PD-L1 testing in triple negative breast cancer

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Corrado D’Arrigo - Poundbury Cancer Institute, Dorchester, UK
background
**Overall Survival in the PD-L1–Positive Subgroup**

<table>
<thead>
<tr>
<th></th>
<th>Median Overall Survival (95% CI)</th>
<th>2-Yr Rate of Overall Survival (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>mo</strong></td>
<td>%</td>
</tr>
<tr>
<td>Atezolizumab + Nab-Paclitaxel</td>
<td>25.0 (22.6–NE)</td>
<td>53.5 (42.3–64.6)</td>
</tr>
<tr>
<td>Placebo + Nab-Paclitaxel</td>
<td>15.5 (13.1–19.4)</td>
<td>36.6 (26.4–46.7)</td>
</tr>
</tbody>
</table>

Stratified hazard ratio for death, 0.62 (95% CI, 0.45–0.86)

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**Abstract**

Atezolizumab and Nab-Paclitaxel in Advanced Triple-Negative Breast Cancer

Indication:
unresectable (locally advanced) or metastatic TNBC

- March 8th 2019: FDA grants accelerated approval
- March 14th 2019: UK MHRA grants Early Access Medicine Scheme (EAMS)
- August 29th 2019: EMA approval
- September 2019: NICE (UK) approval expected
context
SP142 (anti-PD-L1)

• Performance is significantly different from all other clones (SP263, 22C3, 28.8, E1L3N, etc.)

• Recognises an **intracellular** epitope of PD-L1

• Stains proportionally more immune cells (IC)
• Assessment based on PD-L1(+) immune cells only
• Tumour cell (TC) staining not relevant for assessment
• Threshold for positivity is set at 1%

| IC <1% | IC 1% | IC 10% |
What tissue to use for PD-L1 testing?

- Core bx of liver metastasis?
- Core bx chest wall recurrence?
- Primary carcinoma from excision?
- Original diagnostic core bx?
<table>
<thead>
<tr>
<th>Time (h)</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>1 h</td>
<td><img src="10%25_NBF_1h.jpg" alt="Image" /></td>
<td><img src="Zinc-Formalin_1h.jpg" alt="Image" /></td>
<td><img src="Z-5_1h.jpg" alt="Image" /></td>
<td><img src="Prefer_1h.jpg" alt="Image" /></td>
<td><img src="AFA_1h.jpg" alt="Image" /></td>
<td><img src="95%25_Alcohol_1h.jpg" alt="Image" /></td>
</tr>
<tr>
<td>6 h</td>
<td><img src="10%25_NBF_6h.jpg" alt="Image" /></td>
<td><img src="Zinc-Formalin_6h.jpg" alt="Image" /></td>
<td><img src="Z-5_6h.jpg" alt="Image" /></td>
<td><img src="Prefer_6h.jpg" alt="Image" /></td>
<td><img src="AFA_6h.jpg" alt="Image" /></td>
<td><img src="95%25_Alcohol_6h.jpg" alt="Image" /></td>
</tr>
<tr>
<td>12 h</td>
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<td><img src="Zinc-Formalin_12h.jpg" alt="Image" /></td>
<td><img src="Z-5_12h.jpg" alt="Image" /></td>
<td><img src="Prefer_12h.jpg" alt="Image" /></td>
<td><img src="AFA_12h.jpg" alt="Image" /></td>
<td><img src="95%25_Alcohol_12h.jpg" alt="Image" /></td>
</tr>
<tr>
<td>24 h</td>
<td><img src="10%25_NBF_24h.jpg" alt="Image" /></td>
<td><img src="Zinc-Formalin_24h.jpg" alt="Image" /></td>
<td><img src="Z-5_24h.jpg" alt="Image" /></td>
<td><img src="Prefer_24h.jpg" alt="Image" /></td>
<td><img src="AFA_24h.jpg" alt="Image" /></td>
<td><img src="95%25_Alcohol_24h.jpg" alt="Image" /></td>
</tr>
<tr>
<td>72 h</td>
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<td><img src="Zinc-Formalin_72h.jpg" alt="Image" /></td>
<td><img src="Z-5_72h.jpg" alt="Image" /></td>
<td><img src="Prefer_72h.jpg" alt="Image" /></td>
<td><img src="AFA_72h.jpg" alt="Image" /></td>
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PD-L1 positive = Atezolizumab + nab-paclitaxel

PD-L1 negative = Chemotherapy only
aims of the study
Pathologists who report PD-L1 know that expression in TNBC can be heterogeneous.

Does PD-L1 heterogeneity affect diagnosis?

If so, how often?

• What should pathologists and oncologists do?
• What are the best samples to use?
study design
153 TNBC with matched core bx and excision
Final PD-L1 score = all tumour area
findings
Correlation between core bx and excision
results from 73 cases
good correlation!
poor correlation!
<table>
<thead>
<tr>
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<th>PD-L1(+) excision</th>
<th>PD-L1(-) excision</th>
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<tr>
<td>PD-L1(+) core bx</td>
<td>22</td>
<td>0</td>
</tr>
<tr>
<td>PD-L1(-) core bx</td>
<td>16</td>
<td>35</td>
</tr>
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38/73 cases (52%) were PD-L1(+) as final diagnosis. 16/73 cases (22%) had PD-L1(-) on core and PD-L1(+) on final diagnosis. 16% had discordant PD-L1 status between excision blocks.

**Conclusion**: We showed that there are 42% fewer PD-L1 (+) cases when assessed on CB alone. No PD-L1(+) cases on CB became negative on final diagnosis.

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<th>excision</th>
<th>final PD-L1 status</th>
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<tr>
<td>PD-L1(+)</td>
<td>22 (30%)</td>
<td>38 (52%)</td>
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</tr>
<tr>
<td>PD-L1(-)</td>
<td>51 (70%)</td>
<td>35 (48%)</td>
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Conclusions

- Initially, testing should be performed on the needle core biopsy

- If **positive**, the patient can receive PD-L1 inhibitors

- If **negative**, additional testing should be done on the excision specimen (if available)

- It is not necessary to test multiple excision blocks unless distinct morphological subtypes present