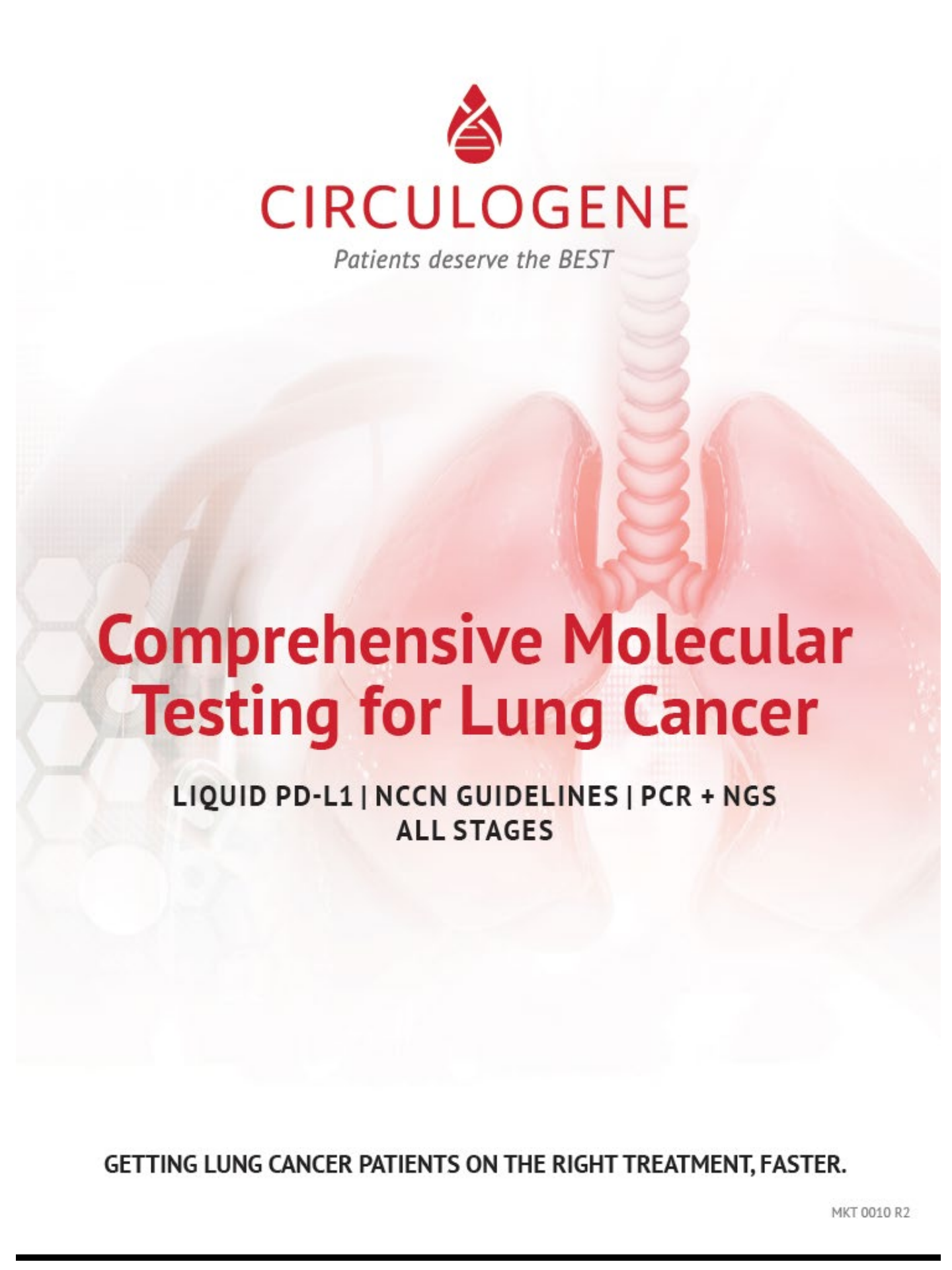
CIRCULOGENE

*Patients deserve the BEST*



# Comprehensive Molecular Testing for Lung Cancer

**LIQUID PD-L1 | NCCN GUIDELINES | PCR + NGS**
**ALL STAGES**

**GETTING LUNG CANCER PATIENTS ON THE RIGHT TREATMENT, FASTER.**

MKT 0010 R2

# Liquid Biopsy is Supported by IASLC for Lung Cancer Patients

International Association for the Study of Lung Cancer (IASLC) Recommendation: Liquid biopsy is emerging as not only complementary to tissue-based analysis but also acceptable as the