North Thames
Genomic Medicine Service

Cancer of the Unknown Primary (CUP) Circulating Tumour Genomic Testing

FAQ Document

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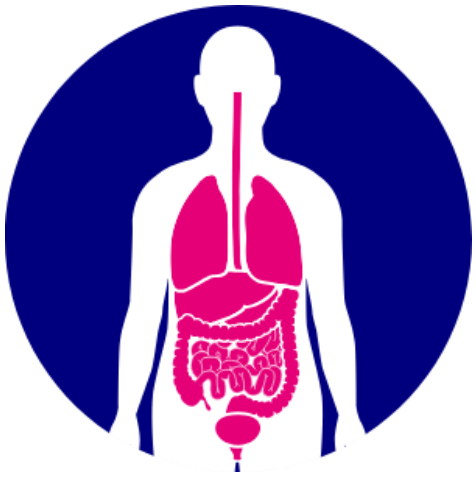

North Thames
Genomic Medicine Service

Purpose

This document covers frequently asked questions for the liquid biopsy genomic CUP testing available to patients in England for regions routing to North Thames Genomic Laboratory Hub.

Whilst this document covers the logistics for the liquid biopsy testing it will refer to the tissue pathways and general eligibility criteria for genomic CUP testing.

GMS Regions covered

- North Thames
- South West
- East

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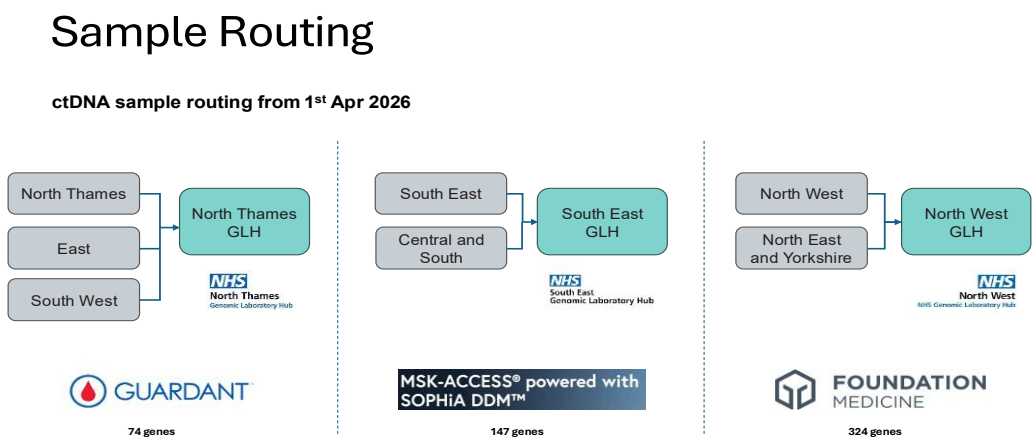
1. Test Routing

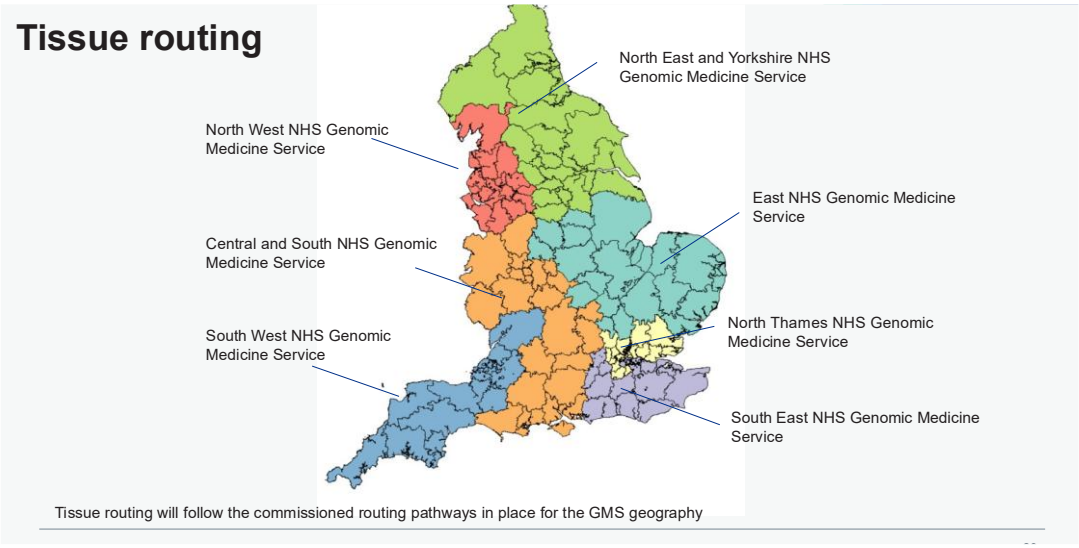
Please note the NT GMS provide liquid biopsy testing for clinicians from the North Thames, East and South West regions. Clinicians should follow their normal tissue sampling and WGS pathways as per their home Genomic Laboratory Hub.

