Case Report

Monoclonal Antibodies Casirivimab and Imdevimab in Pregnancy for Coronavirus Disease 2019 (COVID-19)

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BACKGROUND: For unvaccinated individuals with mild-to-moderate coronavirus disease 2019 (COVID-19), monoclonal antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) decrease the risk of severe disease and hospitalization. We describe the use of the monoclonal antibodies casirivimab and imdevimab for COVID-19 in pregnancy.

CASE: Two unvaccinated pregnant individuals presented with moderate COVID-19, one in the second trimester and one in third trimester; both met criteria for outpatient management. To decrease the risk for severe disease, they were treated with casirivimab and imdevimab. Neither experienced an adverse drug reaction, and neither progressed to severe disease.

CONCLUSION: Monoclonal antibodies such as casirivimab and imdevimab, approved under an emergency use authorization, should be considered in unvaccinated pregnant individuals with mild-to-moderate COVID-19 to decrease the risk of severe disease.

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Teaching Points

1. Pregnant individuals with mild-to-moderate COVID-19, especially those who are unvaccinated, are at high risk for severe disease and hospitalization.
2. In nonpregnant adults with mild-to-moderate COVID-19, use of the monoclonal antibodies casirivimab and imdevimab decreases the likelihood of severe disease and hospitalization.
3. To prevent severe disease in unvaccinated pregnant individuals with mild-to-moderate COVID-19, use of the monoclonal antibodies casirivimab and imdevimab should be considered.

Pregnant adults with coronavirus disease 2019 (COVID-19), caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), are three to four times more likely to develop severe disease and require hospitalization compared with nonpregnant adults with COVID-19.[1–3] They are also 13 times more likely to die from their illness.[1]

According to the Centers for Disease Control and Prevention, only 24% of pregnant individuals had received at least one dose of the COVID-19 vaccine through August 28, 2021.[4] Treatment options for unvaccinated individuals with COVID-19 are limited, but for those with mild-to-moderate illness (Box 1),[5,6] monoclonal antibodies against SARS-CoV-2 may be beneficial.

REGEN-COV, a co-formulated product containing the monoclonal antibodies casirivimab and imdevimab, was introduced on November 21, 2020, after the U.S. Food and Drug Administration (FDA) issued its emergency use authorization for treatment of mild-to-moderate COVID-19 in patients at high risk for progressing to severe COVID-19.[5] Administration of casirivimab and imdevimab reduces the viral load, shortens the duration of symptoms, and decreases the incidence of hospitalization or death by approximately 70%.[7] Although the FDA added pregnancy as a high-risk criteria warranting use of casirivimab and imdevimab on May 14, 2021,[5] there remain limited data on its use among pregnant individuals with COVID-19.[8]

We describe two unvaccinated pregnant individuals with COVID-19 who were treated with casirivimab and imdevimab monoclonal antibodies and recovered without developing severe disease.

CASES

A 36-year-old multiparous patient at 19 1/7 weeks of gestation presented after 8 days of headache, fevers,

nausea, vomiting, and sinus pressure. She was COVID-19 vaccine–naïve. She had one prior cesarean delivery, type 1 diabetes, and hyperlipidemia. Her body mass index (BMI, calculated as weight in kilograms divided by height in meters squared) was 24. Her temperature was 37°C, heart rate was 108 beats per minute, respiratory rate was 18 breaths per minute, and oxygen saturation was 96% on room air. The fetal heart rate was within the normal range. Laboratory evaluation was notable for lymphopenia (absolute lymphocyte count 0.41 k/microliter [normal 1.0–4.5 k/microliter]) and elevated levels of C-reactive protein (97.9 mg/L [normal less than 5 mg/L]), D-dimer (0.88 micrograms/mL [normal less than 0.50 micrograms/mL]), and lactate dehydrogenase (375 units/L [normal 125–220 units/L]). Nasopharyngeal swab was positive for SARS-CoV-2 infection, and chest X-ray demonstrated ground-glass opacities, suggestive of viral pneumonia.

Because the patient was maintaining an oxygen saturation above 96% on room air, she was a candidate for outpatient management of COVID-19. To decrease her risk for severe disease and hospitalization, she was treated with casirivimab and imdevimab monoclonal antibodies. She received them by intravenous infusion (600 mg over 20 minutes) and was observed for 1 hour without evidence of adverse drug reaction and was discharged home. Two weeks later, she reported complete resolution of her symptoms, and she had not required any further medical evaluation or hospitalization for COVID-19.

In the second case, a 29-year-old nulliparous patient presented at 36 4/7 weeks of gestation with 2 days of nasal congestion, fatigue, and cough. She was COVID-19 vaccine–naïve. She had a history of childhood asthma and complement C7 deficiency not requiring treatment. Her BMI was 24. She had no obstetric symptoms.

Her vital signs were within normal limits, and her oxygen saturation was 98–99% on room air. The fetal heart tracing was reassuring. Nasopharyngeal swab was positive for SARS-CoV-2 infection, and the patient had lymphopenia (absolute lymphocyte count 0.76 k/microliter) and elevated levels of C-reactive protein (18.4 mg/L) and D-dimer (2.42 micrograms/L). She was diagnosed with mild COVID-19 and was discharged home without need for hospitalization. She was eligible for casirivimab and imdevimab treatment but declined owing to mild symptoms.

