

ESPS Peer-review Report

Name of Journal: World Journal of Gastrointestinal Oncology

ESPS Manuscript NO: 6426

Title: Thrombocytosis as a prognostic marker in gastrointestinal cancers

Reviewer code: 00289387

Science editor: Cui, Xue-Mei

Date sent for review: 2013-10-18 16:53

Date reviewed: 2013-11-09 21:47

| 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

Dr. Voutsadakis summarized recent clinical studies on a pathologic role of thrombocytosis in gastrointestinal cancers. The author presented a number of gastrointestinal cancers associated with aberrant levels of platelets, including esophageal, gastric, pancreatic, hepatic, and colorectal cancer. In multiple independent clinical trials enrolling large cohorts, thrombocytosis was found to be correlated with adverse clinical outcomes of different types of gastrointestinal cancers in general, such as advanced cancers, high tumor stages, and decreased disease-free survival or overall survival. The review may offer the prognostic value of thrombocytosis in the clinical practice of patients with gastrointestinal cancers. 1) It is well appreciated that inflammation is critical for the development of gastrointestinal cancers, in which multiple cytokines, chemokines, angiogenic factors, and MMPs are derived from tumor infiltrating leukocytes such as infiltrating macrophages as well as tumor cells. Interestingly, platelets also increasingly produce a vast array of cytokines (e.g. ILs), growth factors (e.g. VEGF and TGF- β), and chemokines (e.g. CXCLs) during chronic inflammation. Therefore, there is somehow intimate association between infiltrating macrophages and platelets in terms of these important factor productions in cancers. However, the role of infiltrating macrophages in the paper is missing. 2) With regarding to cytokine production and mechanisms in cancer development, a relatively clear relationship among tumor cells, platelets, and macrophages should be described. 3) A summarized table containing the different types of cancers, platelet counts, correlation data with clinical outcomes, cytokine production, and therapeutic trials targeting cytokines if available, may help highlight the key points demonstrated by the author. 4) It is confused by the statement on p8 the bottom of 3rd paragraph, in which patients with...had a significantly worse survival than patients... the former was 25 months while not reached in the latter.



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If the survival data for the patients with lower counts are absent, how to compare with the survival 25 months? 5) A short section with future directions should be provided prior to the Conclusion.

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Name of Journal: World Journal of Gastrointestinal Oncology

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Title: Thrombocytosis as a prognostic marker in gastrointestinal cancers

Reviewer code: 00542396

Science editor: Cui, Xue-Mei

Date sent for review: 2013-10-18 16:53

Date reviewed: 2013-12-04 18:14

| 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 | 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 review by PhD. Voutsadakis IA discusses the possibility of using the platelet count as a prognosis marker of development and different gastrointestinal cancers. They have compiled very recent publications where the results shown point to that possibility; particularly almost 30% of the references belong to the either the present or the past year. This fact reflects two very important points: 1) the present topic is very interesting for the international community. 2) data that support the present review are very new, thus the review will contribute to update the knowledge regarding this theme. Thus considering the clear presentation of the supporting data, as well as their concise discussion, and finally, the right conclusion that the reach at the end of the manuscript, I have to propose the present manuscript as very suitable for publication in our journal.

ESPS Peer-review Report

Name of Journal: World Journal of Gastrointestinal Oncology

ESPS Manuscript NO: 6426

Title: Thrombocytosis as a prognostic marker in gastrointestinal cancers

Reviewer code: 00289700

Science editor: Cui, Xue-Mei

Date sent for review: 2013-10-18 16:53

Date reviewed: 2013-12-06 02:57

| 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 |
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| <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 |
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COMMENTS TO AUTHORS

The manuscript by Ioannis Voutsadakis is dedicated to reviewing and analyzing existing literature focused on using the high platelet count (thrombocytosis) as a prognostic marker in cancer and on understanding the cellular and molecular mechanisms underlying the link between thrombocytosis and cancer progression. The thorough review of data lead to the conclusion that thrombocytosis may be used in some cases as a marker of poor prognosis and that targeting of the IL-6/IL-6R axis may exert a therapeutic effect in these conditions. This generally well-written manuscript may be improved further by making a few modifications. 1. General: The data analyzed are plentiful, while not always in agreement with each other. It would be very useful to summarize the data reviewed in a summary table. 2. P.4: "Circulating tumor cells may use platelets as a protective shield from the attack of the immune system". This statement needs to be elucidated. How tumor cells use platelets as a shield? 3. Pp.4-5: In the section of the manuscript focused on pathogenesis of thrombocytosis in cancer a substantial part is dedicated to the possible contribution of platelets to carcinogenesis. The analysis is restricted to description of possible effects of soluble factors, produced by platelets. However, these factors may or may not exert these effects in reality; this may depend on the level of their production, location of platelets, etc. It is important to clearly delineate possible, hypothetic effects from those shown directly.

ESPS Peer-review Report

Name of Journal: World Journal of Gastrointestinal Oncology

ESPS Manuscript NO: 6426

Title: Thrombocytosis as a prognostic marker in gastrointestinal cancers

Reviewer code: 02458824

Science editor: Cui, Xue-Mei

Date sent for review: 2013-10-18 16:53

Date reviewed: 2013-12-13 22:04

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COMMENTS TO AUTHORS

The review is very good. I have only two minor comments: -Page 3, introduction, line 13 and 14. When the authors lists causes of secondary thrombocytosis, this reviewer believes that it will be better to write "...or secondary to malignancy, hemorrhage, chronic inflammation, iron deficiency, and splenectomy." -This reviewer wonders if author could summarize main findings of thrombocytosis in diferent gastrointestinal cancers in one table.

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