

## **An update on novel endoscopic techniques for gastric neuroendocrine tumors**

### **Point by point reply to comments**

*We thank the reviewers very much for paying further attention to our manuscript entitled “An update on novel endoscopic techniques for gastric neuroendocrine tumors” and for suggesting further improvements. We re-examined the contents and form of our entire manuscript, hoping to have been thorough in each answer.*

### **Comments from Reviewers:**

#### **Reviewer #1:**

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Dear author: Congratulations! You have given us an informative and detailed narrative article about Gastric neuroendocrine neoplasms, especially the classification and treatments. As a narrative review, although there is no knowledge gap, the detailed information in the manuscript is of substantial reference value for clinical physicians. However, there are some recommendations for you. For the title, I recommend to remove the word “novel” in the title, strictly speaking, the manuscript described numerous conventional endoscopic techniques as well. As an update on novel endoscopic techniques, I recommend that in the introduction part, it would be better to describe what is the conventional concept of treatment and what is the novel concept of treatment. That will make the manuscript more significant and logic. As the abstract consisted of “background”, “aim”, “method”, “results”, “conclusion”, the main text should also consist of such same parts. In the method part, it would be better to describe the literature searching method. As many endoscopic techniques were described. I recommend to have a table, illuminate the different characteristic of the three types of gNENs, such as, proportion, origin, malignant proportion, guideline for treatment, et al. as the article is pretty informative, only select key information in the table. That would be more helpful for the readers.

*We are grateful for the Reviewer’s valuable appreciation of our manuscript.*

*As suggested, we corrected the manuscript title, and effectively it ended up being much more appropriate, with referral to the numerous conventional techniques described in the manuscript.*

*We also introduced a little paragraph in the “introduction” section with a description of the conventional and the novel concepts of treatment.*

*The main text has been developed into chapters which the abstract structure and a detailed description of the literature searching methods used has been provided within the “Methods” section.*

*As suggested, we added a table with key information regarding the possible endoscopic therapeutic approaches for the different types of gNENs (see **Table 1.**)*

#### **Reviewer #2:**

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This narrative review was comprehensively updated the knowledge on the endoscopic treatment options to manage g-NENs.

*We thank very much the Reviewer for the extremely positive feedback given to our manuscript.*

**Reviewer #3:**

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: In general, this review is well conducted and I would not change the scheme or the order of the paragraphs. I think it is precise and complete. Nevertheless, some minor comments are needed. I would quote and integrate the results of three other relevant and recent papers: • “Borbath I, Garcia-Carbonero R, Bikmukhametov D, Jimenez-Fonseca P, Castaño A, Barkmanova J, Sedlackova E, Kollár A, Christ E, Kaltsas G, Kos-Kudla B, Maasberg S, Verslype C, Pape UF. The European Neuroendocrine Tumour Society registry, a tool to assess the prognosis of neuroendocrine neoplasms. *Eur J Cancer*. 2022 Jun;168:80-90. doi: 10.1016/j.ejca.2022.03.007. Epub 2022 Apr 23. PMID: 35472579.” • Sun W, Wu S, Han X, Yang C. Effectiveness of Endoscopic Treatment for Gastrointestinal Neuroendocrine Tumors: A Retrospective Study. *Medicine (Baltimore)*. 2016 Apr;95(15):e3308. doi: 10.1097/MD.0000000000003308. PMID: 27082572; PMCID: PMC4839816. • Xue L, Cai Y, Chen W, Chen S, Xue P. Clinical Spectrum and Endoscopic Treatment of Gastrointestinal Carcinoid Tumour. *J Coll Physicians Surg Pak*. 2022 Oct;32(10):1330-1333. doi: 10.29271/jcpsp.2022.10.1330. PMID: 36205280. In chapter “Traditional EMR”, at line 4 (“EMR, as mentioned earlier, has a lower rate of incomplete resection”) please explain better what EMR is compared to. In chapter “Endoscopic Submucosal Dissection”, when you described the results of the study conduct by Kim et al. about the comparison between ESD and EMR, explain better the reasons of less affection of vertical margins in patients who underwent ESD. It is not clear. Please provide the entire meaning of LNM, I could not find in the text.

*We thank very much the Reviewer for the positive comment to our manuscript. We found the three suggested paper extremely relevant, so we provided the inclusion of their results in our manuscript (see ref 4, 5 and ref 59).*

*We explained that EMR is compared to hot or cold snare resection regarding the lower rate of incomplete resection (see chapter “Endoscopic mucosal resection”, section 1 “traditional EMR”).*

*We also clarified, regarding the study by Kim et al, the reasons for the lower affection of vertical margins in patients undergoing ESD compared to those undergoing EMR (see chapter “Endoscopic submucosal dissection”).*

*The entire meaning of LNM (lymph node metastases) was already provided in the “endoscopic submucosal dissection” section.*