FDA/EMA APPROVED TARGETED THERAPIES, BASED ON NCCN/ESMO GUIDELINES

NCCN/ESMO guideline-recommended targeted therapies, and approved targeted therapies for other indications are also available.

	COLORECTAL	NSCLC	PROSTATE	BREAST	PANCREATIC	OVARIAN
BRCA1			Olaparib, Rucaparib	Olaparib,Talazoparib (germline)	Olaparib	Olaparib, Rucaparib, Niraparib
CDK12			Olaparib			
EGFR		Afatinib, Dacomitinib, Erlotinib, Gefitinib, Osimertinib, Ramucirumab (+Erlotinib)				
NTRK1/2/3	Larotrectinib, Entrectinib (all solid tumors)					
ROS1		Crizotinib, Entrectinib				

TMB-High Pembrolizumab (all solid tumors)

The above table, produced in October 2023, includes a selection of available therapies and should be used for guidance only. NCCN, ESMO, and ASCO guideline-recommended targeted therapies, and approved targeted therapies for other indications are also available. For the latest information on approved targeted therapies, please visit the relevant websites

Pembrolizumab (all solid tumors)

CASE STUDY

Nivolumab, Ipilimumah

A 70-year-old male was diagnosed with stage III laryngeal squamous cell carcinoma, a rare type of cancer

Due to the low incidence rate of this cancer, a larger panel which includes an extensive number of genes and genomic biomarkers is more valuable for the patient, as it increases his chances of identifying an actionable mutation and beneficial treatment.

Pan-Cancer Plus identified a high TMB score of 16mut/Mb as the only therapy associated biomarker.

ForeSENTIA results led to:

Pembrolizumab, a tumor-agnostic FDA-approved immunotherapy drug indicated for high TMB scores, being administered to the patient Identification of **2 clinical trials** related to Pembrolizumab

Identification of **3 genetic alterations** that are associated with:

7 clinical trials

2 FDA/EMA approved therapies for other indications

ABOUT MEDICOVER GENETICS

Medicover Genetics is a leading healthcare company specialising in genetic medicine, with more than 25 years of experience in genetics diagnostics. Medicover Genetics offers genetic testing services and genetic counselling, proprietary CE-IVD marked solutions and a versatile Technology Transfer Platform which enables partners to perform high fidelity genetic tests in-house. With services in over 30 countries across Europe, Asia, and Africa, the company empowers laboratories, healthcare professionals and patients to place genetics at the core of medical decisions. Committed to enhancing health and well-being, Medicover Genetics provides meaningful, actionable diagnostic solutions, improving disease prognosis, clinical management, and therapy selection for genetic disorders. The CAP-accredited, CLIA-, GMP- and ISO9001, 15189, and 13485 certified laboratories ensure the highest quality standards. www.medicover-genetics.com

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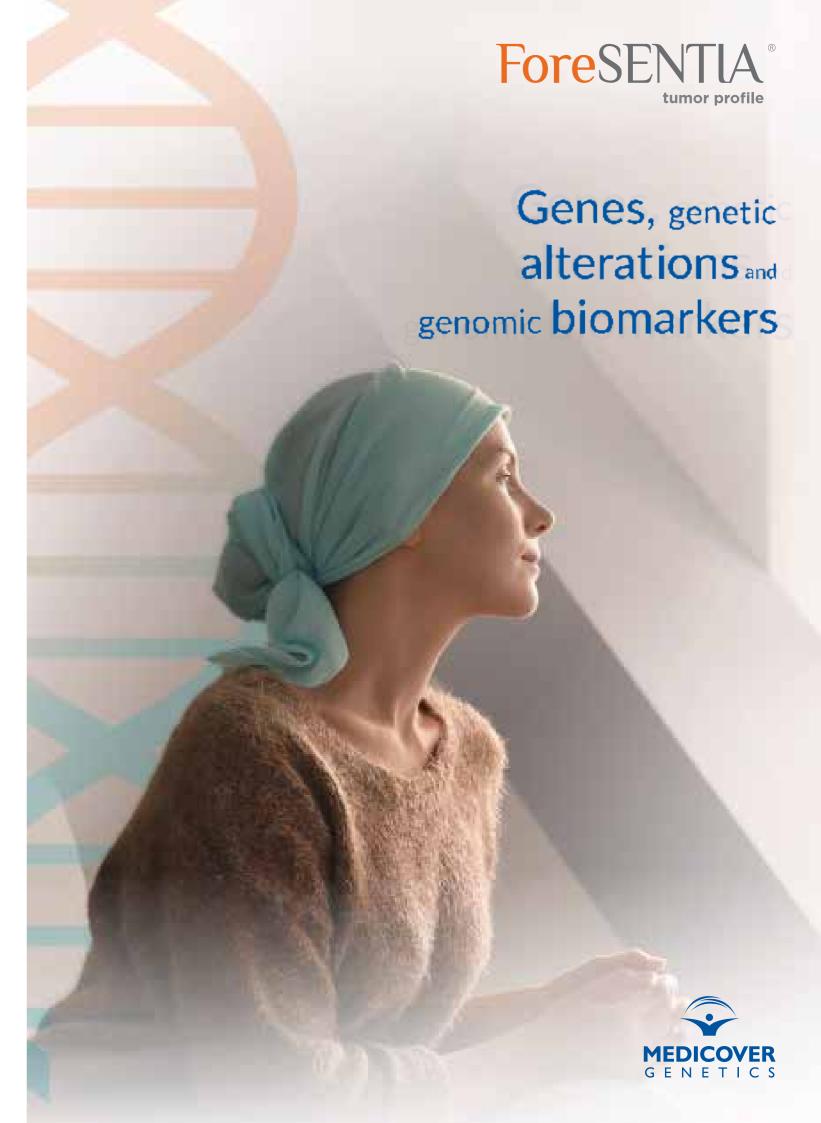












