



Letter to the Editor

## Response to Letter to the Editor entitled: Rethinking biologic and pregnancy research: The importance of assessing postpartum immunosuppression of the infant



Dear Editor,

Important new data have been published that are confirmatory and reassuring for patients and providers since our review on biologic medications used in pregnancy was published in 2017. We thank the authors of this letter for highlighting some important updates. We agree that the recently published study evaluating the pregnancy outcomes of patients with moderate-to-severe psoriasis in the Psoriasis Longitudinal Assessment and Registry provided important confirmation that pregnancy outcomes for women exposed to biologics were similar to those of women exposed to nonbiologics (Kimball et al., 2021).

The comment about the difference between first and third trimester exposure is important to consider. The risks during the first trimester are about malformations, whereas third trimester risks are about active antibody transfer (Chambers and Johnson, 2012). The CRIB clinical trial published in 2018 evaluated the pharmacokinetics of 16 pregnant women with chronic inflammatory receiving certolizumab pegol (CZP) and found no to minimal placental transfer and lack of in utero exposure during the third trimester (Mariette et al., 2018). In addition, the prospective and retrospective study by Clowse et al. (2018) evaluated pregnancy outcomes after exposure to CZP. The study included a large cohort of pregnant women exposed to anti-tumor necrosis factor agents, and the analysis revealed no teratogenic effect of CZP or increased risk of fetal death when compared with the general population (Clowse et al., 2018).

Another agent used in the treatment of some dermatologic conditions is etanercept, which is a receptor fusion protein and therefore not expected to be actively transported. Consistent with this concept, studies on etanercept did not reveal elevated serum levels (Berthelsen et al., 2010; Kurizky et al., 2015; Murashima et al., 2009). Antibody transfer during the third trimester is facilitated through the neonatal Fc receptor on the placenta (Wakefield et al., 2011). Newer technology using smaller nanobodies, some of which can be designed without an Fc receptor, might enable the development of new modalities without this effect during the third trimester (Bannas et al., 2017).

In summary, studies both in dermatology and other fields continue to be reassuring that using biologics during pregnancy does not result in significantly different pregnancy outcomes compared with those of the general population; however, more ro-

bust data sets would be welcome, including the effects of biologics used during pregnancy on infants during the first few months of life.

### Funding

None.

### Study approval

The author(s) confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies.

### Conflicts of interest

Alexa B. Kimball is a consultant and investigator for AbbVie, Eli Lilly, Janssen, BMS, Novartis, Pfizer, UCB, Leo Pharma, Meiji Pharma, and Regeneron; is advisor to the Organization of Teratology Information Services; has received fellowship funding from Janssen and AbbVie; and is on the board of directors for Almirall. Dr. Porter is a consultant and/or investigator for Abbvie, Bristol Meyers Squibb, Janssen, Eli Lilly, Novartis, Pfizer, UCB, and Incyte; also previously received honorarium and fellowship funding from the NPF.

### References

- Bannas P, Hambach J, Koch-Nolte F. Nanobodies and nanobody-based human heavy chain antibodies as antitumor therapeutics. *Front Immunol* 2017;8(NOV):1603.
- Berthelsen B, Fjeldsøe-Nielsen H, Nielsen C, Hellmuth E. Etanercept concentrations in maternal serum, umbilical cord serum, breast milk and child serum during breastfeeding. *Rheumatology (Oxford)* 2010;49(11):2225–7.
- Chambers CD, Johnson DL. Emerging data on the use of anti-tumor necrosis factor-alpha medications in pregnancy. *Birth Defects Res Part A Clin Mol Teratol* 2012;94(8):607–11.
- Clowse MEB, Scheuerle AE, Chambers C, Afzali A, Kimball AB, Cush JJ, et al. Pregnancy outcomes after exposure to certolizumab pegol: Updated results from a pharmacovigilance safety database. *Arthritis Rheumatol* 2018;70(9):1399–407.
- Kimball AB, Guenther L, Kalia S, de Jong EMGJ, Lafferty KP, Chen DY, et al. Pregnancy outcomes in women with moderate-to-severe psoriasis from the

- Psoriasis Longitudinal Assessment and Registry (PSOLAR). *JAMA Dermatol* 2021;157(3):301–6.
- Kurizky PS, de Castro Ferreira C, Nogueira LSC, da Mota LMH. Treatment of psoriasis and psoriatic arthritis during pregnancy and breastfeeding. *An Bras Dermatol* 2015;90(3):367–75.
- Mariette X, Förger F, Abraham B, Flynn AD, Moltó A, Flipo RM, et al. Lack of placental transfer of certolizumab pegol during pregnancy: Results from CRIB, a prospective, postmarketing, pharmacokinetic study. *Ann Rheum Dis* 2018;77(2):228–33.
- Murashima A, Watanabe N, Ozawa N, Saito H, Yamaguchi K. Etanercept during pregnancy and lactation in a patient with rheumatoid arthritis: Drug levels in maternal serum, cord blood, breast milk and the infant's serum. *Ann Rheum Dis* 2009;68(11):1793–4.
- Wakefield I, Stephens S, Foulkes R, Nesbitt A, Bourne T. The use of surrogate antibodies to evaluate the developmental and reproductive toxicity potential of an anti-TNF $\alpha$  PEGylated Fab' monoclonal antibody. *Toxicol Sci* 2011;122(1):170–6.

Ruby S. Gibson MD  
*Department of Dermatology, Beth Israel Deaconess Medical Center,  
Boston, Massachusetts*

Martina L. Porter MD, Alexa B. Kimball MD, MPH\*  
*Department of Dermatology, Beth Israel Deaconess Medical Center,  
Boston, Massachusetts  
Harvard Medical School, Boston, Massachusetts*

\*Corresponding author:  
*E-mail address: [clears@bidmc.harvard.edu](mailto:clears@bidmc.harvard.edu) (A.B. Kimball)*