Background

- The incorporation of immune-checkpoint inhibitors (ICIs) into the multimodal treatment of operable stage III NSCLC is likely to change future treatment standards.
- Programmed cell death ligand-1 (PD-L1) expression on tumor cells is a predictive biomarker for sensitivity to ICIs targeting the PD-1/PD-L1 axis.
- Little is known on the impact of treatment modalities such as chemo-, radiotherapy and/or combinations on PD-L1 expression level.

Methods

Study design

- We collected formalin-fixed, paraffin-embedded tumor tissue samples from patients enrolled in the Swiss Group for Clinical Cancer Research (SAKK) trials 16/96, 16/00, 16/01, 16/04, and analyzed PD-L1 expression (Tumor Proportion Score) by immunohistochemistry using the Ventana PD-L1 SP263 assay.
- The SAKK 16/96, 16/00 and 16/01 trials included patients with operable stage III NSCLC. All patients were treated with 3 cycles of induction chemotherapy (cisplatin/docetaxel), followed in some patients by radiotherapy and/or combinations on PD-L1.

Results

- We obtained matched pre- and post-neoadjuvant tumor tissue samples from 100 patients. Due to low PD-L1 expression and significant inter-trial heterogeneity (SAKK 16/00 vs. 16/96, p = 0.0038), the samples from SAKK 16/96 trial were excluded.
- Overall, pre- and post-neoadjuvant samples from 83 patients were included in the final analysis (Table 1).

Objective

- To investigate the impact of chemotherapy and chemoradiation on the PD-L1 expression in patients with stage III NSCLC.

Figure 1. SAKK 16 trials and PD-L1 analysis.

Figure 2. PD-L1 expression (all patients).

Table 1. Patient demographics and disease characteristics.

<table>
<thead>
<tr>
<th>Trial</th>
<th>Overall (N=83)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAKK 16/96</td>
<td>72 (86.9%)</td>
</tr>
<tr>
<td>SAKK 16/00</td>
<td>11 (13.1%)</td>
</tr>
</tbody>
</table>

PD-L1 status

<table>
<thead>
<tr>
<th>Patient (%</th>
<th>Pre-neoadjuvant</th>
<th>Post-neoadjuvant</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD-L1 0%</td>
<td>54 (65.1%)</td>
<td>49 (58.8%)</td>
</tr>
<tr>
<td>PD-L1 1-5%</td>
<td>13 (15.8%)</td>
<td>21 (25.3%)</td>
</tr>
<tr>
<td>PD-L1 1-5%</td>
<td>12 (14.5%)</td>
<td>16 (19.3%)</td>
</tr>
</tbody>
</table>

Table 2 and Figure 2. PD-L1 expression (all patients).

Conclusions

- Neoadjuvant treatment did not impact on PD-L1 expression. This was the case for both neoadjuvant chemotherapy as well as neoadjuvant chemoradiation.
- If the observation that radiotherapy can sensitize treatment with ICIs holds true, it is unlikely to be mediated through an upregulation of PD-L1 expression.

References:


Acknowledgments: We would like to thank the patients and their families for their participation in the SAKK trials, and the investigators and staff for their contributions.

Funding: This work was supported with grants by the Swiss Cancer Research Foundation (FKS-43841-02-2018), the Peter Bockhoff Stiftung, and the Swiss State Secretory for Education, Research and Innovation (SER).

Poster presented at ESMO Immuno-Oncology Congress 2021

Corresponding author: David König, david.koenig@usb.ch