

NeoThetis<sup>®</sup>  
therapy selection

Liquid biopsy  
for therapy  
selection



**MEDICOVER**  
GENETICS

# WHAT IS NeoThetis THERAPY SELECTION?

NeoThetis is a novel, non-invasive liquid biopsy test for **therapy selection**, that guides patients diagnosed with cancer towards the most optimal **treatment**. NeoThetis can analyze **minute amounts** of circulating tumor DNA (**ctDNA**) which is released from primary and metastatic tumors in the bloodstream of patients. Performed via a simple **blood draw**, NeoThetis is **safe** for the patient and overcomes some of the challenges of tumor biopsy such as the need for hospitalization after surgery.

## CLINICAL UTILITY

- Guides **therapy selection** for primary and metastatic disease, and **treatment re-evaluation** for therapy resistance
  - **FDA/EMA approved therapy** solutions
  - Associated with **ongoing clinical trials**
- Tests for clinically actionable **genetic alterations**, and **immunotherapy** eligibility
- Identifies mutations in distant non-operable **metastatic lesions**
- Captures intra- and intertumor heterogeneity, offering a **comprehensive** genomic tumor profiling
- Offers **fast turnaround** results, ensuring treatment can begin faster

## WHO IS NeoThetis FOR?

NeoThetis can be performed at **initial diagnosis** and during **disease progression** for patients

- whose tumor is inaccessible
- who have limited or unavailable tissue biopsy material
- who are unfit, or are not clinically recommended to undergo invasive tumor biopsy
- who need fast results to select the appropriate therapy
- who do not respond to current treatment and re-evaluation is needed

## NeoThetis TESTS FOR:

### GENETIC ALTERATIONS

*Applicable for Gene Targeted Therapies*

Genetic alterations include any changes in the DNA sequence. They can be responsible for tumor development, therapy resistance and cancer relapse and have been associated with targeted gene therapies which aim to prevent cancer growth and spread.

### MICROSATELLITE INSTABILITY (MSI)

*Applicable for Immunotherapy*

MSI, an immunotherapy biomarker, is caused by defects in the DNA mismatch repair mechanism. This results in the accumulation of short repeated DNA sequences known as microsatellites, which cause genetic hypermutability. MSI can offer prognostic and therapeutic value for patients with different types of solid tumors, including but not limited to: colorectal, endometrial, gastric, prostate and bladder cancer.

### BLOOD TUMOR MUTATIONAL BURDEN (bTMB)

*Applicable for Immunotherapy*

bTMB indicates the total number of mutations found in a tumor per megabase and it is obtained from analyzing ctDNA. bTMB is tumor agnostic and can guide healthcare providers to identify patients who might benefit from immunotherapy.

# NeoThetis TESTS

NeoThetis tests are designed to detect **clinically actionable genetic alterations**, including single nucleotide variants (**SNVs**), insertions and deletions (**INDELs**), copy number amplifications (**CNAs**), and **rearrangements** that drive cancer or are associated with response to treatment. NeoThetis also tests for **MSI**, and **bTMB** predictive biomarkers that guide immunotherapy treatment.

## EXTENDED

<b>Pan-Cancer Plus</b> Targets full exonic coverage* on the genes tested. Testing for MSI and bTMB via Next Generation Sequencing (NGS) is included.	222 genes
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<b>Pan-Cancer</b> Targets specific regions on the genes tested. Testing for MSI via NGS is included.	80 genes
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## CANCER-SPECIFIC

*Target specific regions on the genes tested*

<b>Breast &amp; Gynecological</b>	48 genes
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<b>Colorectal</b>	34 genes
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<b>Gastric</b>	23 genes
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<b>Melanoma</b>	28 genes
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<b>NSCLC</b>	36 genes
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<b>Pancreatic</b>	26 genes
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<b>Prostate</b>	35 genes
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## WHAT IS TESTED IN EACH NeoThetis TEST?

ALTERATIONS	Extended Tumor Profile		Cancer-Specific Tumor Profile
	Pan-Cancer Plus	Pan-Cancer	
SNVs, INDELs	•	•	•
CNAs	•	•	•
REARRANGEMENTS	•	•	•
MSI	•	•	•
bTMB	•		

- Included in the panel

\*Exceptions on regions containing repeats, sequences of high homology (pseudogenes and segmental duplications) or extreme GC-content.

