PD-L1 expression and its association with survival in malignant pleural mesothelioma

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Disclosure slide

• Presenter has no disclosures
PD-L1 (B7-H1)

- PD-L1 is a co-inhibitory immune checkpoint molecule
- PD-L1 is expressed by many malignancies and is associated with advanced disease and poor survival in most of these
Hypothesis

• PD-L1 is expressed in malignant pleural mesothelioma and is associated with poor survival
Study Design

- Archived samples of malignant pleural mesothelioma were identified and evaluated for adequacy.
- Despite clinical diagnosis of malignant pleural mesothelioma, cases that did not have appropriate IHC profile were excluded.
Study Design

IHC criteria

• Specimens must have been positive for at least two mesothelioma markers: WT-1, calretinin, CK5/6, D2-40

• Specimens must have been positive for at least two carcinoma markers: MOC31, pCEA, TTF-1, BerEP4
Study Design

• Tissue blocks were sectioned at 5 microns
• IHC performed with anti-human B7-H1 clone 5H1-A3 as described previously (Frigola et al Clin Cancer Res 2011; 17:1915-23)
Study Design

- Extent and location of positively-stained malignant cells were determined by a pathologist.
- Specimens with 5% or more positively-stained cells were considered positive (Thompson et al. Cancer Res 2006;66:3381-5).
- Patient records were abstracted for clinicopathologic information, treatment and survival.
Study Design

- $X^2$ test used to compare clinicopathologic differences between PD-L1 positive and negative groups
- Survival modeled with Kaplan-Meier method and groups compared by log-rank test
- Cox proportional hazards model used for multivariate analysis
Results

• 224 cases with sufficient tissue were identified from 1986-2006
• 106 cases included after IHC review by a thoracic pathologist
<table>
<thead>
<tr>
<th></th>
<th>PD-L1 positive</th>
<th>PD-L1 negative</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n (%)</strong></td>
<td>42 (40%)</td>
<td>64 (60%)</td>
<td></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td>0.72</td>
</tr>
<tr>
<td>Male</td>
<td>35 (83%)</td>
<td>55 (86%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>7 (17%)</td>
<td>9 (14%)</td>
<td></td>
</tr>
<tr>
<td><strong>Age y (median, IQR)</strong></td>
<td>68 (59-75)</td>
<td>65 (58-73)</td>
<td>0.19</td>
</tr>
<tr>
<td><strong>Decade of Dx</strong></td>
<td></td>
<td></td>
<td>0.57</td>
</tr>
<tr>
<td>1980’s</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>1990’s</td>
<td>22 (52%)</td>
<td>35 (55%)</td>
<td></td>
</tr>
<tr>
<td>2000’s</td>
<td>20 (48%)</td>
<td>28 (43%)</td>
<td></td>
</tr>
</tbody>
</table>

* Univariate analysis
# Table continued

<table>
<thead>
<tr>
<th></th>
<th>PD-L1 +</th>
<th>PD-L1 -</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Subtype</strong></td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Epithelioid</td>
<td>14 (33%)</td>
<td>54 (84%)</td>
<td></td>
</tr>
<tr>
<td>Sarcomatoid</td>
<td>16 (38%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>Biphasic</td>
<td>12 (29%)</td>
<td>9 (14%)</td>
<td></td>
</tr>
<tr>
<td><strong>Surgical treatment offered</strong></td>
<td></td>
<td></td>
<td>0.03</td>
</tr>
<tr>
<td>Yes</td>
<td>7 (17%)</td>
<td>23 (36%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>35 (83%)</td>
<td>41 (64%)</td>
<td></td>
</tr>
<tr>
<td><strong>Lymphocytic infiltration</strong></td>
<td></td>
<td></td>
<td>0.36</td>
</tr>
<tr>
<td>Yes</td>
<td>38 (90%)</td>
<td>54 (84%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>4 (10%)</td>
<td>10 (16%)</td>
<td></td>
</tr>
</tbody>
</table>

*Univariate analysis*
Distribution of expression

Percent expression

n

26-29 March 2014, Geneva, Switzerland
Organisers
Localization of PD-L1

- Cytoplasmic: 18 (43%)
- Membranous: 10 (24%)
- Cytoplasmic and membranous: 14 (33%)
Sarcomatoid
Epithelioid
Biphasic
Overall Survival

PD-L1 negative:
14.5 months (IQR 9-19)

PD-L1 positive:
5 months (IQR 2-9.5)

p<0.0001
Multivariate analysis

- PD-L1 expression remained significantly associated with worse survival after adjusting for age, histology and therapy (risk ratio 1.71, 1.03-2.78, \( p=0.04 \))
- Sarcomatoid histology also remained significantly associated with worse survival (risk ratio 2.18, 1.08-4.23, \( p=0.03 \))
Conclusions

• PD-L1 expression was detected in 40% of specimens of malignant pleural mesothelioma
• Almost all sarcomatoid subtypes expressed PD-L1
• PD-L1 expression is associated with poor survival in malignant pleural mesothelioma
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