FDA/EMA APPROVED TARGETED THERAPIES

	BREAST	COLORECTAL	GASTRIC	MELANOMA	NSCLC	PANCREATIC	PROSTATE
BRAF		Encorafenib		Binimetinib, Cobimetinib, Dabrafenib, Encorafenib, Trametinib, Vemurafenib, Atezolizumab	Dabrafenib, Trametinib		
BRCA1/2	Olaparib, Talazoparib					Olaparib	Olaparib, Rucaparib
EGFR		Cetuximab			Ramucirumab, Atezolizumab, Afatinib, Erlotinib, Dacomitinib, Gefitinib, Osimertinib		
PDGFRA			Avapritinib				
RET					Pralsetinib, Selpercatinib		
ROS1					Crizotinib, Entrectinib		
MSI	Pembrolizumab (all solid tumors)	Ipilimumab, Nivolumab, Pembrolizumab	Pembrolizumab *(all solid tumors)*				

The table above, produced in August 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 therapies, please visit the relevant websites.

CASE STUDY

A 64-year-old female diagnosed with stage III NSCLC

A tissue biopsy molecular profiling was initially performed on the patient's tumor biopsy sample, identifying an in-frame deletion at exon 19 of the EGFR gene. The patient received two EGFR targeted therapies, erlotinib and afatinib (1st and 2nd generation tyrosine kinase inhibitors respectively) approved for the mutation identified, but disease continued to progress.

NeoThetis NSCLC liquid biopsy was then performed for therapy re-evaluation, which found:

- The pre-existing EGFR genetic mutation
- An additional acquired T790M EGFR mutation associated with resistance to 1st and 2nd generation tyrosine kinase inhibitors

NeoThetis results revealed:

- 3 FDA/EMA approved tyrosine kinase inhibitor drugs that the patient will not benefit from
- Osimertinib, an FDA/EMA approved 3rd generation tyrosine kinase inhibitor which the patient is eligible for
- 42 available clinical trials associated with EGFR genetic alterations

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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MEDICOVER GENETICS

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MKT-ONC-NSNT-PANS-DR-EN-V03

NeoThetis®
therapy selection

Genes, genetic alterations and genomic biomarkers

MEDICOVER GENETICS

WHAT IS NeoThetis?

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 cell-free DNA, known as circulating tumor DNA (**ctDNA**), which is released from primary and metastatic tumors in the bloodstream of cancer patients.

Performed via a simple **blood draw**, NeoThetis is **safe** for the patient and overcomes some of the challenges of tumor biopsy including tumor **inaccessibility**, **hospitalization** after surgery, and failure to capture **tumor heterogeneity**.

CLINICAL UTILITY

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

LIST OF GENES AND GENETIC ALTERATIONS TESTED

NeoThetis targets **clinically important** coding regions and selected non-coding regions in genes of interest. It identifies genetic alterations such as single nucleotide variants (**SNVs**), insertions and deletions (**INDELs**), copy number amplifications (**CNAs**), and **rearrangements**, as well as the immunotherapy biomarkers microsatellite instability (**MSI**) and blood tumor mutational burden (**bTMB**). The tables below specify the type of genetic alterations and immunotherapy biomarkers tested.

