Postoperative radioactive iodine administration for differentiated thyroid cancer patients

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Purpose of review
Radioactive iodine (RAI) is administered postoperatively to the majority of thyroid cancer patients. No available study has demonstrated any benefit in low-risk patients.

Recent findings
RAI should be used selectively in low and intermediate-risk patients, based on the surgical and pathological reports and on postoperative serum thyroglobulin level and neck ultrasonography. When used, a low activity (30 mCi) is administered following recombinant human thyrotropin stimulation. High-risk patients are treated with a high activity of RAI (100 mCi or more).

Summary
RAI is not administered in many low-risk patients who can be reliably followed up with serum thyroglobulin determination on L-thyroxine treatment and neck ultrasonography. RAI may be administered in case of abnormality, and this delay will not reduce the chance of cure.

Keywords
ablation, initial treatment, radioiodine, thyroglobulin, thyroid cancer

INTRODUCTION

Before the 1970s, the administration of radioactive iodine (RAI) for remnant ablation in the management of differentiated thyroid cancer (DTC) was restricted to patients with poor prognostic indicators for survival, including age greater than 45 years, aggressive histology of the thyroid tumor and large tumor extension [1]. This was based on the paucity of available data demonstrating benefits and the fear of genetic and carcinogenic effects related to RAI exposure.

However, in a retrospective series published in the late-1970s, Mazzaferri *et al*. [2] demonstrated that remnant ablation reduced the recurrence rate and improved the overall survival of DTC patients. In addition, as subtotal thyroidectomy was frequently performed, leaving a large remnant of thyroid tissue, postoperative follow-up with thyroglobulin (Tg) was difficult. Therefore, beginning in the 1980s, 'remnant ablation' was recommended in nearly all DTC patients, exposing many low-risk patients to the cost, inconvenience, and adverse effects of RAI therapy with little potential benefit. In addition, other researchers demonstrated that the outcome of low-risk patients was favorable after total thyroidectomy even in the absence of RAI ablation [3]. Currently, most thyroid surgeons perform a total thyroidectomy, which leaves only small thyroid remnants and results in many patients having no measurable serum Tg postoperatively.

The last several years have seen a renewed interest in risk-adapted management approaches to DTC, whereby for each patient the intensity of therapy and of monitoring is tailored to the expected aggressiveness of the disease [4–6]. This is relevant because of the increasing incidence of low-risk thyroid cancers, for which limited treatment and follow-up may be sufficient. Unfortunately, most available data regarding this are available only as retrospective studies.

THE GOALS OF POSTOPERATIVE ADMINISTRATION OF RADIOACTIVE IODINE

The goals of the administration of RAI after total thyroidectomy may include [4,5] (Table 1):

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KEY POINTS

- Radioactive iodine should be administered selectively to low and intermediate-risk patients.
- Selection of patients for RAI administration is based on the surgical and pathological reports and on the postoperative serum Tg level and neck ultrasonography.
- When indicated in low-risk DTC patients, low activity RAI (30 mCi) should be administered following stimulation with rhTSH.
- Low-risk patients who have not been given RAI can be followed with serum Tg determination on L-thyroxine treatment.

ablation – eradication of normal thyroid remnants that may facilitate the detection of recurrent disease by serum Tg measurements and treatment – irradiation of persistent disease. Therapy may be adjuvant (intended to improve disease-free survival by destroying suspected, but unproven, persistent disease) or therapeutic (intended to improve disease-specific survival by treating known persistent disease); and assessment of the completeness of surgical resection and of the absence of persistent disease with a post-therapy whole-body scan (WBS).

Indeed, in low-risk patients, when administered RAI is aimed mostly at remnant ablation and in high-risk patients, it is routinely administered both for remnant ablation and for therapy. Each of these aims needs to be critically evaluated according to the recently available data.

