Liquid Biopsy: Clinical Overview

FoundationOne® Liquid CDx

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VP, Medical Affairs
9 Dec 20
Disclosure Information

The speaker is an employee of Foundation Medicine.
The information contained in this presentation is made for the purpose of general education regarding cancer genomics and diagnostic testing, personalized cancer care, genomic research, and other general information concerning Foundation Medicine testing. Nothing contained in this presentation is intended to constitute medical advice, instruction for medical diagnosis, or instruction for treatment.

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Please direct all therapy-related questions to the associated pharmaceutical company. Foundation Medicine can only answer questions about our companion diagnostic tests.
Each Person’s Cancer is Unique
A Complex Treatment Paradigm

Number of targeted oncology therapy indications and approvals in oncology is growing rapidly.

As of April 2020

90+ FDA-approved Targeted Therapies in over 25 cancer types

Recent approvals and label expansions:
- capmatinib
- pemigatinib
- selpercatinib
- olaparib
- rucaparib


*Recent approvals and label expansions
Cancer Treatment Options Have Increased In Recent Decades

Development of targeted therapies has advanced therapeutic strategies from conventional chemo- and radiation-based therapy to molecularly-guided therapy.

- Radiotherapy
- Chemotherapy
- First targeted therapy approved
- First immuno-therapy approved
- Personalized combination therapies

1920  1940  1998  2010  Present

‘One-drug-fits-all’ treatment approach based on cancer histology

Personalised treatment based on comprehensive knowledge of patients’ cancer

Use of NGS to detect mutations in tumors

Sample preparation
DNA is extracted from a biopsy (blood samples might also be used depending on the type of test)

DNA optimization and sequencing
Raw sequencing data identifies 1000s of mutations, not all of which are clinically relevant

Computational biology analysis
Extensive analysis narrows down to the mutations that are most meaningful and relevant to treatment

Clinical report
The analysis is interpreted and a comprehensive report is sent to the physician
BENEFITS OF CGP

CGP opens doors to the innovative treatments of today & tomorrow

Identifies patients who may benefit from targeted therapies, and provides important negative results

Targeted Therapies
Immunotherapies

Clinical Trials

Treatment Plan
Confirmation +
Therapy Avoidance
BENEFITS OF CGP

Supports treatment planning for advanced cancer patients at any line of therapy

First Line

- Develop treatment plan
- Prevent contraindicated therapies
- Avoid trial-and-error treatments
- Helps inform prognosis

Progression/Relapse

- Guide next steps in treatment plan
- Uncover resistance mutations or new alterations
- Predict response to immunotherapies

Refractory

- Investigate clinical trial options
- Explore tumor-agnostic genomically-driven therapies
- Obtain peace of mind further options have been explored

## Our Comprehensive Product Portfolio

Facilitates a precision medicine approach for a broad spectrum of patients in a clinically relevant timeframe

<table>
<thead>
<tr>
<th></th>
<th>FoundationOne®CDx</th>
<th>FoundationOne®Liquid CDx*</th>
<th>FoundationOne®Heme</th>
<th>IHC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FDA-Approved</strong></td>
<td>FDA-approved CDx for 24 targeted therapies</td>
<td>FDA-approved CDx for 7 targeted therapies</td>
<td>Laboratory developed test Not FDA-approved</td>
<td>FDA-approved CDx for 2 immunotherapies</td>
</tr>
<tr>
<td><strong>Target Tumor Types</strong></td>
<td>All Solid Tumors</td>
<td>Liquid Biopsy (ctDNA) for All Solid Tumors</td>
<td>Hematologic Malignancies Sarcomas (Soft Tissue + Bone)</td>
<td>Specific Solid Tumors</td>
</tr>
<tr>
<td><strong>Number of Genes Analyzed</strong></td>
<td>324 (DNA)</td>
<td>&gt;300 (DNA)*</td>
<td>406 (DNA) 265 (RNA)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Genomic Signatures/Biomarkers</strong></td>
<td>Tumor Mutational Burden (TMB) Microsatellite Instability (MSI) Loss of Heterozygosity (LOH)*</td>
<td>Blood Tumor Mutational Burden (bTMB)* Microsatellite Instability (MSI)* Tumor Fraction*</td>
<td>Tumor Mutational Burden (TMB) Microsatellite Instability (MSI)</td>
<td>PD-L1</td>
</tr>
<tr>
<td><strong>Specimen Requirements</strong></td>
<td>FFPE Tissue</td>
<td>Peripheral Whole Blood</td>
<td>FFPE Tissue Bone Marrow Aspirate Peripheral Whole Blood</td>
<td>FFPE Tissue</td>
</tr>
<tr>
<td>10 USS or 1 Block† 1 + 1 H&amp;E slide</td>
<td>2 Tubes of Peripheral Whole Blood</td>
<td>16 USS + 1 H&amp;E slide or 1 FFPE Block or 2.5mL Bone Marrow Aspirate or 1 Filled EDTA tube + 2.5mL Paxgene Tube of Peripheral Whole Blood</td>
<td>4 USS</td>
<td></td>
</tr>
<tr>
<td><strong>Report Features</strong></td>
<td>Point mutations, insertions/deletions, copy number alterations, select rearrangements</td>
<td>Point mutations, insertions/deletions, copy number alterations (amplifications and select deletions), and rearrangements*</td>
<td>Point mutations, insertions/deletions, copy number alterations, rearrangements</td>
<td>Dako 22C3 (CPS/TPS) or Ventana SP-142 (TC/IC) for approved/validated tumor types</td>
</tr>
<tr>
<td><strong>Typical Turnaround Time</strong></td>
<td>&lt;2 weeks</td>
<td>&lt;2 weeks</td>
<td>2 weeks</td>
<td>5 days</td>
</tr>
</tbody>
</table>

