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

## ESPS Peer-review Report

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

**ESPS Manuscript NO:** 4161

**Title:** METASTATIC TYPE 1 GASTRIC CARCINOID - A REAL THREAT OR JUST A MYTH?

**Reviewer code:** 00504704

**Science editor:** Wen, Ling-Ling

**Date sent for review:** 2013-06-18 16:55

**Date reviewed:** 2013-06-21 06:03

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 checked="" 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 is an interesting report and is well written. My only concern is whether or not all the patients they describe as having type I gastric carcinoid actually had type I gastric carcinoid. There should be strong documentation that these patients had atrophic gastritis and not a gastrin producing NET, or a type III carcinoid. This paper would be stronger if the authors show a table with all the features which allowed them to designate their patients as type I carcinoids - when available - B12 levels, gastrin levels, histology showing atrophy, acid secretion, prior use of PPI medicines, etc. The authors stated that gastrin levels fell in all patients on therapy. They should explain how that happens in subjects with a wedge resection of the primary lesion and no other therapy.

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

**ESPS Manuscript NO:** 4161

**Title:** METASTATIC TYPE 1 GASTRIC CARCINOID - A REAL THREAT OR JUST A MYTH?

**Reviewer code:** 00004159

**Science editor:** Wen, Ling-Ling

**Date sent for review:** 2013-06-18 16:55

**Date reviewed:** 2013-07-04 20:01

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)	<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**

This is a useful retrospective study of a rare disease and provides helpful information on risk factors and prognosis in a cohort of 20 patients. Major comments: 1. The description of patient characteristics is confusing, specifically in relation to baseline imaging: a. The paragraph on page 5 entitled "Imaging Assessment" reads: "Seventeen patients underwent 111In-pentetreotide scintigraphy (Octreoscan) or Gallium68-DOTA-TATE/-TOC/-NOC PET at diagnosis. Thirteen patients also underwent computerized tomography (CT) of the abdomen." ...which appears to suggest that of the 17 patients who underwent functional imaging, 13 also had a CT. I assume that this cannot be the case but the manuscript doesn't specify who had functional imaging, who had CT and who had both (or neither). It might be helpful to include these details in the table. It is surprising that not all patients had a CT scan - can the authors explain. b. The following paragraph entitled "Endoscopic and histopathological assessment" (page 5) states that 6/20 patients underwent EUS at baseline but the paragraph on page 6 entitled "Basal evaluation (at diagnosis)" states that EUS was performed in all patients. Can the authors please explain this discrepancy. 2. The same paragraph (page 6) refers to "Signs of aggressiveness or invasiveness at first biopsy" but includes in these the presence of lymph node metastasis. Is this intentional? If so, it needs to be made clear that the "first biopsy" includes surgical/endoscopic resection specimens. 3. Page 6 (methods) - please describe statistical tests used in this study. I am concerned that simple t tests have been used which would not be appropriate as I suspect the datasets were not normally distributed. 4. The observation that serum gastrin levels decreased in all patients (page 9) is interesting and in some cases confusing. a. Presumably, the gastrin levels given in Table 2 are those from baseline assessment. Could post treatment levels also please be included for individual patients? b. There is no value given here for 6



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of the 20 patients – this needs to be clarified when the mean concentration is quoted elsewhere in the manuscript. c. If the value is unknown in these patients, how was the decrease in gastrin levels determined? d. In those patients whose treatment included neither antrectomy nor the use of SSAs, (patients 6, 13 & 14), what mechanism is responsible for a decrease in serum gastrin concentration?. More detail on this would be informative. 5. Please include follow up in each individual patient in the outcome column. It would not be appropriate to consider the patient to be cured if the follow up period was short. 6. Page 10 and table 3: are the subgroup of patients with metastatic GCA1 (n=20) included in the total (n=254)? If so maybe they should be excluded and the comparison made between metastatic and non-metastatic cases. 7. The importance attached to the use of SSAs seems overstated. The authors go so far in discussion as to recommend this as first-line treatment in patients with large (>1cm) tumours. Given the evidence in the literature that, once started, treatment with SSA should be continued indefinitely, it seems that the observed response in this study is insufficient to make such a recommendation and I would suggest a more guarded statement be used instead.

Minor comments

1. Page 6 – It is arguable whether Crohn's disease should be called an autoimmune condition
2. Page 11, 3rd paragraph – change GAC1 to GCA1 for consistency
3. Table 3, column 3 – change GA1 to GCA1 for consistency

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

**ESPS Manuscript NO:** 4161

**Title:** METASTATIC TYPE 1 GASTRIC CARCINOID - A REAL THREAT OR JUST A MYTH?

**Reviewer code:** 01164511

**Science editor:** Wen, Ling-Ling

**Date sent for review:** 2013-06-18 16:55

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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"/> Rejection
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

**COMMENTS TO AUTHORS**

Grozinsky-Glasberg et al. reported a multicenter, retrospective analysis describing characteristics and treatment procedures in a wide group of patients with metastatic gastric carcinoids type 1 (GCA1). The topic is interesting and the paper is well designed and written. The authors should add a short paragraph in the discussion section on the future perspectives in the therapy of advanced and aggressive GCA1. Please, briefly describe the potential applications of interferon-beta (Vitale G. et al. Cancer Res 2006; 66(1):554-62. Vitale G. et al. Am J Physiol Endocrinol Metab 2009; 296(3):E599-66. Caraglia M. et al. Curr Cancer Drug Targets 2009; 9(5): 690-704); pasireotide (Wolin EM, et al. Cancer Chemother Pharmacol. 2013 Jun 14); dopamine agonists and dopamine/somatostatin chimera (Kidd M et al. Regul Pept. 2007 Oct 4;143(1-3):109-17.).

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

**ESPS Manuscript NO:** 4161

**Title:** METASTATIC TYPE 1 GASTRIC CARCINOID - A REAL THREAT OR JUST A MYTH?

**Reviewer code:** 00033061

**Science editor:** Wen, Ling-Ling

**Date sent for review:** 2013-06-18 16:55

**Date reviewed:** 2013-07-09 21:46

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
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<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

**COMMENTS TO AUTHORS**

General observations This manuscript is generally well written and organized. It is quite unexpected the gender distribution in the population studied. Being the population under study composed of type 1 gastric carcinoid, which develop in the context of chronic atrophic gastritis, I would have expected a high prevalence of female gender. If possible, enter a comment about this. Only minor imprecisions should be corrected: - In the "results" section (page 6, Basal Evaluation, second paragraph) the authors said that EUS is done to everyone while in the "methods" section it is written that EUS has been made in 6 out of 20 patients. - Speaking about signs of aggressiveness, the authors write that these one were available in 12 patients .... but they do not explain why these are missing in the other 8 patients (i.e. 40% of the population) ... perhaps because there are no EUS data (but they've just said that it was made in all the patients). - Again in the "results", "Treatment" section, paragraph 2 the authors categorize 11 patients in the group of grade 1 and 9 patients in the group of grade 2 : this does not match Table 2.