ForeSENTIA®

tumor profile

Extensive analysis of tumor molecular markers

MEDICOVER GENETICS

WHAT IS **ForeSENTIA**?

ForeSENTIA is a tumor profiling genetic test for solid tumors that identifies a spectrum of **genetic alterations** and **genomic biomarkers**, such as **microsatellite instability** (**MSI**) and **tumor mutational burden** (**TMB**). The information provided by ForeSENTIA can offer prognostic value, and **guidance** on treatment decisions through **precision medicine** and **targeted therapies**.

CLINICAL UTILITY

- Analysis of clinically actionable genetic alterations, and immunotherapy biomarkers MSI and TMB in a single test.
  - Genes recommended by NCCN guidelines for solid tumors
  - Genes that currently serve as selection criteria in active clinical trials
  - Tumor-agnostic biomarkers
- Guidance on available targeted therapies, including immunotherapies, and ongoing clinical trials. Tailored therapies can reduce the risk of ineffective therapy and adverse side effects, and avoid a 'one-size-fits-all' approach

WHO IS **ForeSENTIA** FOR?

- Patients who require genetic test analysis for targeted therapy
- Patients with treatment resistance or cancer relapse who require alternative treatment options, including immunotherapy
- Patients who want to increase the possibilities of identifying treatment options by testing for immunotherapy biomarkers

ForeSENTIA TESTS FOR:

GENETIC ALTERATIONS

Applicable for Gene Targeted Therapies

Genetic alterations such as single nucleotide variants (**SNVs**), insertions & deletions (**INDELs**), copy number alterations (**CNAs**) and **rearrangements** which can drive tumor development, and can be responsible for therapy resistance and cancer relapse.

GENOMIC BIOMARKERS

Applicable for Immunotherapy

MSI BIOMARKER

MSI is a genetic hypermutability condition caused by defects in the DNA mismatch repair mechanism. It 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.

TMB BIOMARKER

TMB indicates the total number of somatic mutations found in a tumor per megabase. TMB score can offer prognostic value for patients with **solid** tumors, including **rare** types, as well as therapeutic opportunities in a tumor-agnostic manner.

Both MSI and TMB can identify patients eligible for immunotherapy. Although some correlation exists between the two, MSI and TMB scores are not always associated. Results for each biomarker depend on the tumor type, and the underlying pathways involved.

ForeSENTIA PANELS

The ForeSENTIA panels screen for clinically actionable genetic alterations or genomic biomarkers, which are associated with **approved therapies** or are the focus of **ongoing clinical trials**, via Next Generation Sequencing (NGS).

EXTENDED TUMOR PROFILE

Pan-Cancer Plus Targets **all exonic regions**† of the genes tested.	222* genes
Pan-Cancer Targets **specific regions** on the genes tested.	80* genes

CANCER-SPECIFIC TUMOR PROFILE

Target specific regions on the genes tested

Breast & Gynecological	48 genes
Colorectal	34 genes
Glioma	22* genes
Lung (NSCLC)	36 genes
Melanoma	22 genes
Prostate	36 genes

GENE-FOCUSED

Target specific regions on the genes tested

BRAF	**EGFR**	**IDH1 & IDH2**	**KRAS & NRAS**	**PIK3CA & AKT1**

Additionally, histopathology analysis for identification of additional biomarkers, such as PDL-1, can be available upon request

WHAT IS TESTED IN EACH **ForeSENTIA** PANEL?

ALTERATIONS	Extended Tumor Profile		Cancer-Specific Tumor Profile	Gene-Focused
	Pan-Cancer Plus	Pan-Cancer		
SNVs, INDELs	●	●	●	●
CNAs	●	●	●	
REARRANGEMENTS	●	●	●	
MSI	●	●	○	
TMB	●			

● Included in the panel ○ Optionally included in the panel

* 1p/19q codeletion is also tested in these panels and reported only in the context of glioma diagnosis.
† Exceptions on regions containing repeats, sequences of high homology (pseudogenes and segmental duplications) or high GC-content.

