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Similarities and Differences in Follicular Cell-Derived Thyroid Cancer Management Guidelines Used in Europe and the United States

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The management of thyroid cancer has become more refined and complex over the last thirty years. In an effort to provide guidance to both clinicians and patients, several organizations have developed clinical management guidelines that provide specific advice regarding the diagnosis, treatment and follow-up of differentiated thyroid cancer. In this review, we compare and contrast the major management recommendations provided in the guidelines of the European Thyroid Association with those published by thyroid cancer specialty organizations in the United States (American Thyroid Association and National Comprehensive Cancer Network). By carefully examining treatment and management approaches that are applied in other areas of the world, we can identify equally effective alternative treatment or follow-up options that may find applicability to specific patients in our own practice. Despite significant difference in cultures, economies, and health care delivery systems, thyroid cancer management recommendations from the European experts and the American experts are far more similar than they are different. Each of the guidelines strongly endorses an initial management approach that is guided by individualized estimates of risk of recurrence and risk of death. Furthermore, follow up and additional therapeutic recommendations are based on revised risk estimates that reflect an individual patient's response to therapy.
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The management of thyroid cancer has become more refined and complex during the last 30 years. Previously, a "one-size-fits-all" treatment approach (total thyroidectomy and radioactive iodine [RAI] remnant ablation) followed by a recurrence detection paradigm that relied almost exclusively on physical examination and RAI diagnostic scanning would have been recommended in most patients with differentiated thyroid cancer. However, the rapid growth in the availability of highly sensitive biochemical, structural, and functional clinical tests coupled with a renewed desire for individualized treatment recommendations now results in complex treatment and follow-up management plans that are personalized for each patients' individualized risk of recurrence and disease specific mortality.[1,2] The optimal management plan provides the minimum therapy and follow-up testing required to identify and treat clinically significant disease, while avoiding excessive testing/treatments that could lead to excess radiation exposure, and unnecessary treatments or side effects.[3]

In an effort to provide guidance to both clinicians and patients, several organizations have developed clinical management guidelines that provide specific advice regarding the diagnosis, treatment and follow-up of both differentiated thyroid cancer and medullary thyroid cancer.[4-7] The American Thyroid Association (ATA) is also in the process of developing thyroid cancer guidelines specifically for anaplastic thyroid cancer and pediatric thyroid cancer.

It is not surprising that the various guidelines are often in agreement in their recommendations regarding specific major management issues (partly because the data supporting those specific recommendations is quite good and partly because individuals often participate in the development of more than 1 set of guidelines).[8] However, it is also instructive to examine the various guidelines to explore where treatment recommendations differ. Sometimes the recommendations differ based on varying interpretation of the available data. However, oftentimes the recommendations diverge because

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of significant differences either in the availability of specific tests, costs of health care, availability of specialized care, cultural differences, or differences in the health care delivery system.

In this review, we compare the major management recommendations provided in the guidelines of the European Thyroid Association (ETA)[6] with those published by thyroid cancer specialty organizations in the United States (ATA and the National Comprehensive Cancer Network [NCCN][7]). By carefully examining treatment and management approaches that are applied in other areas of the world, we hope to identify equally effective alternative treatment or follow-up options that may find applicability to specific patients in our own practice.

Thyroid Cancer Management Guidelines

In 2006, the ETA (and the European Thyroid Association-Cancer Research Network) published a European consensus for the management of differentiated thyroid cancer which was prepared by a team of 50 multidisciplinary thyroid cancer experts drawn from 25 countries of the European Union. Consensus recommendations are presented without a grading of the strength of the evidence.[6]

The ATA published updated guidelines for the management of thyroid nodules and thyroid cancer in 1996, 2006 and then again in 2009.[4,9] The task force that prepared the 2009 guidelines was a 13-member multidisciplinary team appointed by the board of directors of the ATA. For the 2006 and the 2009 updates, an evidenced-based medicine approach was used with the published data and strength of evidence evaluation performed using a modified schema proposed by the US Preventative Services Task Force.[10]

The NCCN is a not-for-profit consortium of 21 major cancer centers within the United States. The NCCN develops and maintains clinical practice guidelines for most malignancies encountered in clinical practice "through an explicit review of the evidence integrated with expert medical judgment by multidisciplinary panels." The quality of the evidence and level of consensus are noted for each recommendation using a system developed by the NCCN. Another unique aspect of the NCCN guidelines is that they are actively updated at least once a year by review of the member institutions and the disease specific panels. This allows the NCCN guidelines to remain current by being modified through an intentional, active, ongoing process. The NCCN Thyroid Cancer Panel consists of a multidisciplinary team of 26 thyroid cancer specialists representing each of the 21 cancer centers in the consortium.[7]

