Long-Term Outcomes Following Low-Dose Radioiodide Ablation for Differentiated Thyroid Cancer

Liam Welsh, Ceri Powell, Brenda Pratt, Kevin Harrington, Chris Nutting, Clive Harmer, and Kate Newbold

Thyroid Unit, The Royal Marsden Hospital, Sutton, Surrey SM2 5PT, United Kingdom

Context: Randomized trials show that low-dose (1.1 GBq [30 mCi]) radioiodide (RAI) has efficacy equivalent to high-dose RAI (3.7 GBq [100 mCi]) in thyroid remnant ablation (TRA) for differentiated thyroid cancer. Long-term follow-up is required to ensure detection of late recurrences and to confirm equivalence in terms of survival end points. However, median follow-up duration within randomized trials is currently limited.

Patients and Setting: We studied 53 patients undergoing TRA for differentiated thyroid cancer with long-term follow-up in the Thyroid Unit of The Royal Marsden Hospital (Sutton, United Kingdom).

Intervention: Patients were treated with TRA using low-dose (1.1 GBq) RAI.

Main Outcome Measures: Disease-free survival, overall survival, and the incidence of second malignancies were measured. Multivariable analysis was used to determine clinical risk factors for failure to achieve TRA after low-dose RAI.

Results: Median follow-up was 24 (range, 4–34) years. Low-dose RAI TRA was successful in 26 (49%) patients (successful ablation [SA] group), whereas 27 (51%) patients required further treatment (unsuccessful ablation [UA] group). Thirty-year disease-free survival was 92% in the SA group vs 87% in the UA group ($P = .601$). Thirty-year overall survival was 81% in the SA group vs 62% in the UA group ($P = .154$). Nine (17%) patients developed second malignancies (4 in the SA group and 5 in the UA group). Predictors of failure to achieve TRA with low-dose RAI were male sex and stage pT4 disease.

Conclusions: There is no evidence from long-term follow-up of our cohort that treatment outcomes are compromised for patients that fail TRA with low-dose RAI and subsequently receive high-dose RAI. **(*J Clin Endocrinol Metab* 98: 1819–1825, 2013)**

Differentiated thyroid cancer (DTC) is increasing in incidence worldwide (1). Surgery followed by thyroid remnant ablation (TRA) using radioiodide (RAI) 131-I is currently the standard treatment. Long-term survival after treatment is the norm, and multiple published series have found 10-year survival rates of between 90 and 95% (2).

Evidence for a survival benefit from TRA with RAI for DTC has come from nonrandomized, long-term retrospective cohort studies (3–7). Although the results of individual studies of RAI TRA have been inconsistent, one meta-analysis has shown a statistically significant benefit for RAI TRA on locoregional recurrence and distant metastases 10 years after treatment (8), although subsequent updated meta-analyses have not found clear evidence for benefit of RAI TRA in low-risk patients (2, 9).

There has been long-standing uncertainty regarding the dose (administered activity) of RAI required for TRA. This

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Abbreviations: CI, confidence interval; DFS, disease-free survival; DTC, differentiated thyroid cancer; EBRT, external-beam radiotherapy; OS, overall survival; RAI, radioiodide; SA, successful ablation; Tg, thyroglobulin; TRA, thyroid remnant ablation; UA, unsuccessful ablation.

question was addressed by two recent randomized trials (10, 11). The HiLo trial randomized 438 patients with DTC to TRA with low-dose RAI (1.1 GBq [30 mCi]) or high-dose RAI (3.7 GBq [100 mCi]). HiLo included patients with up to stage pT3 and N1 disease but excluded patients with distant metastases. There was no significant difference in the RAI TRA success rates for the low- and high-dose RAI groups, which were 85.0 and 88.9%, respectively, indicating noninferiority for the low-dose RAI group (10). Similar results were obtained from the ESTIMABL trial, which randomized 752 patients with DTC between the same RAI dose levels as HiLo. Importantly, ESTIMABL was limited to low-risk patients, excluding patients with pT3 and including N1 disease only for patients with pT1 tumors (11).

