PD-L1 Testing in Non-Small Cell Lung Carcinoma

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Disclosures

• None

Outline

• Role of PD-1 – PD-L1 in immune system
• Challenges of PD-L1 testing
• Current PD-L1 testing in NSCLC
• Take home points
PD-L1 in the Immune System\textsuperscript{1-3}

• PD1 - PD-L1 interaction
  → Inhibition of T cells → Tumor growth

• Anti-PD1 or anti-PD-L1 drugs
  → Block PD1-PD-L1 interaction
  → Boost host anti-tumor immune response
  → Inhibit tumor growth

• Responses in lung adenoCa and SQCC

\textbf{Anti-PD-1 vs Chemotherapy}

N=305 untreated stage IV NSCLC

PD-L1+ ≥ 50% tumor cells (clone 22C3)

\begin{align*}
\text{Pembrolizumab (anti-PD1)} & \quad P<0.001 \\
\text{Chemotherapy} & \quad \text{OS } P<0.005
\end{align*}

PD-L1 Testing

• Clones - associated with certain drugs (corresponding to clinical trials)
• Companion test: PD-L1-testing using FDA-specified clone required before treatment
• Complementary test: PD-L1-testing using FDA-specified clone strongly encouraged before treatment

PD-L1 Testing in NSCLC

• TPS = Tumor proportion score = [# PD-L1+ tumor cells/all tumor cells]*100
• Any membranous staining
• 100 viable tumor cells
• IC = immune cells = % PD-L1+ tumor-associated immune cells
• If metastasis - know primary tumor (different interpretation guidelines)
<table>
<thead>
<tr>
<th>NSCLC – Therapy</th>
<th>Clone</th>
<th>Test</th>
<th>Cutoff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keytruda (Pembrolizumab)</td>
<td>22C3</td>
<td>Companion</td>
<td>TPS ≥ 1% (2nd line) ≥ 50% (1st line)</td>
</tr>
<tr>
<td>Anti-PD-1</td>
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<tr>
<td>Opdivo (Nivolumab)</td>
<td>28-8</td>
<td>Complementary</td>
<td>TC ≥ 1%</td>
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<tr>
<td>Anti-PD-1</td>
<td></td>
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<tr>
<td>Tecentriq (Atezolizumab)</td>
<td>SP142</td>
<td>Complementary</td>
<td>TC ≥ 50% or IC ≥ 10%</td>
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<tr>
<td>Anti-PD-L1</td>
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**Lung AdenoCa**

PD-L1 (22C3)  
TPS: 100%
Lung AdenoCa met to axilla

PD-L1 (22C3) TPS: 0%

Immune cells with PD-L1 expression
Macrophages express PD-L1
→ Correlation with H&E

PD-L1 (22C3)

PD-L1 (SP263) control – tonsil (placenta also possible)
PD-L1 Clones & Expression on Tumor Cells

- 22C3, 28-8, SP263 - highly comparable
- SP142 - ↓ sensitivity
- 73-10 - ↑ sensitivity
Heterogeneity of PD-L1 Expression

• Within a single tumor (maybe focal or patchy)
• Between independent primary NSCLC (agreement, 52.2%)
• High level of agreement between intrapulmonary metastases (88.9%)
• Sampling might be an issue
PD-L1 Testing in NSCLC

- FFPE tissue – FDA approved
- Cell block, decalcified tissue – not FDA approved → if negative – test another sample, ideally FFPE
- Old FFPE tissue blocks – reduced to no staining
- Test latest specimen (recurrence/metastasis), possibly also original tumor
PD-L1 Evaluation – Our Approach

• FDA-approved clones 22C3, SP263, SP142 (28-8 in validation)
• Oncologist requests clone based on intended treatment
• Report of TPS and IC

Testing Guidelines (NCCN)

• Patients with advanced or metastatic NSCLC (adenoCa, SQCC, large cell Ca, NOS) should be tested for PD-L1 expression
• Response of extensive stage or relapsed SCLC to anti-PD-L1 therapy appears regardless of PD-L1 expression
Take Home Message

- Multiple PD-L1 clones available for testing
- Complementary or companion tests
- Staining might be heterogeneous → sampling
- Oncologist needs to be involved in test planning (clone, specimen)

THANK YOU
References


