

# TruSight™ Oncology Comprehensive

A US FDA–approved next-generation sequencing solution for comprehensive genomic profiling



## General information

### What is TruSight Oncology Comprehensive?

As a global leader in next-generation sequencing (NGS) and microarray-based solutions, Illumina is dedicated to improving human health by unlocking the power of the genome. Illumina continues to innovate by offering TruSight Oncology (TSO) Comprehensive, a US FDA-approved, distributable, comprehensive genomic profiling (CGP) *in vitro* diagnostic (IVD) with pan-cancer companion diagnostic (CDx) claims. TSO Comprehensive can generate a broad molecular profile of solid tumor patient samples from formalin-fixed, paraffin-embedded (FFPE) tissue, maximizing a lab's ability to find actionable alterations that can help inform therapy decisions according to clinical guidelines.

### What is the product's intended use?

TruSight Oncology Comprehensive is a qualitative *in vitro* diagnostic test that uses targeted next-generation sequencing to detect variants in 517 genes using nucleic acids extracted from formalin-fixed, paraffin-embedded (FFPE) tumor tissue samples from cancer patients with solid malignant neoplasms using the Illumina NextSeq™ 550Dx Instrument. The test can be used to detect single nucleotide variants, multi-nucleotide variants, insertions, and deletions from DNA, and fusions in 24 genes and splice variants in one gene from RNA.

The test also reports a Tumor Mutational Burden (TMB) score. The test is intended to be used as a companion diagnostic to identify cancer patients who may benefit from treatment with the targeted therapies listed in [Table 1](#), in accordance with the approved therapeutic product labeling.

In addition, the test is intended to provide tumor profiling information for use by qualified health care professionals in accordance with professional guidelines in oncology for patients with solid malignant neoplasms. Genomic findings other than those listed in [Table 1](#) of the intended use statement are not conclusive or prescriptive for labeled use of any specific therapeutic product.

Table 1: Companion Diagnostic Indications

Tumor Type	Biomarker(s) Detected	Therapy
Solid Tumors	<i>NTRK1/2/3</i> fusions	VITRAKVI® (larotrectinib)
Non-Small Cell Lung Cancer	<i>RET</i> fusions	RETEVMO® (selpercatinib)

### What is a companion diagnostic (CDx)?

A CDx is a medical device, often an *in vitro* diagnostic (IVD), that provides information that is essential for the safe and effective use of a corresponding drug or biological product. A CDx can identify patients most likely to benefit from a particular therapeutic product.

### What types of cancer is TSO Comprehensive approved to test?

TSO Comprehensive is approved for:

- Tumor profiling—solid tumors
- *NTRK1/2/3* CDx—solid tumors
- *RET* CDx—non-small cell lung cancer

**What specimen type is TSO Comprehensive approved to test?**

TSO Comprehensive is approved for use with nucleic acids extracted from FFPE tumor tissue samples.

**Will additional claims be added to TSO Comprehensive?**

Illumina has a pipeline of CDx and tumor profiling claims planned to be added to TSO Comprehensive over time. Inquire with your Illumina sales representative to learn more.

**Where will TSO Comprehensive be sold?**

TSO Comprehensive is US FDA approved and will be for sale in the United States.

**When will TSO Comprehensive be available?**

TSO Comprehensive kits will be available to ship in November 2024. For more information on product availability, including when you can begin placing orders, contact your Illumina sales representative.

**What genes are tested by TSO Comprehensive?**

TSO Comprehensive includes key biomarkers in clinical guidelines, drug labels, and clinical trials across all solid tumor types. Content includes RNA fusions and splice variants in one gene (Table 2 and Table 3, respectively), small DNA variants (Table 4), and the complex genomic signature, TMB. Content is subject to change with additional tumor profiling content under development (Table 5).

Table 2: RNA content included in TSO Comprehensive<sup>a</sup>

<i>AXL</i>	<i>CDK4</i>	<i>ERG</i>	<i>ETV4</i>	<i>FGFR2</i>	<i>KIF5B</i>	<i>NTRK2</i>	<i>RAF1</i>
<i>BCL2</i>	<i>EGFR</i>	<i>ESR1</i>	<i>EWSR1</i>	<i>FGFR3</i>	<i>NRG1</i>	<i>NTRK3</i>	<i>RET</i>
<i>BRAF</i>	<i>EML4<sup>b</sup></i>	<i>ETV1</i>	<i>FGFR1</i>	<i>FLI1</i>	<i>NTRK1</i>	<i>PAX3</i>	<i>TMPRSS2</i>

a. Genes listed are assessed for known and novel fusions.

b. *EML4-ALK* fusions are not included.

