The tumor microenvironment and PD-L1 expression

CLMA/ASCLS Spring Conference 2017 – Little Rock, AR

Denise A Croix, PhD
April 14, 2017
Objectives

1. Understand and describe the different classes of FDA clearances for in vitro diagnostic reagents/assays
2. Understand the tumor microenvironment & programmed death ligand expression
2. Articulate the differences between the various PD-L1 IHC assays
Personalized Healthcare

IVD definitions

PD-L1 & the tumor microenvironment
A key healthcare challenge
Better personalization of cancer care

“Healthcare today is in crisis, as it is expensive, reactive, inefficient & focused largely on one-size-fits-all treatments for events of late stage disease. An answer is personalized, predictive, preventive & participatory medicine.”

—Ralph Snyderman, MD
Chancellor Emeritus, Duke University

Source: The Case for Personalized Medicine, 3rd Edition - The Personalized Medicine Coalition (Oct 2011)
Why are predictive assays important? *Traditional therapy: Same diagnosis, same treatment*
Why are predictive assays important?

*Traditional therapy: Low treatment efficacy*

For every 10 cancer patients treated, an average of only 5 will benefit.*

~1 in 2 respond
Why are predictive assays important?

*Enable personalized care, facilitate better outcomes*

Right therapy, for the right patient, at the right time
Companion diagnostics deliver real value

Help to reduce costs & improve outcomes

$160B of drug spend is ineffective\(^1\)

$15B Savings CDx can deliver to healthcare\(^3\)

$604M Annual savings if patients with metastatic colorectal cancer receive a genetic test prior to treatment\(^2\)

34% Decrease in chemo if women with breast cancer receive a genetic test prior to treatment\(^4\)
Growth of Companion Diagnostics

*FDA approvals flat overall but 600% more likely with bio-target*

**The last ten years in NSCLC**

Number of compounds being investigated +62%

R&D funding has **doubled**

FDA approvals – **flat without a companion**

Biomarker targeted therapies **six-fold increase in clinical trial success**
Targeted therapies

• A type of treatment that uses drugs or other substances to identify and attack specific types of cancer cells with less harm to normal cells. *

• Mutations in specific genes can present as viable targets for therapeutics in lung cancer and melanoma (e.g. ALK, EGFR, BRAF)

• Resistance to these targeted therapies is common, and can arise in a number of ways including
  – Alteration in the target gene
  – Activation of an alternative signaling pathway for cell proliferation, which bypasses the original target gene
  – Activation of other growth receptors independent of the target gene

Oncogene Mutations in NSCLC

Predict Likelihood of Resistance or Response to Targeted Therapies

<table>
<thead>
<tr>
<th>Oncogene</th>
<th>Mutation Prevalence</th>
<th>Mutation-predicted Therapeutic Response</th>
<th>Predicted Overall Response Rates to Targeted Therapies</th>
</tr>
</thead>
</table>
| EGFR     | Asians: 40%  
          Caucasians: 10–15% | Sensitive to EGFR TKIs (most mutations)\(^a\) | Erlotinib: ~82%-83\(^4\)  
          Gefitinib: ~71%-73\(^4\) |
| KRAS     | Asians: 10%  
          Caucasians: 30% | Resistant to EGFR TKIs | 0%-5%\(^2,5,7\) |
| ALK      | 2–7% | Sensitive to ALK inhibitors  
          Resistant to EGFR TKIs | Crizotinib: 50%-61\(^9,10\)  
          0\(^b\) |

TKI, tyrosine kinase inhibitor.

PROFILE I014 Phase 3 Trial

343 randomized patients

crizotinib vs standard chemo

PFS: 10.9 mos  
      7.0 mos (HR =0.45)

ORR: 74%  
      45%  (p<0.001)
Oncogene Mutations in NSCLC Predict Likelihood of Resistance or Response to Targeted Therapies

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</tr>
<tr>
<td></td>
<td>Caucasians: 10–15%</td>
<td></td>
<td>Gefitinib: ~71%–73%&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
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<td>KRAS</td>
<td>Asians: 10%</td>
<td>Resistant to EGFR TKIs</td>
<td>0%–5%&lt;sup&gt;2,5,7&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Caucasians: 30%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALK</td>
<td>2–7%</td>
<td>Sensitive to ALK inhibitors</td>
<td>Crizotinib: 50%–61%&lt;sup&gt;9,10&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Resistant to EGFR TKIs</td>
<td>0%&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

TKI, tyrosine kinase inhibitor.

