

Broad clinical utility built on extensive validation¹⁻⁴

Clinical summary

Our tissue-based comprehensive genomic profiling service for all solid tumours^{1,2,4}

Based on our analytically and clinically validated, FDA-approved comprehensive platform^{1,3}

High concordance with FDA-approved companion diagnostics (CDx)⁴

GENOMIC FINDINGS	POSITIVE PERCENT AGREEMENT (PPA)*	NEGATIVE PERCENT AGREEMENT (NPA)*	COMPARATOR TEST METHOD
<i>EGFR</i> Exon 19 Deletions and L858R Alterations	98.1% (106/108)	99.4% (153/154)	cobas® <i>EGFR</i> Mutation Test v2
<i>EGFR</i> T790M Alterations	98.9% (87/88)	86.1% (93/108)	cobas® <i>EGFR</i> Mutation Test v1 cobas® <i>EGFR</i> Mutation Test v2
<i>ALK</i> Rearrangements	92.9% (78/84)	100% (75/75)	Ventana <i>ALK</i> (D5F3) CDx Assay Vysis <i>ALK</i> Break-Apart FISH Probe Kit
<i>KRAS</i> Alterations	100% (173/173)	100% (154/154)	therascreen® <i>KRAS</i> RGQ PCR Kit
<i>ERBB2</i> (HER2) Amplifications	89.4% (101/113)	98.4% (180/183)	Dako <i>HER2</i> FISH PharmDx® Kit
<i>BRAF</i> V600	99.4% (166/167)	89.6% [†] (121/135)	cobas® <i>BRAF</i> V600 Mutation Test
<i>BRAF</i> V600E	99.3% (149/150)	99.2% (121/122)	
<i>BRAF</i> V600 dinucleotide [‡]	96.3% (26/27)	100% (24/24)	THxID® <i>BRAF</i> kit

- FoundationOne®CDx is concordant with FDA-approved FoundationFocus™ CDx for BRCA 1/2⁴

Cobas is a trademark of Roche Diagnostics Operations, Inc. Therascreen is a trademark of Qiagen. PharmDx is a registered trademark of Dako Denmark A/S. THxID is a registered trademark of bioMérieux. FoundationFocus is a trademark of Foundation Medicine, Inc.

*The reference standard used to calculate positive percent agreement (PPA) and negative percent agreement (NPA) is defined as the consensus calls between the two comparator methods or comparator runs. Agreement calculations solely using consensus calls may overestimate the performance of FoundationOne CDx.

[†]Sensitivity of dinucleotide detection of *BRAF* V600K and V600E was found to be significantly reduced in the cobas® test, in particular for samples in which FoundationOne CDx detected the dinucleotides to be of lower than 40% MAF, leading to low NPA values.

[‡]A study using the THxID™ *BRAF* kit (bioMérieux) was conducted with samples with *BRAF* V600 dinucleotide mutation detected by FoundationOne CDx and *BRAF* V600 negative samples to provide a better evaluation of V600 dinucleotide concordance.

High concordance with externally validated NGS method*⁴

	POSITIVE PERCENT AGREEMENT (PPA)	NEGATIVE PERCENT AGREEMENT (NPA)
All short variants	94.6%	99.9%
Substitutions	96.6%	99.9%
Insertions & deletions	83.4%	99.9%

High concordance with FoundationOne®^{†4}

	POSITIVE PERCENT AGREEMENT (PPA)	NEGATIVE PERCENT AGREEMENT (NPA)
All variants	98.6%	99.9%
All short variants	99.1%	99.9%
Substitutions	99.4%	99.9%
Insertions & deletions	97.0%	99.9%
All copy number variants	94.3%	99.9%
Amplifications	94.0%	99.9%
Losses	94.8%	99.8%
Rearrangements	100.0%	99.9%

- FoundationOne is our pioneering lab-developed test used in over 180,000 patients^{5,6}

*The detection of alterations by FoundationOne CDx was compared to results of an externally validated next-generation sequencing assay (evNGS). Overall there were 157 overlapping genes between the two assays. The comparison between short alterations, including base substitutions and short indels, detected by FoundationOne CDx and the orthogonal method included 188 samples from 46 different tumours. Differences in variants of unknown significance (VUS) alteration calls between the platform were noted, and are expected based on differences in filtering employed by FoundationOne CDx and evNGS. Negative predictive value and positive predictive value were also calculated and were found to be different than percent agreement because the two platforms filter VUS differently. Discordant alterations not related to VUS filtering were primarily caused by deletions with low allelic fraction in homopolymer regions. The FoundationOne CDx variant calling pipeline imposes a filter based on MAF of ≥ 0.10 for indels in homopolymer regions to reduce the likelihood of calling false positives resulting from artifacts introduced by the technology. As such, the difference observed was due to varying filter thresholds between the two platforms.

