

White Paper

Reimagining Cancer Care: The Emerging Role of Circulating Tumour DNA (ctDNA) in Detection, Diagnosis and Management of Cancer

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Introduction

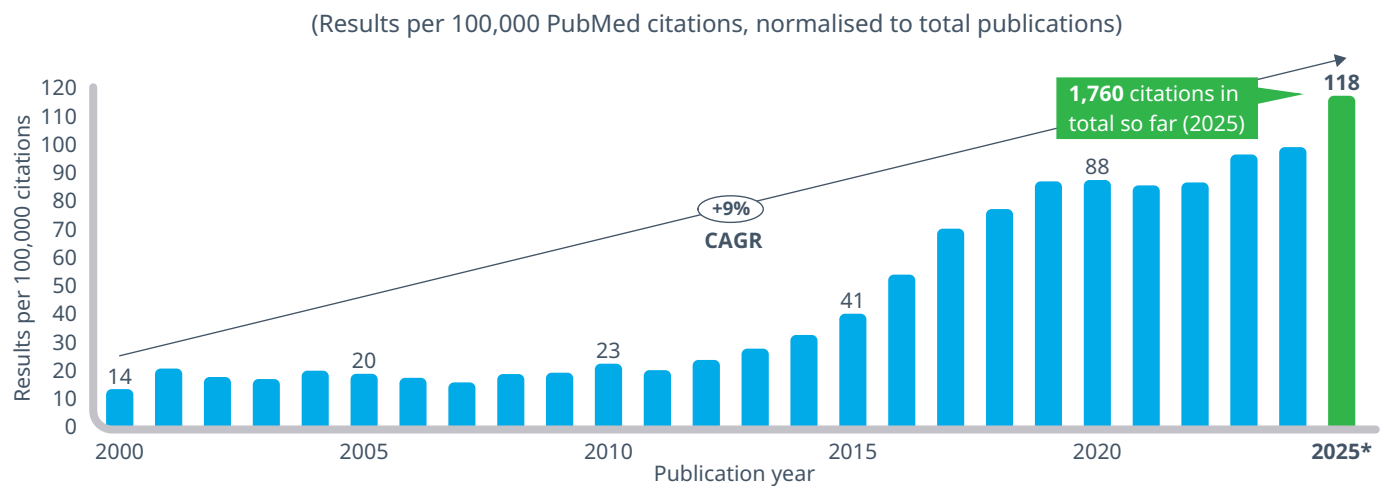
Circulating tumour DNA (ctDNA) testing has the potential to revolutionise cancer care. With ongoing research across applications such as early detection and diagnosis, personalised treatment, and improved surveillance, ctDNA testing holds widespread promise across the cancer care continuum. However, significant technical, regulatory and reimbursement challenges remain. This white paper synthesises the latest evidence and implementation trends, highlighting the key opportunities and challenges that stakeholders face and how they can succeed in this rapidly evolving environment. Ultimately, this paper seeks to raise awareness of the emerging role of ctDNA, whilst also promoting knowledge sharing and collaboration within this dynamic field.

Circulating tumour DNA (ctDNA) comprises fragments of genetic material released from cancer cells into the bloodstream. These harbour tumour-specific mutations and other characteristics which can be detected through minimally invasive “liquid biopsy” techniques. Unlike traditional biopsies that require tissue extraction, ctDNA testing offers the potential for minimally invasive, repeated, low-risk sampling, making it a promising tool for cancer detection, diagnosis, treatment selection, and ongoing monitoring.¹

Recent technological breakthroughs present a novel approach for detecting low-level tumour DNA amidst background noise, overcoming many earlier

limitations. As a result, ctDNA testing is showing promising results in identifying actionable mutations and monitoring tumour evolution and progression, even in challenging clinical scenarios (such as early-stage cancers or post-treatment surveillance). However, further research is ongoing in this rapidly evolving field.¹ Notably, academic interest in ctDNA testing continues to rise, as evidenced by a new peak of 1,760 publications citing ctDNA in 2025 so far (Figure 1).² This surge not only reflects the field’s rapid expansion but also signals increasing research investment and heightened attention from the scientific community.

Figure 1: Global trends in citations for circulating tumour DNA (ctDNA)



Source: PubMed by year analysis: * Search completed in October 2025, Advanced search query included the terms “ctDNA” or “circulating tumour DNA” or “circulating tumor DNA”; IQVIA EMEA Thought Leadership.

Clinical evidence supporting ctDNA testing is also emerging, with some studies demonstrating its value across a range of cancer types, including colorectal, breast and lung cancers.³ For instance, prospective trials have demonstrated that ctDNA testing can inform earlier diagnosis, treatment selection and modification, minimal residual disease (MRD) monitoring and disease progression tracking.

Reflecting this accumulating evidence, leading oncology organisations, including the European Society for Medical Oncology (ESMO), have incorporated ctDNA testing into their clinical guidelines for specific applications.⁴ However, the value of testing has not yet been universally demonstrated, and thus requires further research and supporting clinical studies.

In addition, wider applications such as population-based early screening and routine MRD monitoring are still under investigation and not yet standard practice. There is also a continued need for methods with greater sensitivity and specificity. Nevertheless, promising results announced during ESMO Congress 2025 indicate progress in ctDNA testing for early cancer detection.⁵

International initiatives such as the European Liquid Biopsy Society,⁶ BloodPAC Consortium (U.S.),⁷ and Horizon Europe⁸ projects are working to standardise ctDNA protocols and establish clinical validation. These groups are uniting researchers, clinicians, industry, and regulators to develop quality standards and run multicentre trials to support ctDNA adoption, addressing challenges such as inconsistent assay performance, reimbursement, and regulatory differences, especially within Europe.

