# A new paradigm in testing for targeted therapies in NSCLC and CC with an FDA-approved NGS CDx test

The Ion Torrent™ Oncomine™ Dx Target Test is the first targeted next-generation sequencing (NGS) *in vitro* diagnostic (IVD) test for non-small cell lung cancer (NSCLC) and cholangiocarcinoma (CC), simultaneously delivering multiple biomarker results for multiple targeted therapies from one sample within 4 days.

**This test is reimbursed by Medicare and over 40 commercial payers, covering more than 200 million US enrollees.**

## The Oncomine Dx Target Test enables:

- **Fast results**—The single streamlined sequencing workflow enables concurrent analysis of both DNA and RNA targets. From sample extraction to clinical test report, the total workflow turnaround time is 4 days.
- **Clinical performance**—Based on Ion AmpliSeq™ technology, the test is designed to deliver robust and reproducible results for 23 genes clinically associated with NSCLC and one gene in CC, all from 10 ng of DNA and RNA from formalin-fixed, paraffin-embedded (FFPE) tissue.
- **An automated clinical report**—The Oncomine Dx Target Test results are presented in a single two-part clinical test report that incorporates companion diagnostic (CDx) biomarker results, with associated therapy indications, and other detected cancer-associated gene variant results.

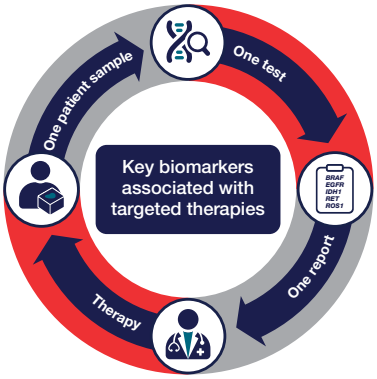


**Table 1. List of genes for therapeutic use.**

| Cancer type | Gene | Targeted therapies |
|---|---|---|
| NSCLC | *BRAF* | TAFINLAR® (dabrafenib) in combination with MEKINIST® (trametinib) |
| | *EGFR* L858R and exon 19 deletions | IRESSA® (gefitinib) |
| | *EGFR* exon 20 insertions | EXKIVITY™ (mobocertinib) |
| | | RYBREVANT™ (amivantamab-vmjw) |
| | *RET* | GAVRETO™ (pralsetinib) |
| | *ROS1* | XALKORI® (crizotinib) |
| CC | *IDH1* | TIBSOVO® (ivosidenib) |

# Complete system: from sample to actionable result, powered by proven Ion Torrent and Ion AmpliSeq NGS technology

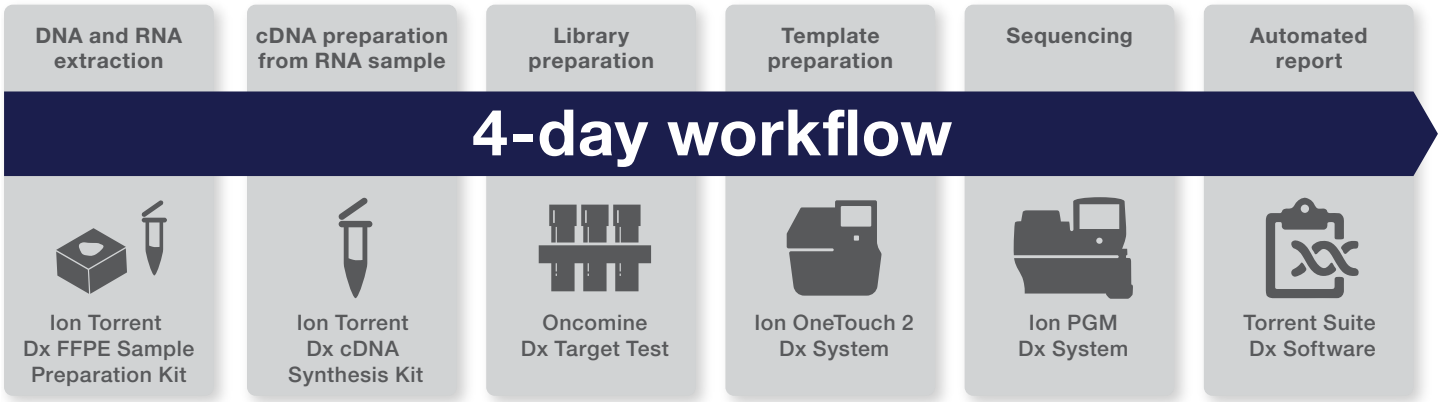


**Figure 1. The Oncomine Dx Target Test utilizes a single streamlined NGS workflow for detecting cancer-associated biomarkers, incorporating reagents, instrument systems, and bioinformatics.** The turnaround time, from FFPE sample to report, is 4 days.

