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315-321 Lockhart Road,
Wan Chai, Hong Kong, China

ESPS Peer-review Report

Name of Journal: World Journal of Diabetes

Ms: 4205

Title: Effects of glucagon-like peptide-1 (GLP-1) receptor agonists on renal function

Reviewer code: 00503339

Science editor: l.l.wen@wjgnet.com

Date sent for review: 2013-06-20 13:52

Date reviewed: 2013-06-20 23:54

| CLASSIFICATION | LANGUAGE EVALUATION | RECOMMENDATION | CONCLUSION |
|----------------------------------------------|----------------------------------------------------------------------|-------------------------------------|--------------------------------------------------------|
| <input type="checkbox"/> Grade A (Excellent) | <input type="checkbox"/> Grade A: Priority Publishing | Google Search: | <input type="checkbox"/> Accept |
| <input type="checkbox"/> Grade B (Very good) | <input type="checkbox"/> Grade B: minor language polishing | <input type="checkbox"/> Existed | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C (Good) | <input type="checkbox"/> Grade C: a great deal of language polishing | <input type="checkbox"/> No records | <input type="checkbox"/> Rejection |
| <input type="checkbox"/> Grade D (Fair) | | BPG Search: | <input type="checkbox"/> Minor revision |
| <input type="checkbox"/> Grade E (Poor) | <input type="checkbox"/> Grade D: rejected | <input type="checkbox"/> Existed | <input type="checkbox"/> Major revision |
| | | <input type="checkbox"/> No records | |

COMMENTS

COMMENTS TO AUTHORS:

Well done and helpful analysis of a concern of growing import to the management of Type 2 Diabetes. The only addition that I would suggest is to note that there have been numerous examples of drugs evaluated in rodents with induced diabetes that when translated into clinical trials were ineffective. The best example is the sequence of failures of advanced glycoylated endproduct (AGE) inhibitors that proved worthless in clinical trials. Thus, caution should be expressed when citing rodent data as a clinical guide.



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Title: Effects of glucagon-like peptide-1 (GLP-1) receptor agonists on renal function

Reviewer code: 00503233

Science editor: l.l.wen@wjgnet.com

Date sent for review: 2013-06-20 13:52

Date reviewed: 2013-06-25 16:58

| CLASSIFICATION | LANGUAGE EVALUATION | RECOMMENDATION | CONCLUSION |
|---------------------------------------------------|--------------------------------------------------------------------------|-----------------------------------------|------------------------------------------------------------|
| <input type="checkbox"/> Grade A (Excellent) | <input type="checkbox"/> Grade A: Priority Publishing | Google Search: | <input type="checkbox"/> [Y] Accept |
| <input type="checkbox"/> [Y] Grade B (Very good) | <input type="checkbox"/> [Y] Grade B: minor language polishing | <input type="checkbox"/> [] Existed | <input type="checkbox"/> [] High priority for publication |
| <input type="checkbox"/> [] Grade C (Good) | <input type="checkbox"/> [] Grade C: a great deal of language polishing | <input type="checkbox"/> [] No records | <input type="checkbox"/> [] Rejection |
| <input type="checkbox"/> [] Grade D (Fair) | | BPG Search: | <input type="checkbox"/> [] Minor revision |
| <input type="checkbox"/> [] Grade E (Poor) | <input type="checkbox"/> [] Grade D: rejected | <input type="checkbox"/> [] Existed | <input type="checkbox"/> [] Major revision |
| | | <input type="checkbox"/> [] No records | |

COMMENTS

COMMENTS TO AUTHORS:

This review is well written, comprehensive and up to date. I only have the following, few, minor comments: 1-it would be helpful to devote a few lines in the Introduction, to the actions(both established and putative)of GLP-1. A figure would also be welcome. I would summarize two tables the studies regarding ezenatide and liraglutide(distinguishing between animal and human studies), besides providing detail in the text



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ESPS Peer-review Report

Name of Journal: World Journal of Diabetes

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Title: Effects of glucagon-like peptide-1 (GLP-1) receptor agonists on renal function

Reviewer code: 00505964

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| CLASSIFICATION | LANGUAGE EVALUATION | RECOMMENDATION | CONCLUSION |
|-------------------------|-------------------------------------------------|----------------|-----------------------------------|
| [] Grade A (Excellent) | [] Grade A: Priority Publishing | Google Search: | [] Accept |
| [] Grade B (Very good) | [Y] Grade B: minor language polishing | [] Existed | [] High priority for publication |
| [Y] Grade C (Good) | [] Grade C: a great deal of language polishing | [] No records | [] Rejection |
| [] Grade D (Fair) | [] Grade D: rejected | BPG Search: | [Y] Minor revision |
| [] Grade E (Poor) | | [] Existed | [] Major revision |
| | | [] No records | |

COMMENTS

COMMENTS TO AUTHORS:

General: This is a highly relevant topic being covered for the first in a dedicated review. The perspective is more on clinical implications than on basic physiology and case reports and safety issues are covered in very great detail. Although the method section states that searches have been performed up to June 2013, important paper are missing. Especially, a paper covering the basic renal physiology of GLP-1 in humans (1) and a paper elucidating a GLP-1 - ANP axis in mice (2) are mandatory in a review as this. In general it should be specified if findings are based on rodent or humans studies. The review has a tendency of becoming a long listing of study findings with only few reflexions from the authors. Abstract/Core Tip/Conclusion: More renal research have been performed with exenatide compared to liraglutide, but there is no evidence that exenatide protects the kidney better than liraglutide (the text could be interpreted that way). Further, it should be stated that this possible protection is based almost solely on rodent studies. Exenatide also affects water-sodium balance in humans (3) (also from studies already cited). Liraglutide also affects water-sodium balance in rodents (2). Sections regarding GLP-1/exenatide/liraglutide actions on renal function: The above mentioned papers (1,2) should be discussed. It should be mentioned that renal receptors in glomeruli and proximal tubules are animal findings which have not been replicated in humans (to my knowledge). Liraglutide safety: Here are two more case reports of acute kidney injury (4) 1. Skov, J., et al. Glucagon-Like Peptide-1 (GLP-1): Effect on Kidney Hemodynamics and Renin-Angiotensin-Aldosterone System in Healthy Men. J Clin Endocrinol Metab 98, E664-671 (2013). 2. Kim, M., et al. GLP-1 receptor activation and Epac2 link atrial natriuretic peptide secretion to



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control of blood pressure. *Nature medicine* (2013). 3. Mendis, B., Simpson, E., Macdonald, I. & Mansell, P. Investigation of the haemodynamic effects of exenatide in healthy male subjects. *Br J Clin Pharmacol* 74, 437-444 (2012). 4. Narayana, S.K., Talab, S.K. & Elrishi, M.A. Liraglutide-induced acute kidney injury. *Practical Diabetes* 29, 380-382 (2012).