North East & Yorkshire GLH Solid Cancer WGS Eligibility & Sample Requirements - 2022

NHS England will fund whole genome sequencing (WGS) analysis for a subset of patients with solid tumours from autumn 2020. These can be seen in the NHSE national cancer test directory at https://www.england.nhs.uk/publication/national-genomic-test-directories/. The list of elibile cancer types is updated annually.

Categories of patients currently eligible for WGS:

- All patients with a sarcoma at initial diagnosis and/or on relapse
- All malignant tumours diagnosed in paediatric, teenage and young adults (≤25 years old) at initial diagnosis and/or relapse other than some subtypes of sarcoma specifically excluded on the sarcoma testing sheet
- Adult patients with any malignant solid tumour type where all standards of care testing and treatment have been exhausted
- All malignant neurological tumours in adults not included in the peadiatric category above
- Both adult and paediatric patient with Cancer of Unknown Primary (CUP). Can be performed at any stage of presentation (e.g. diagnosis, progression, relapse)

Tumour types eligible for WGS as part of a pilot

- High Grade Ovarian Carcinoma. This encompasses histologically proven high grade ovarian carcinoma including endometrioid carcinoma. Patients are eligible at any stage of disease and at any point in the patient pathway
- Triple Negative Breast Cancer. This includes histologically proven triple negative breast carcinoma (negative for ER / PR / HER2 expression), at any stage of diseaseand at any point in the patient pathway

Sarcomas - All patients (adult & paediatric):

Includes cases where specialist sarcoma pathology review indicates that molecular assessment will aid diagnosis or management, and/or those cases deemed eligible at the discretion of the histopathologist. As WGS is a part of the normal diagnostic repertoire in these patients it is recommended that clinicians base decisions on whether to submit samples on similar criteria to those they use for submission of other diagnostic tests.

Disease Group	Test Code	Disease Group	Test Code
Alveolar Rhabdomyosarcoma	M42.4	Sclerosing Epithelioid Fibrosarcoma	M76.2
Alveolar Soft Part Sarcoma	M43.2	Synovial Sarcoma	M77.2
Angiomatoid Fibrous Histiocytoma	M45.3	Undifferentiated Round Cell Sarcoma of Infancy	M78.2
Chondrosarcoma Conventional Central	M46.2	Well Differentiated/Dedifferentiated Liposarcoma	M79.2
Chondroblastoma	M47.2	Bone Forming Soft Tissue Tumour Differential	M196.3
Clear Cell Sarcoma of Soft Tissue	M48.2	Round Cell Sarcoma of Soft Tissue Differential	M197.10

CNS Ewing Sarcoma Family Tumour With CIC Alteration	M49.2	Vascular Soft Tissue Tumour Differential	M198.4
Dermatofibrosarcoma Protuberans	M50.2	Spindle Cell Soft Tissue Tumour Differential	M199.12
Desmoplastic Small Round Cell Tumour	M52.2	Myxoid Soft Tissue Tumour Differential	M200.7
Endometrial Stromal Sarcoma	M53.4	Adipocytic Soft Tissue Tumour Differential	M201.3
Ewing Like Sarcoma/PNET	M55.3	Epithelioid Soft Tissue Tumour Differential	M202.6
Ewing Sarcoma of Bone	M56.2	Uterine Sarcomas (Inc Endometrial)	M203.5
Ewing-Like Soft-Tissue Sarcoma	M57.3	Undifferentiated tumour	M204.1
Extraskeletal Myxoid Chondrosarcoma	M58.2	Cartilage Forming Bone Tumour Differential	M205.7
Giant Cell Tumour of Bone	M60.2	Bone Forming Bone Tumour Differential	M206.7
High-Grade Neuroepithelial Tumour-BCOR Group	M61.3	Osteoclast-Rich Bone Tumour Differential	M207.6
Infantile Fibrosarcoma	M62.2	Round Cell Sarcoma of Bone Differential	M208.6
Inflammatory Myofibroblastic Tumour	M63.4	Vascular Tumour of Bone Differential	M209.4
Low Grade Fibromyxoid Sarcoma	M64.2	Spindle Cell Tumour of Bone Differential	M210.5
Mesenchymal Chondrosarcoma	M65.2	Fibro-Osseous Tumour of Bone Differential	M211.3
Myoepithelial Tumours of Soft Tissue	M66.2	Undifferentiated Round Cell Sarcoma of Infancy	M78.2
Myxoid/Round Cell Liposarcoma	M67.2	Well Differentiated/Dedifferentiated Liposarcoma	M79.2
Myxoinflammatory Fibroblastic Sarcoma	M68.2	Bone Forming Soft Tissue Tumour Differential	M196.3
Osteosarcoma	M70.2	Round Cell Sarcoma of Soft Tissue Differential	M197.10
Phosphaturic Mesenchymal Tumour	M71.2	Vascular Soft Tissue Tumour Differential	M198.4
Primitive Mesenchymal Myxoid Tumour of Infancy	M72.3	Spindle Cell Soft Tissue Tumour Differential	M199.12
Pseudomyogenic Haemangioendothelioma	M73.2	Undifferentiated Round Cell Sarcoma of Infancy	M78.2
Radiation Induced Angiosarcoma	M74.2	Well Differentiated/Dedifferentiated Liposarcoma	M79.2
Round Cell Sarcoma Nos	M75.3		

