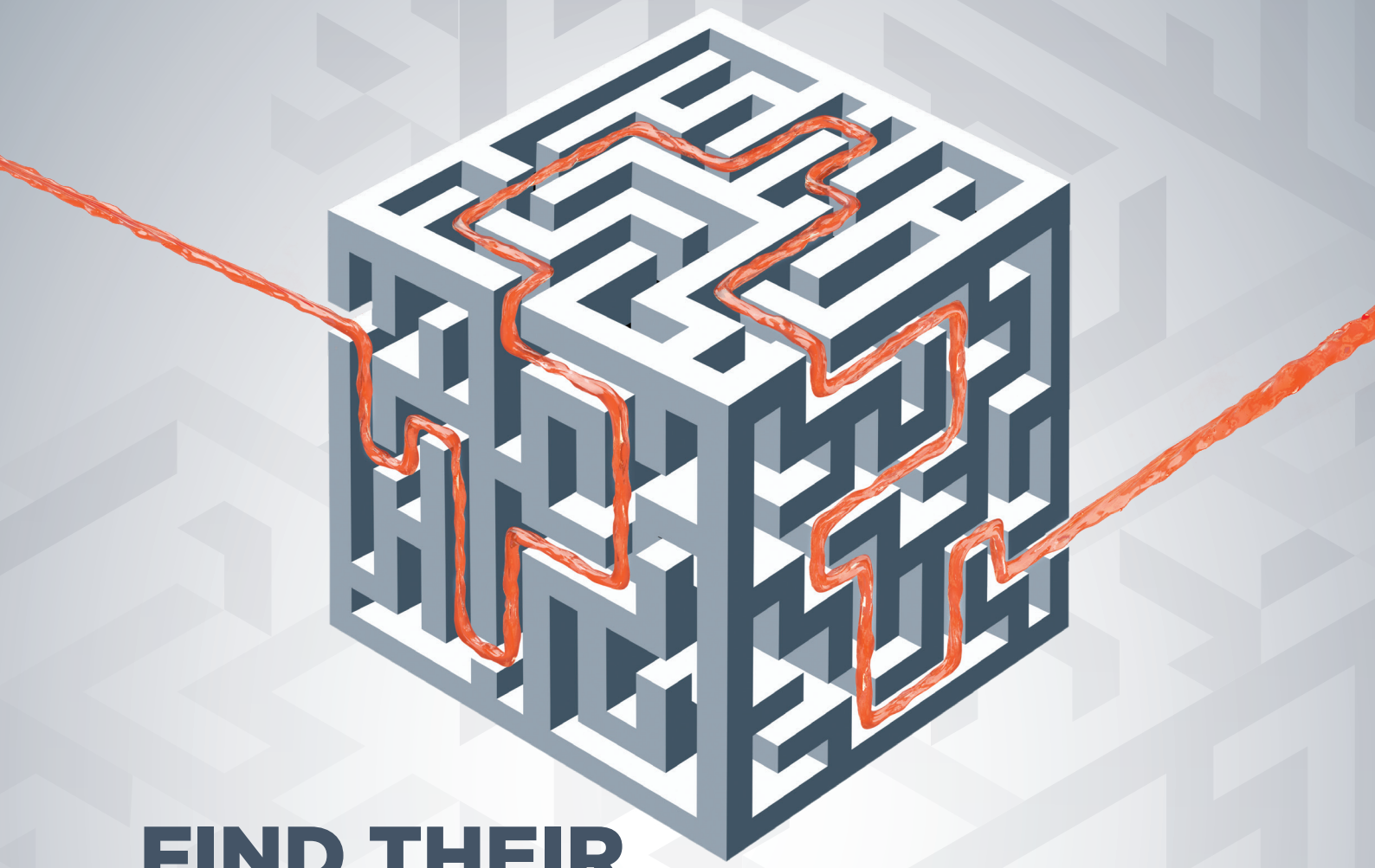
FOUNDATIONONE®LIQUID CDx



FIND THEIR PERSONALIZED PATH WITH LIQUID BIOPSY

See a way forward for all patients with solid tumours – using FoundationOne®Liquid CDx, a **liquid biopsy** comprehensive genomic profiling service, as a **minimally-invasive** option, **alternative or complementary** to FoundationOne®CDx, at **optimal times beneficial to their treatment journey**[1–3]

