Marsden360

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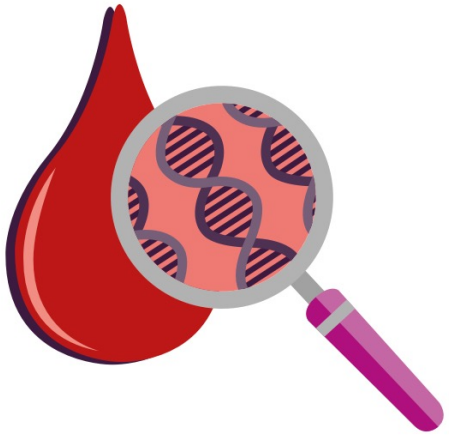
NHS East Genomics

Finding the Fragments: ctDNA in Lung Cancer

Oct 09, 2023

Cambridge, England

This meeting has been organised by NHS East Genomics and sponsored by Guardant Health



Agenda

East Genomics

Time	Title	Speaker
4:00pm	Welcome and introduction to ctDNA / GMSA pilot project	**Dr Brent O'Carrigan** (Medical Oncology Consultant (Melanoma and renal cancer), CUH, Deputy Chair, NCRI Skin Group, Clinical Cancer Lead, NHS East Genomics Laboratory Hub (GLH))
4:10pm	Case Studies	**Dr Frank McCaughan** (Honorary Consultant in Respiratory Medicine and lead clinician for lung cancer, CUH) and **Tiago Verissimo** (Lung Clinical Nurse Specialist, CUH)
4:30pm	Audit of CUH experience	**Dr David Favara** (Clinical Lecturer in Medical Oncology, University of Cambridge)
4:40pm	Current pathway for ctDNA requesting	**Dr Brent O'Carrigan** and **Col Spencer** (Programme Manager, East GMSA)
4:50pm	Audience Q&A	All
5:00pm	Close	All

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NHS East Genomics

National lung cancer circulating tumour DNA (ctDNA) pilot

Dr Brent O'Carrigan

Clinical Cancer Lead, NHS East Genomics

Medical Oncologist

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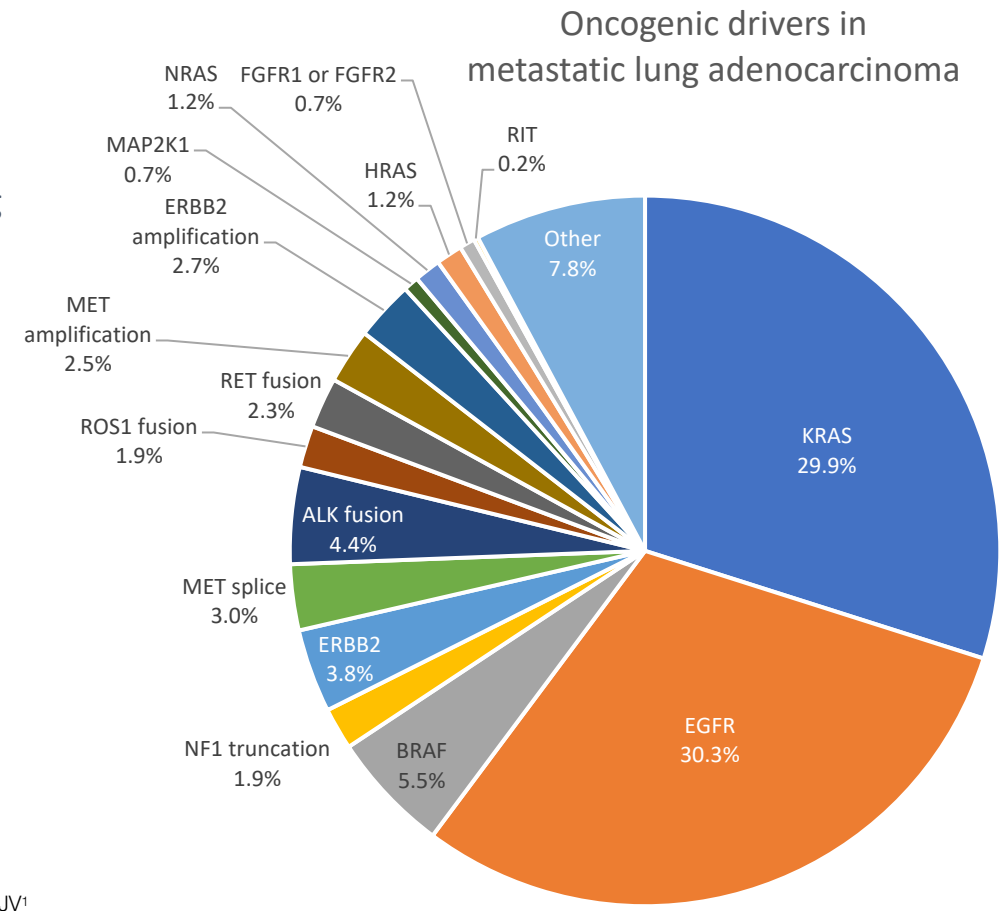
Targetable alterations in advanced cancer: NSCLC example

East Genomics

Many lung adenocarcinoma drivers are known[1,2]

Up to 40% are targetable today

- *EGFR*
- *KRAS* G12C
- *BRAF* V600E
- *MET* exon 14 skipping
- *ALK* fusion
- *ROS1* fusion
- *RET* fusion
- *NTRK* fusion



High prevalence of targetable mutations (~40%)[1]

Increasing demand on lung tissue specimens

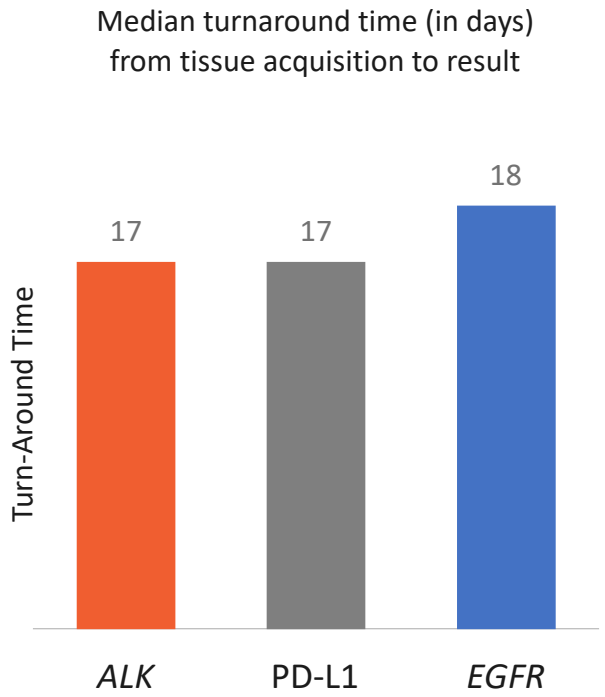
- Histological diagnosis
- Additional stains
- Immunotherapy markers
- Markers for targeted therapy

Figure adapted from Skoulidis F, Heymach JV[1]
NSCLC, non-small cell lung cancer.
1. Skoulidis F, Heymach JV. Nat Rev Cancer. 2019;19(9):495-509: 2. Campbell, JD, et al. Nat. Genet. 2016;48, 607–616.

Slide courtesy Guardant Health

National Lung Cancer Audit: Molecular testing in advanced lung cancer 2019 (for diagnoses in 2017)

East Genomics



- 18-day median turnaround time from tissue acquisition to *EGFR* mutation result
- 11.5% of patients required second biopsies to obtain molecular results

However…There is room for improvement for 'Right drug first time' metric

- 75% of patients with an *EGFR* mutation received a first-line TKI
- 58% of those with an *ALK* translocation received a targeted first-line treatment with an approved TKI

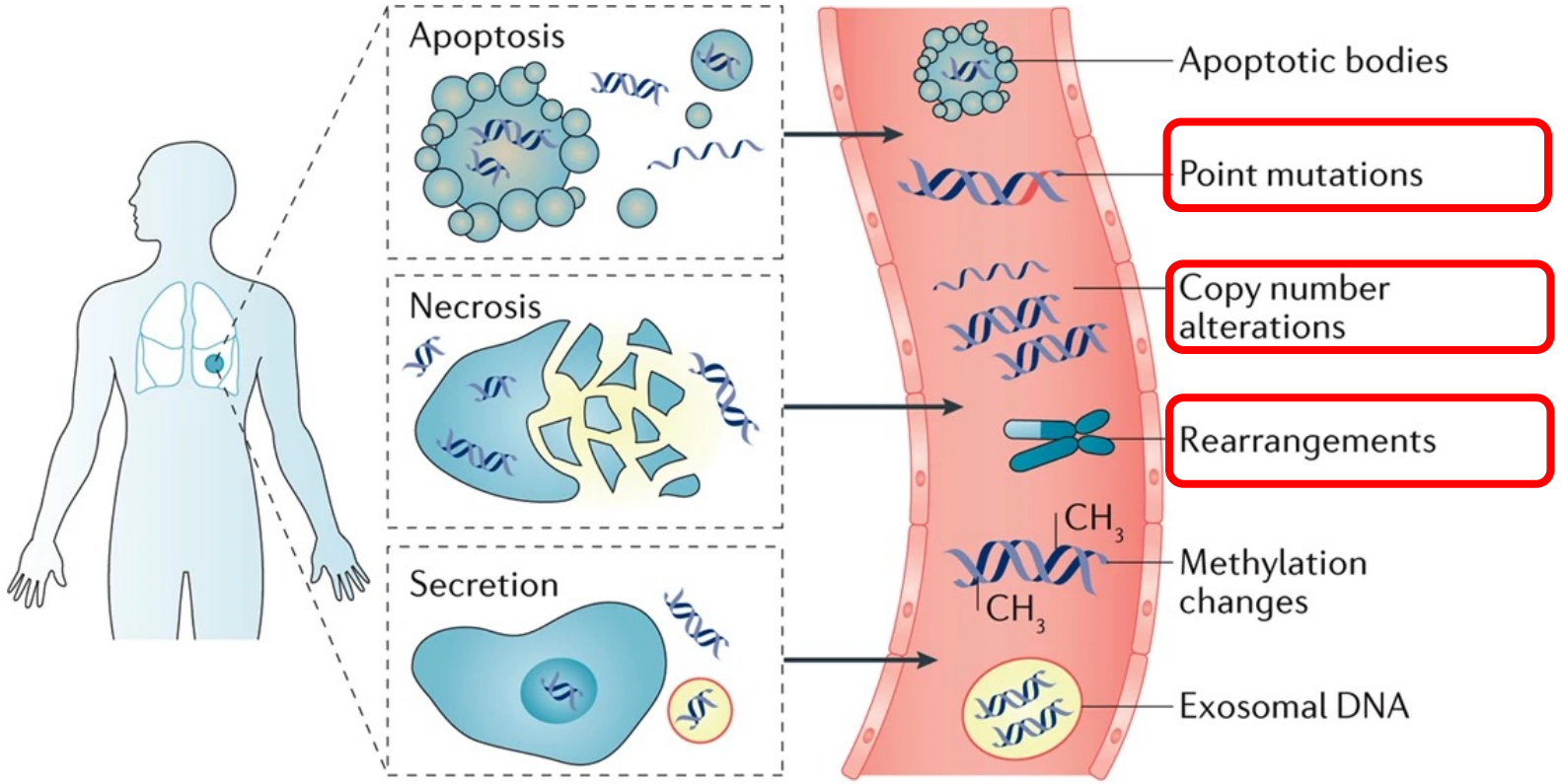
Long turnaround times may lead to inappropriate early chemotherapy in patients with an *EGFR* mutation

