
Supplementary information

Trends in the use of liquid biopsy in oncology

In the format provided by the authors

Clinical trial database construction and analysis

We constructed a proprietary liquid biopsy clinical trial database, which has four components:

- Basic information on the liquid biopsy product: application (therapy guidance, therapy monitoring, residual disease monitoring or early detection), name of product, test manufacturer (test company) and biopharma company collaborator
- Clinical trial information: NCT number, trial title, summary, trial name, phase, start and finish date, current status, country, drug included in the trial, drug type (targeted therapy, chemo, immunotherapy etc.), trial design, cancer indication, size of trial (number of patients), trial outcome (sensitivity, specificity)
- Regulatory status: current regulatory status (in vitro diagnostic (IVD) or laboratory-developed test (LDT), approval entity, approval time
- Technology: next-generation sequencing (NGS)/PCR, panel size, sample type (such as blood, other plasma tissues) etc.

The database was constructed via combined bottom-up and top-down processes:

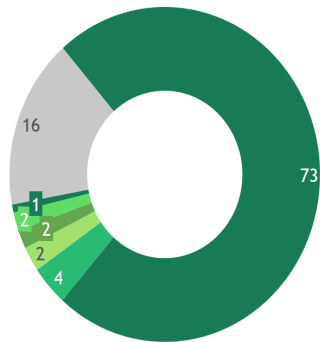
- Top-down approach:
 - First, we obtained a list of any relevant clinical trials by keyword searching for tumour biomarkers, such as ctDNA, ctRNA, extracellular vesicles and circulating tumour cells. A total of ~3,500 trials were obtained with this process.
 - Second, we further scrutinized the results to select the trials that are relevant to liquid biopsy based on the following exclusion criteria:
 - 1) trials not relevant to oncology, such as trials using liquid biopsy technology for acute kidney injury, transplant failure and infectious diseases
 - 2) trials with primarily focus of drug development but included a routine use of diagnostic tests for circulating tumour cells or circulating T cells for blood cancers such as leukaemias and lymphomas
 - 3) trials that only have liquid biopsy as an exploratory objective or exploratory outcome
 - 4) trials primarily assessed tissues other than liquid tissues
 - 5) trials suspended, withdrawn or terminated prematurely.
- Bottom-up approach:
 - First, we compiled a list of key companies and their major products in the liquid biopsy field sourced from analyst reports and literature review. A total of 134 major liquid biopsy and NGS companies were identified.
 - Second, we searched each company's website and company reports (such as 10K filings and investor presentations) to obtain a list of their products and clinical trials. We then searched ClinicalTrials.gov for their major products.

The bottom-up approach results were largely overlapping with those from the top-down approach, so we matched the trials via their NCT numbers to ensure no duplication in the database.

Overall, ~1,500 relevant blood-based liquid biopsy trials in oncology were included in our analysis. Some emerging liquid biopsy analytes such as exosomes and RNA (miRNA and mRNA) are not fully captured in this database given that most of them are in the early exploratory phase with limited clinical application.