initial approach ("plasma first") for biomarker evaluation at the time of diagnosis and for monitoring the efficacy of targeted therapies.

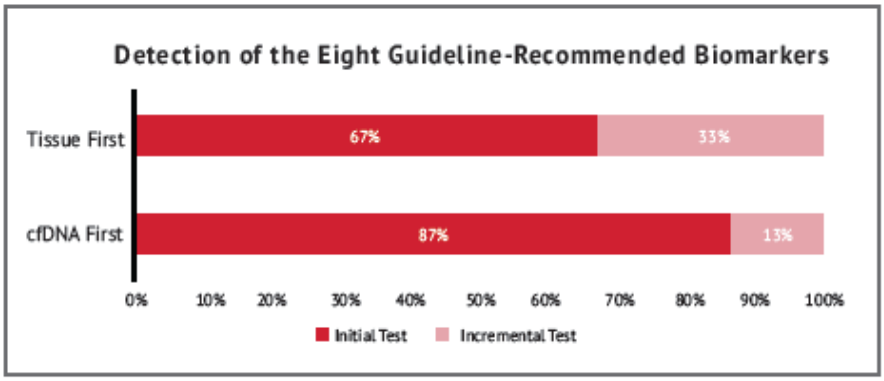
## Combination of Liquid and Tissue Biopsy

**The combination of liquid and tissue biopsy identifies more actionable mutations.**

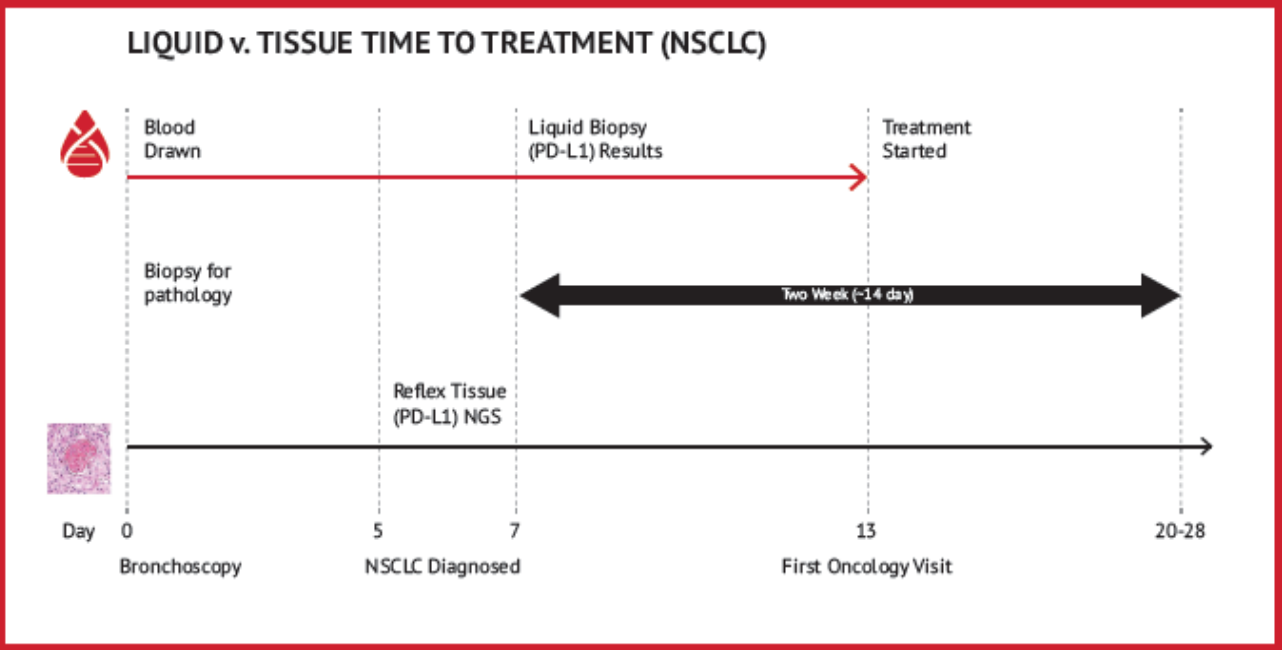
Tissue-only molecular testing only detects 67% of National Comprehensive Cancer Network (NCCN) guideline mutations, missing 33%. Liquid biopsy detects 87% of guideline mutations.