ALK, anaplastic lymphoma kinase; *EGFR*, epidermal growth factor receptor; PD-L1, programmed death ligand 1; TKI, tyrosine kinase inhibitor.
Spotlight audit on molecular testing in advanced lung cancer 2019 (for diagnoses in 2017) https://www.rcplondon.ac.uk/projects/outputs/spotlight-audit-molecular-testing-advanced-lung-cancer-2019-diagnoses-2017 October 2023

Slide courtesy Guardant Health

East Genomics

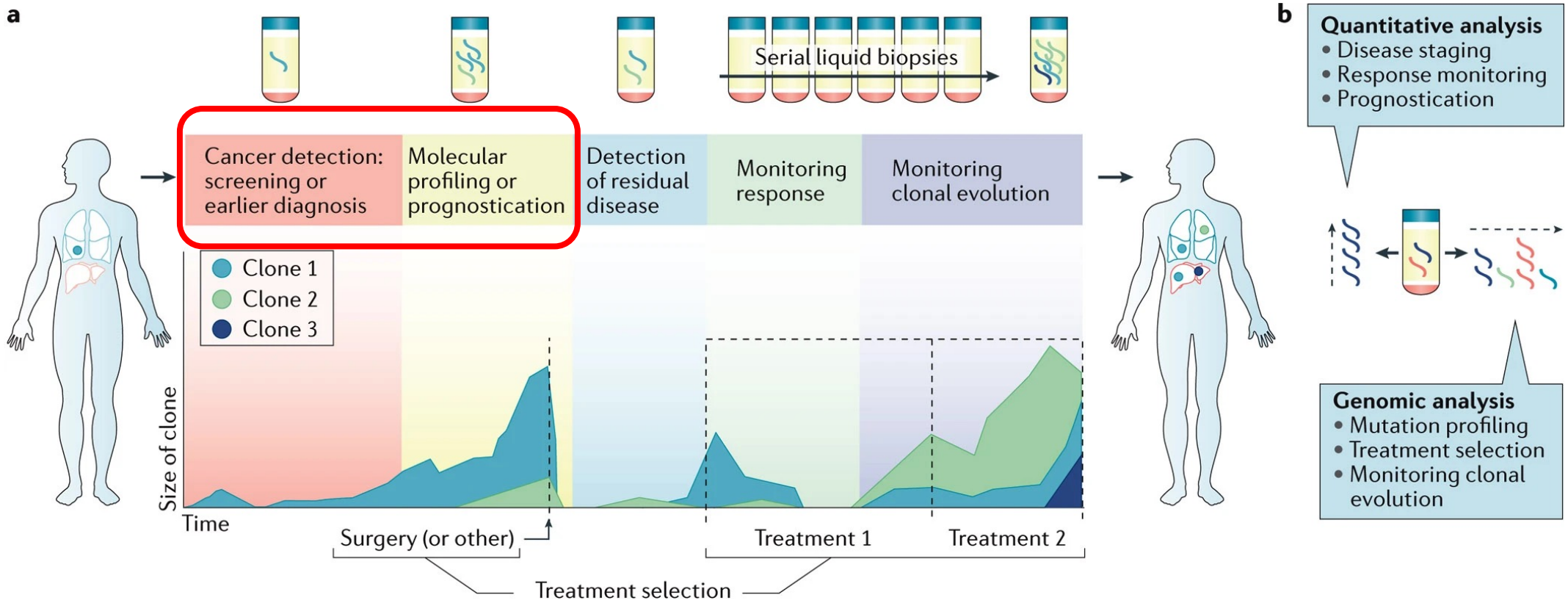
What is circulating tumour DNA? (ctDNA)



Wan JCM *et al*, Nat Rev Cancer, 2017

Potential uses of ctDNA

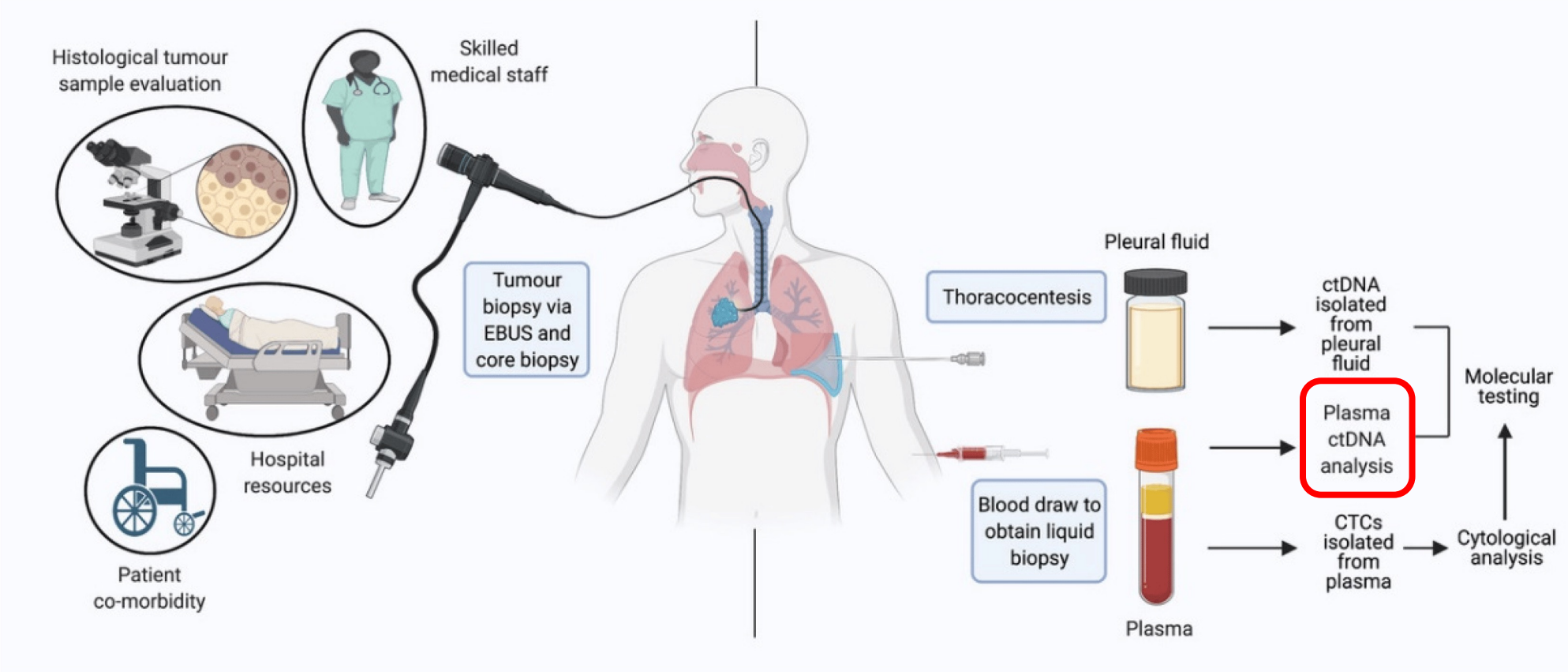
East Genomics



Wan JCM *et al*, Nat Rev Cancer, 2017

ctDNA in lung cancer is non-invasive

East Genomics

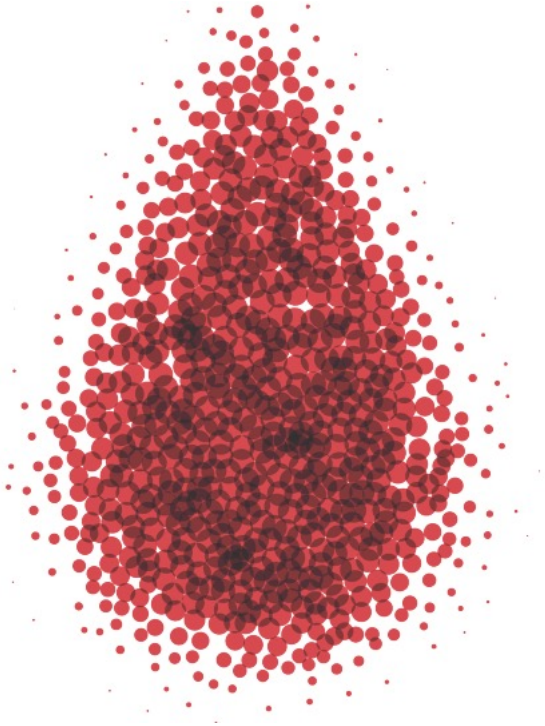


Di Capua et al, Cancers 2021

What is Guardant360?

East Genomics

Clinically validated comprehensive genomic profiling (CGP) liquid biopsy to help guide treatment decisions for patients with advanced solid tumours, including NSCLC[1]



- Simple, non-invasive blood draw
- Detects guideline-recommended genomic alterations for NSCLC[2,3]
- Delivers results in 7 days
- Complementary to molecular testing on tissue biopsy samples
  - Delivers complete results, for more patients, faster than tissue[4]
  - Enables complete testing for 3 times more patients than tissue[4]*
- Can be used ahead of tissue genotyping for every newly diagnosed patient with advanced NSCLC to help accelerate time to complete biomarker results

- NSCLC, non-small cell lung cancer.
- *For the 4 alterations for approved therapies.
- 1. Odegaard JI, et al. *Clin Cancer Res* 2018;24:3539–3549; 2. Mosele F, et al. Ann Oncol 2020;31:1491–1505; 3. NCCN Clinical Practice Guidelines, NSCLC version 6.2021. https:/www.nccn.org/. Accessed 25 October 2021; 4. Leighl NB et al. *Clin Cancer Res* 2019;25:4691–4700.

