



PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Surgery*

Manuscript NO: 66003

Title: Therapeutic strategies for gastro-entero-pancreatic neuroendocrine neoplasms: state-of-the-art and future perspectives

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03738819

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Italy

Manuscript submission date: 2021-03-20

Reviewer chosen by: Ze-Mao Gong

Reviewer accepted review: 2021-07-28 13:27

Reviewer performed review: 2021-08-03 17:37

Review time: 6 Days and 4 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No
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SPECIFIC COMMENTS TO AUTHORS

This review provided an overview of the available treatments for GEP-NENs, and discussed future perspectives and new frontiers regarding the therapeutic approach of GEP-NENs. However, there are several deficiencies that need to be addressed. 1. The manuscript is too long, more than 20,000 words. The language should be more refined and some unimportant parts should be deleted. 2. Future perspectives and open questions of each section are not novel and deep enough. The authors should be added some creative opinions and prospects about the future research. 3. I recommend the authors to add a table to summarize some important clinical trials for the treatment of GEP-NENs in this manuscript.



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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03869952

Position: Peer Reviewer

Academic degree: DO, FACP

Professional title: Associate Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: Italy

Manuscript submission date: 2021-03-20

Reviewer chosen by: Ze-Mao Gong

Reviewer accepted review: 2021-07-28 20:26

Reviewer performed review: 2021-08-05 21:56

Review time: 8 Days and 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



Peer-reviewer statements	Peer-Review: [Y] Anonymous [] Onymous Conflicts-of-Interest: [Y] Yes [] No
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SPECIFIC COMMENTS TO AUTHORS

It was with great interest that I read the very thorough review titled “Therapeutic strategies for gastro-entero-pancreatic neuroendocrine neoplasms: state-of-the-art and future perspectives”. The incidence of neuroendocrine neoplasms is increasing as well as treatment options so therefore this manuscript is very timely. The outline was put together well but have several comments that should be addressed prior to acceptance.

1. There are multiple references to NEN, NET and NEC. This can be confusing for a non-neuroendocrine specialist. Please either define the differences or keep to NET (G1, G2, G3) or NEC (Poorly differentiated G3).
2. Under small bowel NETs page 13, please include that echos are checked to evaluate for carcinoid heart disease.
3. Page 16 under future perspectives and open questions the author should consider emphasizing the only studies showing benefit for adjuvant therapy were in the setting of PD NECs, not WD.
4. Page 19. A reference is needed when discussing prophylactic octreotide for carcinoid crisis.
5. Page 22. Side effects of lanreotide may also include hypoglycemia, abdominal pain and diarrhea.
6. Page 28. Would consider adding other SSTR imaging such as octreoscan and Cu64 DOTATATE.
7. Page 28. A reference is needed about high renal toxicity with Y90 PRRT.
8. Page 29. Please include the updated NETTER1 analysis from ASCO 2021.
9. Page 32. Would consider adding data presented at NANETS 2020 about Pb 212.
10. Page 41. The NCT #00869050 does NOT describe the trial that is discussed. This NCT # corresponds to a single arm phase 2 trial.
11. Would consider adding a section to discuss surufatinib. SANET-P and SANET-EP studies.
12. Please spell check as there are multiple typos and grammatical errors throughout the manuscript.



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