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See more, do more

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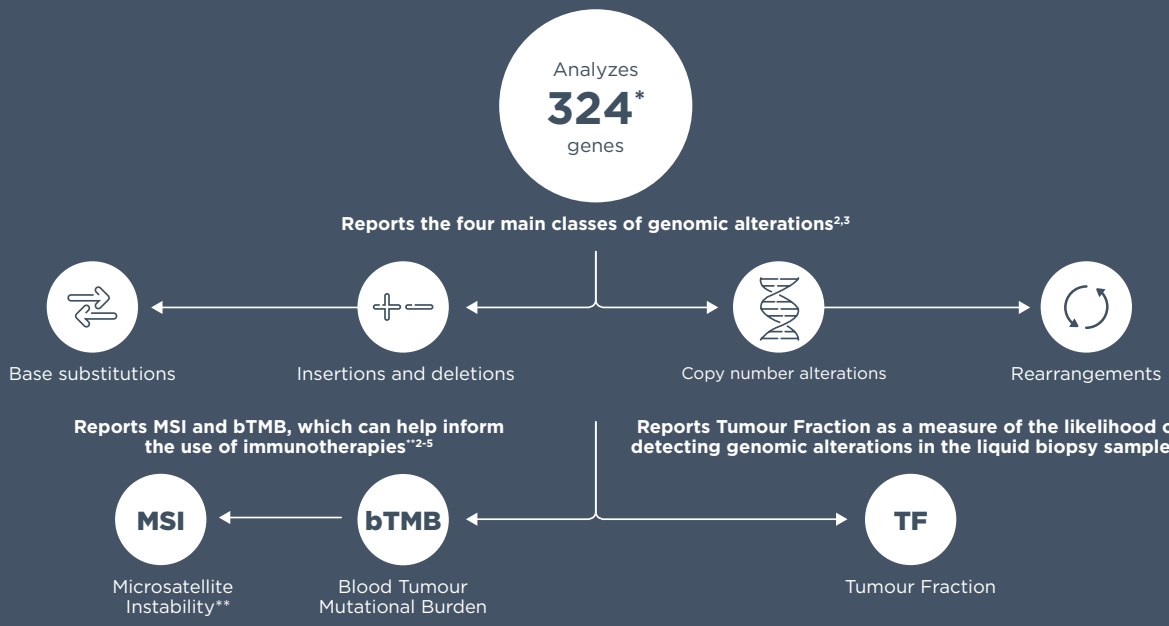
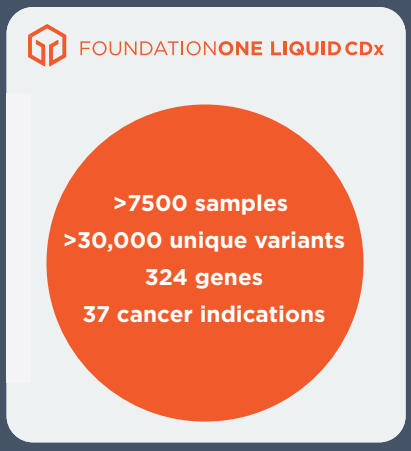
FoundationOne Liquid CDx provides insights that inform research or treatment decisions for individual patients across all solid tumours[2,3]



*309 genes with complete exon coverage, 15 genes with select intronic or non-coding regions only.
**FoundationOne Liquid CDx reports MSI-H status.

FoundationOne Liquid CDx has been validated with >7,500 samples covering >30,000 unique variants across 324 genes and 37 cancer indications[†3]

- 150 X more samples than the typical number of patient samples for laboratory test validation[‡6] and similar to the number of samples used for validation of FoundationOne CDx[7]
- 12 X more variants than the number of variants used for validation of our previous liquid-based test FoundationOne Liquid[8]



†Validation against an externally validated cfDNA assay.
‡According to New York State guidance.

FoundationOne Liquid CDx reports Tumour Fraction, the percentage of tumour-derived DNA in the circulating cell-free DNA, providing you with a measure of the likelihood of detecting genomic alterations in the liquid biopsy sample[2,3]

- FoundationOne Liquid CDx reports Tumour Fraction estimates above ~5%[2,3,9]
- The Tumour Fraction measurement is designed as a decision insight that can guide reflex testing decisions
- A higher Tumour Fraction indicates a higher concordance to tissue-based testing[2,9]

bTMB, blood Tumour Mutational Burden; CDx, companion diagnostic; cfDNA, circulating cell-free DNA; MSI, Microsatellite Instability; TF, Tumour Fraction.