Table 3: Splice variants included in TSO Comprehensive

<i>EGFR</i>
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Table 4: DNA content included in TSO Comprehensive

ABL1	BMPR1A	CTCF	ETS1	FUBP1	ID3	MAP2K4	NOTCH1	PMS2	ROS1	STK11
ABL2	BRAF	CTLA4	ETV1	FYN	IDH1	MAP3K1	NOTCH2	PNRC1	RPS6KA4	STK40
ABRAXAS1	BRCA1	CTNNA1	ETV4	GABRA6	IDH2	MAP3K13	NOTCH3	POLD1	RPS6KB1	SUFU
ACVR1	BRCA2	CTNNB1	ETV5	GATA1	IFNGR1	MAP3K14	NOTCH4	POLE	RPS6KB2	SUZ12
ACVR1B	BRD4	CUL3	ETV6	GATA2	IGF1	MAP3K4	NPM1	PPARG	RPTOR	SYK
ADGRA2	BRIP1	CUX1	EWSR1	GATA3	IGF1R	MAPK1	NRAS	PPM1D	RUNX1	TAF1
AKT1	BTG1	CXCR4	EZH2	GATA4	IGF2	MAPK3	NRG1	PPP2R1A	RUNX1T1	TBX3
AKT2	BTK	CYLD	FAM46C	GATA6	IKBKE	MAX	NSD1	PPP2R2A	RYBP	TCF3
AKT3	CALR	DAXX	FANCA	GEN1	IKZF1	MCL1	NTRK1	PPP6C	SDHA	TCF7L2
ALK	CARD11	DCUN1D1	FANCC	GID4	IL10	MDC1	NTRK2	PRDM1	SDHAF2	TERC
ALOX12B	CASP8	DDR2	FANCD2	GLI1	IL7R	MDM2	NTRK3	PREX2	SDHB	TERT
AMER1	CBFB	DDX41	FANCE	GNA11	INHA	MDM4	NUP93	PRKAR1A	SDHC	TET1
ANKRD11	CBL	DHX15	FANCF	GNA13	INHBA	MED12	NUTM1	PRKCI	SDHD	TET2
ANKRD26	CCND1	DICER1	FANCG	GNAQ	INPP4A	MEF2B	PAK1	PRKDC	SETBP1	TFE3
APC	CCND2	DIS3	FANCI	GNAS	INPP4B	MEN1	PAK3	PRKN	SETD2	TFRC
AR	CCND3	DNAJB1	FANCL	GPS2	INSR	MET	PAK5	PRSS8	SF3B1	TGFBR1
ARAF	CCNE1	DNMT1	FAS	GREM1	IRF2	MGA	PALB2	PTCH1	SH2B3	TGFBR2
ARFRP1	CD274	DNMT3A	FAT1	GRIN2A	IRF4	MITF	PARP1	PTEN	SH2D1A	TMEM127
ARID1A	CD276	DNMT3B	FBXW7	GRM3	IRS1	MLH1	PAX3	PTPN11	SHQ1	TMPRSS2
ARID1B	CD74	DOT1L	FGF1	GSK3B	IRS2	MLL/KMT2A	PAX5	PTPRD	SLIT2	TNFAIP3
ARID2	CD79A	E2F3	FGF10	H3F3A	JAK1	MLLT3	PAX7	PTPRS	SLX4	TNFRSF14
ARID5B	CD79B	EED	FGF14	H3F3B	JAK2	MPL	PAX8	PTPRT	SMAD2	TOP1
ASXL1	CDC73	EGFL7	FGF19	H3F3C	JAK3	MRE11A	PBRM1	QKI	SMAD3	TOP2A
ASXL2	CDH1	EGFR	FGF2	HGF	JUN	MSH2	PDCD1	RAB35	SMAD4	TP53
ATM	CDK12	EIF1AX	FGF23	HIST1H1C	KAT6A	MSH3	PDCD1LG2	RAC1	SMARCA4	TP63
ATR	CDK4	EIF4A2	FGF3	HIST1H2BD	KDM5A	MSH6	PDGFRA	RAD21	SMARCB1	TRAF2
ATRX	CDK6	EIF4E	FGF4	HIST1H3A	KDM5C	MST1	PDGFRB	RAD50	SMARCD1	TRAF7
AURKA	CDK8	ELOC	FGF5	HIST1H3B	KDM6A	MST1R	PDK1	RAD51	SMC1A	TSC1
AURKB	CDKN1A	EML4	FGF6	HIST1H3C	KDR	MTOR	PDPK1	RAD51B	SMC3	TSC2
AXIN1	CDKN1B	EMSY	FGF7	HIST1H3D	KEAP1	MUTYH	PGR	RAD51C	SMO	TSHR
AXIN2	CDKN2A	EP300	FGF8	HIST1H3E	KEL	MYB	PHF6	RAD51D	SNCAIP	U2AF1
AXL	CDKN2B	EPCAM	FGF9	HIST1H3F	KIF5B	MYC	PHOX2B	RAD52	SOCS1	VEGFA
B2M	CDKN2C	EPHA3	FGFR1	HIST1H3G	KIT	MYCL1	PIK3C2B	RAD54L	SOX10	VHL
BAP1	CEBPA	EPHA5	FGFR2	HIST1H3H	KLF4	MYCN	PIK3C2G	RAF1	SOX17	VTCN1
BARD1	CENPA	EPHA7	FGFR3	HIST1H3I	KLHL6	MYD88	PIK3C3	RANBP2	SOX2	WISP3
BBC3	CHD2	EPHB1	FGFR4	HIST1H3J	KRAS	MYOD1	PIK3CA	RARA	SOX9	WT1
BCL10	CHD4	ERBB2	FH	HIST2H3A	LAMP1	NAB2	PIK3CB	RASA1	SPEN	XIAP
BCL2	CHEK1	ERBB3	FLCN	HIST2H3C	LATS1	NBN	PIK3CD	RB1	SPOP	XPO1
BCL2L1	CHEK2	ERBB4	FLI1	HIST2H3D	LATS2	NCOA3	PIK3CG	RBM10	SPTA1	XRCC2
BCL2L11	CIC	ERCC1	FLT1	HIST3H3	LMO1	NCOR1	PIK3R1	RECQL4	SRC	YAP1
BCL2L2	COP1	ERCC2	FLT3	HNF1A	LRP1B	NEGR1	PIK3R2	REL	SRSF2	YES1
BCL6	CREBBP	ERCC3	FLT4	HNRNPK	LYN	NF1	PIK3R3	RET	STAG1	ZBTB2
BCOR	CRKL	ERCC4	FOXA1	HOXB13	LZTR1	NF2	PIM1	RHEB	STAG2	ZBTB7A
BCORL1	CRLF2	ERCC5	FOXL2	HRAS	MAGI2	NFE2L2	PLCG2	RHOA	STAT3	ZFHX3
BCR	CSF1R	ERG	FOXO1	HSD3B1	MALT1	NFKBIA	PLK2	RICTOR	STAT4	ZNF217

