Healthier Scotland
Scottish Government

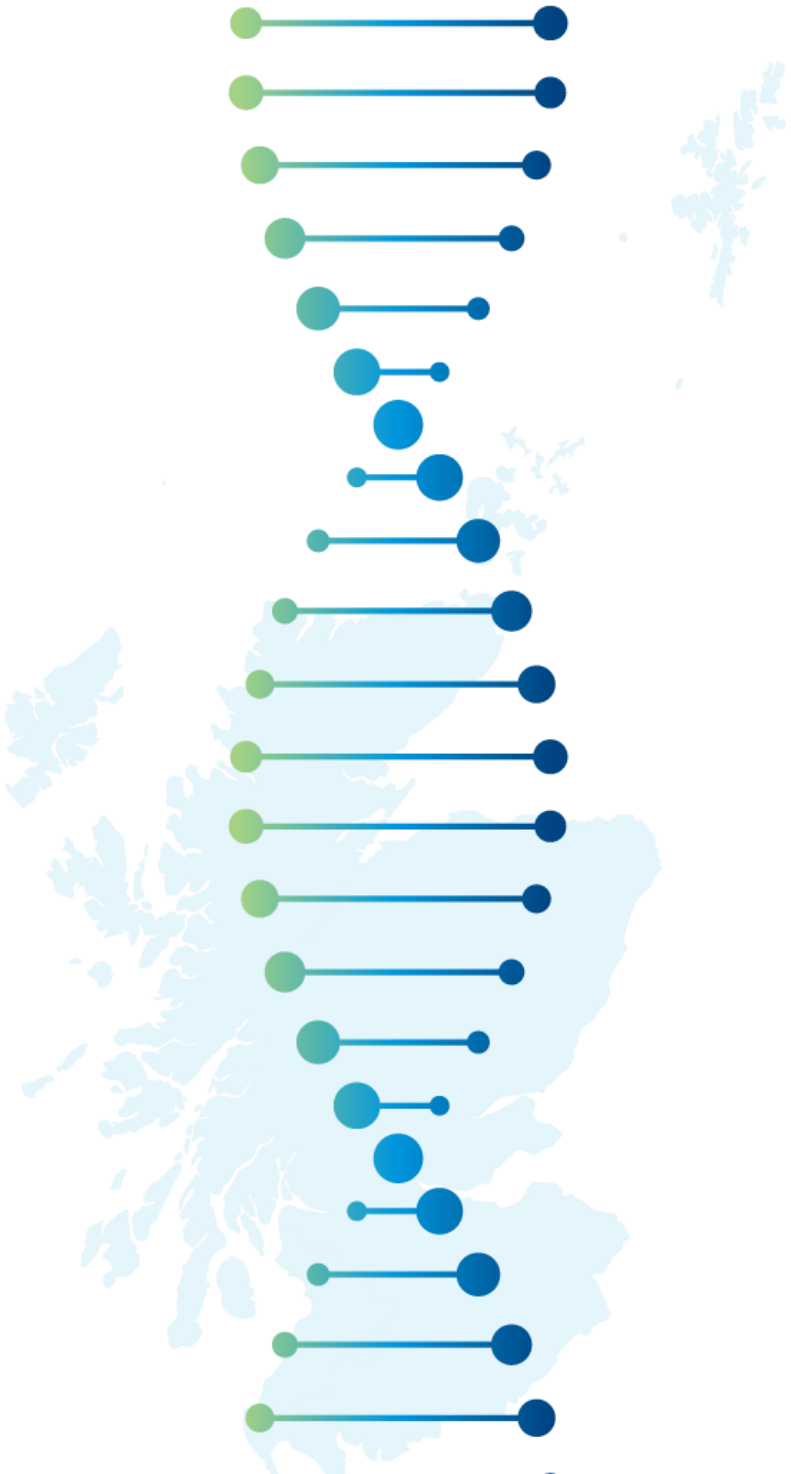
NHS SCOTLAND

Scottish Strategic Network
for Genomic Medicine

Genomic Test Directory

Cancer

Version 2 – May 2023



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INTRODUCTION

NHS SCOTLAND LABORATORY GENETIC SERVICES

NHS Scotland genetics services are delivered through four regional genetics centres in Aberdeen, Dundee, Edinburgh and Glasgow. Each centre offers a closely integrated laboratory and clinical service. NHS National Services Scotland commission the four genetics centres in Scotland work as a formal consortium arrangement, to deliver equitable, high quality genetic testing service for Scotland. All laboratories are accredited by United Kingdom Accreditation Service (UKAS) in accordance with the recognized ISO 15189:2012 standard.

Molecular genetics testing was nationally designated in 1985 and cytogenetics in 2009. Molecular pathology testing services was nationally commissioned as a single designated multi-site national specialist service from 1 April 2013.

Genetics and molecular pathology services are evolving and increasing each year with advancing knowledge, technology, and the increasing utility of stratified medicine. The increase in molecular pathology, in particular, is increasingly being driven by the development and availability of targeted treatment therapies in both solid tumours and haematological malignancies.

Molecular pathology centres deliver the vast majority of services on a regional basis, providing testing for the local and neighbouring healthboards. A limited number of specialist tests are provided in designated centres to cover the population of Scotland.

PURPOSE OF DOCUMENT

The Scottish Strategic Network for Genomic Medicine Cancer Test Directory contains a list of all services currently Available in Scotland.

This document will be reviewed annually.

NHS SCOTLAND GENETIC LABORATORY CONTACT DETAILS

- **Aberdeen (NHS Grampian)**
  Address: Genetics and Molecular Pathology Laboratory Services, Polwarth Building, Foresterhill, Aberdeen AB25 2ZD
  Email address: gram.molgen@nhs.scot
  Website: https://www.nhsgrampian.org/service-hub/north-of-scotland-medical-genetics

- **Dundee (NHS Tayside)**
  Address: East of Scotland Regional Genetics Service, Level 6, Ninewells Hospital, Dundee DD1 9SY
  Email address: Tay.esrg@nhs.scot
  Website: https://www.nhstayside.scot.nhs.uk/OurServicesA-Z/Genetics/PROD_295540/index.htm

- **Edinburgh Genetics (NHS Lothian)**
  Address: South East Scotland Genetic Service, Western General Hospital, Crewe Road, Edinburgh, EH4 2XU
  Email address: edinburgh.dna@nhslothian.scot.nhs.uk / wgh.cytogenetics@nhslothian.scot.nhs.uk
  Phone : 0131 537 1116 / 0131 537 1940
  Website:https://services.nhslothian.scot/clinicalgeneticsservice/GeneticLaboratoryServices/Pages/default.aspx

- **Edinburgh Molecular Pathology (NHS Lothian)**
  Molecular Pathology – Solid Tumours, Department of Laboratory Medicine, Royal Infirmary of Edinburgh, 51 Little France Crescent, Old Dalkeith Road, Edinburgh EH16 4SA
  Email address :molecular.pathology@nhslothian.scot.nhs.uk
  Tel: 0131 242 7141
  Haematology Malignancy Diagnostic Service (HMDS), Haematology/Biochemistry Combined Reception, Department of Laboratory medicine, Western General Hospital, Crewe Road, Edinburgh EH4 2XU
  Email address: HMDS.Lothian@nhslothian.scot.nhs.uk
  Tel: 0131 537 1145/2374

- **Glasgow (NHS Greater Glasgow & Clyde)**
  Address: West of Scotland Centre for Genomic Medicine, Laboratory Genetics, Level 2B Laboratory Medicine & FM Building, Queen Elizabeth University Hospital, Glasgow G51 4TF
  Email address: Genetic.Laboratories@ggc.scot.nhs.uk
  Website: www.nhsggc.scot/laboratory-genetics

TEST REQUESTING

Testing is delivered either in the local centre or the designated centre, according to the test directory. Regardless of testing centre, all samples should be directed to the local genetics laboratory in the first instance, with referrals being forwarded by them where required/if appropriate. Samples should be accompanied with the appropriate completed referral forms (or proforma, if required). For local sample acceptance policies and referral forms, please see the local laboratory website.