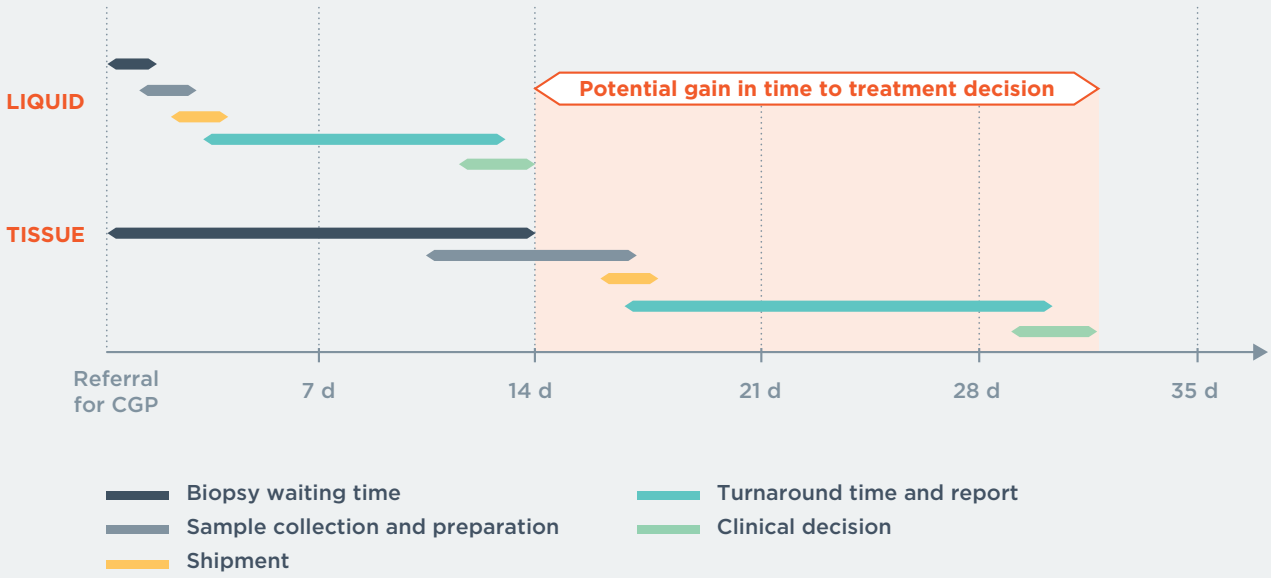
Quick and convenient single blood draw helps avoid invasive biopsies and enables faster treatment decisions[2,3,10–15]

Two tubes of whole blood (8.5 mL each)

<2 weeks

Turnaround time from receipt of sample at our laboratory to report

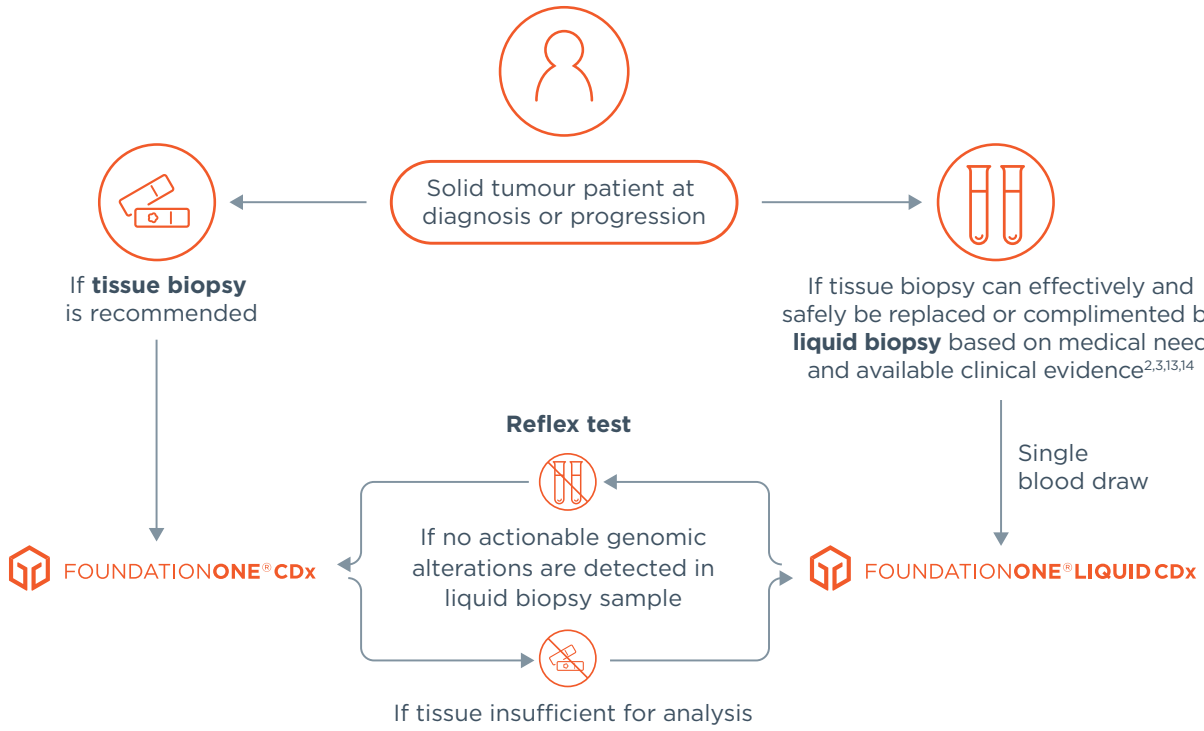
Typical timelines associated with liquid– versus tissue-based CGP



- Liquid biopsy genomic profiling may help reduce the distress which patients may experience from a longer waiting time for scheduling a biopsy and receiving the results of tissue-based testing[11,12]
- FoundationOne Liquid CDx may also help reduce requirements for healthcare infrastructure and resources compared with tissue-based testing[15]
- Phlebotomy services for FoundationOne Liquid CDx are available through Bayshore Infusion Clinics. Please email canada.fmi@roche.com for more information.