If you are unsure how to access testing, please contact your regional GLH for advice and the relevant referral documents and sampling handling instructions. Contact details are in Section 9.

Below is routing diagram for liquid biopsy testing across England on the National Test Directory and the technology partners with each of the GLH's.



Below is the routing for tissue biopsy testing across England on the National Test Directory.



2. Test Patient Eligibility Criteria

2.1 Liquid Biopsy (ctDNA)

Liquid biopsy (ctDNA) is available for patients that meet the following criteria:

- ECOG Performance status 0-2
- Diagnosis of carcinoma unknown primary origin as per the ESMO / NICE guidelines.
- Not currently on treatment
- Discussion at a local CUP MDT confirming diagnosis

References

- ESMO Clinical Practice Guideline: Cancers of Unknown Primary Site | ESMO
- Overview | Metastatic malignant disease of unknown primary origin in adults: diagnosis and management | Guidance | NICE

Exclusion Criteria

Patients with a malignancy of unknown origin or a non-epithelial/non-neuro-endocrine malignancy of unknown origin are NOT eligible for ctDNA testing.

To note:

ctDNA testing:

- Not currently on treatment (as this affects ctDNA yield)
- Metastatic disease in >1 site
- If ctDNA testing fails, consider tissue testing if sufficient tissue is available

2.2 Tissue Testing

Tissue testing is available for patients that meet the following criteria:

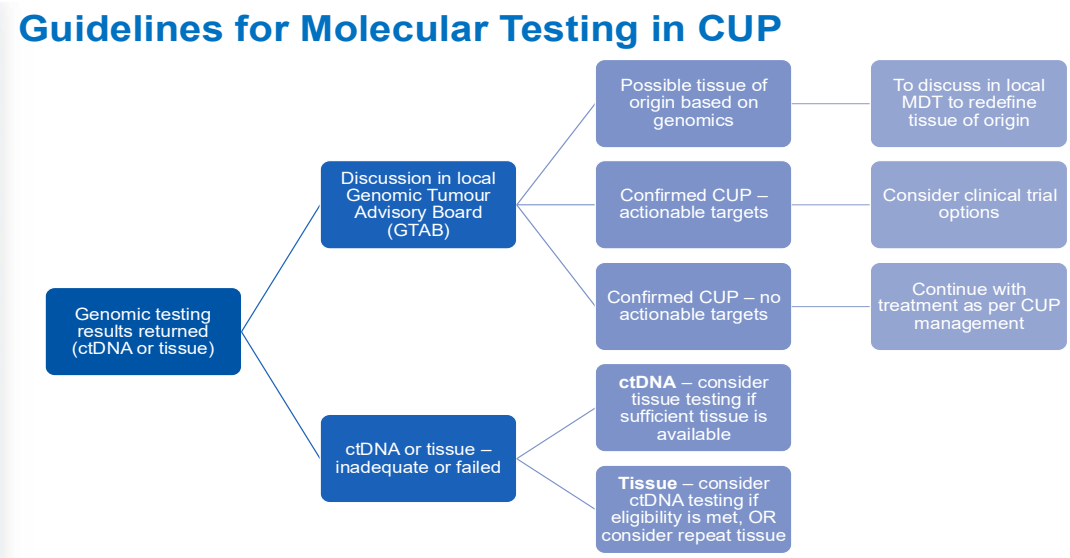
- ECOG Performance status 0-2
- Diagnosis of carcinoma unknown primary origin as per the ESMO / NICE guidelines.
- Discussion at a local CUP MDT confirming diagnosis
- Adequate biopsy material (FFPE) is available for DNA extraction

Exclusion Criteria

Patients with a non-epithelial/non-neuro-endocrine malignancy of unknown origin are NOT eligible for testing.

