Q. Who in my team can consent patients for genetic testing, and what training is offered?

A. Consenting for genetic testing can be carried out by a Clinical Nurse Specialist or a Consultant Oncologist within your team. Instructions on how to consent can be found on the GM Cancer webpage, here.

Additionally, an E-Learning module will become available on the GM Cancer Academy.

Q. How do I ensure I complete the request form correctly?

A. Please use the referral form titled 'NW GLH Genomic Testing Request Form – Rare Disease' which is available on the GLH website: Test Request Forms - Manchester University NHS Foundation Trust (mft.nhs.uk).

When completing the form, the clinical indication code to be used is **R218.** Please use this code instead of listing genes that are being tested.

The form must then be printed and given to the patient to take to the Endocrinology to have their bloods taken. The form and bloods will then be sent together to:

North West Genomic Laboratory Hub – Manchester Site
Manchester Centre for Genomic Medicine
Sample reception 6th Floor
St Mary's Hospital
Oxford Rd
Manchester
M13 9WL

Q. What about patients that do not want testing but would like to store their blood sample for their family to access in the future?

A. Some patients do not consent to have the genetic test but do choose to have their DNA sample stored to give their blood relatives the option to access this at a later date. In these circumstances, the sample would not be tested within that person's lifetime but could provide information for other family members in the future.

In this situation the consent form does not need to be completed. The referral form must be completed as follows:

- Clinical Details (type of test) – tick DNA Storage.
- Clinical Indication Code/Test Code: R218 DNA storage only.

Further guidance on the North West Genomic Laboratory Hub can be found here: https://mft.nhs.uk/nwglh/

Q. What happens if a patient is found to have a variant of unknown significance?

A. It is recommended that patients with VUS are flagged for a 5-year VUS review, using InfoFlex, or an alternative software tracking tool, through the oncology team's aftercare programme (for example Personalised Stratified Follow Up programme). Once a patient qualifies for VUS review at 5 years, please contact the Genomic Laboratory Hub using this email address: mft.genomics@nhs.net

Q. What should I do if a patient has a negative germline variant test and is not eligible for referral to the clinical genetics team, but I am still concerned about their family history?

A. A regional cancer genomics MDT is held on the first Tuesday of the month at 11:00. Clinicians from around the region can request discussion of complex cases, for example, those with an unusual family history or if a clinician has questions about a test result.

If you wish to discuss a patient in more detail with the team please email: mft.nwglh-mdt@nhs.net

Q. What should I do if a patient has another type of thyroid cancer and is not eligible for germline testing but I am still concerned about their family history?

A. A. A regional cancer genomics MDT is held on the first Tuesday of the month at 11:00. Clinicians from around the region can request discussion of complex cases,

for example, those with an unusual family history or if a clinician has questions about a test result.

If you wish to discuss a patient in more detail with the team please email: mft.nwglh-mdt@nhs.net

Q. For patient who require referral to the clinical genetics team, how long will they have to wait for their appointment?

A. Patients referred through the mainstreaming pathway will be seen within 3 months. If a routine appointment is requested, then the patient will be seen within 12 months, or longer.

Q. Is there any support available to patients who have tested positive for the germline RET mutation and are waiting to be seen by Clinical Genetics?

You may find that some patients are feeling very anxious while they wait to be seen by clinical genetics. In this case, they may contact the CNS within your team for support.

Q. What is the difference between germline and somatic variants?

A. There are two ways in which gene variant increase the risk of an individual developing cancer:

Somatic variants occur in the genes of an individual cell and when that cell divides there is a risk of cancer development. Somatic variants are not present when a child is conceived; they are acquired during the individual's lifetime. Smoking, aging, ultraviolet radiation and viruses are examples of causes of somatic variants. Somatic variants can be important in decision-making for cancer treatment and a patient's prognosis, but they are not hereditary.

Germline variants are far less common than somatic variants. They are inherited and therefore are present from the moment a person is conceived. Germline variants can influence whether, and when, an individual might get cancer, what cancer they might develop and what treatments are appropriate and most likely to be successful.

It is important to remember that a very small number of cancers are caused by germline gene variants. Although many families have multiple family members who have been affected by cancer, most of these cases are caused by the combined effects of multiple genetic and environmental factors, with only about 5-10 % being due to an error in a single high risk cancer gene.

Q. What is Multiple Endocrine Neoplasia type 2 (MEN2A)?

A. The Amend MEN2A booklet says:

'Multiple Endocrine Neoplasia Type 2 (MEN2A) is a condition that can be passed down in families. MEN2A causes more than one gland of the body's endocrine (gland) system to develop growths (tumours). The affected glands may then make greater than normal amounts of hormones, the body's chemical messengers, which in turn cause a range of different symptoms. Each type of tumour may occur alone and separate from MEN.

Multiple = more than one

Endocrine = gland system

Neoplasia = increase in growth of normal cells (tumour).

Q. What are the effects on the patient's family if they are found to have MEN2A?

A. The patients' children will also be eligible for testing for MEN2A by looking at the RET gene. If they are found to also have MEN2A, it means that they are likely to develop medullary thyroid cancer (MTC) before the age of 40, and therefore their thyroid will be removed as a precaution. They will also undergo surveillance of other possible cancers they are at an increased risk of developing in their lifetime (adrenal glands and parathyroid glands).