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Thank you very much for considering our manuscript “**Pregnancy and Medications for Inflammatory Bowel Disease: An Updated Narrative Review**” in *World Journal of Clinical Cases*. We replied to reviewers’ comments. Given it is unacceptable to have more than 3 references from the same journal, we revised our reference list accordingly.

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Anti-tumor necrosis factor monotherapy is safe during pregnancy in women with IBD. However, their use in combination with thiopurines may be associated increased risk of neonatal prematurity and infection, although these data are conflicting. According to meta-analyses, vedolizumab and ustekinumab may be associated with early pregnancy loss; however, these data might be biased by IBD activity or small sample sizes. Recent prospective studies have demonstrated these biologics are generally safe during pregnancy. Janus kinase inhibitors are contraindicated during pregnancy as animal studies have demonstrated harmful effects. Calcineurin inhibitors may be considered for pregnant women with IBD who develop clinical relapse.

Response: Thank you for the comments.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: Anti-tumor necrosis factor monotherapy is safe during pregnancy in women with IBD. However, their use in combination with thiopurines may be associated increased risk of neonatal prematurity and infection, although these data are conflicting. It is an interesting manuscript. Authors can succeed to present their idea in a clear way adding information to the existing literature.

Response: We appreciate your comments.

The following papers were replaced with other papers.

6 Abhyankar A, Ham M, Moss AC. Meta-analysis: the impact of disease activity at conception on disease activity during pregnancy in patients with inflammatory bowel disease. *Aliment Pharmacol Ther* 2013; **38**(5): 460-466 [PMID: 23855477 PMCID: PMC3749828 DOI: 10.1111/apt.12417

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5 Rottenstreich A, Shifman Z, Grisaru-Granovsky S, Mishael T, Koslowsky B, Bar-Gil Shitrit A. Factors Associated with Inflammatory Bowel Disease Flare During Pregnancy Among Women with Preconception Remission. *Dig Dis Sci* 2021; **66**(4): 1189-1194 [PMID: 32356256 DOI: 10.1007/s10620-020-06282-7]

20 Wu B, Tong J, Ran Z. Tacrolimus Therapy in Steroid-Refractory Ulcerative Colitis: A Review. *Inflamm Bowel Dis* 2020; **26**(1): 24-32 [PMID: 30980713 DOI: 10.1093/ibd/izz068]

21 Lichtiger S, Present DH, Kornbluth A, Gelernt I, Bauer J, Galler G, Michelassi F, Hanauer S. Cyclosporine in

severe ulcerative colitis refractory to steroid therapy. *N Engl J Med* 1994; **330**(26): 1841-1845 [PMID: 8196726 DOI: 10.1056/NEJM199406303302601]

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16 Loftus CG, Egan LJ, Sandborn WJ. Cyclosporine, tacrolimus, and mycophenolate mofetil in the treatment of inflammatory bowel disease. *Gastroenterol Clin North Am* 2004; **33**(2): 141-169, vii [PMID: 15177532 DOI: 10.1016/j.gtc.2004.02.001]

22 Sandborn WJ, Feagan BG, Wolf DC, D'Haens G, Vermeire S, Hanauer SB, Ghosh S, Smith H, Cravets M, Frohna PA, Aranda R, Gujrathi S, Olson A, Group TS. Ozanimod Induction and Maintenance Treatment for Ulcerative Colitis. *N Engl J Med* 2016; **374**(18): 1754-1762 [PMID: 27144850 DOI: 10.1056/NEJMoa1513248]

23 Sandborn WJ, Feagan BG, D'Haens G, Wolf DC, Jovanovic I, Hanauer SB, Ghosh S, Petersen A, Hua SY, Lee JH, Charles L, Chitkara D, Usiskin K, Colombel JF, Laine L, Danese S, True North Study G. Ozanimod as Induction and Maintenance Therapy for Ulcerative Colitis. *N Engl J Med* 2021; **385**(14): 1280-1291 [PMID: 34587385 DOI: 10.1056/NEJMoa2033617]

46 Sandborn WJ, Feagan BG, Hanauer S, Vermeire S, Ghosh S, Liu WJ, Petersen A, Charles L, Huang V, Usiskin K, Wolf DC, D'Haens G. Long-Term Efficacy and Safety of Ozanimod in Moderately to Severely Active Ulcerative Colitis: Results From the Open-Label Extension of the Randomized, Phase 2 TOUCHSTONE Study. *J Crohns Colitis* 2021; **15**(7): 1120-1129 [PMID: 33438008 PMCID: PMC8256627 DOI: 10.1093/ecco-jcc/jjab012]