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*ctDNA = circulating tumor DNA, H&E = hematoxylin and eosin, IHC = immunohistochemistry, USS = unstained slides.
†For ovarian cancer only.
*FoundationOne®Liquid CDx is FDA-approved to report substitutions and indels in 311 genes, including rearrangements in four (4) genes and copy number alterations in three (3) genes. Comprehensive results across all 324 genes are reported as a laboratory professional service which is not reviewed or approved by the FDA. bTMB, MSI-H status, and tumor fraction are reported as a laboratory professional service which is not reviewed or approved by the FDA.
*MSI status will be reported for samples determined to have high microsatellite instability.
*For full details, refer to specimen instructions at [www.foundationmedicine.com](http://www.foundationmedicine.com).
†FFPE (formalin-fixed paraffin embedded) block is preferred.
*For FDA approved tests, reports contain FDA approved genomic results as well as additional information provided as a professional service that is not reviewed by the FDA.
*Based on typical turnaround time from receipt of specimen.
FoundationOne® CDx is an FDA-Approved Companion Diagnostic for the Following Indications

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Biomarker(s) Detected</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Small Cell Lung Cancer</td>
<td><strong>EGFR</strong> exon 19 deletions and <strong>EGFR</strong> exon 21 L858R alterations</td>
<td>Gilotrif® (afatinib), Iressa® (gefitinib), Tagrisso® (osimertinib), or Tarceva® (erlotinib)</td>
</tr>
<tr>
<td></td>
<td><strong>EGFR</strong> exon 20 T790M alterations</td>
<td>Tagrisso® (osimertinib)</td>
</tr>
<tr>
<td></td>
<td><strong>ALK</strong> rearrangements</td>
<td>Alecensa® (lectinib), Xalkori® (crizotinib), or Zykadia® (ceritinib)</td>
</tr>
<tr>
<td></td>
<td><strong>BRAFV600E</strong></td>
<td>Tafinlar® (dabrafenib) in combination with Mekinist® (trametinib)</td>
</tr>
<tr>
<td></td>
<td><strong>MET</strong> single nucleotide variants (SNVs) and indels that lead to <strong>MET</strong> exon 14 skipping</td>
<td>Tabrecta® (capmatinib) (May 2020*)</td>
</tr>
<tr>
<td>Melanoma</td>
<td><strong>BRAFV600E</strong></td>
<td>Tafinlar® (dabrafenib) or Zelboraf® (vemurafenib)</td>
</tr>
<tr>
<td></td>
<td><strong>BRAFV600E</strong> and V600K</td>
<td>Mekinist® (trametinib) or Cotellic® (cobimetinib) in combination with Zelboraf® (vemurafenib)</td>
</tr>
<tr>
<td>Breast Cancer</td>
<td><strong>ERBB2</strong> (HER2) amplification</td>
<td>Herceptin® (trastuzumab), Kadcyla® (ado-trastuzumab-emtansine), or Perjeta® (pertuzumab)</td>
</tr>
<tr>
<td></td>
<td><strong>PIK3CA</strong> C420R, E542K, E545A, E545D [1635G&gt;T only], E545G, E545K, Q546E, Q546R, H1047L, H1047R, and H1047Y alterations</td>
<td>Piqray® (alpelisib)</td>
</tr>
<tr>
<td>Colorectal Cancer</td>
<td><strong>KRAS</strong> wild-type (absence of mutations in codons 12 and 13)</td>
<td>Erbitux® (cetuximab)</td>
</tr>
<tr>
<td></td>
<td><strong>KRAS</strong> wild-type (absence of mutations in exons 2, 3, and 4), and <strong>NRAS</strong> wild type (absence of mutations in exons 2, 3, and 4)</td>
<td>Vectibix® (panitumumab)</td>
</tr>
<tr>
<td>Ovarian Cancer</td>
<td><strong>BRCA1/2</strong> alterations</td>
<td>Lynparza® (olaparib) or Rubraca® (rucaparib)</td>
</tr>
<tr>
<td>Cholangiocarcinoma</td>
<td><strong>FGFR2</strong> fusions and select rearrangements</td>
<td>Pemazyre® (pemigatinib) (April 2020*)</td>
</tr>
<tr>
<td>Solid tumors</td>
<td>Tumor mutational burden ≥ 10 mutations per megabase</td>
<td>Keytruda® (pembrolizumab) (June 2020*)</td>
</tr>
<tr>
<td></td>
<td><strong>NTRK1/2/3</strong> fusions</td>
<td>Vitrakvi® (larotrectinib) (October 2020*)</td>
</tr>
</tbody>
</table>
Save Valuable Time and Tissue

