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ESPS Peer-review Report

Name of Journal: World Journal of Hepatology

ESPS Manuscript NO: 6852

Title: Insulin Sensitizers for the Treatment of Non-alcoholic Fatty Liver Disease

Reviewer code: 00053433

Science editor: Song, Xiu-Xia

Date sent for review: 2013-10-30 16:40

Date reviewed: 2013-11-24 01:38

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 checked="" type="checkbox"/> Grade B (Very good)	<input checked="" 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)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

This is a review aimed at evaluating the available literature on the use of insulin sensitizers for the pharmacological treatment of NAFLD. The manuscript is well written and has scientific value since it includes a comprehensive compilation of the main articles on that relevant subject. However, there are some issues that need to be addressed. 1. In order to provide readers with a global perspective on the use of insulin-sensitizing medications in NAFLD patients, the recommendations from EASL and AASLD/ACG/AGA guidelines regarding those drugs should be mentioned (Ratziu V et al. J Hepatol 2010 and Chalasani N et al. Hepatology 2012). It would be particularly important to emphasize that those guidelines do not recommend the use of metformin and generally restrict the indication of TZDs, as specific liver-directed therapy, only to patients with biopsy-proven NASH. 2. It has been demonstrated that metformin inhibits hepatocyte proliferation and could inhibit liver oncogenesis, which could reduce the risk of developing hepatocellular carcinoma (Chen HP et al. Gut 2012; Bhalla K et al. Cancer Prev Res 2012; Zhang ZJ et al. J Clin Endocrinol Metab 2012). This should be briefly discussed by authors. 3. For the sake of completeness, the existence of several meta-analyses on the effects of TZDs in patients with NAFLD should be mentioned and their conclusions should be briefly discussed (Musso G et al. Hepatology 2010; Boettcher E et al. Aliment Pharmacol Ther 2012; Mahady SE et al. J Hepatol 2011; Musso G et al. Diabetologia 2012 [already discussed]; Rakoski MO et al. Aliment Pharmacol Ther 2010; and Shyangdan D et al. Health Technol Assess 2011). 4. The lack of evidence on the efficacy of TZDs in diabetic patients should be further discussed. 5. Conclusion section. It would be in the best interest of readers to clearly state authors' opinion on which NAFLD patients are the best candidates to be treated with TZDs. 6. It would also be interesting for readers if the relationship between insulin resistance and NAFLD pathophysiology could be better



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characterized by including a simplified figure.



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ESPS Peer-review Report

Name of Journal: World Journal of Hepatology

ESPS Manuscript NO: 6852

Title: Insulin Sensitizers for the Treatment of Non-alcoholic Fatty Liver Disease

Reviewer code: 00467221

Science editor: Song, Xiu-Xia

Date sent for review: 2013-10-30 16:40

Date reviewed: 2013-12-02 03:04

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" 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)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

This short review article is written well and covering a timely and interesting subject. The opinion presented is fair and agreeable.



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ESPS Peer-review Report

Name of Journal: World Journal of Hepatology

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Title: Insulin Sensitizers for the Treatment of Non-alcoholic Fatty Liver Disease

Reviewer code: 00504962

Science editor: Song, Xiu-Xia

Date sent for review: 2013-10-30 16:40

Date reviewed: 2013-12-12 15:09

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" 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)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

The present review provides an overview of insulin sensitizers in the treatment of non-alcoholic fatty liver disease (NAFLD). The topic of review is very important. It would be better to add the pathophysiological mechanism including several factors related insulin sensitizers.



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ESPS Peer-review Report

Name of Journal: World Journal of Hepatology

ESPS Manuscript NO: 6852

Title: Insulin Sensitizers for the Treatment of Non-alcoholic Fatty Liver Disease

Reviewer code: 00608153

Science editor: Song, Xiu-Xia

Date sent for review: 2013-10-30 16:40

Date reviewed: 2013-12-20 15:44

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" 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 checked="" 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)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

Two points should be addressed in this review. 1. The major pathogenesis of NAFLD is related to obesity that leads to insulin resistance in liver. Insulin resistance may not be the primary deficiency in NAFLD. 2. All the mentioned insulin sensitizer is used as antihyperglycemic agent. Although these agents improve insulin sensitivity, they are not used as insulin sensitizer as only treatment purpose in clinical practice. In several pathological conditions with insulin resistance, such as in subjects with essential hypertension, these agents could not be only used to improve insulin sensitivity.