Used together, liquid and tissue biopsy provides a more complete picture of the tumor's molecular makeup.[1]

Liquid biopsy has the advantage of detecting a multitude of biomarkers which may be an indication of metastasis away from the primary tumor.




## AS QUICK AS 7 DAYS TO RESULTS – FASTER TIME TO TREATMENT



## 80% OF CANCER PATIENTS START TREATMENT WITHOUT MOLECULAR PROFILE

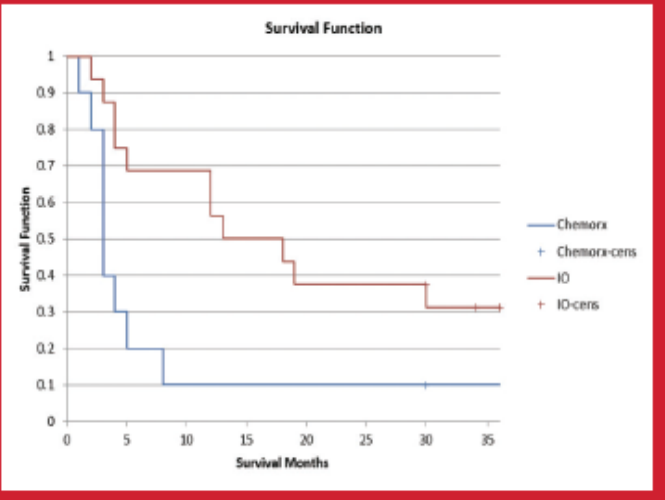
ASCO (2019) reported that only 20% of NSCLC patients have a molecular profile or biopsy to maximize information gathered for optimal treatment decisions.[3]

# CIRCULOGENE Offers the Only Liquid PD-L1

PD-L1 expression has been correlated with clinical effectiveness and improved survival rates when treated with immunotherapy. Utilizing KEYNOTE-042 as a baseline comparison, plasma PD-L1 parallels tissue PD-L1 clinical trial outcomes with a 30% survival over 3 years.[4]

Study demonstrates plasma cfRNA PD-L1 is predictive of immunotherapy benefit in advanced NSCLC (compared to chemotherapy).

The ECU study demonstrated that Plasma PD-L1 expression was predictive of significant survival benefit of immunotherapy treatment over chemotherapy in advanced NSCLC patients. Using pembrolizumab monotherapy study as a baseline comparison, plasma PD-L1 parallels tissue PD-L1 clinical trial outcomea with a 30% survival over 3 years.




# Patients deserve the Best!

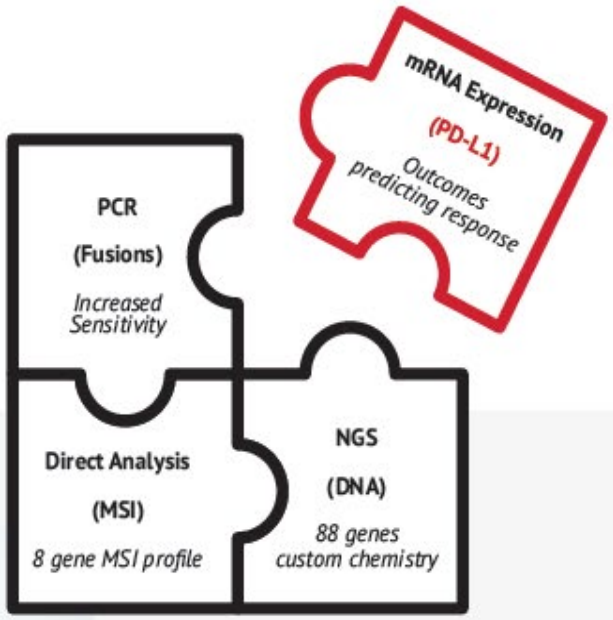
Each patient's cancer is unique, understanding the origins and severity of the cancers aids oncologists to personalize the patient's treatment plan at the time of diagnosis and throughout their cancer journey.