Preoperative Staging

All 3 of the guidelines strongly endorse preoperative neck ultrasonography (US) before initial surgery in patients diagnosed with differentiated thyroid cancer. This preoperative staging US should include not only the thyroid gland itself but also the central and lateral neck lymph node chains so that clinically significant, metastatic lymph nodes can be identified, and verified with fine needle aspiration. Preoperative identification of clinically important lymph node metastases allows a more comprehensive initial surgical plan that addresses not only the primary tumor in the thyroid, but also the metastatic lymph node disease, at the time of the first surgery.

In addition, all 3 guidelines recommend additional structural (computed tomography scan, magnetic resonance imaging) or functional imaging (fludeoxyglucose-positron-emission tomography [FDG-PET]) to be used only in selected patients presenting with signs or symptoms of locally invasive disease. Although not discussed in the ATA guidelines, the NCCN guidelines also recommend evaluating "vocal cord mobility" for all patients even in the absence of clinically apparent locally invasive disease. The ETA guidelines specifically recommend endoscopic examination of aerodigestive structures only if there is clinical or imaging evidence of gross extrathyroidal invasion.

Although the ATA guidelines note that there is some evidence that serum thyroglobulin preoperatively may be useful in the postoperative management, they found the data insufficient to recommend in favor of the routine use of preoperative thyroglobulin (Tg) measurement. Likewise, neither the NCCN nor the ETA guidelines recommend obtaining a serum Tg before primary thyroid surgery.

At our center, preoperative US evaluation of the thyroid as well as central and lateral lymph node chains is routinely done before thyroid surgery. Vocal cord function is routinely evaluated by preoperative visual inspection. Additional functional or cross-sectional imaging is only done if there is clinical evidence of locally invasive disease. Preoperative serum Tg is not routinely obtained.

Extent of Initial Thyroid Surgery

Both the ETA and the ATA strongly endorse total thyroidectomy as the initial thyroid surgery of choice for nearly all well-differentiated thyroid cancers $\geq$1 cm in maximal dimension. Intrathyroidal, unifocal primary tumors $<$1 cm without a history of radiation exposure, lymph node, or distant metastases can be considered for less than total thyroidectomy as the initial surgical procedure. The rationale for total thyroidectomy as the initial surgical procedure includes data showing lower local recurrence rates with initial total thyroidectomy, facilitation of RAI remnant ablation if required, and ease of long term follow-up.

The NCCN guidelines allow for less than total thyroidectomy for intrathyroidal well differentiated thyroid cancers up to 4 cm in primary size in patients between 15 and 45 years of age if there is no history of previous radiation exposure, no aggressive histologic variant (tall cell, columnar cell or poorly differentiated), no evidence of extrathyroidal extension, or metastatic spread (regional or distant). The lack of a proven survival benefit of total thyroidectomy over lobectomy in this select group of low-risk patients is the primary rationale for this specific recommendation. In addition, supporters of lo-

bectomy as initial surgery firmly believe that the loco-regional recurrences that may develop can be identified and treated in a timely fashion without compromising overall survival. Furthermore, RAI ablation is often not recommended for this select group of low-risk patients at many of the NCCN institutions, therefore total thyroidectomy is not a requirement for additional planned treatment or follow-up.

If less than a total thyroidectomy is done for primary lesions between 1 and 4 cm, it is imperative that the multidisciplinary management team is in full agreement with regard to this approach because the choice of initial surgical procedure will have a profound impact on the follow-up management plan. Although still clinically useful tests, follow up US and serum Tg are less sensitive and less specific for detection of persistent/recurrent disease. However, because these low-risk patients are at minimal risk of death from disease and relatively low risk of recurrence, a highly sensitive follow-up management approach is not required.

Completion Thyroidectomy

Not infrequently, a well-differentiated thyroid cancer is diagnosed on histologic examination of a thyroid lobectomy performed for either presumed benign disease or an indeterminate cytology. All 3 guidelines agree that if the primary tumor is unifocal and <1 cm, no additional surgery is required in the absence of other high risk features or known loco-regional or distant metastatic disease.

