Name of journal: World Journal of Diabetes
Manuscript NO: 74740
Title: Immediate-release tofacitinib reduces insulin resistance in non-diabetic active rheumatoid arthritis patients: A single-center retrospective study
Provenance and peer review: Invited Manuscript; Externally peer reviewed
Peer-review model: Single blind
Reviewer’s code: 03737141
Position: Editorial Board
Academic degree: PhD
Professional title: Professor
Reviewer’s Country/Territory: Egypt
Author’s Country/Territory: Taiwan
Manuscript submission date: 2022-01-14
Reviewer chosen by: AI Technique
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Reviewer performed review: 2022-02-08 20:51
Review time: 8 Days and 4 Hours

<p>| Scientific quality          | [ ] Grade A: Excellent       | [Y] Grade B: Very good       | [ ] Grade C: Good       |
|                            | [ ] Grade D: Fair            | [ ] Grade E: Do not publish  |                           |
| Language quality           | [ ] Grade A: Priority publishing | [Y] Grade B: Minor language polishing |
|                            | [ ] Grade C: A great deal of language polishing | [ ] Grade D: Rejection |
| Conclusion                 | [ ] Accept (High priority)   | [ ] Accept (General priority) |
|                            | [Y] Minor revision           | [ ] Major revision           | [ ] Rejection            |
| Re-review                  | [Y] Yes                      | [ ] No                       |                           |</p>
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<th>Peer-reviewer statements</th>
<th>Peer-Review: [Y] Anonymous  [ ] Onymous</th>
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<td>Conflicts-of-Interest: [ ] Yes  [Y] No</td>
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**SPECIFIC COMMENTS TO AUTHORS**

The manuscript fulfillment all the required criteria stated above but the 74740-Institutional Review Board Approval Form or Document is submitted I think in Chinese language.
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Manuscript NO: 74740

Title: Immediate-release tofacitinib reduces insulin resistance in non-diabetic active rheumatoid arthritis patients: A single-center retrospective study

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 03302683

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Chief Physician, Director, Professor

Reviewer’s Country/Territory: China

Author’s Country/Territory: Taiwan

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Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-02-24 02:13

Reviewer performed review: 2022-03-05 02:21

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SPECIFIC COMMENTS TO AUTHORS
The manuscript submitted by Yang Lin, et al. has investigated the effects of 24-week tofacitinib therapy on insulin sensitivity in non-diabetic active rheumatoid arthritis patients naïve or exposed to biologic therapy. In this retrospective study, they found reduced insulin resistance was achieved in non-diabetic active RA patients following 24 wk of tofacitinib therapy, suggesting JAK/STAT signaling may have the potential in treating diabetic. It’s an interesting study, and I have several comments as follows.

Major issues: 1. Glucocorticoids have a great impact on insulin resistance and glucose metabolism. And even with the same daily dose, the effects of long-term use and short-term use on insulin sensitivity vary greatly. So only analyzing the daily dose of prednisolone is not enough to exclude the impact of glucocorticoids. It is suggested to analyze the total exposure of prednisone in the course of treatment. 2. In discussion, “A reduction in IR has been identified in RA patients with a normal weight but not in those with obese status under anti-TNF-α therapy[35]. Despite no identified obesity in the present investigation (all patients had BMI < 27 kg/m2), there were higher BMI levels for patients without IR reduction (n = 7) when compared to those with reduced IR (n = 30) in the high-IR group of patients naïve or exposed to biologic therapy (without vs with IR reduction: 24.53±2.07 vs 22.49±1.91 kg/m2, P= 0.019), reflecting an influence of increased BMI on IR.” But in present study, improvement of insulin sensitivity is more obvious in high-IR group than in low-IR group. While it is known to all that higher BMI is closely associated with more severe insulin resistance. How to explain this contradiction?

Minor issues: 1. There is a mistake in legend of Figure 3, “A: Homeostatic model assessment (HOMA)-insulin resistance (IR) levels in all 30 patients at weeks 0 and 24
after tofacitinib (TOF) therapy (P = 0.016).” According to the results, 30 patients should be 26 patients with active rheumatoid arthritis exposed to biologic agents. This should be corrected.