Number of Slides Required for Traditional Testing

<table>
<thead>
<tr>
<th>Test</th>
<th>Slides Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD-L1 expression</td>
<td>0-1</td>
</tr>
<tr>
<td>EGFR mutation</td>
<td>0-1</td>
</tr>
<tr>
<td>ALK rearrangements</td>
<td>0-1</td>
</tr>
<tr>
<td>ROS1 rearrangements</td>
<td>0-1</td>
</tr>
</tbody>
</table>

After the fourth driver is tested, almost 50% of patients will have run out of tissue¹,²

<table>
<thead>
<tr>
<th>Test</th>
<th>Slides Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAF V600E mutations</td>
<td>0-1</td>
</tr>
<tr>
<td>KRAS mutations</td>
<td>0-1</td>
</tr>
<tr>
<td>MET amplification</td>
<td>0-1</td>
</tr>
<tr>
<td>RET rearrangements</td>
<td>0-1</td>
</tr>
<tr>
<td>HER2 mutations</td>
<td>0-1</td>
</tr>
</tbody>
</table>

Total: 36 slides

FoundationOne®CDx

Comprehensive genomic profiling

Total: 10 slides total or 1 FFPE block
Typical turnaround time is <2 weeks from receipt of tissue

IHC testing for PD-L1
Optional add-on with additional 4 slides

OR

FoundationOne®Liquid CDx

Blood-based genomic profiling

Total: 2 8.5 mL tubes of peripheral whole blood
Typical turnaround time is <2 weeks from receipt of sample

Liquid Biopsy Testing at Foundation Medicine

Important and Growing Part of Our Product Portfolio

2016

Initial launch of FoundationACT, our first liquid biopsy product

2017

Presented validation data for blood TMB and started Phase 3 Blood-First Assay Screening Trial (BFAST) with Roche

Optimized performance of FoundationACT

2018

Launch of updated liquid biopsy, FoundationOne® Liquid, with expanded gene list panel and MSI-H status

Introduced “Automatic Reflex” option for failed tissue specimens to liquid

2019

Analytical and clinical validation of FoundationOne® Liquid CDx

FDA submission

2020

FoundationOne® Liquid CDx launched August 2020

FoundationOne CDx and FoundationOne Liquid CDx are the only FDA-approved in vitro diagnostic tests by Foundation Medicine. FoundationOne Liquid and FoundationAct were developed and their performance characteristics determined by Foundation Medicine. They have not been cleared or approved by the US FDA. For more information on our laboratory developed tests (LDTs) please see their respective Technical Specifications at www.foundationmedicine.com. TMB = tumor mutational burden, MSI-H = microsatellite instability high.
# FoundationOne® Liquid CDx Replaces and Expands Upon FoundationOne® Liquid

