

TRIAL SUMMARY

BACKGROUND

Total thyroidectomy followed by Radioactive Iodine Ablation (RAIAB) is the standard treatment for patients presenting with intermediate or high risk well differentiated thyroid cancer. Radioiodine is mainly used to ablate any residual normal thyroid tissue. In a sub-group of patients characterised as having low risk of recurrence there is debate as to whether RAIAB represents over-treatment. Radioactive iodine (RAI) causes many side effects including increased risk of a second primary cancer.

IoN (Iodine or Not) aims to answer the question of whether RAIAB or NO-RAIAB have similar local recurrence and survival rates in low risk patients who already have been offered the other two important modalities of treatment i.e. Total Thyroidectomy and also optimal TSH suppression. As some patients in the No Ablation arm might feel they are being offered less treatment (therefore less chance of cure) than the patients in the Ablation arm an feasibility trial has been proposed which will move to phase III following satisfactory recruitment.

AIMS

Feasibility– recruitment target is 10 patients per month for a year from at least 10 centres

Phase III– 5 year recurrence free survival rates in the No Ablation arm is non-inferior to the RAI Ablation arm

METHODS

Low risk patients (T1-3, N1a, M0) that have had a total thyroidectomy (ipsilateral level 6 dissection recommended) and meet the inclusion/ exclusion criteria will be randomised to either RAIAB arm or the NO-RAIAB arm.

At 4-8 weeks in both arms the thyroid will be stimulated using rhTSH (Thyrogen) and a RAI scan (^{131}I , 40-110 MBq) will be performed to identify remnant thyroid tissue. A blood sample will also be taken to assess TG levels.

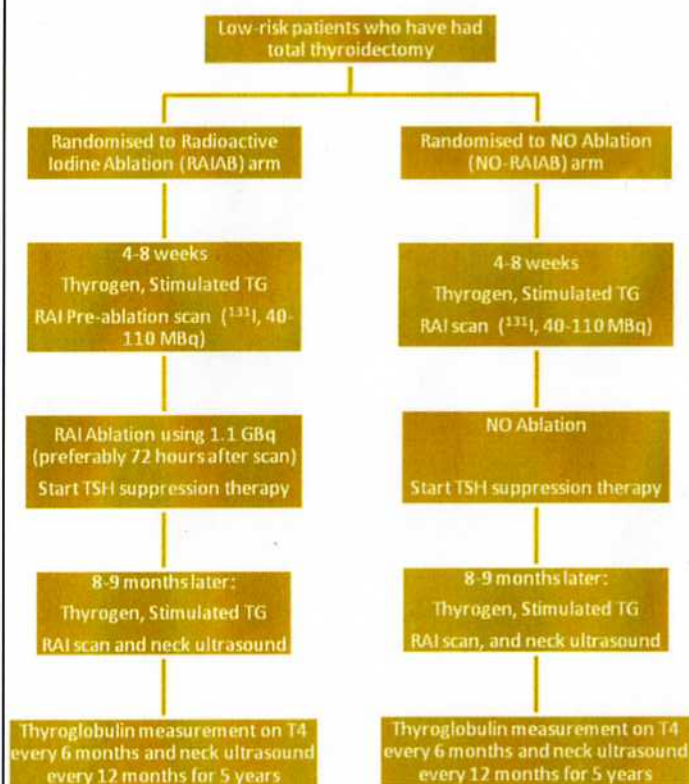
In the RAIAB arm, Ablation will be carried out using ^{131}I at a dose of 1.1 GBq. Patients on both arms will then receive T4 as Thyroid Stimulating Hormone (TSH) suppression therapy.

At 8– 9 months patients will have Thyrogen stimulated TG assessment and a RAI scan and also a neck ultrasound to assess recurrence.

TG levels will be measured every 6 months and a further ultrasound every 12 months for 5 years.

Wider consultation with BAETS and BAHNO surgeons is ongoing to decide whether level 6 dissection should be mandatory or recommended. Also consultation regarding details of inclusion criteria, quality of ultrasound scan, patient information sheet, Trans-IoN and international collaboration is ongoing. Central pathology view, BRFA mutation and highly sensitive TG assay (Beckman assay) have been arranged.

TRIAL DESIGN



INCLUSION CRITERIA

- Negative pregnancy test in females of child bearing potential
- Age greater than 16
- WHO performance status 0 - 2 (self caring)
- Histological confirmation of differentiated thyroid carcinoma:
 - Papillary
 - Minimally invasive (capsular only)
 - Follicular cancer
- Low risk patients (based on ATA guidelines)
 - R0 total thyroidectomy (no residual disease present)
 - Non aggressive histological features
 - Patients with tumour stage (TNM 7th edition 2009)
 - T1b, 1-2cm, intrathyroidal
 - T2, 2-4cm, intrathyroidal
 - T3, 1-4 cm, any age, minimal extrathyroidal extension
 - N1a
 - NO, NX
 - Multifocal microcarcinoma

EXCLUSION CRITERIA

- Pregnant women or women who are breastfeeding
- Patients who have a contrast CT scan up to 3 months before ablation
- Previous treatment for thyroid cancer (not including surgery)
- Tumours with significant infiltrative components.
- Incomplete resection
- Local or distant metastases at diagnosis
- Tumour invasion of locoregional tissues or structures
- Anaplastic or medullary carcinoma
- Widely invasive follicular or Hürthle cell cancer
- Follicular or Hürthle cell cancer > 4cm in size
- Aggressive pathological subtypes of papillary or follicular cancer (including T1a) including:
 - Poorly differentiated tumours
 - Tall cell, columnar cell and diffuse sclerosing papillary variants
 - Insular follicular variants
- Patients with tumour stage (TNM 7th edition 2009)
 - N1b
 - M1
- Macroscopic tumour invasion
- Previous malignancies with limited life expectancy likely to interfere with the patient's ability to be able to comply with treatment and/or follow up
- Severe co-morbid condition/s that would prevent ablation including:
 - Unstable angina
 - Recent myocardial infarction or cerebrovascular accident (CVA)
 - Severe labile hypertension
 - Dementia
 - Any patient who cannot comply with radiation protection including:
 - patients with learning difficulties
 - patients with a tracheostomy that require nursing care
 - patients requiring frequent nursing/medical supervision

CONTACT INFORMATION

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