Consent for genetic testing should be gained for testing before the sample is referred to the laboratories. This is of particular importance in testing where there may be germline implications and a possible impact on family members e.g. BRCA1/2 testing in ovarian tumours, inherited predisposition to haematological malignancies.

Services are provided for the clinical indications listed when referred from the appropriate specialties.

SAMPLE REQUIREMENTS

A range of sample types may be referred for molecular pathology testing including blood, marrow, formalin fixed paraffin embedded (FFPE) tissue etc. For specific sample requirements associated with each test, please see the local laboratory websites.

TESTING METHODOLOGY

Different methods are utilised depending on the scope of testing. These methods include techniques to detect a single variant to genome wide screens including:

- PCR (polymerase chain reaction)
- Sanger sequencing
- Next Generation Sequencing (NGS; DNA or RNA based) panels – vary in size from a small, targeted panels to gene screens and may include detection of fusion genes
- Fragment analysis
- Multiplex Ligation Probe Amplification (MLPA) including methylation specific type (MS-MLPA)
- Fluorescent In Situ Hybridisation (FISH)
- PCR/FLA (fragment length analysis)
- Pyrosequencing (pyroseq), including MS-pyroseq
- Allele specific PCR (COBAS)
- Karyotype
- Microarray (SNP array)
- qRT PCR (quantitative real-time PCR)
- RT-PCR (reverse transcription PCR)
- Real time AS-PCR (allele specific PCR)
- High resolution melt
- Nested RT-PCR

SCOPE AND RANGE OF TEST

The scope and range of testing refers to the extent of testing and the types of variant that will be detected.

The scope of testing includes:

- Targeted screen – testing of specific region(s) e.g. gene rearrangements, amplifications or DNA level variant
- Whole gene screen – sequence of coding region of relevant gene(s)
- Copy number (variant)/(CNV) – assessment of gene level copy number
- Genomic screen – detection of large scale rearrangements

The types of variants detected include:

- Small sequence variants
    - Single nucleotide variants (SNVs)
    - Insertions / deletions (indels)
- Copy number variants (CNVs)
    - Exon level
    - Genome wide level
- Genome wide rearrangements

The targets tested refer to the genes / regions tested for the particular clinical indication.

REPORTING TIMES

Reporting times are listed based on calendar days (except where indicated). These range from 3 to 42 days depending on urgency and complexity of testing. NB. Different reporting times may be evident in some clinical indications due to differences in local clinical practice.

SOLID MALIGNANCIES

ADULT GRANULOSA CELL TUMOUR

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Targeted screen	SNV	FOXL2 p.(Cys134Trp)	14
Dundee	Sanger	Targeted screen	SNV	FOXL2 p.(Cys134Trp)	14
EdinburghMP	Sanger	Targeted screen	SNV	FOXL2 p.(Cys134Trp)	14
Glasgow	Sanger	Targeted screen	SNV	FOXL2 p.(Cys134Trp)	14

Referral criteria

- Ovarian sex cord stromal tumour – differential diagnosis includes adult granulosa cell tumour

Requesting specialties

- Pathology
- Gynaecological MDT

BREAST CANCER

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	FISH	Targeted screen	Copy number	ERBB2 (HER2)	14
Dundee	FISH	Targeted screen	Copy number	ERBB2 (HER2)	14
EdinburghMP	FISH	Targeted screen	Copy number	ERBB2 (HER2)	14
Glasgow	FISH	Targeted screen	Copy number	ERBB2 (HER2)	14

Referral criteria

- Invasive primary breast cancer, recurrent and metastatic tumours identified to have borderline HER2 expression by immunohistochemistry (IHC) (score of 2+)

Requesting specialties

- Pathology
- Oncology

CHOLANGIOCARCINOMA

Available testing

Centre	Method	Scope and range of test		Targets	TAT
EdinburghMP	FISH	Targeted screen	Specific rearrangements	FGFR2 [upon request]	14

Referral criteria

Requesting specialties

- Pathology
- Oncology

COLORECTAL CANCER

Available testing

Centre	Method	Scope and range of test			Targets	TAT
Aberdeen	NGS_DNA	Targeted screen	SNVs, indels		KRAS (codons 12, 13, 59, 61, 117, 146) NRAS (codons 12, 13, 59, 61, 117, 146) BRAF (codon 600)	14
	PCR/FLA	Targeted screen	MSI		NR21, NR24, BAT26, BAT25, MONO27 microsatelllite repeats	14
	MS-MLPA	Targeted screen	methylation		MLH1	14
Dundee	NGS_DNA	Targeted screen	SNVs, indels		KRAS (codons 12, 13, 59, 61,117, 146) NRAS (codons 12, 13, 59, 61, 117, 146) BRAF (codon 600)	14
	PCR/FLA	Targeted screen	MSI		NR21, NR24, BAT26, BAT25, MONO27 microsatelllite repeats	14
	MS-MLPA	Targeted screen	methylation		MLH1	14
EdinburghMP	NGS_DNA	Targeted screen	SNVs, indels		KRAS (codons 12, 13, 59, 61, 117, 146) NRAS (codons 12, 13, 59, 61) BRAF (codon 600) TP53 (if requested by Oncology)	14
	PCR/FLA	Targeted screen	MSI		NR21, NR24, BAT26, BAT25, MONO27 microsatellite repeats	14
	MS-pyroseq	Targeted screen	methylation		MLH1	28
Glasgow	NGS_DNA	Targeted screen	SNVs, indels		KRAS (codons 12, 13, 59, 61, 117, 146) NRAS (codons 12, 13, 59, 61) BRAF (codon 600)	14
	PCR/FLA	Targeted screen	MSI		NR21, NR24, BAT26, Bat25, MONO27 microsatellite repeats	7
	MS-pyroseq	Targeted screen	methylation		MLH1	14

NB Reporting times influenced by local clinical practice

Referral criteria

- All new diagnoses of colorectal cancer
- Pathology
- Oncology

ENDOMETRIAL CANCER

Available testing

Centre	Method	Scope and range of test		Targets	TAT
EdinburghMP	Sanger	Targeted screen	SNVs, indels	POLE (exons 9-14) TP53	14
	PCR/FLA	Targeted screen	MSI	NR21, NR24, BAT26, Bat25, MONO27 microsatellite repeats [upon request]	14
	MS-pyroseq	Targeted screen	Methylation	MLH1	28
Dundee	Sanger	Targeted screen	SNVs, indels	POLE (exons 9-14) TP53	14
	PCR/FLA	Targeted screen	MSI	NR21, NR24, BAT26, Bat25, MONO27 microsatellite repeats [upon request]	14
	MS-MLPA	Targeted screen	Methylation	MLH1	28
Glasgow	Sanger	Targeted screen	SNVs, indels	TP53	14
	PCR/FLA	Targeted screen	MSI	NR21, NR24, BAT26, Bat25, MONO27 microsatellite repeats [upon request]	14
	MS-MLPA	Targeted screen	Methylation	MLH1	28

NB Reporting times influenced by local clinical practice

Referral criteria

- For testing of normal tissue for constitutional MLH1 promoter hypermethylation please refer to the Test Directory for Rare & Inherited Disease Diagnosis of endometrial cancer where considered appropriate
- Stratifies patients into low, intermediate and high risk groups used to predict response to adjuvant therapy, sparing some patients from receiving toxic chemotherapy associated with no outcome benefit

Requesting specialties

- Pathology

GASTRIC CANCER

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	FISH	Targeted screen	Copy number	ERBB2 (HER2)	14
Dundee	FISH	Targeted screen	Copy number	ERBB2 (HER2) EGFR	14
EdinburghMP	FISH	Targeted screen	Copy number	ERBB2 (HER2)	14
Glasgow	FISH	Targeted screen	Copy number	ERBB2 (HER2)	14

Referral criteria

- Upper GI (gastric and gastro-oesophageal) biopsies or excisions

Reflex FISH testing acceptance criteria:

- Testing is initiated by MDT
- Cases scored as HER2 IHC 0, 1+ or 3+ do not require FISH
- HER2 IHC 2+ require FISH testing

Reflex testing is not done on:

- Negative (0, 1+) HER2 IHC cases
- Positive (+++) HER2 IHC cases
- Patients for surgery who may not need Herceptin/chemotherapy treatment
- Very frail patients who will be given "best supportive care" only

Requesting specialties

- Oncology
- Pathology

GASTROINTESTINAL TUMOURS

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS_DNA	Targeted screen	SNVs, indels	KIT (exons 9, 11, 13, 17, region of 8) PDGFRA (exons 12, 14, 18) BRAF (codon 600)	14
EdinburghMP	NGS_DNA	Targeted screen	SNVs, indels	KIT (exons 9, 11, 13, 17) PDGFRA (exons 12, 14, 18) BRAF (codon 600)	14

Referral criteria

- Analysis of all resected moderate-risk and high-risk GISTs, regardless of location, is recommended, as well as all diagnostic biopsies in which neoadjuvant therapy is contemplated and all biopsies of inoperable GIST.