The ATA guidelines recommend completion thyroidectomy for nearly all patients except those with a subcentimeter primary, unifocal, intrathyroidal, node-negative, low-risk tumor. The ETA guidelines recommend completion thyroidectomy for patients with multifocal disease, extrathyroidal extension, vascular invasion, unfavorable histology, prior history of radiation exposure or tumor size >2 cm. The decision regarding a completion thyroidectomy for tumors between 1 and 2 cm in size should be made on the "basis of the risks and benefits of reoperative surgery, including the potential risk of surgical morbidity."[6]

The NCCN guidelines recommend completion thyroidectomy if the primary tumor is >4 cm or demonstrated gross extrathyroidal extension, macroscopic multifocal disease or confirmed nodal metastases. Completion thyroidectomy should also be considered for tumors with aggressive histologies between 1 and 4 cm in primary size. Observation (without completion thyroidectomy) is recommended for tumors <1 cm in the absence of suspicious lesions in the contralateral lobe or loco-regional metastases.

Although not recommended as the preferred treatment option, both the ATA and the ETA guidelines note that radioactive iodine can be used to destroy the remaining normal contralateral lobe (RAI completion thyroidectomy). This approach may be particularly attractive in patients with ipsilateral vocal cord impairment secondary to damage to the recurrent laryngeal nerve during surgery, in patients with follicular thyroid cancer who are unlikely to have disease in the contra-lateral lobe or in patients in whom the potential surgical morbidity from a second intervention is unacceptably high.

At our center, most patients with primary tumors >2-3 cm opt for a total thyroidectomy as the initial procedure of choice. However, as per the NCCN guidelines, low-risk patients with intrathyroidal tumors and normal contralateral lobe on preoperative US are routinely offered the option of thyroid lobectomy provided they will be doing their long term follow-up management within our multidisciplinary team.

Initial Surgical Approach to Cervical Lymph Nodes

All 3 guidelines are in uniform agreement that compartment oriented neck dissection should be done at the time of initial thyroidectomy for patients with known cervical lymph node metastases (therapeutic neck dissection).

Similarly, all 3 guidelines note that routine central neck dissection of clinically uninvolved lymph nodes (prophylactic neck dissection) is controversial. Prophylactic lateral neck dissection (levels 2-5) is not recommended by any of the 3 organizations. Although not recommending routine prophylactic central neck dissection, the ETA guidelines simply note that the information obtained by the procedure may permit more accurate initial staging and therefore could guide subsequent treatment and follow up. The NCCN guidelines note that prophylactic central neck (level VI) dissection should be "considered" but this is a level 2 B recommendation (lower quality evidence, nonuniform agreement). The ATA guidelines note that total thyroidectomy without prophylactic neck dissection "may be appropriate" for small (T1 or T2), noninvasive, clinically node-negative papillary thyroid cancer and most follicular thyroid cancer. However, prophylactic central compartment neck dissection "may be performed" in patients with papillary thyroid cancer, especially those with advanced tumors (T3 or T4).

Therefore, while compartment oriented therapeutic neck dissection is recommended in all 3 guidelines, the role of prophylactic central neck dissection remains to be defined. In the absence of a proven survival benefit, we must carefully weigh the risks associated with central neck dissection (potentially greater rates of hypoparathyroidism and recurrent laryngeal nerve damage) with any potential benefits (improved staging, impact on recommendations for adjuvant therapy or follow up). At our center, we advocate a careful central neck "inspection" intraoperatively by the surgeon, but do not routinely perform prophylactic central neck dissections in the absence of clinically significant lymph node metastases in patients with differentiated thyroid cancer.

RAI Remnant Ablation

All 3 guidelines recommended selective use of radioactive iodine on the basis of the standard clinic-pathologic features that define the risk of recurrence and disease specific mortality. There is uniform agreement that patients with very low