# RECOMMENDATIONS FROM PROFESSIONAL BODIES

*The use of cell-free/circulating tumor DNA testing can be considered when a patient is medically unfit for invasive tissue sampling, or if in the initial diagnostic setting there is insufficient material for molecular analysis following pathologic confirmation.*

NCCN Guidelines NSCLC 2023, Version 3.2023

*“Validated and sensitive ctDNA assays can be used to genotype advanced cancers and select patients for targeted therapies”.*

Pascual et al. 2022, ESMO recommendations<sup>1</sup>

## CASE STUDY



64-year-old female diagnosed with stage III NSCLC

- Tissue biopsy molecular analysis revealed an EGFR exon 19 in-frame deletion
- Patient had previously received targeted therapies (afatinib, erlotinib)
- Progression of disease observed after targeted therapy

### NeoThetis NSCLC results

- New EGFR T790 mutation found
- The patient will not benefit from a continuation of 1<sup>st</sup> or 2<sup>nd</sup> generation TKIs treatment (erlotinib, gefitinib, afatinib)
- The patient is eligible for osimertinib treatment (3<sup>rd</sup> generation TKI)
- Available clinical trials reported

NeoThetis accurately identified the new genetic alteration that contributed to therapy resistance and cancer relapse. NeoThetis also reported the approved therapy associated with the new genetic alteration, as well as the available ongoing clinical trials that the patient could benefit from.

1. Pascual J et al. 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.* 2022 Aug;33(8):750-768. doi: 10.1016/j.annonc.2022.05.520. Epub 2022 Jul 6. PMID: 35809752

# OUR PROPRIETARY TECHNOLOGY PLATFORM

## TARGETED TECHNOLOGY AND NOVEL BIOINFORMATICS

Unparalleled workflow which combines our proprietary **Targeted Capture Enrichment Technology** along with novel **bioinformatic pipelines**, to provide accurate detection of genetic variants. Our high-read depth analysis enables for increased sensitivity and specificity providing reliable results.

## GENETIC ALTERATION DETECTION

Multi-engine analysis incorporating innovative bioinformatic pipelines analyzes the sequencing data produced via NGS. This enables **accurate detection** of different types of genetic alterations, even at low levels. The genetic alterations have thoroughly been selected according to the NCCN guidelines and are associated with FDA/EMA approved therapies.

## MSI AND bTMB ASSESSMENT

MSI testing via NGS detects a higher number of clinically significant loci compared to other MSI testing methods, such as immunohistochemistry, with high sensitivity. MSI assessment:

- has been emphasized by cancer societies including NCCN, ESMO and ASCO
- is associated with FDA/EMA approved immunotherapy drugs

NeoThetis provides >1Mb of genomic coverage for accurate bTMB scoring.

# BENEFITS OF NeoThetis

## SAFE

Non-invasive  
sample collection

## EXTENSIVE

Tests for MSI and  
bTMB immunotherapy  
biomarkers

## VALUABLE

Fast turnaround  
results

## INFORMATIVE

Deep genetic  
insight into a  
patient's tumor

## WHAT WILL THE REPORT TELL ME?

The NeoThetis report provides **clinical interpretation** and **classification** of the results, along with the latest information on **therapy options**, enabling for **precision medicine** tailored to each patient. The report includes:

### MSI STATUS AND bTMB SCORE

The **MSI status** and the **bTMB score** of a tumor is reported along with their current FDA/EMA-approved immunotherapies.

### GENETIC ALTERATIONS RESULTS

Variants of strong, potential, and uncertain significance are reported, along with FDA/EMA- approved or NCCN recommended targeted therapies.



Approved in indication



Included in NCCN guidelines

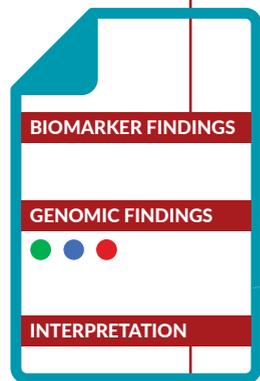


Lack of response

### ELIGIBILITY ON AVAILABLE CLINICAL TRIALS

Ongoing clinical trials are reported, expanding the patient's treatment options.

Comprehensive and insightful information of the results is provided.



## WHAT CAN I DO AFTER NeoThetis?

- Inform your patient about the results and recommend genetic counseling
- Identify the best treatment opportunities tailored to your patient
- Consider eligible clinical trials for your patient

# HOW TO ADMINISTER **NeoThetis**?



Recommend **NeoThetis** to your patient



Collect a peripheral blood sample from your patient



Send the sample to **Medicover Genetics**



The sample will be analyzed at **Medicover Genetics** laboratories



Results will be sent to you within 6-9 working days from sample receipt

## MORE QUESTIONS?

If you have additional questions or concerns, please contact us at [info.genetics@medicover.com](mailto:info.genetics@medicover.com)



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