PROFILE 1014 Phase 3 Trial

343 randomized patients

crizotinib vs standard chemo

PFS: 10.9 mos 7.0 mos (HR =0.45)

ORR: 74% 45% (p<0.001)
Immuno-Oncology Therapies

- Immune therapy is not the same as a targeted therapy.
- Immunotherapeutic agents do not directly kill the tumor cells.
- Instead, the therapy blocks immunosuppressive molecules which allows the normal immune system to expand.
- Cytotoxic T cells can then be activated and kill the tumor cells.

What are some examples of assays & targeted therapies?
Roche’s existing predictive portfolio
*Covers several therapies, uses different technologies*

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Technology</th>
<th>Therapy, indication</th>
<th>Roche Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>HER2</td>
<td>IHC/ISH</td>
<td>Herceptin®, BREAST</td>
<td></td>
</tr>
<tr>
<td>EGFR</td>
<td>PCR (Tissue/Plasma)</td>
<td>Tarceva®, TAGRISSO™, NSCLC</td>
<td>Roche, cobas²</td>
</tr>
<tr>
<td>ALK</td>
<td>IHC</td>
<td>Xalkori®, NSCLC</td>
<td>Roche, VENTANA</td>
</tr>
<tr>
<td>BRAF</td>
<td>PCR</td>
<td>Zelboraf®, MELANOMA</td>
<td>Roche, cobas²</td>
</tr>
<tr>
<td>C-KIT</td>
<td>IHC</td>
<td>GLEEVEC®, GIST</td>
<td>Roche, VENTANA</td>
</tr>
<tr>
<td>KRAS</td>
<td>PCR</td>
<td>Erbitux®, Vectibix®, CRC</td>
<td>Roche, cobas²</td>
</tr>
<tr>
<td>PD-L1</td>
<td>IHC</td>
<td>TECENTRIQ®, Bladder/NSCLC</td>
<td>Roche, VENTANA</td>
</tr>
</tbody>
</table>

Disclaimer: Some of the assay/therapies above are in development and may not be cleared in the US market.
Personalized Healthcare

**IVD definitions**

**PD-L1 & the tumor microenvironment**
Assay Classification

<table>
<thead>
<tr>
<th>Regulatory Classification</th>
<th>RUO</th>
<th>IUO</th>
<th>IVD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intended Use</strong></td>
<td>Research Use Only</td>
<td>Investigational Use Only</td>
<td>Class I, II, III Diagnostics</td>
</tr>
<tr>
<td><strong>Clinical Utility</strong></td>
<td>None Research Use Only</td>
<td>Clinical Trial Assay Enrollment or investigation</td>
<td>Adjunctive, prognostics Predictive or selective</td>
</tr>
<tr>
<td><strong>Used in</strong></td>
<td>Research Use Only</td>
<td>Clinical trial sites &amp; investigations</td>
<td>Pathologist Clinical practice</td>
</tr>
</tbody>
</table>
FDA Medical Device Definition

A device is "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:

- recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
- *intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man* or other animals, or
- intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes."

Source: [http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/ucm051512.htm](http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/ucm051512.htm)
**IVD Assay Classification**

<table>
<thead>
<tr>
<th>Regulatory Classification</th>
<th>I</th>
<th>II</th>
<th>III</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDA Cleared/510(k)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FDA Approved/PMA</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Risk to Public Health   | Low | Moderate | High |

| Clinical Utility        | Adjuvant test | Stand alone assay | Predictive or Selective Diagnostic |

| Characteristics         | Established in literature | Well characterized tissue controls | Claims supported by clinical trials data submission |

| Examples                | CD3 | ER, PR (breast) | HER2, ALK |
## CDx/predictive assay development

### Additional testing needed for a CDx assay

<table>
<thead>
<tr>
<th>Characterization Studies performed</th>
<th>RUO</th>
<th>Analytical</th>
<th>Predictive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product Classification</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FDA Submission</td>
<td>No</td>
<td>No</td>
<td>PMA</td>
</tr>
<tr>
<td>CE Marked</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Immunoreactivity (ToT ToB)</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Robustness</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Repeatability</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Pre-analytical (fixatives, etc)</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Stability Studies</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Design Validation</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Reader Precision</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Inter-laboratory Reproducibility</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Proof of utility in detecting a disease</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Clinical utility proving device performance in relation to drug outcome or potential misdiagnosis</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Possible claims</td>
<td>None</td>
<td>Detects biomarker</td>
<td>Companion diagnostic, Complementary diagnostic</td>
</tr>
</tbody>
</table>
Cost of FDA approval? Length of time?
<table>
<thead>
<tr>
<th>Regulatory Classification</th>
<th>Companion</th>
<th>Complementary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Utility</td>
<td>essential for the <strong>safe and effective use of a corresponding therapeutic product</strong></td>
<td>not required for safe and effective drug use but provide significant information about drug use. These assays may provide additional information for physicians and inform patient dialogue.</td>
</tr>
</tbody>
</table>

