


# Ustekinumab in the Treatment of Generalized Pustular Psoriasis in a Pregnant Patient

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**Abstract:** Although the use of biologics has led to great improvement in psoriasis patients, the treatment of psoriasis during pregnancy still faces many challenges. We herein report on a 29-year-old pregnant woman treated with ustekinumab for generalized pustular psoriasis. Upon becoming pregnant, the woman underwent continued treatment with ustekinumab in the first trimester. We also considered the need for neonatal vaccination. The patient discontinued ustekinumab therapy in the second trimester, and during the period of drug discontinuation we noted a slight rash recurrence. The patient was treated with ultraviolet B phototherapy and topical corticosteroids, and the rash was localized to the abdomen. However, in the 27th week of pregnancy, the patient was infected with COVID-19, which made the condition worse. The rash erupted rapidly and spread throughout her body, and she experienced a high fever with her blood count showing augmented numbers of white blood cells. The patients self-administered 0.3 g of acetaminophen three times per day, and after four days her core body temperature was 38.0°C; the rash, however, did not diminish. We diagnosed an outbreak of generalized pustular psoriasis and treated the patient with ustekinumab. The rash resolved quickly, and a healthy newborn was delivered by caesarean section at 39 weeks.

**Keywords:** Ustekinumab, interleukin-12/-23, generalized pustular psoriasis, pregnancy, COVID-19

## Introduction

Generalized pustular psoriasis during pregnancy is clinically rare, and is often accompanied by fever, leukocytosis, hypoproteinemia, and elevated C-reactive protein (CRP). The impact of generalized pustular psoriasis on pregnant women and fetuses is substantial, and if not treated in time, it can endanger their lives.<sup>1</sup> While treatment of refractory generalized psoriasis is challenging due to the limited treatment options available,<sup>2</sup> the disease has become less lethal through the use of biologic agents. Biologics are molecularly targeted drugs, which have been widely used in the treatment of moderate to severe plaque psoriasis in recent years. With the development of immunology and genetics, biologics with different targets have been gradually applied to the treatment of GPP, such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) inhibitors, IL-1 2/IL-2 3 inhibitors, IL-17A/IL-17A receptor inhibitors, IL-36R inhibitors, IL-1 inhibitors, etc. increased the efficacy of GPP.<sup>3</sup> However, currently reported safety information on the use of biologics in patients with generalized pustular psoriasis and who are pregnant, planning to become pregnant, or who are breastfeeding, remains limited.<sup>4</sup> We herein report successful treatment with ustekinumab (STELARA<sup>®</sup>) in a pregnant patient with generalized pustular psoriasis.

Ustekinumab is a human immunoglobulin G1 monoclonal antibody that binds to interleukin (IL)-12/-23 and thereby inhibits IL-12/-23 activity. In the case we reported here, ustekinumab was used throughout pregnancy, and we posit that it is relevant for the treatment of psoriasis in pregnancy. We also reviewed the literature in order to provide clinicians with guidance on the treatment of this rare and particularly severe skin disease of pregnancy.

## Case Report

We reviewed the case of a 29-year-old female patient with a 13-year history of generalized pustular psoriasis and no family history of psoriasis or other diseases. The patient presented with recurrent erythema and pustules on her entire

integument. The woman had previously undergone ultraviolet (UVB) phototherapy, topical corticosteroids, and topical calcipotriol, but results were unsatisfactory. Although the patient had previously received treatment with tumor necrosis factor (TNF) inhibitors that resulted in significant improvements to her rash, she was unwilling to continue receiving treatment once every two weeks and halted her use of the inhibitors. After curtailing treatment with the inhibitors, the patient's rash gradually increased. On 8 April 2022, the patient first used ustekinumab 45 mg for the treatment of generalized pustular psoriasis, and her disease was completely alleviated after the second injection of ustekinumab 45 mg on 15 May. Six weeks after her second treatment, her urine pregnancy test was positive, and ultrasonographic examination showed intrauterine pregnancy at four weeks of gestation. At 12 weeks, the patient received her third treatment of ustekinumab 45 mg. We then contemplated the need for neonatal vaccination, and the patient decided to suspend treatment with ustekinumab. After discontinuing treatment, she developed erythema and several pustules on her abdomen; these were treated with topical corticosteroid ointment and medium-wave UV light therapy. The rash was initially limited to the trunk, but at the 28th week of pregnancy the patient was infected with SARS-CoV-2 (the virus causing COVID-19), and the patient's rash then erupted again, with large erythematous areas on the abdomen and limbs and dense small pustules on the body surface. The patient's body temperature was 39°C, and she manifested an increased number of blood leukocytes and elevated CRP. While after seven days of penicillin administration the women's body temperature decreased to 37.8 degrees and her white blood cell count returned to normal, her CRP concentration in blood remained higher than normal. Since the generalized pustular psoriasis was exacerbated, we administered a fourth treatment of ustekinumab 45 mg to the patient at 29 weeks of gestation, and her rash subsequently and gradually subsided the next day after injection; most of the rash then subsided after one week. At 39 weeks of gestation, the patient gave birth by cesarean section to a healthy baby boy who is now 24 months old.