Paediatric, teenage and young adult patients:

All malignant tumours diagnosed in paediatric, teenage and young adult patients (≤25 years old) other than some subtypes of sarcoma specifically excluded on the sarcoma testing sheet are eligible for WGS. These include cases where the neuropathologist or specialist paediatric pathology review indicates that molecular assessment will aid diagnosis or management. See table below for eligible disease groups including their test code:

Disease Group	Test Code	Disease Group	Test Code
Anaplastic Astrocytoma	M20.3	Medulloblastoma	M145.13
Diffuse Astrocytoma	M22.4	Medulloblastoma Group 3	M146.6
Embryonal Tumours with Multi-Layered Rosettes	M24.3	Medulloblastoma Group 3/4	M147.7
Ependymoma	M25.6	Medulloblastoma TP53 WT	M148.8
IDH-Wildtype Glioblastoma	M30.2	Melanotic Tumours	M149.2
Pineoblastoma	M37.2	Meningioma	M150.6
Rare Primitive Neuroectodermal Tumours Groups 2/3	M39.2	Midline Carcinoma	M151.5
Diffuse Midline Glioma	M183.5	Neuroblastoma	M152.14
Glioma	M184.2	Nodular Brain Tumour	M153.4
High Grade Glioma	M185.2	Oligoastrocytoma	M155.3
Low Grade Glioma	M186.2	Oligodendroglioma	M156.8
Glial and Glioneuronal Tumour Differential	M213.37	Thyroid Papillary Carcinoma	M157.5
Brain Tumour - No Further Morphological Classification	M189.17	Pilocytic Astrocytoma	M158.5
Embryonal Tumour Differential	M190.30	Pituitary Blastoma	M159.4
Medulloblastoma all Subtypes	M194.22	Pleomorphic Xanthoastrocytoma	M160.14
Paediatric Tumours (general)	M119.1	Pleuropulmonary Blastoma	M161.4
Atypical Teratoid/Rhabdoid Tumour	M120.16	Primitive Neuroectodermal Tumours	M162.8
Clear Cell Kidney Sarcoma	M124.9	Renal Tumours	M165.6
CNS High-Grade Neuroepithelial Tumour with MN1 Alteration	M126.2	Renal Tumour Differential	M212.14
Congenital Mesoblastic Nephroma	M127.3	Rhabdoid Tumours	M167.4
Craniopharyngioma	M195.3	Rosette-Forming Glioneuronal Tumour	M168.5
Cribriform Neuroepithelial Tumour	M130.4	Secondary Glioblastoma	M169.4
Cystic Nephroma	M131.4	SHH Medulloblastoma	M170.6
Desmoplastic Infantile Gangliogliomas	M132.12	SHH Medulloblastoma - TP53 WT	M171.7
Desmoplastic Medulloblastoma	M133.3	SHH Medulloblastoma - TP53 MUTANT	M172.6
Fibrolamellar Hepatocellular Carcinoma	M136.2	t(6;11) Translocation-Associated Renal Cell Carcinoma	M173.2
Ganglioglioma	M137.13	Testicular	M174.3
Glial Tumours	M138.2	Wilms Tumours	M178.3
Glioblastoma	M139.16	WNT Medulloblastoma	M179.8
Lung	M143.4	Xp11.2 Translocation-Associated Renal Cell Carcinoma	M180.6