## Optimized for challenging FFPE samples

Based on Ion AmpliSeq technology, the Oncomine Dx Target Test requires as little as 10 ng of input DNA and RNA. This enables analysis of small and challenging samples. Alternative NGS methods require more FFPE slides and hundreds of nanograms of DNA and RNA, making them less practical for routine analysis of FFPE tumor samples.

## Quality controls included

The Oncomine Dx Target Test incorporates DNA, RNA, and no-template controls for automatic assessment of run success.

## Ion PGM Dx Sequencer

Targeted sequencing is performed on an Ion PGM™ Dx Sequencer using an Ion 318™ Dx Chip, which can accommodate up to 5.5 million reads and 6 patient samples per run (barcode adapters for multiplexing included). Run setup is fast with an easy user interface, and sequencing run time is approximately 4.5 hours. Data analysis and reporting are fully automated and streamlined using Torrent Suite™ Dx Software v5.12.5 or later.

## A complete and flexible system

The Oncomine Dx Target Test is used in conjunction with the Ion PGM Dx sequencing system, which includes a complete NGS system of instruments, reagents, and software, initially validated using challenging germline variants and now validated with the Oncomine Dx Target Test for somatic mutation reporting for FFPE samples. The Ion PGM Dx sequencing system is a Class II 510K Medical Device and incorporates combined functionality, with both “IVD Mode” for molecular diagnostic tests and “Assay Development Mode” for clinical research. The system also facilitates 21 CFR Part 11 compliance, role-based workflows, sample and reagent tracking, QC metrics, and audit trails.

# Oncomine Dx Target Test for NSCLC

## Oncomine Dx Target Test—content

The Oncomine Dx Target Test includes targets for cancer-associated genes that play an important role in NSCLC pathogenesis. Five of them are indicated to aid in selecting patients for approved targeted therapies, while others are currently being investigated in clinical trials and are potentially actionable as referenced in Table 2. The Oncomine Dx Target Test is intended as a companion diagnostic to aid in selecting NSCLC patients for treatment with the six targeted therapies listed in Table 3, in accordance with the approved therapeutic product labeling. See the **Drugs@FDA Database**.

**Table 2. Complete list of gene targets for NSCLC.**

| Gene targets for therapeutic use | | | | |
|---|---|---|---|---|
| *BRAF*: V600E | *EGFR*: L858R, exon 19 deletions, and exon 20 insertions | | *ROS1*: fusions | *RET*: fusions |
| **Analytically validated targets** | | | | |
| | *KRAS* | *MET** | *PIK3CA* | |
| **Additional targets**** | | | | |
| *AKT1* | *ERBB2* | *HRAS* | *MTOR* | *RET* |
| *ALK** | *ERBB3* | *KIT* | *NRAS* | *ROS1* |
| *CDK4* | *FGFR2* | *MAP2K1* | *PDGFRA* | |
| *DDR2* | *FGFR3* | *MAP2K2* | *RAF1* | |

* The test reports fusion/translocation variants for *ROS1* and *RET* only. The test only reports mutations for *ALK and MET*.
** Performance for the additional gene target variants has been validated based on a representative method.

**Table 3. Companion diagnostic biomarkers and their respective therapies.**

| Gene | Variant status | Targeted therapies |
|---|---|---|
| ***BRAF*** | *BRAF* V600E | TAFINLAR® (dabrafenib) in combination with MEKINIST® (trametinib) |
| ***EGFR*** | *EGFR* L858R, exon 19 deletions | IRESSA® (gefitinib) |
| | *EGFR* exon 20 insertions | EXKIVITY™ (mobocertinib)<br>RYBREVANT™ (amivantamab-vmjw) |
| ***RET*** | *RET* fusions | GAVRETO™ (pralsetinib) |
| ***ROS1*** | *ROS1* fusions | XALKORI® (crizotinib) |

Method comparison studies evaluated the accuracy of the Oncomine Dx Target Test for the detection of *BRAF* V600E, *EGFR* exon 19 deletions, *EGFR* L858R, *EGFR* exon 20 insertions, *ROS1* fusions, and *RET* fusions, using a *BRAF* V600E qPCR assay, the *therascreen*™ *EGFR* PCR kit, a *ROS1* fluorescence *in situ* hybridization (FISH) assay, and validated NGS assays, respectively. A summary of the concordance studies' results is included in Table 4. For details, see the Oncomine Dx Target Test User Guide.