WHAT IS ForeSENTIA?

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, ESMO, and ASCO 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.

LIST OF GENES AND GENETIC ALTERATIONS TESTED

ForeSENTIA targets **clinically important** coding regions and selected non-coding regions in genes of interest. ForeSENTIA examines a spectrum of genetic alterations such as single nucleotide variants (**SNVs**), insertions and deletions (**INDELs**), copy number alterations (**CNAs**), and rearrangements, as well as immunotherapy biomarkers microsatellite instability (**MSI**) and tumor mutational burden (**TMB**) via next generation sequencing (NGS). The tables below specify the type of genetic alterations and immunotherapy biomarkers tested per panel.

EXTENDED TUMOR PROFILE SNVs/INDELs **CNAs** Panel Rearrangements Pan-Cancer Plus ABL1, ABL2, AKT1, AKT2, ALK, ANKRD26, APC, AR, ARAF, ASXL1, ATM, ATRX, B2M, 1p/19q ALK. BRAF. CD74. FGFR1. codeletion, AKT1, BAP1, BARD1, BCL2, BCL6, BCOR, BCORL1, BCR, BMPR1A, BRAF, BRCA1, BRCA2, ALK, AR, ATM, BRAF, BRCA1, FGFR2, FGFR3, NTRK1, BRIP1, CALR, CBFB, CBL, CBLB, CBLC, CCND1, CCND2, CCND3, CCNE1, CD274, BRCA2, CCND1, CD274, CDK4, NTRK2, NTRK3, NUTM1, CD74, CDC25C, CDH1, CDK12, CDK4, CDK6, CDKN2A, CEBPA, CHEK2, CIC, CSF1R, CDKN2A, CHEK2, EGFR, ERBB2, PDGFRA. RET. ROS1. CSF3R, CTLA4, CTNNB1, CUX1, CXCR4, DCK, DDR2, DDX41, DEK, DHX15, DICER1, ERBB3, ESR1, FGFR1, FGFR2, TMPRSS2 DNMT3A, DUSP22, EGFR, EIF1AX, EPCAM, ERBB2, ERBB3, ERBB4, ERCC4, ERG, ESR1, FGFR3, JAK2, KIT, KRAS, MDM2, ETNK1, ETV1, ETV4, ETV6, EWSR1, EZH2, FANCA, FBXW7, FGF13, FGF19, FGF2, MET, MYC, MYCN, NCOA3, FGF3. FGFR1. FGFR2. FGFR3. FGFR4. FLT1. FLT3. FLT4. FOXA1. FOXL2. FOXO1. FRS2. NRAS. NRG1. PDGFRA. FUBP1, GATA1, GATA2, GATA3, GNA11, GNAQ, GNAS, H3F3A, HDAC2, HOXB13, PDGFRB, PIK3CA, PIK3CB, PTEN. RAF1. RB1. RET. SMAD4. HRAS IDH1 IDH2 IK7F1 II 3 INHA INSRR IRF4 JAK1 JAK2 JAK3 KDM6A KDR KEAP1, KIT, KMT2A, KMT2C, KMT2D, KRAS, LUC7L2, MALT1, MAP2K1, MAP2K2, MAP3K1, MDM2, MECOM, MET, MITF, MLH1, MLLT3, MPL, MRE11, MSH2, MSH6, MTOR, MUTYH, MYC, MYCN, MYD88, MYH11, MYOD1, NBN, NCOA3, NF1, NF2, NFE2L2, NOTCH1, NPM1, NRAS, NRG1, NTRK1, NUP214, NUTM1, PALB2, PARP1, PBX1, PDCD1, PDCD1LG2, PDGFRA, PDGFRB, PGR, PHF6, PIK3CA, PIK3CB, PIK3R1, PML, PMS2, POLD1, POLE, PPM1D, PPP2R1A, PTCH1, PTEN, PTPN11, RAD21, RAD51C, RAD51D, RAF1, RARA, RB1, RBBP6, RET, RNF43, RPS14, RUNX1, RUNX1T1, SETBP1, SF3B1, SH2B3, SLC29A1, SMAD4, SMARCA4, SMARCB1, SMC1A, SMC3, SMO, SOX10, SPOP, SRSF2, STAG2, STAT3, STAT5B, STK11, SUZ12, TCF3, TCL1A TERT, TET2, TMPRSS2, TP53, TSC1, TSC2, U2AF1, VEGFA, VHL, WT1, XPO1, ZRSR2 Pan-Cancer KT1, ALK, APC, AR, ARAF, ATM, ATRX, BARD1, BRAF, BRCA1, BRCA2, BRIP1, CDH1, 1p/19q codeletion, AR, ALK, BRAF, FGFR3, NTRK1, 30 genes CHEK2, CIC, CTNNB1, DDR2, DICER1, EGFR, ERBB2, ERBB3, ERBB4, ESR1, FBXW7, CDKN2A, EGFR, ERBB2, ESR1, NTRK2, NTRK3, RET, ROS1, FLT3, FOXA1, FOXL2, FUBP1, GATA3, GNA11, GNAQ, GNAS, H3F3A, IDH1, IDH2, FGFR1, FGFR2, FGFR3, KIT, TMPRSS2 JAK2, KEAP1, KIT, KRAS, MAP2K1, MAP3K1, MET, MLH1, MRE11A, MSH2, MSH6, KRAS, MET, MYC, MYCN, MTOR, NBN, NF1, NPM1, NRAS, NTRK1, PALB2, PDGFRA, PIK3CA, PIK3CB, PMS2, PIK3CA, PTEN, RB1, TP53 POLE. PTEN. RAD51C. RAD51D. RAF1. RET. RUNX1, SMAD4. SPOP. STK11. TERT. TP53

