Antibody combination provides strong protection against severe COVID-19 in large international trial

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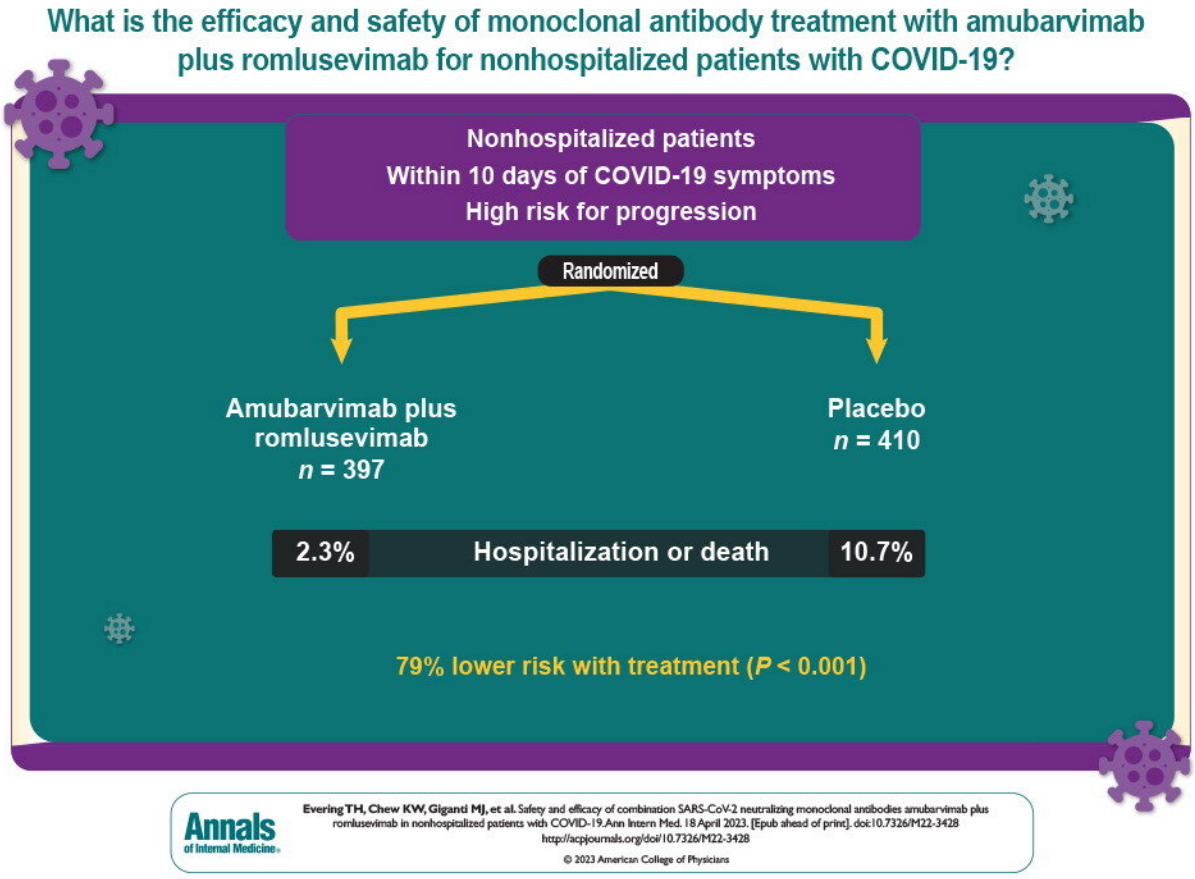

Visual Abstract. Safety and Efficacy of Combination SARS-CoV-2 Neutralizing Monoclonal Antibodies Amubarvimab Plus Romlusevimab in Nonhospitalized Patients With COVID-19. Credit: *Annals of Internal Medicine* (2023). DOI: 10.7326/M22-3428

A treatment combining two antibodies against the coronavirus SARS-CoV-2 strongly protected high-risk people with early COVID-19 symptoms from hospitalization and death in an international Phase 2/3 clinical trial conducted in the first half of 2021 and co-led by researchers at Weill Cornell Medicine and NewYork-Presbyterian.