**Examples**

- VENTANA ALK (D5F3) CDx Assay
- VENTANA PD-L1 (SP142) Assay
- Dako pharmDx 28-8 assay
Companion is required, complementary informs

Both provide information about likely patient response

Examples

VENTANA ALK (D5F3) CDx Assay
VENTANA PD-L1 (SP142) Assay
Dako pharmDx 28-8 assay
Assay Overview

- **Reagent**
- **Detection**
- **Staining instruments and ancillary reagents**
- **Result**
- **Controls (NRC & tissue)**
- **Interpretation Guide**
Personalized Healthcare

IVD definitions

PD-L1 & the tumor microenvironment
The detection, targeting and destruction of cancer cells by the immune system is a multi-step process. The regulation of cytotoxic T cells by co-stimulatory and co-inhibitory molecules plays a key role in cancer immunity.

1. Release of cancer cell antigens (cancer cell death)
2. Cancer antigen presentation (dendritic cells/APCs)
3. Priming and activation (APCs & T cells)
4. Trafficking of T cells to tumors (CTLs)
5. Infiltration of T cells into tumors (CTLs, endothelial cells)
6. Recognition of cancer cells by T cells (CTLs, cancer cells)
7. Killing of cancer cells (immune and cancer cells)

Hallmarks of cancer

- Resistance to cell death
- Immortality
- Angiogenesis
- Sustained proliferation
- Evading growth suppression
- Invasion & Metastasis

Evasion mechanisms utilized by cancer cells

- **Down-regulation of antigen presentation** leading to impaired recognition by T cells

- Reduced expression of ligands for co-stimulatory molecules such as B7.1 and inducible co-stimulator ligand (ICOSL) on APCs leading to defective immune functions

- Creation of an **immunosuppressive microenvironment** leading to recruitment of, or promotion of, suppressive immune cell differentiation or expansion

- Expression of inhibitory ligands, e.g. PD-L1 and PD-L2, leading to T-cell inhibition

References:

Mellman I, Coukos G and Dranoff G. Nature 2011;480:480–9
PD-L1 and PD-1

Part of the immune checkpoint pathway: inhibits T-cell activity

PD-L1, Program death ligand-1, is a ligand that binds PD-1.

PD-1, Program death receptor 1, is a receptor that binds PD-L1.

PD-L1 and PD-1 are part of the immune checkpoint pathway. This pathway limits T-cell proliferation and limits their ability to kill tumor cells.

PD-L1/PD-1 Interaction & Inhibition of Killing

Activated T-cell

PD-1

PD-L1

Tumor cell

(3) The **activated T-cell** is able to destroy **tumor cells** resulting in **tumor cell death**.

Which cancers are being evaluated?

A variety of cancers

Breast cancer

Bladder carcinoma (αPD-L1 and αPD-1 drugs)

Diffuse large B-cell lymphoma

Hodgkin lymphoma

Melanoma (αPD-1 drugs)

Non-small cell lung carcinoma (αPD-L1 and αPD-1 drugs)

Renal cell carcinoma

Squamous cell carcinoma of the head and neck (αPD-1 drugs)

Pancreatic carcinoma

Gastroesophageal cancer

PD-L1 detection in tumors

* Detected in 11% to 100% in a variety of tumors

<table>
<thead>
<tr>
<th>Cancer</th>
<th>PD-L1 positive (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>31-34</td>
</tr>
<tr>
<td>Colon</td>
<td>53</td>
</tr>
<tr>
<td>Esophageal</td>
<td>42</td>
</tr>
<tr>
<td>Gastric</td>
<td>42</td>
</tr>
<tr>
<td>Glioblastoma/mixed glioma</td>
<td>100</td>
</tr>
<tr>
<td>Hepatocellular</td>
<td>45-93</td>
</tr>
<tr>
<td>Leukemias</td>
<td>11-42</td>
</tr>
<tr>
<td>Lymphomas</td>
<td>17-94</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cancer</th>
<th>PD-L1 positive (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoma</td>
<td>40-100</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>93</td>
</tr>
<tr>
<td>Ovarian</td>
<td>33-80</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>39</td>
</tr>
<tr>
<td>Renal cell</td>
<td>15-24</td>
</tr>
<tr>
<td>Urothelial</td>
<td>28-100</td>
</tr>
<tr>
<td>Nasopharyngeal / HNC</td>
<td>46-100</td>
</tr>
<tr>
<td>NSCLC</td>
<td>35-95</td>
</tr>
</tbody>
</table>

