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PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 46649

Title: Prevention of macrovascular complications in patients with type 2 diabetes

mellitus: Review of cardiovascular safety and efficacy of newer diabetes medications

Reviewer's code: 03764245

Reviewer's country: India

Science editor: Fang-Fang Ji

Reviewer accepted review: 2019-04-18 06:38

Reviewer performed review: 2019-04-18 07:01

Review time: 1 Hour

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[] Grade A: Excellent	[] Grade A: Priority publishing	[] Accept	Peer-Review:
[Y] Grade B: Very good	[Y] Grade B: Minor language	(High priority)	[Y] Anonymous
[] Grade C: Good	polishing	[Y] Accept	[] Onymous
[] Grade D: Fair	[] Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
[] Grade E: Do not	language polishing	[] Minor revision	topic of the manuscript:
publish	[] Grade D: Rejection	[] Major revision	[] Advanced
		[] Rejection	[Y] General
			[] No expertise
			Conflicts-of-Interest:
			[] Yes
			[Y] No

SPECIFIC COMMENTS TO AUTHORS

Good study evaluating CV safety and efficacy of glucagon-like peptide-1 receptor agonists (GLP-1 RA) and sodium-glucose cotransporter-2 (SGLT-2) inhibitors.



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PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

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Title: Prevention of macrovascular complications in patients with type 2 diabetes

mellitus: Review of cardiovascular safety and efficacy of newer diabetes medications

Reviewer's code: 02446694

Reviewer's country: Japan

Science editor: Fang-Fang Ji

Reviewer accepted review: 2019-04-16 04:54

Reviewer performed review: 2019-04-21 21:10

Review time: 5 Days and 16 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[] Grade A: Excellent	[] Grade A: Priority publishing	[] Accept	Peer-Review:
[] Grade B: Very good	[Y] Grade B: Minor language	(High priority)	[Y] Anonymous
[Y] Grade C: Good	polishing	[Y] Accept	[] Onymous
[] Grade D: Fair	[] Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
[] Grade E: Do not	language polishing	[] Minor revision	topic of the manuscript:
publish	[] Grade D: Rejection	[] Major revision	[] Advanced
		[] Rejection	[Y] General
			[] No expertise
			Conflicts-of-Interest:
			[] Yes
			[Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors reviewed the recent results of anti-diabetic drugs including GLP1-receptor agonist and SGLT2 inhibitor for prevention of cardiovascular events. This review seems to be educative. I have no requests and questions.



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PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 46649

Title: Prevention of macrovascular complications in patients with type 2 diabetes

mellitus: Review of cardiovascular safety and efficacy of newer diabetes medications

Reviewer's code: 02874819

Reviewer's country: Italy

Science editor: Fang-Fang Ji

Reviewer accepted review: 2019-04-16 09:35

Reviewer performed review: 2019-05-05 07:48

Review time: 18 Days and 22 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[] Grade A: Excellent	[] Grade A: Priority publishing	[] Accept	Peer-Review:
[] Grade B: Very good	[] Grade B: Minor language	(High priority)	[Y] Anonymous
[Y] Grade C: Good	polishing	[] Accept	[] Onymous
[] Grade D: Fair	[Y] Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
[] Grade E: Do not	language polishing	[] Minor revision	topic of the manuscript:
publish	[] Grade D: Rejection	[Y] Major revision	[] Advanced
		[] Rejection	[Y] General
			[] No expertise
			Conflicts-of-Interest:
			[] Yes
			[Y] No

SPECIFIC COMMENTS TO AUTHORS

-The manuscript is very interesting and the topic is very current, however it is not very original, in fact the prevention and the outcome of Macrovascular Complications in Patients with Type 2 Diabetes Mellitus has already been described (Ismail-Beigi F,



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Moghissi E, Kosiborod M, Inzucchi SE. Shifting Paradigms in the Medical Management of Type 2 Diabetes: Reflections on Recent Cardiovascular Outcome Trials. J Gen Intern Med. 2017 Sep;32(9):1044-1051; Rahelić D, Javor E, Lucijanić T, Skelin M. Effects of antidiabetic drugs on the incidence of macrovascular complications and mortality in type 2 diabetes mellitus: a new perspective on sodium-glucose co-transporter 2 inhibitors. Ann Med. 2017 Feb;49(1):51-62) The topic is very long and complex and the authors have well analyzed the main molecules used in the current therapy but it would also be interesting to propose ideas for future therapies that also involve more complex pathogenic mechanisms that are now considered responsible for micro and macro vascular complications in patients diabetics: for example the epigenetics, energetics and therapies that can interact with the microbiota (Forbes JM, Fotheringham AK. Vascular complications in diabetes: old messages, new thoughts. Diabetologia. Nov;60(11):2129-2138.) "....Newer areas such as epigenetics, energetics and the increasing scrutiny of our synergistic inhabitants, the microbiota, also offer novel targets as biomarkers...." (Napolitano A, Miller S, Nicholls AW, Baker D, Van Horn S, Thomas E, Rajpal D, Spivak A, Brown JR, Nunez DJ. Novel gut-based pharmacology of metformin in patients with type 2 diabetes mellitus. PLoS One. 2014 Jul 2;9(7):e100778; Leustean AM, Ciocoiu M, Sava A, Costea CF, Floria M, Tarniceriu CC, Tanase DM. Implications of the Intestinal Microbiota in Diagnosing the Progression of Diabetes and the Presence of Cardiovascular Complications. J Diabetes Res. 2018 Nov 12;2018:5205126.) -for each drug nothing is reported about the glomerular filtrate to which it can be used, if there are contraindications, or if these molecules can cause acute or chronic kidney damage etc or if they have nephroprotective effects: Hahn K, Ejaz AA, Kanbay M, Lanaspa MA, Johnson RJ. Acute kidney injury from SGLT2 inhibitors: potential mechanisms. Nat Rev Nephrol. 2016 Nov 16;12(12):711-712; Gilbert RE.Sodium-glucose linked transporter-2 inhibitors: potential for renoprotection beyond blood glucose



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lowering? Kidney Int. 2014 Oct;86(4):693-700.; Cefalu WT, Leiter LA, Yoon KH, et al. Efficacy and safety of canagliflozin versus glimepiride in patients with type 2 diabetes inadequately controlled with metformin (CANTATA-SU): 52 week results from a randomised, double-blind, phase 3 non-inferiority trial. Lancet 2013;382(9896):941-50; Škrtić M, Cherney DZ. Sodium-glucose cotransporter-2 inhibition and the potential for diabetic nephropathy. Curr Opin Nephrol Hypertens protection in 2015;24(1):96-103; Yamout H, Perkovic V, Davies M, et al. Efficacy and safety of canagliflozin in patients with type 2 diabetes and stage 3 nephropathy. Am J Nephrol 2014;40(1):64-74. -this appears rather relevant considering that chronic renal failure is among the main complications present in diabetes and it itself leads to a greater cardiovascular risk and therefore a worse outcome, therefore it is necessary to add information about it. -the tables are well done and explain the various trials well -the manuscript is not very fluid to read -the manuscript should be revised by a native speaker english There are some typos

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[Y] No