Slide courtesy Guardant Health

Guardant360 detects all NCCN somatic genomic targets and the most important genes in NSCLC with a single test

East Genomics

Guardant360 detects **74 point mutations and insertions/deletions**, with complete (**bold**) or critical exon coverage

AKT1	*ALK*	***APC***	***AR***	*ARAF*	*ARID1A*	***ATM***	***BRAF***	***BRCA1***	***BRCA2***
CCND1	*CCND2*	*CCNE1*	*CDH1*	*CDK4*	*CDK6*	***CDK12***	*CDKN2A*	*CTNNB1*	*DDR2*
EGFR	***ERBB2 (HER2)***	*ESR1*	*EZH2*	*FBXW7*	*FGFR1*	*FGFR2*	*FGFR3*	*GATA3*	*GNA11*
GNAQ	*GNAS*	*HNF1A*	*HRAS*	*IDH1*	*IDH2*	*JAK2*	*JAK3*	***KIT***	***KRAS***
MAP2K1 (MEK1)	*MAP2K2 (MEK2)*	***MAPK1 (ERK2)***	***MAPK3 (ERK3)***	***MET***	*MLH1*	*MPL*	*MTOR*	***MYC***	*NF1*
NFE2L2	*NOTCH1*	*NPM1*	***NRAS***	*NTRK1*	*NTRK3*	*PDGFRA*	***PIK3CA***	*PTEN*	*PTPN11*
RAF1	***RB1***	*RET*	*RHEB*	*RHOA*	*RIT1*	*ROS1*	*SMAD4*	*SMO*	*STK11*
*TERT***	***TP53***	*TSC1*	*VHL*						

Guardant360 detects **microsatellite instability (MSI)**

Guardant360 detects **18 gene amplifications**

AR	*BRAF*	*CCND1*	*CCND2*	*CCNE1*	*CDK4*	*CDK6*	*EGFR*	*ERBB2*
FGFR1	*FGFR2*	*KIT*	*KRAS*	*MET*	*MYC*	*PDGFRA*	*PIK3CA*	*RAF1*

Guardant360 detects **6 gene translocations**

ALK	*FGFR2*	*FGFR3*	*RET*	*ROS1*	*NTRAK*

- Guardant360 Panel version 2.11 (2019)

Slide courtesy Guardant Health

Guardant360 has high sensitivity and high specificity for detecting genomic alterations

East Genomics

Alteration type	Reportable range	Allelic fraction / copy number	Analytical sensitivity	Analytical specificity*
Single Nucleotide Variants (SNVs) 	≥0.04%	>0.25%	100%	97%
		0.05 – 0.25%	64%	
Insertions / Deletions (Indels) 	≥0.02%	>0.20%	100%	100%
		0.05 – 0.20%	68%	
Fusions 	≥0.04%	>0.20%	95%	100%
		0.05 – 0.20%	83%	
Copy Number Variants (CNVs) 	≥2.12 copies	2.24 copies**	95%	100%
MSI	MSH-H detected	>0.1%	95%	100%

Performance specifications based on cell-free DNA input of 30 ng in patient samples of contrived samples; analytical sensitivity cited here are for targeted, clinically important regions. Sensitivity outside these regions or in highly repetitive sequence c

Per sample, over entire genomic reportable range of Guardant360 panel (Guardant360 Panel version 2.11 (2019)))

** Equivalent to 5% tumour fraction and 8 *ERBB2* (*HER2*) gene copies in tumour.

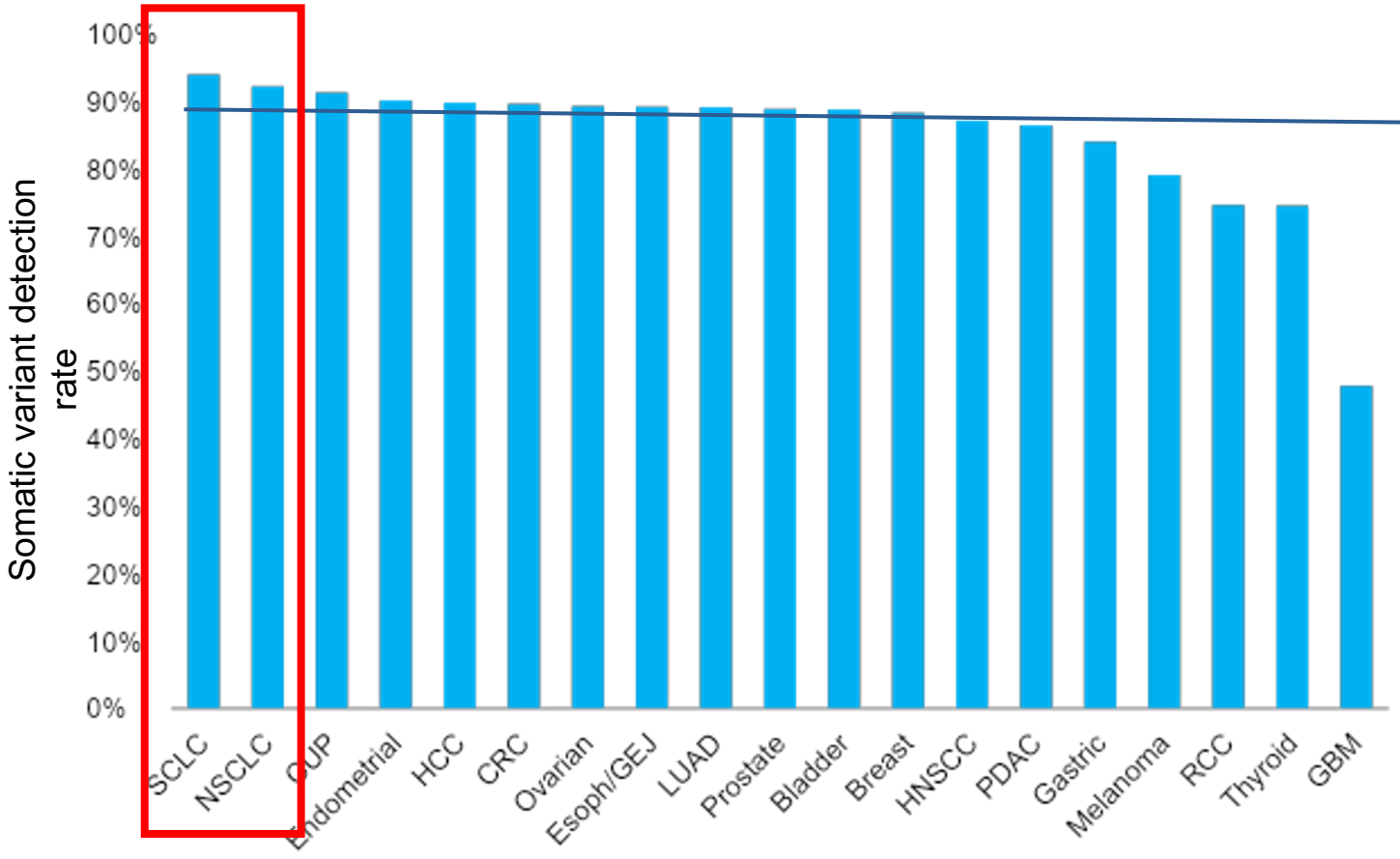
SNV, single nucleotide variants; Indels, insertions and deletions; CNV, copy number variant; MSI-H, microsatellite instability-high

Adapted from Odegaard JI, et al. *Clin Cancer Res* 2018;24:3539–3549 (Supplementary table 1)

Slide courtesy Guardant Health

High ctDNA Detection Rate Across Multiple Solid Cancers

East Genomics



Average across cancer types:
88%

Tumors stabilized by therapy typically do not shed as much DNA into circulation, nor do tumors that are slow-growing.[2] In these clinical contexts, Guardant360 may not detect any tumor DNA in a patient sample.

Based on 46,000 consecutive clinical samples

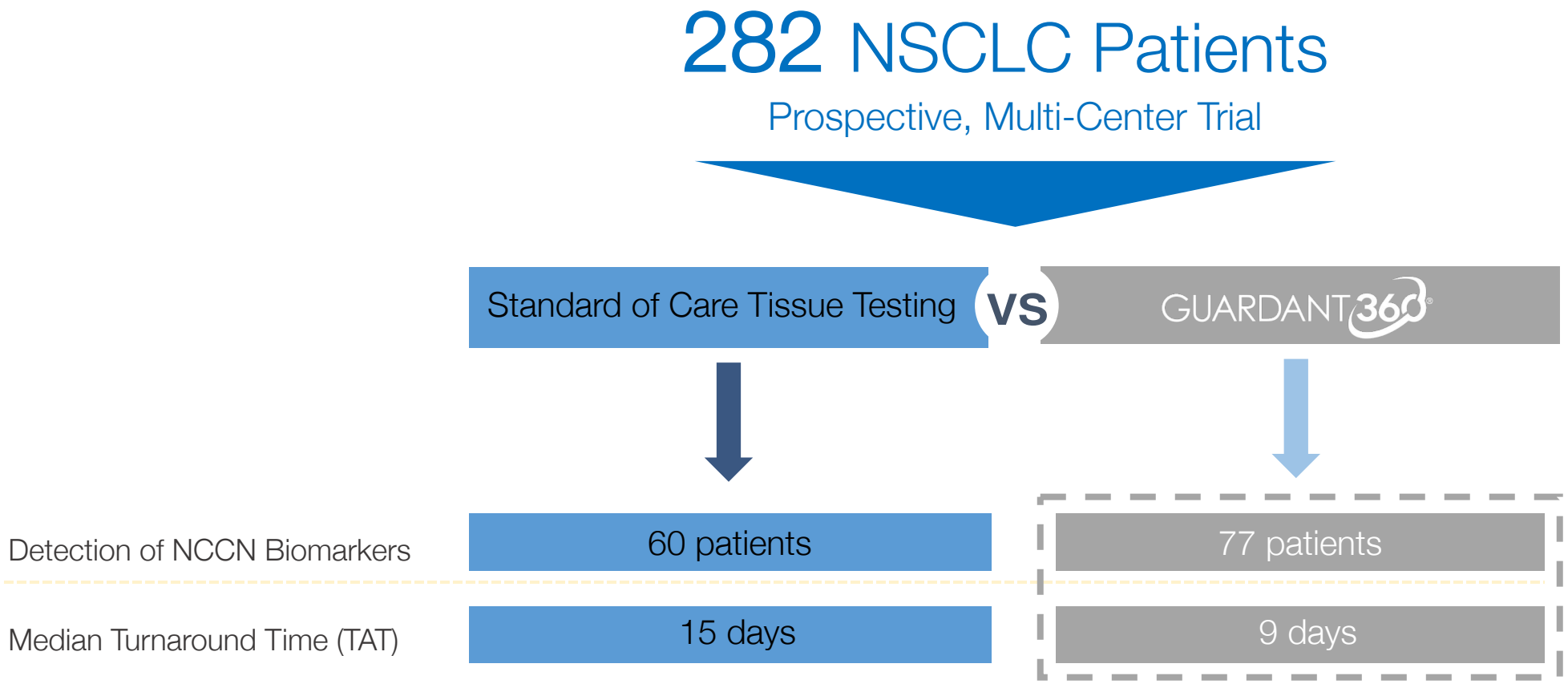
Internal Guardant Data for CY2019

Slide courtesy Guardant Health

Liquid biopsy with Guardant 360 results in more patients successfully genotyped in a shorter TAT than tissue testing

East Genomics

Guardant360 performance matches SoC tissue testing detection rates and delivers a faster turnaround time



NILE study (Non-invasive versus Invasive Lung Evaluation)) Leighl, *et al.* Clin Cancer Res August 1 2019 (25) (15) 4691-4700; DOI: 10.1158/1078-0432.CCR-19-0624

Slide courtesy Guardant Health

Detection of Tier 1 variants with Guardant360 in patients with NSCLC in UK clinical practice

East Genomics

BTOG 2021 Oral – 1st Prize

- 230 UK patients with NSCLC received Guardant360 testing (with matched SOC testing)
- Tier 1 variants defined as variants ready for implementation in routine clinical decisions

Identical results for paired tissue and Guardant360 NGS in 58%

Lower detection rate by tissue vs Guardant360 may reflect more limited tissue panel and limitations of tissue sampling/DNA quantity or quality

		Tier 1 Detection: Tissue		
		Yes	No	Total
Tier 1 Detection: G360	Yes	44 (58%)	32 (42%)	76
	No	7 (6%)	107 (94%)	114
	Total	51	139	190

Negative result with G360 when tissue is positive may reflect lower disease burden and hence low ctDNA level

Good concordance between G360 and tissue tests negative for tier 1 variants

Milner-Watts C, et al. Oral presentation 4, BTOG 2021.