By indication

A % of all active clinical trials



Oncology
Infection
Transplant
Nephropathy
CNS
Cardiovascular
Others

By type of sample¹

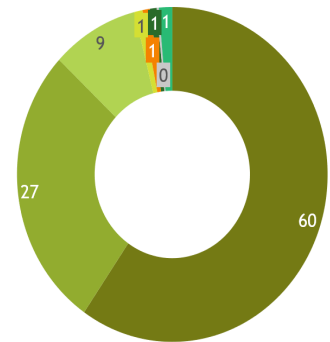
B % of active oncology clinical trials



Blood
Urine
Stool
Saliva
Tumor
Other

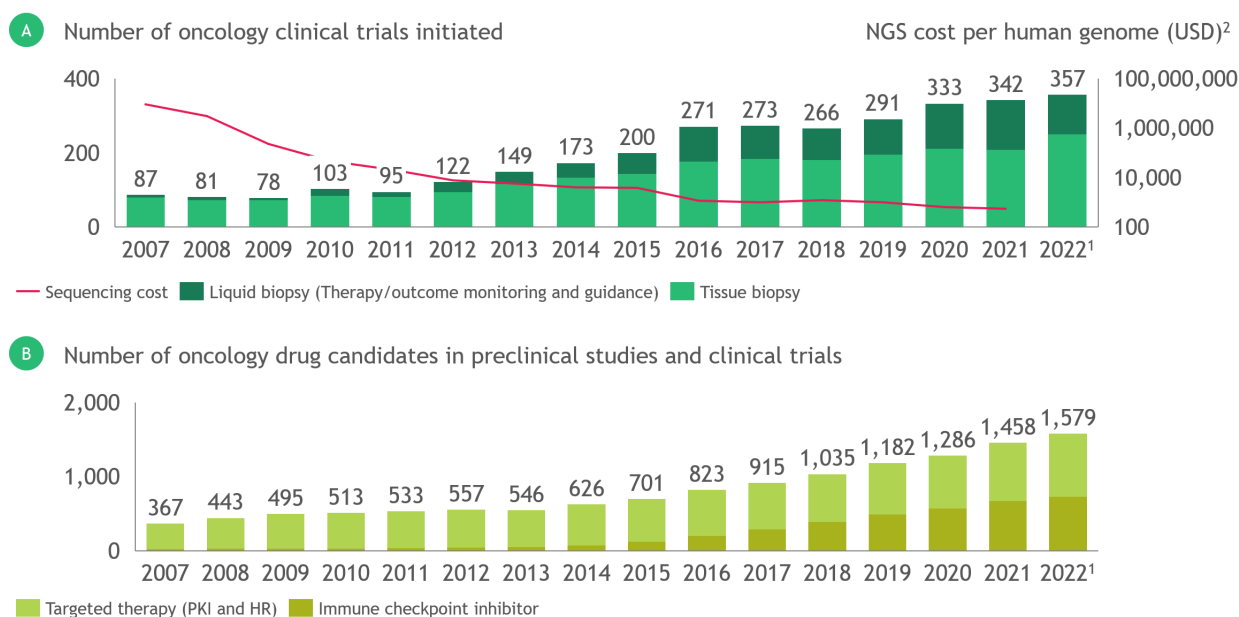
By type of substance¹

C % of active oncology blood sample based clinical trials

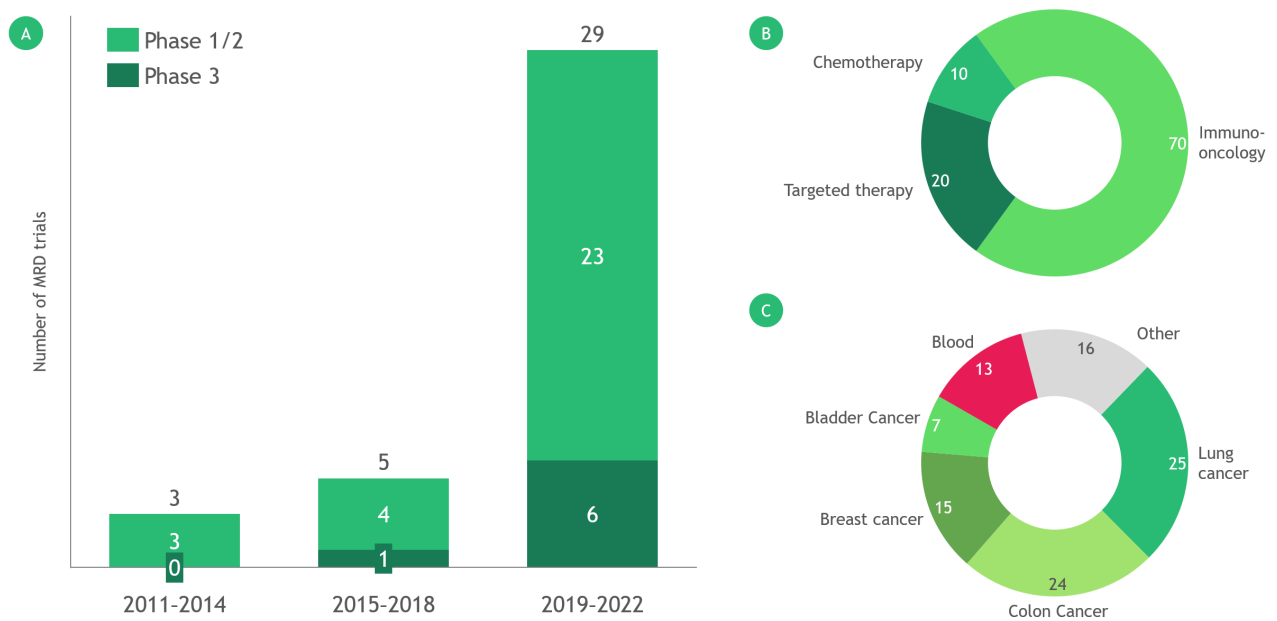


ctDNA
CTC
cfDNA
Protein
ctRNA
Extracellular vesicles
Metabolites
Others

Supplementary Figure 1 | **Overall landscape of liquid biopsy clinical trials.** **A** | Active clinical trials by indication. **B** | Active oncology clinical trials by type of sample. **C** | Active oncology blood-sample-based clinical trials by type of substance. ¹Some trials may contain multiple types of samples, so the number does not add up to total number of trials. Source: ClinicalTrials.gov, company websites and financial reports, BCG analysis.



