Questions and answers by the participants of the ETA-CRN Session on ATA MTC Guidelines
Lisbon, 05 SEP 2009

START OF SESSION

090905 11.15.19

Q A1
Is this your first time in Lisbon?

1. Yes	47%
2. No	53%

n=113

090905 11.15.51

Q B1
Where do you come from?

1. Europe	81%
2. USA	5%
3. Other	14%

n=130

090905 11.16.23

Q C1
What is your profession?

1. Medical Doctor	83%
2. Basic Scientist	8%
3. Student in clinical medicine	2%
4. Student in basic science	1%
5. Pharmaceutical Company	2%
6. Other	4%

n=138

090905 11.16.52

Q D1
If you are in clinical medicine,
what is your Speciality?

1. Medical Endocrinology	62%
2. Oncology	11%
3. Endocrine/Oncological Surgery	13%
4. Paediatrics	0%
5. Nuclear Medicine	7%
6. Clinical Biochemistry	2%
7. Other	5%

n=129

090905 11.17.21

Q E1
Where are you primarily working?

1. University Hospital	72%
2. Regional Hospital	13%
3. Smaller Hospital	2%
4. Private praxis	6%
5. Basic University	1%
6. Pharmaceutical Company	2%
7. Other	4%

n=134

090905 11.18.59

Q 1
The ATA Guideline R52 defers the recommended approach to thyroid nodules, including fine needle aspiration biopsy and serum Ct testing, to the ATA Guideline that addresses thyroid nodules. The European consensus – endorsed by ETA - for management of patients with DTC of the follicular epithelium recommends Ct testing in nodular disease.

What is your opinion?

1. I accept the ATA guideline in its full extent	21%
2. I agree with the European consensus on Ct estimation in all patients with thyroid nodules, and perform it.	45%
3. I agree with the European consensus on Ct estimation in all patients with thyroid nodules, but I am unable to perform it in all patients for financial reasons	15%
4. Obligatory Ct estimation needs better evaluation of its cost-effectiveness	19%

n=120

090905 11.31.46

Q 2
The reference range of basal Ct has a very high inter-laboratory variability and also a gender difference.
Yet, the ATA guidelines refer to fixed cut-off levels.

Do you agree on this practice?

1. Yes. I prefer to have one reference range, with normal values ≤ 10ng/L	43%
2. No. Each laboratory should perform its own specific reference range and ROC curves for cut-off limits	47%
3. I have no opinion on this matter	10%

n=104

090905 11.32.51

Q 3
The ATA guideline R52 defines a basal or stimulated* serum Ct level > 100 ng/L, as suspicious for MTC.

What is you opinion on this?

1. I accept the ATA guideline in its full extent	27%
2. I agree that basal Ct >100 ng/L means a substantial risk of MCT. A pentagastrin stimulated cut-off at 100ng/L should be recommended for the grey zone 10-100ng/L	49%
3. I agree with 2 but prefer to set the cut-off for stimulated Ct at 50 ng/L	13%
4. I agree with 2 but prefer to set the cut-off for stimulated Ct at 200 ng/L or even greater	4%
5. I have no opinion on this matter	7%

n=114

090905 11.50.49

Q 4
Preoperative chest CT, neck CT, and 3 phase contrast enhanced multidetector liver CT or contrast enhanced MRI is recommended for all patients with suspected MTC when local lymph node metastases are detected (N1), or the serum Ct is > 400 pg/ml.

What is you opinion on this?

1. I agree with the ATA guideline	62%
2. Above preoperative imaging is only indicated when serum Ct is larger than 1000-2000 ng/L.	14%
3. These examinations are obligatory in all cases except in case of prophylactic thyroidectomy	13%
4. I have no opinion on this matter	11%

n=108

090905 11.52.24

Q 5
In ATA R71-71, completion thyroidectomy may be postponed after hemithyroidectomy, if unifocal intrathyroidal sporadic MTC, confined to the thyroid, no C-cell hyperplasia, neg surgical margin, no suspicion of persistent disease on neck US and basal serum Ct below upper reference limit > 2 months after surgery

1. I agree with the ATA guideline	29%
2. Completion thyroidectomy is always indicated after unexpected diagnosis of MTC, and should be completed by at least central LND, even if postop Ct is normal	45%
3. The indication depends on the size of the primary tumour. The conditions listed in 2 is valid only if solitary infracentimetric MTC was found	20%
4. I have no opinion on this matter	5%

n=110

FIRST BREAK

090905 12.28.58

Q A2
Where do you come from?

