CORRESPONDENCE

Research Letter

Monoclonal SARS-CoV-2 Antibodies in Pregnancy—a Case Series

In November 2021 the European Medicines Agency (EMA) gave its approval recommendation for regdanvimab and the combination of casirivimab and imdevimab (1). These neutralizing monoclonal antibodies (nMABs) prevent the SARS-CoV-2 virus from entering into cells and thereby from replicating inside cells. The indication for treatment is given for infection with SARS-CoV-2 and for SARS-CoV-2-IgG (immunoglobulin G) seronegativity in the early phase of the infection (<3 days after a positive PCR (polymerase chain reaction) test, <7 days after symptom onset) if there is a risk of a severe disease course (2). Their use is regarded as safe and adverse effects are described as rare. For outpatient application, a risk reduction of 71.3% (1.3% in the intervention group vs 4.6% in the control group) was shown regarding the need for inpatient admission or a fatal disease course (3). The duration of symptoms was reduced to a statistically significant degree.

For use in inpatients, an evaluation of the RECOVERY Trial published as a preprint reported a survival advantage for casirivimab/imdevimab in seronegative patients (n=3151) within 28 days (relative risk [RR] 0.80; 95% confidence interval [0.70; 0.91]; p=0.001); 25 pregnant women were included in the study (4). In spite of the therapeutic recommendation in the context of the current S3 guideline (2), the potential of treatment with SARS-CoV-2-nMABs is currently considered underutilized.

SARS-CoV-2 infection in pregnancy is associated with a severe disease course, independently of additive risk factors (5). This puts not only the pregnant woman at risk but the actual pregnancy too. Furthermore, infected pregnant women are rarely vaccinated nor have they recovered; they are therefore often seronegative, as can be expected.

In a setting of off-label use, five pregnant women with COVID-19 were treated at Jena University hospital by an interdisciplinary team (specialists in obstetrics, internal medicine, and infectious disease) in the time period from 27 November to 1 December 2021 after giving informed consent individually. The *Table* provides an overview of the patients' characteristics. The patients were of age and all were in the third trimester of an intact, singleton pregnancy—developed appropriately for the stage of pregnancy—with normal fetal monitoring parameters. None of the patients had been vaccinated against COVID-19. The serological analysis for SARS-CoV-2-IgG showed a median of 11.2 BAU (binding antibody units)/mL (minimum 4.8 BAU/mL, maximum 20.8 BAU/mL; a value of ≥ 33.8 BAU/mL is considered as positive).

Four patients received inpatient obstetric care and had mild to moderate symptoms without needing oxygen; one patient was treated during an inpatient stare in intensive care and already required oxygen. No adverse effects in the mothers and fetuses

TABLE

Characteristics of pregnant patients with COVID-19 at the time of nMAB treatment using casirivimab and imdevimab

	Case 1	Case 2	Case 3	Case 4	Case 5
Age in years	28	26	34	30	29
Gravidity	1	1	2	1	9
Parity	0	0	0	0	7
Secondary diagnoses	Thrombocytopenia	Gestational diabetes	Gestational diabetes	Typ I diabetes	None
Gestational age in weeks	40 + 3	34 + 2	33 + 0	35 + 2	33 + 4
COVID-19 symptoms	Cough	Nausea, vomiting, cough, fever	Head cold/runny nose	Cough, dyspnea	Cough, nausea, vomiting, moderate pulmonary failure, required oxygen, intensive care ward
nMAB dosage	4 g	4 g	1.2 g	1.2 g	4 g
Discharge from inpatient treatment after	5 days (4 days after nMAB)	5 days (3 days after nMAB)	1 day (0 days after nMAB)	12 days (11 days after nMAB)	9 days (7 days after nMAB)
Outcome, delivery	40 + 4 weeks of gestation, spontaneous birth after premature membrane rupture	34 + 5 weeks of gestation, normal pregnancy	At discharge (33 + 0 weeks of gestation) normal pregnancy; delivery at 35 + 5 weeks of gestation by spontaneous birth after early premature membrane rupture	36 + 2 weeks of gestation, primary cesarean section in suboptimal metabolic adjustment and resulting onset of fetal decompensation	34 + 4 weeks of gestation normal pregnancy

nMABs, neutralizing monoclonal antibodies

were observed in any of the patients. In the symptomatic patients, the symptoms receded rapidly; the disease deteriorated in none of the cases, and no pregnancy had to be terminated prematurely because of COVID-19. All treated pregnant women were discharged within 0–11 days. Especially in the patient (Case 5) who had been admitted to intensive care with severe symptoms on the threshold of requiring intubation and was ventilated non-invasively and treated with dexamethasone, symptoms improved rapidly after treatment with nMABs (transfer to the normal ward on the 2nd day and discharge on the 7th day).

One patient (Case 1) gave birth to an unaffected baby beyond term after premature rupture of the membranes during her inpatient stay, one day after nMAB infusion (*Table*). Serological analysis of the umbilical cord blood showed 222 000 BAU/mL of SARS-CoV-2 specific IgG, which confirms the transplacental transport of nMABs.

In our case series, secondary prophylaxis with nMABs was found to be an effective and safe therapeutic option after SARS-CoV-2 infection in pregnancy. According to the recommendations of the perinatology specialty societies, therapy with nMABs should not be withheld from seronegative pregnant women—especially considering the pregnancy-associated increased risk for a severe disease course—and should be given in the early phase of the infection (5). It should be borne in mind that the respective nMAB used needs to be adapted to the predominant or confirmed SARS-CoV-2 variant. A recent study indicates that the combination of antibodies used in our case series (casirivimab and imdevimab) probably is of notably lesser effectiveness vis-à-vis the omicron variant. The Paul Ehrlich-Institute and the US Food and Drug Administration advise against such therapeutic regimens in omicron infection. Their use should be accompanied by clinical studies and should be documented centrally, for example in the CRONOS registry of the German Society for Perinatal Medicine.

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Conflict of interest statement
The authors declare that no conflict of interest exists.

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