- In some cases, mutational analysis may be of direct diagnostic value. Identification of a typical mutation seen in GISTs may be of value in supporting the diagnosis of GIST, particularly if a broader differential diagnosis had previously been considered.

- The clinical utility of characterising secondary mutations to guide subsequent oncological management remains uncertain.

Requesting specialties

- Oncology
- Pathology

GLIOMA (including high grade)

Available testing

Centre	Method	Scope and range of test		Targets	TAT
EdinburghMP	NGS_DNA	Targeted screen	SNVs, indels	IDH1 (codon 132) IDH2 (codon 172) BRAF (codon 600) TP53 (hotspots)	14
	Sanger	Targeted screen	SNVs	TERT promoter	14
	MS-pyroseq	Targeted screen	methylation	MGMT	7
Glasgow	NGS_DNA	Targeted screen	SNVs, indels	IDH1 (codon 132) IDH2 (codon 172) BRAF (codon 600)	14
	MS-pyroseq	Targeted screen	methylation	MGMT	7

Referral criteria

- Investigations are performed as directed by referral following neuropathological assessment and diagnosis of glioma

Requesting specialties

- Oncology
- Neuropathology

HEAD AND NECK CANCER (Squamous)

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	PCR/FLA	Targeted screen	Types 16 and 18	HPV type 16/18	14

Referral criteria

- Analysis is performed following pathological assessment in patients undergoing investigations for head & neck squamous cell carcinoma (HNSCC).

Requesting specialties

- Oncology
- Pathology

LUNG CANCER

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS_DNA	Targeted screen	SNVs, indels	EGFR (exons 18, 19, 20, 21) KRAS (codons 12, 13, 61) BRAF (codon 600)	14
	NGS_RNA	Targeted screen	Specific rearrangements	ALK ROS1 RET	14
	FISH	Targeted screen	Specific rearrangements	ALK ROS1 RET	14
Dundee	NGS_DNA	Targeted screen	SNVs, indels	EGFR (exons 18, 19, 20, 21) KRAS (codons 12, 13, 61) BRAF (codon 600)	14
	NGS_RNA	Targeted screen	Specific rearrangements	ALK ROS1 RET	14
EdinburghMP	NGS_DNA	Targeted screen	SNVs, indels	EGFR (exons 18, 19, 20, 21) KRAS (codons 12, 13, 61) BRAF (codon 600) Additional targets: FGFR, MET	14
	FISH	Targeted screen	Specific rearrangements	ALK ROS1 RET (upon request)	14
Glasgow	NGS_DNA	Targeted screen	SNVs, indels	EGFR (exons 18, 19, 20, 21) KRAS (codons 12, 13, 61) BRAF (codon 600)	14
	FISH	Targeted screen	Specific rearrangements	ALK ROS1	14

Referral criteria

- Usually non-squamous Non Small Cell Lung Cancer (NSCLC) although there may be scenarios where clinicians wish to test other subtypes of NSCLC e.g. never smokers or long-time ex-smokers with squamous tumours, tumours with unusual phenotype, eligible for tyrosine kinase inhibitor therapy.

Requesting specialties

- Oncology
- Pathology

LUNG CANCER, CELL FREE DNA

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Allele specific PCR (COBAS)	Targeted screen	SNVs, indels	EGFR (exons 18, 19, 20, 21)	7
EdinburghMP	Allele specific PCR (COBAS)	Targeted screen	SNVs, indels	EGFR (exons 18, 19, 20, 21)	7

Referral criteria

- Non-squamous Non Small Cell Lung Cancer (NSCLC)/Lung Cancer patients, where
    - no biopsy material is Available, or
    - biopsy material is unsuitable for molecular analysis, or
    - patient unwell and biopsy cannot be obtained, or
    - for monitoring purposes to detect emergence of resistance mutations, or
    - patient otherwise eligible for tyrosine kinase inhibitor therapy

Requesting specialties

- Oncology

MELANOMA (MALIGNANT, METASTATIC)

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS_DNA	Targeted screen	SNVs, indels	BRAF (codon 600) NRAS (codons 12, 13, 59, 61) KIT (exon 9, 11, 13, 17)	14
Dundee	NGS_DNA	Targeted screen	SNVs, indels	BRAF (codon 600) NRAS (codons 12, 13, 59, 61) KIT (exon 9, 11, 13, 17, 18)	14
EdinburghMP	NGS_DNA	Targeted screen	SNVs, indels	BRAF (codon 600) NRAS (codons 12, 13, 59, 61) KIT (exon 9, 11, 13, 17, 18) GNA11 additional target – reported if present	14
Glasgow	NGS_DNA	Targeted screen	SNVs, indels	BRAF (codon 600) NRAS (codons 12, 13, 59, 61) KIT (exon 9, 11, 13, 17)	14

Referral criteria

- Request from Oncology/MDT for patients with metastatic disease, or locally advanced progression, being considered for adjuvant therapy
- If, following review, the patient's co-morbidities exclude them from adjuvant therapy testing is not indicated

Requesting specialties

- Oncology
- Pathology

MESOTHELIOMA

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	FISH	Targeted screen	Copy number	CDKN2A/CEP9	21
Dundee	FISH	Targeted screen	Copy number	CDKN2A/CEP9	14
Glasgow	FISH	Targeted screen	Copy number	CDKN2A/CEP9	14

NB Reporting times influenced by local clinical practice

Referral criteria

- Diagnostic uncertainty re: mesothelioma or benign or reactive mesothelial proliferation

Requesting specialties

- Oncology
- Pathology

MUCOEPIDERMOID CARCINOMA

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Dundee	FISH	Targeted screen	Specific rearrangements	MAML2	14

Referral criteria

- **Salivary gland excision specimens/core biopsies**
  - To confirm morphological impression of a mucoepidermoid carcinoma (MEC) in challenging/higher grade cases
  - To exclude a MEC when it is among a list of differentials in a hard to classify tumour (such as a tumour comprising predominantly of clear cells or oncocytic cells)
  - In a core biopsy of a salivary tumour where diagnosis is challenging and extensive surgery is planned

- **Jaw cysts**
  - Where mucous cells are prominent to exclude intraosseous MEC

- **Lymph node**
  - Where tumour deposits look like metastatic MEC (primary site may be unknown)

Requesting specialties

- Oncology
- Pathology

NEUROBLASTOMA

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	FISH	Targeted screen	Copy number	MYCN	5
	FISH	Targeted screen	Copy number	1p, 11q and 17 status	21
EdinburghG	FISH	Targeted screen	Copy number	MYCN	3
	SNP array	Genomic screen	Copy number	MYCN, 1p, 11q and 17 status	14
Glasgow	FISH	Targeted screen	Copy number	MYCN	3

Referral criteria

- Investigations are performed as directed by referral following neuropathological assessment and diagnosis of neuroblastoma