<i>BIRC3</i>	<i>CSF3R</i>	<i>ERRF1</i>	<i>FOXP1</i>	<i>HSP90AA1</i>	<i>MAP2K1</i>	<i>NKX2-1</i>	<i>PMAIP1</i>	<i>RIT1</i>	<i>STAT5A</i>	<i>ZNF703</i>
<i>BLM</i>	<i>CSNK1A1</i>	<i>ESR1</i>	<i>FRS2</i>	<i>ICOSLG</i>	<i>MAP2K2</i>	<i>NKX3-1</i>	<i>PMS1</i>	<i>RNF43</i>	<i>STAT5B</i>	<i>ZRSR2</i>

Table 5: Tumor profiling content under development

MSI
Gene amplifications from DNA
Additional gene fusions and splice variants from RNA

**What is comprehensive genomic profiling (CGP)?**

CGP is a type of molecular testing for evaluating advanced stage tumors using a technique called NGS to assess multiple variant classes (eg, SNVs, MNVs, insertions, deletions, fusions, splice variants) in a single test. CGP can interrogate DNA and/or RNA isolated from FFPE tissue, circulating tumor DNA (ctDNA) isolated from peripheral whole blood, as well as other sample types. CGP is a powerful precision medicine tool that better identifies tumor variants sensitive to targeted and immuno-therapies compared to traditional molecular testing, as it simultaneously detects several variant types using one test, sparing usage of valuable tissue specimens.

TSO Comprehensive is approved for use with nucleic acids extracted from FFPE tumor tissue, not ctDNA from peripheral whole blood.