DEFINITION OF ABLATION

Successful remnant ablation can be defined by two criteria [4,5]: an undetectable serum thyroid stimulating hormone (TSH)-stimulated Tg [or a serum Tg <0.2 ng/ml on L-thyroxine (L-T4) treatment with a sensitive method [7]], in the absence of interfering antibodies, and a neck ultrasonography that does not show any evidence of disease. No other imaging studies are required in the majority of cases. WBS following RAI is no longer routinely performed for diagnostic purposes [8,9].

An alternative definition of ablation in cases in which anti-Tg antibodies are present (and in whom serum Tg determination cannot be used) is the absence of visible RAI uptake on a subsequent WBS performed with a diagnostic activity and a neck ultrasonography that does not show any evidence of disease [4,5]. Also, the spontaneous decline of serum titer of anti-Tg antibodies over time in these patients is reassuring.

ABLATION OF NORMAL THYROID REMNANTS AND THE USE OF SERUM THYROGLOBULIN DURING FOLLOW-UP

Serum Tg may be produced by both normal and neoplastic thyroid cells. After ablation of normal thyroid remnants, serum Tg levels should be undetectable; any detectable Tg in the serum signals the presence of neoplastic cells [10]. Therefore, RAI ablation increases the sensitivity and the specificity of serum Tg determination for detecting tumor foci. However, the production of Tg in the serum by the small thyroid remnant after a total thyroidectomy is low during L-T4 treatment. Several retrospective studies have shown that serum Tg determination on L-T4 treatment is useful in patients who had not undergone RAI ablation. In 290 low-risk (T1–T2, N0, and M0) patients who underwent a total thyroidectomy, but were not given RAI postoperatively, the serum Tg on L-T4 treatment was less than 1 ng/ml in 95% after a median follow-up of 5 years; in a subset of 78 of these patients and using a sensitive method

Table 1. Postoperative administration of radioactive iodine

Aim	Definition	Benefits	Limitations
Remnant ablation	Destruction of normal residual thyroid tissue	Facilitates follow-up: improves the sensitivity and specificity of serum Tg determination	Serum Tg can be measured on LT4 treatment
Treatment	Destruction of neoplastic thyroid foci that are either known (treatment) or remote (adjuvant)	Improves disease-free survival (adjuvant) and overall survival (adjuvant and treatment)	Applies only to patients with persistent disease
Postadministration WBS	Sensitive WBS with SPECT/CT	Assess completeness of surgical resection and absence of persistent RAI-avid disease	Low risk of persistent disease by definition in low-risk patients

CT, computed tomography; RAI, radioactive iodine; SPECT, single-photon emission computed tomography; Tg, thyroglobulin; WBS, whole-body scan. Adapted with permission from [4,5].

for serum Tg determination, it was less than 0.2 ng/ml in 60% at 1 year and in 79% at 5 years [11▪]. Similar data have been obtained in another series of patients using a sensitive method [12]. In these series, few patients had a detectable serum Tg that remained reassuringly stable at low levels or decreased with time. In contrast, serum Tg increased with time in patients with persistent disease [13]; these rare patients may benefit from RAI treatment.

RISK OF RECURRENCE AND RISK OF THYROID-CANCER-RELATED DEATH

The individual risk of recurrence depends on the initial prognostic indicators and results of serum Tg measurements and neck ultrasonography after initial surgery. Because the half-life of Tg in the serum is estimated to be 1–2 days, the nadir is obtained at least 1 month after surgery. Benefits of postoperative RAI administration differs among patients from the three American Thyroid Association (ATA) risk groups.

The ATA risk stratification of recurrence is as follows (adapted with permission from [5]):

(1) low risk:
   (a) tumor confined to the thyroid (and probably microscopic N1);
   (b) no aggressive histology, no vascular invasion;
   (c) all macroscopic tumor has been resected and if RAI WBS is done, no uptake outside the thyroid bed;
(2) intermediate risk:
   (a) neck lymph node metastases or RAI uptake outside the thyroid bed (if RAI WBS is done);
   (b) microscopic extrathyroidal extension;
   (c) aggressive histology or vascular invasion;
(3) high risk:
   (a) gross extrathyroidal extension;
   (b) incomplete tumor resection;
   (c) distant metastases;
   (d) inappropriate Tg elevation.

