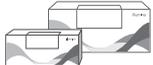
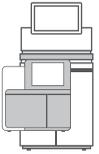


Simplifying the process to identify applicable variants in oncology samples

The TruSight™ Oncology 500 product family, the Illumina variant calling pipeline, and PierianDx Clinical Genomics Workspace™ software enable molecular pathology labs to implement comprehensive genomic profiling (CGP) for quick, easy identification of significant biomarkers.

 <h2>1. Prepare</h2> <p>Analyze 523 cancer-related genes, including biomarkers in key guidelines and clinical trials</p> <p>Assess CNVs, SNVs, indels, fusions, splice variants, and complex genomic signatures, such as MSI and TMB*</p>	<h3>TruSight Oncology 500</h3> <ul style="list-style-type: none"> • Solid tumor samples • DNA and RNA 	<h3>TruSight Oncology 500 High-Throughput</h3> <ul style="list-style-type: none"> • Solid tumor samples • DNA and RNA 	<h3>TruSight Oncology 500 ctDNA</h3> <ul style="list-style-type: none"> • Liquid biopsy samples • DNA
 <h2>2. Sequence</h2> <p>Exceptional data quality</p> <p>Flexible and scalable</p>	<h3>NextSeq™ 550 and NextSeq 550Dx† Systems</h3> <ul style="list-style-type: none"> • Up to 8 samples per run 	<h3>NextSeq 550 and NextSeq 550Dx† Systems</h3> <ul style="list-style-type: none"> • Up to 8 samples per run <h3>NovaSeq™ 6000 System</h3> <ul style="list-style-type: none"> • 16-192 samples per run 	<h3>NovaSeq 6000 System</h3> <ul style="list-style-type: none"> • Up to 24 samples per run
 <h2>3. Call variants</h2> <p>Sophisticated, proprietary algorithms remove errors, artifacts, and germline variants</p> <p>High-sensitivity variant calling from raw sequencing data</p>	<h3>Local Run Manager</h3> <ul style="list-style-type: none"> • On-instrument analysis <h3>Local Server</h3> <ul style="list-style-type: none"> • Off-instrument analysis <h3>PierianDx Clinical Genomics Workspace</h3> <ul style="list-style-type: none"> • Cloud-based analysis (VCF and FASTQ files) 	<h3>Local Server</h3> <ul style="list-style-type: none"> • Off-instrument analysis <h3>PierianDx Clinical Genomics Workspace</h3> <ul style="list-style-type: none"> • Cloud-based analysis (VCF and FASTQ‡ files) 	<h3>DRAGEN™ TruSight Oncology 500 ctDNA Analysis Software</h3> <ul style="list-style-type: none"> • Off-instrument analysis in ~20 hours <h3>PierianDx Clinical Genomics Workspace</h3> <ul style="list-style-type: none"> • Cloud-based analysis (VCF files only)

4. Interpret results and produce meaningful reports with PierianDx Clinical Genomics Workspace



Easy

Upload raw data files (BAM, FASTQ, VCF) and let PierianDx Clinical Genomics Workspace do the interpretation and reporting work

Secure and compliant

Follow privacy best practices, including HIPAA, HITRUST, GDPR, CLIA, and CAP§

Scalable

Run data sets from multiple samples in parallel for fast turnaround of results

Relevant

Identify significant variants using the constantly curated, IVD-ready PierianDx Clinical Genomics Knowledgebase

Comprehensive

Learn from a partner sharing network comprised of world-leading cancer centers and health institutions aggregating real-world knowledge

Applicable

Output an evidence-based final interpretation report with clear, visual results in accordance with commonly accepted nomenclature and reporting guidelines

* CNV = copy number variations, SNV = small nucleotide variants, indel = insertions/deletions, MSI = microsatellite instability, TMB = tumor mutational burden

† NextSeq 550Dx System in Research Mode

‡ Additional fee required

§ HIPAA = Health Insurance Portability and Accountability Act, HITRUST = Health Information Trust Alliance, GDPR = General Data Protection Regulation, CLIA = Clinical Laboratory Improvement Amendments, CAP = College of American Pathologists

From sequence to applicable results

Illumina and PierianDx offer an easy, seamless workflow for turning raw sequence data into an easy-to-understand report.