Patients deserve the right treatment for their cancer and within a time frame that improves their outcomes and chance for survival. Understanding the patient's tumor(s) molecular profile aids oncologists to prescribe the right first-line treatment.

# The CIRCULOGENE Best-in-Class Difference

CIRCULOGENE combines the best-in-class pre-analytical, instrumentation, and technology to provide oncologists (and their patients) with the most comprehensive results. Having results in as little as 7 days could lead to personalized treatment, faster.

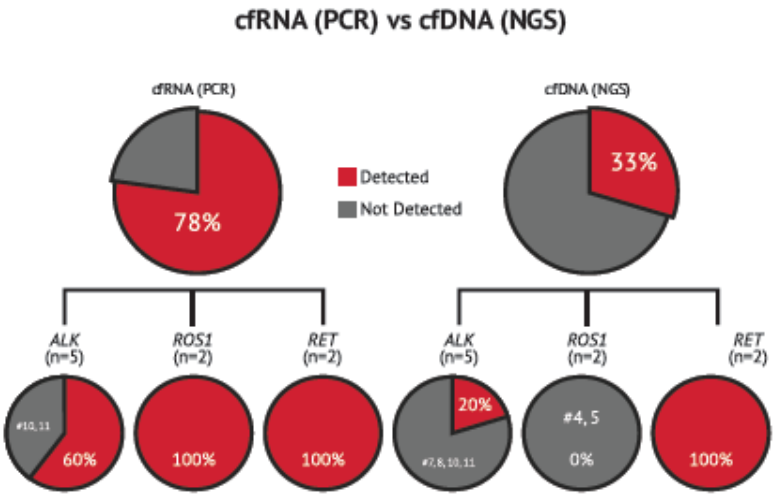
- Combines NGS and PCR
- Increases RNA yields with proprietary LISA technology
- Provides the ONLY liquid PD-L1
- Offers Enhanced MSI
- Clinical utility to detect at all cancer stages
- Early indication of metastasis
- Delivers personalized, actionable reports




# Combining PCR and NGS Leads to Most Comprehensive Assay

Highly sensitive RNA fusions are best detected by PCR versus NGS. CIRCULOGENE's best-in-class approach provides a multi-modality approach combining the breadth of NGS for DNA and accuracy of PCR for RNA.

The fusion detection sensitivities of the cfRNA with PCR and cfDNA with NGS were compared. cfRNA with PCR detected 78% (7/9) of the fusions while cfDNA with NGS only detected 33% (3/9). [2]




**References:**


[1] Combo Liquid and Tissue

Leighl et al. Clinical Utility of Comprehensive Cell-free DNA Analysis to Identify Genomic Biomarkers in Patients with Newly Diagnosed Metastatic Non-small Cell Lung Cancer, Clin Cancer Res (2019) doi: 10.1158/1078-0432.CCR-19-0624

[2] PCR and NGS

Hasegawa et al. Highly sensitive fusion detection using plasma cell-free RNA in non-small-cell lung cancers, Cancer Science (2021) https://doi.org/10.1111/cas.15084

[3] 80% ASCO

Geirman et al. Genomic testing and treatment landscape in patients with advanced non-small cell lung cancer (aNSCLC) using real-world data from community oncology practices. ASCO Annual Meeting (2019) Journal of Clinical Onology

[4] PD-L1

Jayandana et al. Plasma cell free RNA PD-L1 and Clinical Outcomes with Immunotherapy. ASCO Annual Meeting (2021).

