Next-generation sequencing–based circulating tumor DNA testing: clinical promise versus market access reality

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Introduction

The emergence of liquid biopsies using circulating tumor DNA (ctDNA) as a biomarker in early detection and diagnosis has gained significant importance in market access.

For patients, there is a lot of promise in liquid biopsies: earlier diagnosis, more convenient monitoring, and better optimized treatment choice.[1]

Despite the more frequent use of ctDNA testing in clinical trials, important challenges are associated with the use of ctDNA as a prognostic tool that manufacturers will have to overcome to secure patient access to ctDNA testing.[2-4]

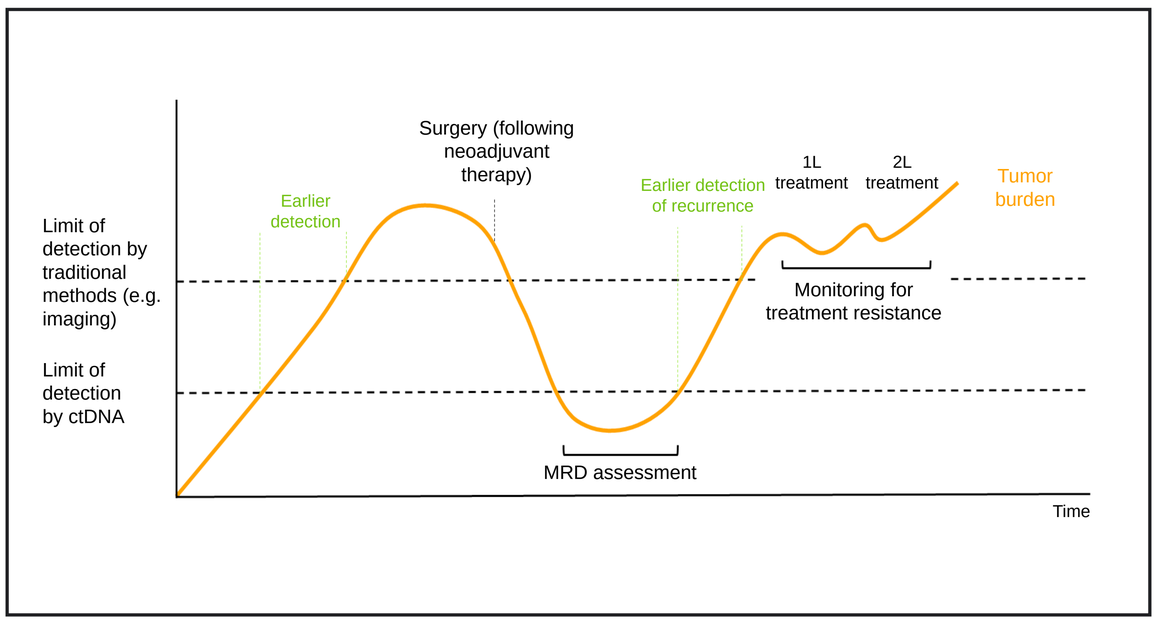
Methods

A targeted literature review (TLR) was carried out to identify both the opportunities and key market access challenges for next-generation sequencing (NGS)-based ctDNA testing, incorporating into clinical trial design, implementation into clinical practice, and payer acceptance.

Results

The clinical promise of ctDNA testing is very clear: reduced tissue biopsies for many solid tumor cancer patients, earlier diagnosis, and precision medicine tailored to the changing genetic profile of patients' cancer.[5-7]

Figure 1: NGS based ctDNA tests in early detection, monitoring, and reducing overtreatment

