Transforming the Lung Cancer Diagnostic Pathway with Liquid Biopsy: Early Genomic Results from the QuicDNA Biomarker Study in Wales

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Authors: Rachel Dodds[1], Rhian White[1], Sian Morgan[1], Richard Adams[2,3], Mick Button [2,] Paul Shaw [2], Mat Jones [4], Ian Williamson [4], Craig Dyer[5], Magda Meissner[2,3]. 1 All Wales Medical Genomics Service, 2 Velindre Cancer Centre, 3 Cardiff University, 4 Aneurin Bevan University Health Board, 5 Cardiff and Vale University Health Board. Rachel.Dodds@wales.nhs.uk & Magdalena.Meissner@wales.nhs.uk

THE QUICDNA STUDY: Liquid Biopsy Samples From Across Wales (2023 – 2025)

In Wales, Lung Cancer is the **fourth** most common cancer and the majority of patients are diagnosed at a **late stage. Lung Cancer is the leading cause of cancer death.** Wales consistently has a **lower survival** rate than other parts of the UK and was ranked **28th out of 29** European countries for lung cancer survival. **There is a critical need to improve and shorten the current diagnostic pathway.**

The discovery of genomic targets has significantly advanced and improved treatment options. **The integration of Liquid Biopsy into the Lung Cancer Pathway has the potential to detect all currently actionable genomic variants earlier in the diagnostic pathway.**

THE STUDY AIMS TO:

1. **INTEGRATE ctDNA testing at an early stage in the diagnostic pathway**
2. **SHORTEN time to treatment compared to current Standard of Care pathway**
3. **INCREASE the number of patients that receive targeted therapy**
4. **IMPROVE patient outcomes**

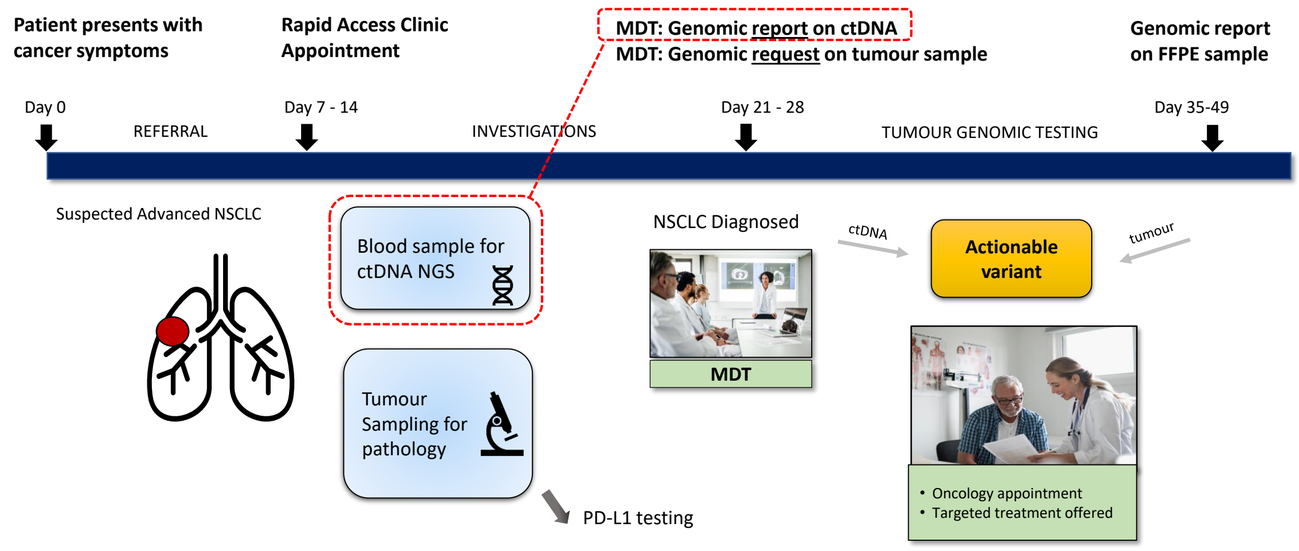
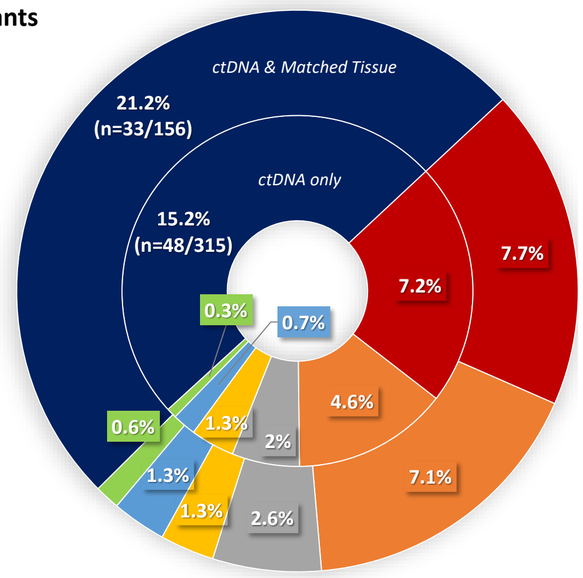