1. Europe	80%
2. USA	5%
3. Other	15%

n=118

090905 12.29.29

Q B2
What is your profession?

1. Medical Doctor	88%
2. Basic Scientist	4%
3. Student in clinical medicine	0%
4. Student in basic science	0%
5. Pharmaceutical Company	0%
6. Other	4%

n=111

090905 12.30.02

Q C2
If you are in clinical medicine,
what is your Speciality?

1. Medical Endocrinology	53%
2. Oncology	9%
3. Endocrine/Oncological Surgery	16%
4. Paediatrics	2%
5. Nuclear Medicine	13%
6. Clinical Biochemistry	2%
7. Other	5%

n=107

090905 12.30.32

Q D2

Where are you primarily working?

1. University Hospital	72%
2. Regional Hospital	12%
3. Smaller Hospital	2%
4. Private praxis	7%
5. Basic University	1%
6. Pharmaceutical Company	3%
7. Other	3%

n=116

090905 12.31.03

Q E2

Do you treat patients with MTC?

1. Yes, > 50	27%
2. Yes, 10 - 50	29%
3. Yes < 10	26%
4. No, I'm not a clinical doctor	9%
5. No, I'm a clinical doctor but don't treat MTC patients	9%

n=127

090905 12.32.30

Q 6

The ATA R61 states “Patients with known or highly suspected MTC with no evidence of advanced local invasion by the primary tumor, no evidence of cervical lymph node metastases on physical examination and cervical US, and no evidence of distant metastases should undergo total thyroidectomy and prophylactic central compartment (level VI) neck dissection”.

Do you agree on this matter?

1. Yes. Because the absence of any enlarged lymph node by ultrasound does not exclude the presence of lymph node metastases in MTC.	80%
2. No. Prophylactic central lymph node dissection may not be necessary in very small tumours detected by Ct screening	13%
3. I have no opinion on this matter	7%

n=126

090905 12.34.05

Q 7

R62 states that if lymph node metastases are not detected by ultrasound, the elective lateral lymphadenectomy is not necessary. However: “A minority of the Task Force favoured prophylactic lateral neck dissection when lymph node metastases were present in the

adjacent paratracheal central compartment".

What is your opinion on this statement?

1. If no enlarged lateral LN are detected, elective lateral lymph node dissection is not obligatory in MTC, irrespective of the status of central neck lymph node	21%
2. With no enlarged lateral LN, elective lateral LND should be done only when lymph node metastases are present in the adjacent paratracheal central compartment	46%
3. Elective lateral lymph node dissection is always obligatory in MTC	29%
4. I have no opinion on this matter	4%

n=120

090905 12.37.30

Q 7/2
R62 states that if lymph node metastases are not detected by ultra-sound, the elective lateral lymphadenectomy is not necessary. However: "A minority of the Task Force favoured prophylactic lateral neck dissection when lymph node metastases were present in the adjacent paratracheal central compartment".

What is your opinion on this statement?

1. If no enlarged lateral LN are detected, elective lateral lymph node dissection is not obligatory in MTC, irrespective of the status of central neck lymph node	14%
2. With no enlarged lateral LN, elective lateral LND should be done only when lymph node metastases are present in the adjacent paratracheal central compartment	35%
3. Elective lateral lymph node dissection is always obligatory in MTC	16%
4. Lymphnode dissection should be performed if in patient with central LND increased basal or stimulated CT is stated	32%
5. I have no opinion on this matter	3%

n=96

090905 12.48.31

Q 8
The ATA guidelines R73-74 recommend postoperative follow-up based on Ct and CEA estimation.

Do you agree on this statement?

