Roche

The Liquid Experience:

From Research to Reality

What have we learnt from the lung liquid biopsy pilots in England and Wales?

Stakeholder group chaired by Professor Alastair Greystoke, Professor of Precision Oncology, Newcastle

FOREWORD BY PROFESSOR SANJAY POPAT

Redefining lung cancer together

The development of this report was supported by Roche Products Ltd, who have funded meetings, medical writing support and co-creation of this report with a stakeholder group of healthcare professionals.

CONTRIBUTORS AND ACKNOWLEDGEMENTS

Developed in collaboration with a steering group of clinical and scientific experts, this report represents the liquid biopsy experience to date in four regions of England and Wales, from programmes such as the NHS England circulating tumour DNA (ctDNA) pilot, Welsh QuicDNA study and Roche's Healthcare Evaluation of the Liquid Pathway (HELP) programme.

Following an initial scoping meeting with the steering group, which included regional representatives Professor Alastair Greystoke, Dr Pooja Bhatnagar, Dr Magdalena Meissner and Dr Helen Winter, small-group virtual meetings were held with representatives from each region to share experience, learnings and insights. A roundtable meeting, chaired by Professor Greystoke, was then held in London to agree the content, structure and narrative; the content of this report has been reviewed and approved by the stakeholder group.

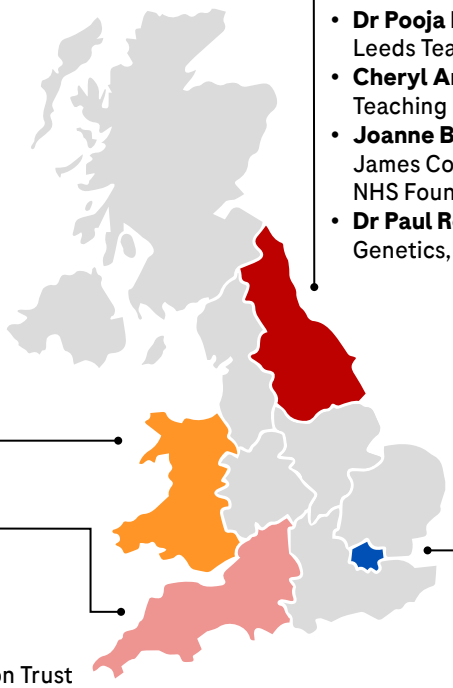
Importantly, this report does not focus on, or endorse, any specific test or treatments, but shares practical learnings to optimise the use of liquid biopsy for patients with advanced lung cancer. We understand regional differences mean that optimal implementation processes will vary between Trusts.

North East England

- **Professor Alastair Greystoke (Group Chair)** – Professor of Precision Oncology, Honorary Consultant in Medical Oncology, Newcastle
- **Dr Pooja Bhatnagar** – Consultant Clinical Oncologist, Leeds Teaching Hospitals NHS Trust
- **Cheryl Armstrong** – Clinical Nurse Specialist, Leeds Teaching Hospitals NHS Trust
- **Joanne Barnett** – Lung Cancer Specialist Nurse, The James Cook University Hospital, South Tees Hospitals NHS Foundation Trust
- **Dr Paul Roberts** – Principal Scientist, Molecular Genetics, Leeds Teaching Hospitals NHS Trust

Wales

- **Dr Magdalena Meissner** – Consultant Medical Oncologist, Clinical Liquid Biopsy Lead for All Wales Genomic Services, Cardiff
- **Dr Sian Morgan** – Consultant Clinical Scientist and Laboratory Director for All Wales Medical Genomics Service, NHS Wales



London

- **Paul Ryves** – Programme Director, North Thames Genomic Medicine Service Alliance
- **Professor Sanjay Popat** – Consultant Thoracic Medical Oncologist, The Royal Marsden Hospital, London
- **Dr Adam Januszewski** – Consultant Medical Oncologist, The Barts Thorax Centre, St Bartholomew's Hospital, London

South West England

- **Dr Louise Medley** – Consultant Medical Oncologist, Torbay and South Devon NHS Foundation Trust
- **Dr Henry Steer** – Respiratory Physician, Gloucestershire Hospitals NHS Foundation Trust
- **Dr Helen Winter** – Medical Oncologist, Bristol Cancer Institute and Clinical Director, Somerset, Wiltshire, Avon and Gloucestershire (SWAG) Cancer Alliance
- **Ms Debbie Farn** – Clinical Nurse Specialist, Torbay and South Devon NHS Foundation Trust
- **Mr Alex Murrell** – Genomics Navigator, Torbay and South Devon NHS Foundation Trust
- **Siobhan Taylor** – Molecular Pathology Lead / Clinical Scientist, Gloucestershire Hospitals NHS Foundation Trust

Acknowledgements: We would like to acknowledge the patients and families who have participated in the pilot and studies; the lung clinical nurse specialist (CNS) teams and phlebotomy services in our centres; our respiratory team colleagues; and third sector community groups who continue to support healthcare equity.

Funding: The development of this publication has been organised and funded by Roche Products Ltd. The contributors listed above have received an honorarium for the activity.

EXECUTIVE SUMMARY

Liquid biopsy offers an exciting opportunity for patients and clinical teams, with the potential to significantly reduce time-to-treatment and optimise care for patients with non-small cell lung cancer (NSCLC) with and without actionable driver mutations.[1] Importantly, this technology can help us address national healthcare inequalities by ensuring all eligible patients have access to molecular testing. However, much of the experience with liquid biopsy to date has been confined to the NHS pilots and studies.[2,3] Our report shares experiences from England and Wales to help others embed this service into routine clinical practice, for when liquid biopsies are widely available within the NHS. The key points are summarised below:

Patient identification

- Liquid biopsy should be offered to all eligible patients with suspected Stage III or IV NSCLC, or as defined by local / national guidelines; hospitals need clear guidance to ensure all potential patients are identified, including emergency admissions
- Patients should be identified by a member of the diagnostic team, which may include either lung cancer nurses or respiratory physicians
- Consent can be obtained verbally when discussing the test with the patient and providing them with the patient information sheet; signed consent is not required
- A nurse-led approach to the liquid biopsy service is recommended. In some centres, this has been achieved without significant impact on the workforce once the pathway process and responsibilities were set up
- Trusts should include liquid biopsy as part of their standard testing bundles – this will help take the decision out of the multidisciplinary team (MDT), bringing results forward and standardising the test into routine practice
- Appointing a Trust or Health Board champion may help drive adoption

Sample collection and logistics

- The blood draw should ideally be done at the first consultation, so the report is ready for the MDT to make timely decisions about treatment
- Blood sample collection and handling of the specialised tubes should be managed through phlebotomy, including storing and restocking kits
- Trusts should explore established routes for sample transport within the region and leverage existing services where possible
- Tracking liquid biopsy samples needs to become routine practice and be managed by a genomics navigator or MDT coordinator. This is vital to ensure samples are sent, received at the laboratory and results are available in a timely manner
- Results need to be incorporated into the electronic patient record (EPR) alongside other molecular results received by the Genomic Laboratory Hub (GLH), and made available to the clinical and pathology teams

Interpreting results

When interpreting liquid biopsy reports, we recommend a stepwise approach to address these questions:

- Is there tumour DNA present? If so:
  - Can I use the results to prescribe a targeted therapy?
  - Can I use the results to exclude a targetable abnormality and proceed with immunotherapy and / or chemotherapy?
- The reports can seem complicated at first and we encourage clinicians to seek support to put the results into context via their local GLH, Genomic Tumour Advisory Board (GTAB), or an experienced colleague
- The European Society of Medical Oncology (ESMO) has published recommendations that provide further guidance on interpreting liquid biopsy reports[4]
- Incidental germline findings are uncommon,[5] but hospitals should ensure a robust process is in place for follow-up[6]

Complementing the tissue pathway

- Liquid biopsy complements tissue molecular testing, providing the opportunity to accelerate time to referral or treatment for many patients. It can also offer molecular profiling to patients who are unfit for, or do not want, tissue biopsy or re-biopsy
- For patients with an actionable mutation, treatment can be initiated without waiting for tissue molecular results and this is permitted within the NHS funding criteria and endorsed by ESMO guidance[4,7,8]
- Patients without actionable variants can also benefit as clinicians may be able to rule out targeted therapy and instead start immunotherapy and / or chemotherapy
- Molecular results from liquid and tissue should be stored together to aid decision-making, in alignment with your local institution's policies. Pathology will need to be aware of all liquid biopsy results to cancel tissue analyses if a patient is starting targeted treatment based on liquid alone

FOREWORD

By Professor Sanjay Popat
Consultant Thoracic Medical Oncologist,
The Royal Marsden Hospital, London

Twenty years ago, two seminal papers identified mutations in the tumour epidermal growth factor receptor *(EGFR)* gene that occur in lung adenocarcinomas, and directly predict response to an *EGFR* kinase inhibitor. Since then, our knowledge of tumour genomics has evolved, new drugs have been approved, and tumour sequencing for multiple genetic alterations is now standard practice. We now have an NHS tumour genotyping service, with seven central GLHs in England and different models in the devolved nations. Nevertheless, the timely delivery of tumour genotyping is complex and problematic in the context of a challenged healthcare system.

In parallel, ctDNA next generation sequencing (NGS) technology has progressed markedly, alongside our understanding of its properties and role. It can be utilised in multiple scenarios, including cancer detection, postoperative monitoring, treatment response evaluation, and most commonly, drug target identification for therapy selection.