Table 1 Major Factors Impacting Decision-Making in RAI Remnant Ablation

Factors	Description	Expected Benefit			RAI Ablation Usually Recommended	Strength of Evidence
		Decreased Risk of Death	Decrease Risk of Recurrence	May Facilitate Initial Staging and Follow-up		
T1a	1 cm or less, intrathyroidal	No	No	Yes	No	E
T1b	1-2 cm, intrathyroidal	No	Conflicting data*	Yes	Selective use*	I
T2	>2-4 cm, intrathyroidal	No	Conflicting data*	Yes	Selective use*	C
T3	>4 cm					
	<45 years old	No	Conflicting data*	Yes	Yes	B
	≥45 years old	Yes	Yes	Yes	Yes	B
	Any size, any age, minimal extrathyroidal extension	No	Inadequate data*	Yes	Selective use*	I
T4	Any size with gross extrathyroidal extension	Yes	Yes	Yes	Yes	B
Nx, N0	No metastatic nodes documented	No	No	Yes	No	I
N1	<45 years old	No	Conflicting data*	Yes	Selective use*	C
	≥45 years old	Conflicting data	Conflicting data*	Yes	Selective use*	C
M1	Distant metastasis present	Yes	Yes	Yes	Yes	A

RAI, radioactive iodine.

*Because of either conflicting or inadequate data, we cannot recommend either for or against RAI ablation for this entire subgroup. However, selected patients within this subgroup with higher risk features may benefit from RAI ablation. A, strongly recommends (good evidence). B, recommends (fair evidence). C, recommends (expert opinion). E, recommends against. I, recommends neither for nor against.

risk thyroid cancers (less than 1 cm confined to the thyroid) do not require routine RAI ablation. The ATA guidelines extend the recommendation against routine use of RAI ablation to include patients with multifocal disease as long as all foci are <1 cm and confined to the thyroid in the absence of other high risk features.

Likewise, there is uniform agreement that high risk patients (gross extrathyroidal extension, primary tumor greater than 4 cm, known distant metastases) should receive RAI remnant ablation as a part of routine care.

Both the ATA and the ETA note that there continues to be controversy regarding the benefit of RAI in patients with tumors between 1 and 4 cm, with or without lymph node metastases. All 3 guidelines call for selective use of RAI in these intermediate-risk patients on the basis of conflicting, retrospective data. The wording used in the ATA guidelines appears to accurately reflect the approach endorsed by both the ETA and the NCCN guidelines and accurately matches the approach used at our center: "RAI ablation is recommended for selected patients with 1-4 cm thyroid cancers confined to the thyroid, who have documented lymph node metastases, or other higher risk features when the combination of age, tumor size, lymph node status, and individual histology predicts an intermediate to high risk of recurrence or death from thyroid cancer."[4] Specific levels of evidence based on specific size of the primary tumor, lymph node status, and presence/absence of distant metastases can be found in Table 5 of the ATA guidelines (Table 1).

Specifics of RAI Remnant Ablation

A low-iodine diet for either 1-2 weeks (ATA) or 3 weeks (ETA), as well as avoidance of iodine contamination from intravenous contrast materials or medications, is routinely recommended. When radiologic imaging with iodine-contrast media had been used, the ETA suggests waiting 2-3 months before performing RAI ablation (ideally with urinary iodine excretion monitoring).

The ETA guidelines note that diagnostic whole-body scanning before ablation has low clinical utility and therefore "may be avoided without loss of information." The ATA recommends diagnostic whole-body scanning before ablation only when the results of the scan would be likely to "alter either the decision to treat or the activity of RAI that is administered." The concern for ^{131}I-induced stunning of normal thyroid remnants (or of thyroid cancer metastases), mentioned in the ETA guidelines, is addressed by the ATA as being avoided with a low ^{131}I activity diagnostic whole-body scan and therapy being given within 72 hours of scanning.

The NCCN guidelines routinely recommend diagnostic scanning for patients being considered for RAI ablation. Information from the diagnostic scan is used to assist in making a final decision about whether ablation is necessary. For example, if the stimulated Tg is <1 ng/mL and the diagnostic scan is negative, then RAI ablation is not given in the absence

Table 2 Initial ATA Risk of Recurrence Classification

Low Risk	Intermediate Risk	High Risk
All the following are present: • No local or distant metastases. • All macroscopic tumor has been resected. • No invasion of loco-regional tissues. • Tumor does not have aggressive histology (eg, tall cell, insular, columnar cell carcinoma, Hürthle cell carcinoma, follicular thyroid cancer). • No vascular invasion. • No ^{131}I uptake outside the thyroid bed on the posttreatment scan, if done.	Any of the following is present: • Microscopic invasion into the perithyroidal soft tissues. • Cervical lymph node metastases or ^{131}I uptake outside the thyroid bed on the posttreatment scan done after thyroid remnant ablation. • Tumor with aggressive histology or vascular invasion (eg, tall cell, insular, columnar cell carcinoma, Hürthle cell carcinoma, follicular thyroid cancer).	Any of the following is present: • Macroscopic tumor invasion. • Incomplete tumor resection. • Distant metastases.

of other high-risk features. Additionally, the scan results also impact the recommendation for administered activity with uptake only in the thyroid bed resulting in a recommendation for 30-100 mCi ^{131}I, whereas uptake in metastatic lesions outside the thyroid bed would result in a recommendation for 100-200 mCi ^{131}I. In effective, all 3 guidelines are in agreement that diagnostic whole body scanning before ablation should only be done if the results of the scan are likely to change the initial treatment recommendation.