Most DTC recurrences occur within the first 5 years after treatment, but they can still occur years or even decades later, particularly in patients with papillary DTC (12, 13). The results of low-dose RAI TRA in HiLo and ESTIMABL are encouraging, but their follow-up data are not mature, with the median follow-up in HiLo being only 13 months at the time of reporting (10). Reassuring data regarding outcomes after low-dose RAI TRA for periods up to 10 years after treatment are available from 2 smaller randomized trials and a large prospective cohort study (12, 14, 15), but there remains concern regarding the possibility of an excess of late recurrences and mortality in patients receiving low-dose RAI TRA. To provide further information on long-term outcomes after low-dose RAI TRA, we report a cohort of patients with DTC treated with 1.1 GBq RAI TRA at a single institution for whom follow-up data over a median interval of 24 years are available.

Patients and Methods

Study design

This is a cohort study of patients identified from records within the prospectively maintained Thyroid Unit database of The Royal Marsden Hospital National Health Service Foundation Trust, United Kingdom (RMH). Approval for this study was obtained from the RMH Committee for Clinical Research. All patients aged > 16 years with DTC (papillary and follicular) treated with total or completion thyroidectomy followed by TRA with low-dose RAI (1.1GBq [30 mCi]) were identified from the database. Patients with Hürthle cell carcinoma, anaplastic thyroid carcinoma, and thyroid lymphoma were excluded. Patients with disease stages [TNM 5th ed] pT1-T4, N0–1, M0 were included if they were considered disease-free after total thyroidectomy and cervical lymph node dissection, when necessary. Although patients with pT4 disease were included in this study, those with extensive extrathyroidal extension, eg, invasion of sc soft tissue, larynx, trachea, esophagus, or recurrent laryngeal nerve were excluded. We identified 63 patients within our database as having undergone TRA with low-dose RAI (1.1 GBq) between 1977 and 1984, and of these, 53 met the inclusion criteria. The 63 patients that form this study cohort represent all the patients undergoing TRA with RAI at RMH in a period during which it was standard practice within the RMH Thyroid Unit to use low-dose RAI, and there was no specific selection policy for low-dose RAI in operation at that time. The 10 exclusions consisted of 1 patient treated for recurrent disease, 3 patients with metastatic disease, 3 patients treated with external-beam radiotherapy (EBRT) immediately after low-dose RAI, and 3 patients whose database records were incomplete.

Treatment

All patients received initial definitive treatment with thyroidectomy followed by low-dose RAI (1.1 GBq) TRA. The median interval between surgery and RAI ablation was 54 (range, 5–631) days. All patients underwent RAI after thyroid hormone withdrawal and were instructed to follow a low-iodide diet for 2 weeks before treatment. Patients were required to have TSH levels > 30 mU/L at the time of RAI administration. Postoperative and preablation serum thyroglobulin (Tg) levels were routinely measured, but these data were available within the Thyroid Unit database for only a minority of patients within this study and, therefore, could not be incorporated into the data analysis.

Response assessment

The success of low-dose RAI TRA was determined after 3 to 6 months by diagnostic RAI scintigraphy (200 MBq [5 mCi]) and measurement of serum Tg. Patients were prepared for post-treatment assessment in an identical fashion to TRA with a low-iodide diet and discontinuation of hormone replacement. Quantitative assessment of RAI uptake was not used to define the success of TRA. Successful TRA was defined by the absence of significant RAI uptake in the neck compared with background activity and an undetectable serum Tg (under TSH stimulation in patients treated since 1980). In the presence of anti-Tg antibodies, serum Tg was considered invalid, and a negative diagnostic RAI uptake scan alone was taken as proof of successful TRA. Failure to achieve TRA with low-dose RAI resulted in subsequent treatment with high-dose RAI (5.5 GBq [150 mCi]) at 6-month intervals until TRA was achieved.

Follow-up

Evidence of the presence of tumor 6 months or more after successful TRA was considered as disease recurrence and was defined as 1 or more of the following: detectable serum Tg level, abnormal clinical findings, or abnormal RAI scintigraphy. All recurrences were confirmed either by fine-needle aspiration cytology or by surgical pathology. Further surgery was considered for patients with resectable disease; otherwise, RAI therapy with 5.5 GBq was administered at 6-month intervals provided that the disease remained iodide avid.