In this important report, colleagues have shared their experiences of implementing ctDNA NGS into routine clinical care across the UK. They highlight marked clinical benefits to patients and clinicians, and importantly several pathway changes affecting all members of the diagnostic and treatment team. Moreover, guidance is given on how to obtain the most information from a ctDNA NGS report, as interpretation may require knowledge of tumour biology and clinical context.

The learnings detailed are of tremendous value, not only to local and regional commissioners, but also clinicians alike. As we move forward, the UK is poised to proudly be the first country globally to lead with a ‘liquid first’ approach at scale, allowing national equity in access to genetic testing, a fundamental tenet of cancer medicine.

> *Circulating free DNA (cfDNA) offers exciting opportunities to patients and clinical teams to speed up diagnosis and treatment. However, it does come with challenges to overcome and will require new ways of working. In our report, we share our experiences to date around the country in the hope that they can help ease implementation of this service into routine clinical practice.*
>
> – Professor Alastair Greystoke,
> Professor of Precision Oncology, Honorary Consultant in Medical Oncology, Newcastle

INTRODUCTION

In April 2024, the NHS England Genomic Medicine Service Alliances (GMSA) transformation ctDNA pilot entered its third phase, aiming to offer a liquid biopsy test to 10,000 patients with suspected lung cancer by March 2025. This initiative marks a significant advancement in cancer diagnostics, with the potential to expedite genomic results and therefore treatment for patients with advanced NSCLC.[2,9]

Why do we need liquid biopsy in lung cancer?

Up to half of all NSCLC adenocarcinomas have an actionable variant, making molecular testing an essential tool for accurate diagnosis and optimal treatment selection.[10]

While most molecular testing is currently performed using tissue biopsies at diagnosis, as many as 30% of patients have an inadequate tumour specimen, and only 18% have sufficient tissue for complete genotyping for guideline-recommended genomic biomarkers.[11,12] Inadequate specimens require repeat biopsies, which may delay treatment and are not even feasible in 19.5% of patients.[13]

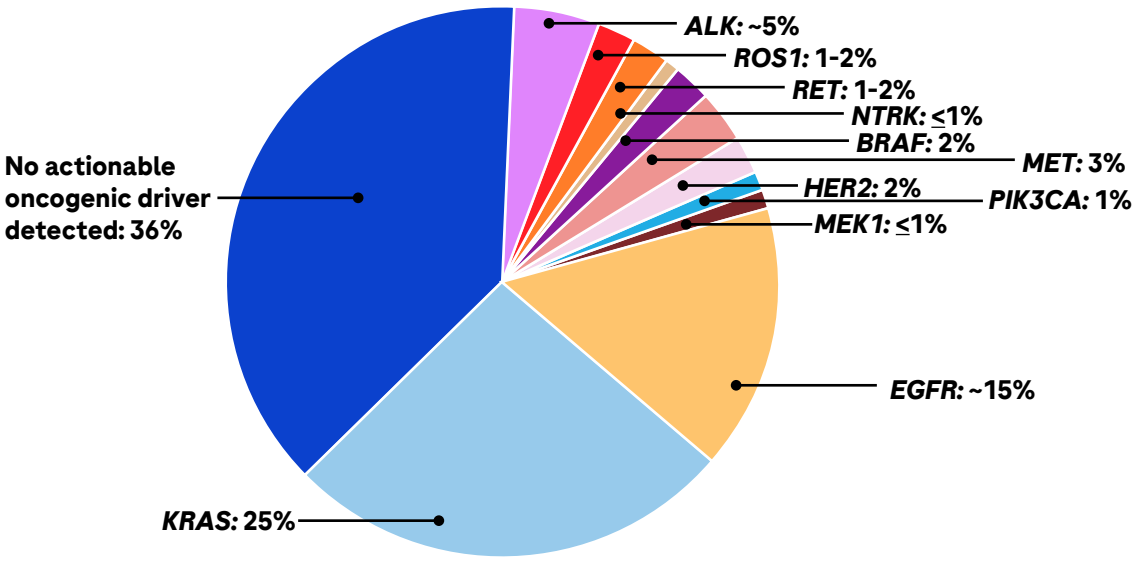
Tissue biopsy may cause delays in initiating treatment due to factors like sample analysis and preparation time, in addition to time in transportation, and logistical and administrative integration prior to assessment by oncologists before starting treatment.

Liquid biopsy offers an alternative method of molecular testing that can circumvent some of these delays. This cutting-edge genomic testing analyses cfDNA isolated from a patient's blood to identify clinically relevant genomic alterations and signatures in ctDNA*. The results from molecular profiling support complex clinical decision-making and can help optimise treatment choice.

The benefits of liquid biopsy are myriad and extend beyond treatment access; the procedure is substantially less invasive and could lower the risk of complications associated with tissue specimen collection.[12]

Liquid biopsy is supported by ESMO lung cancer guidelines, which recommend its use *"in treatment-naïve patients and especially when a significant delay is expected in obtaining tumour tissue for genotyping, when invasive procedures may be risky or contraindicated, or bone is the only site that could be biopsied."* Notably, *"ctDNA can be considered complementary or alternative to tissue NGS for biomarker evaluation"* in treatment-naïve NSCLC patients.[4]

Oncogenic drivers in NSCLC[14]



Adapted from Pakkala S & Ramalingam SS. 2018[14]

*Liquid biopsy refers to the use of a blood sample to analyse ctDNA present in the cfDNA that is released from healthy and tumour tissue. cfDNA is DNA that circulates freely in the bloodstream. Tumour cells that undergo apoptosis or necrosis also shed cfDNA to varying degrees; this tumour-derived cfDNA is called ctDNA.

An opportunity to do more for lung cancer patients

It is clear that UK cancer survival rates lag behind other comparable countries, partly because patients often receive diagnoses at more advanced disease stages. The 2024 National Lung Cancer Audit (NLCA) report showed that 66% of patients diagnosed in 2022 had Stage III / IV disease, and 32% were diagnosed via emergency admission, which is often associated with poor outcomes. It also highlighted that the proportion of patients with Stage IIIB-IVB disease, with a performance status (PS) of 0–1, who did not receive any systemic anticancer therapy (SACT) was 40%.[15]

We are all too aware of the workforce pressures within the NHS, and the performance metrics within oncology make for challenging reading: the 62-day referral target has not been met since 2015, with only 68% of patients treated within this timeframe in June 2024. Moreover, the Faster Diagnosis Standard (FDS), which recommends patients should not wait more than 28 days from referral to diagnosis, has only been met twice since its introduction in October 2021.[16]

Startling statistics from the International Cancer Benchmarking Partnership (ICBP) report highlight opportunities to improve our cancer care, particularly in elderly patients who are not being considered for treatment. In the UK, we treat fewer patients with lung cancer than other comparable countries, and this is particularly marked in older patients, with only 2.4% of patients aged ≥85 years receiving chemotherapy. The ICBP data also highlights the long waits for treatment, which can vary dramatically between regions.[17]

These findings prompt us to consider how we can be more ambitious for our patients – treating more individuals, and earlier in their disease journey. Delays in diagnosis and treatment can have significant consequences in NSCLC, both psychologically as patients wait for test results and treatment, and physically as they may deteriorate rapidly, becoming too unwell for treatment.[18]

The National Optimal Lung Cancer Pathway (NOLCP) has set ambitious timeframes for each stage of the pathway: to enable diagnoses by Day 28, and for most patients to start treatment by Day 49; the maximum time between diagnosis and treatment should be 21 days.[19] In 2022, however, the average time a patient with Stage IV NSCLC waited between diagnosis and treatment was more than double this: 43 days in England and 52 days in Wales.[15]

We believe liquid biopsy has a key role to play in helping us achieve our targets and the NHS England GMSA pilot entering Phase III means it is being offered more widely than ever before. The pilot aims to provide evidence, including health economics, for the expansion of its use.[2] As it progresses and liquid biopsy becomes more routine, lung cancer teams will need to be ready to implement this service within their centres to ensure equitable access and optimal patient outcomes.

> *Being diagnosed at 40 with incurable and inoperable EGFR lung cancer, I have first-hand experience with the cancer diagnostic pathway in Wales. [...] From the point of discovering my tumour, it took a stressful and hard 72 days to identify my cancer but this new technology will help support and deliver results quicker, allowing cancer patients to get treatment sooner and help them plan with their families for the new life that exists in front of them.*
>
> – QuicDNA steering group patient representative, Wales

Supporting our peers: The Liquid Experience report

In our report, we share our experience from using liquid biopsy in four regions of England and Wales, in the hope that this will help ease implementation of this service into routine clinical practice.

We start by focusing on how liquid biopsy can help optimise our testing pathway, then share key learnings and considerations, as well as regional examples and case studies of patients who have benefitted from this technology.

While this report focuses on lung cancer, there is a broader vision for using liquid biopsy in other tumour types. This emphasises the significance of this initiative and the importance of multiprofessional development for clinicians involved in supporting patients throughout their diagnostic and treatment journey.

