Reply to Phillips J et al, "European Crohn's and Colitis Guidelines on sexuality, fertility, pregnancy and lactation: a guideline review"

Goulden B, Nana M, Giles I, Nelson-Piercy C, Wiles K

We read with interest the summary of the European Crohn's and Colitis Guidelines on Sexuality, Fertility, Pregnancy and Lactation (1) but note inaccuracies which may misinform practice.

The authors state that calcineurin inhibitors (CNIs) should, where possible, be avoided in pregnancy due to 'limited data' and avoided in lactation due to 'no data'. These recommendations are not in keeping with the original guideline (2) which acknowledges that they are "low risk", or that of other key speciality guidelines including the British Society for Rheumatology (BSR) (3) and the UK Clinical Practice Guideline on Pregnancy and Renal Disease (4). These guidelines, after systematic literature review, recommend that CNIs are compatible with pregnancy and breastfeeding, with a long history of use in organ transplant recipients in pregnancy. Physicians prescribing CNIs should use them with confidence in pregnancy provided there is consideration for a gestational decrease in blood concentrations, an increased risk of gestational diabetes, and an awareness of potential drug interactions (including erythromycin which may be used for pre-term pre-labour rupture of membranes). Rather than avoidance, we recommend safe, informed use of these agents to optimise pregnancy outcomes.

Ciprofloxacin is appropriately reported as low risk in lactation in the original guideline (2), in contrast to the summary which advocates avoidance. We signpost to contemporary data from the Drugs and Lactation Database (LactMed®) confirming that ciprofloxacin is compatible with breastfeeding.

In the summary article, it is recommended that breastfeeding is delayed for four hours after high-dose corticosteroids with no additional contextual guidance. However, the original guideline describes corticosteroids in lactation as low risk, only advocating a four-hour interval before lactation in long-term, high-dose treatment. LactMed® reports that maternal prednisolone results in very low concentrations in breastmilk, including after short-term use of high-doses and there are no data to support theoretical concerns of infant adrenal suppression. These reassuring data should be weighed along with consideration of the frequent and prolonged feeding patterns of newborns.

The guideline and summary advise avoidance of live vaccines in early life following in-utero exposure to biologics, but both initially state that there is no apparent association between in utero exposure to anti-TNF agents and adverse reactions to vaccinations (1). Whilst all non-live vaccinations are recommended, case report and Medicines and Healthcare products Regulatory Agency alerts detail multiple infant deaths secondary to disseminated BCG following in-utero TNFi exposure and subsequent vaccination. The original guideline clearly outlines these risks later in the article, but this is not covered in the summary piece and may lead clinicians and/or patients to underappreciate the risk.

Prescribing in pregnancy and lactation is undoubtedly challenging. Summary advice on the safe management of inflammatory bowel disease in pregnancy is therefore welcomed, but this information must be appropriately balanced and reflect all available data to allow individualised prescribing and shared-decision making for treatment in pregnancy and lactation. Where evidence gaps exist, consideration should be given to the risks of withholding medication in pregnancy and lactation. We feel that this balance is required in published summary guidance so that maternal, fetal and neonatal health are not compromised by the omission of indicated treatment. Consistency, accuracy, and cross-speciality sharing of knowledge and expertise are essential.

Funding: BG currently supported by Versus Arthritis Clinical Research Fellowship (22975), MN currently supported by NIHR Research Training Fellowship (RE20732)

Acknowledgements: Nil

Competing interests: BG none declared; MN chair of RCP Trainee Committee, honoraria from Exeltis; IG unrestricted research grant from UCB, on advisory board for UCB, speaker fees for UCB, honoraria as co-author of an education review article for MGP, roles within BSR as lead on working group for guideline on prescribing in pregnancy and lactation, and chair of committee overseeing production of all BSR guidelines; CNP consulting and speakers fees for UCB and Sanofi Aventis, KW none declared

Ethics approval: Not applicable

Contributorship: BG, MN and KW conceived the idea. BG and MN prepared the draft manuscript with support and editing from IG, CNP and KW. All authors reviewed and approved the final version of the manuscript. BG is the guarantor of the letter.

1. Phillips J, Archer AJ, Lagnado A, et al. European Crohn's and Colitis Guidelines on sexuality, fertility, pregnancy and lactation: a guideline review. *Frontline Gastroenterology*. Published online first: 06 November 2023. doi: 10.1136/flgastro-2023-0102534
2. Torres J, Chaparro M, Julsgaard M, et al. European Crohn's and Colitis Guidelines on sexuality, fertility, pregnancy, and lactation. *J Crohns Colitis* 2023;17(1):1-27. doi: 10.1093/ecco-jcc/jjac115
3. Russell MD, Dey M, Flint J, et al. British Society for Rheumatology guideline on prescribing drugs in pregnancy and breastfeeding: immunomodulatory anti-rheumatic drugs and corticosteroids. *Rheumatology (Oxford)* 2023;62(4):e48-e88. doi: 10.1093/rheumatology/keac551
4. Wiles K, Chappell L, Clark K, et al. Clinical practice guideline on pregnancy and renal disease. *BMC Nephrol* 2019;20(1):401. doi: 10.1186/s12882-019-1560-2