Given this rapidly evolving landscape, this paper explores the current and emerging roles of ctDNA testing across the cancer care continuum, focusing on European adoption. We highlight key implementation challenges and offer a balanced perspective for stakeholders, such as clinicians, patients, industry and payers, as they consider integrating ctDNA into routine oncology practice.



ctDNA testing: Overview and key considerations

Circulating tumour DNA (ctDNA) tests are emerging as a promising tool in oncology, offering a minimally invasive complement or even an alternative to traditional tissue biopsies. By analysing fragments of tumour-derived genetic material present in blood, ctDNA assays can detect cancer-specific mutations (in addition to other types of genomic alterations or ctDNA characteristics), assess tumour burden, and in some cases, provide insights into the tissue of origin.

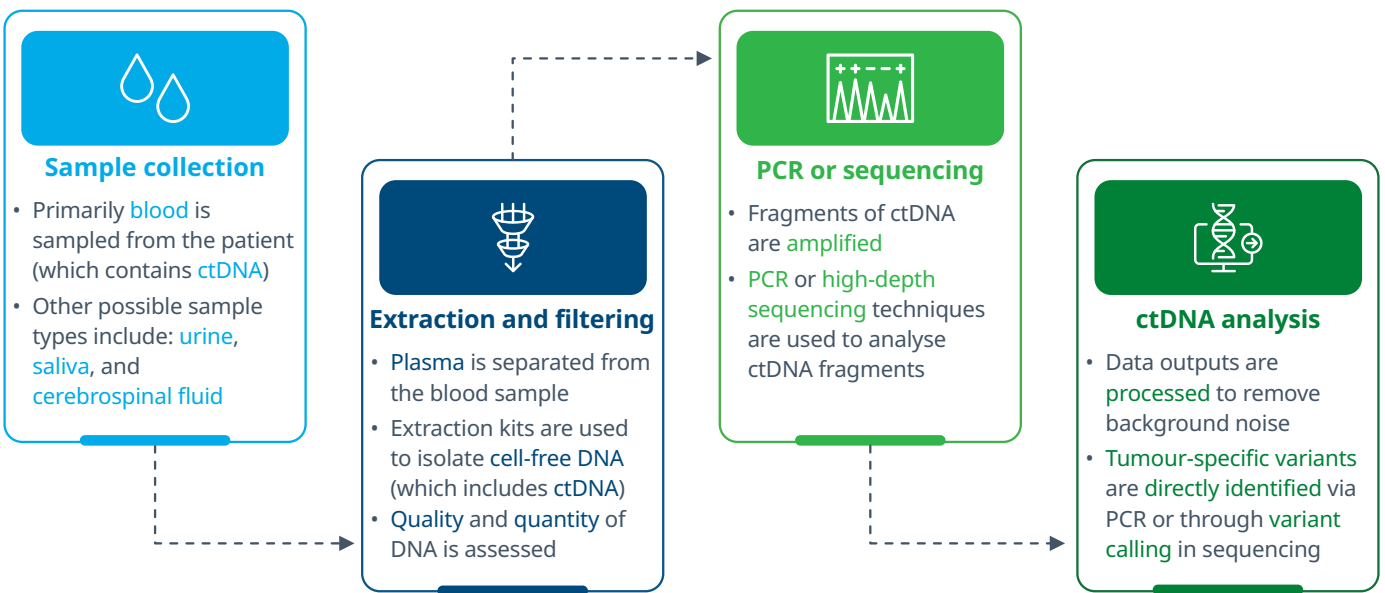
Test designs range from highly targeted (single mutations) to broad panels covering numerous genes or methylation markers (chemical alterations to DNA

that can also serve as biomarkers in cancer detection). A simplified workflow of ctDNA assays is outlined in Figure 2, which highlights the key stages of testing: sample collection, ctDNA extraction and filtering, PCR (a highly sensitive methodology for analysing DNA sample) or sequencing of ctDNA fragments, and data analysis to identify tumour-specific variants.

Whilst ctDNA is often used interchangeably with the term “liquid biopsy,” it is only one type of liquid biopsy. Other approaches include the analysis of circulating tumour cells (CTCs), exosomes, and circulating RNAs. However, ctDNA has gained particular traction due to its stability and the maturity of associated genomic analytical methods.¹

Circulating tumour DNA (ctDNA) tests are emerging as a promising tool in oncology, offering a minimally invasive complement or even an alternative to traditional tissue biopsies.

Figure 2: Simplified workflow of ctDNA assays



Source: IQVIA EMEA Thought Leadership.

Table 1: Comparing liquid biopsy (ctDNA) and tissue biopsy

FEATURE	LIQUID BIOPSY (CTDNA)	TRADITIONAL TISSUE BIOPSY	IMPLICATIONS
Invasiveness	Minimal (simple blood draw)	Invasive (requires needle or surgical extraction)	Liquid biopsy is ideal for patients who cannot undergo surgery or need frequent monitoring
Turnaround time	Fast processing and analysis	Slower due to surgical prep, tissue preservation and lab analysis	Liquid biopsy supports urgent decision-making or real-time treatment adjustments
Sampling scope	Captures biomarkers from multiple tumour sites; can reflect tumour heterogeneity	Samples a small, localised portion of a tumour; may miss heterogeneity	Liquid biopsy supports metastatic or heterogeneous cancer study
Information obtained	Genetic mutations, epigenetic changes, tumour evolution, metastasis potential	Histological structure, localised genetic mutations	Liquid biopsy supports ongoing monitoring; tissue is required for initial diagnosis and staging
Sensitivity	Lower for some cancers (especially those shedding little ctDNA); improving with research	Higher for localised tumours; direct sampling increases diagnostic accuracy	Tissue remains gold standard for cancers with low ctDNA shedding
Cost	Generally lower; fewer resources and personnel needed	Higher due to surgical procedures, pathology, and potential hospitalisation	Liquid biopsy is cost-effective for longitudinal monitoring

Source: IQVIA EMEA Thought Leadership.