Where patients may not benefit from this testing (for example those patients whose management is purely palliative, or where the patient dies soon after diagnosis) submitting sample may not be appropriate.

Patients with metastatic and inoperable solid tumours:

All patients with metastatic or inoperable solid tumours who have exhausted all testing in standard of care approaches and/or treatment are eligible for WGS.

Disease Group	Test Code
Solid Tumour Exhausted all Standards of Care Testing and Treatment- Adult	M232.1

Patients with malignant CNS tumours:

All patients with a malignant CNS tumour are eligible for WGS testing:

Disease Group	Test Code
Atrocytoma	M21.22
Diffuse midline glioma	M23.12
Ependymoma - supratentorial	M26.5
Glioblastoma	M27.16
Glioma	M28.9
High grade glioma	M29.9
Low grade glioma	M31.7
Low grade glioma/glioneural tumours	M32.6
Meningioma	M33.5
Non-midline glioma	M34.8
Oligodendroglioma	M35.9
Pilocytic astrocytoma	M36.16
Pituitary tumours	M38.6
Embryonal tumour differential	M190.3
Low grade intrinsic brain tumor differential	M191.22
High grade intrinsic brain tumour differential	M192.23
Unable to grade intrinsic brain tumour	M193.23
Meningioma	M33.5

Patients with Cancer of unknown primary:

All patients with a CUP are eligibel for WGS where molecular assessment will aid diagnosis and management:

Disease Group	Test Code
Cancer of unknown primary	M226.4

High Grade Ovarian Carcinoma (pilot):

This encompasses histologically proven high grade ovarian carcinoma including endometrioid carcinoma. Patients are eligible at any stage of disease and at any point in the patient pathway

Disease Group	Test Code
High grade ovarian carcinoma	M233.1

Triple Negative Breast Cancer (pilot):

This includes histologically proven triple negative breast carcinoma (negative for ER / PR / HER2 expression), at any stage of disease and at any point in the patient pathway

Disease Group	Test Code
Triple negative breast cancer	M234.1

Sample Requirements - all eligible solid cancers

Tumour:

For optimal, high quality sequencing a fresh tumour sample is required. Tumour tissue for WGS may be taken as a biopsy (e.g. core biopsy, punch biopsy) or resection surgical specimen. Tumour cells must account for at least 30% of the nucleated cells present in the tissue used for DNA extraction. Additionally, the sample should have less than 20% necrosis by area. A minimum of 2µg of tumour DNA must be submitted for WGS at a preferred concentration of 45ng/µl in a minimum volume of 115µl. The following are examples of usual sample quantities which will be adequate to achieve 2µg of DNA:

- 5mm x 5mm x 2mm of tumour tissue
- 15mm x 2mm needle core biopsy

As a general recommendation, in cases where risk to patients is unlikely to be increased by taking more than one biopsy, then 2-3 needle cores or 1-2 standard endoscopic forceps biopsies, if feasible, are recommended.

Frozen sections may be used to assess the tumour of the sample taken for WGS and also for submission to the DNA extracting laboratory.

Formalin fixed tumour tissue cannot be submitted for whole genome sequencing.

Germline:

A peripheral blood sample for direct DNA extraction must be taken for all patients recruited for WGS. Sufficient blood needs to be taken to ensure the required quantities of DNA can be extracted. Two tubes, each filled with 3-5ml of EDTA blood, should be sufficient in the majority of patients. Minimum of 115µl blood required to give a minimum DNA yield of 2µg. DNA should be extracted within 72 hours of taking sample.