Statistical analysis

Patients were divided into 2 groups according to whether or not they achieved successful TRA with low-dose RAI. Disease-free survival (DFS) and overall survival (OS) were calculated dating from the time of DTC diagnosis. Disease recurrence or death ended the DFS period. Survival curves were calculated using the Kaplan-Meier method. The log-rank test was used to compare DFS and OS between patients achieving and failing to achieve successful TRA after low-dose RAI. Predictors of successful

low-dose RAI TRA were analyzed using Pearson's χ^2 test and Fisher's exact test. Individual factors found to predict successful low-dose RAI TRA were subject to stepwise logistic regression analysis, and odds ratios and their 95% confidence intervals (CIs) are presented. The threshold for statistical significance was $P = .05$; all P values are 2-sided and are uncorrected for multiple testing. Data analysis was performed using IBM SPSS version 19.0.0 (IBM SPSS Statistics for Windows, Armonk, New York) (16), R version 2.15.1 (17), and KMWin version 1.52 (18).

Results

Patient characteristics are shown in Table 1. The median follow-up interval was 24 (range, 4–34) years.

Table 1. Baseline Patient Characteristics

	All	SA	UA
n	53	26	27
Age at diagnosis, y			
Median	42	38	53
Range	17–75	21–64	17–75
Age > 45 y at diagnosis	25 (47.2)	7 (26.9)	18 (66.7)
Sex			
Male	10 (18.9)	1 (3.8)	9 (33.3)
Female	43 (81.1)	25 (96.2)	18 (66.7)
Histology			
Papillary	38 (71.1)	17 (65.4)	21 (77.8)
Follicular	15 (28.3)	9 (34.6)	6 (22.2)
Grade			
1	28 (52.8)	16 (61.5)	12 (44.4)
2	19 (35.8)	9 (34.6)	10 (37.0)
3	4 (7.5)	1 (3.8)	3 (11.1)
Multifocal			
Yes	12 (22.6)	6 (23.1)	6 (22.2)
No	41 (77.4)	20 (76.9)	21 (77.8)
T stage			
pT1	8 (15.1)	4 (15.4)	4 (14.8)
pT2	20 (37.7)	15 (57.7)	5 (18.5)
pT3	6 (11.3)	3 (11.5)	3 (11.1)
pT4	19 (35.8)	4 (15.4)	15 (55.6)
N stage			
N0 or NX	38 (71.7)	22 (84.6)	16 (59.3)
N1a	14 (26.4)	4 (15.4)	10 (37.0)
N1b	1 (1.9)	0 (0)	1 (3.7)
Thyroid surgery			
Subtotal thyroidectomy	8 (15.1)	4 (15.4)	4 (14.8)
Near-total thyroidectomy	13 (24.5)	6 (23.1)	7 (25.9)
Total thyroidectomy	10 (18.9)	4 (15.4)	6 (22.2)
Completion thyroidectomy	22 (41.5)	12 (46.2)	10 (37.0)
Time from surgery to ablation, d			
Median	54	66	47
Range	5–631	5–631	6–406

Abbreviations: SA, successful TRA with low-dose RAI; UA, unsuccessful TRA with low-dose RAI. Data are expressed as number (percentage), unless otherwise specified.

Ablation success rate

Of the 53 patients in the cohort, low-dose RAI TRA was successful in 26 (49%) patients (successful ablation [SA] group), whereas the other 27 (51%) patients required further RAI treatment to achieve successful TRA (unsuccessful ablation [UA] group).

Survival

There was no significant difference in the DFS between the SA and UA groups (log-rank test, $P = .601$; Figure 1A), and median DFS was not reached in either group. Group SA had DFS values of 92 and 92% at 10 and 30 years, respectively. Group UA had DFS values of 87 and 87% at