The potential benefits of ctDNA testing compared to traditional tissue biopsy techniques are manyfold (Table 1). Blood-based sampling is less invasive and likely preferred by patients compared to surgical biopsies, enabling repeat testing and improved monitoring of disease progression. Additionally, ctDNA may capture genetic information from multiple tumour sites, potentially providing a broader view of tumour heterogeneity (genetic variation).

In some cases, results can be generated quicker than that of traditional biopsy techniques, supporting timely clinical decisions. Regarding the cost impact of liquid biopsies, this would need to be evaluated for each application, as the economic implications likely differ between assays used for early detection compared to that of treatment selection for example.^{9,10}

Despite these advantages, ctDNA testing is associated with significant limitations. For example, ctDNA may be undetectable in early-stage cancers or post-treatment, therefore potentially leading to false negative results (see box 1 for definitions). Conversely, the generation of false positives may lead to unnecessary interventions for the patient, therefore highlighting sensitivity challenges.

Additionally, false positives can occur due to non-cancer mutations in blood cells (such as those produced from clonal haematopoiesis, the over-representation of blood cells derived from a single clone), so these must be excluded to maintain specificity. Further to this, ctDNA testing may not reliably identify the anatomical site of the tumour or effectively track multiple tumour sites in cases of metastatic disease.^{9,10}

Box 1: Key ctDNA testing-associated definitions

FALSE NEGATIVE

- A test result that incorrectly indicates no presence of cancer when it is actually present.
- May lead to missed or delayed diagnosis, allowing disease progression and reducing treatment options.

FALSE POSITIVE

- A test result that incorrectly indicates the presence of cancer when it is not actually present.
- Can cause unnecessary anxiety, further invasive testing, and potentially harmful interventions.

SENSITIVITY

- The ability of a test to correctly identify patients who do have cancer (true positives).
- High sensitivity reduces the risk of false negatives, improving early detection and outcomes.

SPECIFICITY

- The ability of a test to correctly identify patients who do not have cancer (true negatives).
- High specificity reduces the risk of false positives, avoiding unnecessary procedures and stress.

Analytical complexity, including the low abundance of ctDNA and its highly fragmented nature, poses significant challenges for sequencing and analysis. Additionally, the lack of standardised protocols, and limited breadth of information generated compared to tissue biopsies represent further testing limitations. Moreover, regulatory approval and reimbursement for ctDNA tests vary widely and are not yet consistently established across key markets such as EU4+UK and the U.S.¹¹

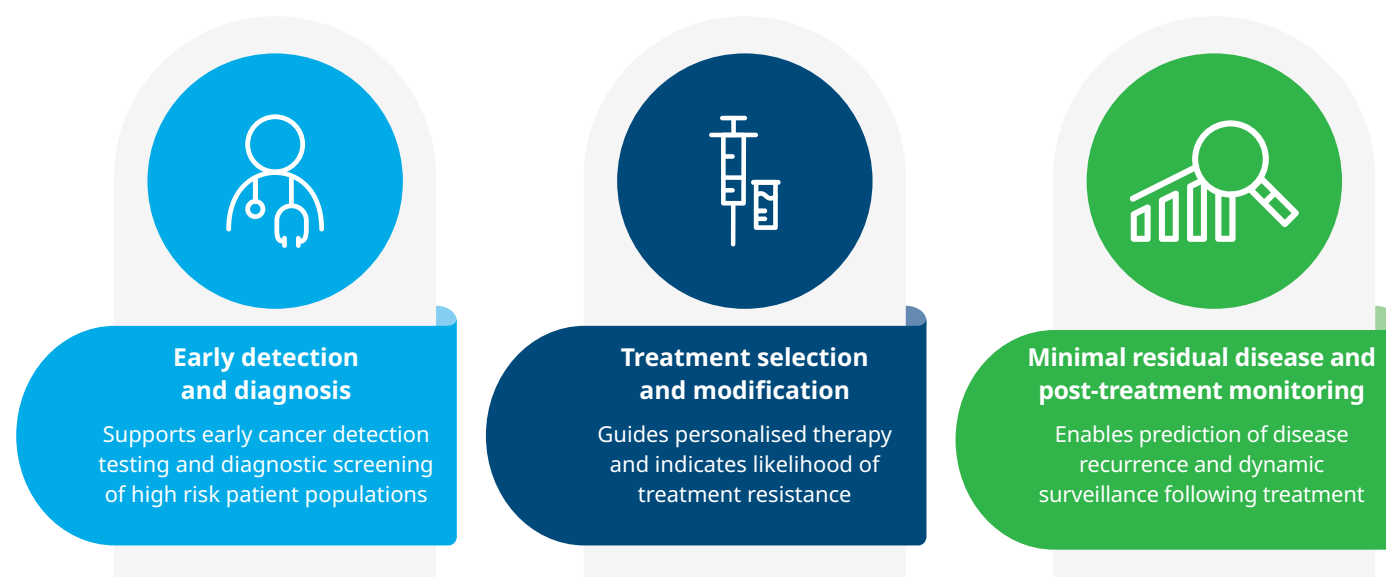
Overall, ctDNA testing should still be viewed as a complement to, rather than a replacement for, tissue biopsy. Its adoption in clinical practice will depend on further validation, standardisation, and real-world evidence demonstrating clinical utility across the cancer care continuum. As the technology and evidence base evolve, ctDNA has the potential to enhance cancer diagnosis and management, but its role must be carefully integrated alongside existing modalities as this technology matures.