CDx, companion diagnostic; CGP, comprehensive genomic profiling; d, days.

Suitable for all solid tumours based on your patient's profile and the available clinical evidence[2,3,13,14]



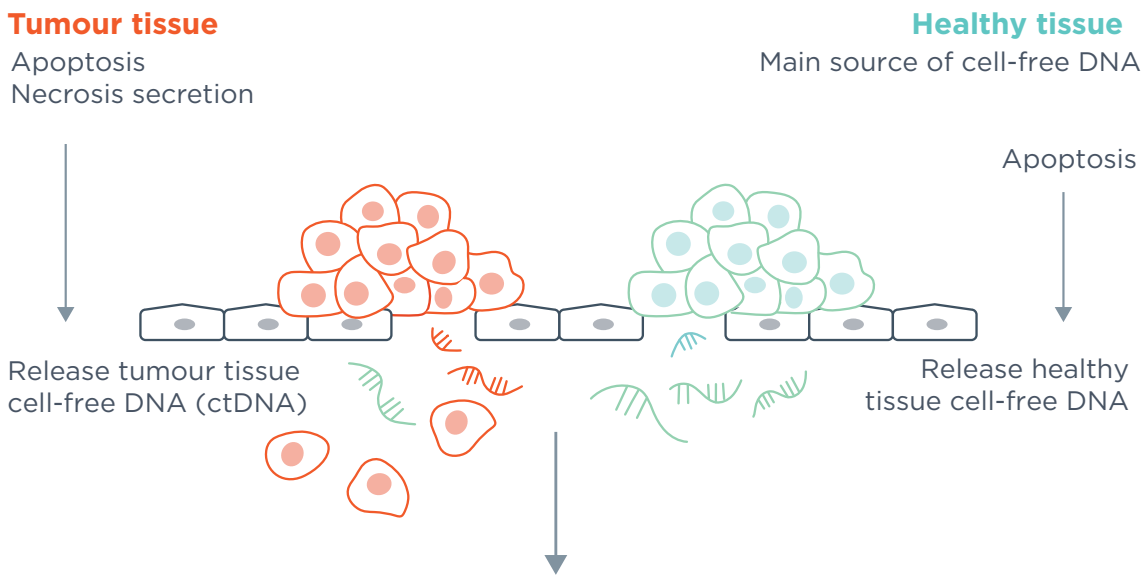
Part of our proven portfolio of high-quality, comprehensive genomic profiling services for all solid tumours, supporting current and future personalized clinical and research decisions at optimal times beneficial to your patients' treatment journeys [1-3,16,17]

Primary diagnosis and therapy initiation	Monitoring	Progression and further lines of therapy selection based on new/evolving resistance mutations
TISSUE (if available) / LIQUID: Use either FoundationOne CDx or FoundationOne Liquid CDx based on medical need and available evidence; reflex to the other service if sample is inadequate or no actionable genomic alterations detected	LIQUID	LIQUID / TISSUE (if available): Use FoundationOne Liquid CDx and reflex to FoundationOne CDx if no actionable genomic alterations detected in the blood sample
TISSUE + LIQUID: Complement FoundationOne CDx with FoundationOne Liquid CDx to capture the full disease heterogeneity	FoundationOne Liquid CDx may also be used to track responses to therapy and for early diagnosis of relapse	LIQUID + TISSUE: Complement FoundationOne Liquid CDx with FoundationOne CDx to capture the full disease heterogeneity
Tissue-based testing is often recommended at diagnosis due to availability of tissue		Liquid-based testing is often suitable at progression due to frequent challenges with tissue biopsy and the increase in ctDNA as the disease progresses

