NHS
South West
Genomic Laboratory Hub

The SW GLH genomic testing service for Haematological Malignancies:

A guide for Clinical Haematologists

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Revision history

Version	Date	Author	Summary of changes

Approved by

This document must be approved by the following people

Name	Signature	Title	Date	Version
Prof Rachel Butler		Operations Director SWGLH		3.0
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1. Introduction

- The South West Genomic Laboratory Hub (SWGLH) was established alongside six other national GLHs in 2018 to drive the standardisation and rapid uptake of new genomic services and technologies and to ensure equity of patient access.

- The SWGLH aims to deliver genomic and genomic analyses for all patients with cancer and rare disease across the SW region.

- The SWGLH is a centralised service that is a partnership between North Bristol NHS Trust (NBT) and the Royal Devon and Exeter NHS Foundation. All cancer genomic services will be delivered from NBT.

This document for NHS clinical haematology services aims to facilitate access to the SWGLH genomic testing for haematological malignancies affecting the bone marrow and for lymphoma.

2. What genomic test technologies for haematological malignancies are available at the SWGLH?

- The indications and test technologies for the SWGLH genomic testing service are defined in a National Genomic Test Directory (NGTD) that is available at https://www.england.nhs.uk/publication/national-genomic-test- /

- For many haematological malignancies, the current NGTD identifies several alternative test technologies that yield similar diagnostic information. SW regional policy about the optimum subsets of tests for each haematological malignancy indication is currently being devised by the SW GLH in partnership with the haematological cancer CAG's, through a series of working groups.

- The NGTD will be regularly updated through an expert peer review process based on advances in best clinical practice. We anticipate future expansion of the NGTD to include additional genes relevant to haematological malignancies. SW regional policy about test adoption will occur in parallel with this process.

Karyotyping, FISH and direct mutation tests

- For many haematological malignancies, karyotypes, FISH panels for gene fusions and/or single gene testing remain the best approach. These services will continue to be available through the SWGLH with unchanged turn-around times.

Gene panel analyses

- The NGTD recommends gene panel analysis for many haematological malignancies for which panel testing is already part of standard care. These tests will continue to be provided by the SWGLH.

- The NGTD also recommends gene panel analysis for new indications such as lymphoma, where gene panel analysis is not currently standard of care. Gene panel analysis will be offered by the SWGLH if the SWGLH/CAG working groups consider gene panels to have better clinical utility than current standard care tests for these indications.

- The SWGLH will progressively implement a new large gene panel platform comprising approximately 500 genes (TSO500 panel) for all cancer panel indications, including those for haematological malignancy.

- **For each haematological malignancy indication, only genes that influence current standard clinical care, or that inform eligibility or stratification in clinical trials will be analysed and reported back to the clinical team.** The selection of which genes will be analysed for each haematological malignancy type is currently being determined through national discussions between SWGLH and clinical experts and will be reviewed on an ongoing basis.

Whole genome sequencing

- All acute leukaemia (AML, ALL and ALAL) in both children and adults is eligible for WGS and will be available through the SWGLH from 2020.

- In order to ensure timely return of clinically actionable genomic test results, standard of care testing will be performed on these samples in parallel with WGS. Dual testing will be reviewed as turnaround times for the national WGS service matures.

3. Which haematological malignancies are eligible for analysis?

- Diagnostic genomic testing for haematological malignancies at first presentation or at relapse and sequential testing for longitudinal monitoring (e.g. BCR-ABL1 in CML), for indications that are specified in the NGTD.

4. What samples are required for the new testing service?

4.1. Haematological malignancies affecting bone marrow

- For the direct mutation and gene panel tests, the best sample is bone marrow aspirate collected into EDTA.

- For the karyotype and FISH, the best sample is bone marrow aspirate collected into lithium heparin or heparinised media.

- For the WGS service for acute leukaemia and haematological malignancy in children (aged ≤19 years), the best sample for somatic WGS is bone marrow aspirate collected into EDTA. The best sample for germline WGS is a punch skin biopsy sent unfixed. More details about the WGS service is provided in the SW GLH guideline *'Sample collection for the acute leukaemia Whole Genome Sequencing: Guidance for clinical haematology services'.*

- Peripheral blood is an alternative to marrow aspirate for acute leukaemia with a high circulating blast count and where taking bone marrow samples is inappropriate. Pleural fluid or other tissue with significant malignant infiltrate may also be suitable but should be discussed directly with the SWGLH.