Requesting specialties

- Oncology
- Neuropathology

OLIGODENDROGLIOMA

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	FISH	Targeted screen	Copy number	1p/19q (PET specimens)	14
EdinburghG	FISH	Targeted screen	Copy number	1p/19q (PET specimens)	14
	SNP array	Genomic screen	Copy number	1p/19q status whole genome (fresh/frozen tissue)	14

Referral criteria

- Investigations are performed as directed by referral following neuropathological assessment and diagnosis of oligodendroglioma

Requesting specialties

- Oncology
- Pathology

OVARIAN CANCER

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS_DNA	Whole gene screen	SNVs, indels	BRCA1 and BRCA2	42
	NGS_DNA	Whole gene screen	SNVs, indels	TP53	14
Dundee	Sanger	Whole gene screen	SNVs, indels	TP53	14
Glasgow	NGS_DNA	Whole gene screen	SNVs, indels	BRCA1 and BRCA2	42
	NGS_DNA	Whole gene screen	SNVs, indels	TP53	14
EdinburghMP	Sanger	Targeted screen	SNVs, indels	High grade serous ovarian cancer: TP53	14

Referral criteria

- First line/maintenance - newly diagnosed, advanced (FIGO stage III or stage IV), high grade epithelial ovarian cancer, fallopian tube or primary peritoneal cancer that is in response (complete or partial) to platinum based chemotherapy

- Second line/relapsed - platinum-sensitive relapsed high grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete response or partial response) to platinum based chemotherapy

N.B. Germline testing of *BRCA1* and *BRCA2* is also available in these patients, and should be performed in parallel. Please refer to the Scottish Genetics Laboratory Consortium Genomic Test Directory for Rare & Inherited Disease

- TP53 aids diagnosis of high grade serous ovarian carcinoma vs. low grade, for treatment decisions.

Requesting specialties

- Oncology
- Pathology

RENAL CELL CARCINOMA (RCC)

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	FISH	Targeted screen	Specific rearrangements	Depending on type; TFE3 VHL/CEP3	21
	Microarray	Genomic screen	Copy number	Whole chromosome or whole chromosome arm gains / losses	21
Dundee	FISH	Targeted screen	Specific rearrangements	TFE3	21
	NGS_DNA Sanger/MLPA	Whole gene screen and CNV	SNVs, indels, exon level CNV	VHL SDH FH FLCN	56
EdinburghMP	FISH	Targeted screen	Specific rearrangements	TFE3 VHL ALK	14

NB Reporting times influenced by local clinical practice

Referral criteria

Testing should be considered in the following cases when the results will impact diagnosis and patient management:-

- A younger age group of less than 30 years (and may be considered for the 30 to 40 year age group)
- A strong family history of renal tumours
- Multiple tumours (in the absence of a known genetic syndrome)
- A rare tumour type with genetic associations
- For the above points germline testing (NGS_DNA/Sanger/MLPA) would be recommended first.
- SDH and FH testing of tumour following on from suggestive IHC but no germline pathogenic variant detected
- Unusual morphology
- TFE3 testing can be used to make a diagnosis of a MiT translocation tumour which may also be important for treatment
- Copy number variant analysis of chromosome 3p aids diagnosis of clear cell renal carcinoma
- Copy number variant analysis can help distinguish between oncocytoma, chromophobe RCC and papillary RCC
- ALK associated RCC can occur in children with sickle cell trait or adults without sickle cell trait (rare)

Requesting specialties

- Oncology
- Pathology

SARCOMA

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	FISH	Targeted screen	Gene rearrangements and amplifications	EWSR1, SS18, FOXO1, FUS, MDM2, USP6	21 14 if urgent
Dundee	FISH	Targeted screen	Specific rearrangements	EWSR1, SS18, COL1A1::PDGFB	14
EdinburghMP	FISH	Targeted screen	Gene rearrangements and amplifications	DDIT3, COL1A1, EWSR1, FOXO1, FUS, JAZF1, MDM2, SS18, TFE3, USP6	14
	NGS_DNA	Targeted screen	SNVs, indels	GNAS, CTNNB1	14
Glasgow	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	28
	FISH	Targeted screen	Gene rearrangements and amplifications	*SS18, EWSR1, FOXO1, PAX7::FOXO1, PAX3::FOXO1, FUS, DDIT3* and *MDM2*	14
	PCR/FLA	Targeted screen	Specific rearrangements	*SS18::SSX1, SS18::SSX2, EWSR1::FLI1, PAX3::FOXO1*, *PAX7::FOXO1*, and *FUS::CREB3L2*	14

Referral criteria

- Translocation sarcoma where differential diagnosis includes such tumours [Ewing's sarcoma / round cell tumours, alveolar rhabdomyosarcoma, myxoid liposarcoma, synovial sarcoma, low grade fibromyxoid sarcoma/sclerosing epithelioid fibrosarcoma, alveolar soft part sarcoma, clear cell sarcomas, endometrial stromal sarcoma, Dermatofibrosarcoma protuberans (DFSP)].
- MDM2 gene amplification for tumours where differential diagnosis includes atypical lipomatous tumour, well differentiated liposarcoma, dedifferentiated liposarcoma, parosteal osteosarcoma, low grade central osteosarcoma.
- CTNNB1 mutation testing to help clinical management for cases where differential diagnosis includes desmoid fibromatosis
- GNAS mutation for fibrous dysplasia.
- USP6 rearrangement for cases where diagnostic clarification is required [myofibroblastic/fibroblastic lesions such as nodular fasciitis and bone lesions such as aneurysmal bone cysts or mimics]

Requesting specialties

- Oncology
- Pathology

THYROID CANCER

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS_DNA	Targeted screen	SNV, indels	BRAF (codon 600) HRAS (codon 12, 13, 61) KRAS (codon 12, 13, 61, 117, 146) NRAS (codon 12, 13, 59, 61) RET mutation (hotspot)	14
	FISH or NGS_RNA	Targeted screen	Specific rearrangements	RET	14
Dundee	NGS_DNA	Targeted screen	SNV, indels	BRAF (codon 600) HRAS (codon 12, 13, 61) KRAS (codon 12, 13, 61, 117, 146) NRAS (codon 12, 13, 59, 61, 117, 146) RET mutation (hotspot)	14
	NGS_RNA	Targeted screen	Specific rearrangements	RET	14
EdinburghMP	NGS_DNA	Targeted screen	SNV, indels	BRAF (codon 600) HRAS (codon 12, 13, 61) KRAS (codon 12, 13, 61, 117, 146) NRAS (codon 12, 13, 59, 61) RET mutation (hotspot) TP53 (hotspots)	
	Sanger	Targeted screen	SNVs	TERT promoter	14
	FISH	Targeted screen	Specific rearrangements	RET	14
Glasgow	NGS_DNA	Targeted screen	SNV, indels	BRAF (codon 600) HRAS (codon 12, 13, 61) KRAS (codon 12, 13, 61, 117, 146) NRAS (codon 12, 13, 59, 61) RET mutation (hotspot)	14

Referral criteria

- BRAF and/or RAS mutations for indeterminate nodules and malignant tumours
- RET fusions for papillary/anaplastic carcinoma
- RET mutations for medullary/anaplastic carcinoma

Requesting specialties

- Oncology
- Pathology

UVEAL MELANOMA

Available testing

Centre	Method	Scope and range of test		Targets	TAT
EdinburghMP	NGS_DNA	Targeted screen	SNV, indels	GNA11, GNAQ (hotspots)	14
Glasgow	NGS_DNA	Targeted screen	SNV, indels	BRAF (codon 600)	14
	FISH	Targeted screen	Specific CNV	Chromosomes 3, 6, 8	14

Referral criteria

- Primary uveal melanoma

Requesting specialties

- Oncology
- Pathology

HAEMATOLOGICAL MALIGNANCIES

ACUTE LYMPHOBLASTIC LEUKAEMIA (all)