> *The use of liquid biopsies is a really exciting development for patients with lung cancer. At St Bartholomew's, we've been involved with some of the earlier phases of the pilot and we've identified mutations we wouldn't have previously tested for and also shortened the time for patients to start treatment. cfDNA in patients with lung cancer is a really exciting opportunity: it brings benefits to patients, it's increasing the genomic literacy of the MDT and, as a result, I think will be an important part of the pathway for patients with lung cancer in the future.*

– Dr Adam Januszewski,
Consultant Medical Oncologist, St Bartholomew's Hospital, London

CASE: A 55-year-old female treated within 22 days of presentation in Middlesbrough

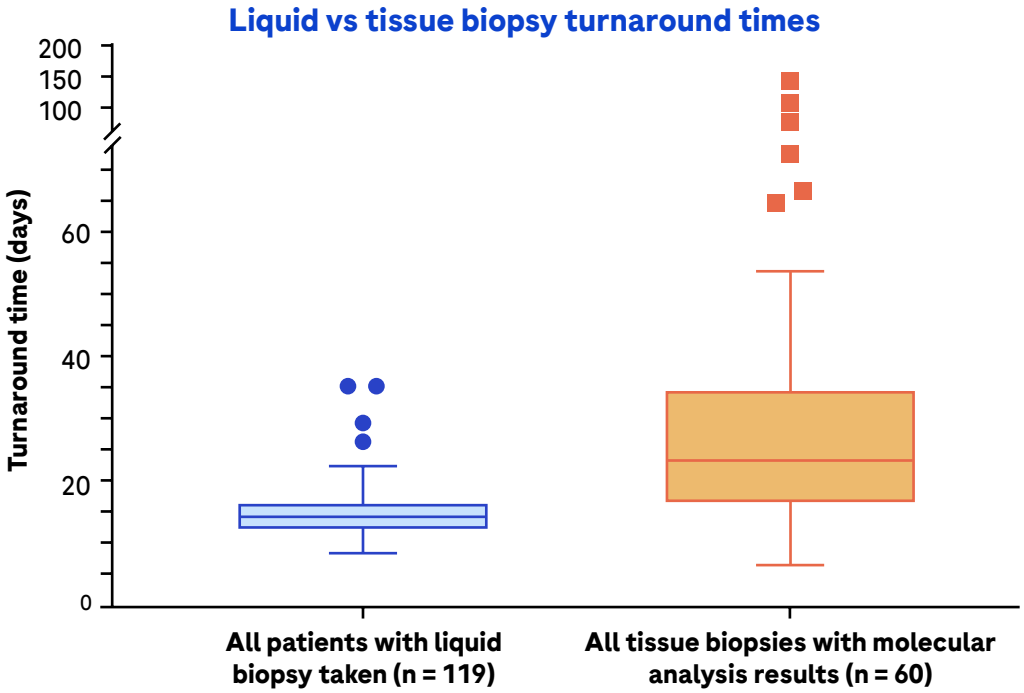
Background: Never-smoker, presented in same-day emergency care (SDEC) with worsening pleuritic chest pain, breathlessness, and headaches. Referred to the Respiratory FDS clinic the next day following computed tomography (CT) scan showing left upper lobe (LUL) nodule, pulmonary and bone metastases. Lung CNS arranged for liquid biopsy to be taken on the day of FDS clinic; endobronchial ultrasound (EBUS) booked for six days later.

Treatment: Liquid results identified an *EGFR* exon 19 deletion and first-line oral targeted treatment commenced 22 days from first presentation to SDEC.

Outcomes: The patient was convinced she only had weeks to live. The ability to shorten the pathway and reduce the anxiety of waiting for the patient was immeasurable. One year on, the patient's symptoms have dramatically reduced, she is holidaying abroad regularly and enjoying her life.

OPTIMISING LUNG CANCER PATHWAYS: THE IMPERATIVE FOR LIQUID BIOPSY

First, let us see how liquid biopsy can impact lung cancer testing pathways and patients' treatment journeys. Our discussions highlighted its significant effect on time-to-treatment, making it a valuable tool for achieving our targets (discussed earlier). Turnaround times (TAT) from one region during the pilot can be seen below:



Adapted, with permission, from NHS England circulating tumour DNA pilot for advanced lung cancer, data from the North East.[20]

Boxplots representing liquid and tissue biopsy TAT. Tissue biopsy TAT was calculated as the difference between the date when the biopsy was taken and the date when the final molecular result was authorised. In this graph, tissue biopsy TAT was considered for patients with molecular analysis results.

Historically, genomic analysis from tissue biopsy had often been requested at the MDT meeting, which could take several weeks after primary referral. Therefore, most centres now reflex test on a diagnosis of NSCLC, otherwise it may be requested following the MDT meeting, which can result in delays of up to a month for results to be returned. Along with other delays in the pathway, this means it can take more than eight weeks from primary referral to receiving treatment.

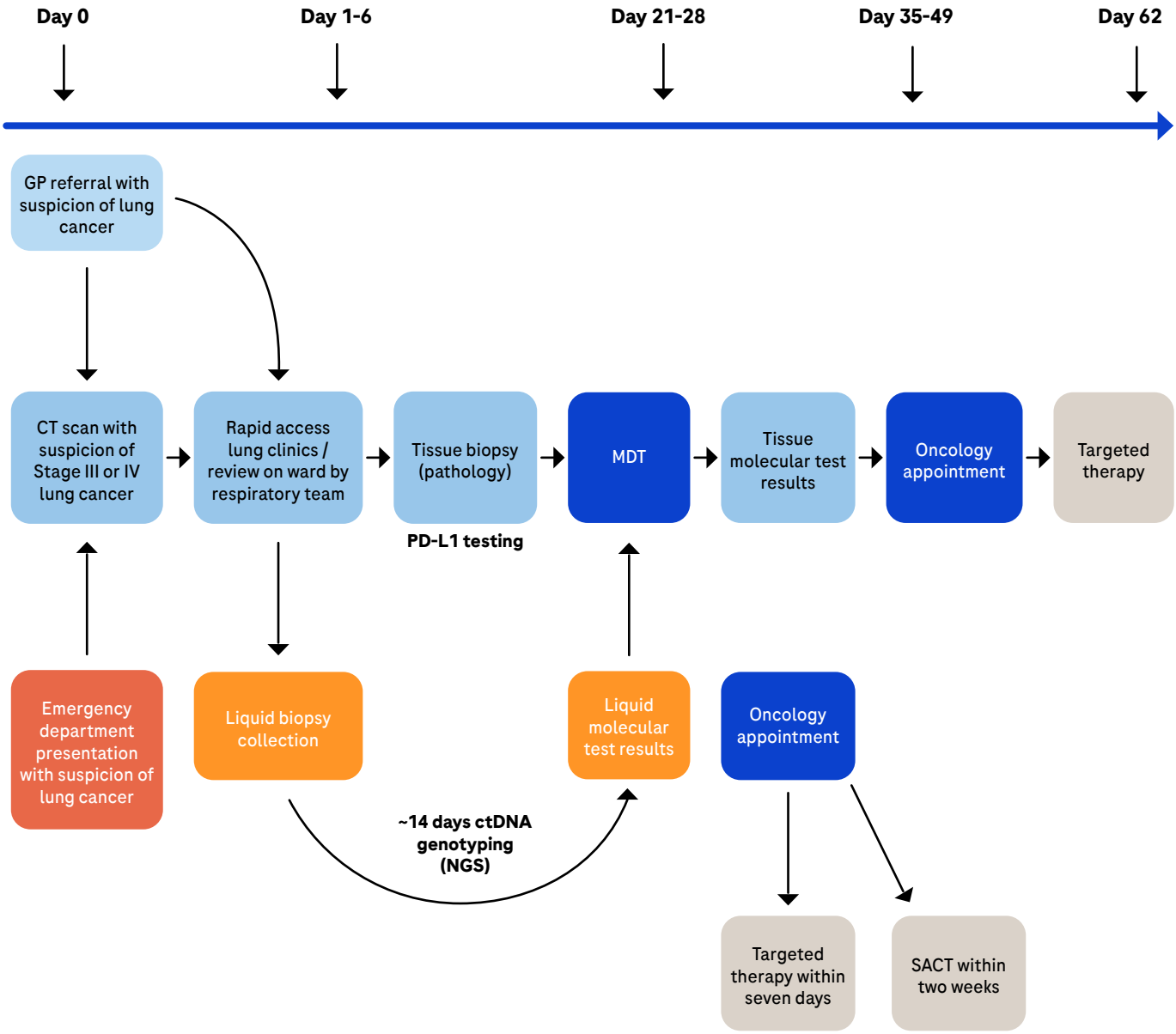
The significant benefits of liquid biopsy in reducing time to molecular analysis and initiation of first-line treatment vs tissue are well established, including in the multicentre, randomised, comparative, open-label LIBELULE study. Here, early liquid biopsy at the first visit significantly reduced time to starting *EGFR*, anaplastic lymphoma kinase (*ALK*), *BRAF* or *ROS1* SACT by 16.4 days (21 vs 37.4 days, p = 0.004), and time to starting any first-line SACT by 9.7 days (29.1 vs 38.8 days, p = 0.01), compared with standard histological sampling with genomic analysis when indicated.[1]

Providing liquid biopsy to all eligible Stage III / IV NSCLC patients earlier in the pathway, e.g., through rapid access clinics, accelerates the availability of molecular test results ahead of the MDT meeting. This provides opportunities for more informed discussions than previously and the potential for earlier treatment.

Following diagnosis, we recommend aiming to deliver oral targeted therapy within seven days (48 hours, if possible) of actionable liquid biopsy results, and that other SACT is delivered within two weeks of the oncology appointment.

While liquid biopsy can play a key role in helping us meet our ambitions, implementing and embedding this service is not without its challenges, which are discussed in more detail in the rest of the report.

How can we treat patients with advanced NSCLC within 49 days?



For illustrative purposes only.
Adapted with permission from QuicDNA Operation Business Case, based on feedback provided by the stakeholder group.[21]

Personalised medicine in lung cancer has been a fantastic evolution but we must have ambitions to treat more patients earlier and faster. For anyone with an actionable mutation, there needs to be a good reason why they're not being treated. We want to ensure equity of access, so all patients are able to benefit.

