Answers to the reviewers' remarks:

Answers to Reviewer #1:

This is a nicely written review on gastroenteric neuroendocrine neoplasm. The authors aimed at summarizing current knowledge.
1. *Currently the manuscript offer a rather shallow overview on the topic. It is such an extense topic that I would recommend to pick a specific subject and develop it better, either diagnostic and therapeutic advances. Also consider to discuss separately functioning and non-functioning NEN, since clinical suspicion, diagnostic approach and treatment are different.*
Answer: We agree with this reviewer that it is indeed a rather extensive topic and both suggested strategies to go deeper into it are worth being considered. However, aim of the present work was to sum-up the current research status for GEP-NENs and to provide a comprehensive overview. We would thus respectfully ask this reviewer to accept our decision to stick to our initial concept.

2. The manuscript would benefit from actual radiology images.
Answer: We agree with this reviewer's thinking that radiological images play a vital role in the diagnosis and treatment of NENs. We discussed this suggestion with all authors and would respectfully ask to accept our decision not to display radiological images. We see the problem that selecting certain subtypes bears a great potential for bias, whereas showing images for all NEN subtypes presented in the manuscript would overload the manuscript. Furthermore many NEN are difficult to detect on certain imaging modalities and displaying examples of all types of imaging methods would be a topic for a separate review.

3. When discussing the use of CgA, I would recommend to develop on what are the causes of false positive results and how to avoid them. Also how and when to interpret and use CgA according to the function/non function status of the neoplasm. What is its role in assessing NEN/carcinoid like symptoms in a patient with no evident neoplasm?
Answer: We want to thank this reviewer for the helpful hint. We tried to clarify these points in the improved version of the manuscript. It now reads: "In clinical diagnosis, CgA is established as a universal routine diagnostic biomarker of neuroendocrine neoplasms[16]. Sensitivity of CgA assays varies between 32% and 92%, depending on the NET type, secretory status, and tumor burden[17]. The specificity can approach 100%; if other diseases elevating serum CgA levels such as kidney insufficiency and chronic atrophic gastritis have to be carefully excluded[17]. Of note, CgA is a general, but not a specific biomarker for GEP-NENs, and is usually found in high concentrations independent of the functional status of a given case[18]. Thus, further more specific biomarkers like serotonin, gastrin, insulin, etc. have to be tested subsequently when assessing a patient with NENs or with carcinoid like symptoms but no evident neoplasm."

4. Regarding PET studies it is mentioned that the right substance should be selected. Please develop when to use DOTA TOC, NOC and TATE.

Answer: We thank this reviewer for this suggestion and modified the manuscript accordingly. It now reads: "^{68}Ga-DOTA-TOC shows a higher affinity to SSR-2, ^{68}Ga-DOTA-NOC towards SSR-2, SSR-3 and SSR-5, whereas ^{68}Ga-DOTA-TATE towards SSR-2 and SSR-5[35]. Clinicians might prefer imaging agents with a broader SSR binding profile like ^{68}Ga-DOTA-NOC. Still, the overall diagnostic accuracy of the three SSAs is very similar[36]."

Answers to Reviewer #2:

Major Points:

1. *Features of GEP-NENs under the endoscope are not described in the section '3. Endoscopy, ultrasonography and ...', and these are important for clinical diagnosis.*

Answer: This is a helpful suggestion which we followed accordingly. The manuscript has been modified and the following has been added: "Under the endoscope, gastrointestinal NENs have various manifestations including oval, hemispherical or polypoid lesions which may present with erosion or ulcer on the surface. Endoscopic ultrasonography (EUS) can show the hierarchical structure of the digestive tract, the size of lesions, the location of NENs, the area, and the invasive depth. In EUS, pancreatic NENs present as round or elliptical lesions with clear boundaries. Highly malignant pancreatic NENs typically are of larger volume with irregular borders compared to lower malignant ones. More importantly, EUS allows fine-needle aspiration for suspicious lesions for pathological assessment."

2. *In the section '4. The Histopathogical ... ', the authors emphasize the important role of CgA and Ki67, while the expression of CK8/18, Cyn and SSTR2 is also very important and should be summarized.*

Answer: Again, this is a very helpful hint which we followed and modified the manuscript accordingly. The following has been added: "Syn and CgA can help to determine whether a NEN is present or not. CK8/18 is the marker of epithelial NENs, and allows to exclude nonepithelial NENs, such as paragangliomas. Moreover, SSRs-expression can be detected on the surface of NEN cells[44], among which SSR2 is the most common one. Thus, detection of SSR2 is also an important biomarker for the diagnosis of NENs."

Minor points：

1. Should line 42 of the abstract be well differentiated grade 3?

Answer: We want to thank this reviewer for the very precise reading. We modified this part to: "According to the most recent clinical guidelines, improved grading standards can help to distinguish poorly differentiated grade 3 neuroendocrine tumors (NETs) from neuroendocrine carcinomas (NECs), which are subclassified into large and small cell NECs."