SNVs/INDELs	CNAs	Rearrangements			
AKT1, ATM, BARD1, BRAF, BRCA1, BRCA2, BRIP1, CHEK2, CTNNB1, DICER1, EGFR, ERBB2, ERBB3, ESR1, FBXW7, FOXA1, FOXL2, GATA3, KIT, KRAS, MAP3K1, MLH1, MRE11A, MSH2, MSH6 MTOR, NBN, NRAS, PALB2, PIK3CA, PIK3CB, PMS2, POLE, PTEN, RAD51C, RAD51D, RAF1, RET, RUNX1, SMAD4, TP53	EGFR, ERBB2, ESR1, FGFR1, FGFR2, FGFR3, KRAS, MET, PIK3CA, PTEN, TP53	NTRK1, NTRK2, NTRK3			
AKT1, APC, ATM, BRAF, BRCA1, BRCA2, CTNNB1, EGFR, ERBB2, FBXW7, GNAS, KRAS, MLH1, MSH2, MSH6, MTOR, NRAS, NTRK1, PALB2, PDGFRA, PIK3CA, PIK3CB, PMS2, POLE, PTEN, RAF1, SMAD4, TP53	EGFR, ERBB2, FGFR1, FGFR2, FGFR3, KRAS, MET, TP53	NTRK1, NTRK2, NTRK3			
ATRX, BRAF, CIC, CTNNB1, EGFR, FUBP1, H3F3A, IDH1, IDH2, NF1, POLE, TERT, TP53	1p/19q codeletion, CDKN2A, EGFR, MET, MYC, MYCN, PTEN	BRAF, FGFR3, NTRK1, NTRK2, NTRK3			
AKT1, ALK, APC, ARAF, ATM, BRAF, BRCA2, CTNNB1, DDR2, EGFR, ERBB2, ERBB3, ERBB4, FBXW7, JAK2, KEAP1, KRAS, MAP2K1, MET, NRAS, PDGFRA, PIK3CA, POLE, PTEN, RAF1, SMAD4, STK11, TP53	EGFR, ERBB2, FGFR1, FGFR2, FGFR3, MET, PIK3CA, PTEN, TP53	ALK, FGFR3, NTRK1, NTRK2, NTRK3, RET, ROS1			
	AKT1, ATM, BARD1, BRAF, BRCA1, BRCA2, BRIP1, CHEK2, CTNNB1, DICER1, EGFR, ERBB2, ERBB3, ESR1, FBXW7, FOXA1, FOXL2, GATA3, KIT, KRAS, MAP3K1, MLH1, MRE11A, MSH2, MSH6 MTOR, NBN, NRAS, PALB2, PIK3CA, PIK3CB, PMS2, POLE, PTEN, RAD51C, RAD51D, RAF1, RET, RUNX1, SMAD4, TP53 AKT1, APC, ATM, BRAF, BRCA1, BRCA2, CTNNB1, EGFR, ERBB2, FBXW7, GNAS, KRAS, MLH1, MSH2, MSH6, MTOR, NRAS, NTRK1, PALB2, PDGFRA, PIK3CA, PIK3CB, PMS2, POLE, PTEN, RAF1, SMAD4, TP53 ATRX, BRAF, CIC, CTNNB1, EGFR, FUBP1, H3F3A, IDH1, IDH2, NF1, POLE, TERT, TP53 AKT1, ALK, APC, ARAF, ATM, BRAF, BRCA2, CTNNB1, DDR2, EGFR, ERBB2, ERBB3, ERBB4, FBXW7, JAK2, KEAP1, KRAS, MAP2K1, MET, NRAS, PDGFRA,	AKT1, ATM, BARD1, BRAF, BRCA1, BRCA2, BRIP1, CHEK2, CTNNB1, DICER1, EGFR, ERBB2, ESR1, FBXW7, FOXA1, FOXL2, GATA3, KIT, KRAS, MAP3K1, MLH1, MRE11A, MSH2, MSH6 MTOR, NBN, NRAS, PALB2, PIK3CA, PIK3CB, PMS2, POLE, PTEN, RAD51C, RAD51D, RAF1, RET, RUNX1, SMAD4, TP53 AKT1, APC, ATM, BRAF, BRCA1, BRCA2, CTNNB1, EGFR, ERBB2, FBXW7, GNAS, KRAS, MLH1, MSH2, MSH6, MTOR, NRAS, NTRK1, PALB2, PDGFRA, PIK3CA, PIK3CB, PMS2, POLE, PTEN, RAF1, SMAD4, TP53 ATRX, BRAF, CIC, CTNNB1, EGFR, FUBP1, H3F3A, IDH1, IDH2, NF1, POLE, TERT, TP53 AKT1, ALK, APC, ARAF, ATM, BRAF, BRCA2, CTNNB1, DDR2, EGFR, ERBB2, EGFR, ERBB2, FGFR1, FGFR2, ERBB3, ERBB4, FBXW7, JAK2, KEAP1, KRAS, MAP2K1, MET, NRAS, PDGFRA, FGFR3, MET, PIK3CA, PTEN, FGFR2, FGFR3, MET, PIK3CA, PTEN, FGFR3,			