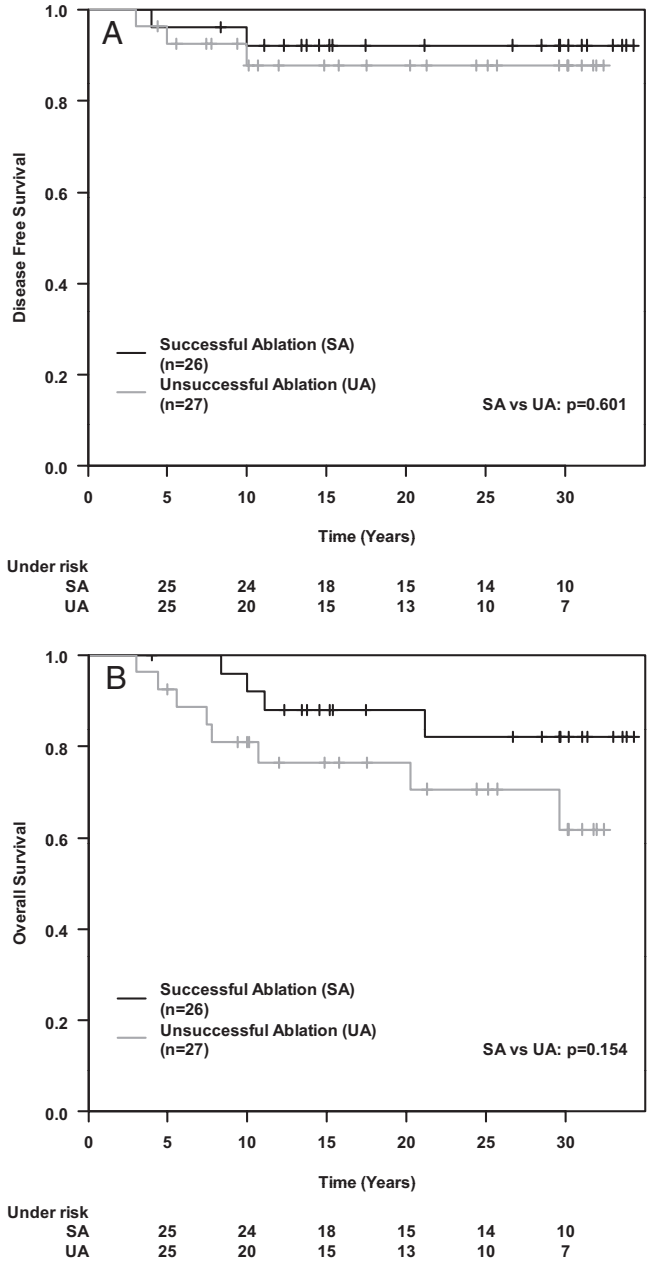

Figure 1. Comparison of DFS (A) and OS (B) between the SA and UA groups.

10 and 30 years, respectively. There was no significant difference in the OS of the SA and UA groups (log-rank test, $P = .154$; Figure 1B), and the median OS was not reached in either group. The OS values of the SA group were 87 and 81% at 10 and 30 years, respectively. For the UA group, the OS values were 77 and 62% at 10 and 30 years, respectively.

Within group SA, 2 of 26 (8%) patients developed recurrent disease, 1 with locoregional failure after 4 years, and 1 with both locoregional and distant failure (lung metastases) after 10 years. Both patients were treated with further RAI therapy, and 1 (with locoregional only relapse) remains alive and disease-free, whereas the other patient (with locoregional and distant relapse) died from stroke 20 years after completing initial treatment and 10 years after completing salvage treatment. Four deaths occurred in group SA during the follow-up period, including the patient with recurrence that died from stroke, but none of these deaths was considered to be attributable to thyroid cancer. One of these patients died from metastatic breast cancer, and the cause of death was unknown in the remaining 2 cases.

The 27 patients in group UA received further treatment with RAI 5.5 GBq (and in 1 case, 3.7 GBq). Ten of these patients required more than 1 RAI therapy dose to achieve successful TRA. Two patients also received EBRT to the neck and thyroid bed as part of ablative therapy. Another 2 patients required neck dissection for cervical lymph node involvement identified during RAI treatment.

A total of 3 (11%) patients in group UA developed recurrent disease. One patient developed locally recurrent disease in the neck 1 year after treatment. This was successfully salvaged by surgery and EBRT. One patient relapsed with lung metastases alone, 4 years after completing initial treatment, and received further RAI therapy. One patient relapsed with both locoregional and distant disease (lung metastases) after 9 years and was treated with neck dissection and further RAI therapy. Eight deaths occurred during follow-up within group UA. None of these deaths was considered to be attributable to thyroid cancer. Three patients died from stroke. Bladder cancer, lung cancer, subglottic anaplastic carcinoma, and pneumonia each accounted for a single death. One patient died from unknown causes.