– Dr Helen Winter,
Medical Oncologist and Clinical Director, SWAG Cancer Alliance

PRACTICAL CONSIDERATIONS FOR IMPLEMENTING LIQUID BIOPSY

Discussions with members of our stakeholder group highlighted several challenges. In this section, we delve into the multifaceted process of implementing liquid biopsy testing in lung cancer, sharing our learnings, considerations, and recommendations in four key areas: patient identification, sample collection and logistics, interpreting reports, and complementing the tissue pathway.

We hope that these insights will prove useful for local teams implementing or embedding liquid biopsy in their lung cancer pathways.

1. Patient identification

To ensure equitable access to the potential benefits of liquid biopsy, clarity is needed on which patients should be offered the test, and who within the MDT can do this.

Patients should be identified for liquid biopsy by a member of the diagnostic team as early in the diagnostic pathway as feasible, ideally at the first consultation.

Depending on your service, patients could be identified by respiratory physicians, lung cancer CNSs, or pathway coordinators. If there are concerns on suitability of a patient for liquid biopsy testing, then the oncologist can help resolve this; however, it does not need to be an oncologist who identifies the patient or orders the test. Respiratory physicians and lung nurses are well placed to do this in fast-track or rapid access clinics, or even at the point of triaging patients with suspected lung cancer on CT scans.

A fundamental step is for the lung MDT to agree clear eligibility criteria. The eligibility criteria for Phase III of the pilot are below and offer broad guidance;[22] however, more specific criteria may be set up by each individual Trust:

- Radiologically suspected Stage III / IV lung cancer, likely unsuitable for curative treatment
- Eastern Cooperative Oncology Group (ECOG) PS 0-3
- Histological diagnosis of NSCLC where molecular testing has failed and the alternative option would be re-biopsy

The QuicDNA real-world study in Wales has similar criteria.[21] Please discuss eligibility criteria within your clinical teams, as these may differ between institutions.

REGIONAL EXAMPLE: Leeds and Middlesbrough took a nurse-led approach

In Leeds, the lung nurses identified the patients, discussing the liquid biopsy with them after they had their CT scan and had been seen by the respiratory consultant.

In Middlesbrough, the lung CNS team led the liquid biopsy service set-up and patient identification using the standard operating procedures (SOPs) from the test providers. Nurses identified potential patients when preparing for fast-track clinics, then discussed the test with patients, depending on their PS.

This approach has proven successful; nurses played a key role in onboarding the broader MDT. The clear eligibility criteria / SOPs have enabled the nurses to take this on with little additional burden to their teams, and South Tees patients have benefitted from:[23]

- 12 days median time from sample to results
- 25-day reduction in time-to-treatment (for mutation-positive patients)
- Earlier treatment, reducing patient stress during an already anxious time

We believe liquid biopsy should be offered to all eligible patients with suspected Stage III or IV lung cancer. This includes patients who are unable or unwilling to undergo traditional tissue biopsy, alongside individuals experiencing disease recurrence post-primary treatment.

Sociodemographic variables and smoking history, for example, must not dictate access to liquid biopsy testing, emphasising the need for unbiased and broad selection protocols. Importantly, liquid biopsy testing is also suitable for patients who enter the pathway from a multitude of ways, including those who present via emergency routes. This highlights the importance of education and awareness across the whole clinical team.

Clearly, use of broad eligibility guidance will increase the number of tests used, many of which will be negative or even lead to alternative diagnoses; however, we believe this is necessary to speed up testing and treatment for as many of our NSCLC patients as possible.

In Cheltenham (Gloucestershire Hospitals NHS Foundation Trust), patients were identified by the respiratory consultant in the two-week wait clinics. Here, liquid biopsy was considered alongside standard diagnostic and fitness tests. To help standardise its use and ensure all eligible patients are offered the test, we recommend Trusts consider including liquid biopsy as part of the standard testing bundles, including those available to lung CNS and respiratory teams managing patients diagnosed via emergency routes.

CASE: A 69-year-old female treated within two weeks, following emergency admission in Torbay

Background: Non-smoker who had a CT scan arranged by GP for a painful hip. She was admitted as an emergency with pulmonary embolism and widespread malignancy. Patient was referred to the cancer of unknown primary (CUP) team and images were suggestive of primary lung cancer. Lung cancer CNS team arranged liquid biopsy as inpatient whilst awaiting a biopsy of the bone metastasis. Blood was taken within 24 hours of admission and liquid biopsy results reported 13 days later.

Treatment: An *EGFR* exon 19 deletion, with a variant allele frequency (VAF) of 18% was identified and first-line oral targeted treatment was commenced 15 days after presentation of metastatic cancer.

Outcomes: This patient presented via emergency route with a new lung cancer diagnosis and an upfront liquid biopsy facilitated first-line treatment within two weeks. After 18 months, she remains well on treatment with a near complete response. Embedding this technology required a whole hospital team approach and the seamless care between acute oncology and respiratory teams facilitated her starting treatment early, with a reduced inpatient stay.

REGIONAL EXAMPLE: Cheltenham considered liquid biopsy alongside the standard diagnostic bundle

Respiratory consultants have been key to identifying patients for liquid biopsy in their two-week wait clinics.

Patients with advanced disease eligible for systemic or targeted therapy were considered, and liquid biopsy was requested alongside the standard diagnostic, staging and fitness tests.

A key reason for taking this approach was to bring this decision ahead of the MDT meeting, ensuring results were available sooner, ideally prior to the meeting, to guide treatment decisions.

Because incidental germline findings can occur, we are often asked how consent is managed for patients undergoing liquid biopsy. In Phase III of the pilot, data collection is no longer required and signed consent is not necessary; the patient can give verbal consent and this should be documented in the case notes. The patient should be fully informed by the team and provided with an information leaflet, so that they understand the possibility of incidental germline findings. These may or may not include mutations that could increase the patient's, and their relatives', chances of getting cancer, e.g., *BRCA 1 / 2*.

As teams are establishing this service, they may wish to consider allocating a Trust champion(s) within the MDT to help drive adoption and reduce inequity of access to liquid biopsy across Trust regions.

Watch a Lunch and Learn webinar with Prof Alastair Greystoke on liquid biopsy testing

Please note, the link above will take you to an external website not controlled by Roche.

CASE: An 89-year-old male in Gloucester who would have missed out on treatment without liquid biopsy

Background: Never-smoker who presented with non-specific symptoms, including fatigue, weight loss and generalised myalgia. PS 2, clinical frailty score 5; CT showed an 8 cm right apical lung cancer; T4N3M0.

Testing discussions: Pros and cons of pursuing tissue biopsy were discussed at length with patient and family; he was not keen on having a bronchoscopy / EBUS and he was not fit for, nor wanted to pursue chemotherapy or immunotherapy. They agreed to do liquid biopsy to look for a targetable mutation, but not to pursue tissue beyond this.

Outcomes: Liquid biopsy results revealed an *EGFR* exon 19 deletion, and he was treated with *EGFR*-targeted treatment on this basis without tissue confirmation.

> *It's actually not as daunting as you think it's going to be. It's just become sort of a standard practice in our team now – we look at our patient list, identify any patients who are eligible, and we just get on with the blood test. It's just part of the CNS role now.*

– Cheryl Armstrong,
Clinical Nurse Specialist, Leeds Teaching Hospitals NHS Trust

2. Sample collection and logistics

Blood sample collection for liquid biopsy is performed using a standard technique; a nurse or phlebotomist uses blood draw and collection kits to collect two tubes of blood from the patient. The key difference here is that the tubes are specialised: these are tubes that contain a small amount of preservative liquid that stabilises cells to ensure any mutations from the tumour remain intact during transportation to the laboratory. This means they have expiry dates that clinicians need to consider.

During the pilot and study, nurses have played a critical role in taking the bloods and ensuring the samples are sent off. As liquid biopsy becomes routine practice and we see the volume and frequency of samples increase, we recommend this is managed through phlebotomy. Not only will this help protect nursing time with patients, but it also provides an opportunity to elevate the role of phlebotomy as a hugely valued part of our oncology service.

Along with training for phlebotomy, hospitals will need to set up a system to ensure adequate storage space for these specialised tubes and kits, and that stock is maintained, expiry dates are regularly reviewed and that stock is readily accessible to all members of the team, including those managing emergency patients.

REGIONAL EXAMPLE: Torbay appointed a genomics navigator who was able to support their liquid service

In Torbay, the genomics navigator role has been central to tracking the samples and supporting lung cancer nurses and clinicians during the pilot.

Tracking was managed via a spreadsheet, capturing key information and tracking numbers for all liquid biopsy samples that were shipped, as well as a testing laboratory contact point, for easy follow-up, if required.

Essentially, it is critical that someone tracks the samples and has oversight of when they are ordered, when they are shipped, where they are going and when they are returned for clinical decision-making.

Liquid biopsy samples should not be refrigerated and need to be received by genomic laboratories as quickly as possible, meaning it is important that samples are shipped to the laboratory the same / next day, following blood draw. However, some stabilising agents can be stable for at least seven days.[24-26] From experience, we recommend that existing post rooms and transportation routes should be used for samples, looking at other send-away tests as examples of what is possible within a region.

Experience has highlighted the clear need for tracking of samples within an organisation, to be aware of samples being sent away. This helps ensure samples are not lost, avoids the risk of duplicate testing and, importantly, helps inform when the report is likely to be available to guide the next steps of the patient's pathway.

During the pilot, Cheltenham had a case where a patient had liquid biopsy testing performed and reported twice by accident, highlighting the importance of effective tracking.