## Validation of performance for additional gene targets

The Oncomine Dx Target Test also detects DNA sequence variations in an additional 19 genes (approximately 343 targets) that are clinically associated with NSCLC. The variants for *KRAS*, *MET*, and *PIK3CA* have been analytically validated. Performance of all other variants identified by the test, other than clinically validated therapeutic variants and analytically validated variants, has not been directly demonstrated and has been validated based on a representative method.

**Table 4. Concordance between the Oncomine Dx Target Test and reference methods for companion diagnostic biomarkers.**

| Variants for therapy selection | Validated comparator methods | Excluding no-calls or unknowns* | | | Including no-calls or unknowns* | | |
|---|---|---|---|---|---|---|---|
| | | Positive percent agreement | Negative percent agreement | Overall percent agreement | Positive percent agreement | Negative percent agreement | Overall percent agreement |
| ***BRAF* V600E** | *BRAF* V600E qPCR test | 100% (67/67) | 100% (114/114) | 100% (181/181) | 91.8% (67/73) | 97.4% (114/117) | 95.3% (181/190) |
| ***EGFR*** ** | *therascreen*™ *EGFR* PCR kit | 98.6% (71/72) | 99.2% (120/121) | 99.0% (191/193) | 81.6% (71/87) | 96.8% (120/124) | 90.5% (191/211) |
| ***EGFR* exon 19 deletions** | | 97.6% (41/42) | 99.3% (147/148) | 99.0% (188/190) | 74.6% (41/55) | 94.2% (147/156) | 89.1% (188/211) |
| ***EGFR* exon 21 L858R** | | 100% (30/30) | 100% (167/167) | 100% (197/197) | 93.8% (30/32) | 93.3% (167/179) | 93.4% (197/211) |
| ***EGFR* exon 20 insertions** | NGS assay 1 | 100% (54/54) | 100% (95/95) | 100% (149/149) | 98.2% (54/55) | 90.5% (95/105) | 93.1% (149/160) |
| | NGS assay 2 | 100% (46/46) | 100% (63/63) | 100% (109/109) | 97.9% (46/47) | 91.3% (63/69) | 94.0% (109/116) |
| ***ROS1* fusions** | *ROS1* FISH test | 100% (9/9) | 100% (62/62) | 100% (71/71) | 90.0% (9/10) | 88.6% (62/70) | 88.8% (71/80) |
| ***RET* fusions** | NGS assay | 90.9% (40/44) | 91.8% (101/110) | 91.6% (141/154) | 90.9% (40/44) | 91.8% (101/110) | 91.6% (141/154) |

* No-calls are for DNA variants and unknowns are for RNA fusions.

** *EGFR* exon 19 deletions and exon 21 L858R combined.

# Oncomine Dx Target Test performance for NSCLC

## Accuracy study

To evaluate the ability of the Oncomine Dx Target Test DNA and RNA panels to identify somatic variants in human specimens, 290 FFPE tumor samples were analyzed using the Oncomine Dx Target Test to demonstrate positive percent agreement (PPA), negative percent agreement (NPA), and overall percent agreement (OPA) concordance with validated reference detection methods. The following reference detection methods were used:

- Validated NGS method to detect single-nucleotide variants (SNVs) and deletion hotspot variants
- Validated *ROS1* FISH test to detect *ROS1* fusions

The study demonstrated a variant level PPA of 98.5%, NPA of 100%, and OPA of 100%, excluding invalids and no-calls; and a PPA level of 98.5%, NPA of 96.8%, and OPA of 96.8% including no-calls. A summary of the data is included in Table 5. For details, see the User Manual.

## Establishment of limit of detection

Four limit of detection (LoD) studies were performed to evaluate DNA variants, *ROS1* fusions, *RET* fusions, and *EGFR* exon 20 insertions.

**Study I:** The LoD was evaluated for 14 representative DNA variants representing 3 variant categories detected by the Oncomine Dx Target Test. The LoD is the lowest allele frequency of SNVs, multi-nucleotide polymorphisms (MNPs), or deletion variants that can be detected at least 95% of the time. The study demonstrated that the Oncomine Dx Target Test can detect DNA variants with 6–8% allele frequencies.

**Study II:** The LoD was calculated for 2 clinical *ROS1* RNA fusion isoforms using the updated RNA library preparation workflow, and determined at 516 fusion reads.

**Study III:** The LoD was calculated for 2 clinical *RET* fusion isoforms using the updated RNA library preparation workflow, and determined at 405 fusion reads.

**Study IV:** The LoD was calculated for 2 clinical *EGFR* exon 20 insertion–positive samples, and determined to be 4.8–5.2% allele frequencies.

