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A case of atopic eczema treated safely with dupilumab during pregnancy and lactation

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Dear editor,

Dupilumab is an IgG4 antibody directed against the common IL-4Ra subunit of both the IL-4- and the IL-13-receptor. The drug is the first biological being licensed for atopic eczema (AE) ^{1, 2}. In pregnancy, AE frequently shows a deleterious course and may relevantly impact on quality of life ^{3, 4, 5}. According to the European Task force on Atopic Dermatitis (ETFAD), when treating pregnant and lactating women with AE, systemic treatment should be restricted to glucocorticosteroids, cyclosporine, and azathioprine. There have been only few data about dupilumab in pregnancy and lactation ^{1, 2}. A possible passage and even active transport and up-concentration across the placentas should be considered ⁶. However, animal studies did not show any direct or indirect harmful influence of dupilumab on reproduction ⁷.

We report on the case of a 35 year old female who suffered from AE since early childhood. She had been treated with topical and systemic glucocorticosteroids, UV therapy and an eighteen month course of cyclosporine. She also suffered from perennial allergic rhinoconjunctivitis and allergic asthma with polyvalent type 1 sensitization.

About 1.5 years ago she had exacerbation of her AE (SCORAD 51.7) and was started on dupilumab 300mg subcutaneously every two weeks. Within six weeks the skin improved significantly.

Eight month later, she became pregnant for the first time and while not being aware of the pregnancy she did not stop dupilumab until the second week of pregnancy (Figure 1). Within the next three months, topical treatment could hardly control the disease and she reintroduced dupilumab on her own. At follow-up one month later, we carefully assessed risks and benefits and decided together to continue dupilumab under frequent monitoring. Eight weeks after reintroduction of dupilumab the skin had improved significantly (Figure 1) and remained stable thereafter. The course of the pregnancy was then without any complications. In week 40, she delivered a healthy baby girl (size 50cm, weight 3460g). With regard to mother and child, the breastfeeding period was uncomplicated during the next four months of observational period.

The European Medicines Agency (EMA) reported 2017 data from one phase-2b- and three phase-3-studies including 2500 AE patients, whereby twenty-three pregnancies of female patients treated with dupilumab resulted in deliveries of eight healthy babies (1 twin birth), two induced abortions and six spontaneous abortions. In two of these six cases patients had at least one risk factor for abortion (i.e. elevated parathyroid hormone, clotting disorders, and history of infertility). Five pregnancies were still ongoing at that point and three pregnancies were lost to follow-up ⁸.

In the EMA assessment report for the indication expansion of dupilumab in treatment for asthma published in 2019, nineteen pregnancies were reported from one phase-2b- and two phase-3-studies.