## Discussion

Generalized pustular psoriasis during pregnancy is a rare type of psoriasis<sup>5</sup> that is mostly acute and often accompanied by severe systemic symptoms. Generalized pustular psoriasis during pregnancy is associated with increased risk of fetal malformations, premature rupture of membranes, intrauterine growth restriction secondary to placental insufficiency, and even stillbirth. The mother is also at risk of infection and sepsis. The treatment of patients with psoriasis during pregnancy remains challenging due to limitations with respect to the medications provided during pregnancy, and careful consideration of the benefits, safety, and effective alternatives to treatment—as well as potential risks to the fetus—is required. The application of biologic agents in the treatment of ordinary psoriasis patients has achieved appropriate efficacy,<sup>6</sup> and TNF- $\alpha$ , IL-17, and IL-23 inhibitors have been reported to produce favorable results. tyrosine kinase 2 (TYK2) inhibitor Deucravacitinib, Phosphodiesterase-4 (PDE-4) inhibitors, has been approved for the treatment of moderate-to-severe plaque psoriasis, but there no use has been reported in pregnant women. Among the guideline recommendations,<sup>7</sup> TNF- $\alpha$  inhibitors may be employed in the first half of pregnancy; and etanercept is also a reasonable choice, as its placental metastasis is less than that of adalimumab or infliximab. Infliximab and ustekinumab have been shown to be secreted through animal milk secretion, and the safety of these drugs for fetuses and infants is unclear. Certolizumab may be considered if biologic therapy is required throughout pregnancy because it does not cross the fetus in large quantities,<sup>8,9</sup> but cercerizumab has not yet been approved for psoriasis in China. There are presently insufficient data as to the use of ustekinumab during pregnancy, and only anecdotal cases have been reported. We herein reported on patients who received ustekinumab before and during pregnancy. Ustekinumab<sup>10</sup> is an IgG1 monoclonal antibody that targets the p40 subunit of IL-12/IL-23 and inhibits IL-12/IL-23 from binding to their surface receptors on T cells, NK cells, and antigen-presenting cells, thereby reducing the inflammatory response. Human IgG antibodies can cross the placental barrier in the second trimester, such that ustekinumab may be transmitted from mother to the developing fetus in the second trimester. The fetal effects of ustekinumab administration during pregnancy in patients with psoriasis have also been reported previously. Galluzzo et al reported<sup>11</sup> that seven patients with psoriasis who used ustekinumab during pregnancy (one of whom exhibited gestational hypertension and diabetes and underwent a third cesarean section after first experiencing two miscarriages) gave birth to a healthy child. The remaining six patients gave birth to seven healthy children. Alsenaid and Prinz reported<sup>12</sup> on a patient with psoriasis who developed impetigo of pregnancy during her first pregnancy, was treated with cyclosporine, and delivered a low-weight preterm infant by cesarean section at 33 weeks.

Four weeks after delivery, the patient was treated with ustekinumab, and at 14 weeks of pregnancy she underwent a third ustekinumab treatment, ustekinumab treatment was stopped during the second pregnancy, the patient developed no complications, with a healthy newborn delivered by cesarean section at 35 weeks of gestation. The remaining patients with plaque psoriasis gave birth to healthy neonates after using ustekinumab in early pregnancy,<sup>13–15</sup> but all women suspended ustekinumab treatment upon discovery of pregnancy. In this study we reported that a patient with generalized pustular psoriasis was found to be pregnant during ustekinumab treatment and that the patient originally planned to halt ustekinumab treatment in the second trimester, but due to an outbreak of a generalized pustular psoriasis rash after infection with COVID-19, during the COVID-19 epidemic, there have been some case reports of onset and exacerbation of psoriasis after COVID-19 Infection,<sup>16,17</sup> COVID-19 vaccination could affect the course of some chronic inflammatory skin diseases, including psoriasis.<sup>18</sup> biologics might reduced the risk of disease severity among these patients<sup>19</sup>. So ustekinumab treatment was again implemented at the 29th week. Thus, in this case, exposure to ustekinumab occurred throughout pregnancy from fertilization of the mature oocyte to the delivery of the fetus; and although the mother experienced COVID-19 infection during pregnancy (with aggravation of her generalized pustular psoriasis rash), these events did not affect fetal growth or development. Additionally, the growth and development of the neonate continued to be normal at follow-up.

## Conclusions

Generalized pustular psoriasis may worsen during pregnancy, and untimely or improper treatment can endanger the life of both the patient and the fetus. Pregnancy-drug options for generalized pustular psoriasis are few and contraindicated, and treatment is therefore challenging. Biologics for psoriasis patients can thus be used as a treatment option for generalized pustular psoriasis in pregnancy, but there are few reports available in the literature. We do, however, expect additional investigations entailing biologics and assessments of their safety and efficacy in future pregnancy studies. Our experience with ustekinumab showed that treatment throughout pregnancy in patients with generalized pustular psoriasis eventually led to the patient's disease being controlled, and resulted in the birth of a healthy newborn. The present case report therefore revealed that treatment throughout pregnancy with ustekinumab possesses significance as a reference for researchers in the future.

## Consent Statement

Informed consent was obtained from the patient to publish her clinical information and relevant images. Ethical approval was also obtained from the hospital ethics committee.

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## Disclosure

The authors report no conflicts of interest in this work.

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