Second malignancies

Four patients within group SA developed second malignancies during follow-up. Three patients developed breast cancer at 2, 23, and 26 years after their diagnosis of DTC. Of these 3 patients, 1 died from unknown causes, while the other 2 remain alive and well. One patient developed leukemia 7 years after low-dose RAI ablation and was subsequently lost to follow-up. Within the SA group, there was also 1 death from metastatic breast cancer, the diagnosis of which predated the diagnosis of DTC.

Five patients in group UA developed second malignancies: 2 patients developed breast cancer after follow-up intervals of 9 and 25 years, and both remain alive and disease-free; 1 patient developed a subglottic anaplastic carcinoma and died from this disease (a poorly differentiated tumor thought to represent a squamous cell carcinoma because it was Tg negative and histologically distinct from the previous papillary DTC); 1 patient died from bladder cancer; and 1 patient died from lung cancer.

For patients that developed a second malignancy, the median time from diagnosis of DTC to diagnosis of second malignancy was 26 years in group SA and 20 years in group UA. Kaplan-Meier analysis of time to diagnosis of second malignancy found no evidence of a significant difference between the SA and UA groups (long-rank test, $P = .525$).

Factors influencing ablation success

Women (25 of 43 [58.1%]) were significantly more likely than men (1 of 10 [10.0%]) to achieve successful TRA after low-dose RAI (Cramer's V = 0.377; $P = .006$). There was a significant difference in the mean age of patients achieving (39.0 ± 11.3 y) and not achieving (49.9 ± 16.8 y) successful TRA (mean difference, 10.9 y; 95% CI, 3.1–18.9; t [46] = 2.796; $P = .008$). There was no significant association between success or failure of low-dose RAI TRA and any of the following factors: tumor histology (Fisher's exact test, $P = .372$), tumor grade (χ^2 [1, n = 51] = 1.605; $P = .448$), or the presence of multifocal tumor (Fisher's exact test, $P = 1.000$). Higher T stages showed a moderately strong and significant association with failure of low-dose RAI TRA (χ^2 [1, n = 53] = 11.354; $P = .010$; $\gamma = 0.502$, $P = .007$). The presence of lymph node metastases also showed an association with failure of low-dose RAI TRA but with borderline significance (χ^2 [1, n = 53] = 4.197; $P = .041$; Fisher's exact test, $P = .066$; $\gamma = 0.582$, $P = .032$).

Consistent with these findings, univariable binary logistic regression analysis identified the following factors as significant predictors of failure to achieve TRA with low-dose RAI: age > 45 years, male sex, stage pT4, and the presence of lymph node metastases (Table 2). However, on stepwise multivariable binary logistic regression, only male sex and the presence of stage pT4 retained statistical significance as predictors of failure to achieve TRA (Table 2).

Discussion

The purpose of our study is to provide data on long-term outcomes for patients treated with low-dose (1.1 GBq)

Table 2. Univariate and Multivariate Logistic Regression Analyses for Predictors of Success of Low-Dose RAI TRA

	Odds Ratio (Ablation Failure)	95% CI	*P* Value
Univariable analysis			
Age at diagnosis (>45 y vs < 45 y)	5.43	1.67–17.66	.005[a]
Sex (male vs female)	12.50	1.45–107.63	.021[a]
Histology (papillary vs follicular)	1.85	0.55–6.24	.320
Grade (2 or 3 vs 1)	1.73	0.57–5.28	.333
Multifocal (present vs absent)	0.95	0.26–3.45	.941
T stage (pT4 vs pT1–3)	6.88	1.86–25.43	.004[a]
N stage (Npos vs Nneg)	3.78	1.02–14.06	.047[a]
Multivariable analysis			
Sex (male vs female)	12.99	1.38–122.36	.025[a]
T stage (pT4 vs pT1–3)	7.07	1.77–28.34	.006[a]
N stage (Npos vs Nneg)			.054
Age (>45 y vs <45 y)			.294

[a] Statistically significant at $P < .05$.

