FREQUENTLY ASKED QUESTIONS

TruSight™ Oncology Comprehensive

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

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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, optimizing the detection of actionable alterations that can 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 qualified health care professionals to use in accordance with oncology guidelines 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	*NTRK1/2/3* fusions	VITRAKVI® (larotrectinib)
Non-Small Cell Lung Cancer (NSCLC)	*RET* fusions	RETEVMO® (selpercatinib)

What is a companion diagnostic (CDx)?

A CDx is a medical device, often an IVD, that provides information 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 profling—solid tumors
- *NTRK1/2/3* CDx—solid tumors
- *RET* CDx—non-small cell lung cancer (NSCLC)

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 is developing a pipeline of CDx and tumor profiling claims for future integration into TSO Comprehensive. Consult your Illumina sales representative to learn more.

Where will TSO Comprehensive be sold?

TSO Comprehensive is US FDA-approved for sale in the United States.

What genes are tested by TSO Comprehensive?

TSO Comprehensive includes key biomarkers referenced 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 TMB. Content is subject to change as tumor profiling content under development is added (Table 5).

Table 2: Fusions from RNA included in TSO Comprehensive[a]

AXL	*CDK4*	*ERG*	*ETV4*	*FGFR2*	*KIF5B*	*NTRK2*	*RAF1*
BCL2	*EGFR*	*ESR1*	*EWSR1*	*FGFR3*	*NRG1*	*NTRK3*	*RET*
BRAF	*EML4*[b]	*ETV1*	*FGFR1*	*FLI1*	*NTRK1*	*PAX3*	*TMPRSS2*

a. Genes listed are assessed for known and novel fusions.
b. *EML4-ALK* fusions are not included.

Table 3: Splice variants from RNA included in TSO Comprehensive

EGFR

Table 4: Small DNA variants 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*
BIRC3	*CSF3R*	*ERRFI1*	*FOXP1*	*HSP90AA1*	*MAP2K1*	*NKX2-1*	*PMAIP1*	*RIT1*	*STAT5A*	*ZNF703*
BLM	*CSNK1A1*	*ESR1*	*FRS2*	*ICOSLG*	*MAP2K2*	*NKX3-1*	*PMS1*	*RNF43*	*STAT5B*	*ZRSR2*

Table 5: Tumor profiling content under development

MSI
ERBB2 and *MET* gene amplifications from DNA
ALK and *ROS1* fusions from RNA
MET splice variants from RNA

What is comprehensive genomic profiling (CGP)?

CGP is a molecular test that uses NGS to evaluate advanced-stage tumors by assessing multiple variant classes (eg, single nucleotide variants, multi-nucleotide variants, insertions, deletions, fusions, and splice variants). 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 more effectively identifies tumor variants sensitive to targeted treatments and immunotherapies compared to traditional molecular testing, as it can detect multiple variant types in a single test and conserve valuable tissue specimens.

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

What are the key attributes of the TSO Comprehensive assay?

TSO Comprehensive:

- Is the first US FDA–approved and distributed IVD CGP solution with pan-cancer CDx claims
- Includes both DNA and RNA content and detects several variant classes, plus TMB
- Identifies fusions from RNA to maximize detection sensitivity
- Provides a kitted, US FDA–approved IVD solution that can be implemented by local laboratories to generate CGP results in-house with a 4–5 day workflow
- Can alleviate 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[1]
- Provides physicians with a results 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 results report is generated as part of the TSO Comprehensive workflow. Contact your Illumina sales representative to view an example TSO Comprehensive results report.

What are the workflow steps from sample preparation to results 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 results report generation (Figure 1).

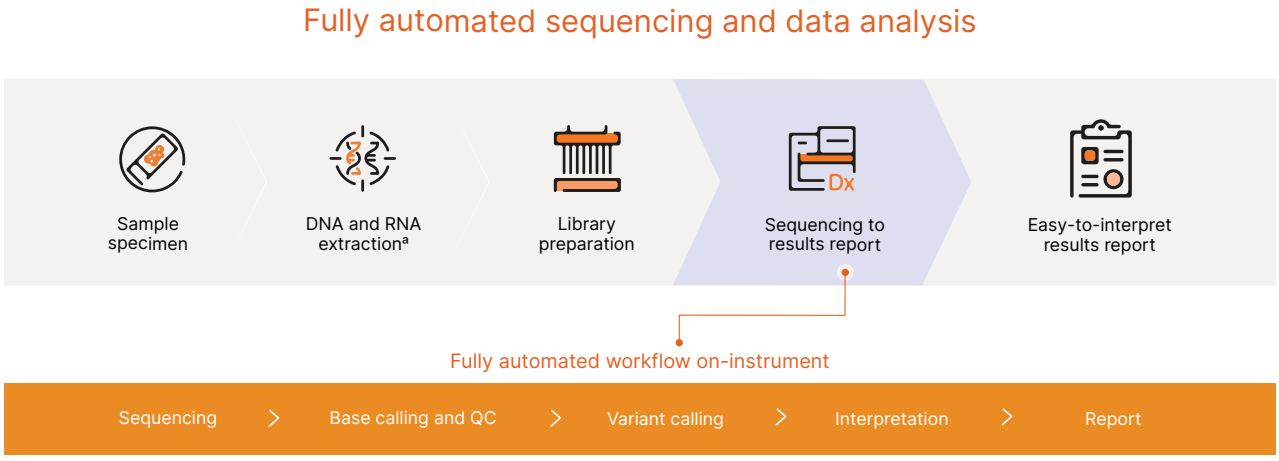

Figure 1: TSO Comprehensive sample to report workflow—The fully automated workflow on the NextSeq 550Dx System sequences samples; performs base calling and QC, variant calling, and interpretation; and generates a results report. The entire workflow is complete in 4–5 days.
a. Extraction kits must be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

Learn more

TruSight Oncology Comprehensive

Reference

1. Policy Reporter. Data pulled in 2023.

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