Slide courtesy Guardant Health

Guardant360 improves detection of Tier 1 variants in patients with NSCLC

East Genomics

BTOG 2021 Oral – 1st Prize

Guardant360 ctDNA NGS reported results rapidly (median **9 days**)

Guardant360 increased breadth of detection of tier 1 genomic variants

- Should be considered routinely in first-line and relapsed advanced NSCLC
- May be of most importance in those with non-squamous histology

Guardant360 may lessen the need for tissue NGS testing or salvage pathway testing if a tier 1 variant is identified

ctDNA, circulating rumour DNA; NGS, next-generation sequencing; NSCLC, non-small cell lung cancer..

Milner-Watts C, et al. Oral presentation 4, BTOG 2021.

Slide courtesy Guardant Health

A Pilot of Blood-first – in 50 UK image-suspected Lung cancers

East Genomics

Background

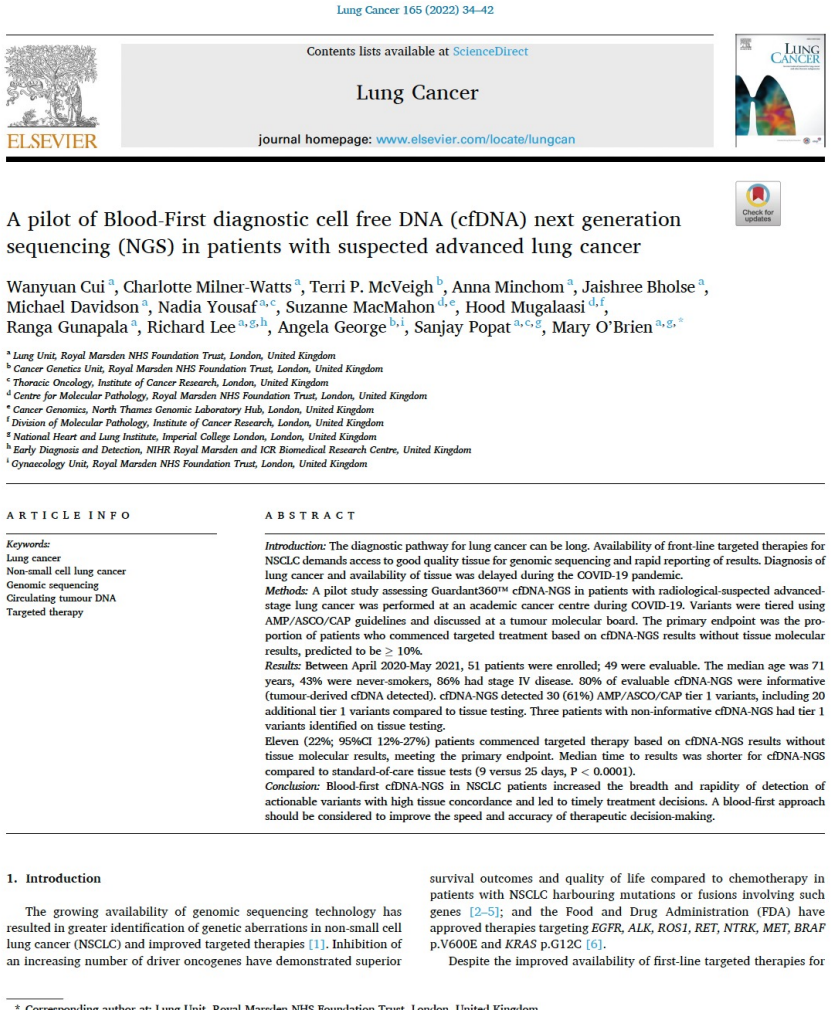
- 50 radiologically-suspected advanced Lung cancer patients were tested in a single centre during the Covid-19 pandemic.

Primary endpoint

- Proportion of patients who commenced targeted treatment based on cfDNA-NGS results without tissue molecular results, predicted to be ≥ 10%

Results:

- 22% of patients were able to start targeted therapy before a tissue result was returned
- An additional 15% of patients were able to start chemotherapy based on a ctDNA result alone
- Guardant360 detected 30 (61%) AMP/ASCO/CAP tier 1 variants, including 20 additional tier 1 variants compared to tissue testing.
- Median TAT for Guardant360 was 9 days vs 25 for SOC tissue test
- Results lead to the first NHSE-backed pilot to access ctDNA in image suspected lung cancer (700 patients) currently running in England



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A pilot of Blood-First diagnostic cell free DNA (cfDNA) next generation sequencing (NGS) in patients with suspected advanced lung cancer

Wanyuan Cui [a], Charlotte Milner-Watts [a], Terri P. McVeigh [b], Anna Minchom [a], Jaishree Bholse [a], Michael Davidson [a], Nadia Yousaf [a,c], Suzanne MacMahon [d,e], Hood Mugalaasi [d,f], Ranga Gunapala [a], Richard Lee [a,g,h], Angela George [b,i], Sanjay Popat [a,c,g], Mary O'Brien [a,g,*]

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ARTICLE INFO

Keywords:
Lung cancer
Non-small cell lung cancer
Genomic sequencing
Circulating tumour DNA
Targeted therapy

ABSTRACT

Introduction: The diagnostic pathway for lung cancer can be long. Availability of front-line targeted therapies for NSCLC demands access to good quality tissue for genomic sequencing and rapid reporting of results. Diagnosis of lung cancer and availability of tissue was delayed during the COVID-19 pandemic.
Methods: A pilot study assessing Guardant360™ cfDNA-NGS in patients with radiological-suspected advanced-stage lung cancer was performed at an academic cancer centre during COVID-19. Variants were tiered using AMP/ASCO/CAP guidelines and discussed at a tumour molecular board. The primary endpoint was the proportion of patients who commenced targeted treatment based on cfDNA-NGS results without tissue molecular results, predicted to be ≥ 10%.
Results: Between April 2020-May 2021, 51 patients were enrolled; 49 were evaluable. The median age was 71 years, 43% were never-smokers, 86% had stage IV disease. 80% of evaluable cfDNA-NGS were informative (tumour-derived cfDNA detected). cfDNA-NGS detected 30 (61%) AMP/ASCO/CAP tier 1 variants, including 20 additional tier 1 variants compared to tissue testing. Three patients with non-informative cfDNA-NGS had tier 1 variants identified on tissue testing.
Eleven (22%; 95%CI 12%-27%) patients commenced targeted therapy based on cfDNA-NGS results without tissue molecular results, meeting the primary endpoint. Median time to results was shorter for cfDNA-NGS compared to standard-of-care tissue tests (9 versus 25 days, P < 0.0001).
Conclusion: Blood-first cfDNA-NGS in NSCLC patients increased the breadth and rapidity of detection of actionable variants with high tissue concordance and led to timely treatment decisions. A blood-first approach should be considered to improve the speed and accuracy of therapeutic decision-making.

1. Introduction

The growing availability of genomic sequencing technology has resulted in greater identification of genetic aberrations in non-small cell lung cancer (NSCLC) and improved targeted therapies [1]. Inhibition of an increasing number of driver oncogenes have demonstrated superior survival outcomes and quality of life compared to chemotherapy in patients with NSCLC harbouring mutations or fusions involving such genes [2–5]; and the Food and Drug Administration (FDA) have approved therapies targeting *EGFR, ALK, ROS1, RET, NTRK, MET, BRAF* p.V600E and *KRAS* p.G12C [6].

Despite the improved availability of first-line targeted therapies for

* Corresponding author at: Lung Unit, Royal Marsden NHS Foundation Trust, London, United Kingdom

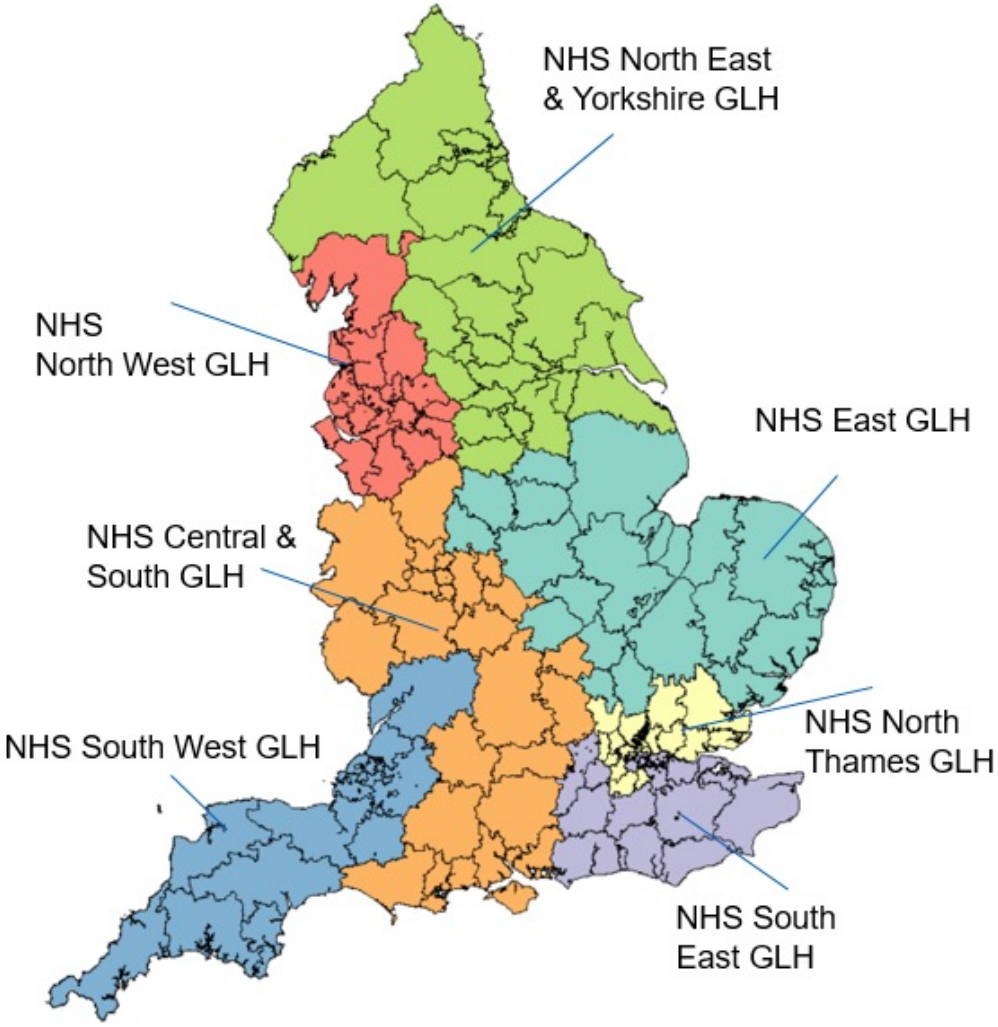
- Cui W, Milner-Watts C, McVeigh TP, et al. A pilot of Blood-First diagnostic cell free DNA (cfDNA) next generation sequencing (NGS) in patients with suspected advanced lung cancer [published online ahead of print, 2022 Jan 20]. Lung Cancer. 2022;165:34-42. doi:10.1016/j.lungcan.2022.01.009