Supplementary Figure 2 | **Relevant trends in oncology clinical trials.** **A** | Clinical trials initiated in each year associated with genetic testing from 2007 to 2022. Note the liquid biopsy trials only include the therapy/outcome monitoring and guidance applications for fair comparison to tissue biopsy, and do not include early disease detection and residual disease monitoring applications. **B** | Number of immune-oncology drug candidates and targeted oncology drug candidates in preclinical studies and clinical trials from 2007 to 2022. Targeted drugs include protein kinase inhibitors and hormone receptor modulators. ¹2022 data include only January to November 2022. ²Source: ClinicalTrials.gov, NIH National Human Genome Research Institute, Citeline Pharmaprojects, Evaluate Pharma, BCG analysis.



Supplementary Figure 3 | **Trends in clinical trials assessing minimum residual disease (MRD) to test drug effectiveness.** **A** | The number of clinical trials conducted by biopharma aiming to use MRD to test drug effectiveness is increasing. **B** | Drug categories tested in MRD clinical trials. **C** | Indications tested in MRD clinical trials. Numbers in panel B and C refer to % trials. ‘Other’ includes head and neck cancer, brain tumors, ovarian cancer, renal cancer, melanoma, esophageal cancer and liver cancer. Trials that are not conducted by biopharma companies, with an undisclosed drug or without a drug, not aiming to test drug effectiveness, or with an undisclosed clinical phase, are not included. Source: ClinicalTrials.gov, BCG analysis.

Supplementary Table 1 | **Commercialized products for liquid biopsy**

| Product | Company | Approval or launch status | Panel size category | Primary application |
|---|-----------------------|--|----------------------------|----------------------------|
| Abbott RealTime IDH1 | Abbott Molecular | Launched 2018 Approved by FDA 2018 | small | Therapy guidance |
| Abbott RealTime IDH2 | Abbott Molecular | Launched 2017 Approved by FDA 2017 | small | Therapy guidance |
| ARNA Breast | Arna Genomic | Launched n.a | small | Early detection |
| AR-v7 assays | Epic Sciences | Launched n.a | small | Therapy guidance |
| Astra™ | Genosity | Launched 2020 | large | MRD |
| AVENIO ctDNA Expanded Kit | Roche | Launched 2017 | mid | Therapy monitoring |
| AVENIO ctDNA Surveillance Kit | Roche | Launched 2017 | mid | Therapy monitoring |
| AVENIO ctDNA targeted kit | Roche | Launched 2017 | small | Therapy monitoring |
| BRACAnalysis CDx® | Myriad Genetics | Launched 2014, Approved 2014 | small | Therapy guidance |
| brProphet | Burning Rock Biotech | Launched n.a | large | MRD |
| CancerSEEK | Thrive/Exact Sciences | Launched 2019 | small | Early detection |
| CatALLyst™ | Amgen | Launched 2022 | unknown | Early detection |
| CellSearch | Veridex | Launched 2004 Approved 2004 | n/a | Therapy guidance |
| clonoSEQ | Adaptive | Launched 2018 Approved 2018 | small | MRD |
| Cobas EGFR Mutation Test v2 | Roche | Launched 2016, Approved by FDA 2018 | small | Therapy guidance |
| COLVERA | Clinical Genomics | Launched 2016 | small | MRD |
| Epi proColon | Epigenomics | Launched 2016 Approved 2016 | small | Early detection |
| Epi proLung | Epigenomics | Launched n.a | small | Early detection |
| FoundationACT | Foundation Medicine | Launched 2017 | mid | Therapy monitoring |
| FoundationOne Heme | Foundation Medicine | Launched 2013 | large | Therapy monitoring |
| FoundationOne® Liquid CDx | Foundation Medicine | Launched 2020, Approved 2020 | large | Therapy guidance |
| Freenome multianalyte test for colon cancer | Freenome | Launched 2014 | (blank) | Early detection |
| Galleri | Grail/Illumina | Launched 2021 | large | Early detection |
| Guardant Reveal | Guardant Health | Launched 2021 | large | MRD |
| Guardant360 | Guardant Health | Launched 2014, Approved 2014 | small | Therapy guidance |

