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Developing effective ctDNA testing services for lung cancer

Executive summary

September 2017

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Acknowledgements:

The PHG Foundation is grateful for the contributions of consultees and the speakers and participants of a workshop held on 7th March 2017. While their contribution has been invaluable, the responsibility for the content and analysis in the report rests with the authors.

NHS
National Institute for Health Research

NIHR Cambridge Biomedical Research Centre

NB: URLs in this report were correct as at 31 July

This report can be downloaded from our website:
www.phgfoundation.org

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How to reference this report:

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PHG Foundation (2017)
ISBN: 978-1-907198-28-1

1. Executive summary

Personalised medicine – a revolution in cancer care?

The era of personalised medicine is upon us, but amid all the promise, and the hype, what does this mean for patients? For patients with cancer, personalised medicine can mean monitoring or clinical intervention based on family history or evidence of inherited susceptibility mutations, or it could mean a therapy that targets tumours with specific genetic mutations. For a sub-set of patients with non-small cell lung cancer (NSCLC) a group of drugs called tyrosine kinase inhibitors (TKIs) treat tumours with mutations in the *EGFR* gene. These patients require a genetic test in order for the clinician to prescribe the therapy. Due to the challenges associated with carrying out a biopsy to collect a solid tumour sample for testing, many patients miss out on genetic testing. In patients for whom biopsies are possible approximately 30% of biopsies fail or do not yield enough material for a genetic test.

Circulating tumour (ct) DNA testing – a pioneering technology to meet clinical need

A new genomic technology, circulating tumour DNA testing, can bridge the gap for these patients. ctDNA testing analyses patient blood samples for mutations in the fragments of tumour DNA found in the circulation. This non-invasive biopsy method has advantages in terms of accessibility and ease of use, allowing patients who would not have received a genetic test from a solid biopsy the chance to have a test carried out using another method.

While there are still technological challenges to overcome in terms of the use of ctDNA technologies, the evidence from clinical trials, combined with the availability of targeted therapies, has been sufficient to see the adoption of ctDNA testing within a small number of NHS laboratories in the UK. Testing is currently used at diagnosis, to determine if a patient's tumour has mutations in *EGFR*, and at progression, to determine if resistance to therapy is caused by an additional mutation in *EGFR* called p.T790M, for which a second line TKI is available.

ctDNA testing is already benefiting some patients with NSCLC; however, this technology is not in widespread use throughout the NHS and not all eligible patients receive testing. The question is how this technology might be delivered in the most effective and equitable way across the health system to ensure that every eligible NSCLC patient receives a ctDNA test as appropriate to their care.

How can the health system maximise the impact of ctDNA testing for NSCLC patients?

A multidisciplinary workshop was held on 7th March 2017 to investigate the current position of NHS ctDNA services for NSCLC patients, with participation from key experts including NHS clinical scientists, clinicians and the commercial sector.

The discussions at the workshop informed the content of this report, which describes the early experiences of some of the laboratories that have pioneered the introduction of this testing into the NHS. It outlines the steps that stakeholders, both internal and external to the health system, will need to take to maximise the impact of this technology for lung cancer patients. Finally, details are provided on emerging possibilities to applying this technology across the care pathways for the management of advanced lung cancer and other cancers.

The workshop also focused on what needs to be done to strengthen and support implementation, improve quality of testing and ensure that more patients receive testing. The key findings are that:

The NHS should consider offering ctDNA testing of *EGFR* in lung cancer to all eligible patients. The evidence of clinical utility demonstrates that ctDNA testing makes a difference to patients, increasing accessibility to targeted therapies. While some improvements are needed to laboratory techniques, these are not a barrier to adoption, since the alternative is that patients miss out on testing, and therefore some will not receive appropriate targeted therapy, which has been assessed as cost-effective treatment for NHS use.

The NHS should use existing ctDNA testing to maximise access to TKIs. To do this, we recommend that the health system support existing services – ctDNA testing at diagnosis and for p.T790M – and establish current services as centres of excellence for ctDNA testing in lung cancer. Clinical guidelines from NICE, or developed by the clinical community, are crucial for raising awareness and providing reassurance to clinicians that these tests have clinical utility and benefit patients. Ongoing NHS service evaluations will provide critical evidence to support wider NHS implementation.

There are lessons that can be learned from existing ctDNA services that will support the wider use of ctDNA tests in future. The laboratory case studies presented demonstrate that there are different paths to take in terms of test development and delivery, which are affected by the resources and infrastructure available in each laboratory. The meeting highlighted the importance of ongoing external quality assurance efforts, which will provide benchmarks on the quality of testing services. Active engagement efforts to inform the health system about ctDNA testing are effective, as demonstrated by the example of the All Wales Medical Genetics Service, but require the laboratories to invest time and resource. Further efforts such as these will be required, however, to improve further engagement within the health system.

Recommendations to support the development of effective ctDNA testing services

Evidence from early adopters of ctDNA technology revealed that whilst testing benefits NSCLC patients in terms of accessing the most appropriate treatment, there are issues that need to be addressed in order to support the implementation of comprehensive, effective and equitable ctDNA testing for NSCLC. Based on the findings, we make seven recommendations to meet these challenges. Establishing a solid foundation now in terms of service development and delivery will be an investment for the future, when more uses of this technology are likely to become available.

- Healthcare commissioners should formally consider the provision of ctDNA services in lung cancer and improve and strengthen current service provision
- Ongoing service evaluation is required to ensure that the health system has the appropriate information for further implementation
- Laboratory websites should include up-to-date and clear electronic referral information and resources, including testing information, costs and logistics
- Engagement about ctDNA testing can take place within the multidisciplinary team (MDT) – ideally via an individual who can act as a point of contact for queries and information. This person could be a clinician, clinical scientist or a pathologist
- Clinical guidelines on the use of ctDNA testing in NSCLC should be developed
- Service establishment and validation should be supported, by and within the health system, by promotion of available funding, promotion of test funding structures, linking of test development into accelerated access of technologies and support of collaborative test development
- NHS England should consider how patients can have improved access to funded targeted therapies and take steps through policy development to ensure that the health system is better prepared to implement targeted therapies when commissioned

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About the PHG Foundation

The PHG Foundation is a pioneering independent think-tank with a special focus on genomics and other emerging health technologies that can provide more accurate and effective personalised medicine. Our mission is to make science work for health. Established in 1997 as the founding UK centre for public health genomics, we are now an acknowledged world leader in the effective and responsible translation and application of genomic technologies for health.

We create robust policy solutions to problems and barriers relating to implementation of science in health services, and provide knowledge, evidence and ideas to stimulate and direct well-informed discussion and debate on the potential and pitfalls of key biomedical developments, and to inform and educate stakeholders. We also provide expert research, analysis, health services planning and consultancy services for governments, health systems, and other non-profit organisations.

ISBN: 978-1-907198-28-1

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