All 3 guidelines support the use of recombinant human thyroid-stimulating hormone (rhTSH) as an alternative to traditional thyroid hormone withdrawal in the absence of known metastatic disease. Obviously, the use of rhTSH varies between countries on the basis of cost, health care delivery systems, and other details that are specific to each country.

All 3 guidelines provide only broad guidance as to the recommended administered activity of ^{131}I that should be used for ablation. The ETA notes that standard activities range from 1110 MBq (30 mCi) to 3700 MBq (100 mCi) or even higher. The ATA recommends using the "minimum activity" necessary to achieve successful ablation (usually 1110 MBq [30 mCi] to 3700 MBq [100 mCi]). If residual microscopic disease is suspected or documented, then higher administered activities would be considered for adjuvant therapy (100-200 mCi). The NCCN recommendations (as discussed above) closely mirror the ATA guidance. All 3 guidelines endorse the utility of a posttherapy scan obtained 3-5 days after remnant ablation.

Staging Systems

While all 3 guidelines endorse using the American Joint Cancer Committee/Union Internationale Contre le Cancer (AJCC/UICC) staging system for estimating the risk of disease-specific mortality, the NCCN and ATA guidelines also point out the importance of using additional tumor and patient specific risk factors to guide treatment and follow up recommendations. The ATA specifically recommends using an additional clinic-pathologic staging system to "improve prognostication and to plan follow up for patients with differentiated thyroid cancer."[4] The NCCN guidelines specifically state that AJCC/UICC staging is not used to direct management recommendations but instead rely on specific "tumor and patient characteristics" to guide recommendations.

Recognizing that the AJCC/UICC staging system was not designed to predict risk of recurrent/persistent disease, the ATA guidelines also proposed a novel three-tiered risk of recurrence stratification system (Table 2). In a recent publication, we have verified that this newly proposed classification system accurately predicts the risk of recurrence and persistent disease in a cohort of more than 500 patients following total thyroidectomy and RAI remnant ablation.[11]

In all 3 guidelines, treatment recommendations are often made based on the "risk" of recurrence and/or death from thyroid cancer. Although varying slightly with regard to the specific staging systems used, all 3 guidelines are in agreement that AJCC/UIC staging can be used to stratify for risk of disease-specific death while an additional clinic-pathologic staging system should be used to estimate risk of recurrence/persistent disease and guide long term management.

TSH-Suppressive Therapy

In the absence of specific contraindications, the ETA recommends using levothyroxine to achieve an initial TSH goal of $\leq$0.1 mU/L for all patients. This level of suppression is maintained indefinitely in patients with persistent biochemical or structural evidence of disease and for 3-5 years in high-risk patients who are apparently in remission. However, as soon as the patient has achieved remission (no clinical or biochemical evidence of disease), the goal of therapy changes from thyroid hormone suppression (TSH $\leq$0.1 mU/L) to thyroid hormone replacement (TSH 0.5-1.0 mU/L).

The ATA and NCCN guidelines follow a similar risk adapted strategy where the degree of TSH suppression is titrated to the ongoing estimated risk of recurrence/death from disease. The ATA guidelines specifically note that the initial goal TSH for intermediate and high risk patients is $<$0.1 mU/L, but only 0.1-0.5 mU/L in low-risk patients. Persistent TSH suppression ($<$0.1 mU/L) is recommended for

patients with persistent/recurrent disease in the absence of medical contraindications. High risk patients who are free of disease are recommended to maintain a TSH of 0.1-0.5 mU/L for 5-10 years whereas low-risk patients with no evidence of disease can have simple thyroid hormone replacement with a goal TSH of 0.3-2.0 mU/L. Although they are less specific about the precise TSH goals, the NCCN guidelines are consistent with the more detailed approach outlined in the ATA guidelines.