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|--|---------------------------|------------------------------|---------|--------------------|
| Guardant360 LDT | Guardant Health | Launched 2020 | mid | Therapy monitoring |
| Idylla™ ctBRAF Mutation Assay | Biocartis | Launched n.a | small | Therapy guidance |
| Idylla™ ctKRAS Mutation Assay | Biocartis | Launched 2016 | small | Therapy guidance |
| Idylla™ ctNRAS-BRAF Mutation Assay | Biocartis | Launched n.a | small | Therapy guidance |
| Idylla™ ctEGFR Mutation Assay | Biocartis | Launched 2015 | small | Therapy guidance |
| InvisionFirst® | Inivata | Launched 2020 | small | MRD |
| KIT D816V Assay | ARUP Laboratories | Launched 2015, Approved 2015 | small | Therapy guidance |
| LeukoStrat® CDx FLT3 Mutation Assay | Invivoscribe Technologies | Launched 2014 Approved 2017 | small | Therapy guidance |
| Lunar 2 | Guardant Health | Launched n.a | large | Early detection |
| LungLB | LungLifeAI | Launched 2022 | large | Therapy guidance |
| MRDx BCR-ABL Test | MolecularMD/Icon | Launched 2017 Approved 2017 | small | Therapy guidance |
| NavDx® HPV ctDNA testing | Naveris | Launched n.a | unknown | Early detection |
| OncoBEAM™ RAS Colorectal | Sysmex | Launched n.a | small | Therapy guidance |
| OncoCEE™ | Biocept | Launched 2011 | unknown | Early detection |
| OncoCompass Target™ | Burning Rock Biotech | Launched 2021 | small | Therapy guidance |
| Oncomine | ThermoFisher | Launched 2017 Approved 2017 | mid | Therapy guidance |
| Oncomine focus | ThermoFisher | Launched 2015 Approved 2017 | mid | Therapy guidance |
| Onconscreen plus 520 Panel | Burning Rock | Launched n.a | large | MRD |
| OncoReveal® | Pillar Biosciences | Launched 2021 | large | Therapy guidance |
| OncoScreen Plus panel | AlphaGenomix | Launched n.a | large | Therapy guidance |
| Oncotype DX The Breast Recurrence Score® | Exact Sciences | Launched n.a | small | MRD |
| OncotypeSEQ Liquid Select assay | Genomic Health | Launched 2016 | small | Therapy guidance |
| PANAMutyper™ R EGFR | PNA Bio | Launched prior 2016 | small | Therapy guidance |
| PANAMutyper™ R KRAS | PNA Bio | Launched prior 2016 | small | Therapy guidance |

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|--|-------------------------|--|---------|-----------------------|
| PANAMutyper™ R NRAS (31 Mutations) | PNA Bio | Launched prior 2016 | small | Therapy guidance |
| PCM™ | ArcherDx/Invitae | Launched n.a | unknown | MRD |
| PGDx elio™ plasma resolve* | PGDx | Launched 2018 Approved 2018 | large | Therapy guidance |
| POMC/PCSK1/LE PR CDx Panel | PreventionGenetics | Launched 2022 Approved 2022 | small | Therapy guidance |
| PredicineCARE | Predicine | Launched 2022 | mid | Therapy guidance |
| QIAamp | Qiagen | Launched prior 2019 | mid | Therapy monitoring |
| RaDAR | Inivata | Launched 2021 Approved by FDA 2021 | small | MRD |
| RadTox | Diacarta | Launched n.a | (blank) | Therapy monitoring |
| Signatera | Natera | Launched 2021 | small | MRD |
| Super-ARMS® EGFR kit | AmoyDx | Launched prior 2017 | small | Therapy guidance |
| therascreen PIK3CA RGQ PCR Kit | Qiagen | Launched 2019, Approved 2019 | small | Therapy guidance |
| THERASURE CNI Monitor | Chronix | Launched 2018 | small | MRD |
| TruSight Oncology 500 (TSO500) | Illumina | Launched 2019 | large | Therapy monitoring |
| HCCscreen | Genetron | Launched 2021 | unknown | Early detection |
| ColonAiQ | Singlera | Launched 2022 | small | Therapy guidance |
| OverC™ Multi- Cancer Early Detection | Burning Rock Biotech | received CE mark in May 2022 | large | Therapy guidance |
| BGI SENTISTM C ancer + Discovery Panel | BGI | received CE mark in May 2021 | large | Therapy guidance |
| GENESEEQLITE TM | GeneSeeq | Launched 2021 | mid | Therapy guidance |
| BRCASCAN™ | GeneSeeq | Launched n.a | small | Therapy guidance |

MRD, minimum residual disease; n.a, not available.

References

1. Preethi KA, et al. Mol Cancer. 2022 Feb 16;21(1):54.
2. Galiveti CR, et al. Head Neck. 2023 Jan;45(1):212-224
3. Guo T, et al. Mol Cancer. 2022 Dec 12;21(1):21