Tissue FFPE can be considered if:

- Adequate biopsy material (FFPE) is available for DNA extraction
- Only one site of metastatic disease (i.e. isolated lymph node) so low ctDNA yield is likely
- If already on systemic treatment
- Can also be done if ctDNA testing fails and patient meets the eligibility criteria



- If in doubt always discuss at your regional GTAB

2.3 WGS Testing

WGS testing is available for patients that meet the following criteria:

- Adult, paediatric and TYA patients with Cancer of Unknown Primary (CUP) are eligible for WGS
- Adequate fresh tissue is available for DNA extraction
- Not restricted to but permitted where non informative results from ctDNA or tissue and WGS may provide additional actionable information

FAQs

- **Are there any additional clinical criteria beyond that can be considered for testing patients?**

  Within the commissioned service provision there is no further eligibility criteria that can be considered however, we will notify all Trusts if criteria changes.

- **Is written patient consent required for the test?**

  For liquid biopsy and tissue testing, there is no signed consent required from the patient. Informed consent is taken following a verbal explanation of the test.

  For WGS please refer to our website for consenting information: Test request forms and information.

- **When should bloods be taken?**

  Ideally the blood draw should be done at the earliest opportunity, normally this is in the patients outpatient consultation following discussion at the CUP MDT. This ensures the test report is ready for timely treatment decisions and can be discussed at your local Genomic Tumour Advisory Board (GTAB) (see Section 8).

  Blood samples should arrive in the laboratory within 7 days of venepuncture. Blood samples taken on a Friday should be posted on the day, using the Royal Mail pre-paid blood collection kit, to ensure samples arrive in the laboratory Monday/ Tuesday the following week.

3. Ordering and Receiving Liquid Biopsy Blood Collection Kits

RMH laboratories recommend using Alpha Laboratories' Laboratory Suppliers | Alpha Laboratories research use only venous blood transport kit which has: -

- Two specialist Cell-Free DNA blood collection tubes
- Royal Marsden Royal Mail Track24 return to laboratory shipping label
- Fully compliant UN3373, Category B transport packaging (mandatory requirement for the safe and effective transport of the patient samples)

To purchase the correct kits to be able send blood samples to the NT GLH there are two options a Trust can consider: -

1. Please send quote requests to solutions@alphalabs.co.uk and send purchase orders directly to Alpha Labs at sales@alphalabs.co.uk using product code **RM-VBC-KIT.**
2. Alternatively, the kit components can be ordered separately via your local procurement system using the following product codes: -

- cfDNA Blood Collection Tubes - 218997
- UN3373 sample transport box - SHU-01-3-2
- Absorbent bay pouch - AB010-100

4. Blood Collection Protocol

- **Where can we find detailed instructions for blood collection and handling?**

  Please refer to the 'Instructions for Use' document.

- **Who do we contact if there are issues or questions regarding blood collection procedures?**

  Please contact marsden360@rmh.nhs.uk.

- **How should the blood samples be packaged and labelled before shipping?**

  Please refer to the 'Instructions for Use' document.

5. Test Request Form

- **What specific information is required on the test request form?**

  Please refer to the test request form.

- **Are there any mandatory fields that must be completed on the form?**

  All sections on the test request form must be completed for samples to be accepted for testing.

- **Who should we contact if there is missing or unclear information on the form?**

  Please contact marsden360@rmh.nhs.uk.

6. Shipping

- **What are the shipping requirements for the blood samples?**

  Please refer to the 'Instructions for Use' document.

- **How do we track the shipment of the samples?**

  Record locally the Royal Mail Tracking number on the postage label to enable tracking during transit.

- **What should we do if the samples do not arrive at the NT GLH within the specified time frame?**

  The samples should arrive within 48 hours using the pre-paid Royal Mail Track24 service. Please send samples as soon as they are taken. Samples must arrive in the lab latest within 7 days of venepuncture, to ensure the sample integrity meets the requirements for processing.

7. Results and Turnaround Time

- **How will the test results be communicated to us?**

  Results will be sent securely to the emails provided on the test request form via NHS.net or hospital email (.nhs.uk). The form will as for the responsible clinician, regional Genomic Medicine Service (GMS) contact (normally the laboratory) if this is needed and any other additional individual or team email.