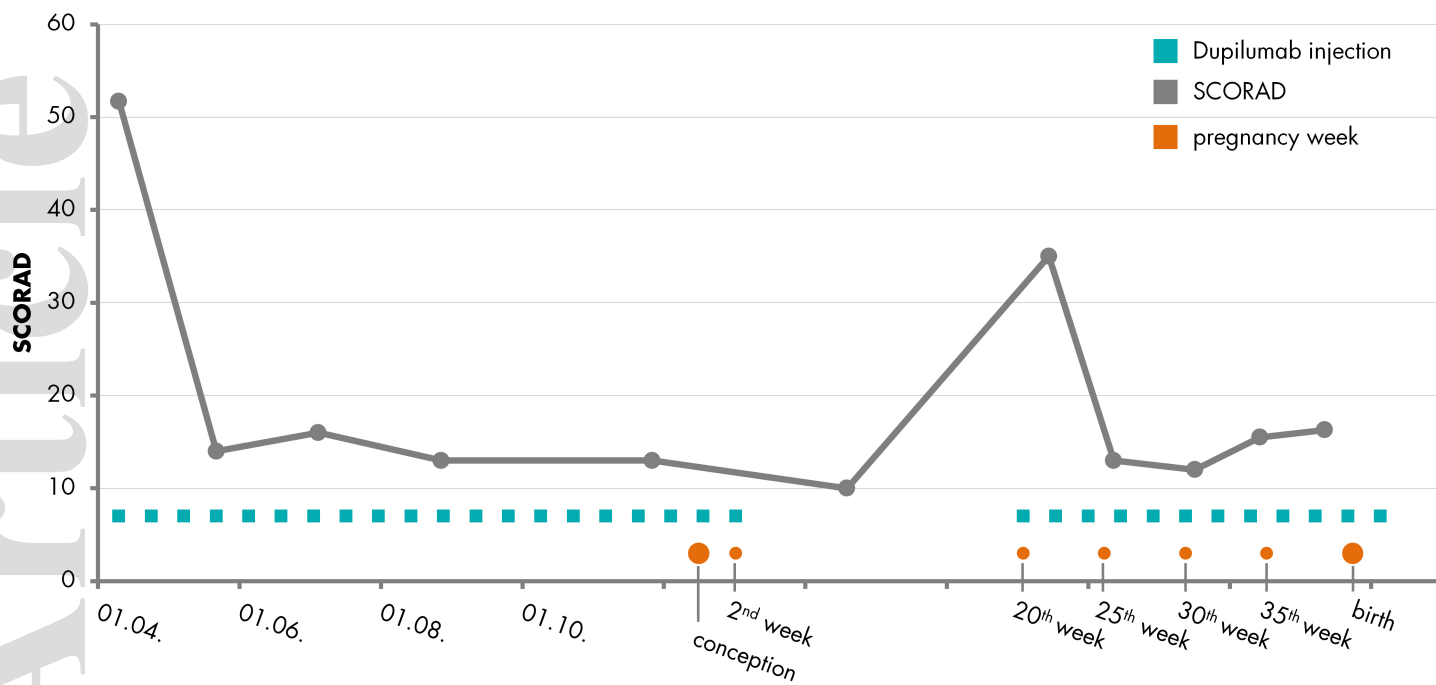
Pregnancies resulted in eight healthy babies (one twin birth), one baby with Turner's syndrome, five spontaneous and three induced abortions. Of the five spontaneous abortions three patients had at least one risk factor for abortion (i.e. clotting disorders, infertility treatments, advanced age, and twin pregnancy). Three pregnancies were still ongoing. The spontaneous abortion rate did not exceed the general spontaneous abortion rate ⁹.

Accordingly, until today, neither clinical nor experimental data nor theoretical considerations point to dupilumab's teratogenic capacity. However, the ETAD advises that other systemic drugs should be used instead of dupilumab in pregnant women with AE until more experience is available ⁶.

Our case supports the idea that dupilumab may be used after careful risk benefit assessment in pregnancy and lactation if all other therapies have failed.

References

1. Simpson EL et al., Two Phase 3 Trials of Dupilumab versus Placebo in Atopic Dermatitis. *N Engl J Med*. 2016 Dec 15;375(24):2335-2348
2. Blauvelt A et al., Long-term management of moderate-to-severe atopic dermatitis with dupilumab and concomitant topical corticosteroids (LIBERTY AD CHRONOS): a 1- year, randomized, double-blinded, placebo-controlled, phase 3 trial. *Lancet*. 2017 Jun 10;389(10086):2287-2303.
3. Treudler R. [Allergic diseases in pregnancy. Overview of diagnosis and therapy]. *Hautarzt*. 2010 Dec;61(12):1027-33. doi: 10.1007/s00105-010-2008-6.Review. German. PubMed PMID: 21088817.
4. Kage P, Simon JC, Treudler R. [Atopic dermatitis and psychosocial comorbidities]. *JDDG* (in press)
5. Treudler R et al. Depression, anxiety and quality of life in subjects with atopic eczema in a population-based cross-sectional study in Germany. *J Eur Acad Dermatol Venereol*. 2019 Dec 14. doi: 10.1111/jdv.16148. [Epub ahead of print] PubMed PMID: 31838777.
6. Vestergaard C, et al. European task force on atopic dermatitis position paper: treatment of parental atopic dermatitis during preconception, pregnancy and lactation period. *J Eur Acad Dermatol Venereol*. 2019 Sep;33(9):1644-1659.
7. German prescribing information on Dupixent®. October 2019
8. Committee for Medicinal Products for Human Use (CHMP) Assessment report Dupixent 20 July 2017 EMA/512262/2017. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Public_assessment_report/human/004390/WC500236509.pdf (last accessed 05 November 2019).
9. Committee for Medicinal Products for Human Use (CHMP) CHMP assessment report on extension of marketing authorization and an extension of indication variation 28 February 2019 EMA/188111/2019. Available at: https://www.ema.europa.eu/en/documents/variation-report/dupixent-h-c-4390-x-0004-g-epar-assessment-report-variation_en.pdf (last accessed 05 November 2019).



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