Whether the responsibility of the MDT coordinator or genomics navigator (where the role exists), tracking liquid biopsy samples needs to become routine practice.

REGIONAL EXAMPLE: Cheltenham managed their pilot samples through phlebotomy

The nurses saw patients after clinic as part of their usual care, discussed liquid biopsy with them, requested the test and printed the forms. The patients took these to phlebotomy with their standard blood forms and tubes to have their bloods taken. When the patients returned to clinic, the nurses organised the tubes into postage bags ready for collection from the post room.

During scale up, phlebotomy is likely best placed to hold the tubes and coordinate postage collection after the blood draw.

> *Some centres are doing blood draws very close to tissue biopsy. To get the maximum benefit this should be done as early as possible, at the first consultation.*

– Professor Sanjay Popat,
Consultant Thoracic Medical Oncologist,
The Royal Marsden Hospital, London

CASE: Reducing the time to treatment for a 75-year-old lady near Torbay after excluding actionable variants with liquid biopsy

Background: Six-week history of hoarse voice. Seen by ear, nose and throat (ENT) physician and diagnosed with a left vocal cord palsy. Patient was a non-smoker, with a history of screen-detected breast cancer and endometrial cancer. CT of the thorax, abdomen and pelvis (TAP) confirmed likely Stage IV lung cancer, with a PS of 0. Liquid biopsy was taken two days before lymph node biopsy and reported 16 days later with a primary lung cancer.

Treatment: An actionable variant was excluded using liquid biopsy, and the patient was counselled and consented for chemo-immunotherapy, which commenced 10 days after the clinic.

Outcomes: Liquid biopsy findings reduced the patient's anxiety regarding the uncertainty of what treatment, if any, was possible for her.

CASE: Using liquid biopsy to support prompt referral to best supportive care for an 83-year-old in Torbay

Background: Never-smoker, presented with a six-month history of dry cough. CT TAP confirmed likely Stage IV lung cancer; liquid biopsy was taken 15 days before lymph node biospy. Liquid biopsy was reported with a primary lung cancer 17 days later; the patient was already booked to be seen in clinic with the results, due to the predictable TAT.

Treatment: Results excluded actionable variants and when the patient was reviewed in clinic her PS was 3. The decision was made to focus on symptom control and she was referred to palliative care.

Outcomes: Results of the liquid biopsy facilitated discussion and referral to community-based palliative care two weeks earlier than waiting for tissue NGS. The predictable TAT of liquid biopsy enabled forward planning for the oncology clinic bookings, with a view to ensuring the patient had a plan to move their care forward, at a difficult time for them and their families.

Once results are returned, we regard it as mandatory that these are integrated into the Electronic Patient Record (EPR), where this exists. As these are returned as PDFs, loading them onto a clinical system has presented some challenges. In Cheltenham, for example, their molecular pathology lead, who was helping to coordinate the pilot project, took responsibility for uploading the reports into their Laboratory Information Management System (LIMS) to ensure they were accessible by the clinical team. It is important to consider that the test may have been coordinated by a different hospital to where the patient will be treated.

The Wales Clinical Portal gives NHS health professionals across the country access to patients' digital health records. In future, all genomic reports for patients in Wales will be uploaded to this system.

Ultimately, teams may need to better understand their Trusts' or Health Boards' IT systems and explore efficient ways to incorporate liquid biopsy results. Relevant staff training will be crucial, especially as liquid biopsy expands to other tumour types. We encourage nurses and allied health professionals to participate and maximise professional learning opportunities, including the Aspirant Cancer Career and Education Development (ACCEND) programme, which aims to enhance workforce education and development for cancer care. Other solutions may also be available to incorporate liquid biospy results. Solutions should be discussed within organisations and teams involved to understand best practice.[27]

Click for more about the ACCEND programme

Please note, the link above will take you to an external website not controlled by Roche.

3. Interpreting results

Turnaround times for liquid biopsy results are currently around two weeks. This means the results can accelerate decision-making and should ideally be available ahead of the MDT meeting for discussion and referral as required – **provided this does not delay MDT discussions, should the results not yet be available.** It is therefore important to consider allocating someone to be responsible for tracking the sample and return of results. Whether they are received before or after the MDT, the oncologist can treat based on positive liquid biopsy results, as highlighted in the NHS England funding criteria and ESMO recommendations. If in doubt, oncologists may wish to discuss the results with their clinical scientist / GLH or local GTAB to understand them and put them into clinical context.

When interpreting the reports, we recommend a stepwise approach, starting with understanding whether ctDNA is present. This is based on identifying an oncogenic mutation in a reasonable percentage of the patient's cfDNA. Experts within the GLH or GTAB will help with interpreting what would constitute reasonable % (VAF) of actionable oncogenic mutations to suggest the presence of ctDNA.

Next, it is important to determine, as with any test, whether the results fit with the clinical-radiological context, whether they suggest an oral targeted therapy may be indicated or not, whether the patient could now proceed to unselected treatment with chemotherapy and / or immunotherapy, or whether they need to wait for any other tests.

Watch VJOncology Lung Cancer videos on how to interpret reports

Please note, the link above will take you to an external website not controlled by Roche.

The reports may seem complicated at first and, while some will come with interpretation, healthcare professionals (HCPs) will need to learn what to look out for. This will largely come down to experience and practice, and we recommend that HCPs seek support from experienced colleagues, clinical scientists, or the molecular tumour board / GTAB until they feel comfortable. ESMO recommendations on the use of cfDNA assays for patients with cancer are also a useful resource for further information.[4]

For ESMO recommendations see Pascual J, et al. Ann Oncol. 2022;33:750-68.

Please note, the link above will take you to an external website not controlled by Roche.

Clinical teams can be reassured that incidental germline variants are uncommon, occurring in around 2% of patients with NSCLC, but can go up to 15% depending on patient population.[5,28] Therefore, it is still essential that a process is established for handling potential germline findings using available multidisciplinary expertise.[6] For example, establishing a monthly local meeting with the clinical genetics team could be useful. We also recommend an annual audit for potential germline results to ensure we continue to learn from this process.

Read "Family Matters: Germline Testing in Thoracic Cancers" (ASCO Educational Book)

Please note, the link above will take you to an external website not controlled by Roche.

Example liquid biopsy report

Please note, this example report is for illustrative purposes only and is not representative of a real report. For more information and advice, please contact your GMSA.

Regional Genomics Laboratory
Regional Hospital, Local Street, City

web: email:

GENOMIC REPORT

Referring clinician
Ms Jeanette Bloggs
Role:

Patient name:
DOB:
Sex:
Hospital no.
Lab no.

Your ref:
Sample type: Blood
Date rec'd: 01/06/2023
Report date: 12/06/2023

Genomic findings	VAF (%)
EGFR L858R	20
EGFR T790M	15
EGFR amplification	N/A
TP53 Q192*	4
BRCA2	1
DNMT3A	1.5

VAF:
The frequency at which the variant is detected within a specimen

Follow-up germline testing may be required to distinguish between germline and somatic findings; considered more likely to be germline if VAF approximately 50% or higher (the low VAF represented here suggests a subclonal somatic mutation); expert opinion.

Clonal haematopoiesis of indeterminate potential (CHIP):
An age-related source of biological noise, due to haematopoietic cell variations that can falsely appear as ctDNA variations

Somatic mutations:
An alteration in DNA that occurs after conception and can occur in any of the body's cells except the germ cells. These are not hereditary.

Germline mutation:
An alteration to a reproductive cell that becomes incorporated into the DNA of every cell in a child's body. These are inherited during conception.

Other things you may see on a liquid biopsy report:

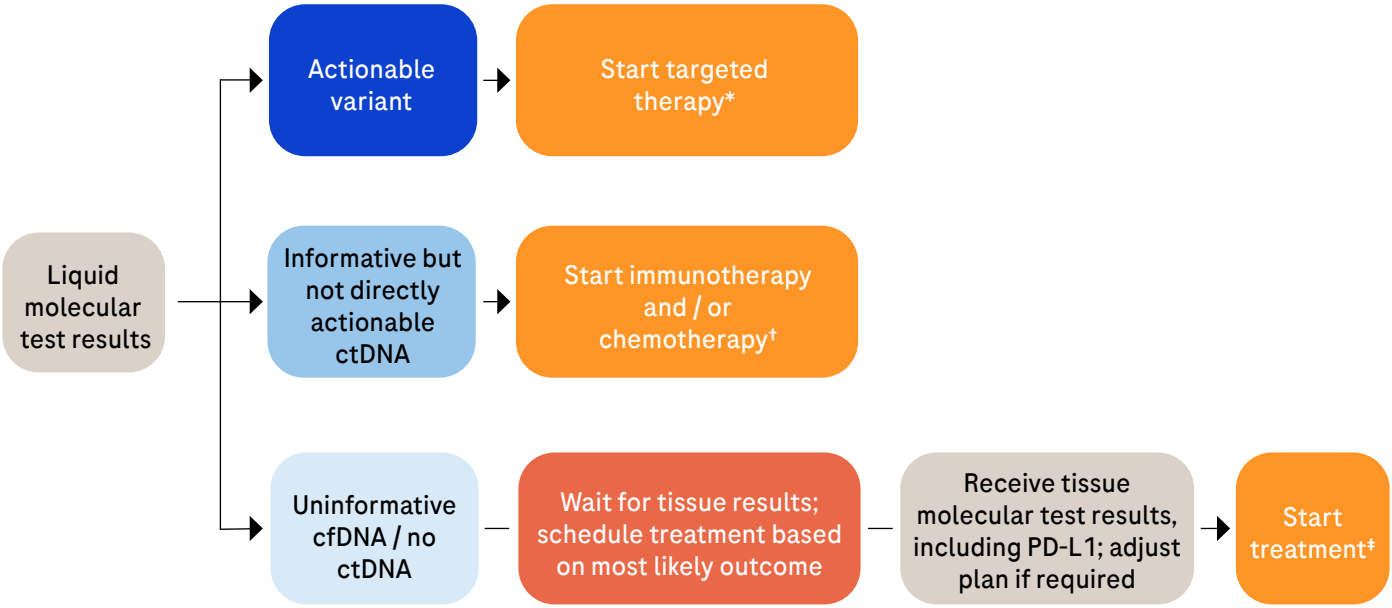
- **Microsatellite status:** MSI stands for 'microsatellite instable' and MSI-H means there is a high amount of instability in a tumour; an increased number of insertions or deletions in the genome. MSI-H is a biomarker for favourable response to immune checkpoint inhibitor therapy
- **Tumour fraction:** The approximate percentage of ctDNA present in a cfDNA sample; this should be taken into consideration when interpreting VAFs. Tumour fraction can be an indicator of the robustness of the report
- **Blood tumour mutational burden:** The total number of somatic variations per coding area of a tumour genome
- **Therapy / clinical trial recommendations** will only be included in some liquid biopsy reports

Read Krebs M, et al. JAMA Oncol. 2022;8(12):1830–9.