RAI TRA. The HiLo and ESTIMABL trials confirmed low-dose RAI plus thyrotropin alfa as an effective and convenient treatment with reduced radiation exposure and equivalent TRA success to high-dose RAI. Following the results of these pivotal trials, low-dose RAI TRA is now the standard-of-care for patients meeting the HiLo and ESTIMABL inclusion criteria. The results of HiLo and ESTIMABL relate to TRA success and do not currently address future recurrences or survival end points (10, 11). Our long-term follow-up data show no significant difference in either DFS or OS for patients achieving TRA with low-dose RAI and those requiring higher doses of RAI for TRA after unsuccessful TRA with low-dose RAI. In addition, there were no deaths from DTC in our study. The patients in our study were treated before the availability of thyrotropin alfa, and therefore our data provide insight into long-term outcomes only for patients undergoing low-dose RAI TRA after thyroid hormone withdrawal.

The pattern of relapses seen in our study demonstrates the need for long-term follow-up of patients with DTC. After successful TRA with low-dose RAI (group SA), the DFS at 30 years was 92%. Of 2 relapses that occurred after low-dose RAI (group SA), one occurred at 4 years and the other at 10 years. These results show that the risk of subsequent disease recurrence is low after successful low-dose RAI TRA, and we found no evidence of an increased recurrence rate over the long-term for such patients. Importantly, we found no evidence that treatment outcomes are compromised for patients that fail to achieve TRA with low-dose RAI and subsequently receive high-dose RAI.

Within the HiLo trial, median follow-up was 13 months at the time of reporting, during which time a total of 6 recurrences were found (3 each in the low- and high-dose RAI groups) (10). ESTIMABL has so far not reported data on recurrences (11). Our data are consistent with results from other studies with intermediate durations of follow-up (12, 14, 15). Two smaller randomized trials of low-dose RAI provide longer term follow-up data than currently available from HiLo. Mäenpää et al. (15) reported a trial in 160 patients with DTC randomized to TRA with either low-dose (1.1 GBq) or high-dose (3.7 GBq) RAI. Eighty-one patients were allocated to low-dose RAI, TRA was successful in 42 (52%) of these cases, and the median duration of follow-up was 51 (range, 18–77) months. There was no significant difference in DFS between patients treated with low-dose (68 of 81 [84%]) and high-dose (65 of 79 [82%]) RAI. Kukulska et al (14) randomized 309 patients with DTC to TRA using 1 of 3 RAI doses of 1.1 (n = 86), 2.2 (n = 128), or 3.7 GBq (n = 95). Median follow-up after RAI was 10 (range, 2–11) years for patients treated with 1.1 GBq. After successful TRA, there was no significant difference in rates of local relapse between RAI dose groups, which occurred in 2 (2.4%), 4 (3%), and 3 (3%) patients treated with RAI doses of 1.1, 2.2, and 3.7 GBq, respectively. In a prospective cohort study of 715 patients undergoing RAI TRA, 35 patients received low-dose RAI (1.11–1.85 GBq), and after a median follow-up of 6.2 (range, 0.75–9.6) years, there were 32 recurrences (12). All recurrences occurred in the high-dose RAI group. The low recurrence rate observed in the SA group of our cohort is in keeping with the results of these previous prospective studies, and because our cohort has significantly longer follow-up, our data provide substantial additional reassurance with regard to the risk of late relapse after low-dose RAI TRA.

The rate of successful low-dose RAI TRA in our cohort was only 49%, in contrast to success rates of 85 and 89% in the low-dose RAI arms of HiLo and ESTIMABL, respectively (10, 11), but in keeping with the success rate of 52% in the low-dose RAI arm of the Mäenpää et al (15) trial. The most likely cause for this difference is a systematic difference in the amount of residual thyroid tissue

present in our cohort and in patients within HiLo and ESTIMABL. The success of RAI ablation is known to depend on thyroid remnant size (19). Preablation scanning in HiLo showed that only 2.3% of patients had a large thyroid remnant (10). No preablation measurements of thyroid remnant size were made for patients in our study. Preablation Tg levels were routinely measured for our patients, but these data were available for too few of the patients to enable meaningful analysis. The HiLo and ESTIMABL trials excluded patients with pT4 disease, whereas patients with pT4 disease comprised 36% (n = 19) of our study cohort. Another contributory factor to the difference in low-dose RAI TRA success rates may be that patients in both our study and the Mäenpää et al (15) trial, underwent post-TRA assessment at earlier time points (3–6 and 4–8 mo, respectively) than patients in HiLo and ESTIMABL (6–9 and 6–10 mo, respectively) (10, 11).