The trial, described in a paper appearing online Apr. 18 in *Annals of Internal Medicine*, enrolled more than 800 non-hospitalized patients with COVID-19 at high-risk of progression of the disease in the United States and five other countries.

Those who were randomly assigned to be treated with the combination of the two antibodies, amubarvimab and romlusevimab, had only a 2.3 percent rate of progression to hospitalization and/or death, compared to 10.7 percent in the placebo group, a highly significant difference. The treatment also appeared safe.

"This was a randomized, blinded, placebo-controlled clinical trial—the gold standard as we call it—that was conducted as a large international collaboration in the midst of a global pandemic, and demonstrated strong effectiveness and safety for this treatment," said study co-first author Dr. Teresa Evering, an assistant professor of medicine in the Division of Infectious Diseases at Weill Cornell Medicine and an infectious disease specialist at NewYork-Presbyterian/Weill Cornell Medical Center.

The study, which is part of the ACTIV-2 Study of Outpatient Monoclonal Antibodies and Other Therapies was also co-led by researchers at the University of California-San Diego, The Geffen School of Medicine at UCLA, and the Lundquist Institute at Harbor-UCLA Medical Center. ACTIV-2 is sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National

Institutes of Health (NIH), and is part of NIH's Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) public-private partnership.

The combination monoclonal antibody treatment was jointly developed by the China and U.S.-based company Brii Biosciences, Tsinghua University and the Third People's Hospital of Shenzhen. The two antibodies, which are based on antibodies originally isolated from recovering COVID-19 patients, hobble SARS-CoV-2's ability to spread by targeting two non-overlapping structures in the virus's receptor binding domain.

The trial enrolled non-hospitalized patients with early, mild to moderate COVID-19 who were considered at high risk of progression to severe COVID-19. The participating medical centers were in Argentina, Brazil, Mexico, the Philippines, South Africa and the United States. Enrollment took place during January to July of 2021, and the final analysis covered 807 patients, the vast majority of whom were from the United States, South Africa or Argentina.

Although the treatment and placebo groups were roughly equal in number (397 and 410), 44 of the 53 total hospitalizations and/or deaths occurred in the placebo group, compared with only 9 in the treatment group—a 79 percent reduction in risk for the latter. The analysis also found that the antibody treatment worked about as well for patients enrolled 6 to 10 days after symptom onset as it did for patients enrolled earlier.

It also appeared to be effective against the delta variant of SARS-CoV-2, which emerged and spread worldwide during the study. Moreover, the safety analysis found that reports of treatment-related side effects were significantly lower in the treatment group compared to the placebo group , suggesting that the treatment was safe.

The amubarvimab-plus-romlusevimab treatment was granted approval by the National Medical Products Administration (NMPA) of China in late 2021 and was later used in hundreds of Chinese hospitals. It was found to be effective in lab tests against early omicron variants. However, it was never approved for use in the U.S., and like other anti-SARS-CoV-2 antibody treatments, it may have reduced efficacy for currently circulating variants. Brii Biosciences announced last month that it was shelving production of the treatment.

"We were honored to play a role in a study that clearly demonstrated the safety and efficacy of a monoclonal antibody combination therapy in reducing hospitalizations and deaths among those with mild to moderate COVID-19 at high risk for clinical progression, prior to the emergence of omicron variants," Dr. Evering said.

More information: Teresa H. Evering et al, Safety and Efficacy of Combination SARS-CoV-2 Neutralizing Monoclonal Antibodies Amubarvimab Plus Romlusevimab in Nonhospitalized Patients With COVID-19, *Annals of Internal Medicine* (2023). DOI: 10.7326/M22-3428

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