Slide courtesy Guardant Health

National GMSA lung ctDNA pilot

East Genomics

- Initially n=700 patients nationally
  - n=100 for each of the 7 GLHs
  - Providers: Clinically validated providers of liquid biopsies, including Guardant Health
- Pilot expansion: n=2000
  - Provider: Marsden360*
- Expected to expand to 10,000 patients nationally in 2023/24

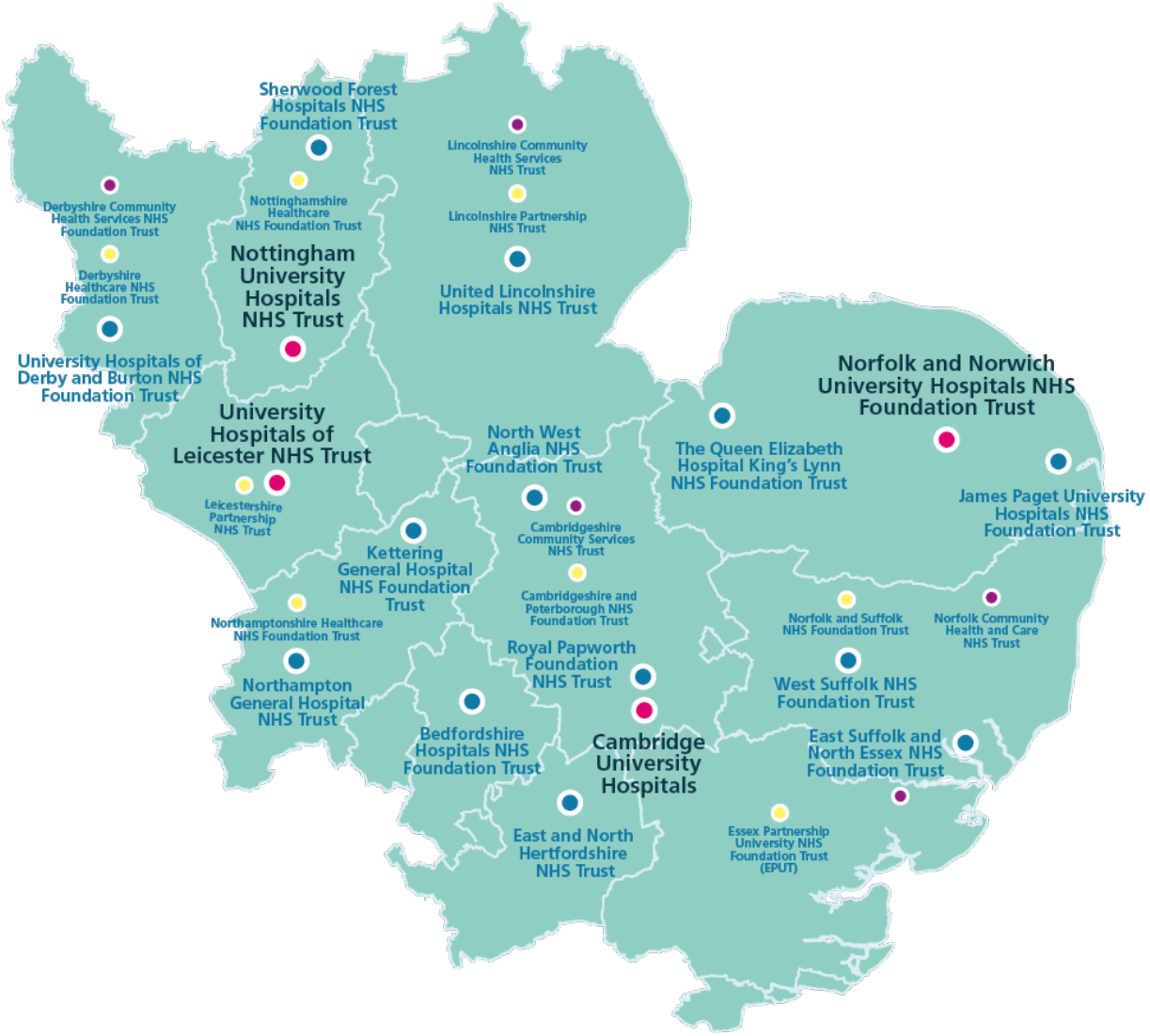


- M360 is a test based on Guardant technology, modelled on Guardant360 CDx being offered at RM

East GMSA

East Genomics

- Active:
  - Cambridge University Hospitals
  - University Hospitals Leicester
  - West Suffolk
  - Kettering
- In setup:
  - Norfolk & Norwich
  - University Hospitals of Derby & Burton
  - East & North Herts



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NHS
East Genomics

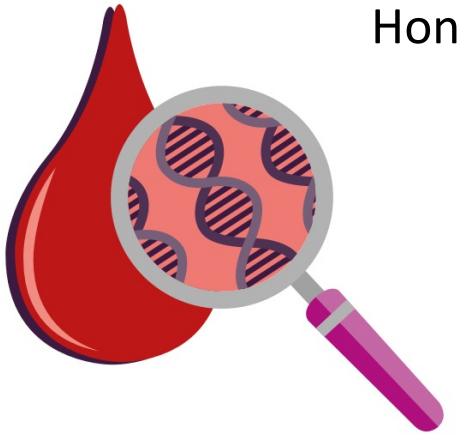
Case Studies

Dr Frank McCaughan

Honorary Consultant in Respiratory Medicine and lead clinician for lung cancer, CUH