The European Thyroid Association consensus. Indications for the postsurgical administration of RAI is as follows (adapted with permission from [4]):

(1) very low-risk patients: T less than 1 cm, unifocal (and probably limited multifocal), intrathyroid and N0 (and probably microscopic N1): no benefits, no indication.
(2) high-risk patients: T3–T4, extensive N1, M1 or known persistent disease, aggressive histology, inappropriately elevated serum Tg level: Treatment with a high activity (100 mCi or more) following withdrawal of thyroid hormone treatment
(3) low-risk patients: all the other patients (T1–T2, 1–4 cm; micro-N1–N0–Nx with normal neck ultrasonography; nonaggressive histology). Controversial benefits: selective indications, and when indicated, a minimal activity (30 mCi or less) is administered following the best tolerated method [recombinant human thyrotropin (rhTSH)].

ATA high risk

The overall and disease-specific mortality, as well as disease-free survival, were improved after postsurgical RAI therapy in TNM stage III and IV patients [14]. Furthermore, prospectively collected data suggest that postsurgical RAI therapy is associated with improved overall survival in patients aged greater than 45 years with papillary thyroid cancer with distant metastases, tumor size greater than 2 cm and positive lymph nodes [15], and in patients with follicular thyroid cancer with distant metastases in whom it more than doubled [16]. Thus, routine postsurgical RAI treatment with a high activity is recommended in high-risk DTC patients and in those with distant metastases or persistent disease in the neck.

ATA intermediate risk

Multivariate analyses suggest that postsurgical RAI treatment is associated with improved overall survival for aggressive papillary thyroid cancer histology, such as tall cell and diffuse sclerosing variants [17]. It may improve disease-specific survival, as well as disease-free survival, in PTC patients with nodal metastases aged at least 45 years but not in younger patients [14], and lymph node failure-free survival in patients with node-positive papillary thyroid cancer [18]. However, a retrospective study from the Mayo Clinic suggested no benefit in the 20-year cause-specific mortality and recurrence rate in papillary thyroid cancer patients with a MACIS score of less than 6, including those who had positive lymph nodes [3].

The risk of recurrence may be different within ATA intermediate-risk patients. The greatest potential benefit may be observed in those with adverse thyroid cancer histology, increasing volume of nodal disease, lymph node disease outside the central neck, and advancing age [18]. Indeed, several groups recommend the administration of a high activity of RAI in those intermediate-risk patients with the highest risk of recurrence. The efficacy of RAI treatment in improving long-term thyroid

cancer outcomes in patients with isolated microscopic central neck nodal disease in the absence of other adverse features is unknown. In this regard, prophylactic central neck dissection may help to exclude N0 patients from RAI administration, but should not lead to the RAI administration in all patients with minimal lymph node involvement [19].

Intermediate-risk patients may be selected for RAI administration according to the postoperative data. RAI-avid metastatic foci outside the thyroid bed was detected in 12% of patients with a suppressed Tg of less than 0.6 ng/ml [20], and in another series in 6% of patients with a suppressed Tg less than 1.0 ng/ml [21], and in 7% T1–T2, N1 patients with stimulated serum Tg less than 1 ng/ml [22]. Also, a combination of postoperative neck ultrasonography and TSH-stimulated serum Tg level less than 10 ng/ml individualizes a group of N1 patients with a risk of recurrence after RAI administration of 6% [23]. Therefore, neither a stimulated nor a suppressed postoperative Tg less than 1 ng/ml can completely eliminate the possibility that a post-therapy RAI scan will identify metastatic foci outside the thyroid bed, but it should be taken into account together with other prognostic indicators to select patients for RAI administration. The risk of persistent disease increases with higher postsurgical serum Tg levels.