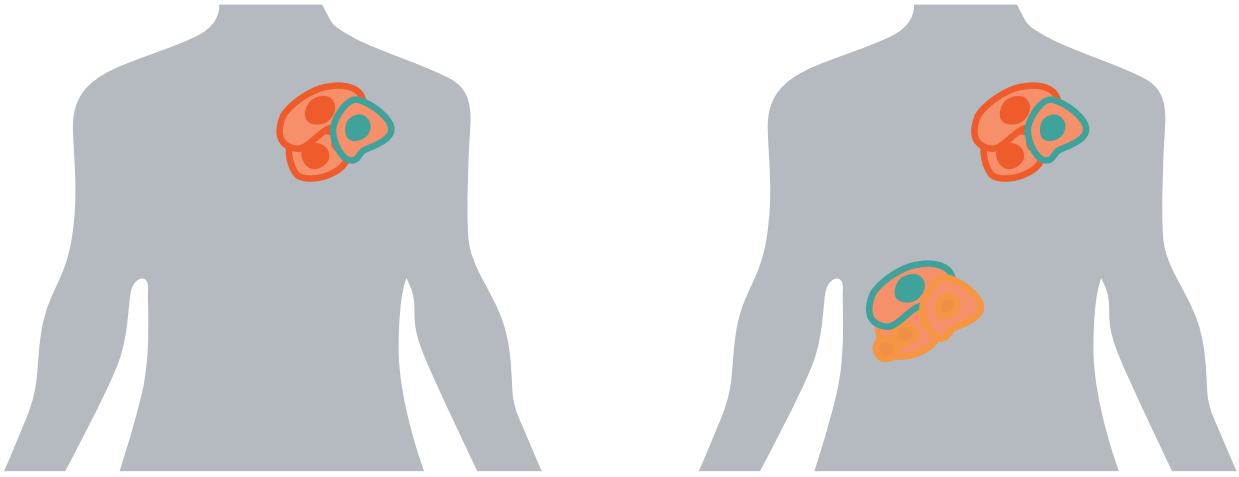
*FoundationOne Liquid CDx reports MSI-H status.

CDx, companion diagnostic; ctDNA: circulating tumour DNA.

FoundationOne Liquid CDx sequences cfDNA which can originate from primary and metastatic tumour sites, thereby capturing the full disease heterogeneity across the body as the disease evolves[2,3,13,14]



Circulating cells release genomic DNA when lysed (circulating cell-free DNA, cfDNA)
Blood contains circulating cell-free DNA released from healthy tissue and from tumour tissue (circulating tumour DNA, ctDNA)



Tumour heterogeneity within the primary tumour

Tumour heterogeneity across the body

CDx, companion diagnostic; cfDNA, circulating cell-free DNA; ctDNA, circulating tumour DNA.

FoundationOne Liquid CDx can help inform therapy selection at progression[13,14,18]

- Tumour heterogeneity is associated with the development of new and evolving resistance mutations and relapse[18]
- FoundationOne Liquid CDx is often suited at progression owing to the increase in ctDNA levels and clonal evolution of the tumour as the disease progresses[13,14]