## Assay reproducibility study

Four reproducibility studies were performed to evaluate DNA variants, *ROS1* fusions, *RET* fusions, and *EGFR* exon 20 insertions.

**Study I:** The reproducibility and repeatability of the Oncomine Dx Target Test was evaluated for 30 representative variants from 18 DNA samples. The study was designed to evaluate within-run precision performance (repeatability) and variability across sites, operators, and instruments (reproducibility). Due to the large number of variants detected by the test and the rarity of some of the variants, a representative variant approach was used. Variants were selected in the following categories:

- Simple SNVs
- Complex SNVs and MNPs, including SNVs in di- or tri-nucleotide repeat regions and SNVs in high-GC (>60%) or low-GC (<40%) content regions
- Deletions (including deletions of 6, 9, 15, and 18 bp)

Excluding no-calls, the percent of correct calls was >96%. The estimate of repeatability at each DNA variant location across all the samples was ≥98.8% (95% CI lower limit of ≥97.5%). A summary of the results of Study I is included in Table 6. For details, see the User Manual.

**Table 5. A summary of the variant level accuracy study results.**

| Variant level measure of agreement | Percent agreement excluding no-calls | Percent agreement including no-calls |
|---|---|---|
| Positive percent agreement | 98.5% (195/198) | 98.5% (195/198) |
| Negative percent agreement | 100.0% (118,155/118,159) | 96.8% (118,155/122,012) |
| Overall percent agreement | 100.0% (118,350/118,357) | 96.8% (118,350/122,210) |

**Table 6. Study I—assay reproducibility study results.**

| Description | No. of variants | Call rate excluding no-calls | | Call rate including no-calls | |
|---|---|---|---|---|---|
| | | Mean | Median | Mean | Median |
| **DNA positive variants (positive calls)** | 46 | 96.60% | 97.10% | 94.50% | 95.80% |
| **WT DNA variant locations (negative calls)** | 872 | 96.10% | 95.00% | 96.10% | 95.00% |

**Study II:** An additional study was performed to evaluate the reproducibility and repeatability of the Oncomine Dx Target Test for 6 representative variants from 11 DNA samples and 4 RNA samples. One wild-type (WT) DNA sample and 4 WT RNA samples were included in the study.

The study was designed to evaluate within-run precision performance (repeatability) and variability across sites, operators, and instrument platforms (reproducibility). The updated RNA library preparation workflow was used. Due to the large number of variants detected by the test and the rarity of some variants, a representative variant approach was used. Variants were selected in the following categories:

- 15 bp deletion
- Simple SNVs
- Complex SNVs and MNPs
- Fusions

Excluding no-calls, the estimate of repeatability at each DNA variant location across all the samples was ≥94.4% (95% CI lower limit of ≥72.7%). The estimate of repeatability at each RNA clinical variant location was 100%. A summary of the reproducibility results of Study II is included in Tables 7 and 8.

**Study III:** An additional study was performed to evaluate the reproducibility and repeatability of the Oncomine Dx Target Test for 4 *RET* fusion–positive samples and 2 *RET* fusion–negative samples.

The study was designed to evaluate within-run precision performance (repeatability) and variability across sites, operators, and instrument platforms (reproducibility). The updated RNA library preparation workflow was used.

Excluding unknowns, estimates of the repeatability ranged from 98.1–100% for two *RET* variants. A summary of the reproducibility results of Study III is included in Table 9.

**Study IV:** A study was performed to evaluate the reproducibility and repeatability of the Oncomine Dx Target Test for detection of *EGFR* exon 20 insertion variants using FFPE DNA from 2 *EGFR* variant–positive samples (blended with WT clinical samples) and 2 *EGFR* variant–negative (WT) samples.

The study was designed to evaluate within-run precision performance (repeatability) and variability across sites, operators, and instrument platforms (reproducibility).

Excluding no-calls, estimates of the repeatability is 100% for both *EGFR* exon 20 insertion variants. A summary of the reproducibility results of Study IV is included in Table 10.