EXTENDED

Test	SNVs/INDELs	CNAs	Rearrangements
NeoThetis Pan-Cancer Plus *222 genes*	ABL1, ABL2, AKT1, AKT2, ALK, ANKRD26, APC, AR, ARAF, ASXL1, ATM, ATRX, B2M, BAP1, BARD1, BCL2, BCL6, BCOR, BCORL1, BCR, BMPR1A, BRAF, BRCA1, BRCA2, BRIP1, CALR, CBFB, CBL, CBLB, CBLC, CCND1, CCND2, CCND3, CCNE1, CD274, CD74, CDC25C, CDH1, CDK12, CDK4, CDK6, CDKN2A, CEBPA, CHEK2, CIC, CSF1R, CSF3R, CTLA4, CTNNB1, CUX1, CXCR4, DCK, DDR2, DDX41, DEK, DHX15, DICER1, DNMT3A, DUSP22, EGFR, EIF1AX, EPCAM, ERBB2, ERBB3, ERBB4, ERCC4, ERG, ESR1, ETNK1, ETV1, ETV4, ETV6, EWSR1, EZH2, FANCA, FBXW7, FGF13, FGF19, FGF2, FGF3, FGFR1, FGFR2, FGFR3, FGFR4, FLT1, FLT3, FLT4, FOXA1, FOXL2, FOXO1, FRS2, FUBP1, GATA1, GATA2, GATA3, GNA11, GNAQ, GNAS, H3F3A, HDAC2, HOXB13, HRAS, IDH1, IDH2, IKZF1, IL3, 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	AKT1, AKT2, ALK, AR, BRAF, CCND1, CCND2, CCND3, CCNE1, CD274, CDK4, CDK6, EGFR, ERBB2, ERBB3, ESR1, FGF19, FGF2, FGF3, FGFR1, FGFR2, FGFR3, FGFR4, JAK2, KIT, KRAS, MDM2, MET, MYC, MYCN, NCOA3, NRAS, NRG1, PDGFRA, PDGFRB, PIK3CA, PIK3CB, RAF1, RET, TERT	ALK, BRAF, CD74, FGFR1, FGFR2, FGFR3, NTRK1, NTRK2, NTRK3, NUTM1, PDGFRA, RET, ROS1, TMPRSS2
NeoThetis Pan-Cancer *80 genes*	AKT1, ALK, APC, AR, ARAF, ATM, ATRX, BARD1, BRAF, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, CIC, CTNNB1, DDR2, DICER1, EGFR, ERBB2, ERBB3, ERBB4, ESR1, FBXW7, FLT3, FOXA1, FOXL2, FUBP1, GATA3, GNA11, GNAQ, GNAS, H3F3A, IDH1, IDH2, JAK2, KEAP1, KIT, KRAS, MAP2K1, MAP3K1, MET, MLH1, MRE11A, MSH2, MSH6, MTOR, NBN, NF1, NPM1, NRAS, NTRK1, PALB2, PDGFRA, PIK3CA, PIK3CB, PMS2, POLE, PTEN, RAD51C, RAD51D, RAF1, RB1, RET, RUNX1, SMAD4, SPOP, STK11, TERT, TP53	AR, CDKN2A, EGFR, ERBB2, ESR1, FGFR1, FGFR2, FGFR3, KIT, KRAS, MET, MYC, MYCN, PIK3CA	ALK, BRAF, FGFR3, NTRK1, NTRK2, NTRK3, RET, ROS1, TMPRSS2

CANCER-SPECIFIC

Test	SNVs/INDELs	CNAs	Rearrangements
NeoThetis Breast / Gynecological *48 genes*	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	NTRK1, NTRK2, NTRK3
NeoThetis Colorectal *34 genes*	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	NTRK1, NTRK2, NTRK3
NeoThetis Gastric *23 genes*	APC, CDH1, ERBB2, KIT, KRAS, MLH1, MSH2, MSH6, NF1, NTRK1, PDGFRA, PIK3CA, PMS2, SMAD4, STK11, TP53	EGFR, ERBB2, FGFR1, FGFR2, FGFR3, MET, PIK3CA	FGFR3, NTRK1, NTRK2, NTRK3
NeoThetis Melanoma *28 genes*	AKT1, BRAF, CTNNB1, ERBB2, FGFR1, FGFR2, FGFR3, GNA11, GNAQ, KIT, KRAS, MAP2K1, NF1, NRAS, PDGFRA, PIK3CA, POLE, PTEN, STK11, TP53	FGFR1, FGFR2, FGFR3, KIT, KRAS, MET, MYC, PDGFRA	ALK, BRAF, NTRK1, NTRK2, NTRK3, RET, ROS1
NeoThetis NSCLC *36 genes*	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	ALK, FGFR3, NTRK1, NTRK2, NTRK3, RET, ROS1
NeoThetis Pancreatic *26 genes*	ATM, ALK, BRAF, BRCA1, BRCA2, CDKN2A, CHEK2, ERBB2, FBXW7, KRAS, MLH1, MSH2, MSH6, NTRK1, PALB2, PMS2, ROS1, SMAD4, STK11, TP53	FGFR1, FGFR2, FGFR3, MYC	ALK, NTRK1, NTRK2, NTRK3, ROS1
NeoThetis Prostate *35 genes*	AKT1, APC, AR, ATM, BARD1, BRAF, BRCA1, BRCA2, CTNNB1, CHEK2, FOXA1, MLH1, MSH2, MSH6, NRAS, PALB2, PIK3CA, PIK3CB, PMS2, POLE, PTEN, RAD51C, RAD51D, SPOP, TP53	AR, ERBB2, FGFR1, FGFR2, FGFR3, MYC, MYCN, PIK3CA	NTRK1, NTRK2, NTRK3, TMPRSS2

TECHNICAL SPECIFICATIONS PER TEST

		EXTENDED		CANCER-SPECIFIC
		Pan-Cancer Plus	Pan-Cancer	
Technical features and markers analyzed	bTMB	●		
	MSI	●	●	●
	SNVs/INDELs	●	●	●
	CNAs	●	●	●
	Rearrangements	●	●	●
	Full exonic coverage*	●	○	○
	Reported variants	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		
Other test details	Turnaround time (TAT)	6-9 days		
	Sample type	Blood sample		

● Included ○ Applicable for selected genes

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