The patient returned 5 days later (symptom day 7) at 37 2/7 weeks of gestation with worsening cough and shortness of breath. Her vital signs were within normal limits, and her oxygen saturation was 96–97% on room air. She had no obstetric symptoms, and the fetal heart tracing was reassuring. Laboratory evaluation revealed worsening of C-reactive protein (71.5 mg/L) and liver transaminase levels (alanine transaminase 110 units/L [normal 5–34 units/L], aspartate transaminase 103 units/L [normal 0–55 units/L]). Chest X-ray showed extensive bilateral infiltrates, suggestive of viral pneumonia and moderate COVID-19. Because the patient met criteria for outpatient management, she was treated with casirivimab and imdevimab (600 mg by intravenous infusion over 20 minutes). She remained on continuous fetal heart monitoring during the infusion and was observed for 1 hour with no adverse reactions. She was discharged home in stable condition.

She returned at 38 1/7 weeks of gestation in active labor. Her cough and shortness of breath had resolved. Her D-dimer level remained elevated, but liver transaminase levels had improved significantly (alanine transaminase 39 units/L, aspartate transaminase 35 units/L). She had an uneventful labor and a normal spontaneous vaginal delivery without complication. The neonate was admitted to the neonatal intensive care unit owing to intermittent tachypnea and an oxygen requirement for presumed transient tachypnea of the newborn (COVID-19 test result was negative). The patient's postpartum course was otherwise uncomplicated, and she was discharged home on postpartum day 2 in good health. She did not require oxygen supplementation throughout her labor or postpartum course and did not develop severe COVID-19.

Box 1. Clinical Spectrum of Coronavirus Disease 2019 (COVID-19)

Mild illness: Individuals with various signs and symptoms of COVID-19 (eg, fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea, or abnormal chest imaging.
Moderate illness: Individuals with evidence of lower respiratory disease during clinical assessment or imaging and who have an SpO_2 level of 94% or higher on room air.
Severe illness: Individuals with SpO_2 levels lower than 94% on room air, a PaO_2/FiO_2 ratio less than 300 mm Hg, respiratory frequency greater than 30 breaths per minute, or lung infiltrates greater than 50%.
Monoclonal antibody treatment: The co-formulated product containing casirivimab and imdevimab received emergency use authorization by the FDA for treatment of mild-to-moderate COVID-19 in adult and pediatric patients (12 years of age and older, weighing at least 40 kg) with positive SARS-CoV-2 test results and who are at high risk for progression to severe COVID-19, including pregnant individuals. Casirivimab and imdevimab treatment is not recommended in patients who require oxygen therapy, have severe disease, or are hospitalized due to COVID-19.

COVID-19, coronavirus disease 2019; FDA, U.S. Food and Drug Administration; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
Data from U.S. Food and Drug Administration fact sheet for health care providers emergency use authorization (EUA) of REGEN-COV™ (casirivimab and imdevimab). Accessed September 13, 2021. https://www.fda.gov/media/145611/download
Data also from the National Institutes of Health. COVID-19 treatment guidelines. Accessed September 13, 2021. https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum/

DISCUSSION

We describe the use of the monoclonal antibodies casirivimab and imdevimab in two unvaccinated pregnant individuals with moderate COVID-19. Both improved after administration of casirivimab and imdevimab, and neither progressed to severe disease. These cases highlight the potential benefit of monoclonal antibodies to prevent hospitalization and death in pregnant individuals, though it is important to note that casirivimab and imdevimab were approved under an emergency use authorization and safety and efficacy data are still being collected.

Monoclonal antibody treatments such as casirivimab and imdevimab have not been tested specifically in pregnant people, and therefore the National Institutes of Health has concluded that there is insufficient evidence for or against monoclonal antibodies in pregnant individuals with COVID-19.[9] Although data are limited, monoclonal antibody therapies are particularly critical in unvaccinated pregnant individuals because they are at higher risk for severe disease and death compared with vaccinated individuals. Under the FDA's emergency use authorization, monoclonal antibodies may also be given as postexposure prophylaxis in pregnant individuals who are not fully vaccinated or who are not expected to mount an adequate immune response to complete COVID-19 vaccination.[5,6]

Health care professionals and patients should practice joint decision making before casirivimab and imdevimab administration to discuss individualized risks and benefits. At our institution, criteria for casirivimab and imdevimab administration are derived from the FDA's emergency use authorization: age 12 years or older, weight 40 kg or more, positive SARS-CoV-2 PCR test result, symptomatic for 10 days or less, stable for outpatient management, ability to provide informed consent, and presence of a high-risk condition such as pregnancy.[5] Potential benefits of treatment include reduction in severe disease and hospitalization and possibly a decrease in preterm birth due to COVID-19. However, patients should be counseled that monoclonal antibodies such as casirivimab and imdevimab may cross the placenta and that fetal effects are unknown. Known risks of casirivimab and imdevimab include hypersensitivity reactions and anaphylaxis; clinical worsening of COVID-19 has been reported, but this may be a result of the natural progression of COVID-19 rather than administration of monoclonal antibodies.

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