- **What is the typical turnaround time for receiving the results?**

  Results usually available within 10 calendar days.

- **Who will receive the results?**
    - Referring lead oncologist
    - The regional GLH hub
    - Any additional names that are provided

- **Where should the results be stored?**

  Results need to be incorporated into Trusts electronic patient record (EPR) alongside other molecular results received by the Genomic Laboratory Hub (GLH) and made available to the clinical and pathology teams.

- **What should we do if there is a delay or we do not receive the results within the expected time frame?**

  Reach out to marsden360@rmh.nhs.uk if you have any concerns.

- **Who should determine if a result is informative or not?**

  It's recommended that all results are either reviewed by your local Genomics Tumour Advisory Board or by a CUP Oncologist colleague experienced in the interpretation of ctDNA results. This will help inform the answers to whether the result is informative and the level of confidence.

8. Genomic Tumour Advisory Board (GTAB) Details

- **How do I access a GTAB?**

  The North Thames GTAB will accept referrals from North Thames clinicians. To request for a patient to be added to the GTAB please email rmh-tr.mdt.gel@nhs.net. The GTAB occurs weekly on a Wednesday.

  If you are based in the South West region, please email rduh.swgmsaadmin@nhs.net.

  If you are based in the East region, please email cuh.genomics-mdtgtab@nhs.net.

9. General Queries

- **How can we provide feedback or report issues encountered?**

  For general liquid biopsy queries all three regions can reach out to marsden360@rmh.nhs.uk with any feedback or issues or via 0208 915 6565 / 6514. North Thames clinicians can also use the same email for tissue or WGS samples.

  For the South West region please contact your regional Genomic Laboratory Hub via SWGLHcancer@nbt.nhs.uk.

  For the East region, please contact your regional Genomic Laboratory Hub via cuh.geneticslaboratories@nhs.net

- **What is the cost of the test?**

  The testing has been commissioned by NHS England for Trusts across England and is available on the National Test Directory. Therefore, no individual cost per test will be incurred by a requesting Trust.

  As described in section 1, Trusts will need to purchase blood kits locally as there is no national funding in place via NHSE.

10. Target Genes Tested

10.1 Liquid (ctDNA) Biopsy

SNV

AKT1	APC	ALK	BRCA1	BRCA2	BRAF
CDKN2A	CTNNB1	EGFR	ESR1	HRAS	IDH1
FGFR2	FGFR3	KIT	KRAS	MLH1	NF1
NRAS	PDGFRA	PIK3CA	PTEN	RB1	RET
TSC1	TP53	TERT promoter	VHL		
ERBB2	CDK12	FGFR1	IDH2		

CNV

PTEN	BRCA1	BRCA2

SV

ALK	EML4	FGFR2	FGFR3	NTRK1	NTRK2
NTRK3	ROS1	MET* (including exon 14 skipping)	RET	BRAF::	

(Red targets are clinical trial targets)

10.2 Tissue Biopsy

SNV					
AKT1	APC	ALK	BRCA1	BRCA2	BRAF

CDKN2A	CTNNB1	DICER1	EGFR	ELOC	ESR1
FGFR2	FGFR3	FH	FOXL2	HRAS	IDH1
KIT	KRAS	MLH1	MSH2	MSH6	MET* (incuding exon 14 skipping)
NF1	NRAS	PDGFRA	PIK3CA	POLD1	POLE
PMS2	PTEN	RB1	RET	SDHA	SDHB
SDHC	SDHD	SMARCA4	TP53	TSC1	TSC2
TERT promoter	VHL	ERBB2	PALB2	RAD51C	RAD51D
NF2	CDK12	FGFR1	IDH2		
CNV					
CDKN2A	FGFR2	FGFR3	MET	PTEN	TP53
ERBB2	BRCA1	BRCA2	MLH1	MSH2	MSH6
PALB2	RAD51C	RAD51D	NF1	NF2	CDK12
FGFR1	MTAP				
SNV					
ALK	EML4	FGFR2	FGFR3	MAML2	MET* (including exon 14 skipping)
MYB	NFIB	NTRK1	NTRK2	NTRK3	RET
ROS1	TFE3	TMPRSS2	ERG	BRAF::	MET::
FGFR1::					

(Red targets are clinical trial targets)