**Table 7. Study II—assay reproducibility study results (DNA variants).**

| Description | No. of variants | Call rate excluding no-calls | | Call rate including no-calls | |
|---|---|---|---|---|---|
| | | Mean | Median | Mean | Median |
| DNA positive variants (positive calls) | 11 | 99% | 100% | 98% | 99% |
| WT DNA variant locations (negative calls) | 367 | 100% | 100% | 99% | 100% |

**Table 8. Study II—assay reproducibility study results (*ROS1* fusions).**

| Description | No. of variants | Call rate including or excluding unknowns | |
|---|---|---|---|
| | | Mean | Median |
| *ROS1* positive variants (positive calls) | 4 | 100% | 100% |
| WT RNA variant locations (negative calls) | 4 | 99% | 100% |

**Table 9. Study III—assay reproducibility study results (*RET* fusions).**

| Description | No. of variants | Call rate including or excluding unknowns | |
|---|---|---|---|
| | | Mean | Median |
| *RET* positive variants (positive calls) | 4 | 100% | 100% |
| WT RNA variant locations (negative calls) | 2 | 99% | 100% |

**Table 10. Study IV—assay reproducibility study results (*EGFR* exon 20 insertions).**

| Description | No. of variants | Call rate excluding no-calls | | Call rate including no-calls | |
|---|---|---|---|---|---|
| | | Mean | Median | Mean | Median |
| *EGFR* insertion positive variants (positive call) | 2 | 100% | 100% | 100% | 100% |
| WT DNA variant locations (negative calls) | 2 | 100% | 100% | 100% | 100% |

# Oncomine Dx Target Test report for NSCLC

The clinical test report for the Oncomine Dx Target Test is automatically generated as a PDF and incorporates relevant patient, sample, and test information required to help ensure high performance standards, and to assist with regulatory compliance and quality control (Figure 2). The test results are presented in two parts: companion diagnostic biomarker results with associated therapy indications, and analytically detected NSCLC-associated biomarker results in a separate section. The report is laboratory information management system (LIMS)–compatible and customizable for sample details.

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www.testlabs.com

**Clinical Test Report: Oncomine™ Dx Target Test US**

Patient ID: Date Of Birth:

**Sample Details**

| | | | |
|---|---|---|---|
| Cancer Type: | **Non-small Cell Lung Cancer** | Ordering Physician: | Sample Type: |
| Accession Number: | | Physician Org: | Sample ID: |
| Patient ID: | | Physician Phone: | Collection Date: |
| Gender: | | Physician Fax: | Receive Time: |
| Date Of Birth: | | Pathologist: | %Cellularity: |
| Sample Condition: | | Pathology Lab Org: | Sample Source: |
| MRN: | | Pathology Lab Phone: | Reference Interval: |
| | | Pathology Lab Fax: | % Necrosis: |

**Results for Sequence Variations for Therapeutic Use (For illustrative purposes only. *EGFR*, *BRAF*, *ROS1*, and *RET* are mutually exclusive.)**

DNA Sequence Variants

| Gene | Display Name | Amino Acid Change | Nucleotide Change | Test Result | Hotspot ID | Associated Therapy |
|---|---|---|---|---|---|---|
| *EGFR* | *EGFR* L858R | p.Leu858Arg | c.2573T>G | **POSITIVE** | COSM6224 | IRESSA® (gefitinib) |
| *BRAF* | *BRAF* V600E | p.Val600Glu | c.1799T>A | **POSITIVE** | COSM476 | TAFINLAR®+MEKINIST® (dabrafenib in combination with trametinib) |
| *EGFR* | *EGFR* exon 20 insertions | p.Ala767_Ser768insSerValAsp | c.2311_2312insGCGTGGACA | **POSITIVE** | COSM13428 | EXKIVITY™ (mobocertinib) RYBREVANT™ (amivantamab-vmjw) |

Gene Fusions

| Gene | Display Name | Test Result | Associated Therapy |
|---|---|---|---|
| *ROS1* | *ROS1* Fusions | **POSITIVE** | XALKORI® (crizotinib) |
| *RET* | *RET* Fusions | **POSITIVE** | GAVRETO™ (pralsetinib) |

**Results for Analytical Sequence Variations Detected**

DNA Sequence Variants Detected

No DNA sequence variations detected

| | | | | |
|---|---|---|---|---|
| *MET* | p.His1112Arg | c.3335A>G | **NEGATIVE** | COSM703 |
| *KRAS* | p.Ala146Pro | c.436G>C | **NEGATIVE** | COSM19905 |
| *FGFR2* | p.Lys659Asn | c.1977G>T | **NO CALL** | COSM49173 |
| *AKT1* | p.Glu17Lys | c.49G>A | **NEGATIVE** | COSM33765 |
| ..... | | | | |

The Oncomine Dx Target Test assay definition file includes prevalent RET isoforms, but not all rare or newly identified RET isoforms. The Oncomine Dx Target Test may miss a subset of patients carrying rare or newly identified RET isoforms who may derive benefit from GAVRETO (pralsetinib).

For additional questions on no call results please contact testing service laboratory.

