

Prof Godefridus J Peters,
Editor in Chief World Journal of Clinical Oncology

Dear prof Peters,

Please find enclosed the revised manuscript entitled "Watch & wait policy in advanced neuroendocrine tumors: what does it mean?" that I would like to submit for publication in the World Journal of Clinical Oncology as a revised invited Editorial.

The manuscript has been revised in accordance with the reviewers' comments. Please, below you can find a point by point list of revisions.

Point by point answers:

Reviewer 1:

This is an Editorial about "watch and wait policy in advanced NETs" by Dr Nicola Fazio who has many years of experience on NETs. The "W and W" policy is mentioned in the new guidelines of ENETS and the readers of the journal will benefit from the present Editorial by Dr N. Fazio.

I have some minor suggestions:

Q: At the abstract (line 2) and at the introduction (line 2) it is written that NETs may develop in "any" organ. I suggest the word "any" to be substituted by various or many.

A: I thank the reviewer for this pertinent comment; I modified that accordingly.

Q: Furthermore, in introduction the grading system for G1 NETs should be changed according to the WHO reference (G1 $\leq 2\%$ Ki67 index).

A: I thank the reviewer for this editorial comment; I modified that accordingly.

Q: Page 2 where the results of the Clarinet study are presented, I suggest to add a meaning that lanreotide was not effective in rectal NETs.

A: the text was modified accordingly.

Q: 3) Where the good performance status I asymptomatic patients with advanced NETs is discussed I suggest that it should be made a comment why the characterization of the disease make take months rather than weeks (delay in referral to centers that focus on these tumors? Other reasons?)

A: I thank the reviewer for this comment; I changed to weeks, that is less misleading than months.

Q: 4) Second last page: "Nonetheless patients..... and that this means..." please make the proper changes so that the meaning will be correct

A: Thanks for this. I changed that accordingly.

Q: 5) Second last page, last meaning. The phrase is 5 lines long and difficult for the reader to follow. Furthermore, please change "share" to "shares".

A: Thanks for the suggestion. I shortened the sentence.

Q: 6) Reference 1: classification. Please correct.

A: Thanks for this editorial suggestion. I corrected that.

Q: 7) Reference 2: tymus. Please correct.

A: Thanks for this suggestion. I corrected that.

Q: 8) Reference 5 Wied i. Please correct the first name of the author.

A: Thanks for noticing this mistake. I corrected that.

Q: 9) Reference 11: Pavel Ma, O'Toole Db, Costa Fc Please correct the first names of the authors.

A: Thanks for this suggestion. I corrected that.

Reviewer 2:

Watch and wait policy in advanced neuroendocrine tumors: what does it mean? Fazio N. This review article discusses "Watch & wait policy" for neuroendocrine tumor, especially for advanced tumor. They concluded that this policy may be justified in good performance asymptomatic patients with low- grade neuroendocrine tumor. However, they showed serious concern to introduce this policy into patients with advanced disease. This review article is well-written with adequate references. In addition, it is very useful to understand recent reports regarding the follow up policy for neuroendocrine tumors. One point I found in this article is that they described $<3\%$ Ki-67 as definition of G1 tumor (line 4-5 of Introduction section). According to the WHO classification of tumours of the digestive system, which they referred as Reference 1, this should be $\leq 2\%$ (See p13 of this book). I think this article is very useful for many readers who participate in the treatment of patients with neuroendocrine tumors and suitable for publication in "World Journal of Clinical Oncology".

A: I thank the reviewer for the suggestion. I replaced Ki-67 $< 3\%$ with Ki-67 $\leq 2\%$.

Sincerely yours.

Milan, on November 20th 2016

Nicola Fazio, M.D., Ph.D.