PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 78469

Title: Molecular factors, diagnosis and management of gastrointestinal tract neuroendocrine tumors: An update

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03763614

Position: Peer Reviewer

Academic degree: PhD

Professional title: Academic Fellow, Associate Chief Physician, Doctor, Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Greece

Manuscript submission date: 2022-06-28

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-06-28 12:19

Reviewer performed review: 2022-06-28 12:58

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No

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

SPECIFIC COMMENTS TO AUTHORS

NO specific comments

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Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
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SPECIFIC COMMENTS TO AUTHORS

The approached topic regarding the latest news in the field of molecular markers, diagnosis and management of NEN is very modern. Yet, the manuscript "Molecular factors, diagnosis and management of gastrointestinal tract neuroendocrine tumors: An update" cand be much updated instead of listing the common knowledge on this subject. A systematic review and the description of the methodology would add value to this narrative review. I suggest a distinct approach to GI and pancreatic NETs as their molecular pathology and treatment is quite different. Key words could be improved. Please develop the ideas regarding NETEST utility in NETs. The imagistic section cand be updated. Statements should be supported by solid scientific data. "Long-acting release of somatostatin analogs"- please correct to "Long-acting release somatostatin analogs" "Progress in PET-CT and scintigraphy with new radioactive agents (64Cu-DOTATATE or 68Ga-DOTATATE) replacing octreotide have improved the current diagnostic imaging."- please correct to "has improved"; the sentence is not quite scientifically exact . GI-NETs and GIS -NETs are pretty similar, I suggest you should choose one of these terms "The vast majority of them are sporadic, but at a rate less than 5%, they are found in genetic syndromes mainly in MEN 1 (multiple endocrine neoplasia), predominantly pancreatic islet cell neoplasia (gastrinoma, insulinoma, glucagonoma, in order), which is malignant at a high rate [4]."- please be more specific and clear I suggest a consistent approach to abbreviations in text eg: Positron emission tomography-computerized tomography (PET-CT) vs SPECT (single photon emission computed tomography) "Small intestine NET is its most common cancer."- please explain, or give exact data   "The correct identification of cell origin could be implicated

in cancer development [27]."- I would rephrase this as it is not very clear Molecular factors – Genomic profile -I would suggest a more integrated approach instead of a simple enumeration of factors "The clinical presentation is influenced by hormone secretion or lack thereof in order to define them as functional or nonfunctional."- I would recommend a reconstruction of this sentence "NET carcinoma"- is not adequate "PPI use"- define abbreviations at the first use in text somatostatin receptor (SSTR) scintigraphy is no longer the preferred imaging investigation There is a type 4 ECL-Cell NET described "A new immunohistochemical neuroendocrine marker for staining is the transcription factor insulinoma-associated protein 1 (INSM1)"- I suggest you to develop this idea "5-HIAA is the main metabolic product of serotonin. Its assessment in 24-hour urine determines serotonin levels in NETs, which secrete serotonin and are associated with the tumor burden".- please use comma in the correct place; there are also a few other sentences in which comma is not used properly\ "The modalities of somatostatin receptor scintigraphy used in clinical practice include radiolabeled metaiodobenzylguanidine, 11indium pentetreotide (octreoscan), radiolabeled vasointestinal peptide, radiolabeled monoclonal antibodies and the abovementioned positron emission radionuclides [63]." the information is inexact   APUDomas- is rather an outdated terminology I would split the pathology and prognostic factors sections The treatment section is not easy to follow and can be updated eg: IFN, telotristat, somatostatin receptor antagonists therapy I recommend the princeps references to be used Conclusions do not appropriately summarize the data and they should outline the future directions of the topic described in this manuscript   Quality of written English: needs minor typing error corrections

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Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

In general, the research in the article "Molecular factors, diagnosis and management of gastrointestinal tract neuroendocrine tumors: an update" is of high quality. The text needs minor linguistic amendments. For example, at the Introduction, paragraph 1 "The vast majority of them... at a high rate" I would recommend something like this: "The vast majority of them are sporadic. However, at a rate less than 5%, they are found in genetic syndromes, mainly MEN 1, in the form of pancreatic islet cell neoplasms (gastrinoma, insulinoma, glucagonoma, in order) which carry a high rate of malignancy". Or, in Diagnosis-Clinical picture, paragraph 4: "In small bowel locations, regardless of the primary lesion..." instead of "despite the primary lesion". Regarding the content, it is up-to-date and comprehensive. I would suggest an addition in the Section "Clinical picture (which I would rename "Clinical presentation") that would mention intussusception as a manifestation of SI-NETs (relevant citations by DOI: 10.1016/j.ijscr.2020.10.091;   10.1016/j.cgh.2022.04.016;   10.12998/wjcc.v7.i21.3517). Finally, perhaps it would be worth mentioning about the role of artificial intelligence in the diagnosis and management of GI-NETS, as a future perspective towards the end of the text. I understand that it is no established standard of practice yet, but as it has been recently shown by our workgroup (10.3390/diagnostics12040874) it may serve as a useful adjunct in current practices.