The safe and effective use of the variants reported in the Analytical Sequence Variations Detected section has not been established for selecting therapy using this device.The variants for KRAS(COSM512/p.Gly12Phe/c.34_35delGGinsTT and COSM516/p.Gly12Cys/c.34G>T), MET (COSM707/ p.Thr1010Ile/c.3029C>T) and PIK3CA (COSM754/p.Asn345Lys/c.1035T>A) have been analytically validated. Performance of all other variants identified by the test, other than clinically validated therapeutic variants and analytically validated variants has not been directly demonstrated.

**Lab Director: Max Smith** **CLIA number: 03C1021009**

Report generated by Life Technologues PGM Dx Torrent Suite Software v5.5.15
For In Vitro Diagnostic Use.

ion torrent
by Thermo Fisher Scientific

1

**Section 1.** Includes the patient ID, date of birth, date of the report, and specifics such as the cancer type, sample type, and quality, source, and pathologic characteristics customizable by the laboratory.

2

**Section 2.** Includes results of the companion diagnostic markers, with associated therapy indications. For illustrative purposes only. *EGFR*, *BRAF*, *ROS1*, and *RET* are mutually exclusive.

3

**Section 3.** Contains results of the additional analytically detected DNA biomarkers—for illustrative purposes, only a few rows are shown. The real report will, however, contain results of all remaining over 300 variants detectable by the test, and will therefore be several pages long.

**Figure 2. Example of an Oncomine Dx Target Test report for NSCLC.**

# Oncomine Dx Target Test for CC

## Oncomine Dx Target Test—content

The Oncomine Dx Target Test includes a target for *IDH1* R132 mutations as a companion diagnostic to aid in selecting CC patients for TIBSOVO® (ivosidenib), in accordance with the approved therapeutic product labeling, referenced in Table 11. See the **Drugs@FDA Database**.

### Table 11. Gene targets for CC.

| | Gene targets | Targeted therapy |
|---|---|---|
| **List of gene targets for therapeutic use** | *IDH1* R132C<br>*IDH1* R132G<br>*IDH1* R132H<br>*IDH1* R132L<br>*IDH1* R132S | TIBSOVO® (ivosidenib) |

### Establishment of limit of detection

The limit of detection (LoD) was evaluated for 5 *IDH1* R132 variants detected by the Oncomine Dx Target Test. The LoD is the lowest allele frequency of SNVs that can be detected at least 95% of the time. The study demonstrated the LoD of the 5 *IDH1* R132 variants ranged from 4.5–5.7% allele frequencies, including 4.5% for R132C, 5.7% for R132G, 4.9% for R132H, 5.1% for R132L, and 5.3% for R132S.

### Assay reproducibility study

The reproducibility and repeatability of *IDH1* R132 variant detection using the Oncomine Dx Target Test were assessed with 1 *IDH1* WT sample and 3 *IDH1* R132 variant–positive samples at two allelic frequency (AF) levels. Testing was performed at 4 testing sites using 4 lots of reagents, and each site had 2 PGM Dx instrument systems and 2 operators. The overall positive call rate for *IDH1* R132 variants was 92.6% when including no calls and 97.1% when excluding no calls. The negative call rate for *IDH1* WT sample was 100% at all *IDH1* R132 variant locations (Table 12).

### Clinical study

To evaluate the ability of the Oncomine Dx Target Test to identify 5 *IDH1* biomarkers in FFPE CC tumor specimens, 168 specimens from patients that tested positive and 181 specimens that tested negative using the Sanger assay were tested using the Oncomine Dx Target Test to demonstrate PPA, NPA, and OPA concordance with the Sanger assay as a validated reference detection method.

The study demonstrated PPA of 99.4%, NPA of 96.5%, and OPA of 97.9%, excluding invalids and no calls; and PPA of 97.0%, NPA of 90.6%, and OPA of 93.7%, including no calls. A summary of the data is included in Table 13. For details, see the User Manual.

# Oncomine Dx Target Test for CC

Table 12. Reproducibility results.