Follow-Up Recommendations

All 3 guidelines provide remarkably similar recommendations with regard to follow-up of patients who were initially treated with thyroidectomy and RAI remnant ablation. Serum Tg (and antithyroglobulin antibodies), TSH, and neck US are performed initially at 6- to 12-month intervals during the first 1-2 years of follow-up. Once the suppressed Tg is <1 ng/mL, a stimulated Tg with the use of either rhTSH or thyroid hormone withdrawal is recommended 6-12 months after RAI ablation to identify those patients who are very unlikely to recur (stimulated Tg less than 1 ng/mL). These patients are considered low risk and the TSH goal is changed to generous replacement (rather than suppression) with long-term follow up consisting primarily of yearly TSH, Tg, and anti-Tg antibodies with neck US performed occasionally, if at all.

Diagnostic whole-body RAI scans are not considered clinical helpful if the suppressed Tg is undetectable and the neck US is unremarkable. However, all 3 guidelines note that diagnostic RAI scanning may be helpful in intermediate to high risk of recurrence patients or in patients with biochemical or structural evidence of persistent disease. Fludeoxyglucose position emission tomography scanning is not routinely used in the follow-up of low- to intermediate-risk thyroid cancer patients but may be useful in localizing disease in Tg-positive, diagnostic scan-negative patients and patients with locally aggressive tumors (especially with high risk histologies like poorly differentiated tumors, Hürthle cell carcinoma or insular variants). Traditional cross-sectional imaging is used only if functional or biochemical testing indicates persistent/recurrent disease or if the patient is at high risk of developing recurrent disease.

Both the ATA and the ETA guidelines make specific recommendations regarding management of the very small abnormal lymph nodes often identified on follow up neck US. The ETA recommends serial US observation of abnormal lymph nodes <5 mm. The ATA recommends fine-needle aspiration for lymph nodes <5-8 mm only if a positive result would change management. Because these small lymph nodes often grow very slowly (if at all) and are of doubtful clinical significance, the risk of surgery may outweigh the benefit of surgical resection. Therefore, cautious observation of small lymph nodes with compartment oriented surgical resection only with documented structural growth is probably in the best interest of most patients.

Management of Loco-Regional Recurrent Disease

Management recommendations regarding loco-regional recurrence are very similar across all 3 guidelines. Compartment oriented surgical resection with additional RAI (if the lesions are likely to be RAI avid) is recommended as the treatment of choice in each guideline. Furthermore, all 3 guidelines endorse repeated administrations of RAI for loco-regional or distant metastases provided a meaningful clinical response is being seen. The ETA guidelines note that external beam irradiation "may be indicated" if complete surgical excision is not possible and there is no significant RAI uptake within the tumor. Likewise, the ATA recommends consideration of external beam radiation therapy in the management of non-RAI avid, grossly unresectable residual or recurrent cervical disease.

Management of Distant Metastases

Furthermore, there is uniform agreement with regard to the management of distant metastases. RAI is recommended as long as a therapeutic effect is being demonstrated. External beam irradiation is used both for unresectable, structurally significant disease with actual or impending local compressive symptoms and for pain control in bone metastases. Because traditional systemic therapies have been so disappointing, all 3 guidelines recommend proceeding directly to experimental therapies instead of cytotoxic chemotherapy in patients with structurally progressive disease that is not amenable to resection or external beam irradiation therapy. Fortunately, the last 5 years have seen an explosion in clinical trials and novel agents specific for thyroid cancer.[12,13] Many of the novel therapies appear to have a clinical benefit in 50%-60% of patients with non-RAI avid progressive structural distant metastases.

Conclusions

Despite significant difference in cultures, economies, and health care delivery systems between Europe and the United States, thyroid cancer management recommendations from the European experts (ETA) and the American experts (ATA, NCCN) are far more similar than they are different. Each of the guidelines strongly endorses an initial management approach that is guided by individualized estimates of risk of recurrence and risk of death. Furthermore, follow up and additional therapeutic recommendations are based on revised risk estimates that reflect an individual patient's response to therapy.

This risk adapted approach to the management of thyroid cancer allows the clinician to tailor both treatment and follow-up recommendations to the specific risks of recurrence and death of each individual patient. In this way, low-risk patients are spared unnecessary treatment and follow up studies whereas high-risk patients are subjected to more ag-

gressive therapy and more intense follow-up. This approach appropriately balances the risk and benefit of each treatment and follow-up study with the risk of recurrence and death of each patient.

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