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	14
	FISH	Targeted screen	Specific rearrangements	B-ALL: BCR::ABL1 ETV6::RUNX1 TCF3::PBX1 TCF3::HLF FIP1L1::PDGFRA KMT2A PDGFRB ABL1 and 2 Others if required e.g. ploidy T-ALL: ABL1 ABL2 FIP1L1::PDGFRA PDGFRB	14 (BCR::ABL-3)
	Array	Genomic screen	Genomic screen Ploidy and (specific) deletions	*EBF1*, *IKZF1*, *CDKN2A/B*, *PAX5*, *ETV6*, *BTG1*, *RB1* and *PAR1* (CRLF2)	14
	NGS_RNA	Targeted screen	Specific rearrangements	Including: BCR::ABL1 (qualitative) ETV6::RUNX1 TCF3::PBX1 TCF3::HLF KMT2A::AFF1 KMT2A::MLLT1 KMT2A::MLLT3 KMT2A::MLLT4 KMT2A::MLLT10 KMT2A::ELL	14
Dundee	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	21 (if urgent - 14)
	FISH	Targeted screen	Specific rearrangements	BCR::ABL1 ETV6::RUNX1 KMT2A (MLL) Ploidy If required screening for ABL-class gene fusions ABL1,ABL2, PDGRFA and PDGRFB::CSF1R, FIP1L1::PDGFRA T-CELL TCRA/D	14 (BCR-ABL-3)
	Array	Genomic screen (if requested by clinician)	Genomic screen Ploidy and (specific) deletions	EBF1, IKZF1, CDKN2A/B, PAX5, ETV6, BTG1, RB1 and PAR1 (CRFL2), iAMP21	14
EdinburghG	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	14

	FISH	Targeted screen	Specific rearrangements	B-cell: BCR::ABL1, ETV6::RUNX1, TCF3::-PBX1 TCF3::HLF KMT2A If required screening for ABL-class fusions:- ABL1, ABL2, FIP1L1::PDGRFA PDGRFB T-cell: KMT2A, BCR::ABL1 If required screening for ABL-class fusions:- ABL1, ABL2, FIP1L1::PDGRFA PDGRFB	7
	Array	SNP Array	Genomic screen Ploidy and (specific) deletions	*EBF1*, *IKZF1*, *iAMP21, CDKN2A/B*, *PAX5*, *ETV6*, *BTG1*, *RB1* and *PAR1* (CRLF2)	14
EdinburghMP	RT-PCR	Targeted screen	Specific rearrangements	BCR::ABL1 ETV6::RUNX1 TCF3::PBX1 KMT2A::AFF1 KMT2A::MLLT1 KMT2A::MLLT3 KMT2A::AFDN KMT2A::ELL	3*
Glasgow	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	14
	Array	Genomic screen	Genomic screen Ploidy and (specific) deletions	BTG1, CDKN2A/b, EBF1, ETV6, IKZF1, PAX5, PAR1 (CRLF2) and RB1 Ploidy group determination iAMP21	14
	FISH	Targeted screen	Specific rearrangements	B-cell: *BCR::ABL1*, *ETV6::RUNX* *TCF3::PBX1* *TCF3::HLF* *KMT2A* *KMT2A::AFF1* *KMT2A::MLLT1*Ploidy. If required screening for ABL-class fusions:- *ABL1, ABL2,* *FIP1L1:: PDGRFA* *PDGRFB* T-cell: Screening for ABL-class fusions:- *ABL1, ABL2* *FIP1L1::PDGRFA* *PDGRFB*	7 (if urgent - 3)
	PCR/FLA	Targeted screen	Specific rearrangements	BCR::ABL (qualitative)	14 (if urgent - 7)

* refers to working days

NB Reporting times influenced by local clinical practice

Referral criteria

- New diagnosis of acute lymphoblastic leukaemia (ALL)
- Relapsed ALL

Requesting specialties

- Haematology

ACUTE LYMPHOBLASTIC LEUKAEMIA (all), MINIMAL RESIDUAL DISEASE (MRD)

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	qRT-PCR	Targeted screen	Specific rearrangements	BCR::ABL1 quantitation [E1A2 and E13A2/E14A2]	21
Dundee	qRT-PCR (GeneXpert)	Targeted screen	Specific rearrangements	BCR::ABL1 quantitation [E1A2 and E13A2/E14A2]	14
Edinburgh MP	RT-PCR	Targeted screen	Specific rearrangements	BCR::ABL1 quantitation [E1A2 and E13A2/E14A2] ETV6::RUNX1 (relative) TCF3::PBX1 (relative)	14
Glasgow	qRT-PCR	Targeted screen	Specific rearrangements	BCR::ABL1 quantitation [E1A2 and E13A2/E14A2]	14
	Seq/qPCR	Targeted screen	Specific rearrangements	IgH/TCR gene rearrangement work up	28
	qPCR	Targeted screen	Specific rearrangements	MRD patient specific monitoring (day 29 and week 14)	7

NB Reporting times influenced by local clinical practice

Referral criteria

- BCR-ABL1
  - All patients with a BCR-ABL1 rearrangement identified at diagnosis
  - Patients on tyrosine kinase inhibitor therapy (treatment response assessment)
  - Patients undergoing reduced intensity conditioning (RIC) allograft for BCR-ABL1 positive ALL require BCR-ABL monitoring every 3 months post-transplant for a minimum of 2 years.
- IgH/TCR minimal residual disease
  - Paediatric and young adult patients (≤45 years) with a new diagnosis of ALL should be referred for MRD target identification (IgH/TCR gene rearrangements) and follow up as per trial protocols (ALLTogether trial)
  - ***We had previously received an amendment for the test directory from our Glasgow colleagues for referral criteria for when we were going to do the updates – have added here so it doesn't get missed but you may already have had notification of this direct from Glasow in this call out…. The revision was

    IgH/TCRG mimimal residual disease - amend upper age limit "paediatric and young adult patients (≤ 45 years) with a new diagnosis" to 29 years and **364 days (29 years effectively)**
  - 'Off-trial' MRD analysis and monitoring is available for paediatric and young adult patients who are not enrolled on the trial
  - Older adults requiring MRD are referred on a case-by-case basis by the managing team and samples are sent to the adult reference laboratory in London

Requesting specialties

- Haematology

ACUTE MYELOID LEUKAEMIA (AML)

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	14
	NGS_RNA	Targeted screen	Specific rearrangements	Including: BCR::ABL1 (qualitative) RUNX1::RUNX1T1 CBFB::MYH11 PML::RARA (qualitative) KMT2A::AFF1 KMT2A::MLLT1 KMT2A::MLLT3 KMT2A::MLLT4 KMT2A::MLLT10 KMT2A::ELL	14
	PCR/FLA	Targeted screen	Specific rearrangements	FLT3 ITD & TKD, NPM1	14 (FLT3- 7)
	FISH	Targeted screen	Specific rearrangements	As required/indicated : BCR::ABL1 RUNX1::RUNX1T1 PML::RARA DEK::NUP214 KMT2A CBFB MECOM Chr 5 and 7 (copy number)	14 (PML::RARA - 3)
	NGS_DNA	Targeted screen	SNV, indels	Myeloid NGS Panel (agreed whole gene / hot-spots	28
Dundee	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	14
	Array	Genomic screen (Used if karyotype poor quality)	Large scale and targeted rearrangements	All (within resolution of method)	14
	FISH	Targeted screen	Specific rearrangements	As required/indicated BCR::ABL1 RUNX1::RUNX1T1, CBFB::MYH11 PML::RARA KMT2A MECOM	14 (PML::RARA or BCR::ABL1 - 3)
EdinburghG	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	14
	FISH	Targeted screen	Specific rearrangements	KMT2A MECOM and others as required/indicated FAST FISH: MDS5, MDS7 and 3q26	14 (3 if urgent)
EdinburghMP	RT-PCR	Targeted screen	Specific rearrangements	BCR::ABL1 RUNX1::RUNX1T1 CBFB::MYH11 PML::RARA KMT2A::AFF1 KMT2A::AFDN KMT2A::MLLT1 KMT2A::MLLT3 KMT2A::ELL	3*
	PCR/FLA	Targeted screen	Specific rearrangements	FLT3 ITD & TKD NPM1	3*