## PD-L1 expression & prevalence in tumors

**Phase I trial of atezolizumab (PCD4989g)**

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Number (n)</th>
<th>PD-L1+ Immune Cells (IC)</th>
<th>PD-L1+ Tumor Cells (TC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSCLC</td>
<td>184</td>
<td>26%</td>
<td>24%</td>
</tr>
<tr>
<td>RCC</td>
<td>88</td>
<td>25%</td>
<td>10%</td>
</tr>
<tr>
<td>Melanoma</td>
<td>58</td>
<td>36%</td>
<td>5%</td>
</tr>
<tr>
<td>HNSCC</td>
<td>101</td>
<td>28%</td>
<td>19%</td>
</tr>
<tr>
<td>Gastric cancer</td>
<td>141</td>
<td>18%</td>
<td>5%</td>
</tr>
<tr>
<td>CRC</td>
<td>77</td>
<td>35%</td>
<td>1%</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>83</td>
<td>12%</td>
<td>4%</td>
</tr>
<tr>
<td>Bladder</td>
<td>205</td>
<td>27%</td>
<td>11%</td>
</tr>
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The detection, targeting and destruction of cancer cells by the immune system is a multi-step process:

1. Release of cancer cell antigens (cancer cell death)
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3. Priming and activation (APCs & T cells)
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5. Infiltration of T cells into tumors (CTLs, endothelial cells)
6. Recognition of cancer cells by T cells (CTLs, cancer cells)
7. Killing of cancer cells (immune and cancer cells)

The regulation of cytotoxic T cells by co-stimulatory and co-inhibitory molecules plays a key role in cancer immunity.
Cell recognition and immune checkpoints

**TC or IC**

**T cell**

**CD8+ CTL**

CD3 complex

TCR

MHC class I

CD8

Tumor cell

**MHC I**

B7.1

B7.1

PD-L1

PD-L1

CD137-L

OX40-L

CD40-L

CD70

Light

TCR

CTLA-4

CD28

B7.1

**Inhibitory Receptors**

PD-1

VISTA

LAG-3

**Activating Receptors**

CD28

OX40

CD137

CD27

HVEM

**T cell targets for modulating activity**

**Agonistic Antibodies**

CD28

OX40

CD137

CD27

HVEM

**Blocking Antibodies**

CTLA-4

PD-1

BTLA

TIM-3

PD-L1 and PD-1

Part of the immune checkpoint pathway: inhibits T-cell activity

PD-L1, Program death ligand-1, is a ligand that binds PD-1.
PD-1, Program death receptor 1, is a receptor that binds PD-L1.

PD-L1 and PD-1 are part of the immune checkpoint pathway. This pathway limits T-cell proliferation and limits their ability to kill tumor cells.

Blocking **PD-L1** could have the potential to restore T cell activation and proliferation

**B7.1**
Potentially restores its ability to **sustain T cell activation and proliferation**

**PD-L1**

**PD-1**

Potentially **prevents T cell deactivation** through binding PD-L1

**Dual Blockade of PD-1 and B7.1 could potentially lead to durable activation and proliferation of T Cells**

Chen DS, Mellman I. *Immunity*. 2013
# Examples of cancer immunotherapy drugs

<table>
<thead>
<tr>
<th>Target</th>
<th>Drug / indication</th>
<th>FDA status</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTLA-4</td>
<td>Yervoy® (ipilimumab) / melanoma</td>
<td>Approved 2010</td>
</tr>
<tr>
<td>CTLA-4</td>
<td>Tremelimumab</td>
<td>In clinical trials</td>
</tr>
<tr>
<td>PD-1</td>
<td>KEYTRUDA® (pembrolizumab) / advanced melanoma, NSCLC, HNSCC</td>
<td>Approved 2014</td>
</tr>
<tr>
<td>PD-1</td>
<td>OPDIVO® (nivolumab) / metastatic melanoma, NSCLC</td>
<td>Approved 2015</td>
</tr>
<tr>
<td>PD-L1</td>
<td>Durvalumab</td>
<td>In clinical trials</td>
</tr>
<tr>
<td>PD-L1</td>
<td>TECENTRIQ® (atezolizumab) / Urothelial carcinoma (UC), NSCLC</td>
<td>Approved 2016</td>
</tr>
</tbody>
</table>

*Disclaimer: Some of the assay/therapies above are in development and may not be cleared in the US market.*

TECENTRIQ® (atezolizumab) is a registered trademark of Genentech, Inc. All rights reserved. OPDIVO® (nivolumab), YERVOY® (ipilimumab) are registered trademarks of Bristol-Myers Squibb Company. All rights reserved. KEYTRUDA® (pembrolizumab) is a registered trademark of Merck & Co. All rights reserved.

