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) to facilitate consent.

Further information to support the guides can be found at www.genomicseducation.hee.nhs.uk.

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

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.
- Uncertainty of genomic information: 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.
- Germline variant(s) may be shared for relatives to access testing (limited identifiers to process test); medical information will not be shared with relatives.
- 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

- National Genomic Research Library: 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

- Wider benefits of learning more about cancers to guide management, where any new significant findings will be shared with the NHS.
- Individuals may be re-contacted for further information, regarding new findings, other clinical trials or other research.

Use of samples

- Samples can be sent to approved organisations within and outside of the UK for research.
- 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.
- **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. As well as an order form, patient choice forms are required to record each individual (patient and relative)'s choices to consent to WGS and the NGRL:

	Individuals aged 16+ years with capacity	Children (less than 16 years)	Patient representative /consultee (for adults without capacity)	Deceased
Clinical test	RoD signed by individual	RoD signed by parent/guardian	RoD signed by person acting in best interests of patient	RoD signed by appropriate relative
NGRL	Research choice captured within RoD; additional form to note choice about NGRL if not made at time of clinical test discussion			
	No additional forms	OPTIONAL Assent form signed by child	MANDATORY Consultee form signed by consultee	No additional forms

Note: The process of requesting WGS may be adapted for local needs, so please make sure you have checked with your Genomics Laboratory Hub, which can assist with queries about submitting patient clinical information, which family members to include, and ensuring you have the correct forms.

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.
- Consider referral for genetic counselling for further discussion about inherited predisposition to cancer, and/or where there may be family communication barriers related to this.
- If the patient is deemed to not have capacity to consent, a parent, guardian, or other person representing the patient's interests should be available. Where possible, the patient should be involved to provide assent.
- Additional materials/support may be required for patients who are non-English speaking, hearing impaired, visually impaired, or have learning disabilities.
- Further resources may be informative and/or supportive for patients (such as NHS Choices, Macmillan).