1. Yes	41%

2. No. Only basal Ct should be measured	11%
3. Stimulated Ct is more sensitive than basal Ct level and should be performed annually	14%
4. Pentagastrin test should be performed at first postoperative evaluation if basal Ct is low.	30%
5. I have no opinion on this matter	3%

n=119

090905 12.51.40

Q 9
The ATA R75 guideline proposes a cut-off of <150 ng/L, below which postoperative imaging may be limited to US only.
R76 recommends that post-operative MTC patients with detectable serum Ct levels <150 ng/L may be considered for additional imaging (CT/MRI) to serve as baseline examinations for future comparison even though these studies are usually negative.

Do you agree?

1. I agree with R75. Additional imaging can subsequently be implemented should the serum Ct rise over time.	22%
2. I agree with R75 and R76	65%
3. Postoperative imaging is indicated in every case post surgery to serve as baseline examinations even in patients with undetectable Ct	6%
4. I have no opinion on this matter	7%

n=120

090905 12.52.57

Q 10
R78 states that in the absence of residual anatomically identifiable disease (neck US and CT) in a thyroidectomized patient with a measurable Ct level without previous level VI LND, an empiric central LND dissection may be considered, but may not be successful.

Do you agree?

1. I agree with the ATA guideline	54%
2. Central LND should be performed, due to a high probability of lymph node metastases in this compartment even without visible lymph nodes on US.	38%
3. I have no opinion on this matter	8%

n=114

090905 13.02.17

Q 11
Postoperative adjuvant EBRT to the neck and mediastinum may be considered in patients who are found to have microscopic positive margin(s) (R1 resection) following surgery for moderate to high volume disease involving the central compartment (level VI) and one or both lateral neck compartments (levels 2A-V).

1. I agree with the ATA guideline	53%
2. This recommendation may be accepted only in patients with evidence of incomplete resection (R2 resection)	22%
3. I do not agree, as EBRT will lead to considerable toxicity without any evidence for improved overall survival	16%
4. I do not have an opinion on this matter	9%

n=116

090905 13.03.10

Q 12
The routine use of cytotoxic chemotherapy should be discouraged in patients with MTC. It may be considered for selected patients with rapidly progressive disease not amenable to clinical trials.

Do you agree?

1. Yes.	84%
2. No. Cytotoxic chemotherapy is standard of care in patients with metastatic MTC	7%
3. I do not have an opinion on this matter	9%

n=116

090905 13.05.01

Q 13
R66 states that in patients with extensive distant metastases a palliative neck operation may still be needed when there is pain, or evidence of tracheal compromise and the need to maintain a safe airway. Otherwise, in the setting of moderate to high volume extra-cervical disease, neck disease may be observed and surgery deferred (Task Force opinion was not unanimous).

Do you agree?

1. Yes	72%
2. No	24%
3. I have no opinion on this matter	4%

n=114

090905 13.13.44

Q 14
ATA guidelines do not recommend FDG PET imaging
in primary preoperative evaluation.

Do you agree?

1. Yes.	68%
2. No. FDG PET helps in preoperative staging	4%
3. No. Receptor PET imaging is more useful in primary MCT staging and should be recommended	4%
4. F dopa seems the best one	18%
5. I have no opinion on this matter	6%

n=113

090905 13.14.42

Q 15
Do you agree that FDG PET should be performed
in cases of asymptomatic hypercalcitoninaemia
to localize foci of MTC?

1. Yes	31%
2. No. FDG PET is not sufficiently sensitive for detection of small metastatic MTC foci	20%
3. No. FDG PET should be applied to detect metastatic foci only if Ct>400 ng/L	7%
4. No. Due to both 2 + 3	34%
5. I do not have own opinion in this matter	6%

n=120

090905 13.15.31

Q 16
Do you agree that MIBG therapy and peptide
receptor radiotherapy may be useful in
palliative therapy of advanced MCT

1. Yes.	59%
2. No.	32%
3. I have no opinion on this matter	9%

n=117

090905 13.26.06

Q 17
Do you agree with the ATA guideline statement
that somatostatin analogues are not recommended
as antitumor agents in MTC?

1. Yes	38%
2. MCT associated symptomatic diarrhea or Cushing syndrome may be treated with somatostatin analogues	13%
3. Both 1 and 2 apply	44%
4. I have no own opinion in this matter	3%

n=111

090905 13.27.06

Q 18
Do you agree that residual disease as documented
by any increase of Ct level without localization
of the disease should not constitute an absolute
contraindication to pregnancy?