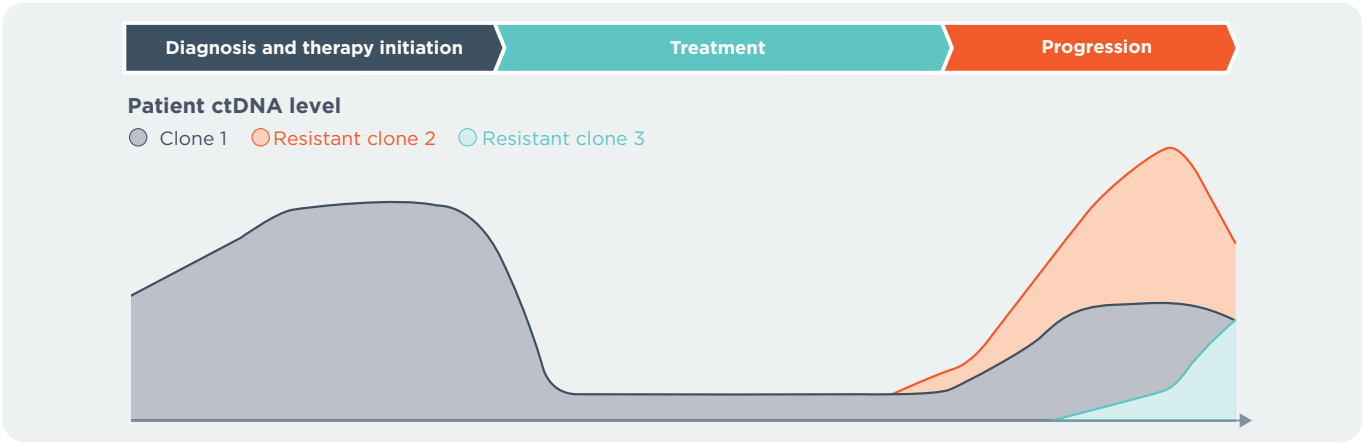


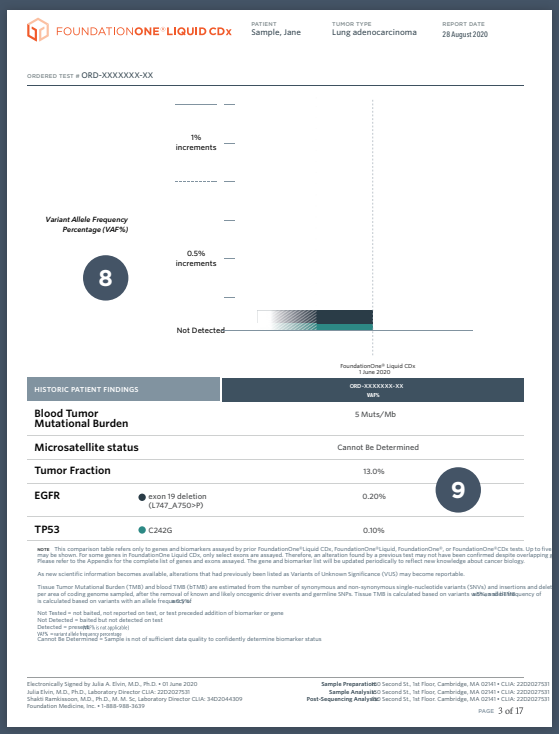
Figure adapted from reference 18.

FoundationOne Liquid CDx is suited for NSCLC, breast cancer, ovarian cancer, prostate cancer, and other solid tumours[2,3,19-39]

- FoundationOne Liquid CDx covers professional guidelines, and other clinically relevant genomic alterations and signatures* for NSCLC, breast, ovarian and prostate cancer[2,3,19-31,33-39]

*FoundationOne Liquid CDx reports MSI-H status.
CDx, companion diagnostic; ctDNA: circulating tumour DNA; NSCLC, non-small cell lung cancer.

In-depth report helps inform clinical decision-making[40]



1. Patient and specimen details
2. Summary of all identified genomic alterations and biomarkers as well as the number of therapy and clinical trial options
3. Genomic alterations, clinically relevant targeted therapies and clinical trials for each alteration, to help guide your treatment strategy
4. bTMB and MSI* status to help inform the use of immunotherapies
5. Therapies ranked alphabetically within NCCN therapy categories†
6. Tumour Fraction, the percentage of tumour-derived DNA in the liquid biopsy sample, providing you with a measure of the likelihood of detecting genomic alterations in the liquid biopsy sample
7. Genomic alterations associated with no reportable therapeutic or clinical trial options
8. Variant allele frequency percentage (VAF%) for base substitutions and insertions and deletions (indels)
9. Historic patient findings from earlier FoundationOne tests, allowing you to follow your patient's genomic profile across their disease journey

- Consistency in the reports across different FoundationOne services aids comparison of the results across the patient journey[40,41]

*FoundationOne Liquid CDx reports MSI-H status
†For additional information on the NCCN categories please refer to the NCCN Compendium® (www.nccn.org).

bTMB, blood Tumour Mutational Burden; CDx, companion diagnostic; MSI, Microsatellite Instability; NCCN, National Comprehensive Cancer Network; VAF, variant allele frequency

FoundationOne Liquid CDx is able to detect novel and known variants of all four main classes of genomic alterations in 324 cancer-related genes in all solid tumours[2,3]

Genes baited with enhanced sensitivity† (selected based on increased actionability with current or future targeted therapies) are highlighted[2,3]