Fig. 1: QuicDNA ctDNA NGS testing added to diagnostic pathway at cancer suspicion. All Standard of Care testing remains unchanged

EARLY GENOMIC RESULTS: Actionable Variants Detected in 315 ctDNA Tests (156 with Matched Tissue Samples)

Fig. 2: Pick-up rates for actionable variants

- **KRAS (G12C) - Sotorasib**
- **EGFR (various) - Osimertinib**
- **MET exon 14 skipping - Tepotinib**
- **BRAF (V600E) – Dabrafenib & Trametinib**
- **ALK fusion – Alectinib**
- **RET fusion - Selpercatinib**
- **Total with Actionable Variant**



ABOVE/RIGHT Fig 2: Frequency of Actionable Variants. Inner circle - frequency detected in ctDNA samples (cancer suspicion); outer circle - frequency in matched ctDNA and tumour-tissue samples (confirmed NSCLC); Numbers = % of samples with successful testing. Based on 315 completed QuicDNA ctDNA tests and 156 QuicDNA patients with completed genomic testing on ctDNA and tumour samples.

Illumina TSO500 and TSO500 ctDNA NGS testing performed. Sequencing on a NovaSeq 6000. Analysis of named genes only.

Table 1: ctDNA test statistics (n=156)	
Sensitivity	86.4% (72.7% - 94.8%)
Specificity	100% (96.5% to 100%)
Positive Predictive Value	100% (90.8% - 100%)
Negative Predictive Value	94.6% (89.2% - 97.3%)

KEY FINDINGS (Data updated on 16 October 24 as a genomics snapshot from the ongoing study)**:**

- **Concordance between successful ctDNA and tumour-tissue genomic testing for the presence or absence of actionable variants (treatment indication) = 91.03%.**
- All actionable variants (n=33) reported for ctDNA were confirmed during successful genomic tissue testing
- 6 patients had an actionable variant detected through genomic tissue testing which was not detected during the ctDNA test

ADDITIONAL FINDINGS:

- Non-actionable variants were detected in 50 ctDNA samples (concordance for non-actionable variants has not been assessed)
- *At least* 3 patients had actionable variants detected through ctDNA but tissue testing failed and *at least* 6 patients were diagnosed with a different cancer type (includes 4 with CUP) – Benefit to wider group of patients?

Table 2: Potential reasons for discordant testing	VARIANTS NOT DETECTED	ADDITIONAL VARIANT(S) DETECTED
cfDNA/ctDNA	low/absent ctDNA - tumour shedding. Location of tumour/metastases	tumour heterogeneity/sub-clonal variants, CHIP, additional malignancy
Tumour tissue	poor quality DNA/RNA. Low tumour content. Sampling bias	confirmed tumour content. Sampling of metastatic sites

LEFT Table 1: ctDNA test statistics - ctDNA test statistics generated with data from 156 QuicDNA patients with completed genomic testing on ctDNA and tumour samples using MedCalc*.
ABOVE Table 2: potential reasons for discordant testing - variants may not be detected, or additional variants detected during genomic testing of either sample type**, reports are cautiously worded.

TIME TO REPORT: ctDNA vs Tissue Total TAT (left), Timing in Diagnostic Pathway (right) 156 Patients

ctDNA can guide earlier treatment because liquid biopsies can be taken earlier in the diagnostic pathway AND processed faster

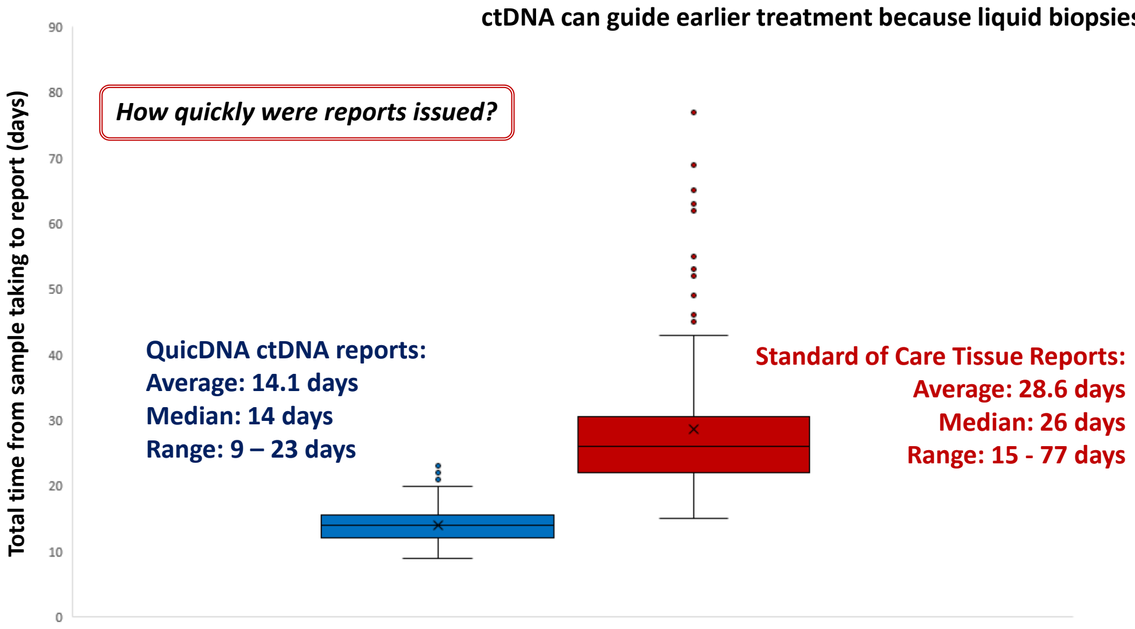


Fig 3: ctDNA results are CONSISTENTLY issued FASTER than Standard of Care results

