

Na Ma

Editor-in-Chief, World Journal of Clinical Oncology

We are very thankful to the Reviewers for the valuable comments and suggestions performed to improve our paper. All changes were marked in yellow in the manuscript. We hope that with these changes, our manuscript is now suitable for publication.

With my best regards,

Fabian Pitoia, MD, PhD

#1. Editor.

Please check and confirm that there are no repeated references! Please verify that the references are cited by Roman numerals in brackets and superscripted in the text and that the numbering order is correct. There should be no space between the bracket and the preceding word or the following punctuation. When references in the text and tables are cited with author name(s), it is necessary to manually verify that the name(s) is consistent with the first author's surname in the corresponding reference list. Please don't include abbreviations in the title of the figure/table. Please explain all the abbreviations in the figure/table legends as full name (abbreviation). Please explain all the abbreviations of each figure/table under each piece of figure/table legends. Please provide the decomposable figure of Figures, whose parts are movable and editable. So you can put the original pictures in PPT and submit it in the system. Please provide the decomposable figure of all the figures, whose parts are all movable and editable, organize them into a PowerPoint file, and submit as "Manuscript No. - image files.ppt" on the system. Make sure that the layers in the PPT file are fully editable. For figures, use distinct colors with comparable visibility and consider colorblind individuals by avoiding the use of red and green for contrast. Please read these four important guidelines carefully and modify your figure(s) accordingly: First, all submitted figures, including the text contained within the figures, must be editable. Please provide the text in your figure(s) in text boxes. Second, for line drawings that were automatically generated with software, please provide the labels/values of the ordinate and abscissa in text boxes. Third, please prepare and arrange the figures using PowerPoint to ensure that all graphs or text

portions can be reprocessed by the editor. Fourth, in consideration of color-blind readers, please avoid using red and green for contrast in vector graphics or images.

The changes were addressed as suggested by the editor. Images files were attached separately in a “.ppt” file.

#2 Reviewer’s code: 05194798

1. Please clarify the selection and exclusion criteria and the search results: how many literatures were found and how many was excluded by what reasons. Authors may add a figure of the selection tree.

We added the figure according to the reviewer observation

2. Abstract should be a summary of the article. The authors should modify the Abstract.

We do not agree with the reviewer considering that this is a review article we cannot make a structured abstract. The text that appears in it clearly reflects our complete topic review.

3. Minor 1. (P13L7) Please replace “%” to a correct value.

Seventeen percent is the correct frequency value of the patients with tumor enlargement reported in the cited article: “Active surveillance in papillary thyroid carcinoma : not easily accepted but possible in Latin America”. Smulever & Pitoia. Arch. Endocrinol. Metab. 2019; 63:462-469

4. Figure 3: The authors should add some explanations in the figure legend.

We added a legend in order to clarify the figure (now figure 4).

#3 Reviewer’s code: 00505511

1. MCPs in page 2 and 3 should be PMC

The change was addressed as suggested by the reviewer.

2. Please cite the below publication and discuss about that. Davies L et al. JAMA Otolaryngol Head Neck Surg 2019;145:363-370.

The suggested publication was discussed in "Non-biological aspects of active surveillance" section, as: "Conversely, "maximalist" patients chose the immediate surgical option as the only possible alternative, expressing rush to undergo the intervention. They perceived PMC as a life-threatening disease that could be cured by surgery and expressed anxiety about development of local and/or distant metastases during the follow-up[66,67]. These causes were reported as the main sources of worry in a recent research which describe the experiences of patients with low-risk PMCs under an active surveillance program [68].

#4 Reviewer's code: 03767436

1. In the present paper the Authors discuss an important topic related to the evaluation of criteria for selecting papillary thyroid microcarcinomas patients for active surveillance describing also the epidemiology, clinical evolution, prognostic factors and mortality of these tumors. It is well known that active surveillance can be considered as an alternative to immediate surgery in low-risk papillary thyroid microcarcinoma (PTMC) without clinically apparent lymph nodes, gross extrathyroidal extension (ETE) and/or distant metastasis according to American Thyroid Association. However, active surveillance has been controversial, in particular the most important of these controversies is represented by limited accuracy and utility of ultrasound in the detection of potential ETE, malignant lymph node involvement or the advent of novel lymph node malignancy during tumor progression. In the current opinion, the utility of active surveillance for low-risk PTMC patients requires improvements to stratify patient risk and the combined use

of US and CT imaging technologies is strongly recommended in identifying ETE and cervical LNM involvement. Therefore, on the light this consideration I suggest that, in the conclusion section, should be stressed the need of sophisticated imaging technologies and reliable prognostic biomarkers to increase our ability in the screening of high risk patients. In few words a great caution should be proposed in order to exclude the risk of an underdiagnosis of PTMC patients.

We agree with the reviewer, so we emphasized this aspect in the conclusions section.

2. Add some significant and recent published papers on in this topic such as:

- Implementation of active surveillance: the correct moment for diagnosis section: Low-risk papillary thyroid microcarcinoma: Optimal management toward a more conservative approach. Ramundo V et al. J Surg Oncol. 2020.
- Models of proper patient selection section: The increasing prevalence of chronic lymphocytic thyroiditis in papillary microcarcinoma. Vita R et al. Rev Endocr Metab Disord. 2018.
- Risk factors for tumor progression section: BRAF Status in Papillary Microcarcinomas of the Thyroid Gland: a Brief Review. Ieni A et al. Curr Mol Med. 2019.

We added the suggested papers in the appropriate sections.