	NGS_DNA	Targeted screen	Specific rearrangements	CBF Leukaemia only: KIT (exons 9, 11, 13, 17)	14
	NGS_DNA	Targeted screen	SNVs, indels	Myeloid NGS panel Panel (agreed whole gene / hot-spots)	42
	NGS_RNA	Targeted screen	Multiple rearrangements	Myeloid NGS panel Panel	42
Glasgow	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	7
	RT-PCR	Targeted screen	Specific rearrangements	BCR::ABL (quantitative and qualitative), RUNX1::RUNX1T1 CBFB::MYH11 inv (16) PML::RARA (qualitative) FLT3 ITD & TKD, NPM1	14
	Sanger	Targeted screen	Specific rearrangements	FLT3 (codon 835, 836)	14
	FISH	Targeted screen	Specific rearrangements	As required/indicated e.g. *BCR::ABL1* *RUNX1::RUNX1T1* *PML::RARA* *DEK::NUP214* *KMT2A* *KMT2A::AFF1* *KMT2A::MLLT3* *KMT2A::MLLT10* *KMT2A::MLLT1* *MECOM* *CBFB* Chr 5 and 7 (loss/deletion) *TP53*/17 centromere	3 (same day PML-RARA if received before 1pm)
	NGS_DNA	Targeted screen	SNVs, indels	Myeloid NGS panel Panel (agreed whole gene / hot-spots)	14

*refers to working days
NB Reporting times influenced by local clinical practice

Referral criteria

Morphologically or immunophenotypically identified acute myeloid leukaemia or likely AML

- Intensive-treatment eligible AML :
- Not fit for intensive treatment: FLT3 NPM1 G-banding and MLL MECOM/3q26 FISH as appropriate
- Relapse – in accordance with clinical requirements and diagnostic findings.

Myeloid NGS panel - All intensive treatment-eligible AML patients (<65).
Selected relapsed AML patients to provide therapeutic information.

Requesting specialties

- Haematology

ACUTE MYELOID LEUKAEMIA (AML)
REMISSION STATUS ASSESSMENT (MINIMAL RESIDUAL DISEASE, MRD)

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	qRT-PCR	Targeted screen	Specific rearrangement	BCR::ABL1 quantitation	21
Dundee	qRT-PCR (GeneXpert)	Targeted screen	Specific rearrangement	BCR::ABL1 quantitation	14
Edinburgh MP	RT-PCR	Targeted screen	Specific rearrangements	BCR::ABL1 [quantitative] RUNX1::RUNX1T1 [quantitative] PML::RARA [quantitative] CBFB::MYH11 [quantitative]	14
	RT-PCR	Targeted screen	Specific rearrangements	NPM1 (type A, B, D) [quantitative]	7 (3* post cycle 2)
Glasgow	qRT-PCR	Targeted screen	Specific rearrangements	BCR::ABL1 quantitation	14

*refers to working days
NB Reporting times influenced by local clinical practice

Referral criteria

First assessment

- Molecular analysis : PML::RARA, CBFB::MYH11, RUNX1::RUNX1T1, BCR::ABL1 fusion or NPM1 mutation (type A, B, D)
- Other abnormalities (e.g. KMT2A; uncommon NPM1 mutation – by arrangement/send away)

Subsequent assessments

- Molecular analysis : PML::RARA, CBFB::MYH11, RUNX1::RUNX1T1, BCR::ABL1 fusion or NPM1 mutation (type A, B, D)
- Other abnormalities (e.g. KMT2A; uncommon NPM1 mutation – by arrangement/send away)

Note – NGS is not routinely used for monitoring of remission status.

Requesting specialties

- Haematology

CHIMAERISM

Available testing

Centre	Method	Scope and range of test	Targets	TAT
Glasgow	PCR/FLA	STR pre-transplant assessment	Screening performed for 11 EuroChimerism STR markers	30
		Whole blood post-transplant chimerism Lineage-specific post-transplant chimerism	Informative markers as selected during pre-transplant assessment	14
	FISH	X/Y sex markers	X and Y chromosome	7

Referral criteria

- All patients and potential donors being considered for allogeneic stem cell transplant for any indication should be referred for STR pre-transplant assessment
- Whole blood post-transplant chimerism is performed at day 14-28 and then from Day 50 as required
- Lineage-specific post-transplant chimerism monitoring is performed for adult patients from Day 50 and for paediatric patients by request

Requesting specialties

- Haematology

CHRONIC LYMPHOCYTIC LEUKAEMIA (CLL)

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	FISH	Targeted screen	Specific rearrangements	TP53 IGH::CCND1 if requested	21
	NGS_DNA	Whole gene screen	SNVs, indels	TP53	21
Dundee	Array	Genomic screen	Large scale and targeted rearrangements	TP53, ATM, 13q14, trisomy 12. Any other relevant findings including CNN LOH	21
	Sanger	Whole gene screen	SNVs, indels	TP53	21
EdinburghG	FISH	Targeted screen	Specific rearrangements	TP53, ATM IGH::CCND1 if requested	21
EdinburghMP	Sanger	Whole gene screen	SNVs, indels	TP53 IGHV mutation status	21
Glasgow	FISH	Targeted screen	Specific rearrangements	TP53, ATM Differential diagnoses: TP53, ATM and *IGH::CCND1*, 13q14, 13q34, and 12 centromere	21
	NGS_DNA	Whole gene screen	SNVs, indels	TP53	28

NB Reporting times influenced by local clinical practice

Referral criteria

- Prior to treatment – Assessment of TP53 status (even if previously performed)
- IGH/CCND1 undertaken to aid in differential diagnoses

Requesting specialties

- Haematology

CHRONIC MYELOID LEUKAEMIA (CML)

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	14
	FISH	Targeted screen	Specific rearrangements	BCR::ABL1	3
	NGS_RNA	Targeted screen	Specific rearrangements	BCR::ABL1 (qualitative)	14
Dundee	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	14 (if urgent - 10)
	FISH	Targeted screen	Specific rearrangements	BCR::ABL1	3
	~~qRT-PCR (GeneXpert)~~	~~Targeted screen~~	~~Specific rearrangements~~	~~BCR::ABL1 (qualitative)~~	~~14~~
EdinburghG	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	14
	FISH	Targeted screen	Specific rearrangements	BCR::ABL1	3
EdinburghMP	RT-PCR	Targeted screen	Specific rearrangements	BCR::ABL1 (qualitative and quantitative)	3
Glasgow	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	21
	FISH	Targeted screen	Specific rearrangements	*BCR::ABL1*	7 (if urgent - 3)
	RT-PCR	Targeted screen	Specific rearrangements	*BCR::ABL1* (qualitative and quantitative)	14 (if urgent - 7)

NB Reporting times influenced by local clinical practice

Referral criteria

- Chronic Myeloid Leukaemia (CML) or suspected Chronic Myeloid Leukaemia. Molecular assessment will aid diagnosis or management (identify fusion variant for MRD).

Requesting specialties

- Haematology

CHRONIC MYELOID LEUKAEMIA (CML), MINIMAL RESIDUAL DISEASE (MRD)

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	qRT-PCR	Targeted screen	Specific rearrangement	BCR::ABL1 quantitation [E1A2 and E13A2/E14A2]	21
	Sanger	Targeted screen	SNVs, indels	BCR::ABL1 kinase domain mutation (KDM)	21
Dundee	qRT-PCR (GeneXpert)	Targeted screen	Specific rearrangement	BCR::ABL1 quantitation [E1A2 and E13A2/E14A2]	14
EdinburghMP	qRT-PCR	Targeted screen	Specific rearrangement	BCR::ABL1 quantitation [E1A2 and E13A2/E14A2]	14
	Sanger	Targeted screen	SNVs, indels	BCR::ABL1 kinase domain mutation (KDM)	21
Glasgow	qRT-PCR	Targeted screen	Specific rearrangement	*BCR::ABL1* quantitation [E1A2 and E13A2/E14A2]	14

NB Reporting times influenced by local clinical practice

Referral criteria

- MRD assessment to aid management.
- Clinically thought to have BCR-ABL1 TKD resistance mutations.

