

PEER-REVIEW REPORT

Name of journal: World Journal of Transplantation

Manuscript NO: 62523

Title: Chances and Risks of SGLT-2 inhibitors in Solid Organ Transplantation: a Review of the Literature

Reviewer's code: 04122500

Position: Peer Reviewer

Academic degree: MD

Professional title: Academic Fellow, Academic Research

Reviewer's Country/Territory: Italy

Author's Country/Territory: Switzerland

Manuscript submission date: 2021-01-11

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-04-10 12:04

Reviewer performed review: 2021-04-11 18:46

Review time: 1 Day and 6 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 Grade E: Do not publish
Language quality	<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
Conclusion	<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
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	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

I have read with interest the present minireview by Schwarzenbach M. and colleagues on the efficacy and side effects of SGLT2-inhibitors in diabetes management specifically in solid organ recipients. The authors reviewed current literature on the use of oral anti-diabetic drugs in solid organ transplantation, focusing on SGLT2-inhibitors which are showing favourable risk/benefit ratio. Still, current available literature is not sufficient to make strong recommendations for the use of these drugs in transplanted patients, so the author conclude that further studies are warranted to assess the potential role of these agents in the management of post-transplant diabetes (PTDM), which is a very actual issue. The discussed topics are of high interest and well written, still I would like to suggest a few observations that may improve the manuscript: **MAJOR** - I would suggest to reduce the introduction on general DM complications and general risk factors, in favor of the chapter analyzing those specifically related to transplanted patients. For example, pre- and peri-transplant risk factors for PTDM and prevention strategies could be discussed; - PTDM diagnostic criteria could be added as well; - I would recommend to add short chapter on potential diabetogenic effects of different immunosuppressive drugs, and drug-drug interferences with SGLT2-inhibitors; - Interestingly, Jin et al. (2017, American Journal of Transplantation) demonstrated in an experimental model that empagliflozin decreases tacrolimus induced hyperglycemia, and increases plasma insulin levels and pancreatic islet size. In addition, it reversed tacrolimus-induced renal dysfunction. It could be interesting to have the authors opinion about this potential additional beneficial effects that SGLT-2 inhibitors may exert on transplanted patients, by reversing immunosuppressive treatment's side effects **MINOR** - There are a few non-defined abbreviations throughout the manuscript: OPTN/SRTR, CNI, TPL, OLT. The manuscript contains numerous abbreviations, it may be easier for readers to reduce

them to the most frequently cited ones; - The manuscripts contains a few typos: o
 "...By blocking glucose and sodium re-uptake in the proximal convoluted tubule these
 compounds reduces..." -> reduce o "...by pancreatic β -cell function or the degree of
 insulin resistance, what allows their use in any stage of typ 2 diabetes" -> which
 allows....type 2 diabetes o "...Therefore, apart from reduction of glucosemia, SGLT2-
 inhibitores have a benefitial..." -> SGLT2-inhibitors...positive o "...SGLT-2 inhibitors
 may induce normoglycemic ketoacidosis, notably in settings of dehydration..." ->
 dehydration o "...although the CANVAS study included patients with eGFR von..." ->
 of o "...In line, several retrospective cohort studies in kindey transplant recipients under
 SGLT2-inhibitors reported a high tolerability of the drug class with minimal infecious/
 infectious complications..." -> minimal infectious complications o "...In our literature
 search, were did not identify..." -> we o "...Currently, several prospective trials
 investiagting..." -> investigating o "...The EMPTRA-DM trial from Vienna
 (NCT03113110) investigates glucose control in 16 stable kindey..." -> kidney

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<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
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer statements	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



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I appreciate the answers from authors. All suggestions were adequately addressed.