Please note, the link above will take you to an external website not controlled by Roche.

Adapted from Krebs M, et al. 2022.[29]

How can the various outcomes of liquid biopsy testing influence our patients' treatment pathway?



The Liquid Experience Roundtable Meeting, 15th March 2024.
For illustrative purposes only. Treatment decisions may vary depending on the test results and clinical context of the patient. The treating HCP is responsible for making all treatment decisions and this is not meant to replace clinical discussions that may be required.

*Ensure therapy is matched to presenting genomic alterations and is in accordance with NHS guidelines. †Start therapies according to NHS guidelines as informed by the genomic report. Alternatively, consider trials matched to novel actionable alterations. ‡According to NHS guidelines.

A non-randomised clinical trial with 150 participants, conducted in Ontario, Canada, found that of 90 patients with advanced NSCLC, 51% had actionable driver alterations detected, 22% had nonactionable, informative driver alterations and 27% had uninformative results, including 18% with no detectable cfDNA.[30]

The utility of liquid biopsy is not just confined to identification of actionable variants where we can speed up time-to-treatment with an oral targeted therapy. An informative result, e.g., significant levels of a *KRAS* mutation (non-*G12C*), can be used to rule out targeted therapy and plan for and start chemo-immunotherapy. On the other hand, if the results are uninformative, we can plan the patient's most likely next steps and await further results; in the event that a tissue molecular test identifies an actionable variant, we can always revisit our plans and prescribe an appropriate targeted therapy.

Alongside licensed treatment, there is also the potential to reduce inequity in the UK by identifying patients who may be eligible for ongoing clinical trials.

> *"I'm finding the 'negative' reports, where no actionable variant is detected, as helpful as the 'positive' reports in moving patients through the pathway. With predictable TATs for cfDNA, I can plan patient's clinic appointments from MDT, often reducing time to see an oncologist by 7–10 days.*
>
> – Dr Louise Medley,
> Consultant Medical Oncologist, Torbay and South Devon NHS Foundation Trust

Another common question is about the concordance between liquid and tissue molecular testing. Real-world data generally confirm high concordance between liquid and tissue biopsies. A retrospective analysis of data from 6,491 patients who received comprehensive genetic profiling in routine clinical practice found that targetable genomic alterations were detected in 20% of liquid and 22% of tissue samples.[8]

These data highlight the utility of liquid biopsy in complementing tissue testing and support the idea that we can be confident making clinical decisions based on the results. Discrepancies are to be expected and can be confusing when they occur; however, for the majority of patients there is likely to be concordance. As with any test, there may be some anomalies and challenging samples, including necrotic biopsies or samples from patients whose tumour is not shedding ctDNA. Therefore, it is crucial to understand the clinical history and context of the patient alongside the interpretation of results.

Importantly, this presents a valuable learning process for all roles involved in the lung oncology pathway, and highlights the need for ongoing professional development for teams involved in interpreting lung biopsy reports, to embed these skills into diagnostic and clinical teams. There are several valuable educational resources already available – see the back page for more information.

REGIONAL EXAMPLE: An oncologist in Leeds summarised the report in the patient notes

The reports came back to the oncologist, lung nurses and pathology, with the GLH email address copied in. The lung nurses uploaded the report to the electronic note system along with the patient notes.

As the reports are often returned before the tissue results, they can be viewed straight away by the oncologist, who can add a summary of the results and their significance to support the respiratory physician or oncologist who would pick it up next. Where there was uncertainty, the oncologist would contact the clinical scientist for support.

CASE: Expediting diagnosis for a 76-year-old male in Newcastle

Background: Patient presented with a large, ulcerated lesion on his scalp. This was excised and reported as squamous cancer with high PD-L1. Staging showed a large lung primary and multiple lung and bone metastases. Lung tissue biopsy was planned as it was unclear if the skin lesion was a metastasis or a separate primary.

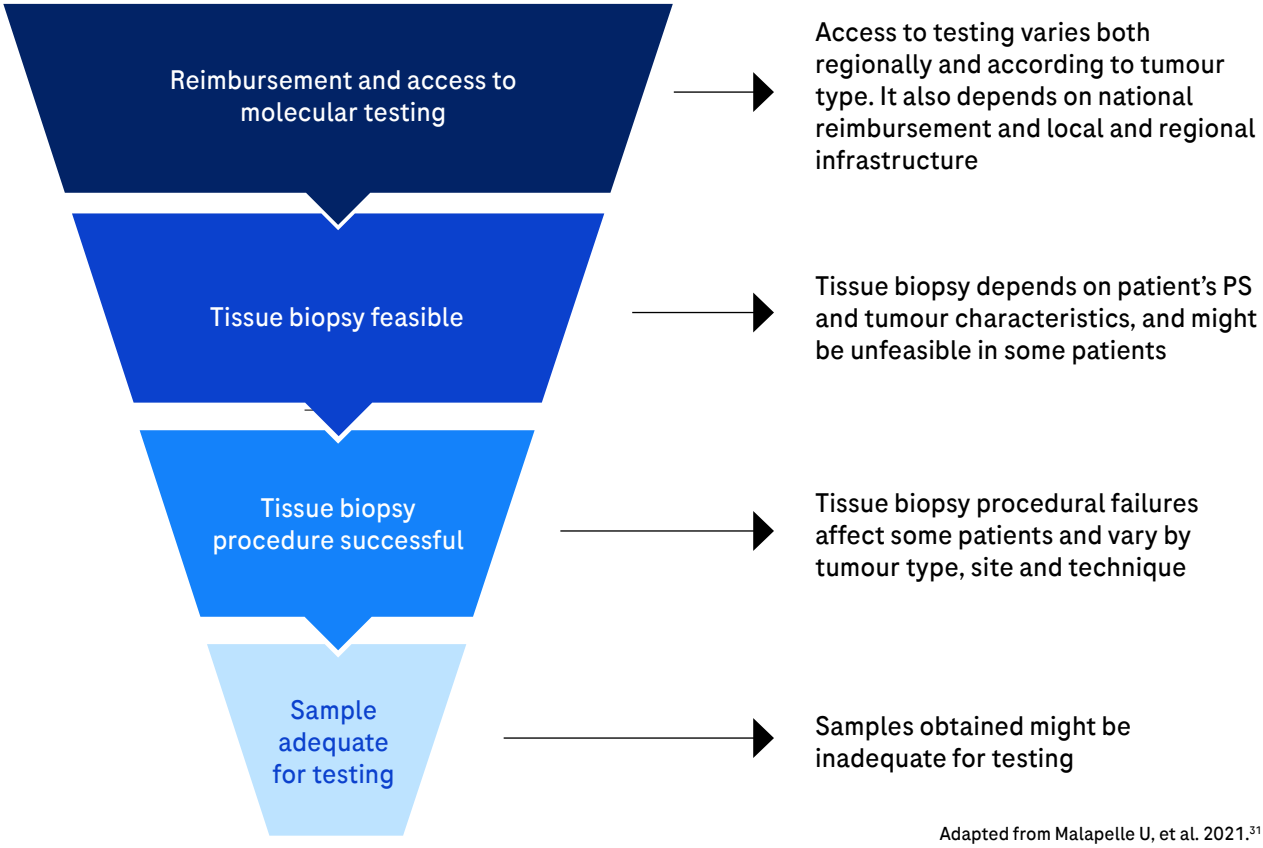
Treatment: Liquid biopsy was also sent and results showed an *EGFR* exon 19 deletion (VAF 5.5%). The planned lung tissue biopsy was cancelled and the patient started on oral targeted therapy.

Outcomes: He was able to avoid lung biopsy and access oral therapy, which he has been on for eight months with response in lung and bones and no recurrence in scalp.

4. Complementing the tissue pathway

While liquid biopsy is not set to replace tissue molecular testing, it effectively complements the tissue pathway by accelerating time to referral or treatment for some patients, or offering molecular profiling to patients who wouldn't otherwise receive this through tissue biopsy.[1]

Reasons why patients may miss out on biomarker testing / molecular diagnosis from tissue biopsy



Adapted from Malapelle U, et al. 2021.[31]

There are massive discrepancies in turnaround times for tissue genotyping between centres in the UK, which ctDNA just normalises.