Tiago Verissimo

Lung Clinical Nurse Specialist, CUH

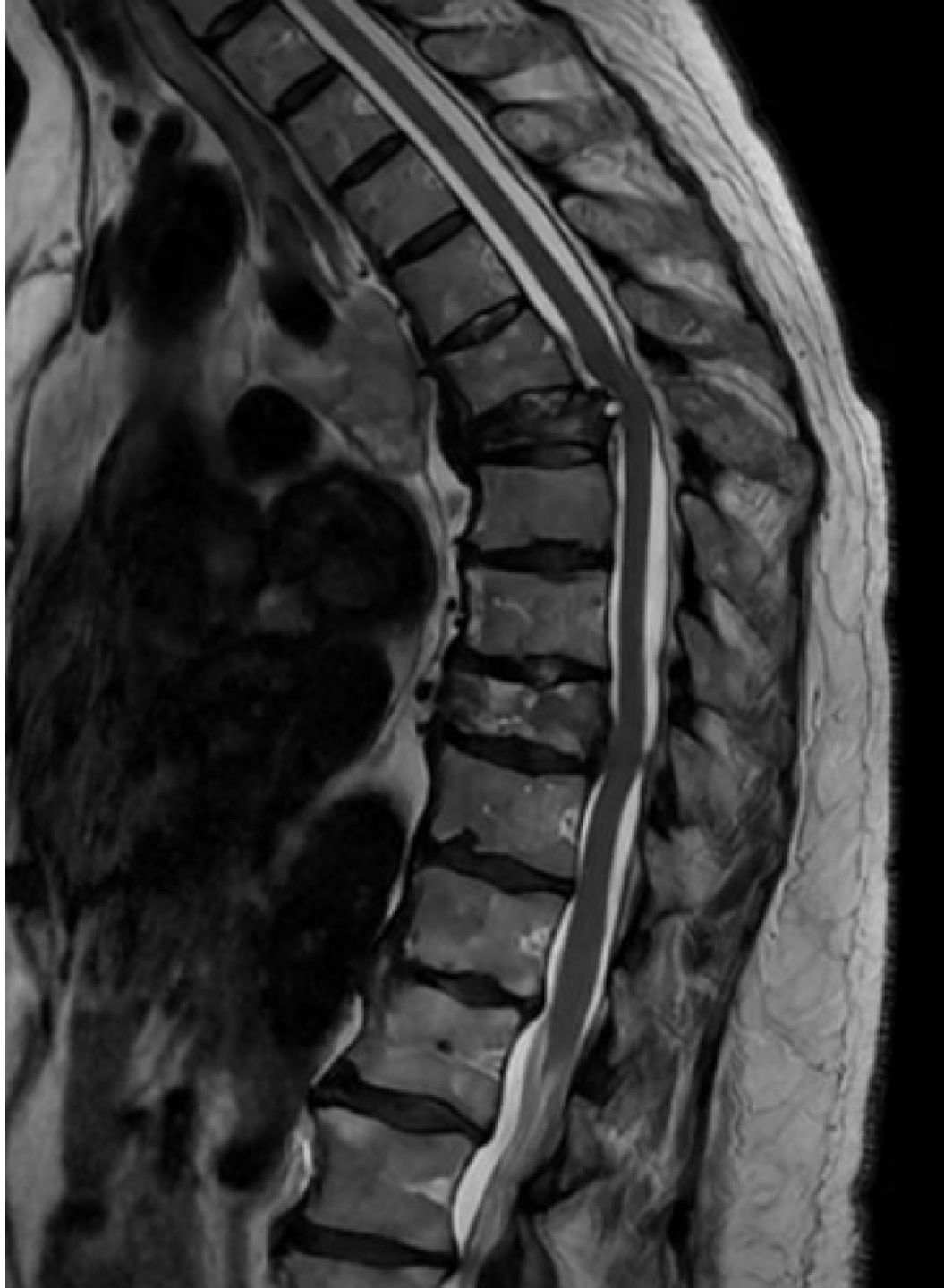


NHS
Cambridge
University Hospitals
NHS Foundation Trust

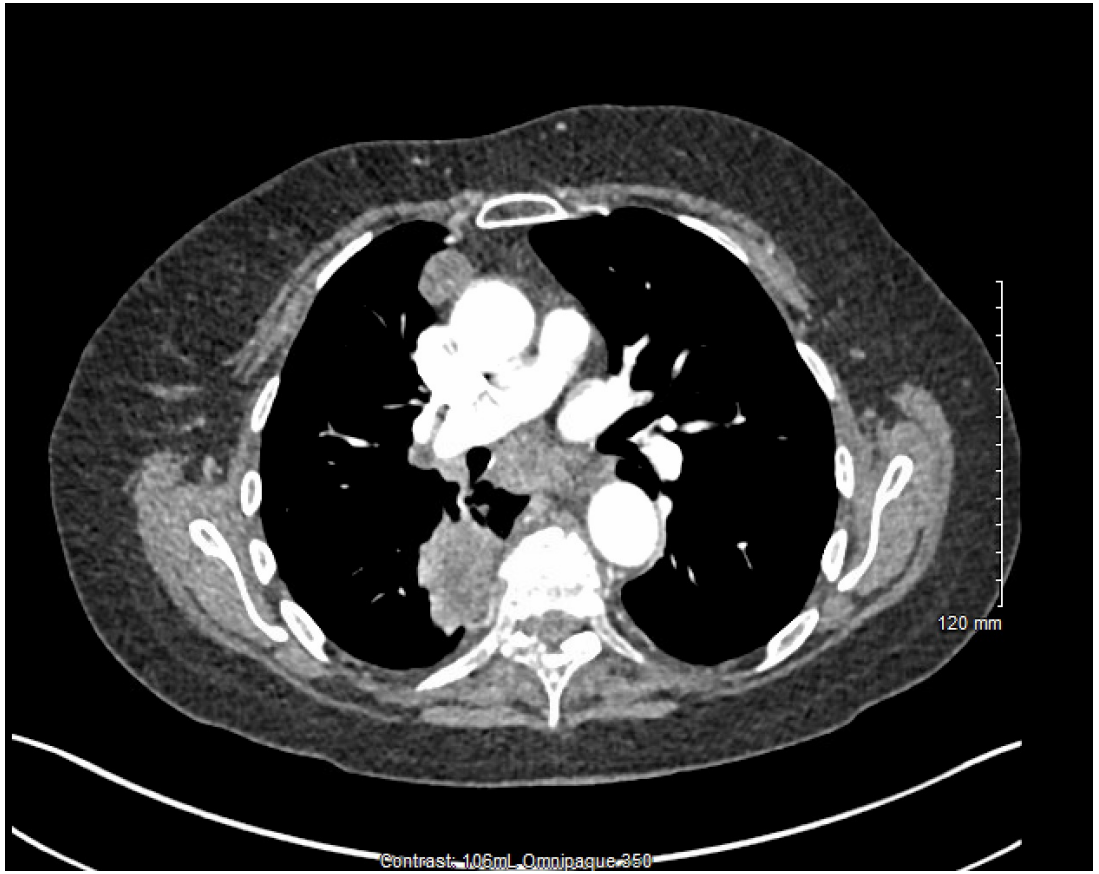
Case 1

Background

- 65 y/o female
- Never smoker
- PMHx
  - Hypertension
- Baseline PS 0
- Presentation
  - 6 weeks progressive back pain
  - Associated with moving furniture
  - Unbearable despite high dose codeine phosphate
- No clinical features of cord compression
- Hyponatraemia
- Imaging investigations were performed



Diagnostic work-up



- SCL Biopsy 22 March 2023
- Cytology report 27 March
  - CK7/TTF1 +ve cells
  - NSCLC – adenocarcinoma
  - Molecular profile requested (reflex)
  - Reported 19 April
- Guardant360® CDx
  - Blood taken 21 March 2023
  - Reported 28 March

Guardant360® CDx result

Cambridge University Hospitals NHS Foundation Trust

Summary of Detected Somatic Alterations, Immunotherapy Biomarkers & Associated Treatment Options

KEY CDx Guardant360 CDx approved indication ✓ Approved in indication ~ Approved in other indication ⊗ Lack of response

Detected Alteration(s) / Biomarker(s)	Associated EMA-Approved Therapies	Clinical Trial Availability (see page 3)	% cfDNA or Amplification	Biomarker Category
EGFR E746_A750del (Exon 19 deletion)	CDx TAGRISSO® (osimertinib) is EMA-approved for this indication ✓ Afatinib, Dacomitinib, Erlotinib, Erlotinib+ramucirumab, Gefitinib, Osimertinib	Yes	8.37%	1
BRAF G469V	None	Yes	0.21%	4
STK11 V66V	None	No	0.55%	4
TP53 Y205C	None	Yes	4.27%	4

Management

- Dexamethasone
- Radiotherapy
- Analgesia

- Osimertinib 3 April
- 19 April – confirmed tissue EGFR Exon 19 deletion

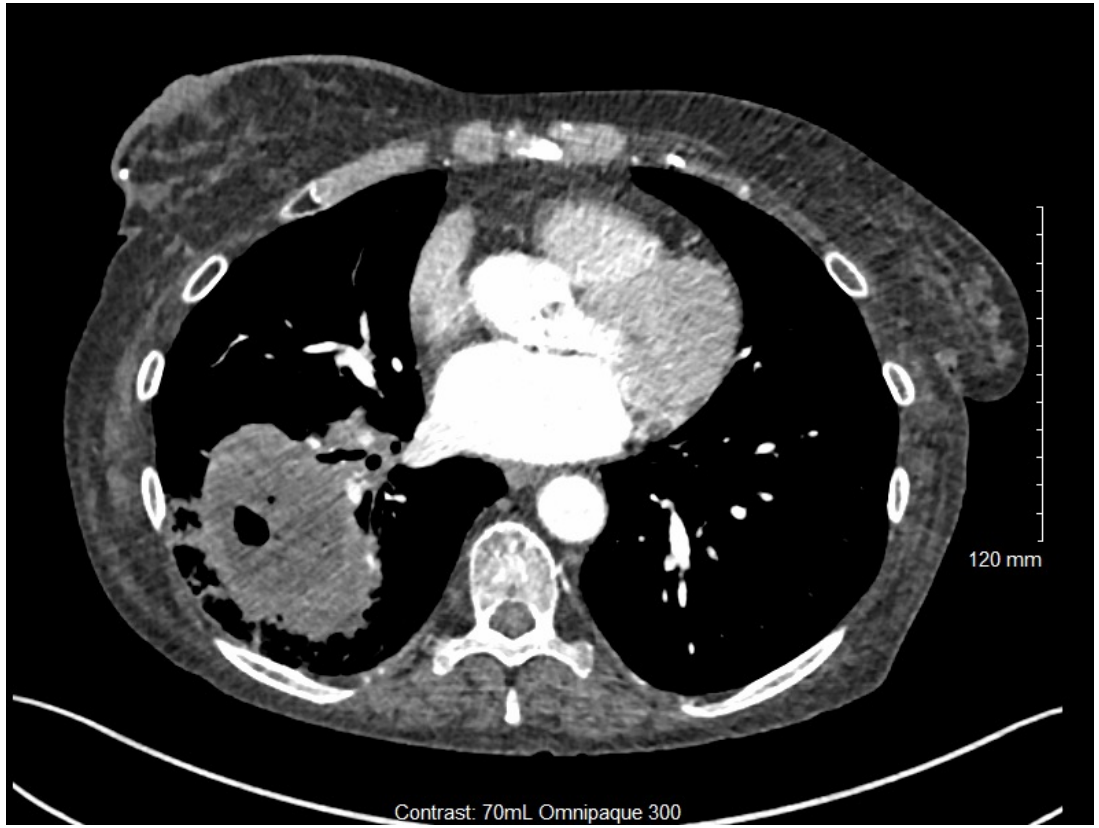
Conclusions

- Earlier diagnosis of EGFR mutated disease via Guardant compared to normal pathway in previously well never-smoker who was admitted in some distress
- Treatment instituted approximately 3 weeks earlier than otherwise would have been the case

Case 2

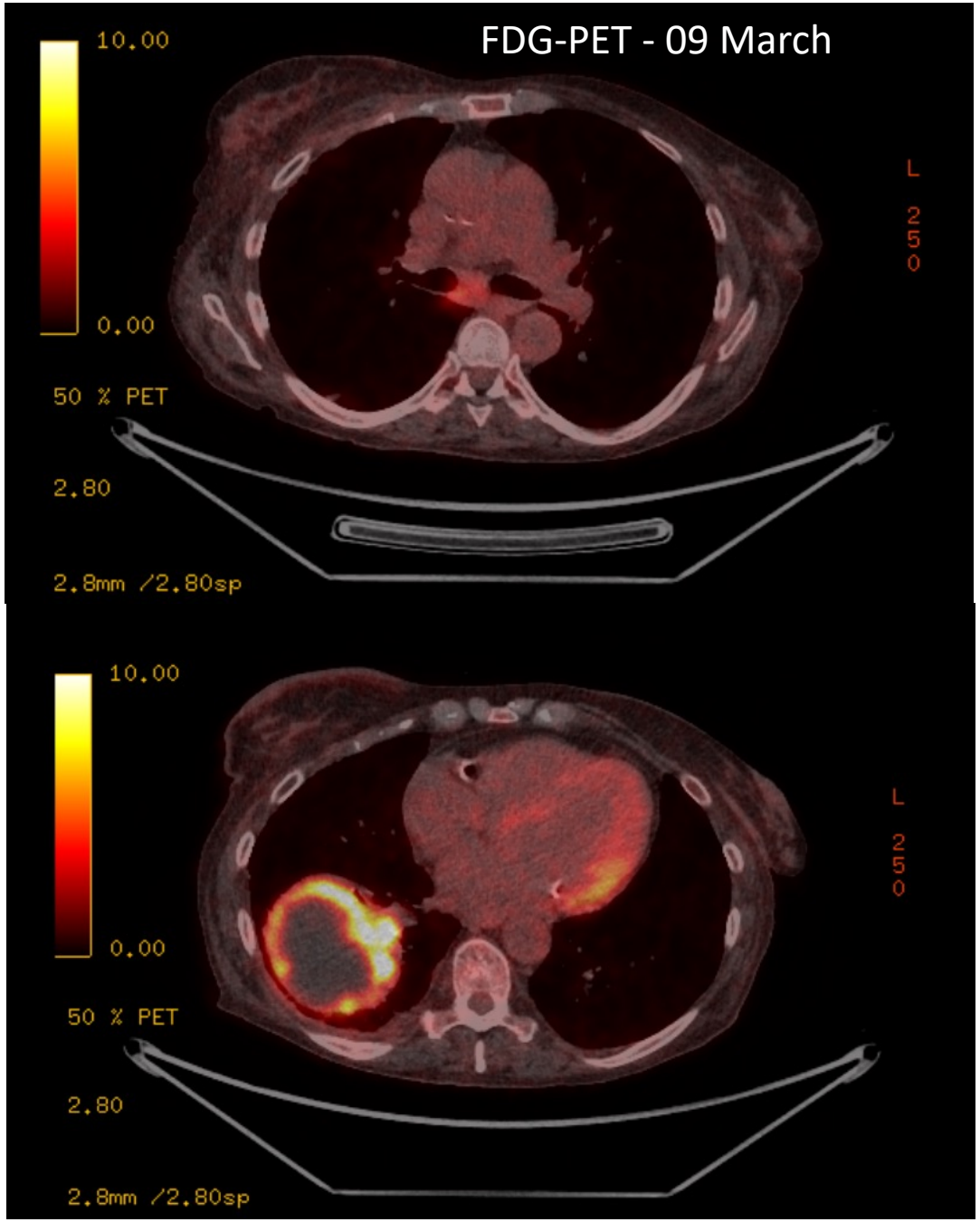
Background

- 61 yr old female
- Current smoker
- Prior breast cancer (Right)
  - Wide local excision
  - Radiotherapy
- Admitted end December
  - 4 weeks cough/pleuritic chest pain
  - Swinging fever
  - CRP>300
  - Enterobacter cloacae in sputum