Source: [http://www.clinicaltrials.gov](http://www.clinicaltrials.gov)
What is the rationale for PD-L1 testing?

Identify patients who are most likely to benefit from therapy

**PD-L1 positive** associated with **1.6x-9x higher response** rates versus PD-L1 **negative**


Response to atezolizumab in PD-L1+ UC patient

Overall Survival in PD-L1 Immune Cell groups in UC

* historic overall survival at 12 months is 20%

PD-L1 detection
Via immunohistochemistry in FFPE samples

PD-L1 is expressed on tumor cells and immune cells. It is a transmembrane protein. Localized to the cell membrane and cytoplasm.
## FDA Approved PD-L1 Assays
### As of 2/2/2017

<table>
<thead>
<tr>
<th>Assay</th>
<th>TECENTRIQ™ (atezolizumab)</th>
<th>OPDIVO® (nivolumab)</th>
<th>KEYTRUDA® (pembrolizumab)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Classification</strong></td>
<td>Complementary</td>
<td>Complementary</td>
<td>Companion</td>
</tr>
<tr>
<td><strong>Tested Cells</strong></td>
<td>Tumor Cells (TC), Immune Cells (IC)</td>
<td>Tumor Cells (TC)</td>
<td>Tumor Cells (TC)</td>
</tr>
<tr>
<td><strong>PD-L1+ Expression UC</strong></td>
<td>≥5% IC</td>
<td>Approved/no scoring algorithm</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>PD-L1+ Expression 2L NSCLC</strong></td>
<td>≥50% TC or ≥10% IC</td>
<td>≥1% TC</td>
<td>≥1% TC (≥50% for 1L)</td>
</tr>
</tbody>
</table>

TECENTRIQ® (atezolizumab) is a registered trademark of Genentech, Inc. All rights reserved.
OPDIVO® (nivolumab) is a registered trademark of Bristol-Myers Squibb Company. All rights reserved.
KEYTRUDA® (pembrolizumab) is a registered trademark of Merck & Co. All rights reserved.
Comparison of fixation methods for SPI42 Assay

<table>
<thead>
<tr>
<th>Time Point</th>
<th>Fixative</th>
<th>10% NBF</th>
<th>Zinc Formalin</th>
<th>Z-5**</th>
<th>Prefer*</th>
<th>AFA*</th>
<th>95% Alcohol*</th>
</tr>
</thead>
<tbody>
<tr>
<td>One hour</td>
<td></td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
<td><img src="image5.png" alt="Image" /></td>
<td><img src="image6.png" alt="Image" /></td>
</tr>
<tr>
<td>Six hours</td>
<td></td>
<td><img src="image7.png" alt="Image" /></td>
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<td><img src="image29.png" alt="Image" /></td>
<td><img src="image30.png" alt="Image" /></td>
</tr>
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</table>

All images at 10X magnification
Antigen Stability

NSCLC specimens
Antigen Stability

UC specimens

Day 0

After 3 months
Tonsil Control

Acceptable Staining

Superficial squamous epithelium

Crypt-epithelium

Interfollicular region

Germinal Center
VENTANA PD-L1 (SPI42) Assay

Examples of NSCLC staining

NSCLC tissue showing moderate to strong circumferential TC membrane staining

NSCLC tissue showing dark brown punctate and linear IC staining
Summary

1. PD-L1 is the ligand for PD-1 and B7.1 receptors and are part of the immune checkpoint pathway that inhibits T-cell activity.

2. PD-L1 is a co-inhibitory molecule that is expressed in the tumor microenvironment of numerous cancers and may be detected on both immune cells and tumor cells.

3. There are several FDA-approved assays that enumerate PD-L1 in various tumors. Each assay has unique scoring algorithms and is tied to patient outcomes for specific therapeutics and indications.

4. Substitution of any component of an FDA approved assay is considered on off-label use of assay

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