RECOMMENDATIONS FROM PROFESSIONAL BODIES

- *NGS represents another type of molecular test to assess MSI. Its main advantages are represented by the possibilities of coupling MSI analysis with the determination of TMB.*
- *All common or rare tumor types not belonging to the spectrum of Lynch syndrome with low prevalence of MSI and little data available on the reliability of IHC and MSI-PCR, to be tested using NGS.*

ESMO, 2019[1]

CASE STUDY

A 67-year-old female was diagnosed with stage III colorectal cancer

ForeSENTIA Pan-Cancer Plus results

Genomic Biomarkers

- MSI-high and TMB score of 12 mut/Mb
- 3 FDA/EMA approved immunotherapies
- >90 clinical trials

Genetic Alterations

- 7 genetic alterations in BRCA2, CTNNB1, RET, IDH2 and other genes
- 6 off-labeled drugs
- 11 clinical trials

ForeSENTIA accurately identified the genomic biomarkers and genetic alterations of the patient's tumor, as well as the associated approved therapies and available ongoing clinical trials offering a detailed guidance on the best clinical management of the patient.

1. *Luchini C et al. ESMO recommendations on microsatellite instability testing for immunotherapy in cancer, and its relationship with PD-1/PD-L1 expression and tumour mutational burden: a systematic review-based approach. Ann Oncol. 2019 Aug 1;30(8):1232-1243. doi: 10.1093/annonc/mdz116. PMID: 31056702.*

OUR **PROPRIETARY** TECHNOLOGY PLATFORM

TARGETED TECHNOLOGY AND NOVEL BIOINFORMATICS

ForeSENTIA is based on a novel, **Target Capture Enrichment Technology** which utilizes Next Generation Sequencing, and has been developed in-house and ensures high accuracy and precision. The proprietary technology is combined with novel **bioinformatic pipelines**, to provide accurate detection of genetic variants even at low allele frequencies. Our high read-depth analysis enables for increased sensitivity and specificity providing reliable results.

GENETIC ALTERATION DETECTION

Multi-engine analysis incorporating innovative bioinformatic pipelines analyze the sequencing data. These enable **accurate detection** of different types of genetic alterations, even at low levels.

MSI AND TMB ASSESSMENT

ForeSENTIA can accurately detect both MSI and TMB. MSI testing via NGS detects a **higher number** of clinically significant loci compared to other MSI testing methods, such as immunohistochemistry, with high sensitivity. ForeSENTIA provides **>1Mb** of genomic coverage for accurate TMB scoring.

BENEFITS OF **ForeSENTIA**

COMPREHENSIVE
Charts the mutational landscape of tumors

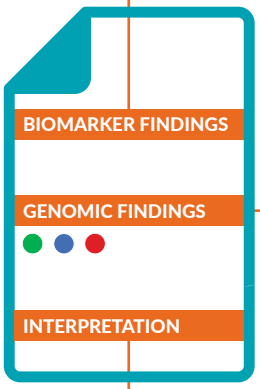
EXTENSIVE
Tests for MSI and TMB

INFORMATIVE
Provides tailored therapy options

VALUABLE
Identifies eligible clinical trials

WHAT WILL THE **REPORT** TELL ME?

The ForeSENTIA report will empower you to take **informed** and **accurate decisions** on the best clinical management of your patient. The information provided can guide you to select currently approved therapies and ongoing clinical trials that are most applicable for your patient's tumor profile results.



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

GENETIC ALTERATIONS RESULTS
Based on the genetic alterations reported, information is provided on associated FDA/EMA-approved or NCCN-recommended therapies, and ongoing clinical trials.

- 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 opportunities.

VARIANTS OF UNCERTAIN SIGNIFICANCE
A genetic change has been detected, but it is currently unknown whether that change is associated with cancer development.

Comprehensive analysis of findings. The report will explain all the genetic and biomarker findings as well as their clinical significance, according to the latest guidelines and scientific literature.

WHAT CAN I DO AFTER **ForeSENTIA**?

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

HOW TO ADMINISTER **ForeSENTIA**?

Recommend **ForeSENTIA** to your patient

Let the histopathology lab know that additional testing will be required on the tissue biopsy sample

The histopathology lab will send the tumor sections to **Medicover Genetics**

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

The results will be sent to you within 2-3 weeks from sample receipt

MORE **QUESTIONS**?

If you have additional questions or concerns, please contact us at **info.genetics@medicover.com**

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