1. Yes.	66%
2. No. Pregnancy is contraindicated in any case of persistent MTC, with or without positive imaging	15%
3. No. Pregnancy may be considered only if doubling time of Ct is less than 2 years	17%

n=108

SECOND BREAK

090905 14.36.27

A3
Where do you come from?

1. Europe	85%
2. USA	5%
3. Other	10%

n=99

090905 14.36.55

Q B3
What is your profession?

1. Medical Doctor	86%
2. Basic Scientist	10%
3. Student in clinical medicine	1%
4. Student in basic science	1%
5. Pharmaceutical Company	0%

6. Other	2%

n=102

090905 14.37.18

Q C3
If you are in clinical medicine,
what is your Speciality?

1. Medical Endocrinology	55%
2. Oncology	16%
3. Endocrine/Oncological Surgery	19%
4. Paediatrics	2%
5. Nuclear Medicine	4%
6. Clinical Biochemistry	0%
7. Other	3%

n=98

090905 14.37.44

Q D3
Where are you primarily working?

1. University Hospital	79%
2. Regional Hospital	11%
3. Smaller Hospital	1%
4. Private praxis	5%
5. Basic University	0%
6. Pharmaceutical Company	0%
7. Other	4%

n=101

090905 14.38.08

Q E3
Do you treat patients with MTC?

1. Yes, > 50	28%
2. Yes, 10-50	28%
3. Yes, < 10	28%
4. No, I'm not a clinical doctor	12%
5. No, I'm a clinical doctor but don't treat MTC patients	4%

n=104

090905 14.39.00

Q 19
ATA guideline R1 recommends RET testing in patients
with personal medical history of primary C hyperplasia
in whom no diagnosis of MTC has been made because new
carriers of RET germline mutation can be detected in
this way. Do you agree on this procedure?

1. Yes	62%
2. No, because the risk of finding a germline RET mutation carrier is too low	21%
3. No, because this will not be covered by the insurance system	6%
4. I have no opinion on this matter	8%

n=102

090905 14.40.37

Q 20
Guideline R10 recommends to consider (Grade A) RET testing in all patients with Hirschprung disease (HD). Do you agree to test all HD patients in view of HD as a common disease with few RET positive cases?

1. Yes	60%
2. No	6%
3. No,Further research is necessary to disclose the significance of testing for activating mutations in HD	18%
4. I have no opinion on this matter	13%

n=102

090905 14.41.40

Q 21
ATA guideline R11 recommends to perform MEN 2-specific exons of RET (10, 11, 13, 14, 15, 16) as either as single or multi-tiered approach. Do you agree?

1. Yes	35%
2. No, RET mutation screening should be completed by exon 8 analysis in all regions where it was described to be present	23%
3. No. Systematic screening for RET mutations in exon 8, 10, 11, 13, 14, 15 and 16 should be performed in all patients diagnosed with MTC	26%
4. I have no opinion on this matter	16%

n=102

090905 14.43.01

Q 22
If the routine analysis is negative in the clinical setting of MEN 2 or when there is a discrepancy between the genotype and phenotype, do you agree with recommen-

dation R12 to perform sequencing of the entire coding region of RET to identify MTC causative mutations:

1. Yes	46%
2. No. it has a poor cost effectiveness since there are 14 "remaining" exons (1-7, 9, 12, 17, 18, 19, 20, 21) where activating mutations have never been reported	8%
3. No. There is no need to sequence the remaining exons with the exception to look for rare mutations in exon 5 (R321G)	5%
4. 2 + 3	23%
5. I have no opinion on this matter	17%

n=95

090905 14.44.15

Q 23
Conflicting results have been published in recent years about the possible role of RET polymorphisms as genetic modifiers, either in sporadic or hereditary MTC. Do you agree that ETA comments should include that no definite clinical significance can be given to the presence/absence of RET polymorphic variants and no further research seems necessary

1. Yes	43%
2. No. The data are still insufficient to add this statement	47%
3. I have no opinion on this matter	10%

n=92

090905 14.57.15

Q 24
ATA gives in Table 6 a division of RET germline carriers into 4 risk categories (A – lowest, D – highest) which differs from the previous division into 3 risk categories by separation of the high risk RET 634 and (ATA B class) and moderately high risk of other exon 10 mutations (ATA A class). Do you agree on this ATA modification?