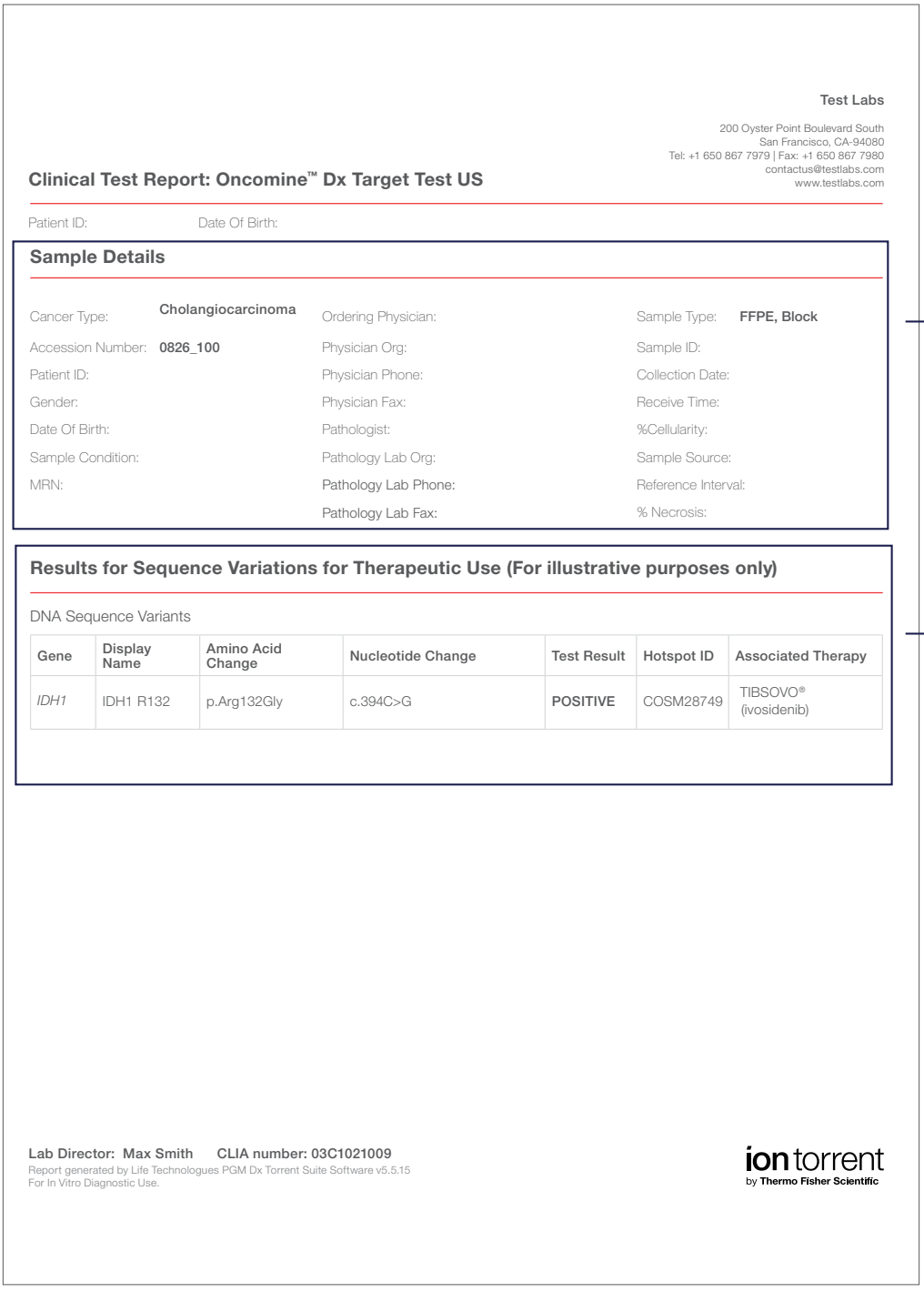
| Sample COSMIC ID, variant | No. of valid sample results | Call rate (95% CI) | |
|---|---|---|---|
| | | Including no calls | Excluding no calls |
| **D1**<br>**COSM28747, R132C** | 36 | 100%<br>(90.3%, 100%) | 100%<br>(90.3%, 100%) |
| **D2**<br>**COSM28747, R132C** | 36 | 97.2%<br>(85.5%, 99.9%) | 100%<br>(90.0%, 100%) |
| **D3**<br>**COSM28749, R132G** | 36 | 100%<br>(90.3%, 100%) | 100%<br>(90.3%, 100%) |
| **D4**<br>**COSM28749, R132G** | 36 | 100%<br>(90.3%, 100%) | 100%<br>(90.3%, 100%) |
| **D5**<br>**COSM28750, R132L** | 36 | 100%<br>(90.3%, 100%) | 100%<br>(90.3%, 100%) |
| **D6**<br>**COSM28750, R132L** | 35 | 57.1%<br>(39.4%, 73.7%) | 76.9%<br>(56.4%, 91.0%) |
| **D1-D6**<br>**All variants, R132** | 215 | 92.6%<br>(88.2%, 95.7%) | 97.1%<br>(93.7%, 98.9%) |
| **D7**<br>**Wild-type** | 36 | 100%<br>(90.3%, 100%) | 100%<br>(90.3%, 100%) |

Table 13. Concordance between the Oncomine Dx Target Test and a reference method for *IDH1* R132 mutations.

