Letter to the Editor – Vedolizumab safety in pregnancy: extricating drug from disease related effects.

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We read with interest the recently published manuscript by Bell et al entitled Systematic review and meta-analysis: Safety of vedolizumab during pregnancy in patients with inflammatory bowel disease. This review aims to evaluate the safety of vedolizumab exposure in pregnancy utilizing a composite endpoint for adverse pregnancy outcomes comprising preterm births, early pregnancy loss, congenital abnormalities, late fetal death and elective termination of pregnancy. Four studies of varying designs, variable control cohorts and variable timing/perinatal duration of vedolizumab exposure were included. The authors concluded that vedolizumab exposure is associated with an increased risk of unfavorable pregnancy outcomes, acknowledging the potential of confounding due to a higher prevalence of active disease in vedolizumab exposed women at both conception and during pregnancy in two of the four studies. We wish to emphasize the later point. Our group has previously shown the disparate frequency of active disease in pregnancy between those receiving anti-TNF and vedolizumab. This was not commented upon in Bell’s review, and adds weight to the significance of disease activity as a potential confounder.

Clinically active IBD in pregnancy is associated with increased risks of adverse pregnancy and neonatal outcomes, including preterm labour, early pregnancy loss and small for gestational age. As such, continuing biologic agents (including vedolizumab) antenatally to maintain clinical remission is recommended, with withdrawal of biologics associated with increased rates of IBD relapse. 35% of the vedolizumab exposed women in the PICCOLO cohort had active disease in pregnancy. This significantly exceeded rates of active disease in the infliximab and adalimumab exposed cohorts of 9% and 0%, respectively (p=0.012). Two of the three adverse pregnancy outcomes described in the vedolizumab exposed cohort (the preterm deliveries) occurred in women with significant IBD activity. This included a participant who warranted vedolizumab induction in second trimester.
thus suggest these adverse outcomes were largely attributable to active disease, as opposed to the vedolizumab exposure independently.

Women exposed to vedolizumab in pregnancy often have anti-TNF refractory disease, and are more likely to Ulcerative Colitis (UC) compared to Crohn’s disease (CD)\(^3\). In of itself, UC is associated with an increased risk of flare in pregnancy relative to CD\(^8,9\). 71% of the 17 of the vedolizumab exposed women in PICCOLO had UC. This compared to only 7% receiving adalimumab and 17% on infliximab\(^5\). Likewise, 15% in the anti-TNF cohort in Moens’ study had UC, compared to 45% in the vedolizumab group\(^3\). 21% and 49% in the anti-TNF and vedolizumab exposed group in Wils’ study had UC respectively\(^4\). The discrepant proportion of UC patients warrants consideration when comparing rates of disease flare, and thus interpreting the significance of disparate pregnancy outcomes.

Bell et al described the increased rates of active disease in pregnancy noted in Moens’ vedolizumab exposed groups (36%) as compared to their unmatched anti-TNF exposed controls (17%)\(^1,3\). We feel the difference in rates of active disease warrants greater emphasis, particularly considering the high rates of active disease in the vedolizumab exposed women in the PICCOLO cohort. Although disparate rates of disease activity were not seen in the Wils’ cohort, more women were receiving steroids at conception in the vedolizumab as opposed to anti-TNF exposed groups\(^4\), suggesting active disease. Rates of live births and preterm delivery were equivalent when women with active disease were excluded from analysis in Moens’ study, with no increased risk of miscarriage in those exposed to vedolizumab vs anti-TNF with disease remission (16% vs 17%)\(^3\).

The findings of this systematic review and meta-analysis and the included studies highlight the confounding effects of IBD activity on pregnancy outcomes in vedolizumab exposed women. We agree with Bell et al that further prospective data with clear disease activity stratification is warranted. However, we do not feel there is adequate data currently to support modifying vedolizumab prescribing practices prior to conception or during pregnancy for women with IBD, and suggest that the priority in management of pregnancy...
women with IBD remain the control of active disease, including with the use of vedolizumab where indicated.

References:
