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Professor Lian-Sheng Ma
Editorial Office Director
Company Editor-in-Chief
World Journal of Clinical Cases

Dear Professor Ma,

RE: Manuscript NO: 71264, entitled 'Safety of dual biologic therapy in a patient receiving ocrelizumab for multiple sclerosis and vedolizumab for Crohn's disease. A case report and literature review update.'

Thank you for considering our manuscript. We appreciate the feedback that was given by the reviewers and have given absolute consideration into the feedback received.

Please see the additional pages where reviewer comments have been responded to on a point-by point basis.

Please find attached the manuscript with tracked changes.

Should you have any additional feedback or questions, please do not hesitate to contact myself at michael.au@my.jcu.edu.au or via phone on +61 414 656 163.

Thank you once again for considering the manuscript. We look forward to hearing from you.

Sincerely,

Michael Au
Principal Investigator on behalf of the research team
Nikola Mitrev, Rupert W Leong, Viraj Kariyawasam

Reviewer 1

Feedback	Response
The ethical approval document is lacked.	We have now updated the ethical rigour of our case report and have included an ethics declaration on the title page.
Line 112 “A 45-year-old female with a four-month history of newly diagnosed ileal CD” How to diagnose diagnosed ileal CD? Pathological diagnosis?	<p>We have now updated this to provide strengthened evidence on how the diagnosis of ileal CD was reached: clinically, radiologically, endoscopically, histologically, and biochemically. We have now updated the case report to state:</p> <p>“Active ileitis with involvement of 30 cm from the ileal-caecal junction and increased bowel wall thickness of 5 mm without upstream small bowel dilatation was confirmed on magnetic resonance enterography. Colonoscopy demonstrated active ileitis with a Simple Endoscopic Score for Crohn’s disease of 5 (2, 1, 2, 0). Histopathology from biopsy of the terminal ileum demonstrated patchy mild active inflammation. Her faecal calprotectin was elevated at presentation (> 1000 µg/g). Other pathogenic causes of diarrhoea from bacteria, parasites, and viruses were excluded from blood tests and stool cultures.”</p> <p>Radiology images are now included as Figure 1 and Figure 2.</p>
Line147. 148 “To date, the patient has safely received five months of DBT without adverse side-effects.” The case Will been taken longer to observe the patient’s curative effect.	Thank you for your feedback. We have now discussed this as a potential limitation in our case report. The primary focus of this case report, as the title suggests, is on the <u>safety</u> of dual biologic therapy, rather than efficacy. We have now added a limitations section to discuss this further.
The literature review update isn’t been seen in the article	We have now made it clear for the reader where the review of literature occurred in our article. We sought to provide a narrative review on this small topic area of dual biologic therapy in immune-mediated conditions.
Except CRP, whether there are other indexes, such as inflammatory factors (IL-6), oxygenation index.	We have included ESR as a marker of inflammation. IL-6 and oxygenation index are not routine markers of inflammation performed in Australia.
The article is not detailed, The case of the article is too simple.	We have now included images, histopathology results, and further detail to strengthen the case report.
There are no figures and tables, this case needs more evidences.	We have now included radiology images to strengthen the evidence. Please see Figure 1 and Figure 2. We have also included

	histology results in the case report.
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Reviewer 2

Feedback	Response
1. Title, "A case report and literature review update", it is hard to understand. I can't see literature review update.	We have now made it clear for the reader where the review of literature occurred in our article. We sought to provide a narrative review on this small topic area of dual biologic therapy in immune-mediated conditions.
2. Abstract, "There were no adverse reactions for the duration of treatment", the authors should present the case more gentle. How to proof that "no adverse reactions"?	The patient was reviewed monthly whilst on treatment with dual biologic therapy and reported no adverse reactions. We reclarified this statement in the body case report to support this statement. We have now rephrased this statement to present it more gently as recommended by the reviewers.
3. Introduction, "Furthermore, the COVID-19 pandemic presents new challenges in the clinical setting with concerns to the safety of biologic therapy", please supply references.	We have now provided a reference for this statement: Christina Dimopoulos, MD, Badr Al-Bawardy, MD, SARS-CoV-2 Infection and Dual-Biologic Therapy for Crohn's Disease, Inflammatory Bowel Diseases, Volume 26, Issue 12, December 2020, Pages e153–e154, https://doi.org/10.1093/ibd/izaa275
4. The language is needed to be improved. There are some mistakes for the grammar and language problems. For example, line 113, "stricturing" is a wrong word.	As native English speakers, we have now thoroughly revised the grammar of the article, and gave careful consideration to our word choices for an international audience.
5. Line 140, "Unfortunately, 5 months in to therapy she developed diarrhoea despite having therapeutic levels of vedolizumab of 33 ug/mL", could you please give the discussion for the developed diarrhoea. This should be adverse reactions, which is inconsistent to the point 1.	We believe the diarrhoea was a continuation of her initial presenting symptom, rather than new onset diarrhoea as a result of initiation of vedolizumab. Therefore, the recrudescence of her diarrhoea on this second occasion should not be considered as an adverse reaction.
6. Except CRP, whether there are other indexes, such as inflammatory factors (IL-6), oxygenation index.	We have included ESR as a marker of inflammation. IL-6 and oxygenation index are not routine markers of inflammation performed in Australia.
7. The ethical approval document is lacked.	We have now updated the ethical rigour of our case report and have included: (1) An ethics declaration on the title page
8. "Funding, Nil.", please provide the full name of Nil..	We have now updated this to state "There was no funding awarded or required for this case report."
9. There are no figures and tables, this case needs more evidences.	We have now included radiology images to strengthen the evidence. Please see Figure 1 and Figure 2. We have also included histology results in the case report.

Science Editor

Feedback	Response
It is unacceptable to have more than 3 references from the same journal. To resolve this issue and move forward in the peer-review/publication process, please revise your reference list accordingly.	We have now selected other sources to support our statements.