Review of: "The Association Between The Interval of Radioiodine Treatment and The Response and Adverse Effect in Patients with Non-Progressive Lung Metastases From Differentiated Thyroid Cancer"

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Potential competing interests: The author(s) declared that no potential competing interests exist.

This retrospective study deals with a problem of the recommended interval between the courses of radioiodine therapy (RT) in patients with pulmonary metastases of differentiated thyroid carcinoma. In order to evaluate treatment efficacy and adverse events of RT, the authors analyzed treatment pairs with regard to the change in stimulated thyroglobulin and in lesion diameter between the former and next RT course, as well as frequency of adverse effects. The treatment efficacy and adverse effects were compared between the subgrous of RT pairs with the interval between courses below and above 12 months. The design of the study is correct and the quality of the study is generally good. Here are, however, some issues that require clarification:

The L-thyroxin withdrawal is recommended to last for ca. 4 weeks. Why do you practice 2-3 weeks withdrawal only? Is it sufficient to achieve TSH values above 30 IU/L?

In the methods section, the LLD has not been described. How was LLD defined in case of single, multiple and disseminated pulmonary lesions?

Table 3 is difficult to understand. It is indicated in the headline that the numbers in the table correspond to number of patients and percentage. There are, however, only simple complete numbers in each line. When analyzing the data in Table 3, it seems that patients from the >12 m group had better initial parameters than those from the <12 m group, e.g. abnormal leukocytes, platelets, AST, ALT and calcium were found in 0,1,0,1 and 12 patients respectively in the >12 m group and in 17, 22, 16, 10 and 54 patients in the <12 m group. This difference is striking but it seems that it was not analyzed in deep. The statistical test did not show any significant differences, but I presume, that the test evaluated the impact of each treatment on each parameter only, without taking into account the striking differences in the initial values. Could you, please, look at it more closely? Perhaps there is some bias or a pitfall in this table? What does 'Missing' in the Table 1 mean?

page 4 typo: comparison Table 1 typo: ETE (not ENE) page 7: The interval ranges from 126 to 937 days. page 9: A representative patient who responded... page 11: ...considering balance of the benefit and adverse effects?

page 11: On the other side, a longer interval may shorten the time of unnecessary stimulation of thyroid cancer cells, reduce the frequency...

page 12: what do you mean by 'permissive'?

page 12: ...we did not identify any potential indication to prolong the interval.

- page 12: ...for micrometastases with no recommendation for macronodular metastases.
- page 12: ...additional treatments and patient's preferences [4,5,19]...
- page 12: The 65-year-old male presented in Fig. 3 had undergone three RTs...