Logistic regression analysis of our data identified male sex and pT4 disease as significant risk factors for failure to achieve successful TRA with low-dose RAI (Table 2). Both of these factors are already well-established risks for DTC recurrence (20). Logistic-regression analysis of the results of the HiLo trial showed no significant difference in TRA success rates between the low-dose and high-dose RAI arms of the trial on the basis of tumor or lymph node stage. There were too few disease recurrences within group SA (n = 2 [8%]) to enable analysis of risk factors for recurrence after RAI within this group.

An important part of the rationale for adopting low-dose RAI TRA is to minimize the radiation dose to patients because RAI for DTC is associated with an excess risk of second malignancies (21, 22). Due to the tissue expression of the sodium iodide symporter and the routes of RAI uptake and excretion, an increased risk for salivary gland, breast, bladder, and gastrointestinal cancers after RAI treatment is plausible (23, 24). The risk of acute myeloid leukemia is also increased after RAI (25). In our cohort, 9 of 53 patients (17%) developed second malignancies. This seemingly high rate is predominantly due to the prolonged duration follow-up of our cohort, and some of these malignancies will probably be sporadic. The crude incidence of breast cancer for women in our cohort over the total duration of follow-up is 5 of 43 (11.6%), which is close to what would be expected from the lifetime risk of developing breast cancer for women in the United Kingdom of 12.5% (CR-UK 2008 data) (16). We cannot determine whether RAI therapy had an etiological role in any of these malignancies, although 8 of 9 cases were of cancers with a plausible link to RAI treatment. However, 1 of 5 cases of breast cancer, and the single case of lung cancer, occurred too soon after treatment to be attributable to RAI. All the other secondary malignancies occurred 7 or more years after the diagnosis of DTC. Patients in the UA group received significantly higher radiation doses than those in the SA group, having had 1 or more doses of RAI at 5.5 GBq (mean, 1.89 additional RAI doses; range, 1–9) after their initial TRA with RAI 1.1 GBq, but there was no significant difference in the second malignancy-free survival between the SA and UA groups.

There are clear limitations to our study. Given the long duration of follow-up, most of the patients have now been discharged from, or lost to, ongoing follow-up. Nevertheless, most patients within both the SA and UA groups were still under active follow-up after a period of 15 years, and after 25 years, 14 (54%) of the SA group and 10 (40%) of the UA group remained under follow-up (Figure 1). The number of patients within our cohort is limited and, therefore, despite the prolonged follow-up of our cohort, this intrinsically limits the potential for disease recurrence within the cohort and our ability to detect a difference between treatment groups. Small cohort size could also result in bias due to a skewed distribution of known risk factors for DTC recurrence. However, our cohort consists predominantly of higher-risk patients (Table 1), including 19 [35%] patients with pT4 disease. The high DFS over prolonged follow-up after low-dose RAI TRA in our cohort is, therefore, reassuring and unlikely to be due to selection bias.

There is now level 1 evidence for the efficacy of low-dose RAI TRA for patients with DTC in terms of TRA success rates (10, 11). The long-term follow-up data from our cohort of patients treated with low-dose RAI TRA are indicative rather than definitive but nevertheless provide evidence that the efficacy of low-dose RAI is very likely to be maintained over time in the HiLo and ESTIMABL trials. Our data lend further support to the routine use of low-dose RAI for TRA in patients with DTC.

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Address all correspondence and requests for reprints to: Dr Kate Newbold, MBChB, MD, MRCP, FRCR, Royal Marsden Hospital, Thyroid Unit, Downs Road, Sutton, Surrey SM2 5PT, United Kingdom. Email: Kate.Newbold@rmh.nhs.uk.

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