The application of ctDNA testing across the cancer care continuum

Across the cancer care continuum, circulating tumour DNA (ctDNA) testing has key potential applications that extend from early detection and diagnosis, through to guiding treatment selection and modification, as well as detecting minimal residual disease and facilitating post-treatment monitoring (Figure 3). Thus, this highlights the widespread potential capabilities of this rapidly evolving field.

Figure 3: Key applications of ctDNA testing across the cancer care continuum



Source: IQVIA EMEA Thought Leadership.

Early detection and diagnosis

The application of ctDNA for early cancer detection and diagnosis is an area of accumulating research. Multi-cancer early detection (MCED) tests, such as GRAIL's Galleri, analyse methylation patterns in ctDNA from a single blood sample to signal the potential presence of multiple cancer types and, in some cases, indicate the organ of origin.¹²

Early pilot programmes, including the UK's NHS study involving approximately 140,000 participants, are assessing whether these technologies can identify cancers earlier and reduce late-stage diagnoses with

final outcomes expected in 2026.^{13,14} Separately at ESMO 2025, the PATHFINDER-2 study reported that adding GRAIL's Galleri test increased cancer detection compared to standard screening and could identify many cancers at early stages and at a low false-positive rate.⁵ However, the absolute yield was low with only 3 cancers detected per 1000 people tested, and the study had more false negatives than true positives.¹⁵

Globally, adoption trends of MCED tests are varied, with reimbursement and broad clinical integration remaining limited.¹⁶ The U.S. market has seen more rapid commercialisation, whilst most European

countries have not yet adopted MCED testing outside clinical studies. Other innovators include Israel and China, both of which are developing blood-based screening solutions.¹⁷ Israel's health sector for example, is notable for its rapid integration of liquid biopsy innovations and collaborative research.¹⁸

In contrast, most European health systems are prioritising the generation of robust clinical and economic evidence before considering large-scale deployment. As more data emerges from ongoing pilots and trials, the role of ctDNA in early cancer detection and diagnosis will be better defined, with a continued emphasis on balancing innovation with clinical rigor and health system sustainability.

Globally, adoption trends of MCED tests are varied, with reimbursement and broad clinical integration remaining limited

Beyond MCED testing, ctDNA assays can also assist in diagnosing symptomatic patients when tissue biopsies are infeasible or inconclusive. For example, in particularly challenging cases, such as inaccessible lung tumours, ctDNA assays can be harnessed to help inform clinical diagnoses. However, sensitivity limitations mean that, in practice, ctDNA is generally used adjunctively rather than as a standalone diagnostic tool.

Treatment selection and modification

The application of ctDNA as a real-time biomarker for monitoring disease progression, tumour burden and informing treatment strategies is an area of growing interest, especially in advanced cancers. Regular ctDNA testing during therapy can indicate early response or resistance, often before changes are seen on scans. Falling ctDNA levels suggest better outcomes, whilst rising levels may signal resistance. However, these associations are not yet fully validated and should be interpreted with care.



Adaptive clinical trials are increasingly being explored to optimise treatment strategies through the integration of real-time data. In these studies, ctDNA levels are evaluated as dynamic biomarkers to guide therapy adjustments. Although early findings are encouraging, further validation is needed to confirm the clinical utility of this approach and its effect on patient outcomes.¹⁹ Two recent trials, DYNAMIC-III and PEGASUS-II, did not meet their primary endpoints for ctDNA-guided adjuvant therapy in colon cancer. These results highlight the need for improved sensitivity of ctDNA testing.²⁰

The co-development of therapies and ctDNA-based companion diagnostics (CDx) is increasingly shaping the oncology landscape, as more products launch with integrated predictive biomarker testing (including CDx testing). Therapies with predictive biomarkers tend to achieve greater commercial success than those without; average 5-year U.S. sales for oncology new active substances (NAS) launches were 60% higher for those with predictive biomarkers than those without.²¹ Recent technological advances are driving the shift towards sophisticated biomarker screening, with next-generation sequencing now accounting for over 70% of testing in common tumours and ctDNA-based screening gaining prominence.²²

Therapies with predictive biomarkers tend to achieve greater commercial success than those without

Commercially available CDx (companion diagnostics) ctDNA assays, such as Guardant360 CDx and FoundationOne Liquid CDx, enable mutation profiling and have secured regulatory approval or certification in certain markets. These tools can facilitate matching targeted therapies to patients with lung, colon and breast cancers for example.¹ While the U.S. has seen faster regulatory progress and uptake, Europe is seeing a gradual emergence of ctDNA CDx, with ongoing efforts by pharmaceutical companies to bring such tests to market. Early collaborations, such as AstraZeneca's partnership with GRAIL, illustrate the potential for integrating early detection and therapy selection.²³

Tumours are inherently heterogeneous and acquire new mutations as they evolve, highlighting the importance of conducting regular sampling to track disease progression. Serial ctDNA testing enables real-time detection of emerging mutations associated with treatment resistance and supports timely therapeutic adjustments. For example, the identification of EGFR T790M mutation in lung cancer²⁴ or RAS mutations in colorectal cancer²⁵ can directly inform changes in targeted therapy. In lung and breast cancers, ctDNA analyses have been used to detect resistance mutations and guide the selection of targeted therapies, often before changes are visible on imaging.²⁶

Minimal residual disease and post-treatment monitoring

The use of ctDNA for minimal residual disease (MRD) detection and post-treatment monitoring is advancing the oncology landscape, but its integration into clinical practice remains complex. MRD refers to the presence of small numbers of cancer cells that may persist after curative treatment, posing a risk of recurrence. Traditional monitoring, such as imaging, often detects recurrence only once a tumour is visible. ctDNA testing, in contrast, can identify molecular signs of residual disease in blood samples, potentially signalling recurrence months before conventional methods.²⁷