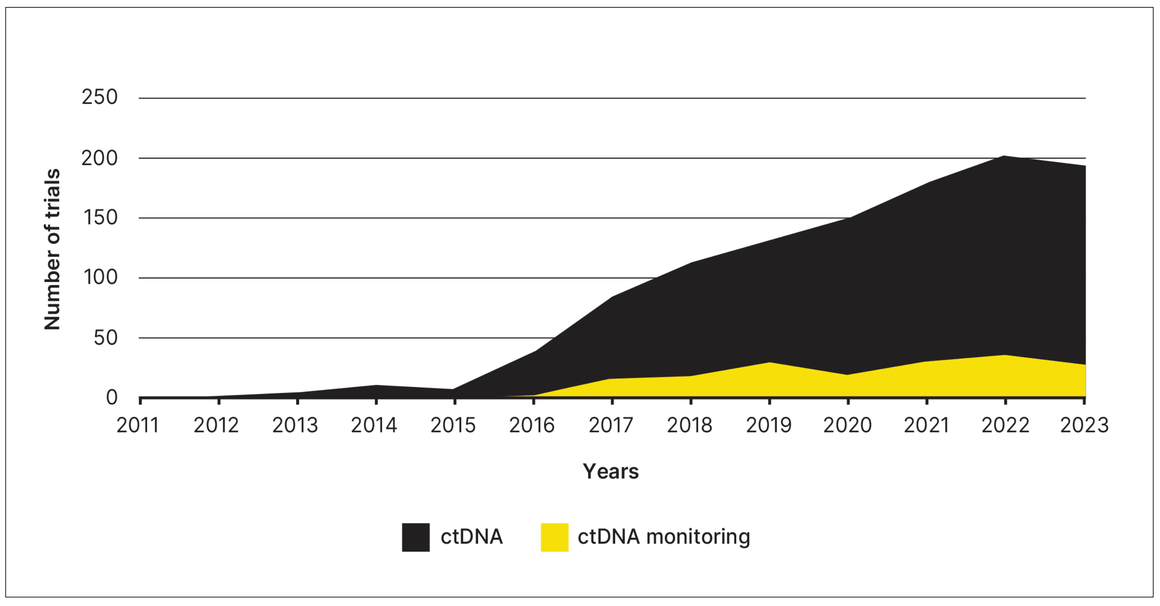


1L, first line; 2L, second line; MRD, minimal residual disease.

Source: Graph developed based on Febbo PG, et al. *JCO Precis Oncol*. 2024;8:e2300382.

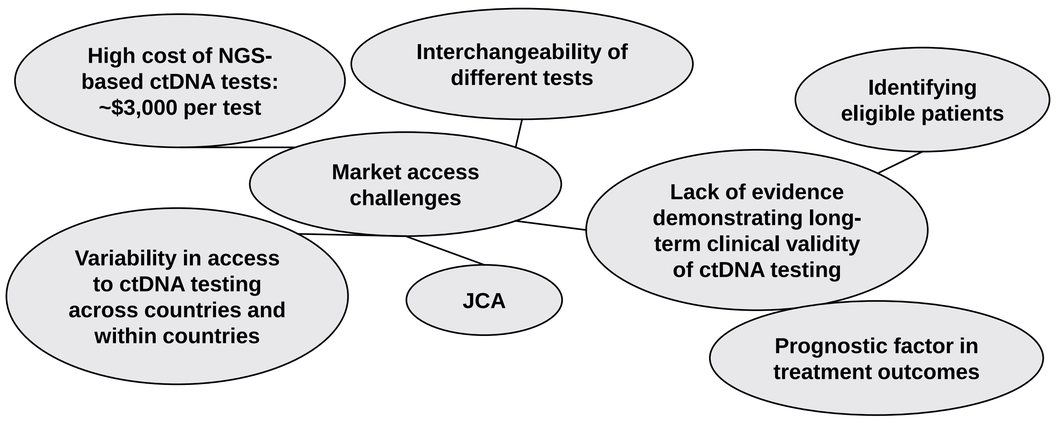
Considering the clinical promise of testing, there is a growing interest in ctDNA, including ongoing trials using ctDNA for monitoring.