**What are the key attributes of the TSO Comprehensive assay?**

TSO Comprehensive:

- Is the first US FDA–approved, distributed IVD CGP solution with pan-cancer CDx claims
- Includes both DNA and RNA content and detects several variant classes, plus TMB
- Calls fusions from RNA to maximize sensitivity for detection
- Provides a kitted, US FDA–approved IVD solution that can be implemented by local labs in house to generate CGP results with a 4–5 day workflow
- Can alleviate much of the resource-intensive validation and regulatory requirements associated with implementing Laboratory-Developed Tests (LDTs)
- Has a clear pathway to public payer reimbursement under the [CMS National Coverage Determination \(NCD\) 90.2](#) as an IVD CGP test with CDx claims, and may be eligible for increased commercial payer coverage<sup>1</sup>
- Provides physicians with a clear, integrated, clinical report for each sample as part of the standard workflow

## Workflow

### What is the recommended sample input?

TSO Comprehensive requires 40 ng RNA and/or 40 ng DNA extracted from FFPE tissue.

### How are results reported for TSO Comprehensive?

A clear, integrated report is generated as part of the TSO Comprehensive workflow. Contact your Illumina sales representative to view an example TSO Comprehensive report.

### What are the workflow steps from sample preparation to final report?

The TSO Comprehensive workflow includes the following steps: sample acquisition and processing, DNA and RNA extraction, library preparation and enrichment, fully automated sequencing and analysis, and report generation (Figure 1).

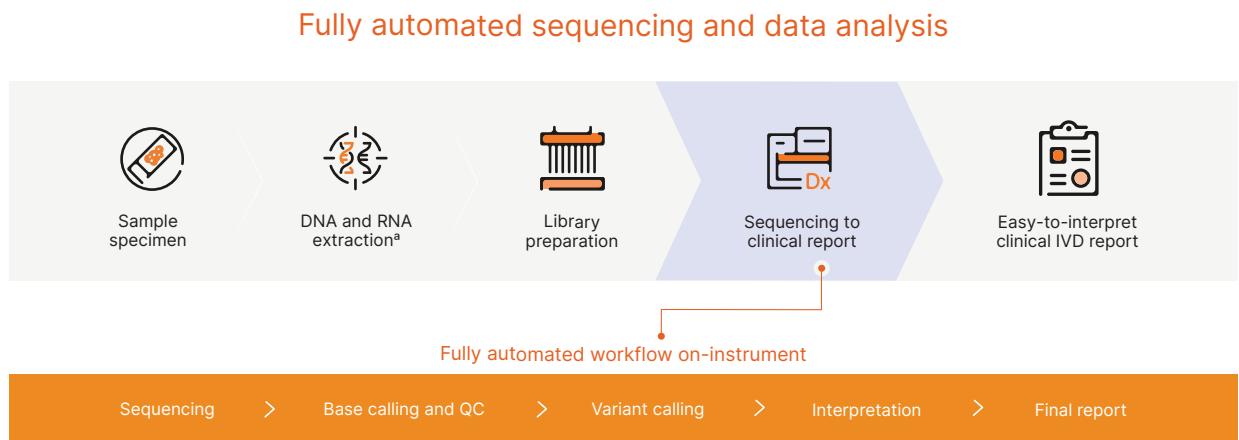


Figure 1: TSO Comprehensive sample to report workflow—The fully automated workflow on the NextSeq 550Dx System sequences samples; performs base calling and QC, variant calling, and interpretation; and generates a clinical report. The entire workflow is complete in 4-5 days.

a. Extraction kits must be purchased separately.

### How long is the turnaround time (TAT) from sample to report?

The TAT is 4–5 days from extracted DNA and/or RNA to the final clinical report.

### What sequencing platform is needed?

TSO Comprehensive is run on the NextSeq 550Dx Instrument, an FDA-regulated high-throughput sequencing platform. For platform acquisition options available, inquire with your Illumina sales representative.

### What is the expected analysis time for a sample batch processed in a sequencing run?

Analysis time is 8–10 hours.

## Reimbursement

### What reimbursement is available for NGS-based oncology tests in the US?

IVD CGP tumor profiling assays with CDx claims across solid malignant neoplasms are covered for eligible Medicare beneficiaries throughout the US under [National Coverage Determination \(NCD\) 90.2](#). Commercial coverage for assays with this indication increases by more than a third of US commercially insured lives as compared to assays without CDx claims.<sup>1</sup>

## Learn more

[TruSight Oncology Comprehensive](#)

## Reference

1. Policy Reporter. Data pulled in 2023.



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