Emerging evidence suggests that ctDNA-guided MRD assessment can inform adjuvant therapy decisions (adjuvant therapy is the treatment given after a primary therapy such as surgery to increase the chances of a cure or delay in disease progression). For example, the DYNAMIC phase II trial in stage II colon cancer demonstrated that patients with negative ctDNA post-surgery could safely avoid chemotherapy, reducing exposure to unnecessary treatment without compromising recurrence-free survival.²⁸ However, the DYNAMIC-III trial did not meet its primary endpoint, therefore highlighting the need for further research and validation.²⁹

Emerging evidence suggests that ctDNA-guided MRD assessment can inform adjuvant therapy decisions

These developments represent a shift towards personalised therapy, although the broader applicability across cancer types is still under investigation, with ongoing trials in breast, lung, and other cancers seeking to validate clinical utility. Moreover, MRD assessment is increasingly recognised as a surrogate endpoint in clinical trials for haematological cancers such as acute myeloid leukaemia (AML), with evidence showing that MRD provides a sensitive and quantitative assessment of disease burden.³⁰

From a patient perspective, ctDNA-based monitoring could offer practical benefits, such as reducing scan frequency and associated burdens if blood results are stable. It may also enable earlier detection of molecular changes. In terms of real-world adoption, this varies with some oncologists in the U.S. utilising commercial ctDNA assays off-label for challenging cases, including those where tissue biopsy is not feasible due to inaccessible tumours. Additionally, example diagnostics companies, such as Natera,³¹ Adaptive Biotech,³² and Roche,³³ are developing personalised MRD assays, with commercial availability and insurance coverage again varying by geography and cancer type.

Across Europe, ctDNA-based MRD testing is largely confined to research settings due to limited test access and reimbursement constraints.³⁴ Key European initiatives include the GUIDE.MRD consortium, a Horizon Europe-funded public-private partnership aiming to standardise ctDNA assays, develop reference materials, and validate tests for lung, pancreatic, and colorectal cancers.⁸ Beyond trials, some progress towards clinical implementation is also emerging: Germany's MVZ HPH Institute recently launched an in-house MRD test, improving local access to ctDNA assays previously limited to the U.S.³⁵ Despite these developments, continued adoption requires further outcome data and regulatory guidance.



Current status of ctDNA testing

The current status of circulating tumour DNA (ctDNA) testing shows substantial progress, with advances in technology and artificial intelligence (AI) enhancing sensitivity and specificity. Academic institutions remain pivotal in driving research and the validation of ctDNA assays. Looking ahead, the ctDNA testing market is expanding alongside the clinical pipeline, yet persistent challenges such as sensitivity, specificity, protocol standardisation, regulatory issues, and the need for strong clinical evidence remain.

Technology development and the role of AI

The ctDNA testing landscape has evolved rapidly, propelled by developments in high-throughput sequencing, digital PCR, and AI. Enhanced sequencing and digital PCR have greatly improved assay sensitivity and specificity, making detection and monitoring of cancer-related genetic changes more accurate. In addition, associated fields such as fragmentomics (the study of cell-free DNA fragments, including ctDNA) have helped to drive academic interest in liquid biopsy research.³⁶

AI tools, especially machine learning, can now integrate genomic, epigenomic, and proteomic data, enhancing cancer detection and minimising false positives. Improved bioinformatics and error

suppression techniques have also made assays more robust and reliable, while the use of longitudinal data analysis supports tracking disease progression and treatment response, further increasing the clinical value of ctDNA assays.¹ Recent studies already demonstrate the capabilities of AI to improve ultra-low detection limits and specificity in the context of ctDNA testing, and highlight the potential of this continued technological evolution.³⁷

Role of academia and the “Make vs. Buy” options for testing labs

Academic institutions and research consortia remain pivotal in developing ctDNA assays and frequently spearhead innovation. In Europe, centres and initiatives like the European Organisation for Research and Treatment of Cancer (EORTC)³⁸ and the European Liquid Biopsy Society (ELBS)⁶ are working to standardise and validate ctDNA for routine oncology use. This leadership leaves testing labs with a key choice: to “make” bespoke in-house ctDNA assays, allowing for customisation but requiring major investment in expertise and infrastructure, or to “buy” commercial, often regulatory-approved, assays, which are less flexible and may be more costly over time. Beyond panel design, labs must also decide whether to conduct testing onsite or outsource it to reference labs, and select the most appropriate technology platform, with these decisions influenced by factors such as regulatory requirements, available resources, test volume, financial viability and turnaround times.



Companies in the marketplace, offerings, and commercial potential

The commercial potential of ctDNA testing is substantial, underpinned by the growing demand for personalised oncology and non-invasive diagnostics. A subset of landmark ctDNA tests at various stages of the approval process, and their associated applications are highlighted in Table 2.¹ The market is projected to

expand significantly as more assays receive regulatory approvals and as real-world evidence accumulates to support broader clinical adoption. European startups, academic spin-offs, and collaborative studies are also contributing to market growth and innovation, with the region’s innovation climate supporting both homegrown and international solutions.