ATA low risk

In this group, the risk of disease-specific mortality and of persistent and recurrent disease is low, and there is no demonstration that delayed treatment of persistent disease may decrease the chance of cure. In 1298 low-risk patients who were followed for a median of 10.3 years, there was no benefit of postoperative RAI administration on overall or disease-free survival [24]. Prospective data suggest that overall, disease-specific and disease-free survivals are not improved by RAI treatment in Tumor Node Metastases stage I and II patients [14,25]. In a retrospective series on 290 low-risk patients (T1–T2, N0, and M0) who did not receive any RAI, only one had a neck recurrence with a median follow-up of 6 years [11▪], and in another series of 136 patients who had a postoperative stimulated Tg level less than 1 ng/ml and a normal neck ultrasonography, only one had a neck recurrence [26].

The risk of persistent disease is even lower in some low-risk patients. Retrospective studies have shown that the 136 low-risk (T1–T2) patients who had no lymph node involvement and a postoperative TSH-stimulated serum Tg less than 1 ng/ml had no evidence of disease on the posttherapy WBS and probably do not require any RAI administration [22]. Similarly, no uptake outside the thyroid bed was identified in 63 low-risk patients with a non-stimulated postoperative Tg of less than 0.2 ng/ml using a sensitive method [27] or in 132 low-risk patients with a thyroid hormone withdrawal Tg of less than 1 ng/ml [21].

In conclusion, RAI remnant ablation is unlikely to improve disease-specific or disease-free survival in papillary microcarcinoma (<1 cm, unifocal or multifocal), in the absence of other higher risk features [28–30]. In other low-risk patients, there is little evidence to suggest that RAI may improve disease-specific mortality and risk of recurrence, and RAI should be administered selectively, based on the prognostic indicators and on the serum Tg level and neck ultrasonography performed after surgery. The risk of persistent disease is low when postoperative serum Tg is undetectable, so that RAI administration may not be justified. This is particularly the case in N0 patients with minimal lymph node involvement. On the contrary, the likelihood of identifying RAI-avid metastatic disease on the post-therapy WBS increases with postoperative Tg values greater than 5–10 ng/ml, suggesting that RAI should be administered to such patients [20,31,32].

There are currently insufficient data regarding whether the BRAF V600E mutation in papillary thyroid cancer patients may impact the success of RAI administration or whether RAI activity adjustments are warranted for any planned treatment. A retrospective study on T1aN0M0 patients who received 30 mCi postoperatively found that 13% of BRAF-positive patients had biochemical persistence of disease, compared to 1.7% in BRAF negative patients [33]. There are no recommendations that BRAF status should modify the indication of RAI administration in either low or high-risk patients.

In conclusion, the role of RAI remnant ablation in ATA low risk should be clarified by performing randomized trials in well defined subgroups of patients, such as the Iodine or Not (IoN) trial for low and intermediate-risk patients [34] and Essai Stimulation Ablation 2 for low-risk patients (Leboulleux, 2013, registration number NCT01837745). The Essai Stimulation Ablation 2 study will also analyze the relevance of BRAF mutation status on outcome.

SHOULD A POSTTHERAPY SCAN BE PERFORMED FOLLOWING REMNANT ABLATION?

The post-therapy WBS is more reliable when uptake is less than 2% of the administered activity in small thyroid remnants following total thyroidectomy. In

comparing the results of pretherapy RAI scans to post-therapy scans, the rate of newly discovered lesions on post-therapy scans was reported to be between 6 and 13% [35–37], suggesting that a post-therapy WBS should be performed in all patients in whom a high RAI activity has been administered.

The availability of superimposed functional images provided by single-photon emission computed tomography (SPECT) and anatomical images provided by CT scan is a major advantage for imaging DTC patients. SPECT-CT is useful for differentiating neck uptake in normal thyroid remnants from uptake in neck lymph node metastases, or chest uptake in bones (ribs, sternum, or vertebrae) from uptake in lungs and pelvis, and uptake in the urinary or digestive tract from uptake in pelvic bones [38]. The routine addition of neck and chest SPECT-CT to all post-therapy scans has been estimated to alter the postsurgical ATA recurrence risk estimate in 6.4% of patients [39], impact therapeutic planning in about 2% of cases [40], and reduce the need for additional cross-sectional imaging in 20% of cases. SPECT-CT is useful for identifying noniodine-avid lesions [39].