AKT1, BRAF, CTNBB1, ERBB2, GNA11, GNAQ, KIT, KRAS, MAP2K1, NF1,

AKT1, APC, AR, ATM, BARD1, BRAF, BRCA1, BRCA2, CTNNB1, CHEK2,

FOXA1, MLH1, MSH2, MSH6, NRAS, PALB2, PIK3CA, PIK3CB, PMS2, POLE,

GENE-FOCUSED						
BRAF	EGFR	IDH1 & IDH2	KRAS & NRAS	PIK3CA & AKT		

ERBB2, KIT, KRAS, MYC, TP53

AR, ERBB2, FGFR1, FGFR2,

FGFR3, MYC, MYCN, PIK3CA,

PTEN, RB1, TP53

ALK, BRAF, NTRK1, NTRK2,

NTRK3,

NTRK3, RET, ROS1

NTRK1, NTRK2,

TMPRSS2

TECHNICAL SPECIFICATIONS PER PANEL

NRAS, PIK3CA, POLE, PTEN, TP53

PTEN, RAD51C, RAD51D, SPOP, TP53

CANCER-SPECIFIC TUMOR PROFILE

		EXTENDED		CANCER-SPECIFIC	GENE-EOCUSED	
		Pan-Cancer Plus	Pan-Cancer	CANCEN SI ECII IC	GLIVE I GCGSED	
Technical features and markers analyzed	TMB	•				
	MSI	•	•	o		
	SNVs/INDELs	•	•	•	•	
	CNAs	•	•	•		
	Rearrangements	•	•	•		
	Full exonic coverage	•	*	*		
	Reported variants	Tier I/II	Tier I/II	Tier I/II	Tier I/II	
	Variants of unknown clinical significance (VUS) reported	•	•	•	•	
	Target selected intronic regions of clinical importance	•	•	•	•	
	Technology	Target capture enrichment technology via NGS				
er st ails	Turnaround time (TAT)	10-15 days				
Other test details	Sample type	FFPE sample				

Included

Melanoma

22 genes

Prostate

Optionally included

Selected genes

^{*}Exceptions on regions containing repeats, sequences of high homology (pseudogenes and segmental duplications) or high GC-content