Table 2: Sample of ctDNA tests and their uses

ASSAY	CORPORATION	APPROVAL STATUS	KEY APPLICATION	CLINICAL UTILITY
Guardant360 CDx	Guardant Health	FDA approved	Treatment selection and modification	Companion diagnostic for therapies in NSCLC and breast cancer
FoundationOne Liquid CDx	Foundation Medicine (affiliate of the Roche Group)	FDA approved	Treatment selection and modification	Companion diagnostic for pan-cancer (including NSCLC, prostate and breast)
Cobas EGFR Mutation Test v2	Roche	FDA approved	Treatment selection and modification	Companion diagnostic for NSCLC
Signatera	Natera	CLIA-certified for clinical use (FDA)	Minimal residual disease detection and post-treatment monitoring	MRD detection and recurrence (including colorectal cancer)
Galleri	GRAIL	CLIA-certified for clinical use (FDA)	Early detection and diagnosis	Early pan-cancer detection (including over 50 cancer types)
NavDx	Naveris	CLIA-certified for clinical use (FDA)	Minimal residual disease detection and post-treatment monitoring	HPV positive cancer and surveillance
GuardantOMNI	Guardant Health	Research use only	Treatment selection and modification	Clinical trials; patient selection and monitoring response to investigational drugs
TruSight Oncology 500	Illumina	Research use only	Treatment selection and modification	Pan-cancer tumour profiling (solid tumours)
OncoBEAM EFGR v2	Sysmex Inostics	Research use only	Treatment selection and modification	NSCLC therapy selection and monitoring

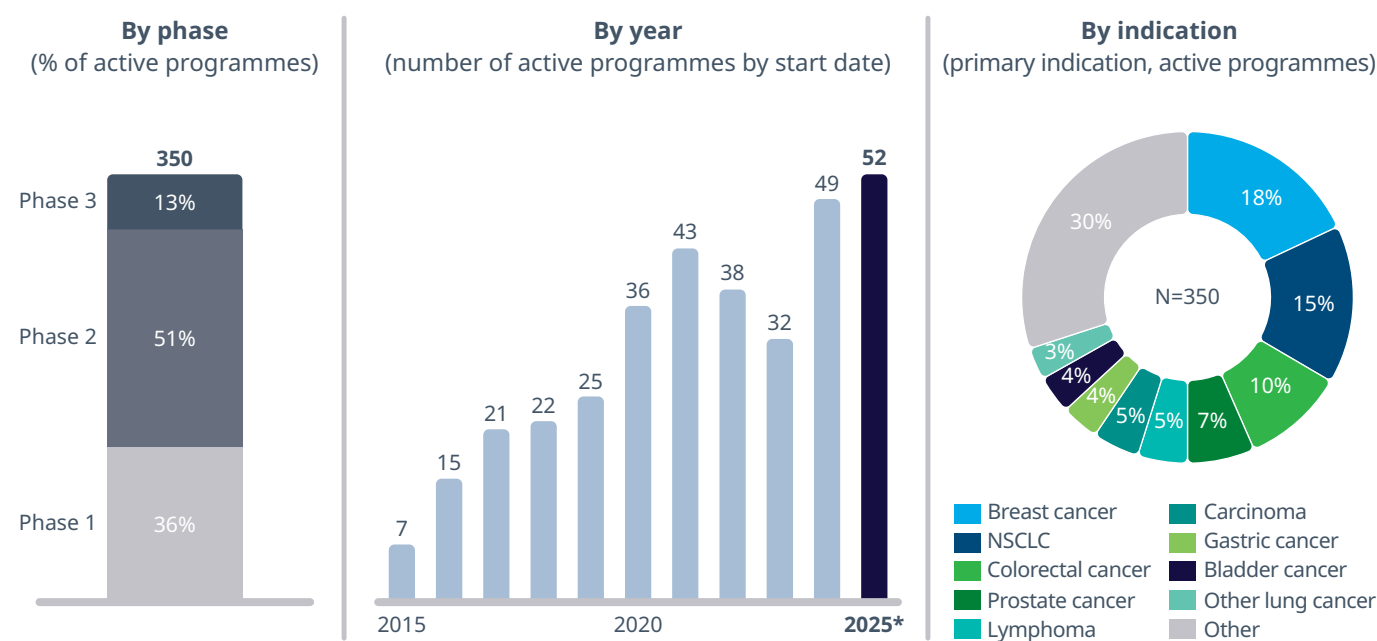
Source: Regina de Abreu et al; IQVIA EMEA Thought Leadership.

The growing clinical pipeline

Drawing on the latest clinical trial data, it is clear that the ctDNA testing clinical pipeline is expanding (Figure 4).³⁹ There are currently 350 active clinical trials, with a new peak of 52 programmes beginning or entering the next phase in 2025 so far. This surge in activity underlines the heightened clinical and scientific interest in the potential of ctDNA as a transformative

tool in oncology. When examining these trials by disease type, breast cancer leads with nearly a fifth of ctDNA clinical trials, followed by non-small cell lung cancer (NSCLC), colorectal cancer, and prostate cancer. These trends highlight the growing momentum and broad horizons for ctDNA research across multiple cancer indications.

Figure 4: The growing ctDNA-guided clinical pipeline



Source: Clinicaltrials.gov: Search query included clinical trials in phases 1 through 3 that were industry-funded, using the search terms “ctDNA,” “circulating tumor DNA,” or “circulating tumour DNA.” Trials with a status of “terminated,” “withdrawn,” or “suspended” were excluded from the results. * Accessed October 2025; IQVIA EMEA Thought Leadership.

Hurdles and barriers to success

Sensitivity and specificity remain significant hurdles, impacting the reliability of detecting clinically meaningful genetic alterations. The processes of curation, annotation, and interpretation of results require robust standards and a highly skilled workforce to ensure results are both accurate and actionable. Added to this, more research is needed to build a compelling case, particularly for applications in MRD detection and screening.

