Dupilumab for Atopic Dermatitis during Pregnancy and Breastfeeding: clinical experience in 13 patients

Dear editor,

Atopic dermatitis (AD) affects patients of reproductive age and can worsen or start during pregnancy.[1] The high prevalence of AD in childbearing age women highlights the need to determinate the safety of biologics during pregnancy and lactation. Currently, data is limited regarding the use of dupilumab in pregnant/breastfeeding women.[2] The aim of this report is to describe our experience using dupilumab during pregnancy/breastfeeding in 13 women with AD.

We conducted a multicentre retrospective case series study with eleven pregnant and two breastfeeding women included. All suffered from moderate-to-severe AD with mean EASI score before initiating dupilumab of 34.9 (0-72). The mean time of exposure to dupilumab was of 6.8±2.9 and 11.5±3.2 months during pregnancy and breastfeeding, respectively. Patients' characteristics, treatments received before dupilumab, reasons that led to initiate this treatment as well as the cause of treatment discontinuation are mentioned in Table 1. The 83.3% of the patients reached EASI-75 at week 16 and this percentage was even better at weeks 24 (90.9%) and 52 (90.0%). At week 16, pruritus NRS and DLQI scores were considerably reduced, maintaining these good results at weeks 24 and 52 (Fig. 1). Regarding materno-fetal outcomes, eleven pregnant women gave birth to twelve babies. Eight were eutocic, vaginal deliveries and three were dystocic deliveries (one vacuum-assisted and two caesarean-deliveries). Ten (90.9%) were full-term pregnancies, without complications during delivery and giving birth to normal weight babies. One was a twin pregnancy that required a caesarean-section, giving birth two premature babies (week 35) with low

weigh (1.5 and 2.0kg respectively) but with a proper development and weight gain. None of the women suffered a miscarriage neither complications during pregnancy or puerperium. Moreover, none of the babies have suffered from AD to date.

Management of AD during both pregnancy and breastfeeding is challenging, especially in severe forms, due to the lack of clinical studies investigating effects of novel treatments on fertility, pregnancy and lactation. Dupilumab, as other IgG antibodies, is expected to cross the placental barrier, especially in the second and third trimesters of pregnancy.[3] However, studies using animal models have shown no direct or indirect harmful effects in terms of reproductive toxicity.[4] The European Medicines Agency reported that the spontaneous abortion rate in patients treated with dupilumab did not exceed that of the general population.[4] Additionally, a study that assessed the safety profile of dupilumab during pregnancy using pharmacovigilance data did not find any adverse effects.[5] Moreover, seven case reports published of pregnant women treated with dupilumab resulted in livebirths, with only one premature birth and another infant with low birth weight reported.[1,2,6-10] Regarding breastfeeding, secretion and absorption of dupilumab is thought to be minimal due to its high molecular weight and its degradation by acid and proteolytic enzymes in the infant's gut, respectively. Notwithstanding, during the first three days postpartum there are wide gaps between the breast alveolar cells which may allow the passage of immunoglobulins through them.[1] For these reasons it is recommended to avoid breastfeeding or the use of dupilumab during a short postpartum period and in preterm infants who are likely to have an immature gastrointestinal tract. There is only one case report published of a woman treated with dupilumab whom breastfeed her infant for at least 4 months in which no complications were reported.[2]

In conclusion, data is limited regarding the use of dupilumab during pregnancy/breastfeeding. We report the largest case series yet described of patients with moderate-to-severe AD treated with this drug during pregnancy/lactation. In our series maternal-fetal outcomes were excellent, highlighting that dupilumab use in this subgroup of patients has its place but should be preceded by careful assessment.

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Tables and figures:

Figure 1. Evolution of EASI (A), itch (B) and DLQI (C) scores in weeks 0,16, 24 and 52 in 12 patients (P) during pregnancy and/or breastfeeding.

Table 1. Patient population characteristics