Requesting specialties

- Haematology

LEUKAEMIA, OTHER

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	21
	FISH	Targeted screen	Specific rearrangements	As indicated/required	7
	NGS_RNA	Targeted screen	Specific rearrangements	As indicated/required	14
Dundee	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	21
	FISH	Targeted screen	Specific rearrangements	As indicated/required	7
EdinburghG	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	21
	FISH	Targeted screen	Specific rearrangements	As indicated/required	7
Glasgow	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	21
	FISH	Targeted screen	Specific rearrangements	As indicated/required	7

Referral criteria

- Suspected acute leukaemia with clinical reasons to suspect translocation, or indication of likely translocation on karyotyping. Assessment will aid diagnosis or management.

Requesting specialties

- Haematology

LYMPHOMA/LYMPHOPROLIFERATIVE DISEASE

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	FISH	Targeted screen	Specific rearrangements	DLBCL: MYC with BCL2 and BCL6 where required.	21 (Burkitt- 14)
				Burkitt lymphoma: MYC with BCL2 and BCL6 where required.	
				Burkitt-like lymphoma (if MYC negative) : 11q23/q24/cen	
				Follicular lymphoma: BCL2	
				Mantle cell lymphoma : IGH::CCND1	
				Anaplastic large cell lymphoma (ALCL) : ALK, DUSP22::IRF4	
				MALT lymphoma: MALT1	
				T-PLL: TCL1	
	PCR/FLA	Targeted screen	Clonality studies	IgH, IgK PCR assay TCRG, TCRB PCR assay	21
	Real time-ASO PCR	Targeted screen	Specific variant	MYD88 (p.L265P) as requested	21
	Sanger	Targeted screen	Specific variant	Hairy cell leukaemia: BRAF (p.V600E)	21
Dundee	FISH	Targeted screen	Specific rearrangements	High Grade B cell MYC, IGH::MYC with BCL2 and BCL6 where required.	21 High grade/Burkitt MYC - 14
				Burkitt: MYC, IGH::MYC with BCL2 and BCL6 where required.	
				Follicular lymphoma: BCL2, IGH::BCL2	
				Mantle cell lymphoma: CCND1, IGH::CCND1	
				Anaplastic large cell lymphoma: ALK, DUSP22::IRF4	
				MALT: MALT1, IGH::MALT1, with BIRC3::MALT1, BCL6 if required	
				DLBCL: MYC, BCL2, BCL6, IGH::MYC, IGH::BCL2, IRF4::DUSP22 where required	
	PCR/FLA	Targeted screen	Clonality studies	IgH, IgK PCR assay TCRG, TCRB PCR assay	21
	Pyro	Targeted screen	Specific variant	Hairy cell leukaemia: BRAF (p.V600E)	21
EdinburghG	FISH	Targeted screen	Specific rearrangements	High-grade B Cell lymphoma : MYC - with BCL2, BCL6, IGH-MYC, IGH, IGK, IGL where required	14
				Burkitt-like lymphoma (if MYC negative) : 11q23/q24/cen	
				Follicular lymphoma : BCL2 (and BCL6 if requested)	
				Mantle cell lymphoma : IGH-CCND1	
				ALCL: ALK (if negative then DUSP22/IRF4 and/or TP63 on request)	
				MALT lymphoma : MALT1	
EdinburghMP	PCR/FLA	Targeted screen	Clonality studies	IGH IGK IGL clonality TCRB TCRG clonality [TCRD if appropriate]	14
	Real time AS-PCR	Targeted screen	Specific variant	MYD88 (p.L265P)	14
	Pyroseq	Targeted screen	Specific variant	Hairy cell leukaemia: BRAF (p.V600E)	14
Glasgow	Karyotype (if fresh	Genomic screen	Large scale rearrangements	All (within resolution of method)	28

	material available)				
	FISH	Targeted screen	Specific rearrangements	High grade lymphoma: MYC, *IGH::MYC*. If MYC rearranged, *IGH::BCL2* and *BCL6*	14 (MYC-3) 14 for NHL (if urgent - 3)
				Follicular lymphoma: *IGH::BCL2*. If *BCL2* not rearranged, *BCL6*	
				Mantle cell lymphoma IGH::CCND1	
				ALCL: ALK, DUSP22/IRF4	
				MALT lymphoma : MALT1. If MALT rearranged, *BIRC3::MALT1*	
				T-PLL: TCL1	
	PCR/FLA	Targeted screen	Clonality studies	IgH, IgK PCR assay TCRG, TCRB PCR assay	21
	Sanger	Targeted screen	Specific variant	MYD88 (p.L265P)	14

NB Reporting times influenced by local clinical practice

Referral criteria

- Investigations to aid diagnosis and classification of lymphoma / lymphoproliferative disorder.
    - G-banding [where bone marrow involvement has been confirmed]
    - IG and TCR clonality where required
    - Appropriate FISH and molecular assay depending on suspected disease sub type [see table]

Requesting specialties

- Haematology

MYELOMA

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	FISH	Targeted screen	Specific rearrangements	IGH::FGFR3 IGH::CCND1 (if requested) IGH::MAF IGH::MAFB TP53 CDKN2C CKS1B	21
Dundee	FISH	Targeted screen	Specific rearrangements	IGH::FGFR3 IGH::MAF IGH::MAFB CKS1B::CDKN2C D13S319::13q34 TP53	21
EdinburghG	FISH	Targeted screen	Specific rearrangements	IGH::FGFR3 IGH::MAF TP53 CKS1B and CDKN2C	21
Glasgow	FISH	Targeted screen	Specific rearrangements	*IGH::FGFR3* *IGH::MAF* *IGH::MAFB* IGH BAR *TP53* *CDKN2C and CKS1B* *ATM* *IGH::CCND1*	21

Referral criteria

- Transplant eligible only: FISH analysis on CD138+ plasma cells
- Patients with poor response to initial therapy (WoSCAN CMG guidelines)
- Patients in whom the treating clinician thinks it will alter therapy (WoSCAN CMG guidelines)

Requesting specialties

- Haematology

MYELOPROLIFERATIVE NEOPLASMS (MPN)

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	21
	FISH	Targeted screen	Specific rearrangements	FIPL1::PDGFRA PDGFRB	21
	NGS_RNA	Targeted screen	Specific rearrangements	FIPL1::PDGFRA PDGFRB FGFR1	21
	PCR/FLA	Targeted screen	Specific variants; SNVs, indels as indicated	Differential diagnoses: JAK2 p.(V617F) JAK2 (exon 12) CALR exon 9 insertions and deletions MPL p.(W515L)	21
	Real time-ASO PCR	Targeted screen	SNV	KIT D816V	21
	NGS_DNA	Targeted screen	SNV, indels	Myeloid NGS Panel (agreed whole gene / hot-spots	42
Dundee	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	21 (10 if urgent)
	Array	Genomic screen (Used if karyotype poor quality)	Large scale and targeted rearrangements	All (within resolution of method)	21
	FISH	Targeted screen	Specific rearrangements	FIPL1::PDGFRA PDGFRB	21
	PCR/FLA and Sanger	Targeted screen	Specific variants; SNVs, indels	JAK2 p.(V617F) JAK2 (exon12) CALR exon 9 insertions and deletions MPL exon 10 KIT p.D816V	21
EdinburghG	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	21
	FISH	Targeted screen	Specific rearrangements	BCR::ABL1 (if requested) Eosinophilia and Hypereosinophilia: FIPL1::PDGFRA PDGFRB FGFR1	21
EdinburghMP	RT AS-PCR	Targeted screen	Specific variants	KIT D816V	14
	RT AS-PCR	Targeted screen	Specific variants	JAK2 (V617F)	21
	High resolution melt analysis	Targeted screen	Specific variants; SNVs, indels	JAK2 exon 12 mutation MPL exon 10 p.(W515 and S505)	28
	PCR/FLA	Targeted screen	Specific variants; SNVs, indels	CALR exon 9 mutation	28
	Nested RT-PCR	Targeted screen	Specific rearrangements	FIP1L1::PDGFRA	14
Glasgow	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	21
	FISH	Targeted screen	Specific rearrangements	*BCR::ABL* if requested *FIP1L1::PDGFRA* *PDGFRB* *FGFR1*	7 (3 if urgent)

				20q deletion	
	PCR/FLA	Targeted screen	Specific variants; SNVs, indels	JAK2 p.(V617F) JAK2 (exon12) CALR exon 9 insertions and deletions MPL exon 10 p.(W515L)	21
	NGS_DNA	Targeted screen	SNVs, indels	Myeloid NGS panel Panel (agreed whole gene / hot-spots)	14

NB Reporting times influenced by local clinical practice

Referral criteria

- Myeloproliferative neoplasm (MPN) or suspected Myeloproliferative Neoplasm. Molecular assessment will aid diagnosis or management.
- For extended Myeloid NGS panel: Atypical MPNs (triple negative PMF phenotype, MDS/MPN overlap). Molecular assessment will aid diagnosis or management.

