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## ESPS Peer-review Report

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

**Ms:** 3865

**Title:** The role of bevacizumab in malignant tumor growth and its adverse effects: a review

**Reviewer code:** 00186131

**Science editor:** Song, Xiu-Xia

**Date sent for review:** 2013-05-29 10:53

**Date reviewed:** 2013-06-10 14:03

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)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

the manuscript is interesting, original and well written. However, the authors have to add and discuss also the role of VEGF in other diseases such as allergic and immune-mediated diseases (see Ciprandi G, et al. Serum vascular endothelial growth factor in allergic rhinitis and systemic lupus erythematosus. *Hum Immunol.* 2008 Aug;69(8):510-2; Ciprandi G, et al. Serum vascular endothelial growth factor and sublingual immunotherapy. *Allergy.* 2008 Jul;63(7):945-6) and the potential positive effect of other biological drugs (Murdaca G, et al. Effects of TNF- $\alpha$  inhibitors upon the mechanisms of action of VEGF. *Immunotherapy.* 2013 Feb;5(2):113-5).



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### ESPS Peer-review Report

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

**Ms:** 3865

**Title:** The role of bevacizumab in malignant tumor growth and its adverse effects: a review

**Reviewer code:** 00367760

**Science editor:** Song, Xiu-Xia

**Date sent for review:** 2013-05-29 10:53

**Date reviewed:** 2013-06-11 06:48

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)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

### COMMENTS TO AUTHORS

In this review, Dr. Pavlidis ET et al. summarized the role of bevacizumab in malignant tumor growth and its adverse effects. It will be useful if the application of bevacizumab in medical treatment is well reviewed. However, there are several problems in this review. Comment: 1. The author should summary the key points of this review in abstract or introduction. Lack of summary makes the review lose the questions to be addressed. 2. A summary is also needed at the end of the paper. 3. The “experimental use perspectives” should put into the main text to support the data in human. 4. Some of the basic concepts need to be carefully corrected, such as page 7 “ small dose of the drug may be bound to all the VEGF receptors”. It binds to VEGF, not receptors. That is one example, and there are many of those issues. 5. Also, the review need be edited by professorial language service to make it readable.



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## ESPS Peer-review Report

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

**Ms:** 3865

**Title:** The role of bevacizumab in malignant tumor growth and its adverse effects: a review

**Reviewer code:** 02494908

**Science editor:** Song, Xiu-Xia

**Date sent for review:** 2013-05-29 10:53

**Date reviewed:** 2013-06-23 20:34

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)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

The work is interesting and represent a good overview concerning bevacizumab and mCRC. However, some general points should be addressed before this paper be resubmitted: 1 - language review is mandatory. 2 - highlight the main clinical trials involved in the bevacizumab FDA and EMA approval - specific and discuss those trials issues, such as design, pitfalls, consistence of results, toxicities and limitations. 3 - create tables inserting those trials issues due to facilitate readers understanding your article. 4 - insert figures explaining the VEGF-VEGFR interactions. 5 - highlight medical oncologists practice issues whether choose bevacizumab to treat mCRC. How we should proceed ? what we should consider in this setting of patients? 6 - a brief paragraph of pharmaco-economic approaches concerning bevacizumab should be interesting 7 - How should mananger bevacizumab side effects ? what onocologists should be aware ? 8 - and finally, what about the future ? what oncologists expects toward the world regarding anti-angiogenic therapies for mCRC? phase II clinical trials ? important results from ASCO 2013? a new table containing this studies could help in this topic ...