1. Yes, it rationalizes the differences in phenotype and is clinically relevant	82%
2. No, I prefer the previous division of risk into three categories	10%
3. Yes, but would prefer a 5 categories division, including the lowest risk RET mutations, which haven't been proven fully (example: RET 649)	8%

n=78

090905 14.59.16

Q 25
ATA guideline R2 recommends RET testing of MEN 2B only in cases of intestinal ganglioneuromatosis, because intestinal ganglioneuromatosis is often diagnosed before the diagnosis of MEN2B. Do you agree on this?

1. Yes	32%
2. No, bumby lips with mucosal neuromas should also be considered as indication	13%
3. No, both bumby lips with mucosal neuromas and corneal fibres should also be considered.	55%

n=77

090905 15.02.02

Q 26
Ad R2 Do you accept inclusion of Tearless crying sign as indication for RET testing in small children without any other MEN2 symptoms and with negative family history?

1. Yes, because it is necessary to diagnose de novo MEN2 cases as soon as possible	34%
2. No, the prevalence of tearless crying is not well defined in normal children and high risk of false	25%
3. No, more data necessary. However, I find this sign worth mentioning in the comments.	41%

n=76

090905 15.03.10

Q 27
The ATA R4 recommends RET testing in cases of lichen planus (Grade B). The proposal is to strengthen this recommendation: Lichen planus amyloidosis or pruritus in the central upper back may indicate the presence of a RET mutation and should prompt Ct measurement in adults and genetic testing in children. Do you accept this proposal?

1. Yes.	62%
2. No, I prefer the more cautious standpoint of ATA Guidelines	16%
3. I propose to mention it in the comments but not change the ATA R4 recommendation.	20%

n=78

090905 15.14.37

Q 28
ATA guidelines (R6-8) recommend to consider ATA risk class and patient's age and allow to "delay prophylactic thyroidectomy beyond age 5 years in patients with ATA Level A and B RET mutations in the setting of a normal annual basal +/- stimulated* serum Ct, normal annual neck US, less aggressive MTC family history and family preference.". "For higher risk mutations consider treatment before age 5 in an experienced tertiary care setting".

1. I accept this statement fully	61%
2. Prophylactic thyroidectomy should be done when stimulated Ct starts to rise	26%
3. Prophylactic thyroidectomy should be done before Ct starts to rise at the age of 3-5 years	8%
4. I have no opinion on this matter	5%

n=80

090905 15.15.40
Q 29
The ATA guidelines state that there is rarely a need for stimulated Ct testing for deciding on prophylactic Tx.

Do you agree?

1. Yes. It is a burden for a young patient, with a risk of not being cured after surgery.	31%
2. Yes, in addition to 1, sensitive Ct assays have to prove their value in these circumstances	25%
3. No. Stimulated Ct helps to define the optimal time point for prophylactic Tx.	37%
4. I have no opinion on this matter	7%

n=84

090905 15.16.24

Q 30
When prophylactic thyroidectomy is delayed beyond the fifth year of life, Ct should be measured:

1. every 6 months	36%
2. every year	52%
3. every year until age of 20, then every 2-3 years	12%

n=90

090905 15.18.19

Q 31
Ad R6-8. Please select the level of Ct which is allowed to delay the prophylactic/preemptive thyroidectomy in ATA class A and ATA class B RET mutation carriers, who have less aggressive family history

1. At normal basal Ct (≤10 ng/L) and normal stimulated Ct (≤ 30 ng/L)	45%
2. At normal basal Ct (≤10 ng/L) and only slightly elevated stimulated Ct (≤50 ng/L)	20%
3. At normal basal Ct (≤10 ng/L) and only moderately elevated stimulated Ct (≤ 100 ng/L)	12%
4. I do not see the role for stimulated calcitonin estimation in this setting, evaluation of normal basal Ct is sufficient	17%
5. I do not have an opinion on this matter	6%

n=84

090905 15.28.16

Q 32
Do you agree to complete ETA comments with the statement: It is also of high importance that high volume surgeons perform pre-emptive thyroidectomies with or without additional lymph node dissection