<table>
<thead>
<tr>
<th><strong>FoundationOne® Liquid CDx</strong></th>
<th><strong>FoundationOne® Liquid</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FDA Status</strong></td>
<td>FDA approved as CDx for 7 targeted therapies</td>
</tr>
<tr>
<td><strong>Target Tumor Types</strong></td>
<td>All Solid Tumors</td>
</tr>
<tr>
<td><strong>Number of Genes Analyzed</strong></td>
<td>&gt;300 (DNA)*</td>
</tr>
<tr>
<td><strong>Genomic Signatures / Biomarkers</strong></td>
<td>bTMB, MSI-High*, Tumor Fraction*</td>
</tr>
<tr>
<td><strong>Specimen</strong></td>
<td>Peripheral Whole Blood</td>
</tr>
<tr>
<td><strong>Report Features</strong></td>
<td>Point mutations, insertions/deletions, copy number alterations (amplifications and select losses) and rearrangements</td>
</tr>
<tr>
<td><strong>Turnaround Time (TAT)</strong></td>
<td>Typically within 2 weeks from receipt of specimen</td>
</tr>
</tbody>
</table>

*FoundationOne® Liquid CDx is FDA-approved to report substitutions and indels in 311 genes, including rearrangements in four (4) genes and copy number alterations in three (3) genes. Comprehensive results across all 324 genes are reported as a laboratory professional service which is not reviewed or approved by the FDA. bTMB, MSI-H status, and tumor fraction are reported as a laboratory professional service which is not reviewed or approved by the FDA.*

US-FLDX-2000120
## FoundationOne® Liquid CDx Enhancements Compared With FoundationOne® Liquid

| Increased coverage of key oncologic drivers* | • 324 genes* compared to 70 genes on previous test (FoundationOne® Liquid)  
• Alterations in 75 genes detected with increased sensitivity |
| New genomic signature added* | • Blood tumor mutational burden (bTMB) provides additional information for decision-making in patients who may be candidates for immunotherapy* |
| Extensive pre-approval evaluation, as FDA required for CDx approval | • Validation studies included >7,000 sample replicates involving >31,000 unique variants in >30 tumor types, representing all 324 genes targeted by the assay¹ |

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FoundationOne® Liquid CDx and FoundationOne® CDx: Complementary Options for Comprehensive Genomic Profiling
# Complementary FDA-Approved Genomic Profiling Tests for Blood and Tissue Across All Solid Tumors

<table>
<thead>
<tr>
<th></th>
<th><strong>FoundationOne® Liquid CDx</strong></th>
<th><strong>FoundationOne® CDx</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FDA-Approved</strong></td>
<td>FDA approved CDx for 7 targeted therapies</td>
<td>FDA approved CDx for 24 targeted therapies</td>
</tr>
<tr>
<td><strong>Target Tumor Types</strong></td>
<td>All Solid Tumors</td>
<td></td>
</tr>
<tr>
<td><strong>Number of Genes Analyzed</strong></td>
<td>&gt;300 (DNA)*</td>
<td>324 (DNA)</td>
</tr>
<tr>
<td><strong>Genomic Signatures / Biomarkers</strong></td>
<td>bTMB, MSI-High®, Tumor Fraction*</td>
<td>TMB, MSI, LOH**</td>
</tr>
<tr>
<td><strong>Specimen</strong></td>
<td>Peripheral Whole Blood</td>
<td>FFPE Tissue</td>
</tr>
<tr>
<td><strong>Variant Types Identified</strong></td>
<td>Point mutations, insertions/deletions, copy number alterations (amplifications and select losses) and rearrangements</td>
<td>Point mutations, insertions/deletions, copy number alterations and rearrangements</td>
</tr>
<tr>
<td><strong>Turnaround Time</strong></td>
<td>Typically within 2 weeks from receipt of specimen</td>
<td></td>
</tr>
</tbody>
</table>

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Considerations for the Use of ctDNA in Genomic Profiling

ctDNA is tumor-derived, fragmented DNA released by cell death (apoptosis/necrosis) that circulates in the bloodstream\(^1,3\).

>75% of advanced cancer cases have ctDNA\(^3,4\).

In metastatic disease, ctDNA can potentially capture genomic alterations found at more than one tumor site\(^3\).

Factors impacting the amount of ctDNA shed by tumors include:\(^1\)
- Tumor burden (amount and location)
- Tumor type
- Timing and type of last therapy

Tumor content in blood may be less than 1% of total cell free DNA in plasma, compared to ~20-40% tumor DNA in a biopsy specimen\(^2\).

ctDNA usually represents a small fraction of the cell-free DNA found in the bloodstream\(^2\).