Early Investigations/Management

- Broad spectrum antibiotics
- Bronchoscopy/EBUS
  - Negative cytology Station 7,11R
  - Negative microbiology
- Post EBUS sepsis
  - Further broad spectrum antibiotics
  - DRESS syndrome
- New diagnosis severe aortic stenosis



Further Diagnostics

Cambridge University Hospitals NHS Foundation Trust

- Diagnostic biopsy (March 3rd)
- Biopsy
  - cytology – NSCLC NOS (March 13th)
  - GLH report – no mutations detected (March 21st)
- Guardant360® CDx (March 9th)
  - Report 19th March

Summary of Detected Somatic Alterations, Immunotherapy Biomarkers & Associated Treatment Options

KEY CDx Guardant360 CDx approved indication ✓ Approved in indication ~ Approved in other indication ⊗ Lack of response

Detected Alteration(s) / Biomarker(s)	Associated EMA-Approved Therapies	Clinical Trial Availability (see page 3)	% cfDNA or Amplification	Biomarker Category
APC N372fs	None	No	11.76%	4
BRCA1 A1708T	~ Olaparib, Talazoparib	Yes	8.59%	4
CCNE1 R240H	None	No	0.22%	4
DDR2 L610L	None	No	7.07%	4
ESR1 V422V	None	No	4.92%	4
STK11 P221L	None	Yes	2.29%	4
TP53 G334V	None	Yes	8.45%	4

Further Investigation and Management

- Patient management
  - Deep SCL node (negative)
  - Repeat EBUS (negative)
  - Transcatheter Aortic Valve Implantation
  - Surgical resection

Discussion / Learning Points

Cambridge University Hospitals NHS Foundation Trust

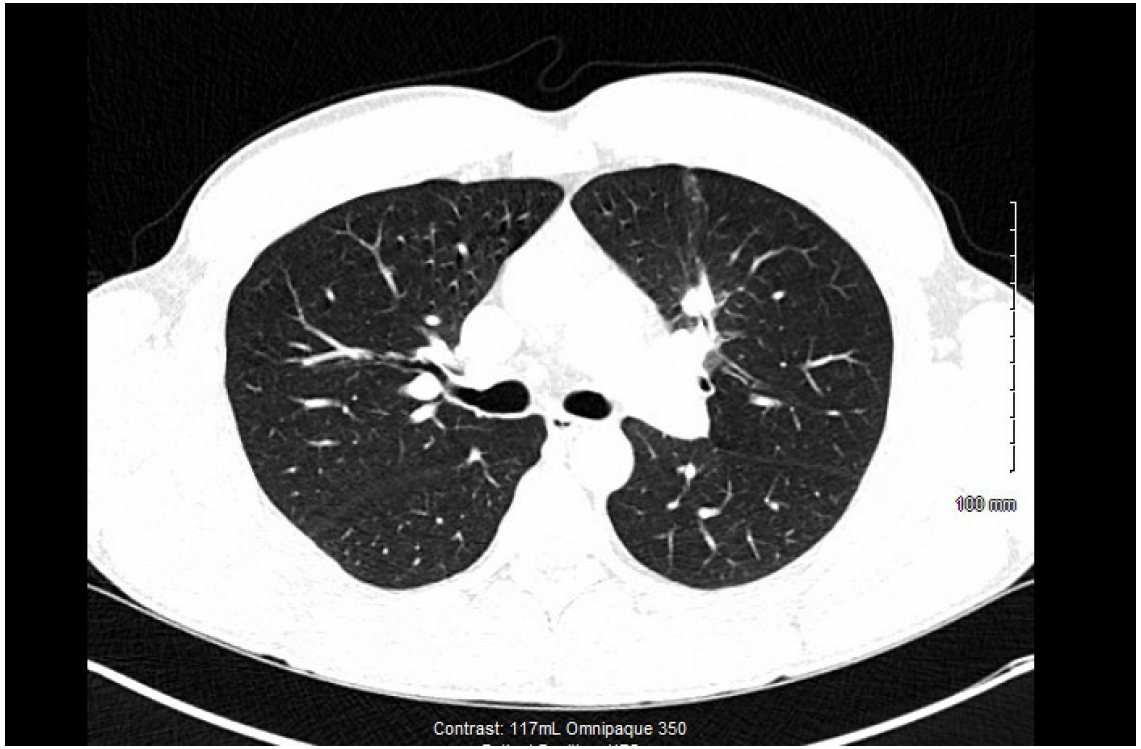
- Protracted diagnostic work-up
- ctDNA has the potential to help resolve diagnostic dilemmas in challenging cases
- In this case Guardant360® CDx yielded a mutational profile that was not detected from tissue NGS panel

Cambridge University Hospitals NHS Foundation Trust

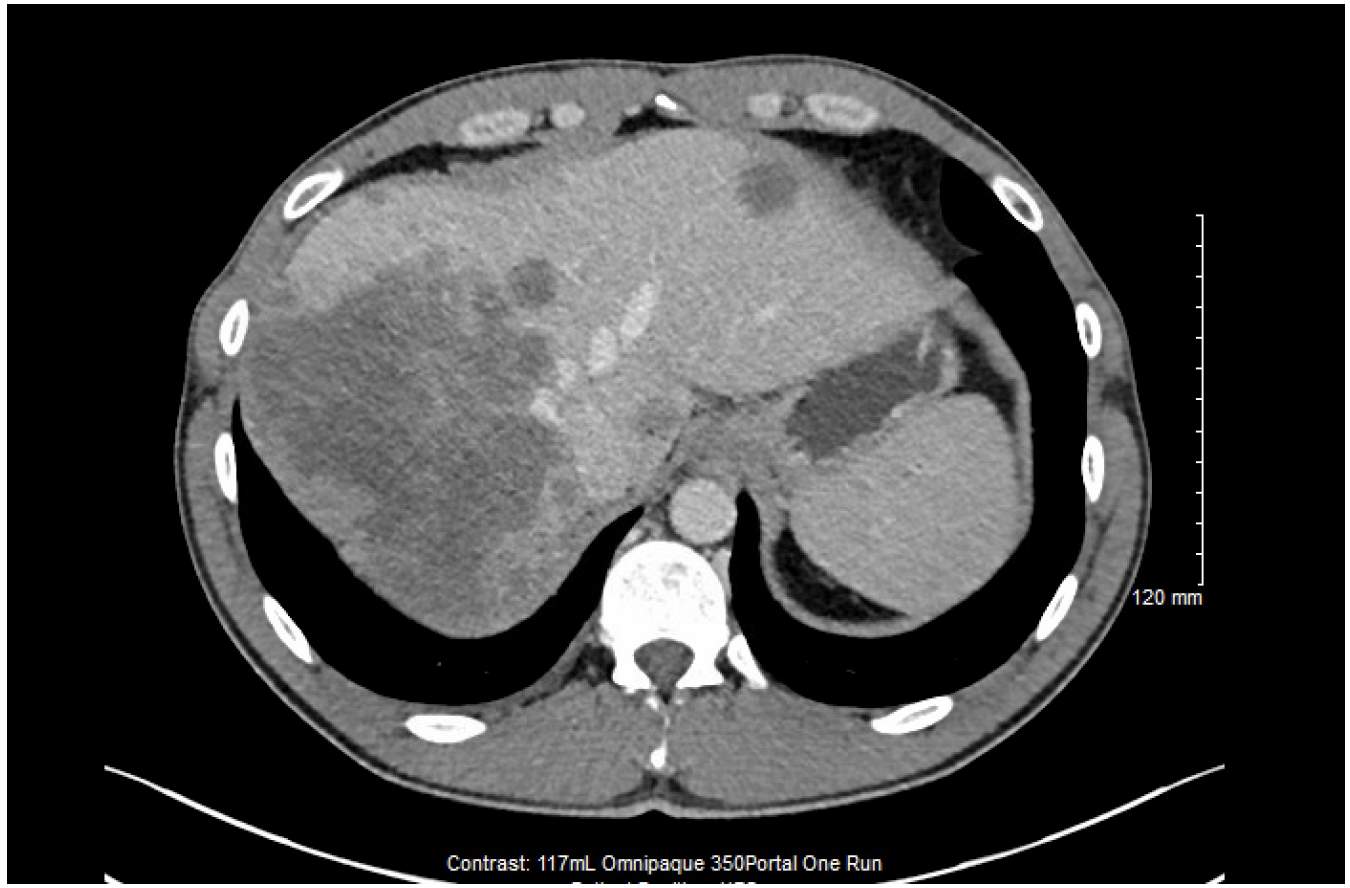
Case 3

Background

- 39 yr old male, army engineer
- Never smoker
- Extremely fit baseline
- Few weeks of fatigue and reduced appetite



Diagnostic work-up



- ctDNA 05/09
  - Reported 27/09
  - (Marsden)
- Liver biopsy 07/09
  - NSCLC (CK7/TTF1+ve) 11/09
  - Reflex molecular profile requested 11/09
  - Molecular report 06/10
  - ALK+ve IHC 14/09

Marsden 360 Result

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NHS Cambridge University Hospitals NHS Foundation Trust

Analysis results: Clinically relevant variants detected

1 Variant of strong clinical significance, Tier 1	Approved treatments	Trials and Supplementary Information
EML4-ALK, fusion, Pathogenic	Alectinib Brigatinib Ceritinib Crizotinib Lorlatinib	Trials: 1 Phase 4 1 Phase 3 2 Phase 2 2 Phase 1/Phase 2 1 Phase 1
1 Variant of potential clinical significance, Tier 2	**Approved treatments**	**Trials and Supplementary Information**
TP53, c.559+1G>A, VAF 6.32%, Pathogenic	-	Trials: 1 Phase 1

Interactions

None

Guidelines

Potentially relevant guidelines are reported in the "guidelines" section starting on page 6.