4.2. Lymphoma and lymphoproliferative disorders not affecting the bone marrow

- For lymphoma and other lymphoproliferative disorders without BM involvement, gene panel and direct mutation tests will be performed on FFPE samples obtained at biopsy or surgical resection or from cytology samples.

- For the gene panel analyses, the new panel technology offered by the SWGLH requires some small changes in the way that tissue samples are processed. These are described in more detail in the SW GLH guideline '*The SW GLH genomic testing service for solid tumours: A guide for Cellular Pathologists'.*

- A pathologist's assessment of lymphoma tissue samples is essential to ensure that sufficient neoplastic cells are present for genomic analysis. If the SWGLH does not receive a sufficient sample for complete genomic analysis a single tumour-specific test may need to be prioritised.

- Other sources of tissue such as fine needle aspirate, csf or pleural fluid may be suitable for testing is they contain sufficient tumour material. Clinicians are invited to discuss with the SW GLH.

4.3 Longitudinal monitoring of haematological malignancy

- Peripheral blood or bone marrow aspirate collected into in EDTA is the preferred is the best sample for longitudinal monitoring.

- Samples must be transported rapidly to ensure arrival at the laboratory within 72 hours of collection to facilitate RNA extraction.

5. How can cancer genomic tests be requested?

- Tests for haematological malignancy should be requested using Bristol haematology-Oncology Diagnostic Service request form <insert link to BHODs request form vs 6>.

- For all haematological malignancy genomic tests other than the WGS indications, the SWGLH does not currently require confirmation of patient consent for testing. Clinicians are advised to follow host Trust consent policy.

- **To ensure clinically acceptable test turnaround times, it is essential that genomic test requests are initiated as early in the patient pathway as possible and that samples are transported to the SWGLH using the rapid transport routes that have been established from all SW Trusts.** Further information about sample transport has been given to the local Pathology teams at each Trust. Transport arrangements for samples are described in <Insert link to transport document>.

6. How will test results be reported?

- The SWGLH will issue a genomic report containing the results only for those genes that are clinically relevant for the specific haematological malignancy tested. A clinical interpretation will also be given for standard of care (NICE approved) treatments.

- To ensure rapid communication, genomic test reports will be issued by expert Clinical Scientists at the SWGLH

- The preferred route for return of results is via SIHMDS integrated diagnostic reporting software such as HILIS. If clinical haematology teams do not have access to this service, then results will be issued via an email addressed to members of the clinical team identified on the test request form, preferably via a generic, continuously monitored email address. Improved reporting through

electronic distribution direct to local Pathology systems is currently being developed by the SWGLH.

- For the infrequent cases that require further discussion, genomic test results will be discussed at a weekly SW GLH Genomics Tumour Advisory Board (GTAB), held by Webex. The GTAB will be open to the haematology clinical team and will also include a pathologist and a clinical scientist. The referring clinical team will be notified that their case is being discussed. The forum is also open for local teams to bring any reported cases for discussion. The GTAB is intended to discuss cases rapidly after completion of laboratory analyses.

- Clinicians and Pathologists may request analysis of other genes from the 500-gene panel that are not part of the core group assessed for that tumour type, in discussion with the SW GLH team.

7. What will be the turnaround time for genomic tests?

- The SWGLH will continue to maintain current TATs for different haematological malignancies and points in the clinical care pathway. As a guide these are as follows:
    - PML-RARA <24 hours
    - BCR-ABL1 PCR, ALL FISH <3 days
    - Urgent karyotype/FISH <7 days
    - Urgent panel, simple targeted mutation tests, CML monitoring <14 days
    - Routine karyotype, FISH, panel <21 days

- These targets may be refined as a result of the ongoing review of testing standards by the SWGLH/CAG working groups and NHSE.

- To enable rapid turnaround times, it is critical that decisions to request genomic testing and transport of tissue samples to the SW GLH occurs as rapidly as possible after sample collection.

8. How will tests be funded?

- The genomic and genomic analysis of cancer samples specified in the NGTD will be funded centrally by NHSE from April 2020. The existing funding for these services is currently being calculated and will be removed from local budgets.

- Genomic laboratory testing outside the NGTD will not be centrally funded. However, some of these tests may be available at the SW GLH. Please contact us if there is a test that you are interested in.

9. Where can more information be found?

For further information about these new and exciting services, or for feedback, please contact:

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