Figure 2: Number of clinical trials that mention ctDNA and ctDNA monitoring, based on start date



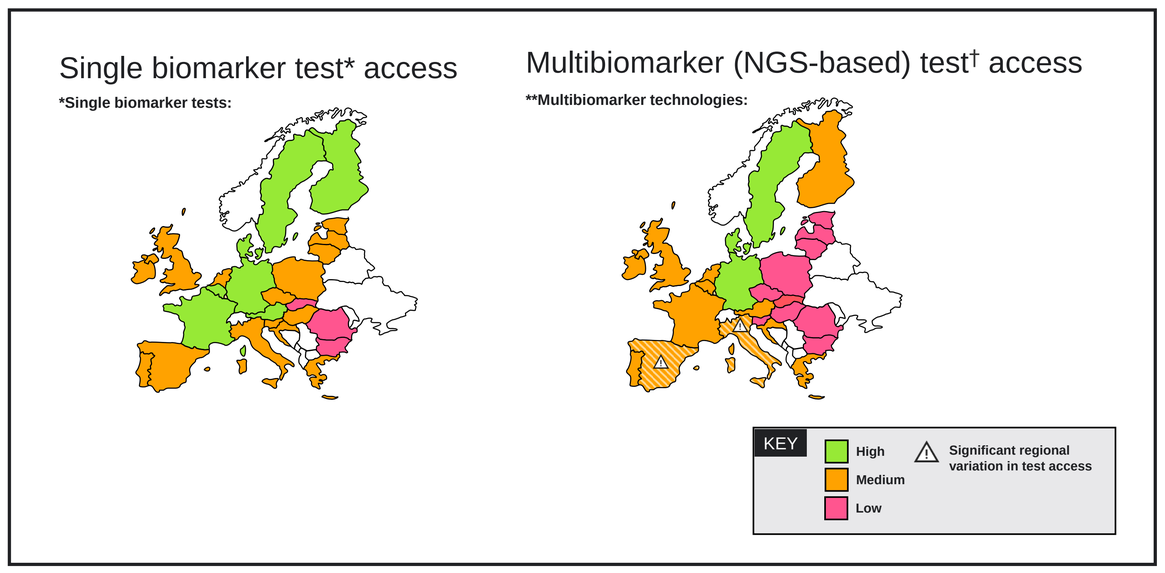
Source: Graph developed based on Clinical trials.gov

However, the use of ctDNA tests does not come without challenges that manufacturers will have to overcome to secure patient access to both the tests and treatments dependent on ctDNA testing.[2-4]



JCA, Joint Clinical Assessment

Figure 3: Regional variation in test access



Source: Graph developed based on Martak A (2022) graph: NGS in clinical routine–where are we in 2022?

Several approaches to addressing these market access barriers need to be considered.

1. Clinical validation of ctDNA testing by tumor type as a prognostic factor via indication-specific trials
   - Assess the value of ctDNA testing, separately from value of treatment, in clinical trials for a specific indication that would support implementation of ctDNA in clinical practice.
   - More rigorous study designs that can provide reliable evidence for JCAs (eg, adaptive trial design that adjusts the treatment regimen based on ctDNA response and what is available in each market, and longitudinal studies collecting ctDNA data at regular intervals to monitor changes).
   - Apply Artificial Intelligence and Machine Learning (AI/ML) algorithms to analyze ctDNA changes over time to predict long-term outcomes.
2. Real-world evidence to demonstrate the long-term outcomes associated with using ctDNA as a prognostic factor or to drive treatment decision-making
   - Establish multicenter prospective studies where ctDNA levels are monitored at regular intervals along with clinical outcomes.
   - Create a ctDNA-specific registry where clinical data and treatment outcomes are prospectively collected from real-world patients undergoing routine clinical care.
3. Provision of clear guidance on the incorporation of ctDNA testing in the treatment pathway
   - Cross-functional collaboration and primary research with key opinion leaders (KOLs) and other stakeholders.
   - Development of testing protocols to be integrated across the referral pathway.
4. Addressing issues of equitable access by removal of local barriers and variation
   - Early engagement with HTA agencies to understand potential local barriers of equitable access.
   - Engagement with cancer patient advocacy groups to promote ctDNA testing and push for policy changes that ensure wider access to cutting-edge diagnostics.
   - Work with international organizations like the World Health Organization (WHO) to include ctDNA testing in global cancer control strategies.

Conclusion

The scientific promise of ctDNA testing is clear, however, considerable efforts remain before payers reimburse the NGS-based ctDNA tests required for proactive detection.

Scan here for poster references

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