

## Letter to the Editor

Recently, the Martinique Working Group (MWG) composed of representatives from the American Thyroid Association (ATA), the European Association of Nuclear Medicine (EANM), the European Thyroid Association (ETA), and the Society of Nuclear Medicine and Molecular Imaging (SNMMI) published a white paper entitled “The Martinique Principles” [1].

As defined by Wikipedia [2], “. . . a white paper is an authoritative report or guide that informs readers concisely about a complex issue and presents the issuing body's philosophy on the matter. It is meant to help readers understand an issue, solve a problem, or make a decision.” Although not infrequently, “white papers” are characterized as exactly that: mostly “white with very little black ink used to communicate nothing of substance,” *tout au contraire!* The article by Tuttle et al. [4] entitled “Martinique Principles” documented multiple important accomplishments.

First and foremost, this “white” paper documents the important establishment of an honest and collegial discussion of differences of practices and opinions regarding the diagnosis and management of differentiated thyroid cancer among prominent members of four societies. Arguments can be divisive or constructive. This group’s efforts were constructive and help us all move toward understanding and resolving controversial issues, thereby hopefully improving patient care. Again, the establishment of this new collegial dialogue is the foremost accomplishment of the MWG as demonstrated in this white paper from the 2108 meeting.

Second, the MWG compiled nine principles (see Figure 1 in the on-line supplement), and the reader is encouraged to read the entire article for a more detailed discussion and appreciation of the value of these principles. Overall, the nine principles established a valuable

foundation from which to proceed. In addition, each principle has its specific value, and I have selected several of the nine principles to present examples of the value of the individual principles themselves.

Third and as an example of the above, the MWG established common terminology for the discussion of  $^{131}\text{I}$  therapies, and this was based upon a combination of definitions proposed by Cooper et al. [3], Van Nostrand et al. [4], and further supported by Haugen et al. [5]. These terms are  $^{131}\text{I}$  remnant ablation,  $^{131}\text{I}$  adjuvant treatment, and  $^{131}\text{I}$  treatment of known locoregional or distant metastases. These definitions are based on different objectives of those  $^{131}\text{I}$  therapies (see Table 1 in the on-line supplement). In order to make any dialogue about controversies more productive and less confusing, it is paramount that we use the same terms with the same meanings. The MWG established common terminology that was accepted by all the members of the MWG of the four societies. I encourage the members of the SNMMI to also accept and use these terms. To use different terms or to use the same terms but with our own individual definitions and objectives will only aggravate the futility of our discussions of controversies. The WMG has achieved reasonable and workable terminology for  $^{131}\text{I}$  therapies.

Fourth, the MWG presented various viewpoints followed by constructive discussions regarding three controversial areas (i.e., indications for  $^{131}\text{I}$  adjuvant treatment, the amount of activity for  $^{131}\text{I}$  adjuvant treatment, and what is radioiodine refractory disease). These presentations and discussions allowed a better understanding of the arguments of the opposing sides and that we need better evidence based medicine.

There are other benefits specific to the individual principles, which I do not discuss here. However, there are also less frequently discussed benefits from the Martinique Principles such as the following two examples. By developing the nine principles through sharing the differences of opinion and, hopefully, understanding those differences better, the MWG will help influence the development of future guidelines to continue to incorporate the spectrums of expert

opinions and recognize the frequently inadequate evidence available to us. In addition, I believe that the nine principles will offer facilitators of Continuing Medical Education programs a document for “needs assessment” to encourage more presentations discussing the various viewpoints of these three controversies. These presentations will, in turn, help practicing physicians to better individualize their care to a specific patient in a specific facility in a specific location of the world.

In summary, the Martinique Work Group and its past 2018 and 2019 meetings have been extremely valuable in organizing our collaborative efforts to establish common terminology, to help identify areas of differences of opinions, to better understand what our differences are, and to recognize that, overall, our intentions of improved diagnosis and management of patients with differentiated thyroid cancer are aligned.

It is now the tasks of the MWG and its present and future members to continue the honest and collegial dialogue to order to move forward toward an every-better understanding of best practices for our patients with DTC.

In the end, follow those who seek the truth and not those who think they know the truth.

Respectfully submitted

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## References

<sup>1</sup>Tuttle RM, Sukhjeet A, Avram AM, Bernet V, Bourguet P, Daniels GH, Dillehay G, Draganescu C, Giovanella L, Flux G, Fuehrer D, Greenspan B, Luster M, Muylle K, Smit J, Van Nostrand D, Verburg F, Hegedus L. Controversies, consensus and collaboration in the use of I-131 therapy in differentiated thyroid cancer. *Thyroid*. 2019 Mar 22. doi: 10.1089/thy.2018.0597 [Epub ahead of print].