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17 Paik J. Ozanimod: A Review in Ulcerative Colitis. *Drugs* 2022; **82**(12): 1303-1313 [PMID: 35994200 PMCID: PMC9499884 DOI: 10.1007/s40265-022-01762-8]

24 Mahadevan U, Robinson C, Bernasko N, Boland B, Chambers C, Dubinsky M, Friedman S, Kane S, Manthey J, Sauberan J, Stone J, Jain R. Inflammatory Bowel Disease in Pregnancy Clinical Care Pathway: A Report From the American Gastroenterological Association IBD Parenthood Project Working Group. *Inflamm Bowel Dis* 2019; **25**(4): 627-641 [PMID: 30821832 DOI: 10.1093/ibd/izz037]

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18 Mahadevan U, Robinson C, Bernasko N, Boland B, Chambers C, Dubinsky M, Friedman S, Kane S, Manthey J, Sauberan J, Stone J, Jain R. Inflammatory Bowel Disease in Pregnancy Clinical Care Pathway: A Report From the American Gastroenterological Association IBD Parenthood Project Working Group. *Am J Obstet Gynecol* 2019; **220**(4): 308-323 [PMID: 30948039 DOI: 10.1016/j.ajog.2019.02.027]

52 Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. ACG Clinical Guideline: Ulcerative Colitis in Adults. *Am J Gastroenterol* 2019; **114**(3): 384-413 [PMID: 30840605 DOI: 10.14309/ajg.0000000000000152]

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42 Hindryckx P, Jairath V, D'Haens G. Acute severe ulcerative colitis: from pathophysiology to clinical management. *Nat Rev Gastroenterol Hepatol* 2016; **13**(11): 654-664 [PMID: 27580687 DOI: 10.1038/nrgastro.2016.116]

The following papers were deleted.

4 de Lima-Karagiannis A, Zelinkova-Detkova Z, van der Woude CJ. The Effects of Active IBD During Pregnancy in the Era of Novel IBD Therapies. *Am J Gastroenterol* 2016; **111**(9): 1305-1312 [PMID: 27349339 DOI:

10.1038/ajg.2016.254]

14 Sandborn WJ, Feagan BG, Rutgeerts P, Hanauer S, Colombel JF, Sands BE, Lukas M, Fedorak RN, Lee S, Bressler B, Fox I, Rosario M, Sankoh S, Xu J, Stephens K, Milch C, Parikh A, Group GS. Vedolizumab as induction and maintenance therapy for Crohn's disease. *N Engl J Med* 2013; **369**(8): 711-721 [PMID: 23964933 DOI: 10.1056/NEJMoa1215739]

15 Sands BE, Sandborn WJ, Panaccione R, O'Brien CD, Zhang H, Johanns J, Adedokun OJ, Li K, Peyrin-Biroulet L, Van Assche G, Danese S, Targan S, Abreu MT, Hisamatsu T, Szapary P, Marano C, Group US. Ustekinumab as Induction and Maintenance Therapy for Ulcerative Colitis. *N Engl J Med* 2019; **381**(13): 1201-1214 [PMID: 31553833 DOI: 10.1056/NEJMoa1900750]

32 Broms G, Granath F, Linder M, Stephansson O, Elmberg M, Kieler H. Birth outcomes in women with inflammatory bowel disease: effects of disease activity and drug exposure. *Inflamm Bowel Dis* 2014; **20**(6): 1091-1098 [PMID: 24810137 DOI: 10.1097/MIB.0000000000000060]

33 Cleary BJ, Kallen B. Early pregnancy azathioprine use and pregnancy outcomes. *Birth Defects Res A Clin Mol Teratol* 2009; **85**(7): 647-654 [PMID: 19343728 DOI: 10.1002/bdra.20583]

50 Reddy D, Murphy SJ, Kane SV, Present DH, Kornbluth AA. Relapses of inflammatory bowel disease during pregnancy: in-hospital management and birth outcomes. *Am J Gastroenterol* 2008; **103**(5): 1203-1209 [PMID: 18422816 DOI: 10.1111/j.1572-0241.2007.01756.x]

Comments for reviewers and editors

We have carefully considered removing some papers published from *Aliment Pharmacol Ther* in the reference list to reduce the number of citation from this journal. Since four pivotal studies introduced in this review article were published from *Aliment Pharmacol Ther*, we left them. If we need to delete one of them, the content of article would not be updated. Readers will notice this point easily. Please check them.