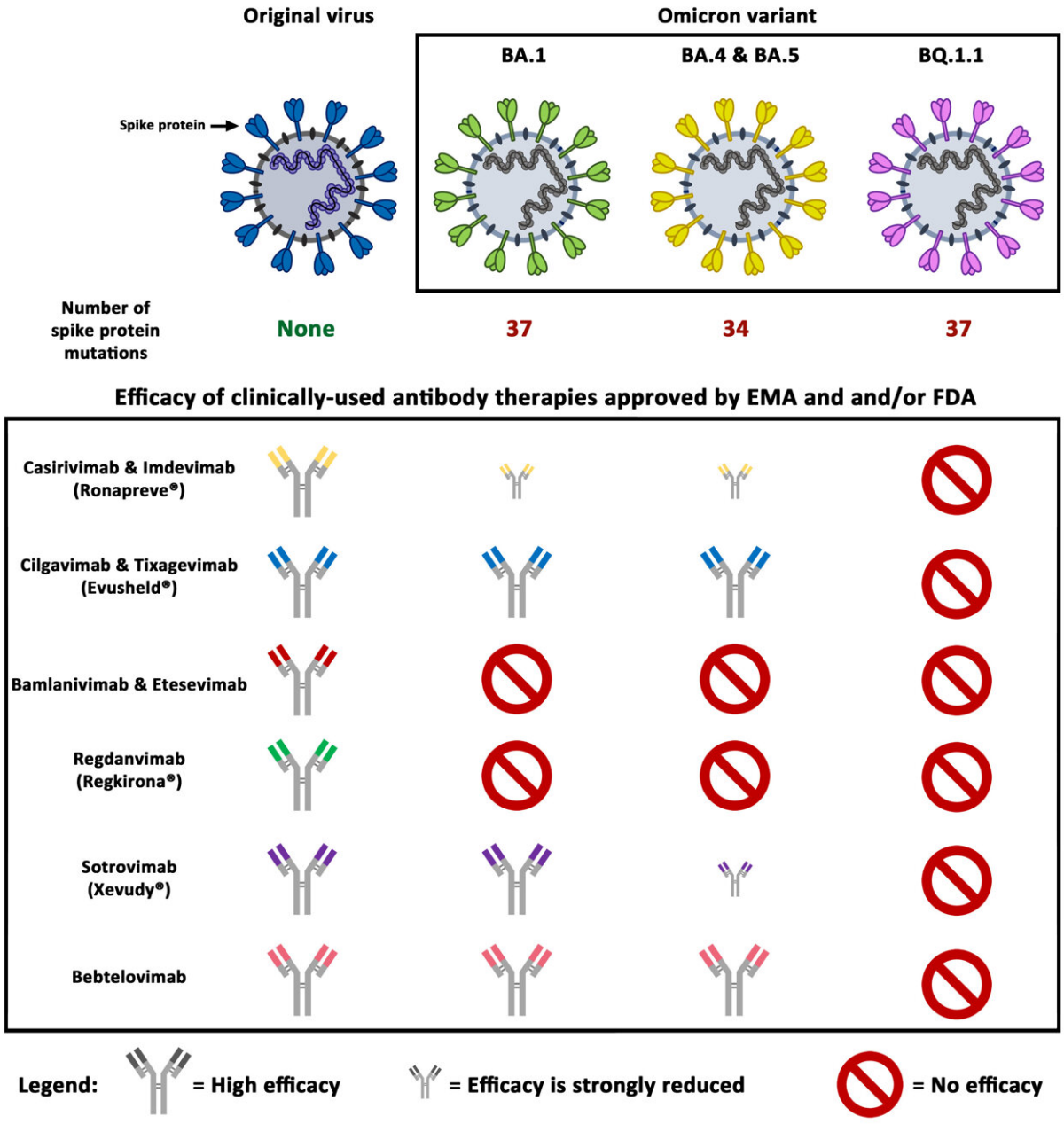
A combined team of researchers from Leibniz Institute for Primate Research and Friedrich-Alexander University of Erlangen-Nürnberg, both in Germany, has found that the SARS-CoV-2 omicron variant BQ.1.1 is resistant to all known monoclonal antibody treatments. In their study, published in *The Lancet—Infectious Diseases*, the group tested a host of omicron sublineages against all known antibody treatments.

Monoclonal antibody treatments, as their name suggests, are therapies that prompt antibody production in people already infected with a pathogen. As the pandemic has worn on, medical researchers have continually searched for new monoclonal antibody treatments to fight off future variants of the virus. But now, it seems researchers are losing that race. In this new effort, the researchers looked at COVID-19 variants and the effectiveness of monoclonal antibody treatments used to combat them.

In their work, the researchers looked at BJ.1, BA.4.6, BA.2.75.2 and BQ.1.1—all subvariants of the omicron strain of the SARS-CoV-2 virus. They tested each against all of the currently available monoclonal

antibody treatments to see how well the treatments are working. They found that all of the variants were resistant to some of the treatments and that BQ.1.1 was resistant to all of them.

The finding is alarming in one respect—BQ.1.1, along with BQ.1, currently comprise nearly half of all infections in the U.S. The good news is that because of the multi-pronged attack the medical community has taken against the virus, together with large numbers of people infected, overall numbers of infections are low.



The Omicron subvariants BA.1, BA.4, BA.5 as well as Q.1.1 have a high number of mutations in the spike protein. Some of these mutations are escape mutations that allow the virus to escape neutralization by antibodies. In addition, resistance to biotechnologically produced antibodies, which are administered to high-risk patients as a preventive measure or as therapy for a diagnosed SARS-CoV-2 infection, is also developing. Omicron sub-lineage BQ.1.1 is the first variant resistant to all antibody therapies currently approved by the EMA (European

Medicines Agency) and/or FDA (US Food and Drug Administration). Credit: Markus Hoffmann, Deutsches Primatenzentrum

Also, monoclonal antibody treatments are typically only given to infected people with underlying conditions that are believed to be at great risk of serious complications from the disease. On the other hand, because of the unpredictable nature of the virus, no one really knows what this new development might mean for the progression of the pandemic—except for those unlucky people with underlying conditions who, in the near future, happen to catch the BQ1.1. version of COVID-19.

More information: Prerna Arora et al, Omicron sublineage BQ.1.1 resistance to monoclonal antibodies, *The Lancet Infectious Diseases* (2022). DOI: 10.1016/S1473-3099(22)00733-2