Regulatory challenges further complicate the pathway to implementation. The absence of standardised assay protocols leads to variations in test performance and comparability across jurisdictions. Increasingly stringent requirements, exemplified by the introduction of Europe’s In Vitro Diagnostic Regulation

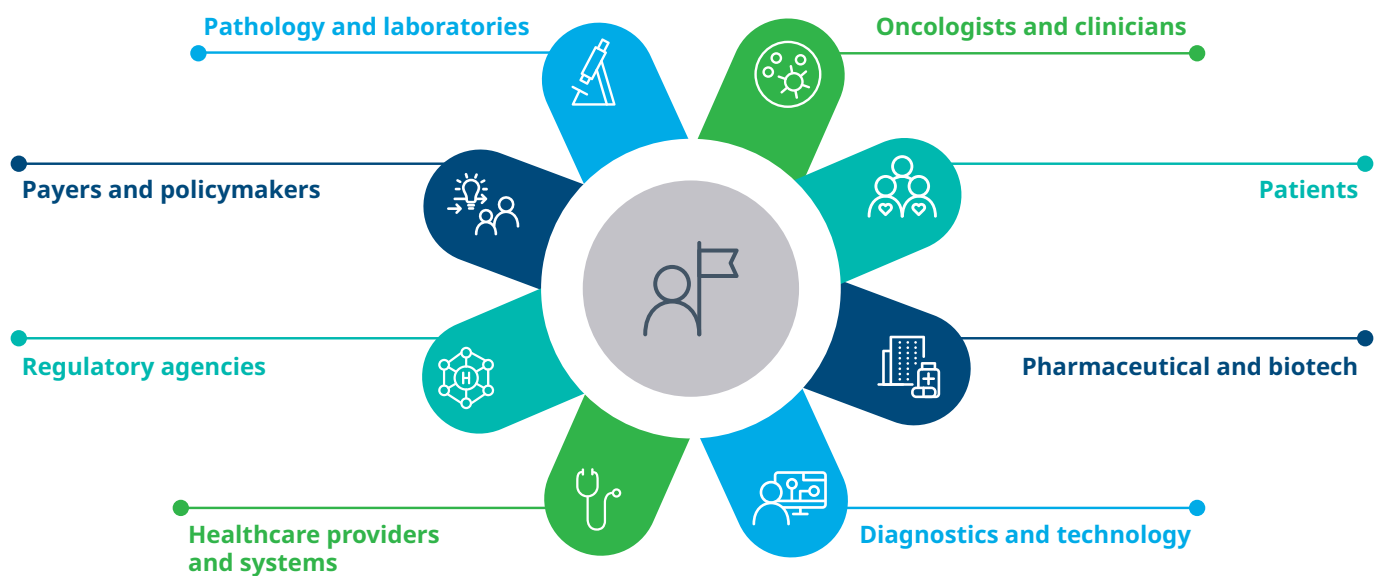
(IVDR), demand continuous adaptation from laboratories and diagnostics manufacturers, often at considerable financial and administrative cost.

Infrastructure and operational realities represent equally formidable barriers. Successful ctDNA testing depends on access to high-quality laboratory facilities, rapid turnaround, and a workforce with advanced technical expertise. Challenges such as inconsistent reimbursement, fragmented funding pathways, and pronounced access disparities impede integration into clinical practice. Addressing these challenges will require not only harmonised guidelines and supportive policy frameworks, but also a concerted effort to foster multidisciplinary collaboration and ensure equitable access for patients across all healthcare systems.

Realising the promise of ctDNA: Stakeholder implications

The integration of circulating tumour DNA (ctDNA) testing into routine oncology practice presents both promise and complexity for stakeholders across the cancer care pathway. Whilst ctDNA offers potential for earlier detection and more personalised treatment, its adoption requires thoughtful consideration of clinical, operational, economic, and ethical factors. Below, we offer an overview of the anticipated impact on key stakeholder groups, reflecting emerging evidence as well as ongoing uncertainties. Concerted collaboration across these stakeholder groups will be crucial to ensure ctDNA testing becomes a success story for all those involved.

Figure 5: Key Stakeholders with the potential to benefit from ctDNA testing



Source: IQVIA EMEA Thought Leadership.

Pathology and molecular laboratories

Laboratories are central to ctDNA testing, driving assay quality and result interpretation. Increased demand will require investment in advanced equipment, informatics, and specialised training. Operational challenges include managing higher sample volumes and integrating ctDNA results into clinical workflows for timely decision-making. Collaboration among regional labs and participation in external quality assessment schemes will support standardisation and scalability. Labs must also address the analytical limitations of ctDNA, such as variable sensitivity, specificity, and interpretation challenges.

Oncologists and clinicians

Clinicians face the dual challenge of incorporating ctDNA findings into complex treatment decisions while ensuring patients understand the implications. Updated guidelines and decision support tools will be crucial to mitigate information overload and ensure appropriate use. Multidisciplinary tumour boards may need to adapt to interpret ctDNA data alongside traditional pathology. Change management, ongoing education for both clinicians and patients, clear protocols and treatment guidelines will help clinicians navigate a landscape where ctDNA augments, but does not replace, established monitoring modalities.



Patients

For patients, ctDNA testing offers the potential for less invasive monitoring and more tailored care, in addition to the logistical benefits associated with liquid biopsies compared to traditional biopsies. However, earlier or more frequent detection of recurrence can cause anxiety and uncertainty, underscoring the need for robust counselling and psychological support. Access and affordability remain critical concerns, with disparities likely unless reimbursement and health system support expands. Patient advocacy groups are influential in driving adoption, but there is a need for clear communication to ensure informed consent regarding the interpretation of positive test results, the risk of false positive results and clarity on genetic testing for hereditary cancer predisposition.

Pharmaceutical and biotech companies

Pharmaceutical and biotech companies are increasingly turning to ctDNA testing to improve clinical trial efficiency, optimise patient selection, and gather real-world evidence. Additionally, the growing evidence that MRD assessment can be used as a surrogate endpoint for clinical drug approval, highlights significant opportunities. Broader adoption may refine patient populations for targeted therapies and enable more personalised treatment durations

based on molecular response. To gain regulatory approval and payer reimbursement, companies must provide rigorous supporting evidence of both clinical utility and cost-effectiveness, ensuring their strategies align with evolving industry standards. Their strategies must also stay in step with changing requirements from regulators and payers, ensuring that evidence standards are consistently met.