| Variant for therapy selection | Validated comparator method | Excluding invalid results and no-calls | | | Including invalid results and no-calls | | |
|---|---|---|---|---|---|---|---|
| | | Positive percent agreement | Negative percent agreement | Overall percent agreement | Positive percent agreement | Negative percent agreement | Overall percent agreement |
| *IDH1* R132 | Sanger assay | 99.4%<br>(163/164) | 96.5%<br>(164/170) | 97.9%<br>(327/334) | 97.0%<br>(163/168) | 90.6%<br>(164/181) | 93.7%<br>(327/349) |

# Oncomine Dx Target Test report for CC

The clinical test report for the Oncomine Dx Target Test is automatically generated as a PDF and incorporates relevant patient, sample, and test information required to help ensure high performance standards, and to assist with regulatory compliance and quality control (Figure 3). The test results are presented in two parts: companion diagnostic biomarker results with associated therapy indications and analytically detected biomarker results in a separate section. The report is LIMS-compatible and customizable for sample details.



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**Clinical Test Report: Oncomine™ Dx Target Test US**

Patient ID: Date Of Birth:

**Sample Details**

| | | | | | |
|---|---|---|---|---|---|
| Cancer Type: | **Cholangiocarcinoma** | Ordering Physician: | | Sample Type: | **FFPE, Block** |
| Accession Number: | **0826_100** | Physician Org: | | Sample ID: | |
| Patient ID: | | Physician Phone: | | Collection Date: | |
| Gender: | | Physician Fax: | | Receive Time: | |
| Date Of Birth: | | Pathologist: | | %Cellularity: | |
| Sample Condition: | | Pathology Lab Org: | | Sample Source: | |
| MRN: | | Pathology Lab Phone: | | Reference Interval: | |
| | | Pathology Lab Fax: | | % Necrosis: | |

**Results for Sequence Variations for Therapeutic Use (For illustrative purposes only)**

DNA Sequence Variants

| Gene | Display Name | Amino Acid Change | Nucleotide Change | Test Result | Hotspot ID | Associated Therapy |
|---|---|---|---|---|---|---|
| *IDH1* | IDH1 R132 | p.Arg132Gly | c.394C>G | **POSITIVE** | COSM28749 | TIBSOVO® (ivosidenib) |

**Lab Director: Max Smith** **CLIA number: 03C1021009**

Report generated by Life Technologues PGM Dx Torrent Suite Software v5.5.15
For In Vitro Diagnostic Use.

ion torrent by Thermo Fisher Scientific

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**Section 1.** Includes the patient ID, date of birth, date of the report, and specifics such as the cancer type, sample type, and quality, source, and pathologic characteristics customizable by the lab.

2

**Section 2.** Includes results of the companion diagnostic markers, with associated therapy indications.

**Figure 3. Example of an Oncomine Dx Target Test report for CC.**

## Ordering information

| Product | Cat. No. |
|---|---|
| **Oncomine Dx Target Test, which includes:** | **A51695** |
| Ion Torrent Dx FFPE Sample Preparation Kit | A32445 |
| Oncomine Dx Target Test, Controls, and Diluent Kit | A49756 |
| Ion PGM Dx Library Kit | A49758 |
| Ion PGM Dx OneTouch Template Kit | A49759 |
| Ion PGM Dx Sequencing Kit | A49760 |
| Ion PGM Dx 318 Chip Kit | A18937 |
| Oncomine Dx Target Test User Guides and Assay Definition File | A51694 |
| **Ion PGM Dx Instrument System includes:** | **A25511** |
| Ion PGM Dx Sequencer | |
| Ion OneTouch Dx Instrument | |
| Ion PGM Dx System Installation and Training Kit | |
| Ion PGM Dx Chip Minifuge | |
| Ion PGM Wireless Scanner | |
| Ion Torrent Server with Ion PGM Dx Software Pack v5.12.5<br>(Torrent Suite Dx Software v5.12.5 and Torrent Suite Assay Development Software v5.12.5) | |

Learn more at **thermofisher.com/oncomine-dxtarget**



**Abbreviated Intended Use:** The Oncomine Dx Target Test is a qualitative *in vitro* diagnostic test that uses targeted high-throughput, parallel-sequencing technology to detect single-nucleotide variants (SNVs) and deletions, and insertions in 23 genes from DNA and fusions in *ROS1* and *RET* from RNA isolated from formalin-fixed, paraffin-embedded (FFPE) tumor tissue samples from patients with non–small cell lung cancer (NSCLC) and *IDH1* R132 mutations from FFPE tumor tissue samples from patients with cholangiocarcinoma (CC), using the Ion PGM Dx System (MAN0018948).