– Professor Sanjay Popat,
Consultant Thoracic Medical Oncologist, The Royal Marsden Hospital, London

While the turnaround times for tissue molecular results can be quick, delays may occur at various stages in the pathway, including requesting and performing the tissue biopsy procedure, analysis and preparation in pathology, and time in transport. Considering these potential issues and the reasons patients may miss out on biomarker testing (listed above), the ease of sample acquisition with liquid biopsy means it offers more rapid molecular results. As described in the previous section, this can help plan the next steps of the patient's pathway and is particularly important for certain higher-risk patient groups, e.g., those with high symptom burden who are at risk of rapid deterioration.

For those patients who are found to have actionable variants on their liquid biopsy results, we should be able to start treatment before the tissue molecular results are returned; this is permitted within the NHS funding criteria, and we would recommend this approach unless there is a significant clinical concern or uncertainty.[7]

Blueteq criteria permits treatment based on liquid biopsy results in England

2. I confirm that the patient has histological or cytological evidence of NSCLC that carries a sensitising *EGFR* mutation based on a validated test **OR** there is documented agreement by the lung MDT that the radiological appearances are in keeping with locally advanced or metastatic NSCLC **AND** there is an informative cfDNA test result confirming the presence of a sensitising *EGFR* mutation. Please mark below on which basis the diagnosis of *EGFR* mutation-positive NSCLC has been made in this patient: ◯ Histological or cytological evidence ◯ Documented agreement by the lung MDT that the radiological appearances are in keeping with locally advanced or metastatic NSCLC and there is an informative cfDNA test result confirming the presence of a sensitising *EGFR* mutation *Required	◯ Yes ◯ No * Required

Adapted from NHS England Cancer Drugs Fund (CDF) List August 2024.[7]

CASE: A 70-year-old female who was able to start targeted therapy two weeks before tissue results in Velindre, Wales

Background: A CT scan arranged by her GP for low back pain and right hip pain revealed suspicious bronchogenic primary cancer with multiple pulmonary, bone, and subcutaneous metastases. Patient was referred to a Rapid Access Lung Clinic, where ctDNA collection was arranged while awaiting a skin biopsy. ctDNA results were available by Day 18 and showed an *EGFR* exon 19 deletion with a VAF of 3.3%.

Treatment: Oral targeted therapy was initiated two weeks before the genomic report from skin tissue biopsy became available.

Outcomes: Patient has been on treatment for over 10 months, showing a positive response in the lung and bone, with complete resolution of the subcutaneous metastases.

OPERATIONALISING LIQUID BIOPSY IN THE NORTH THAMES GENOMIC MEDICINE SERVICE

Interview with Paul Ryves – *Programme Director, North Thames Genomic Medicine Service Alliance*

What do you think are the benefits of liquid biopsy for patients and HCPs?

For patients, it offers the chance of an improved quality of life with faster access to precision treatment. Patients often have anxiety about waiting for results, and knowing that this can be quicker than the current standard of care pathway can make a massive difference to them. Liquid biopsy is less invasive and will be helpful when managing patients who are too unwell for tissue biopsy; however, the test will not be replacing the tissue biopsy. It is there to enhance the current pathway, even for those who aren't eligible for targeted treatments. Having those results earlier means that patients know they are on the best treatment option for them.

From a clinician perspective, it can help speed up the pathway, which will be helpful in meeting NHS waiting time targets in the 62-day pathway.

What do you think were the biggest challenges encountered during the pilot?

The logistics were always going to be challenging with regards to the distribution of kits sent out to referring Trusts and back to the various testing laboratories in the different phases of the pilot. This is due to the specialist consumables, like specific tubes, that are required. There were also significant barriers to overcome regarding the amount of information governance (IG) required in the pilot – that was probably the biggest challenge and necessitated time and effort to onboard the clinical teams involved in the data collection that was required for the health economics analysis. We also identified broader educational needs because, whilst genomics is not new in the NHS, the interpretation and understanding of liquid biopsy will be a new concept to the majority of clinical and nursing teams involved in patient care.

How did you get people engaged?

In North Thames specifically, we benefitted from having clinicians who were very experienced in performing liquid biopsies and were involved in leading the pilot. They made very good inroads into linking in with many of their colleagues about the benefits of the test. I was aware that colleagues in other GMSA regions held educational events that were filmed for on-demand availability. Overall, nationally there was a mix of formal education and one-to-one discussions. We have learnt a lot from the first phases of this pilot and will be working with patient groups, charities and key workforces as we onboard new Trusts for the next phase.

In terms of taking on the pilot, are there any success stories you'd like to share?

The obvious success is how we've been able to improve patient care and speed up access to precision treatment. We have had some fantastic patient stories; for example, one patient in our region was able to attend our North Thames end-of-year genomic showcase to talk about their experience of the test. This patient had been struggling to come to terms with a totally unexpected diagnosis and the pilot meant he could spend Christmas time with his family, with full knowledge about his diagnosis and the next steps for his treatment. He was so grateful for all the work our team had done; without it, he wouldn't have been able to share his story with us.

How will Phase III of the pilot differ to the earlier phases?

Phase III is a major step change between the small-scale pilot and what we would call 'business as usual'. This means any Trusts in England with a lung pathway that have patients who meet the eligibility criteria can now access the test. A key difference is in the IG; we no longer need to provide data for this phase, which will save time for clinical teams embedding the test in the pathway and hopefully means we can bring on board more Trusts.

How do you envisage liquid biopsy becoming standard of care?

Ultimately, it needs to be on the National Genomic Test Directory for it to be a true standard of care test. But just because something is on the Test Directory doesn't mean it's readily accessible, so it's ensuring we raise awareness of the test, but also making sure we have the educational resources to support adoption of liquid biopsy by the workforce that will use the test in their clinical practice.

Will this extend beyond lung cancer?

Our next focus is the Circulating Tumour Biomarker Network of Excellence, which is being set up to expedite the introduction of liquid biopsy tests into other cancer care pathways in the NHS. Jointly led by North Thames and Northwest GMSA regions, it will bring together a range of experts to assess which clinical cancer pathways could benefit from liquid biopsy. This could include CUP, breast and paediatrics. It's an exciting time, and this network is built on the success of the lung transformation pilot.

What are your ambitions and hopes for the future of the service?

That this is eventually introduced onto the National Test Directory to ensure all eligible patients across England can benefit. I believe this can be a world-leading first in implementing liquid biopsy within a national health service. That's a great achievement.

What performance metrics will you be using?

There can be various metrics, looking at uptake and clinical impact for example, but it's also ensuring there is equity of access across the country. It's all about impact, because there's no point doing this if it's not going to change anything. Patient stories are always a fantastic way of looking at whether a pathway change has been successful, but hopefully from a cost-benefit perspective this can relieve some pressure on the NHS, helping to avoid costs downstream in the pathway, and lastly help improve the percentage of patients accessing treatment within the 62-day cancer waiting times target.

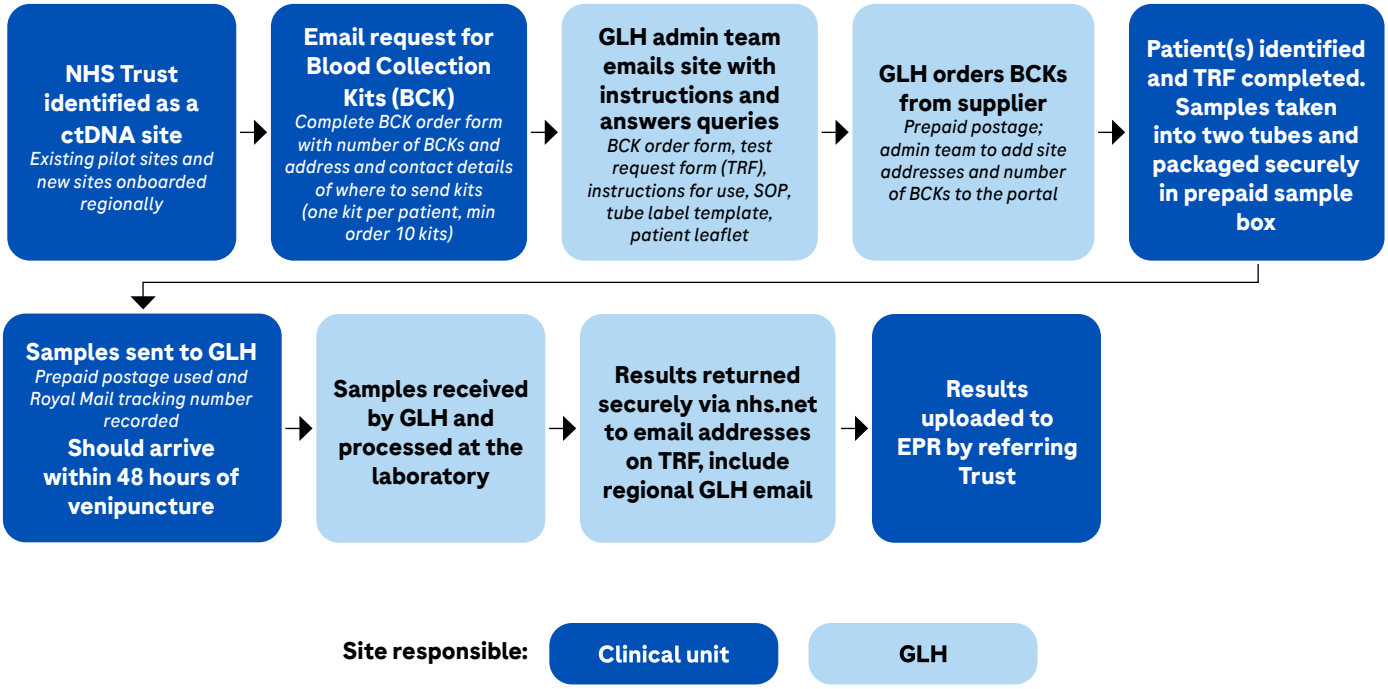
What advice do you have for anyone looking to integrate liquid biopsy into their lung pathway?

