

Research team demonstrates rapid clearance of culturable SARS-CoV-2 following monoclonal antibody treatment

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The AIDS Clinical Trials Group (ACTG), the largest global HIV research network, which expanded to conduct research into COVID-19,

today announced the publication of "Monoclonal Antibody Treatment Drives Rapid Culture Conversion in SARS-CoV-2 Infection," in the journal *Cell Reports Medicine*. The publication reports on findings from the ACTIV-2/A5401 study of Outpatient Monoclonal Antibodies and Other Therapies, and found that treatment with the monoclonal antibody bamlanivimab led to a rapid clearance in culturable virus from the nose that was far faster than the decline in viral RNA levels. While bamlanivimab is not currently in clinical use, the identical mechanisms of action of all clinically used SARS-CoV-2-targeting monoclonal antibodies make it likely that these findings will translate to other monoclonal antibodies.

Bamlanivimab is a neutralizing monoclonal antibody that received an Emergency Use Authorization (EUA) as a treatment for people with mild to moderate COVID-19 in November 2020. Lilly voluntarily asked the Food and Drug Administration to revoke the EUA for bamlanivimab 700 mg alone in April 2021 due to reduced activity against circulating variants (there were no new safety concerns).

This publication reports on a study that included viral culture analysis of participants enrolled in the ACTIV-2 randomized placebo-controlled trial of bamlanivimab monotherapy for adults with mild to moderate COVID-19 who were not hospitalized, to understand how monoclonal antibody treatment impacts the dynamics of shedding culturable SARS-CoV-2, a potential marker of SARS-CoV-2 infectivity.

"These findings may provide important insights into the impact of [monoclonal antibodies](#) on SARS-CoV-2 transmission," said ACTG Chair Judith Currier, M.D., M.Sc., University of California, Los Angeles.

"Within 24 hours of monoclonal antibody treatment, culture-positive virus could not be detected in any of the treated participants. This suggests that viral culture could be a more sensitive marker of monoclonal antibody activity than viral RNA levels."

The publication reports on 69 participants, 39 in the placebo arm and 30 in the bamlanivimab arm. Baseline participant characteristics, including age, race, comorbidities, days of symptoms before enrollment, and serostatus were similar between groups. Participants received either placebo or bamlanivimab on day zero of the study. Anterior nasal sample SARS CoV-2 RNA levels were assessed prior to treatment and one, two, three, and seven days after treatment. Shedding of culturable virus was assessed at the same timepoints for all samples with viral loads greater than $2 \log_{10}$.

One day after treatment, while the anterior nasal sample viral RNA levels were similar between participants receiving bamlanvimab or placebo, a significant difference in culture positivity was observed: The culture positivity rate in the placebo arm was 41 percent compared to zero in the bamlanivimab arm. Two days after treatment, 18 percent of participants in the placebo arm were still culture-positive; three days after treatment, 22 percent of placebo participants remained culture-positive; and seven days after treatment one placebo participant remained culture-positive. All bamlanivimab-treated participants without bamlanivimab-resistant virus remained culture-negative from day one onward.

The study also found that individuals with emerging drug resistance to bamlanivimab had rebound of culturable virus, highlighting the fact that individuals with symptom rebound after monoclonal antibody treatment should re-isolate, as they might be infectious again, and possibly with virus containing new monoclonal antibody-resistant mutations, although the association between symptom rebound and return of culturable virus was not assessed in this study.

"These data suggest that monoclonal antibodies may have an additional role beyond treatment of the individual, to include reducing the risk of secondary transmission," said Jonathan Z. Li, M.D., Brigham and

Women's Hospital and Harvard Medical School, Co-Chair of this sub-study.

His co-chair, Amy K. Barczak, M.D., Massachusetts General Hospital and Harvard Medical School, continued, "As such, the findings raise the question of whether we should consider reduced forward transmission as a goal of monoclonal antibody treatment and if so, what endpoints might be useful in determining how [therapies](#) impact the duration of infectiousness."

ACTIV-2 is a randomized, blinded, controlled adaptive platform that allows promising therapies to be added and removed over the course of the study to efficiently test a variety of new agents against placebo within the same trial infrastructure.

This substudy was led by Dr. Li and Dr. Barczak. ACTIV-2 is led by Kara W. Chew, M.D., M.S., UCLA and Davey Smith, M.D., University of California, San Diego (protocol chairs) and David Alain Wohl, M.D., University of North Carolina (UNC) and Eric S. Daar, M.D., Lundquist Institute at Harbor-UCLA Medical Center (vice-chairs), and supported by Dr. Currier and Joseph J. Eron, M.D., UNC (ACTG Co-Chair).

More information: Julie Boucau et al, Monoclonal antibody treatment drives rapid culture conversion in SARS-CoV-2 infection, *Cell Reports Medicine* (2022). [DOI: 10.1016/j.xcrm.2022.100678](https://doi.org/10.1016/j.xcrm.2022.100678)

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