



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 48807

Title: Retrospective study on mixed neuroendocrine non-neuroendocrine neoplasms from five European centres

Reviewer’s code: 03548113

Reviewer’s country: Japan

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-05-07 03:42

Reviewer performed review: 2019-05-08 06:02

Review time: 1 Day and 2 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good		<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer’s expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Minor revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This retrospective study is well written and very interesting. I think this is worthy for WJG.



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INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 48807

Title: Retrospective study on mixed neuroendocrine non-neuroendocrine neoplasms from five European centres

Reviewer’s code: 00050849

Reviewer’s country: Sweden

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-05-04 16:20

Reviewer performed review: 2019-05-10 20:34

Review time: 6 Days and 4 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This is an interesting manuscript focusing on MANETs by Frizziero MF. Minor points: At “Clinical characteristics of patients and pathological data on tumour samples” last paragraph, “Additional pathological material from synchronous or metachronous



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metastatic sites was available for 15 patients“ how many patients had synchronous and how many metachronous metastatic sites? Major points: Can the authors present biochemical markers (CgA, NSE etc) before and during treatment? Can statistics be applied? In which studies do the authors base there algorithm to offer surgery in localized disease? A Nordic study included only pancreatic NECs (Annals of Surgical Oncology May 2016, Volume 23, Issue 5, pp 1721-1728). How the authors address the possible hematogenous metastases of the NEC counterpart before the surgery is done.

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- Y] No

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- Y] No



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 48807

Title: Retrospective study on mixed neuroendocrine non-neuroendocrine neoplasms from five European centres

Reviewer's code: 02445679

Reviewer's country: Italy

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-05-04 14:35

Reviewer performed review: 2019-05-14 09:25

Review time: 9 Days and 18 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The manuscript by Frizziero et al reports data on histological features and clinical management of a series including 69 patients with mixed adeno-neuroendocrine carcinoma (MANEC). Although this work has some limitations (stated by the authors in



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the discussion) consisting in the retrospective design, the relatively small number of patients, and the long period of observation (> 30 years), it has some merits which make it interesting for physicians dealing with neuroendocrine tumors. Since MANEC is an extremely rare entity, literature focusing on this topic is scanty. This is the reason why also retrospective studies are welcomed. Below are my comments, which should be taken into account before considering this manuscript suitable for publication: 1. Introduction: it is correctly reported that the recent WHO 2017 changed the definition of MANEC rising from the pancreas into MiNEN. I believe this change should be applied also in the results section. This could make this work more up to date with the current knowledge, and even more easy to use in the clinical practice. 2. Additional histological revision should be done, in order to add Ki67 value. Although Ki67 role is widely understood in NETs in general, its prognostic accuracy in MANEC (or MiNEN) is unknown, and this could add an additional value to the manuscript 3. Results and table 2. I understand that multivariate analysis was not performed due to the low number of cases included in the subgroups. However, I think it should be attempted, and data (even if not significant) should be given 4. authors should shorten the discussion section by 1/3, particularly in the final section (page 17) 5. Table 1. I wonder why NE proportion was unknown in 1/3 of cases. Please double check, if confirmed add a comment to explain the reason. The same observation refers to % of cell morphology (small vs large), which was unknown in 72.4% of cases. This is quite easy to obtain by checking histological slides. 6. Table 1, add Ki67 if possible (see point 2) 7. Table 2. Add multivariate, if possible (see point 3) 8. Figure 2. Please add patients' "number at risk" in the horizontal axis. try to cut horizontal axis of figures PFS Adv and OS Adv at 36 months

INITIAL REVIEW OF THE MANUSCRIPT



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