Somatic ctDNA alterations were detected in 85% of patients (n=21,807) across all cancer types.

Alteration-positive samples had average of 3-4 alterations including copy number amplifications.

CRC had the highest average ctDNA fraction while pancreas, renal, and glioblastoma had the lowest.
ctDNA was analyzed in 640 patients with a range of solid tumors

cDNA levels increased with stage of cancer and tumor burden
- ctDNA was detectable in 55% of patients with localized disease (stages I-III)
- ctDNA was detectable in >80% of patients with metastatic disease (stage IV)

cDNA may be particularly useful in tumors such as prostate and breast that tend to metastasize to bone, which can be challenging to biopsy

ctDNA = circulating tumor DNA
New clones may:
Carry subclonal genomic alterations with differing implications for treatment, for example, targeted therapy resistance
Seed in areas that are easier or more difficult to biopsy, for example, liver vs bone

By capturing shed tumor DNA, ctDNA has the potential to capture heterogeneity that may not be apparent in a solid tumor biopsy

ctDNA = circulating tumor DNA.
Tumor Heterogeneity: ctDNA Can Capture Multiple Mechanisms of Acquired Resistance in mCRC

Multiple solid tumor biopsies show diverging resistance mechanisms in different metastases in a patient with advanced *BRAF* V600E CRC

Liquid biopsy captured all 4 resistance mechanisms

**Brain lesion**
- *BRAF* V600E, AF 54.7%
- *EGFR* amp
- *KRAS* G12S not detected
- *NRAS* Q61R not detected

**Liver biopsy 1**
- *BRAF* V600E, AF 36.4%
- *EGFR* amp, not detected
- *KRAS* G12S, AF 6.4%
- *NRAS* Q61R, AF 3.1%

**Liver biopsy 2**
- *BRAF* V600E, AF 61.6%
- *EGFR* amp, not detected
- *KRAS* G12S, AF 22.4%
- *NRAS* Q61R, not detected

**Subcutaneous lesion**
- *BRAF* V600E, AF 45.4%
- *EGFR* amp, not detected
- *KRAS* G12S, AF 0.2%
- *NRAS* Q61R, not detected

**cfDNA**
- *BRAF* V600E, AF 24%
- *EGFR* amp
- *KRAS* G12S, AF 2.1%
- *NRAS* Q61R AF 0.6%

AF = allelic fraction, cfDNA = cell-free DNA, mCRC = metastatic colorectal cancer.

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## Comprehensive Genomic Profiling by Liquid and Tissue Builds on the Strengths of Each Type of Assay

<table>
<thead>
<tr>
<th>Strengths</th>
<th>Blood</th>
<th>Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Less invasive/less morbidity(^1,2)</td>
<td>• Remains the gold standard(^2)</td>
<td></td>
</tr>
<tr>
<td>• Simpler to obtain/faster results(^1,2)</td>
<td>• More confidence in negative results(^1)</td>
<td></td>
</tr>
<tr>
<td>• Less biased detection of genomic alterations versus single tissue biopsy site(^1,2)</td>
<td>• Higher sensitivity for certain types of alterations(^1)</td>
<td></td>
</tr>
<tr>
<td>• Makes a repeat biopsy more feasible(^1,2)</td>
<td>• Tumor heterogeneity may not be captured(^1)</td>
<td></td>
</tr>
<tr>
<td>• Could allow for real-time monitoring(^1,2)</td>
<td>• Finite resource in many tumor types(^2)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Limitations</th>
<th>Blood</th>
<th>Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Not all patients have ctDNA(^1,2)</td>
<td>• Tumor heterogeneity may not be captured(^1)</td>
<td></td>
</tr>
<tr>
<td>• Negative result should be confirmed with tissue testing(^1)</td>
<td>• Finite resource in many tumor types(^2)</td>
<td></td>
</tr>
</tbody>
</table>


cDNA = circulating tumor DNA.
Clinical Utility of Liquid Biopsy and Comprehensive Genomic Profiling
Patients Who May Benefit From Liquid Biopsy

1. Patients in whom traditional biopsy is inaccessible or impractical
   - Anatomically inaccessible/unacceptable risk
   - Resource-limited settings (e.g. leading to delayed biopsy)
   - Time sensitivity (acutely ill)

2. Patients in whom traditional biopsy is insufficient
   - Tissue exhausted by immunohistochemistry, PD-L1 or other single marker testing, hotspot testing, or smaller tumor-specific panels
   - Highly necrotic tumor with inadequate nucleated tumor cells
   - Low tumoral content in specimen