1. Yes	39%
2. No, children should be operated by pediatric surgeons only	0%
3. It depends on the experience of the given centre, but prophylactic/preemptive Tx should be performed only in experienced tertiary reference centers	57%
4. Don't have an opinion	4%

n=82

090905 15.29.31

Q 33
The ATA R20 recommends preoperative Ct testing in children-RET carriers with the exception of the MEN2B carriers younger than 6 month old.
Do you agree?

1. Yes	59%
2. No. It is unclear why children younger than age 6 months should not have Ct assessment.	15%
3. Reference ranges for small children not well set, thus prophylacticTx should be as early as possible independent of Ct level	24%

n=77

090905 15.40.29

Q 34
R38 and R42 state that in asymptomatic MEN 2A and FMTC patients who present at age >5 years and asymptomatic MEN 2B patients who present at age >1 year, further evaluation prior to surgery, and more extensive surgery, is needed if the basal serum Ct is >40 ng/L, if thyroid nodules are > 5 mm, or if suspicious lymph nodes are identified on neck US. Do you agree?

1. Yes	57%
2. Preoperative basal and stimulated Ct, thyroid sonography are always necessary to decide whether resignation of central LND is possible	25%
3. Cut-offs of basal Ct>40 pg/ml and thyroid nodules of >5mm may be regarded as cut-off between prophylactic and therapeutic Tx but not define extent of surgery	18%

n=65

090905 15.41.53

Q 35
The ATA guidelines recommend screening for hyperparathyroidism (PHPT) in asymptomatic RET mutation carriers by 8th year of age in ATA C (634 and 630) RET mutation carriers and by 20th year of age in other RET mutations associated with MEN2A.
Agree?

1. Yes	67%
2. No, 8 years is very early as there are only a few cases of PHPT before the third decade, 20 years more appropriate if no specific family data	28%
3. I have no opinion on this matter	3%

n=80

090905 15.43.21

Q 36
ATA R49-50 guidelines recommend surgical treatment for PHPT in MEN2A, preferred to medical therapy, in the absence of contraindications such as excessive surgical risk or limited life expectancy. Do you agree?
Your choice is:

1. Yes	52%

2. The optimal surgical management of HPT in MEN2A is not yet defined. Decision for surgery for mild HPT should be assessed per individual patient	42%
3. I have no opinion on this matter	5%

n=80

090905 15.57.33

Q 37
ATA guidelines recommend that screening for PHEO is necessary by 8th year of age in ATA D class (MEN2B) and ATA C (634 and 630) RET mutation carriers.
Do you agree?

1. Yes	32%
2. Age of 8 years seems very early, only few cases of PHEO before 3rd decade, 18 years more appropriate unless specific family data on earlier appearance	11%
3. Always if an operation or pregnancy is planned	11%
4. 2+3	42%
5. I have no opinion on this matter	4%

n=73

090905 15.58.54

Q 38
In MTC diagnosed/suspected preoperatively in which the familial anamnesis is negative if no RET data are available prior to surgery ATA R53 guideline recommends at least one test – biochemical or CT/MRI.
What is your opinion?

1. PHEO biochemical screening is mandatory in any case of suspected MTC.	33%
2. CT/MRI imaging is an alternative to exclude adrenal tumor	16%
3. 1+2 are necessary	47%
4. No additional investigations are necessary if no hypertension present	4%

n=73

090905 16.00.13

Q 39
ATA guidelines recommend that PHEO should be surgically resected after appropriate preoperative preparation and prior to surgery for MTC or PHPT. ATA R54-55 and R60 do not require scintigraphy

to exclude extraadrenal pheo/malignancy. You opinion is

1. Yes I agree with ATA guideline because the risk for extraadrenal pheo is extremely small in MEN2A.	58%
2. No, scintigraphy should be included in the preop assessment of PHEO in MEN2A to exclude rare cases of malignancy/multiple pheos.	35%
3. I have no opinion on this matter	7%

n=74

END OF SESSION