Requesting specialties

- Haematology

MYELODYSPLASTIC SYNDROME

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	21
	FISH	Targeted screen	Specific rearrangements	monosomy 5/5q- monosomy 7/7q- TP53 (on 5q- syndrome) others as required	21
	NGS_DNA	Whole gene screen	SNVs, indels	TP53 (5q- syndrome)	21
	NGS_DNA	Targeted screen	SNV, indels	Myeloid NGS Panel (agreed whole gene / hot-spots	42
Dundee	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	21
	Array	Genomic screen (Used if karyotype poor quality)	Large scale and targeted rearrangements	All (within resolution of method)	21
	FISH	Targeted screen	Specific rearrangements	monosomy 5/5q- monosomy 7/7q- TP53 (on 5q- syndrome) others as required	21
	Sanger	Whole gene screen	SNVs, indels	TP53 (5q- syndrome)	21
EdinburghG	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	21
	FISH	Targeted screen	Specific rearrangements	High risk MDS patients: monosomy 5/5q- monosomy 7/7q- EVI1 (3q26) TP53 (on 5q- syndrome)	21 (3 – HR MDS)
EdinburghMP	NGS_DNA	Targeted screen	SNVs, indels	Myeloid NGS panel Panel (agreed whole gene / hot-spots)	42
	NGS_RNA	Targeted screen	Multiple rearrangements	Myeloid NGS panel Panel (agreed fusion panel)	42
Glasgow	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	21
	FISH	Targeted screen	Specific rearrangements	monosomy 5/5q- monosomy 7/7q- TP53 (on 5q- syndrome) 20q , and others as required	3
	NGS_DNA	Targeted screen	SNVs, indels	Myeloid NGS panel Panel (agreed whole gene / hot-spots)	14

NB Reporting times influenced by local clinical practice

Referral criteria

- Known or suspected / high risk for the development of myelodysplasia. Assessment will aid diagnosis or management.
- Myeloid NGS panel: All transplant-eligible MDS patients (both low- and high-risk patient cohorts)(<65) / For differentiation of hypoplastic MDS/aplastic anaemia.

Requesting specialties

- Haemataology

PRIMARY MYELOFIBROSIS (under 70Years)

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	21
	PCR/FLA	Targeted screen	Specific variants; SNVs, indels	MPD: JAK2 p.V617F CALR exon 9 MPL exon 10 p.(W515L)	21
	NGS_DNA	Targeted screen	SNV, indels	Myeloid NGS Panel (agreed whole gene / hot-spots	28
Dundee	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	21
	PCR/FLA / Sanger	Targeted screen	Specific variants; SNVs, indels	JAK2 p.V617F CALR exon 9 insertions and deletions MPL exon 10	21
EdinburghG	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	21
EdinburghMP	Real time AS-PCR	Targeted screen	Specific variants; SNV, indels	JAK2 p.(V617F)	21
	High resolution melt analysis	Targeted screen	Specific variants; SNVs, indels	CALR exon 9 MPL exon 10 p.(W515 and S505)	28
	PCR/FLA	Targeted screen	Specific variants; SNVs, indels	CALR exon 9	28
	NGS_DNA	Targeted screen	SNV, indels	Myeloid NGS Panel (agreed whole gene / hot-spots	42
	NGS_RNA	Targeted screen	Multiple rearrangements	Myeloid NGS Panel	42
Glasgow	Karyotype	Genomic screen	Large scale rearrangements	All (within resolution of method)	21
	PCR/FLA	Targeted screen	Specific variants; SNVs, indels	MPD: JAK2 p.V617F CALR exon 9 MPL exon 10 p.(W515)	21
	NGS_DNA	Targeted screen	SNVs, indels	Myeloid NGS panel Panel (agreed whole gene / hot-spots)	14

NB Reporting times influenced by local clinical practice

Referral criteria

- Primary Myelofibrosis (PMF) or suspected PMF. Assessment will aid diagnosis or management.
- Myeloid NGS panel: All transplant-eligible patients with PMF (<65)

Requesting specialties

- Haematology

PHARMACOGENOMIC TESTING

DIHYDROPYRIMIDINE DEHYDROGENASE DEFICIENCY (DPYD)

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Targeted screen	Specific SNVs	*c.1236G>A/HapB3 c.1679T>G c.1905+1G>A c.2846A>T	14
Dundee	Real-Time PCR	Targeted screen	Specific SNVs	*c.1236G>/HapB3 c.1679T>G c.1905+1G>A c.2846A>T	14
EdinburghMP	PCR/FLA	Targeted screen	Specific SNVs	*c.1236G>/HapB3 c.1679T>G c.1905+1G>A c.2846A>T	14
Glasgow	PCR/FLA	Targeted screen	Specific SNVs	*c.1236G>/HapB3 c.1679T>G c.1905+1G>A c.2846A>T	14

*c.1236G>A may be reported as c.1129-5923C>G (HapB3 – in linkage disequilibrium)

Referral criteria

- Patients potentially receiving fluoropyrimidine treatment

Requesting specialties

- Oncology

THIOPURINE S-METHYLTRANSFERASE (TPMT) DEFICIENCY

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	PCR/FLA	Targeted screen	Specific SNVs	c.238G>C c.460G>A c.719A>G	14
Dundee	Real-Time PCR	Targeted screen	Specific SNVs	c.238G>C c.460G>A c.719A>G	14

Referral criteria

- Patients potentially receiving thiopurine treatment.
- Patients with chronic inflammatory and autoimmune conditions, leukaemia and who may be subject to post-transplant rejection.

Requesting specialties

- Oncology
- Gastroenterology
- Haematology

UDP-GLUCURONOSYLTRANSFERASE 1A1 (UGT1A1) DEFICIENCY

Dundee	Real-Time PCR	Targeted screen	Specific SNV	UGT1A1*28 (UGT1A1 c.-41_40dupTA)	14

- Patients potentially receiving irinotecan treatment

ASTHMA ß2-ADRENERGIC RECEPTOR (ADRB2) p.(Gly16Arg) GENOTYPING

Dundee	Real-Time PCR	Targeted screen	Specific SNV	*ADRB2* p.(Gly16Arg)	14

- Asthma patient who may be using or about to be prescribed long acting B2 agonist therapy.
- Some evidence to suggest that homozygotes for arginine at codon 16 (*ADRB2* p.(Arg16Arg)) may not benefit from long acting B2 agonist therapy

Requesting specialties

- Clinical Genetics
- Respiratory

AMINOGLYCOSIDE RELATED DEAFNESS MT-RNR1 M.1555A>G GENOTYPING

Available testing

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Targeted screen	SNV	MT-RNR1 m.1555A>G	5

Referral criteria

Significant exposure to aminoglycosides posing risk of ototoxicity.
This indication would be relevant to:

1. Individuals in whom aminoglycoside therapy may be required
2. Individuals who have been exposed to aminoglycosides in whom mt.1555A>G status needs to be determined because of concern regarding hearing loss

Requesting specialties

- Clinical Genetics
- Any specialty considering aminoglycoside treatment