

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 84451

**Title:** Azathioprine Monotherapy withdrawal in Inflammatory Bowel Diseases: A Retrospective Mono-centric Study

**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 03009698

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Chief Doctor, Professor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2023-03-27

**Reviewer chosen by:** Geng-Long Liu

**Reviewer accepted review:** 2023-05-01 03:37

**Reviewer performed review:** 2023-05-01 09:17

**Review time:** 5 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

This paper performed a retrospective monocentric study aiming to evaluate azathioprine monotherapy withdrawal in inflammatory bowel diseases. I enjoyed reading this paper. However, there are some problems to be resolved. 1. I would strongly suggest that the author evaluate the recurrence rate of CD and UC after AZA suspension separately, instead of evaluating the recurrence rate of IBD. 2. Please add a section where potential clinical implications of these findings in real world clinical practice are presented. Moreover, please also discuss the limitations of this study. 3. English should be improved.

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**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 02441180

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** South Korea

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2023-03-27

**Reviewer chosen by:** Geng-Long Liu

**Reviewer accepted review:** 2023-05-07 02:10

**Reviewer performed review:** 2023-05-14 12:56

**Review time:** 7 Days and 10 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
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<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

#### **SPECIFIC COMMENTS TO AUTHORS**

The manuscript entitled Azathioprine Monotherapy Withdrawal in Inflammatory Bowel Diseases: A Retrospective Monocentric Study was reviewed and considered there is no new remarkable fact in this research. For advanced evidence, prospective research could be needed as outcomes after withdrawal of AZA after long term remission of IBD. Thanks.

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**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05562008

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** Australia

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2023-03-27

**Reviewer chosen by:** Geng-Long Liu

**Reviewer accepted review:** 2023-05-08 01:08

**Reviewer performed review:** 2023-05-17 19:48

**Review time:** 9 Days and 18 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
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	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

It is a nice study which tries to address an unanswered question but with a small number of patients. I would suggest using the word cessation rather than suspension through out the paper. (suspension implies something temporary) Aim: We described the events that led to and following the cessation of AZA in IBD Under Materials and Methods to define your cohort: We selected IBD patients aged >18 years who were already on AZA or started then discontinued AZA monotherapy. (this takes into account some of your data that you presented for the <18 year old) 3rd Paragraph under Materials and Methods. Sentence to restructure : All patients were assessed every six months in our outpatients clinic or earlier when needed using clinical and laboratory parameters. Under results the 69 patients that were in remission that AZA was stopped is a crucial group. How long was this group in sustained remission Figure 1 - Is it showing patients that were started or remained on Azathioprine? the body and discussion implies started the legend says remained. It is somewhat surprising before 2011 the use of Azathioprine was low Discussion IBD is an inflammatory disease of the gastrointestinal tract with a chronic intermittent course. 2nd paragraph 2nd line



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consistent with published data regarding the efficacy... However we found a higher percentage of CD patients started AZA before 18 years when compared to UC patients.

At the end of paragraph 2 I would include anti TNF together with vedlizumab and ustekinumab Paragraph 4 and table 2 don't seem to correlate. Your criteria in Table 2 says ALT X2?? Myelosuppression in your table says 8.4% in the discussion you say 9.9%

At the end of the discussion you have quoted a very low relapse rate in your cohort which is a crucial outcome in your study. You will need to hypothesise why - maybe data of how long these 69 patients were in remission before stopping may shed some light. Your study is much smaller compared to the other 2 studies (N when it comes to sustained remission n=69 vs =237 and 215) and that limitation must be highlighted.