Because post-therapy WBS has been shown to be more sensitive than diagnostic pretherapy WBS and because pretherapy WBS may induce stunning, pretherapy WBS is not performed on a routine basis (only when the extent of thyroid remnants cannot be assessed) and only a post-therapy WBS is performed [4,5] in many centers. With the use of modern techniques, it appeared that diagnostic WBS with SPECT-CT may be as sensitive as post-therapy WBS [41]. However, in many centers, RAI is administered on the basis of initial prognostic indicators either alone or in combination with results of postsurgical serum Tg determination and of neck ultrasonography, and no pretherapy WBS is performed. Furthermore, when no RAI is administered, the risk of persistent disease is by definition so low that there is no need for diagnostic WBS.

TSH STIMULATION IS REQUIRED FOR REMNANT ABLATION

Endogenous TSH elevation can be achieved by thyroid hormone withdrawal that consists either in stopping L-T4 and switching to L-T3 for 2–4 weeks followed by withdrawal of L-T3 for 2 weeks or discontinuation of L-T4 for 3 weeks without the use of L-T3. Both methods of preparation can achieve serum TSH levels above an arbitrary level greater than 30 mU/l in more than 90% of patients, a level of serum TSH that is associated with RAI uptake in tumors [42]. A prospective study showed no difference in hypothyroid symptoms between these two approaches [43]. Children with thyroid cancer achieve adequate TSH elevation within 14 days of L-T4 withdrawal [44], but elderly patients may only achieve lower serum TSH levels [45].

rhTSH is an alternative method for TSH stimulation prior to RAI administration. It consists of two intramuscular injections of rhTSH (10 IU) on two consecutive days with the administration of RAI on the day following the second injection. L-T4 treatment is initiated after initial surgery and is maintained during the procedure, and hypothyroid-related symptoms are avoided and the health-related quality of life (HRQOL) is maintained [46,47,48▪▪,49▪▪]. This difference in HRQOL may persist during 6 weeks or even longer after the administration of RAI, but the HRQOL was similar in both groups at 3 months after RAI administration [47,48▪▪,49▪▪]. The other benefits of using rhTSH are a shorter duration of stay in isolation in those centers requiring hospitalization [50], a shorter duration of sick leave, and a lower radiation dose to the body [51,52], compared with hypothyroidism following withdrawal of thyroid hormone treatment.

IS A LOW-IODINE DIET NECESSARY BEFORE REMNANT ABLATION?

It is important to inquire about the history of possible high-dose iodine exposure (e.g., intravenous contrast, amiodarone, or others) in considering the timing of RAI administration. Excess iodine is eliminated 1 month after the administration of an iodinated CT scan [53]. The urinary iodine excretion can be obtained to confirm clearance. The most commonly studied low-iodine diets (LIDs) allowed for 50 μg/day or less of iodine for 1–2 weeks that appeared to be associated with an increase in RAI uptake, compared with no LID [54]. However, there is conflicting evidence on the impact of a LID on the outcome of remnant ablation success [54–56].

RADIOIODINE ACTIVITY ADMINISTERED FOR REMNANT ABLATION

Most clinicians prescribe an empiric fixed RAI activity for ablation that usually ranges between 30 and 150 mCi, but radiation dosimetry is used in some centers [57]. The administered activity depends not only on the center, but also on the aim of RAI administration: in high-risk patients, a high activity is administered because it is aimed at irradiating remote or known tumor foci; in low and intermediate-risk patients, it is mostly aimed at ablating normal thyroid remnants, and both a low activity and the best tolerated TSH stimulation method are used.

In patients with distant metastases, retrospective studies have shown that the short-term outcome was similar after preparation with either rhTSH injections or prolonged withdrawal [58], but no comparative data on long-term outcome is available. Also, whole-body and blood dosimetry studies were performed in all patients and these results may not be extrapolated to patients treated with standard and lower activities. The few available data on dosimetry suggest that the radiation dose delivered to neoplastic foci by a given RAI activity following rhTSH injections may be lower than after prolonged withdrawal [59]. This is the rationale for administering RAI following prolonged withdrawal in patients with known distant metastases, as well as in many centers, in patients with high-risk disease.