523

Genes sequenced

10000+

Variants called

<10

Relevant variants identified

1

Meaningful report

File format: BAM, FASTQ VCF PDF

G C C C C A T C A G T A G C C C G A A T A **MSI** G C T T T T C G G G T C C T G G G C C G A G G A G C G A T A C C
 C C G T T C G T T A A T T C T T G T T G C G T T C C T A G C G C C T A T **CNV** T G T C T C T T T G C C G G **SNV**
 A G C C A T T T A T C G G A G C G C C T C G G T A C A **SPLICE VARIANT** G A C C A G A G C C C T C G T G A G A C C A T T
 C T G T G A G C A G C G A A G G C C C A T A C G C G A G A T A C A C T G C C A **INDEL** C G T G A T T A C G
 A T C T G G C T G T G G T C T A G A C A T T C C A G G C G G T G C G T C T G C T G T C G G G T G C C **FUSION**
 T G C C G C T G G T A A A C A C A C C A T G A C C C C G C **TMB** C A T T G A T G C C A C G G C G A A T G T C G G

Variants and signatures identified by variant calling tools Pathogenic variants identified by PierianDx CGW

Comprehensive Genomic Report

Reviewed by PierianDx

TEST NAME: John Doe |
 DOB: 02/04/1951 |
 TUMOR: Non-small cell Lung Cancer |
 HISTORICAL NCI CRIP #: 6563465346 |
 REPORT DATE: 09/19/2019 |
 REPORT STATUS: Final

REPORT SUMMARY

Executive Summary

The patient tumor specimen harbors an **NCOA4-RET** fusion, **KRAS G12D** and **PDGFRα D842Y** mutations and an amplification in the **MDM2** gene. **RET** fusions/rearrangements are an emerging biomarker and NSCLC patients harboring these are recommended to target therapies involving cabozantinib or vandetanib by NCCN. Presence of **EGFR** mutations in NSCLC patients indicates poor prognosis independent of therapy, reduced responsiveness to EGFR TKI therapy and no impact on chemotherapeutic efficacy, as per recent NCCN guidelines. Targeted therapies against **RET** fusions, **KRAS** mutations, **PDGFRα** mutation or **MDM2** amplification are available in clinical trials for patients with NSCLC.

Other Biomarkers

BIOMARKER	LEVEL
TMB	High
MSI	Stable

Genomic Findings

IA	IB	IIC	IID
NCOA4, RET NCOA4-RET fusion	No variants reported.	PDGFRα p.D842Y L2525A>Y	No variants reported.
KRAS p.G12D C359A		MDM2 MDM2 amplification	

10 Clinical Trials | 5 Clinical Trials

RELEVANT RESULTS

Tier I - Strong Significance

VARIANT	POTENTIAL IMPACT
NCOA4, RET NCOA4-RET fusion	May benefit from - Cabozantinib or Vandetanib in non-small cell lung cancer

INTERPRETATION

RET encodes a receptor tyrosine kinase involved in cell growth and differentiation which is known to undergo oncogenic activation in vivo and in vitro by cytogenetic rearrangement (RefSeq, Jul 2008).

NCOA4 encodes an androgen receptor coactivator which interacts with the androgen receptor in a ligand-dependent manner to enhance its transcriptional activity. Chromosomal translocations between NCOA4 and RET, both located on chromosome 10, have been associated with papillary thyroid carcinoma (RefSeq, Feb 2009).

NCOA4-RET fusions have been reported in lung adenocarcinoma (COSMIC, September 2019). NCCN recommends cabozantinib (FDA approved for treatment of advanced renal cell carcinoma (RCC) and patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib) and vandetanib (FDA approved symptomatic or progressive metastatic thyroid cancer in patients with unresectable locally advanced or metastatic disease, category 2A) as targeted agents for NSCLC patients harbouring RET rearrangements (NCCN, NSCLC v.7.2019).

TruSight Oncology 500

- Sequence 523 genes in key cancer guidelines and clinical trials

Secondary analysis

- Identify genomic alterations present in sample data
- Call variants with 99.9998% analytical specificity and >95% analytical sensitivity¹
- Determine multiple variant types, including genomic signatures such as MSI and TMB
- Run Illumina secondary analysis pipeline in the PierianDx cloud, reducing risk, cost, and time

PierianDx Clinical Genomics Workspace

- Determine variant significance using literature, guidelines, drug labels, and trials information
- Filter out variants of uncertain significance or that are benign/likely benign
- Classify variants in tiers by clinical significance
- Map variants to guidelines and clinical trials
- Annotate and interpret relevant variants

Customizable genomic report

- Consolidate relevant information in one, easy-to-read report
- Adhere to AMP, CAP, ASCO, and ACMG guidelines*
- Generate meaningful information for oncologists

Learn more

Enable CGP with TruSight Oncology 500 at www.illumina.com/products/by-brand/trusight-oncology-500
 Request a demo of PierianDx Clinical Genomics Workspace at www.pierianDX.com/request-a-demo/

* AMP = Association of Molecular Pathology, CAP = College of American Pathologists, ASCO = American Society of Clinical Oncology, ACMG = American College of Medical Genetics

1. Illumina. (2020) TruSight Oncology 500 and TruSight Oncology 500 High-Throughput. Accessed May 4, 2020.

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