# Why CIRCULOGENE?

CIRCULOGENE's comprehensive tumor DNA and RNA sequencing is the only plasma testing available that combines the most advanced next-generation sequencing (NGS) and polymerase chain reaction (PCR) technology to detect and monitor cfDNA and cfRNA within well-characterized, well-documented, actionable cancer-associated genes.

## FULL GENE

| | | | | |
|---|---|---|---|---|
| AKT1 | CDK6 | GNA11 | MLH1 | **RET** |
| ALK | CDKN2A | GNAQ | MTOR | ROS1 |
| AR | CHEK1 | GNAS | MYC | SETD2 |
| ARAF | CHEK2 | HNF1A | NF1 | SMAD4 |
| ARID1A | CRKL | HRAS | NOTCH1 | SMARCA4 |
| ATM | CSF1R | IDH1 | NRAS | SMARCB1 |
| ATR | CTNNB1 | IDH2 | NTRK1 | SMO |
| AXL | DDR2 | IGF1R | NTRK2 | SRC |
| BAP1 | **EGFR*** | JAK2 | NTRK3 | STAT3 |
| BARD1 | **ERBB2** | JAK3 | PALB2 | STK11 |
| **BRAF*** | ERBB4 | KDR | PDGFRA | TERT |
| BRCA1 | ESR1 | KEAP1 | PIK3CA | TOP1 |
| BRCA2 | EZH2 | KIT | POLD1 | TP53 |
| CCND1 | FBXW7 | **KRAS** | POLE | TSC1 |
| CCNE1 | FGFR1 | MAP2K1 | PTEN | TSC2 |
| CDH1 | FGFR2 | MAP2K2 | PTPN11 | VHL |
| CDK12 | FGFR3 | MAPK3 | RAF1 | |
| CDK4 | FOXL2 | **MET** | RB1 | |

## CNV

| | |
|---|---|
| AR | ERBB2 |
| CCND1 | FGFR1 |
| CCNE1 | FGFR2 |
| CDK4 | KIT |
| CDK6 | MET |
| EGFR | MYC |

## FUSION

**ALK***
**NTRK1***
**NTRK2***
**NTRK3***
**ROS1***

## IMMUNOTHERAPY

MSI
PD-L1 RNA Expression

## HEREDITARY GENES

| | | |
|---|---|---|
| APC (2,3) | CHEK2 (1,2,4) | POLE (2) |
| ATM (1,2,3,4) | EPCAM (1,2,3,4,5) | PTEN (1,2) |
| BMPR1A (2) | MLH1 (1,2,3,4,5) | RAD51C (1) |
| BRCA1 (1,3,4) | MSH2 (1,2,3,4,5) | RAD51D (1,4) |
| BRCA2 (1,3,4) | MSH6 (1,2,3,4,5) | SMAD4 (2) |
| BRIP1 (1) | MUTYH (2) | STK11 (1,2,3) |
| CDK (4) | PALB2 (1,3,4) | TP53 (1,2,3,4) |
| CDH1 (1,2) | PMS2 (1,2,3,4,5) | VHL |
| CDKN2A (3) | POLD1 (2) | |

1 = Hereditary Breast/Ovarian/Uterine Cancer (HBOUC) Panel
2 = Colorectal Cancer Panel
3 = Pancreatic Cancer Panel
4 = Prostate Cancer Panel
5 = Lynch Syndrome

**EXPERT-RECOMMENDED BIOMARKERS**
***NCCN TARGETABLE MARKERS**

## When to Test with Liquid Biopsy

CIRCULOGENE offers the most advanced NGS and PCR methods to both detect and continually monitor cfDNA and cfRNA.

**1. At diagnosis to guide treatment**

**2. At 6-8 weeks post treatment to assess response**

**3. To assess symptomatic or radiographic concern for recurrent or progressing cancer**

## GET STARTED TODAY.

Talk to your CIRCULOGENE representative to request our collection kit and requisition form.

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