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## ESPS Peer-review Report

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

**Ms:** 3865

**Title:** The role of bevacizumab in malignant tumor growth and its adverse effects: a review

**Reviewer code:** 00503623

**Science editor:** Song, Xiu-Xia

**Date sent for review:** 2013-05-29 10:53

**Date reviewed:** 2013-06-25 23:55

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)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

This manuscript presents a short review of the preclinical and clinical data on bevacizumab, an IgG monoclonal antibody against VEGF. The presentation, while reasonable in details when dealing with clinical aspects, suffers considerably in description and wording when describing the mechanism of bevacizumab action. Hence, it is absolutely mandatory that you revise the following sections; Abstract- line 7 'it cannot be banded'??? Page 5, line 5. It is not 'phosphorization' but phosphorylation. Page 7, first paragraph - This entire section needs restructuring, so the words such as "inhered" and "humanized" are substituted with the more appropriate. There should be a separate section describing the mechanism of VEGF signaling, possibly with schematic drawing of the receptor and how it interacts with the antibody. Sorry, but these suggestions are meant to be constructive.

**ESPS Peer-review Report**

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

**Ms:** 3865

**Title:** The role of bevacizumab in malignant tumor growth and its adverse effects: a review

**Reviewer code:** 02446379

**Science editor:** Song, Xiu-Xia

**Date sent for review:** 2013-05-29 10:53

**Date reviewed:** 2013-07-03 02:54

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	BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

**COMMENTS TO AUTHORS**

As regarding the trial titled “The role of bevacizumab in malignant tumor growth and its adverse effects: a review” by Theodoros E Pavlidis MD, PhD which was submitted for publication consideration in WJGO I have the follow comments: The author has provided a comprehensive review focusing on the role of bevacizumab in malignancy. Overall the manuscript is well written and well organised. Nevertheless, there are some minor concerns: a) In the section of the clinical application in rectal cancer page 10. The author has stated that a large randomized multicenter trial has shown that the addition of bevacizumab in the treatment with capecitabine plus or without mitomycin improved significantly the progression-free survival (PFS) and the quality of life without inducing further toxicity [32]. Actually, the quality of life (QoL) was neither improved nor attenuated with the addition of bevacizumab and specific toxicity related to bevacizumab such proteinuria, hypertension, and arterial thromboembolic events, hemolytic uremic syndrome was added in the two arms of bevacizumab plus chemo. Furthermore there were 11 treatment-related deaths: one in the capecitabine arm (sepsis); seven in the CB arm (hemorrhage, myocarditis, bowel perforation, and sepsis); and three in the CBM arm (hemorrhage, pulmonary embolism, and neutropenic colitis). I strongly believe that this should be corrected and clarified. b) In the section of Bevacizumab in other malignancies page 12. I recommend that a small paragraph regarding the role of bevacizumab in primary brain gliomas should be added, since bevacizumab’s role in such tumours is nowadays increasingly investigated. E.g Bevacizumab had been investigated extensively in patients with primary brain malignant gliomas and has been approved as second line chemotherapy alone or in combination with irinotecan following first or second recurrence after radiotherapy and temozolomide [1. Vredenburgh JJ, Desjardins A, Herndon JE 2nd, et al. Bevacizumab plus



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irinotecan in recurrent glioblastoma multiforme. *J Clin Oncol.* 2007;25:4722-4729. 2. Kreisl TN, Kim L, Moore K, et al. Phase II trial of single-agent bevacizumab followed by bevacizumab plus irinotecan at tumor progression in recurrent glioblastoma. *J Clin Oncol.* 2009;27:740-745. 3. Friedman HS, Prados MD, Wen PY, et al. Bevacizumab alone and in combination with irinotecan in recurrent glioblastoma. *J Clin Oncol.* 2009;27:4733-4740]. Furthermore, the efficacy and safety of combining bevacizumab with standard-of-care therapy in patients with newly diagnosed glioblastoma multiforme of the brain is now investigating by AVAGLIO phase III randomized trial [O. L. Chinot, T. de La Motte Rouge, N. Moore, et al. AVAGlio: Phase 3 Trial of Bevacizumab Plus Temozolomide and Radiotherapy in Newly Diagnosed Glioblastoma Multiforme. *Adv Ther* (2011) 28(4):334-340. DOI 10.1007/s12325-011-0007-3]. My final decision is accept it after the correction of the above mentioned concerns.