In 63 patients with intermediate and low-risk disease, preparation using rhTSH or thyroid hormone withdrawal has been compared using an RAI activity of 100 mCi, and the rate of successful remnant ablation was 100% with both methods [46]. The dose delivered to thyroid remnants was similar with both methods, and the dose to the body was 50% lower in euthyroid, rhTSH prepared patients relative to hypothyroid patients with decreased renal iodine clearance. Furthermore, the use of rhTSH is able to minimize hypothyroid symptoms and maintains the HRQOL. In the above study, follow-up data was reported a median of 3.7 years later for 51 of the original 63 patients, and rates of reoperation for cervical neck recurrence were similar between groups (4% of patients), with no deaths; repeat RAI treatment for detectable serum Tg or imaging showing evidence of disease was performed in four of 28 patients in the rhTSH group and five of 23 patients in the hypothyroid group [60]. The low number of thyroid-cancer-related deaths and recurrences limit the ability to make meaningful statistical comparisons of long-term outcomes. A retrospective study using a high RAI activity (median: 4 GBq, 108 mCi) and a preparation with either rhTSH or prolonged withdrawal showed similar efficacy on the recurrence rate in intermediate and high-risk patients [61▪], and similar data were reported in another study [62].

Two prospective randomized trials have addressed the question of whether rhTSH can be used prior to the administration of RAI to allow for a lower 131-I dose (Table 2).

Essai stimulation ablation was supported only by the French Institut National du Cancer [48▪▪]. This randomized phase III trial performed in 24 French centers compared four strategies for postoperative RAI in a 2×2 factorial design using an equivalence framework: each strategy combined a TSH stimulation method (either thyroid hormone withdrawal or rhTSH) and a RAI activity (either 30 or 100 mCi). The ablation rate at 6–10 months was assessed with neck ultrasonography and stimulated Tg determination (or with neck ultrasonography and WBS in the presence of anti-Tg antibodies). A total of 752 low-risk patients (79% women, mean age 49 years) were included: 92% had papillary cancer [30% of tumors were pT1N0, 18% were pT1N1 (with minimal involvement), 39% were pT1, Nx and 12% were pT2N0]. A total of 68 patients were excluded from the final analysis, including the 27(3%) patients who had persistent disease at ablation. Among the remaining 684 patients, neck ultrasonography was normal in 652 patients (95%), stimulated Tg level was 1.0 ng/ml or less in 621 of the 652 (95%) patients without Tg antibodies, and thyroid ablation was complete in 631 of 684 (92%) patients. The ablation rate was equivalent both for the 131-I activity and for the TSH stimulation method.

High or Low was conducted at 29 centers in the UK using the same equivalence framework [49▪▪]. A total of 438 patients who had tumor stage T1–T3 with possible N1, M0 disease underwent randomization.

Table 2. Comparison of High or Low and Essai Stimulation Ablation trials

	Essai stimulation ablation	High or Low
Patients (*n*)	752	438
pT1N0, pT1Nx, and pT2N0	75%	54%
Preablation stimulated Tg	<1 ng/ml in 45%	<2 ng/ml in 28%
Definition of complete ablation	Normal neck ultrasonography and Tg/rhTSH <1 ng/ml in the absence of Tg Ab	Normal diagnostic WBS and Tg/TSH <2 ng/ml
Persistent disease at ablation (WBS or neck ultrasonography) (%)	3%	Nd
Complete ablation (%)	92%	87%
Non inferiority of rhTSH vs. withdrawal	Yes	Yes
Non inferiority of 30 vs. 100 mCi	Yes	Yes

rhTSH, recombinant human thyrotropin; Tg, thyroglobulin; WBS, whole-body scan. Data from [48▪▪,49▪▪].

