

## ESPS Peer-review Report

**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 5780

**Title:** Meta-analysis of HIF-1a Immunohistochemical Expression as a Prognostic Role in Gastric Cancer

**Reviewer code:** 00503539

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-09-26 18:32

**Date reviewed:** 2013-10-04 08:59

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 checked="" 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)		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 TO AUTHORS

ESPS Manuscript No.5780 Ms. title: Meta-analysis of HIF-1a Immunohistochemical Expression as a Prognostic Role in Gastric Cancer by Shuang L, et al. General comments: Nine articles were selected from the Pubmed, EMBASE, and Web of Science databases to conduct a meta-analysis to evaluate prognostic role of HIF-1a expression in gastric cancer. They founded that HIF-1a positive expression in gastric cancer correlated with lower 5-year overall survival, worse tumor differentiation, deeper invasion, higher rate of lymph node metastasis, lymphatic invasion, vascular invasion and (III+IV) TNM staging. They concluded that HIF-1a positive expression indicates a poor prognosis for patients with gastric cancer. Some problems are, however, still remained to be clear. In particular, the authors could not fully demonstrate the significance of the present study. Therefore, the results between the present meta-analysis study and each selected nine studies [8-16] should be fully compared. Specific comments: 1. Abstract: The authors described that "Further studies are required to confirm these results." in Abstract. There is, however, no further description about this problem. The concrete proposal about this problem should be provided in Discussion. 2. Introduction: The authors referred "low-quality" and "high-quality" studies. Is this description appropriate? If appropriate, what are the criteria of both qualities? 3. Methods: The criteria of HIF-1a positive case are not clear. What the proportion of positive cancer cells per total cancer cells in HIF-1a positive cases? 4. Methods: It may be better that tumor location and tumor size could be included in clinicopathological features. 5. Discussion: "Gastric cancers do not usually express HIF-1a, and 548 (50%) of 1,103 gastric cancer patients had HIF-1a positive expression in this meta-analysis." Is this sentence right? It seems that the 50% may be unusual. "However, once



## **Baishideng Publishing Group Co., Limited**

Flat C, 23/F., Lucky Plaza,  
315-321 Lockhart Road,  
Wan Chai, Hong Kong, China

---

gastric cancer cells acquire HIF-1a expression, ....." What is the mechanism of acquisition of HIF-1a expression by gastric cancer cells?

**ESPS Peer-review Report**

**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 5780

**Title:** Meta-analysis of HIF-1a Immunohistochemical Expression as a Prognostic Role in Gastric Cancer

**Reviewer code:** 00722213

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-09-26 18:32

**Date reviewed:** 2013-10-07 23:38

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 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 checked="" type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input checked="" type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input checked="" 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 TO AUTHORS**

**META-ANALYSIS OF HIF-1A IMMUNOHISTOCHEMICAL EXPRESSION AS A PROGNOSTIC ROLE IN GASTRIC CANCER** In this paper the authors tried to perform a meta-analysis about the role of HIF-1A in gastric cancer, based on only 9 from about 100 studies published in the literature. Although the idea of paper is valuable, it is quite similar with a recent paper published by Zhang ZG et al. in 2013, Asian Pac J Cancer Prev (Title 7 from Reference list). There are several aspects that do not allow publication of the paper in the present format. However, the paper can be modified and submitted to other journal, according to the following suggestions: 1. **TITLE PAGE** Title - I suggest replacing the meta-analysis with Review because meta-analysis should involve a higher number of studies, nine of them being enough for such statistical study Authors - although the paper reports a pathological aspect of gastric cancer, the seven authors are surgeons. I suggest reducing the number of authors - two many for nine studies - and to ask for a pathologist point of vision and include him in the list of authors. 2. **ABSTRACT** - Aim: A meta-analysis should include more than 24 titles, as in this paper. - Results: This part of the abstract is partially incorrect. One hand, because the authors mentioned that HIF1a expression correlated with worse tumor differentiation.....what about the other types of gastric tumors excluding the adenocarcinomas??? - what about mucinos, poorly cohesive, neuroendocrine, lymphomas....if it is a metaanalysis of gastric CANCER, it should include all tumors form WHO classification. If not, the title and study design should be changed. On the other hand, the nine studies included in this analysis were published before and after 2010 - this is a very important aspect that disqualify the study for publication - a pathologist would be contacted for a restaging of the tumors - according with the AJCC classification

VIIth edition or VIIth edition used from 2010.....WITHOUT THIS RESTAGING THIS STUDY IS TOTALLY UNADEQUATED. More than, because HIF1a is involved in angiogenesis, a correlation with serum and histological aspects of VEGF is mandatory to be included.... 3. INTRODUCTION -

first paragraph - second phrase - both histological differentiation (tumor differentiation is an improper term) and tumor type should be taken into account; fifth phrase - wrong spelling -

second paragraph - second phrase - last part (from '....which was known...' should be removed - the authors already mentioned this aspect in first paragraph); same for last phrase 4.METHODS -

Study selection? First paragraph - 'gastric carcinoma'should also be included as keyterm -

Outcomes of interest? First paragraph - both histological differentiation (tumor differentiation is an improper term) and tumor type should be taken into account and TNM staging system should be mentioned - ideally, it is to restaging the tumors according to the VIIth edition of AJCC ?

Second paragraph - to exclude papers wrote by same team all authors should be extracted, not only first one 5. RESULTS - Selection of trials? It is not a proper selection - few studies (9) - only one study from Europe, with several genetic differences compared with Asian patients - this is the reason why the study from Turkey had results discordants to the other studies (see the graphics) - papers published before and after 2010, with different staging systems - after consulting of results, I can see that the studies are inhomogenous, reason why, in graphics, an improper reporting of results occurred, only 4-5 studies being included for specific parameters...?I suggest to reduce this paragraph and to resume it in tables - there are too many numbers and data, very difficult to understand them 6. DISCUSSION - First paragraph? first phrase should be reworded, being difficult to be understood - second phrase - this is not a comprehensive study or a detailed meta-analysis.....It is a review - Second

## ESPS Peer-review Report

**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 5780

**Title:** Meta-analysis of HIF-1a Immunohistochemical Expression as a Prognostic Role in Gastric Cancer

**Reviewer code:** 02445717

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-09-26 18:32

**Date reviewed:** 2013-10-09 23:08

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	<input type="checkbox"/> ] No records	<input type="checkbox"/> ] Rejection
<input type="checkbox"/> Grade D (Fair)	language polishing	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 TO AUTHORS

This manuscript describes an interesting meta-analysis of the HIF-1a positive expression was associated with a poor prognostic factor for 5-year overall survival and clinicopathological features in patients with gastric cancer. In addition, HIF-1a positive expression could be a useful prognostic marker of gastric cancer. The manuscript is well written. The abstract summarizes the purpose of the study. The introduction covers the literature and explains the basis for this study. The methods are sound and accurately performed. The results are also a straightforward description of the HIF-1a positive expression in gastric cancer correlated with lower 5-year overall survival. The results are supported with good illustrations. The discussion is well orchestrated. This section summarizes the present data and correlates these observations with appropriate information from the literature. In sum, this is a competent review addressing a subject of interest and potential value for the scientific community, and it should be useful for interdisciplinary correlative studies. However, there are some recommendations that I would make: Check the text there is some minor spelling