Regulatory agencies

Regulatory agencies, including the FDA and European bodies, are crucial in guiding the adoption of ctDNA assays. They set standards for assay validation, clinical utility, and analytical performance, with the FDA previously issuing guidance on MRD assay requirements for example.⁴⁰ Agencies must balance robust oversight with timely innovation access and address international harmonisation challenges to support global trials. Ongoing collaboration between regulators and other stakeholder groups is vital to ensure patient safety and the responsible integration of ctDNA testing into cancer care.

Diagnostics and technology developers

As the ctDNA testing market matures, diagnostics and technology developers must set themselves apart with excellent test accuracy, faster turnaround times, and strict regulatory compliance. Success requires robust health economic data, adept management of complex reimbursement processes, and strong data security. Collaborating with pharmaceutical partners and engaging in national testing programmes can boost market adoption. Ultimately, sustained innovation and rigorous quality assurance will be vital to maintaining credibility and long-term success.

Healthcare providers and systems

Hospitals and health systems must coordinate across departments to implement ctDNA testing, revising care pathways and investing in technology and training. Potential benefits include better patient outcomes and efficiency gains (due to the ease of liquid biopsy sampling compared to traditional biopsies for example). Resource allocation and workflow digitisation are required to manage increased testing

volume and integrate results into electronic health records. Variation in adoption rates between centres raises equity concerns, highlighting the importance of referral networks and potential central funding to ensure broad access.

Payers and policymakers

Funding decisions for ctDNA testing depend on strong clinical and economic evidence. ctDNA testing is already used as an alternative to tissue biopsies in specific cases, such as in advanced or inaccessible cancers. Future uses like population-wide cancer screening are still under evaluation and require significantly more robust and extensive data. Expanding coverage will also require guideline support, health technology assessments, and solutions to regulatory and data privacy challenges, especially as new indications and direct-to-consumer marketing emerge.



Conclusion and future outlook: ctDNA at an inflection point

ctDNA testing is poised to redefine the landscape of cancer care. As a minimally invasive technique for capturing tumour-specific genetic information, ctDNA offers transformative potential across the oncology continuum, from early detection and diagnosis to treatment selection and modification, and post-treatment surveillance including MRD monitoring. Looking ahead, the convergence of artificial intelligence and advanced sequencing technologies, is set to further accelerate the evolution of ctDNA testing and position this technique as a cornerstone of precision oncology.

Realising this promise requires concerted multi-stakeholder collaboration to establish best practice frameworks, share knowledge, and address systemic access barriers. Targeted initiatives and real-world evidence generation will be essential to demonstrate clinical utility and cost-effectiveness, paving the way for regulatory approval and reimbursement. Importantly, ctDNA is not the endpoint but the beginning of a new era in cancer care. Future advances will integrate complementary technologies such as exosome analysis and proteomics, further refining early detection, treatment, and monitoring. The journey to routine ctDNA testing is ongoing, and its legacy will be a foundation for ever more precise, personalised, and effective cancer care.



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Julia leads oncology, genomics and precision medicine Real-World Solutions design and delivery in the UK and Ireland. She has more than 20 years' experience in Life Sciences including roles in global strategy, sales and marketing at GSK and GE Healthcare. She previously helped establish the Collaboration for Oncology Data in Europe at IQVIA and led the International COVID-19 Data Alliance at HDR UK.

She has also held leadership roles in healthcare policy think tanks and start-ups including e-health business, radioisotopes manufacturing for use in radio-pharmaceuticals. She is a Trustee of Picker Institute, a charity that promotes person-centred care. Julia holds a BSc in Biochemistry from the University of Bristol and an MBA from INSEAD.



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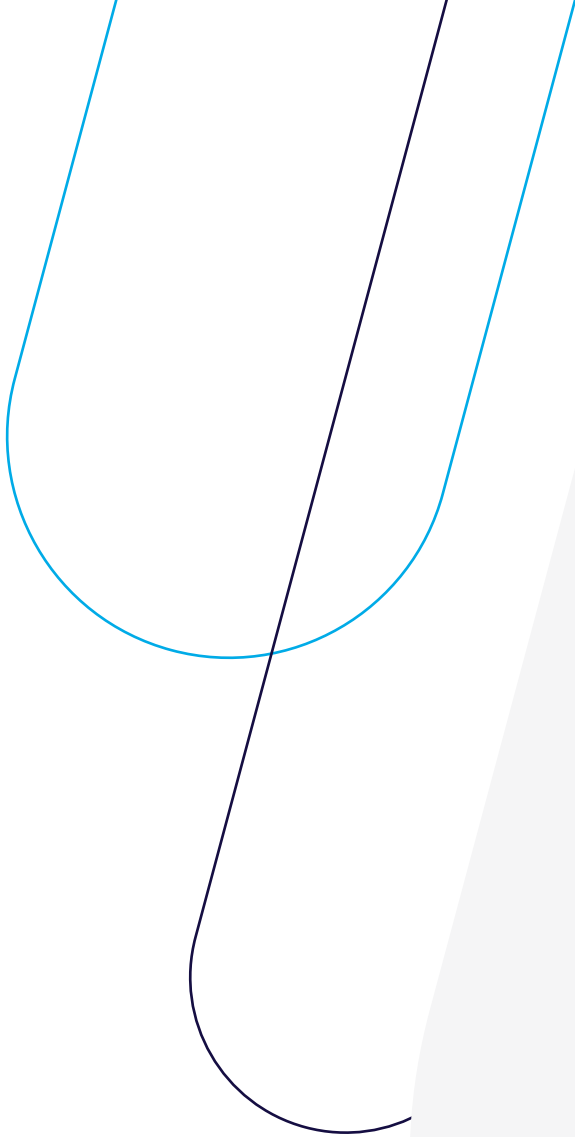
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