I would encourage clinical teams to get involved, understand what liquid biopsy means and that it's an opportunity to improve your genomic literacy. This is a test that can help improve patient care and speed up patients' time-to-treatment and is funded by the NHS.

I would say reach out to your GMSA team, learn about it, and learn how to access it.

Example pathway for Phase III of the NHS England liquid biopsy pilot

This is an example pathway and may be subject to change. Trusts and clinical teams should check with their GMSA / GLH to find out what the most up-to-date and appropriate process is.



CONCLUSION

Liquid biopsy has emerged as an important tool to help improve and accelerate diagnostic and treatment pathways for our patients with lung cancer.

The evidence for timely diagnosis and treatment of lung cancer is clear; we know we need to be more ambitious to ensure more patients receive appropriate treatment sooner, and liquid biopsy can help us achieve this.

The NHS England lung cancer cfDNA pilot offers exciting opportunities for clinical teams to accelerate diagnosis and treatment. However, it does come with challenges and will require new ways of working.

In our report, we have shared our experiences to date around the country in the hope that they can help upskill clinical teams and ease implementation of this service into routine clinical practice.

We look forward to you joining us and becoming part of The Liquid Experience.

> *cfDNA is a tool that we can use to improve the care of patients and the work of lung MDTs regardless of hospital size, site or population.*
>
> – Professor Alastair Greystoke
> Professor of Precision Oncology, Honorary Consultant in Medical Oncology, Newcastle

References

1. Swalduz A, et al, *JCO.* 2023;41:9019.
2. NHS. North Thames Genomic Medicine Service. Circulating tumour DNA testing in the NHS. Available at: https://norththamesgenomics.nhs.uk/circulating-tumour-testing-in-the-nhs/ [last accessed: August 2024].
3. Cardiff University. Centre for Trials Research. QuicDNA. Available at: https://www.cardiff.ac.uk/centre-for-trials-research/research/studies-and-trials/view/quicdna [last accessed: August 2024].
4. Pascual J, et al. *Ann Oncol.* 2022;33:750–68.
5. Vallabhaneni E, et al. *Cancers (Basel)* 2024;16:1150.
6. Mandelker D, et al. *Ann Oncol.* 2019;30:1221–31.
7. NHS England. National Cancer Drugs Fund list – version 1.306. Available at: https://www.england.nhs.uk/publication/national-cancer-drugs-fund-list/ [last accessed: August 2024].
8. Madison R, et al. *Lung Cancer*. 2020;148-78.
9. NHS England. News. Thousands more lung cancer patients to get innovative blood test as part of NHS pilot. 22 March 2024.
10. Navani N, et al. *Lung Cancer.* 2022;172:142–53.
11. Mlika M, et al. *Curr Respir Med Rev.* 2018;14:48–60.
12. Rolfo C, et al. *J Thorac Oncol.* 2021;16:1647-1662.
13. Chouaid C, et al. *Lung Cancer*. 2014;86:170-3.
14. Pakkala S & Ramalingam SS. *JCI Insight*. 2018;3(15):e120858.
15. National Lung Cancer Audit. State of the Nation Report 2024. Published April 2024.
16. Cancer Research UK. Cancer News. Cancer waiting times: Latest updates and analysis. May 2024. Available at: https://news.cancerresearchuk.org/2024/08/08/cancer-waiting-times-latest-updates-and-analysis/ [last accessed: August 2024].
17. McPhail S, et al. *Lancet Oncol*. 2024;25:338–51.
18. Adizie JB, et al. *JTO Clin Res Rep*. 2021;2:100176.
19. NHS National Optimal Lung Cancer Pathway, V3.0, 2020.
20. Data on File: Newcastle Trust Turnaround Time Data Report, 2024.
21. QuicDNA. Integration of Liquid Biopsy into Lung cancer Diagnostic Pathway. Operational Business Case. Version 1.4. August 2022.
22. Marsden360 ctDNA Pathway - Pilot Phase 3 SOP.
23. Ainsley J, et al. Presented at LCNUK Annual Conference 2023.
24. Gerber T, et al. *J Mol Diagn.* 2020;22:1070–86.
25. FDA. FoundationOne® Liquid CDx Technical Information.
26. FDA. Guardant360® CDx Technical Information.
27. NHS England. Workforce, training and education. ACCEND Framework. Available at: https://www.hee.nhs.uk/our-work/cancer-diagnostics/aspirant-cancer-career-education-development-programme/accend-framework [last accessed: August 2024].
28. Mezquita L, et al. *J Clin Oncol*. 2022;40(16).
29. Krebs MG, et al. *JAMA Oncol.* 2022;8:1830–9.
30. Garcia-Pardo M, et al. *JAMA Netw Open.* 2023;6:e2325332.
31. Malapelle U, et al. *J Mol Pathol.* 2021;2:255–73.

FURTHER READING AND RESOURCES

Please note, some links on this page may take you to external pages that are not controlled by Roche Ltd.

Publications, guidelines and recommendations

- **Optimising Tissue Acquisition and the Molecular Testing Pathway for Patients With Non-Small Cell Lung Cancer: A UK Expert Consensus Statement.**
  Navani N, et al. *Lung Cancer*. 2022;172:142–53.
- **ESMO Recommendations on the Use of Circulating Tumour DNA Assays for Patients With Cancer: A Report From the ESMO Precision Medicine Working Group.**
  Pascual J, et al. *Ann Oncol*. 2022;33:750-768.
- **ASCO Guideline: Selection of Germline Genetic Testing Panels in Patients with Cancer.**
  Tung N, et al. *J Clin Oncol*. 2024;42:2599-615.
- **Family Matters: Germline Testing in Thoracic Cancers.**
  Hathaway F, et al. *Am Soc Clin Oncol Educ Book*. 2023:43:e389956.

Webinars and video resources

- VJOncology: **How to Interpret ctDNA Reports for Patients With Lung Cancer in the UK** – *A roundtable series featuring UK experts including Professor Sanjay Popat and Professor Alastair Greystoke*
  https://www.vjoncology.com/event/btog-vjoncology-lung-cancer-sessions-how-to-interpret-ctdna-reports/
- North East & Yorkshire Genomics Webinar: **Lunch and Learn: ctDNA Testing** (YouTube) – *Professor Alastair Greystoke discusses the progress made in adopting liquid biopsy testing across the NHS*
- Central & South GMSA Webinar: **Unlocking the Potential – Advancing Cancer Detection with ctDNA** (YouTube) – *Dr Marcus Remer, Dr Tom Geldart, Jo Wilson, Professor Alastair Greystoke and Kat Omer discuss the GMSA pilot project, case studies, sampling, report interpretation and current pathways*
- Macmillan Webinar: **The Impact of Genomics on the Prevention, Diagnosis and Treatment of NSCLC** – A webinar available to those with a Macmillan login

Genomics education

- **GeNotes (Genomic notes for clinicians)** – *Quick, concise information to help healthcare professionals make the right genomic decisions at each stage of a clinical pathway*
  https://www.genomicseducation.hee.nhs.uk/genotes/
- **NHS England Genomics Education Programme** – *Health Education England's Genomics Education Programme to deliver and advise on learning and development opportunities that prepare current and future NHS professionals to make the best use of genomics in their practice*
  https://www.genomicseducation.hee.nhs.uk/about-us/
- **The Royal College of Radiologists: The Fundamentals of Cancer Genomics*** – *A four-module e-learning resource on the fundamentals, targeting clinical and medical oncologists and healthcare professionals involved in the care of cancer patients*
  https://www.rcr.ac.uk/cpd-and-events/rcr-learning-hub/the-fundamentals-of-cancer-genomics/
- **NHS Workforce, Training and Education: ACCEND** – *A cancer career and education development programme that supports aspirant cancer nurses and allied health professionals towards increasing their knowledge, skills and capability*
  https://www.hee.nhs.uk/our-work/cancer-diagnostics/aspirant-cancer-career-education-development-programme
- Your local GMSA / GLH may be organising more educational resources. Please contact them for further information

More about your GLH, GMSA and GTAB

- NHS England National Genomics Education Programme: Genomic Laboratory Hubs – https://www.genomicseducation.hee.nhs.uk/genotes/knowledge-hub/genomic-laboratory-hubs/
- Search for your local NHS Genomic Medicine Service Alliance website – For more about how your GMSA is working to improve equity of access to genomic testing and patient outcomes
- Find out more about your local GTAB by contacting your local GMSA

Other relevant information

- ECMC Experimental Cancer Trial Finder
  https://www.ecmcnetwork.org.uk/ec-trial-finder
- Contact your GMSA / GLH for the patient information leaflet
- NHS National Genomic Test Directory https://www.england.nhs.uk/publication/national-genomic-test-directories/

Reporting suspected adverse reactions after authorisation of a medicinal product is important. It allows continued monitoring of the benefit / risk balance of the medicinal product. Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Roche Products Ltd. Please contact Roche Drug Safety Centre by emailing welwyn.uk_dsc@roche.com or calling +44 (0)1707 367554.

*This activity has been supported by a grant from Roche Products Ltd.

The content of this report was accurate at the time of publication.
M-GB-00018455 | August 2024

This report is intended for healthcare professionals and other relevant decision makers only.

Roche