3. Patients who have disease progression or relapse on targeted therapies
   - Detection of suspected resistance mutations
   - To consider new therapy options including clinical trials

Biomarkers for Immunotherapy
Liquid Biopsy Can Provide Accurate Detection Of Microsatellite Instability

Microsatellite instability (MSI) is a measure of DNA replication errors due to deficient mismatch repair\(^1\)

MSI is assessed by identifying and quantifying “unstable” loci, or loci with lengths that are inconsistent with a reference genome\(^1\)

On FoundationOne\textsuperscript{\textregistered} Liquid CDx, about 2000 repetitive loci (mono, di, or trinucleotide context of >5 repeats) are assessed for instability relative to an internal database of >3000 clinical samples\(^2\)

Samples with >0.5% unstable loci are considered to be MSI-High\(^2\)

MSI-High Tumors Show High Response To Immune Checkpoint Inhibitors

Data led to tumor-agnostic approval of pembrolizumab

Pembrolizumab response rates (RR) across tumor types*

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>N</th>
<th>RR</th>
<th>Tumor type</th>
<th>N</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal (CRC)</td>
<td>90</td>
<td>36%</td>
<td>Bladder</td>
<td>1</td>
<td>NE</td>
</tr>
<tr>
<td>Endometrial</td>
<td>14</td>
<td>36%</td>
<td>Sarcoma</td>
<td>1</td>
<td>PR</td>
</tr>
<tr>
<td>Biliary tract</td>
<td>11</td>
<td>27%</td>
<td>Thyroid</td>
<td>1</td>
<td>NE</td>
</tr>
<tr>
<td>Gastro-esophageal</td>
<td>9</td>
<td>56%</td>
<td>Unknown primary</td>
<td>1</td>
<td>PR</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>6</td>
<td>83%</td>
<td>Small cell lung</td>
<td>1</td>
<td>CR</td>
</tr>
<tr>
<td>Small intestine</td>
<td>8</td>
<td>38%</td>
<td>Renal cell</td>
<td>1</td>
<td>PD</td>
</tr>
<tr>
<td>Breast</td>
<td>2</td>
<td>100%</td>
<td>Esophageal</td>
<td>1</td>
<td>PR</td>
</tr>
<tr>
<td>Prostate</td>
<td>2</td>
<td>50%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>149</td>
<td>40%</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

*Data reported in pembrolizumab prescribing information

Clinical validation of bTMB using >1000 ctDNA samples from advanced pretreated NSCLC

Blood Tumor Mutational Burden (bTMB)

Computational Methodology and Study Design

Blood collection, plasma isolation & cfDNA extraction → Sequencing → bTMB
- All base substitutions with ≥0.5% allele frequency
- Remove germline polymorphisms & predicted driver mutations

POPLAR (training) → OAK (validation)

*This study used previous versions of FoundationOne®CDx and FoundationOne®Liquid CDx.

cfDNA = cell free DNA, ctDNA = circulating tumor DNA, NSCLC = non-small cell lung cancer.
Key Takeaways
Key Takeaways

1. FoundationOne® Liquid CDx expands on FoundationOne® Liquid with more genes and additional biomarkers, including new blood tumor mutational burden (bTMB).* Coverage of the same 324 genes* as FoundationOne® CDx creates a set of highly complementary tissue and liquid options for comprehensive genomic profiling.

2. Using both blood and tissue diagnostic tools can help reduce chances of missing key alterations. ctDNA can help to inform targeted therapy selection by uncovering tumor heterogeneity. Positive ctDNA results can be acted upon, but negative results should be confirmed by tissue testing.¹

3. Liquid biopsy has shown clinical utility in multiple solid tumors, including lung, breast, and prostate, as well as in pan-tumor applications. Clinical evidence shows that genomic alterations in ctDNA are predictive biomarkers for immunotherapy and targeted therapy response, including TKIs and PARP inhibitors.²

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*FoundationOne® Liquid CDx is FDA-approved to report substitutions and indels in 311 genes, including rearrangements in four (4) genes and copy number alterations in three (3) genes. Comprehensive results across all 324 genes are reported as a laboratory professional service which is not reviewed or approved by the FDA. MSI-H status, tumor fraction are reported as a laboratory professional service which is not reviewed or approved by the FDA.

ctDNA = circulating tumor DNA, TKI = tyrosine kinase inhibitor.

Questions?