1. SYNOPSIS

Background: Ustekinumab is increasingly used for the treatment of inflammatory bowel disease (IBD) in women of reproductive age. Due to its IgG1 structure, placental transfer occurs predominantly during the second and third trimesters of pregnancy. Although available evidence has generally been reassuring, a recent observational study (Meyer 2025) suggested a potential increase in the risk of small for gestational age (SGA) infants among pregnancies exposed to ustekinumab compared with anti-TNFα therapy.

Objectives: The objective of the present study was to evaluate the risk of SGA in infants born to women with IBD exposed to ustekinumab during pregnancy using prospectively collected data from the DUMBO registry.

Methods: This observational cohort study analyzed pregnancies recorded in the Spanish prospective multicenter DUMBO registry. Pregnancies were categorized according to treatment exposure at conception or at any time during pregnancy into 4 groups:

- Group 1: no biologics and no immunomodulators or systemic corticosteroids
- Group 2: immunomodulators and/or systemic corticosteroids
- Group 3: anti-TNFα therapy
- Group 4: ustekinumab

The primary outcome was SGA, defined as birth weight below the 10th percentile for gestational age and sex according to the INTERGROWTH-21st international standards (Villar 2014).

Associations between treatment exposure and SGA were evaluated using multivariable logistic regression adjusting for clinically relevant confounders. Inverse probability of treatment weighting (IPTW) was not performed due to limited sample size.

Results: A total of 954 pregnancies with 980 live births were included in the analysis. The overall incidence of SGA was 11%, and the proportion of infants classified as SGA was similar across treatment groups (37 cases [11%] in the non- treated group, 27 [11%] in the immunomodulator group, 37 [12%] in the anti-TNFα group, and 10 [11%] in the ustekinumab group). In multivariable analysis, ustekinumab exposure was not associated with an increased risk of SGA compared with anti-TNFα therapy, immunomodulators including corticosteroids, or no immunosuppressive treatment : compared with ustekinumab exposure, adjusted OR (95% CI) were: 1.17 (0.53–2.78) for immunomodulators/corticosteroids, 1.37 (0.65–3.16) for anti-TNFα therapy, and 1.37 (0.61–3.33) for no immunosuppressive therapy. Independent predictors of SGA included female infant sex, maternal diagnosis of Crohn's disease and disease activity during pregnancy (higher risk of SGA).

Conclusions: In this prospective cohort of pregnancies in women with IBD, exposure to ustekinumab during pregnancy was not associated with an increased risk of SGA infants compared with other treatment groups. These findings provide reassuring real-world evidence regarding the fetal growth safety profile of ustekinumab in pregnancy.

References

Meyer A, Miranda A, Drouin J, et al. Safety of Vedolizumab and Ustekinumab Compared With Anti-TNF in Pregnant Women With Inflammatory Bowel Disease. Clinical Gastroenterology and Hepatology 2025;23:144–153

Villar J, Cheikh Ismail L, Victora CG, et al. International standards for newborn weight, length, and head circumference by gestational age and sex: the Newborn Cross-Sectional Study of the INTERGROWTH-21st Project. Lancet 2014; 384: 857–68