

Thessaloniki 9 November 2023

Dr. Lian-Sheng Ma, Founder and Chief Executive Officer

Baishideng Publishing Group, Inc.

Dear Editor:

Thank you for your preliminary decision regarding our invited paper entitled “Update on current diagnosis and management of anaplastic thyroid carcinoma” (Manuscript NO: 88665), which was sent to the *World Journal of Clinical Oncology* for publication as a *Review*.

I would like to thank the reviewers for their earnest efforts in reviewing the manuscript. I accepted and responded step by step to all considerations by the reviewer improving the manuscript. The changes are highlighted by yellow.

Reviewer 1

Many thanks for his considerable comments. He made a concise review. It seems that he knows the subject well and in-depth. I absolutely agree with him. I am having a bit of a hard time understanding where we are disagreeing. Every author has his own way of expression and writing style. So do I, an Emeritus Professor with a lot of both experience and published papers in high-impact international journals. We have exactly the same views on this matter. However, I will make a few clarifications to make things more clear.

1. This is a comprehensive review presenting all the available published main knowledge. In every case, it is not an opinion review.

2. a. Fine needle aspiration cytology is referred in the diagnosis section with its disadvantages compared to core needle biopsy (*page 9, lines 12-18*). For further clarification, it has been added, before the above-mentioned text for FNA, the following text: “*It is obvious, that in cases of rapidly enlarging neck nodules, the necessary first step is an ultrasound imaging performance. Advances in the ultrasound technology provide precise diagnostic capability by high resolution ultrasound. However, then biopsy is fundamental to make the diagnosis.*” (*page 9, lines 11-14*). FNA (*fine needle aspiration*) cytology using a 21-25 gauge needle under ultrasound guidance has been widely used as an initial step in diagnosis by cytologic examination [20,21,34,45,60]. However, due to its high

false-negative results, low sensitivity of 54-61% vs. 77-80% of CNB, and specificity of 87% vs. 100% of CNB [20,21] or often inconclusive results, this option tends to be omitted recently in favor of CNB. Because of performance, using it is considered a vain spending of time [21,45]." This whole final text is in page 9, lines 11-20. Also, the diagnostic approach is shown schematically in Figure 1.

b. Surgical resection and complete lymph node dissection are referred to the text of NCCN guidelines *" The guidelines of the NCCN (National Comprehensive Cancer Network) and ATA (American Thyroid Association) recommend surgical resection by lobectomy or near total thyroidectomy with wide lymphadenectomy in stage IVA and IVB, even in stage IVC when an R0 or at least R1 intervention could be achieved in locally resectable tumors [36,43,68-70]. However, many locally unresectable cases may respond to neoadjuvant external beam radiation, chemotherapy or even targeted therapy (dabrafenib and trametinib) for BRAF gene mutation, thus becoming resectable and ensuring surgical excision [43]. Timely detection and proper treatment reduce the number of advanced cases with distant metastases [9]."*(page 11 , lines 22-30). Also, the management policy is shown schematically in Figures 2 and 3.

c. Radiotherapy and chemotherapy are referred already in the following text: *"It should be emphasized overall that patients undergoing extended surgical intervention and receiving adjuvant radiation and chemotherapy gain the chance of the best overall survival [9,48]. Aggressive locoregional surgery and radiotherapy must be performed whenever possible, and adding chemotherapy can lead to further improvement; however, in unresectable cases, radiotherapy and chemotherapy must be preferred [9]."* (page 12, lines 18-23). Also, there is a separate section for chemotherapy (page 12) and radiotherapy (page 13). The management policy is shown schematically in Figures 2 and 3.

3. It has been added the suggested consideration: *"Although, the overall prognosis of anaplastic thyroid carcinoma is very poor, in some cases is relatively good. There is evidence that patients with anaplastic carcinoma clearly transformed from papillary thyroid carcinoma, or those with mutated BRAF gene had a significantly better prognosis than other patients. Despite, the conflicting aspects for the above mentioned, it could be possibly explained by the higher expression of PD-L1 in papillary than in anaplastic carcinoma and response to immunotherapy [59] and anti-BRAF targeted therapy [24]."* (page 19 , lines 25)

Reviewer 2

Many thanks for his positive comments.

I am sending the revised manuscript and hope to receive a favorable final decision.

We look forward to hearing from you at your earliest convenience.

Sincerely,

Theodoros E Pavlidis MD, PhD

Emeritus Professor of Surgery

School of Medicine, Aristotle University of Thessaloniki, Greece,

Hippocraton Hospital, Konstantinoupoleos 49, 546 42, 2nd Surgical Propedeutic
Department

e-mail: pavlidth@auth.gr

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