Genomics Education Programme

NHS
Health Education England

Clinician's guide for requesting whole genome sequencing: cancer

Introduction

This guide has been developed to support clinicians who will be requesting whole genome sequencing (WGS) for patients with cancer. The guide highlights key points to cover during conversation(s) with patients about WGS and contributing to the National Genomic Research Library (NGRL), based on the statements in the record of discussion (RoD) form.

SEE PAGE 2...
... for a handy pre-appointment checklist

Further information to support this guide can be found at www.genomicseducation.hee.nhs.uk/supporting-the-nhs-genomic-medicine-service/.

Key points to cover when discussing clinical WGS

Introduction and context of the test

- Primary aim of WGS is to provide additional information regarding cancer diagnosis and potentially inform treatment decisions.
- Sequencing the whole genome will take place, although analysis will focus on gene panels (known genes associated with cancer prognosis, treatment, or underlying predisposition).

Results

- Test may not yield any significant findings.
- Any results may or may not affect treatment plan, or provide insight to prognosis.
- Interpretation and knowledge about results may change over time.
- Somatic variants: exclusive to cancer and not heritable.
- Germline variants: rare; may indicate an underlying predisposition to cancer and other health issues. Some of these findings may be uncertain and require future follow-up.
- Incidental findings: rare; unexpected results not related to reason for test may be found.
- Results will not inform all health conditions (currently no additional looked-for findings).
- Confirm approximate timeline for results and communication process (how any results are fed back, by whom, and with whom they would be shared).

Implications for the patient

- Potential therapeutic indications including clinical trials.
- Onward referrals may be made for screening or management based on results.
- Potential psychosocial impact of receiving results and support available.
- Implications for family planning and reproductive choices.
- Association of British Insurers' code for disclosing genetic test results vs medical/family history.

Implications for family members

- Opportunities based on germline results or family history where relatives could have access to preventative screening, predictive testing, and/or information about reproductive choices.
- Discuss the importance of sharing results with family members if a germline variant is found, as it may impact blood relatives, and strategies that may be used (such as 'To whom it may concern' letter).

Use of samples

- Samples taken from cancer and germline (i.e. blood, skin biopsy) for comparison.
- DNA from solid tumour, or from germline samples from liquid cancers, is not always good enough quality to obtain a result.
- Samples stored and accessed within the Genomic Laboratory Hub, other local labs (such as pathology) and other labs within the NHS Genomic Medicine Service.
- Stored samples can be used for further genomic tests with appropriate consent.
- Germline sample can be used as a control for testing others, including relatives.
- De-identified samples may be used for lab test development or quality control procedures.

Use of data

- Data includes patient's health and genomic information, which can be securely accessed on an ongoing basis by NHS healthcare professionals.
- National (identifiable) and international (not identifiable) comparison of data for greater understanding of significance of any results found.
- Genetic variant(s) may be shared (with limited identifiers) for relatives to access testing.
- Genomic data may be reanalysed in future as new evidence can occasionally change results.

Key points to cover when discussing the NGRL

Introduction and context

- The NGRL is a collection of data from patients that can be accessed by researchers.
- Aim and potential benefits of having a large dataset and access to research to improve diagnostic potential of genomic information.
- Patient can request to withdraw from the NGRL at any time, either partially (no future contact) or fully (no future data use) at any time.

Implications for the patient

- Individuals would be giving permission to Genomics England to manage access to their health and genomic data.
- Each individual may or may not benefit, but increases the chance of a diagnosis in future.
- Wider benefits of learning more about cancers to guide management.
- Individuals may be re-contacted for further information, regarding new findings, other clinical trials or other research.

Use of samples

- Genomics England can access DNA as well as additional tissue/other samples stored in the NHS if this would not otherwise affect clinical care.
- Samples are held securely within the UK and not sent outside without explicit consent.
- Patient may be invited to donate additional samples for research.

Use of data

- Data and samples will have name, contact and other personal identifiers removed.
- Data includes genomic information as well as other health and social care records.
- Controlled, read-only access by approved researchers both in and outside of the UK including not-for-profit and commercial (for-profit) organisations.

PRE-APPOINTMENT CHECKLIST

- **Is your patient eligible for WGS?**
  Check the National Genomic Test Directory (www.bit.ly/NatGenTests), which specifies which patients may be offered a whole genome sequencing test. If you need advice, you may wish to discuss with your local GLH.
- **Do you have the forms you need?**
  A WGS order form must be completed with relevant clinical and pathology information about the patient's cancer. There are also nationally standardised RoD forms to record each individual's choices to have clinical WGS and take part in the NGRL:

	Individuals aged 16+ years with capacity	Children (less than 16 years)	Adults without capacity)	Individuals who are deceased
Clinical test	RoD reviewed with individual	RoD reviewed with parent/guardian	RoD reviewed with person acting in best interests of the patient	RoD reviewed with appropriate relative
NGRL	The research choice is captured within the RoD. There is an additional 'Participation in the NGRL' form to note the individual's choice if this was not made at time when the clinical test was discussed.			
	No additional forms	OPTIONAL assent form signed by child	MANDATORY form signed by consultee	No additional forms

Notes: For results to be released to the GLH, an RoD must be received for each individual undergoing WGS. The process may be adapted for local needs, so do check with your GLH.
When recording patient choices in exceptional circumstances:

- If the RoD is not submitted when WGS is requested but discussions have taken place, the 'Form to follow' box can be selected at the bottom of the WGS order form. An RoD form is required before results can be released.
- Where patient's choices have been obtained through phone or video consultation, the clinician may sign the RoD and note that the patient has agreed to this remotely. This should be recorded in their notes, and a copy of the form sent to the patient.
- Where it may not be possible for the patient to provide consent, the clinician may decide to proceed with clinical WGS in patient's best interests. This should be noted on the RoD form and an appropriate record kept locally of the basis of this decision.

Additional points to consider

- The patient may decide to not proceed with the clinical test and/or research offer, or may wish to have more time to consider following the initial discussion.
- You may wish to draw on or refer for additional support from your clinical genetics service, for further discussion about inherited predisposition to cancer and/or where there are complex social, family communication or ethical issues related to this.
- Patient information has been developed by Genomics England, NHS England and NHS Improvement, and charities to support your discussions. Additional materials and support may be required for patients who are non-English speaking, hearing impaired, visually impaired, or have learning disabilities.