Report content

- RNA: Fusion EML4-ALK confirmed
- Tissue correlation
  - Also reported EML4-ALK fusion
  - No *TP53* mutation reported

Management

- Brigatinib commenced 18 September
- Already responding

Discussion / Learning Points

Cambridge University Hospitals NHS Foundation Trust

- “ctDNA” assays can also detect actionable fusion events – ALK, NTRK1-3, ROS1
- Potential to instigate treatment earlier with ctDNA assay
- CNS role in expediting investigations and management decisions including ctDNA assays in appropriate patients

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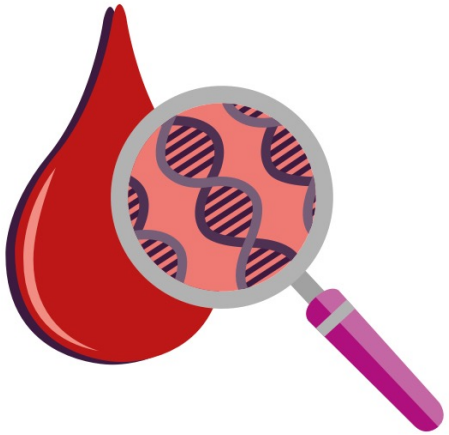
NHS
Cambridge University Hospitals
NHS Foundation Trust

Audit of CUH experience

Dr David Favara

(Clinical Lecturer in Medical Oncology, University of Cambridge)



cfDNA testing in lung cancer: NHS real-world results from a single centre

Main finding: *lung cancer patients with a cfDNA detected targetable driver mutation started treatment 3.5 weeks earlier than those without (2.5 weeks versus 6 weeks; p=0.02).*

David M Favara[1,2], Tiago Verissimo[1,3], Frank McCaughan[3,4]

[1] Oncology Department, Cambridge University Hospitals NHS Foundation Trust, Cambridge UK

[2] Oncology Department, University of Cambridge, UK

[3] Respiratory Department, Cambridge University Hospitals NHS Foundation Trust, Cambridge UK

[4] Department of Medicine, University of Cambridge, UK

	n	%
Total cases	32 (100%)	100%
Female	18	56%
Mean age (years; range)	71 (57-87)	
Lung diagnoses	25	78%
Non lung cancer diagnoses	7	28%
Biopsy Histology		
Lung:		
Adenocarcinoma	12	48%
SCC	1	4%
Small cell	3	12%
Not otherwise specified (NOS)	2	8%
Other lung type*	3	12%
No histology (radiological diagnosis)	4	16%
Non-lung		
Lymphoma	4	57%
Breast cancer	1	14%
Renal cell carcinoma	1	14%
Head and neck SCC	1	14%
Lung cancer patient characteristics		
Female	17	68%
Mean age (years; range)	69.8 (61-87)	
Lung cancer biopsy source		
EBUS	15	60%
Other	9	36%
No biopsy	1	4%
Lung stage		
Stage 1-IIIA	3	12%
Stage IIIB-IV	22	88%

Table 1: patient characteristics (*large cell lung cancer; spindle cell lung cancer; undifferentiated lung cancer)

	n	%
cfDNA assay		
Mean time (days) from collection to arrival at US lab	2.8 (2.1-3.7 95% CI)	
Mean time (days) from arrival in US lab to result	6.4 (5.2-7.6 95% CI)	
Mean time (days) from collection to result	9.3 (4.6-10.9 95% CI)	
Tumour biopsy profiling:		
Mean time (days) from biopsy to histology result	10.2 (7.5-12.8 95% CI)	
Mean time from histology to profiling result	16.74 (13.2-20.2 95% CI)	
Mean time (days) from biopsy to profiling result	26.89 (22.3-31.5 95% CI)	
Lung cancer treatments		
Patients treated	16	64%
Patients not treated (poor PS or death)	8	32%
Unknown (patient transferred to another hospital)	1	4%
cfDNA detected targetable driver alterations		
EGFR exon 21 Leu858Arg	3	43%
EGFR exon 19 Glu746_Ala750del	3	43%
EGFR exon 19 Leu747_Pro753delinsSer	1	14%
Biopsy concordance with cfDNA testing		
Yes	17	68%
No	2	8%
No biopsy	6	24%
Treatment implications		
cfDNA expedited 1st line treatment	7	
Time from cfDNA to treatment if ctDNA actionable result	17.6 (13.1-22.2 95% CI)	p=0.02
Time from cfDNA to treatment for non-actionable ctDNA result	42 (21.4-62.6 95%CI)	

Table 2: cfDNA and biopsy profiling results and effect on treatment

Results:

	n	%
cfDNA assay		
Mean time (days) from collection to arrival at US lab	2.8 (2.1-3.7 95% CI)	
Mean time (days) from arrival in US lab to result	6.4 (5.2-7.6 95% CI)	
Mean time (days) from collection to result	9.3 (4.6-10.9 95% CI)	
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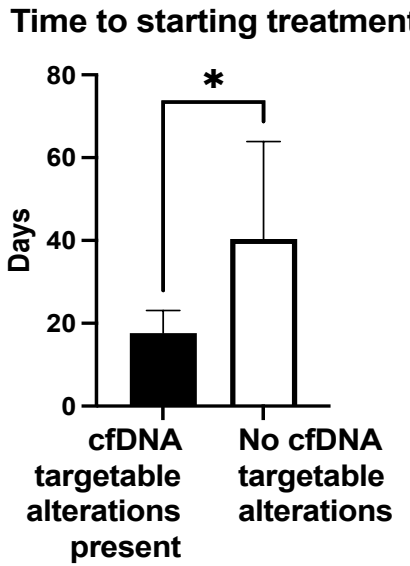
cfDNA expedited 1st line treatment	7	
Time from cfDNA to treatment if ctDNA actionable result	17.6 (13.1-22.2 95% CI)	*p*=0.02
Time from cfDNA to treatment for non-actionable ctDNA result	42 (21.4-62.6 95%CI)	

Table 2: cfDNA and biopsy profiling results and effect on treatment



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NHS East Genomics

Lung ctDNA pilot: Clinical pathway

Dr Brent O'Carrigan

Clinical Cancer Lead, NHS East Genomics

Medical Oncologist

b.ocarrigan@nhs.net

Trust onboarding / activation

East Genomics

- Contact:
  - Brent O’Carrigan b.ocarrigan@nhs.net

Documentation	
Patient Leaflet	☐
Marsden360 SOP	☐
Electronic test request form	☐
Instructions for use leaflet	☐
Marsden360 annotated report to help facilitate interpretation of the results	☐
Access to national data collection tool (excel spreadsheet)	☐

Supplies	
Streck Tubes received	☐
Safeboxes received	☐
Marsden360 return address labels received for safeboxes received	☐
Marsden360 tube labels for Streck tubes received	☐
Access to Royal Mail tracking system	☐

East Genomics

Ordering a Marsden360

1. For Test Requisition Form (TRF), Instruction leaflet, tube label template and enquiries, please email **Marsden360@rmh.nhs.uk** or telephone **020 8915 6565**

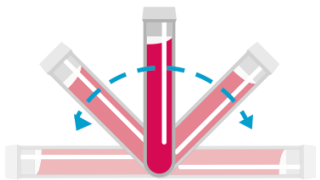
For Streck tubes and Royal Mail Safeboxes (Special Delivery; UN3373 compliant) please contact your lead GMSA site.

East Genomics

Blood draw instructions

1. Collect specimen by venipuncture, filling the two Streck tubes completely

2. Mix by gentle inversion 8 to 10 times



3. Ensure tubes are labelled as instructed in step 2 on the following page

Do not refrigerate or freeze blood samples

Shipping instructions

1. Complete the Test Requisition Form (TRF)

2. Fill out labels on each tube including:
   - Patient name
   - Hospital number
   - Date of birth (dd/mm/yyyy)
   - Collection date (dd/mm/yyyy)

3. Open the Safebox and wrap the sample tubes in the absorbent sheet and place into the grip seal bag and close. Please note one Safebox for two sample tubes only

4. Place the filled grip seal bag into the PathoSeal bag

5. Close the PathoSeal bag following the instructions printed on the bag

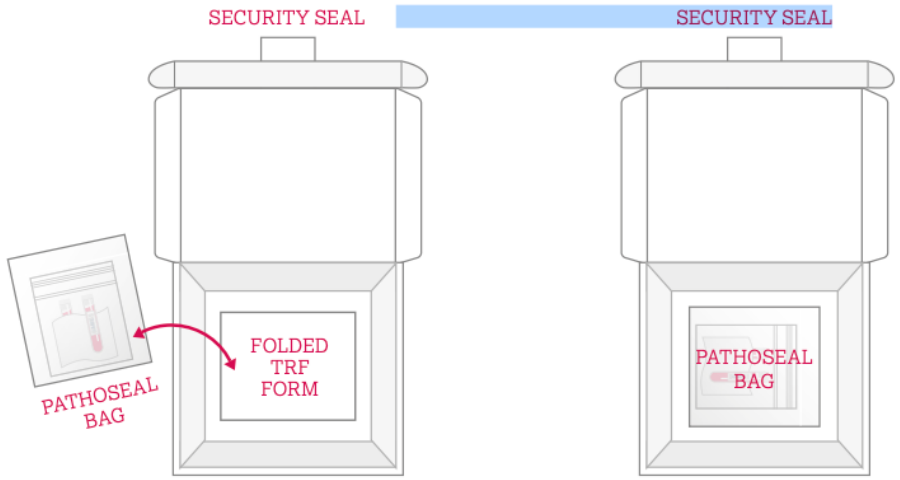
3

East Genomics

Shipping instructions

6 Place the completed PathoSeal bag and Test Requisition Form (TRF) into the Safebox

7 **CHECK** all contents are included as required before closing



8 Close the Safebox ensuring the security tab is tucked in

East Genomics

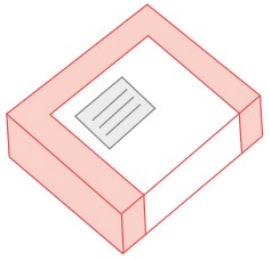
Shipping instructions

9 Complete the Send and Return address details.

Clinical Genomics The Centre for Molecular Pathology
The Royal Marsden NHS Foundation Trust |
Cotswold Road Sutton Surrey | SM2 5PT

10 Apply prepaid postage label over these instructions ensuring it wraps round and over the tuck in security tab.

Please record the Tracking number, to enable the Safebox to be tracked during transit



11 Please take the Safebox to your Trust Postroom for delivery to Clinical Genomics, The Royal Marsden NHS Foundation Trust.

Samples should be received within 48 hours of venepuncture

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NHS

East Genomics

Q&A / Discussion