***ABL1* [Exons 4–9]**	*CALR*	*CYP17A1*	*FGFR4*	*KDM6A*	*MYCL (MYCL1)*	*POLD1*	*SMAD4*
ACVR1B	*CARD11*	*DAXX*	*FH*	*KDR*	***MYCN***	*POLE*	*SMARCA4*
***AKT1* [Exon 3]**	*CASP8*	*DDR1*	*FLCN*	*KEAP1*	***MYD88* [Exon 4]**	*PPARG*	*SMARCB1*
AKT2	*CBFB*	***DDR2* [Exons 5,17,18]**	*FLT1*	*KEL*	*NBN*	*PPP2R1A*	***SMO***
AKT3	*CBL*	*DIS3*	***FLT3* [Exons 14,15,20]**	***KIT* [Exons 8,9,11,12,13,17,** Intron 16]	***NF1***	*PPP2R2A*	*SNCAIP*
***ALK* [Exons 20–29, Introns 18,19]**	***CCND1***	*DNMT3A*	***FOXL2***	*KLHL6*	*NF2*	*PRDM1*	*SOCS1*
ALOX12B	*CCND2*	*DOT1L*	*FUBP1*	*KMT2A (MLL)* [Introns 6,8–11, **Intron 7**]	*NFE2L2*	*PRKAR1A*	*SOX2*
AMER1 (FAM123B)	*CCND3*	*EED*	*GABRA6*	*KMT2D (MLL2)*	*NFKBIA*	*PRKCI*	*SOX9*
APC	*CCNE1*	***EGFR* [Introns 7,15,24–27]**	*GATA3*	***KRAS***	*NKX2–1*	*PTCH1*	*SPEN*
AR	*CD22*	*EP300*	*GATA4*	*LTK*	*NOTCH1*	***PTEN***	*SPOP*
***ARAF* [Exons 4,5,7, 11,13,15,16]**	*CD70*	*EPHA3*	*GATA6*	*LYN*	*NOTCH2* [Intron 26]	***PTPN11***	*SRC*
ARFRP1	*CD79A*	*EPHB1*	***GNA11 [Exons 4,5]***	*MAF*	*NOTCH3*	*PTPRO*	*STAG2*
ARID1A	*CD79B*	*EPHB4*	*GNA13*	***MAP2K1 (MEK1)* [Exons 2,3]**	***NPM1* [Exons 4–6,8,10]**	*QKI*	*STAT3*
ASXL1	***CD274* (PD-L1)**	***ERBB2***	***GNAQ* [Exons 4,5]**	***MAP2K2 (MEK2)* [Exons 2–4,6,7]**	***NRAS* [Exons 2,3]**	*RAC1*	***STK11***
ATM	*CDC73*	***ERBB3* [Exons 3,6,7, 8,10,12,20, 21,23,24,25]**	***GNAS* [Exons 1,8]**	*MAP2K4*	*NSD3 (WHSC1L1)*	*RAD21*	*SUFU*
ATR	***CDH1***	*ERBB4*	*GRM3*	*MAP3K1*	*NT5C2*	*RAD51*	*SYK*
ATRX	***CDK12***	*ERCC4*	*GSK3B*	*MAP3K13*	***NTRK1* [Exons 14,15, Introns 8–11]**	*RAD51B*	*TBX3*
AURKA	***CDK4***	*ERG*	*H3F3A*	*MAPK1*	*NTRK2* [Intron 12]	*RAD51C*	*TEK*
AURKB	***CDK6***	***ERRFI1***	*HDAC1*	*MCL1*	***NTRK3* [Exons 16,17]**	*RAD51D*	*TERC*‡ {ncRNA}
AXIN1	*CDK8*	***ESR1* [Exons 4–8]**	*HGF*	***MDM2***	*P2RY8*	*RAD52*	***TERT*‡ {Promoter}**
AXL	*CDKN1A*	***EZH2* [Exons 4,16,17,18]**	*HNF1A*	*MDM4*	***PALB2***	*RAD54L*	*TET2*
BAP1	*CDKN1B*	*FAM46C*	***HRAS* [Exons 2,3]**	*MED12*	*PARK2*	***RAF1* [Exons 3,4,6,7,10,14,15,17,** Introns 4–8]	*TGFBR2*
BARD1	***CDKN2A***	*FANCA*	*HSD3B1*	*MEF2B*	*PARP1*	*RARA* [Intron 2]	*TIPARP*
BCL2	*CDKN2B*	*FANCC*	*ID3*	*MEN1*	*PARP2*	***RB1***	*TNFAIP3*
BCL2L1	*CDKN2C*	*FANCG*	***IDH1* [Exon 4]**	*MERTK*	*PARP3*	*RBM10*	*TNFRSF14*
BCL2L2	*CEBPA*	*FANCL*	***IDH2* [Exon 4]**	***MET***	*PAX5*	*REL*	***TP53***
BCL6	*CHEK1*	*FAS*	*IGF1R*	*MITF*	*PBRM1*	***RET* [Introns 7,8, Exons 11,13–16, Introns 9–11]**	*TSC1*
BCOR	***CHEK2***	*FBXW7*	*IKBKE*	*MKNK1*	*PDCD1 (PD-1)*	*RICTOR*	*TSC2*
BCORL1	*CIC*	*FGF10*	*IKZF1*	*MLH1*	***PDCD1LG2 (PD-L2)***	*RNF43*	*TYRO3*
***BRAF* [Exons 11–18, Introns 7–10]**	*CREBBP*	*FGF12*	*INPP4B*	***MPL* [Exon 10]**	***PDGFRA* [Exons 12,18, Introns 7,9,11]**	***ROS1* [Exons 31,36–38,40, Introns 31–35]**	*U2AF1*
***BRCA1* [Introns 2,7, 8,12,16,19,20]**	***CRKL***	*FGF14*	*IRF2*	*MRE11A*	***PDGFRB* [Exons 12–21,23]**	*RPTOR*	***VEGFA***
***BRCA2* [Intron 2]**	*CSF1R*	*FGF19*	*IRF4*	*MSH2* [Intron 5]	*PDK1*	*SDHA*	*VHL*
BRD4	*CSF3R*	*FGF23*	*IRS2*	*MSH3*	*PIK3C2B*	*SDHB*	*WHSC1*
BRIP1	*CTCF*	*FGF3*	*JAK1*	*MSH6*	*PIK3C2G*	*SDHC*	*WT1*
BTG1	*CTNNA1*	*FGF4*	***JAK2* [Exons 14]**	*MST1R*	***PIK3CA* [Exons 2,3,5–8,10,14,19,21] (Coding Exons 1,2, 4–7,9,13,18,20)**	*SDHD*	*XPO1*
BTG2	***CTNNB1* [Exon 3]**	*FGF6*	***JAK3* [Exons 5,11,12,13,15,16]**	*MTAP*	*PIK3CB*	*SETD2*	*XRCC2*
***BTK* [Exons 2,15]**	*CUL3*	***FGFR1*** [Introns 1,5, **Intron 17**]	*JUN*	***MTOR [Exons 19,30,39,40,43–45,47,48,53,56]***	*PIK3R1*	*SF3B1*	*ZNF217*
C11orf30 (EMSY)	*CUL4A*	***FGFR2*** [Intron 1, **Intron 17**]	*KDM5A*	*MUTYH*	*PIM1*	*SGK1*	*ZNF703*
C17orf39 (GID4)	*CXCR4*	***FGFR3* [Exons 7,9 (alternative designation exon 10),14,18, Intron 17]**	*KDM5C*	***MYC* [Intron 1]**	*PMS2*	*SMAD2*	