[†]To support the use of retrospective data generated using FoundationOne, a concordance study was conducted with FoundationOne CDx. This study evaluated a test set of 165 specimens. PPA and NPA between FoundationOne CDx and FoundationOne, using the FoundationOne assay as the reference method, was calculated for all alterations, as well as for alterations binned by type: short variants, copy number alterations (CNAs) and rearrangements. A total of 2325 variants, including 2026 short variants, 266 CNAs and 33 rearrangements were included in the study. NGS, next-generation sequencing.

Broad clinical utility across common cancers

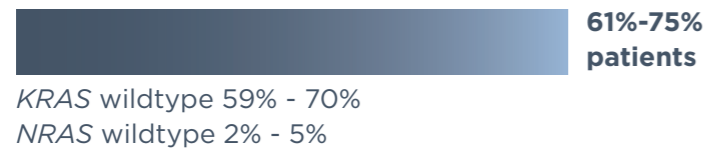
% patients with genomic alterations that the FoundationOne CDx platform is clinically validated to detect **Benefits vs other tests**

Melanoma⁷⁻¹²



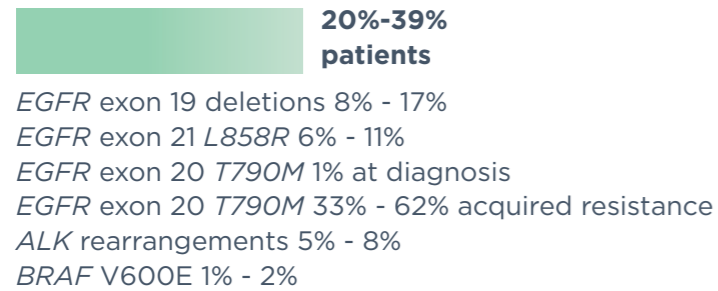
Identifies 37% more patients with clinically relevant *BRAF* alterations compared with PCR, IHC and other NGS testing methods⁴⁰

Colorectal cancer¹³⁻²⁰



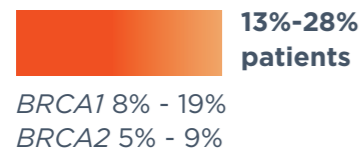
Identifies up to 12% more patients with resistance-associated KRAS alterations compared with traditional PCR-based methods⁴¹

NSCLC²¹⁻³¹



Identifies up to 35% and 17% more patients with *ALK* fusions and *EGFR* alterations, respectively, compared with traditional FISH and PCR-based methods^{42,43}

Ovarian³²⁻³⁵



Identifies patients with *BRCA1/2* alterations who may benefit from PARP inhibitors⁴⁴

Breast³⁶⁻³⁹



Identifies patients with *ERBB2* alterations who may benefit from HER2 therapy⁴
Detects drug resistance mechanisms, including various *ESR1* and *RB1* alterations⁴ that may inform patient management regarding hormone therapy and CDK4/6 inhibitors^{44,45}

* FoundationOne CDx does not distinguish between germline and somatic alterations. FISH, fluorescence in situ hybridisation. IHC, immunohistochemistry. NGS, next-generation sequencing. NSCLC, non-small cell lung cancer. PCR, polymerase chain reaction.

Comprehensive analysis of the tumour genome in a single test⁴

Genes with full coding exonic regions included in FoundationOne CDx for the detection of substitutions, insertion-deletions (indels), and copy-number alterations (CNAs).

Assesses 324 cancer-related genes⁴

Genes with full coding exonic regions included in FoundationOne CDx:

For detection of substitutions, insertion-deletions and copy-number alterations

ABL1	ACVR1B	AKT1	AKT2	AKT3	ALK	ALOX12B	AMER1 (FAM123B)	APC
AR	ARAF	ARFRP1	ARID1A	ASXL1	ATM	ATR	ATRX	AURKA
AURKB	AXIN1	AXL	BAP1	BARD1	BCL2	BCL2L1	BCL2L2	BCL6
BCOR	BCORL1	BRAF	BRCA1	BRCA2	BRD4	BRIP1	BTG1	BTG2
BTK	CT1orf30 (EMSY)	CALR	CARD11	CASP8	CBFB	CBL	CCND1	CCND2
CCND3	CCNE1	CD22	CD274 (PD-L1)	CD70	CD79A	CD79B	CDC73	CDH1
CDK12	CDK4	CDK6	CDK8	CDKN1A	CDKN1B	CDKN2A	CDKN2B	CDKN2C
CEBPA	CHEK1	CHEK2	CIC	CREBBP	CRKL	CSF1R	CSF3R	CTCF
CTNNA1	CTNNB1	CUL3	CUL4A	CXCR4	CYP17A1	DAXX	DDR1	DDR2
DIS3	DNMT3A	DOT1L	EED	EGFR	EP300	EPHA3	EPHB1	EPHB4
ERBB2	ERBB3	ERBB4	ERCC4	ERG	ERRF1	ESR1	EZH2	FAM46C
FANCA	FANCC	FANCG	FANCL	FAS	FBXW7	FGF10	FGF12	FGF14
FGF19	FGF23	FGF3	FGF4	FGF6	FGFR1	FGFR2	FGFR3	FGFR4
FH	FLCN	FLT1	FLT3	FOXL2	FUBP1	GABRA6	GATA3	GATA4
GATA6	GID4 (C17orf39)	GNAI1	GNAI3	GNAQ	GNAS	GRM3	GSK3B	H3F3A
HDAC1	HGF	HNF1A	HRAS	HSD3B1	ID3	IDH1	IDH2	IGF1R
IKBKE	IKZF1	INPP4B	IRF2	IRF4	IRS2	JAK1	JAK2	JAK3
JUN	KDMSA	KDMS5C	KDM6A	KDR	KEAP1	KEL	KIT	KLHL6
KMT2A (MLL)	KMT2D (MLL2)	KRAS	LTK	LYN	MAF	MAP2K1 (MEK1)	MAP2K2 (MEK2)	MAP2K4
MAP3K1	MAP3K13	MAPK1	MCL1	MDM2	MDM4	MED12	MEF2B	MEN1
MERTK	MET	MITF	MKNK1	MLH1	MPL	MRE11A	MSH2	MSH3
MSH6	MST1R	MTAP	MTOR	MUTYH	MYC	MYCL (MYCL1)	MYCN	MYD88
NBN	NF1	NF2	NFE2L2	NFKB1A	NKX2-1	NOTCH1	NOTCH2	NOTCH3
NPM1	NRAS	NT5C2	NTRK1	NTRK2	NTRK3	P2RY8	PALB2	PARK2
PARP1	PARP2	PARP3	PAX5	PBRM1	PDCC1 (PD-1)	PDCC1LG2 (PD-L2)	PDGFRA	PDGFRB
PDK1	PIK3C2B	PIK3C2G	PIK3CA	PIK3CB	PIK3R1	PIM1	PMS2	POLD1
POLE	PPARG	PPP2R1A	PPP2R2A	PRDM1	PRKARIA	PRKCI	PTCH1	PTEN
PTPN11	PTPRO	QKI	RAC1	RAD21	RAD51	RAD51B	RAD51C	RAD51D
RAD52	RAD54L	RAF1	RARA	RB1	RBM10	REL	RET	RICTOR
RNF43	ROSI	RPTOR	SDHA	SDHB	SDHC	SDHD	SETD2	SF3B1
SGK1	SMAD2	SMAD4	SMARCA4	SMARCB1	SMO	SNCAIP	SOC3	SOX2
SOX9	SPEN	SPOP	SRC	STAT3	STAT3	STAT3	SUFU	SYK
TBX3	TEK	TET2	TGFB2	TIPARP	TNFAIP3	TNFRSF14	TP53	TSC1
TSC2	TYRO3	U2AF1	VEGFA	VHL	WHSC1 (MMSET)	WHSC1L1	WT1	XPO1
XRCC2	ZNF217	ZNF703						

Select rearrangements:

Genes with select intronic regions for the detection of gene rearrangements, one gene with a promoter region and one non-coding RNA gene.

ALK	BCL2	BCR	BRAF	BRCA1	BRCA2	CD74	EGFR	ETV4
ETV5	ETV6	EWSR1	EZR	FGFR1	FGFR2	FGFR3	KIT	KM2A (MLL)
MSH2	MYB	MYC	NOTCH2	NTRK1	NTRK2	NUTM1	PDGFRA	RAF1
RARA	RET	ROSI	RSPO2	SDC4	SLC34A2	TERC*	TERT (promoter only)*	
TMPRSS2								

In the same test reports:⁴

- Tumour mutational burden
- Microsatellite instability

*TERC is a non-coding RNA gene. *TERT is a gene with a promoter region.

Broad clinical utility built on extensive validation¹⁻⁴



Extensive validation¹⁻³

- » Based on our analytically and clinically validated, FDA-approved comprehensive platform^{1,3}
- » High concordance with FDA-approved companion diagnostics and with NGS methods⁴



Broad clinical utility

- » Clinically relevant results across common cancers: colorectal cancer, melanoma, NSCLC, ovarian and breast⁷⁻³⁹

324
GENES
TMB+MSI

Goes beyond common genomic alterations⁴

- » Assesses 324 cancer-relevant genes⁴
- » Reports TMB and MSI⁴

Intended use statement

FoundationOne®CDx is a next generation sequencing based *in vitro* diagnostic device for detection of substitutions, insertion and deletion alterations (indels), and copy number alterations (CNAs) in 324 genes and select gene rearrangements, as well as genomic signatures including tumour mutational burden (TMB) and microsatellite instability (MSI) using DNA isolated from formalin-fixed paraffin embedded (FFPE) tumor tissue specimens. The test is intended as a companion diagnostic to identify patients who may benefit from treatment with therapies in accordance with approved therapeutic product labeling. Additionally, FoundationOne CDx is intended to provide tumour mutation profiling to be used by qualified health care professionals in accordance with professional guidelines in oncology for patients with solid malignant neoplasms.

For more information, please contact your Roche representative

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