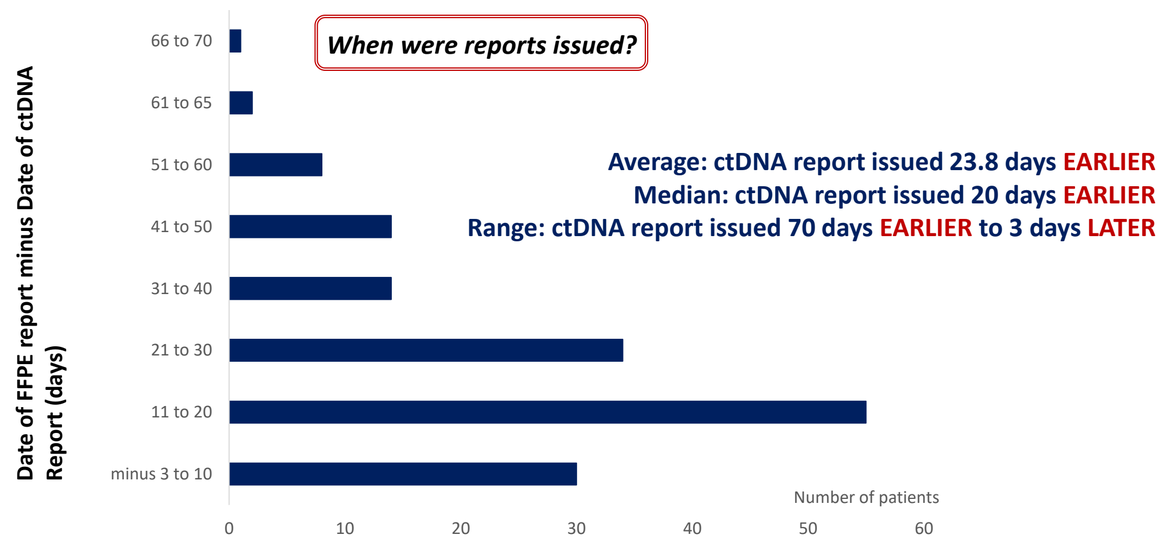


Fig 4: ctDNA results are CONSISTENTLY issued EARLIER than Standard of Care results

PATIENT CASE STUDIES: Treatment Guided by QuicDNA ctDNA Result

372-064 - Hip pain, skin lesions
EGFR c.2239_2248delinsC p.(Leu747_Ala750delinsPro) 3.30% VAF

- Day 0 - primary care referral. Blood sample received Day 9
- ctDNA Report issued Day 21
- Tissue sample taken Day 15, received Day 37
- NSCLC confirmed and Osimertinib initiated Day 37
- Concordant tissue genomic report issued Day 49
- Significant and ongoing response to treatment. Regression of multiple metastatic deposits

ACTIONABLE VARIANT REPORTED 28 DAYS EARLIER

264-002 - ?chest infection
BRAF c.1799T>A p.(Val600Glu) 0.45% VAF

- Day 0 – in-patient CT scan. Blood sample received Day 4
- ctDNA Report issued Day 14
- Multiple biopsies taken but histological diagnosis not confirmed. Rapid patient deterioration Days 50-60.
- Absence of diagnosis or further tissue
- Dabrafenib & Trametinib initiated Day 62
- Dramatic response achieved, normal lifestyle resumed

STANDARD OF CARE TISSUE TESTING NOT POSSIBLE

399-015 - dysphagia, vomiting
Predicted EML4-ALK Fusion EML4(Ex18)::ALK(Ex20) 0.11% VAF

- Day 0 – in-patient CT scan. Blood sample received Day 2
- ctDNA Report issued Day 14
- Alectinib initiated Day 18
- Tissue sample taken Day 2. Delayed in pathology laboratory. Received for testing Day 50
- EML4-ALK Fusion reported on tissue Day 64
- Partial response to treatment reported at follow-up scan

ACTIONABLE VARIANT REPORTED 50 DAYS EARLIER

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QuicDNA study managed by the Centre for Trials Research at Cardiff University

References: Table 1: *MedCalc statistical analysis at: https://www.medcalc.org/calc/diagnostic_test.php. Table 2: **Pascual et al. (2022). ESMO recommendations on the use of circulating tumour DNA assays for patients with cancer: a report from the ESMO Precision Medicine Working Group. Ann Oncol. Aug;33(8):750-768