*Overall 309 genes with complete coding exonic coverage, 15 genes with selected intronic or non-coding regions only.

†**75 genes are baited for enhanced sensitivity** using ultra-deep sequencing coverage; other genomic regions are baited for high sensitivity using high sequencing coverage.

‡Genes with selected non-coding coverage only; additional genes with selected non-coding coverage only are: ***BCR*** (introns 8,13,14); ***CD74*** (introns 8–6); ***ETV4*** (introns 5,6); ***ETV5*** (introns 6,7); ***ETV6*** (introns 5,6); ***EWSR1*** (introns 7,13); ***EZR*** (introns 9–11); ***MYB*** (intron 14); ***NUTM1*** (intron 1); ***RSPO2*** (intron 1); ***SDC4*** (intron 2); ***SLC34A2*** (intron 4); ***TMPRSS2*** (introns 1–3).

CDx, companion diagnostic; ncRNA, non-coding RNA.

Use FoundationOne Liquid CDx, our liquid biopsy comprehensive genomic profiling service, as a minimally invasive option, alternative or complementary to FoundationOne CDx, for all patients with solid tumours at optimal times beneficial to their treatment journey[1-3]

Comprehensive panel

- Assesses all four main classes of genomic alterations in 324 genes plus MSI* and bTMB
- Complete exon coverage of 309 genes
- Additional coverage of selected intronic or non-coding regions
- Enhanced sensitivity for 75 genes associated with increased actionability with targeted therapies

Tumour Fraction

- Reports Tumour Fraction as a measure of the likelihood of detecting genomic alterations in the liquid biopsy sample

Extensively analytically and clinically validated comprehensive platform

- High sensitivity and specificity† for key genomic alterations, MSI* and bTMB across all solid tumours
- Analytical and clinical validation based on >7,500 samples covering >30,000 unique variants in 324 genes and 37 cancer indications‡

Faster treatment decisions

- Quick and convenient single blood draw and improved turnaround time of <2 weeks to enable faster treatment decisions
- Helps avoid invasive biopsies

Supporting personalized decision-making across the patient journey

- Part of our proven portfolio of high-quality, comprehensive genomic profiling services for all solid tumours, supporting current and future personalized clinical and research decisions at optimal times beneficial to your patients' treatment journeys
- Option of reflex testing to FoundationOne CDx if no actionable genomic alterations are detected in the liquid biopsy sample

High accuracy

- Accurately detects the main types of genomic alterations, MSI* and bTMB at very low allele frequencies, Tumour Fractions or percent unstable loci
- Low overall false positive rate of 1 in 8000

*FoundationOne Liquid CDx reports MSI-H status.

†75 genes are baited with enhanced sensitivity for all variant types (selected based on increased actionability with current or future targeted therapies; for more information of these 75 genes, please refer to our full gene list); other genomic regions are baited with high sensitivity.

‡Validation against an externally validated cfDNA assay.

bTMB: blood Tumour Mutational Burden; CDx, companion diagnostic, MSI, Microsatellite Instability, TAT; turnaround time; TF, Tumour Fraction.

Contacts

For more information, please contact Roche at canada.fmi@roche.com

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