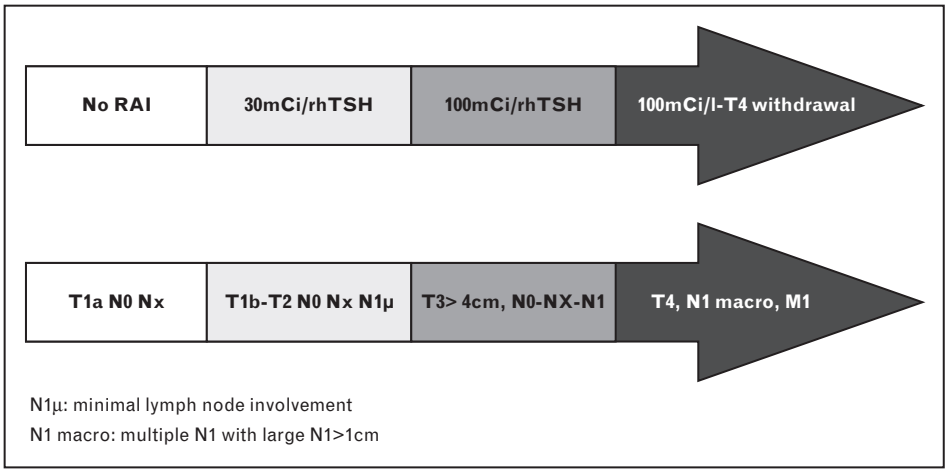

FIGURE 1. Proposed protocol for radioactive iodine administration as a function of the American Thyroid Association risk of recurrence.

Ablation success rates were 85–89% in the four subgroups with no evidence of inferiority.

Short-term salivary and lacrimal side-effects in the weeks following remnant ablation were more frequent in patients treated with 100 mCi, compared with those treated with 30 mCi [48▪▪,49▪▪]. Medicoeconomic evaluation of these four strategies confirmed that the use of rhTSH permits the maintenance of a good quality of life, although not significantly increasing the cost of treatment from a societal perspective. Patients in these two studies are currently being followed up to assess the long-term risk of recurrent disease and thus to confirm retrospective studies that showed no increased risk of recurrence in patients who had received a low activity (30 mCi) after rhTSH stimulation [63,64].

These results validate the use of rhTSH and 30 mCi for remnant ablation of low-risk patients, and this has led to the product labeling of rhTSH for ablation with low activity RAI (30 mCi) in North America and Europe. Ongoing randomized clinical studies in France (ESTIMABL 2) and the UK (IoN) [34] will compare the outcome after either the administration of 30mCi after rhTSH or no RAI administration in low-risk patients. A practical guide to achieve a well tolerated and convenient treatment plan for DTC patients is summarized in the list below.

Proposed protocol for ablation in low and intermediate-risk patients is as follows:

(1) Start L-thyroxine treatment immediately after surgery.
(2) Schedule ablation at a time that is convenient both for the patient and for the treating team (can be performed 1–3 months or more after surgery).
(3) Administer rhTSH (10 IU intramuscularly on days 1 and 2).
(4) Administer RAI on day 3 (1.1 GBq to 30 mCi).
(5) Perform a WBS with neck SPECT–CT on days 5–8.

CONCLUSION

Significant progress has been made toward the selective use of RAI in DTC patients. In many low-risk patients, postoperative RAI may be avoided and when indicated, should be of low activity (30 mCi) administered after rhTSH administration. In patients with known distant metastases, treatment consists of the administration of high activity RAI (100 mCi or more) following withdrawal of thyroid hormone treatment, although rhTSH may be used especially in elderly patients who do not tolerate hypothyroidism well. In patients with intermediate or high-risk but without known distant metastases, a high activity (100 mCi) is administered following a preparation with either rhTSH or prolonged withdrawal (Fig. 1). Further prospective trials are needed to better delineate the indications of RAI administration, and when indicated, the protocol to be used in each of these DTC patient subgroups to improve the consistency of postoperative RAI use among different centers.

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Conflicts of interest

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- ■ of special interest
- ■■ of outstanding interest

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