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A monoclonal antibody stands out against omicron subvariants: a call to action for a wider access to bebtelovimab

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We read with great interest the Correspondence by Daichi Yamasoba and colleagues,¹ which highlighted the efficacy of all commercially-available monoclonal antibodies against dominant omicron subvariants. In this Correspondence, similar to others,² one monoclonal antibody stands out, namely, bebtelovimab. Among all available monoclonal antibodies, bebtelovimab is the only one that has shown remarkably preserved in vitro activity against all SARS-CoV-2 variants, including the omicron variant and the most recent BA.4 and BA.5 subvariants that are now becoming dominant.

Bebtelovimab (175 mg dosage), which is licensed by Eli Lilly, is a neutralising immunoglobulin (Ig)-G1 monoclonal antibody targeting the spike protein of SARS-CoV-2. Bebtelovimab received emergency-use authorisation from the United States Food and Drug Administration in February 2022, for early therapy

against mild-to-moderate COVID-19 in high-risk adults and in children older than 12 years. Authorisation was based on the results of the phase 2 BLAZE-4 trial³ and bebtelovimab's shown activity against omicron subvariants.⁴ Of note, there are still no phase 3 data available (clinicaltrials.gov NCT04634409).

Despite bebtelovimab's crucial interest related to COVID-19 treatment strategy, as a single intravenous dose administered in 30 s with no drug-drug interactions, it has not been submitted to regulatory authorities anywhere outside the USA, either for clinical care or for research purposes. However, Eli Lilly has just decided to supply an additional 150 000 doses of bebtelovimab solely to the US Government.⁵

Bebtelovimab would be an important antiviral globally, especially when nirmatrelvir boosted ritonavir, a major oral direct anti-SARS-CoV-2 drug with conserved efficacy against all omicron variants but with many drug-drug interactions, is contraindicated. Remdesivir has proven efficacy as early treatment but currently requires 3 days of intravenous administration, which limits its use in outpatients. Molnupiravir has not been recommended in international guidelines, or is only recommended when no other treatment options exist due to questions regarding its efficacy and safety. Other currently commercially-available monoclonal antibodies have decreased in vitro activity against new variants.^{1,2}

Beneficence is one of the basic principles of health-care ethics and should be respected by all actors in the health arena, including by those entities who develop therapeutic options. Here, we advocate that bebtelovimab should be made available outside the USA for patients worldwide. Bebtelovimab should be evaluated against current predominant

variants in clinical independent research, alone or in combination with other antiviral options, and should be used for clinical care when no other therapeutic options exist, especially in immunocompromised populations.

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- 5 Lilly Investors. Lilly will supply an additional 150,000 doses of bebtelovimab to U.S. government in ongoing effort to provide COVID-19 treatment options. <https://investor.lilly.com/news-releases/news-release-details/lilly-will-supply-additional-150000-doses-bebtelovimab-us> (accessed July 5, 2022).