<sup>2</sup>[https://en.wikipedia.org/wiki/White\\_paper](https://en.wikipedia.org/wiki/White_paper). April 4, 2019

<sup>3</sup>Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, Mazzaferri EL, McIver B, Pacini F, Schlumberger M, Sherman SI, Steward DL, Tuttle RM. Revised Volume 19, Number 11, 2009 Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer. 2009;19:1-48.

<sup>4</sup>Van Nostrand, D. The Benefits and Risks of I-131 Therapy in Patients with Well-Differentiated Thyroid Cancer. *Thyroid* 2009;19: 1381-1391.

<sup>5</sup>Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, Pacini F, Randolph GW, Sawka AM, Schlumberger M, Schuff KG, Sherman SI, Sosa JA, Steward DL, Michael Tuttle RM, Wartofsky L. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid* 2016;26:1-133.

Figure 1. Summary of the Nine Martinique Principles from the 2018 Martinique meeting recently published in Thyroid (Reproduced with permission by Mary Ann Liebert, Inc.) [1]

### Martinique Principles

1. Advancing our understanding of optimal thyroid cancer management requires a commitment by clinicians, researchers, patients and organizations to engage in proactive, purposeful, and inclusive inter-disciplinary cooperation.
2. The goal of I-131 therapy should be characterized as remnant ablation, adjuvant treatment, or treatment of known disease using standardized definitions.
3. Assessment of post-operative disease status is required to optimize proper patient selection for I-131 therapy (remnant ablation, adjuvant treatment, or treatment of known disease).
4. Post-operative disease status evaluations should be standardized and integrated into routine clinical care.
5. Optimal patient selection for I-131 adjuvant treatment requires consideration and evaluation of multiple factors beyond post-operative disease status and risk stratification.
6. The optimal administered activity for adjuvant treatment cannot be definitely determined from the published literature. Until definitive data are available, selection of the administered activity for adjuvant treatment should be based on multidisciplinary management recommendations.
7. Characteristics used to classify patients as I-131 refractory should be used to risk stratify patients with regard to the likelihood that a tumor will respond to I-131 therapy and not necessarily as definitive criteria to mandate whether or not I-131 therapy should be recommended.
8. I-131 refractory criteria will continue to evolve as a) additional studies address important limitations and technical issues confounding the current literature, b) techniques for radioiodine imaging are optimized and standardized, and c) re-differentiation therapies enhance the effectiveness of I-131 therapy.
9. Major gaps in knowledge and evidence regarding optimal use of I-131 therapy should be addressed with properly designed prospective studies.

Table 1

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**Definitions of <sup>131</sup>I Therapies Based on Objectives [3]**

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**<sup>131</sup>I remnant ablation:**

“Remnant ablation refers to the use of <sup>131</sup>I to destroy post-operatively residual, presumably benign thyroid tissue to facilitate initial staging and follow-up studies [such as serum thyroglobulin (Tg) and radioiodine imaging].”

**<sup>131</sup>I adjuvant treatment:**

“. . . <sup>131</sup>I administered in an effort to destroy subclinical tumor deposits that may or may not be present after surgical resection of all known primary tumor tissue and metastatic foci. The goals of adjuvant treatment are to improve disease specific survival, decrease recurrence rates, as well as to improve progression free survival. It is important to remember that since adjuvant treatment is given for a risk, rather than for known disease, it is accepted that some patients who receive adjuvant treatment might already have been treated sufficiently by their primary surgery. Therefore, selection for adjuvant treatment involves both an assessment of risk of differentiated thyroid cancer (DTC) recurrence/persistence and risk of dying of DTC as well as the prediction of the likelihood that <sup>131</sup>I treatment may have a meaningful impact on an individual patient’s course of disease.”

**<sup>131</sup>I treatment of locoregional and/or distant metastases:**

“Treatment of known biochemical or structural disease refers to the goal of destroying persistent or recurrent DTC foci with <sup>131</sup>I in order to improve progression free, disease specific and overall survival. It can be given either with curative or palliative intent.”

**<sup>131</sup>I Therapy:**

Refers to <sup>131</sup>I remnant ablation, <sup>131</sup>I adjuvant treatment, or <sup>131</sup>I treatment of known disease.