percentages of diagnostic status change were HNSCC (CPS ≥20) with a remarkable 83.3% (130) followed by UC (CPS ≥10) at 46.3% (57) and ESCC (CPS ≥10) at 36.6% (45) of the specimens reclassified as negative.

\[
\text{a) TPS} = \left( \frac{\text{PD-L1 Staining TC}}{\text{Total Number of Viable TC}} \right) \times 100
\]

\[
\text{b) CPS} = \left( \frac{\text{PD-L1 Staining Cells (TC, lymphocytes and macrophages)}}{\text{Total Number of Viable TC}} \right) \times 100
\]

\[
\text{c) QID} = \text{CPS} - \text{TPS}
\]

Abstract 81 Figure 1 PD-L1 Scoring Algorithms

The TPS algorithm (a) is defined as the number of PD-L1 staining tumor cells divided by the total number of viable TC, multiplied by 100. The CPS algorithm (b) includes TC and IC and is defined as the number of PD-L1 staining cells (TC, lymphocytes and macrophages) divided by the total number of viable TC, multiplied by 100. In addition to TPS and CPS, QID (c) was also calculated to quantify the contribution from PD-L1 expressing IC, QID is defined as the CPS minus the TPS.

Conclusions PD-L1 IHC 22C3 pharmDx (Dako, USA) stains both TC and immune cells. Removal of the PD-L1 staining TC from the CPS algorithm reduces the number of specimens scored as positive for each indication’s respective diagnostic cut-off(s). Scoring only IC reduces the number of specimens scored as positive for each indication’s respective cutoff.

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Abstract 82 Table 1 Agilent Tumor Bank CPS and QID

<table>
<thead>
<tr>
<th>Indication</th>
<th>Diagnostic Cut-off</th>
<th>Number of Specimens</th>
<th>Number CPS Positive Cases</th>
<th>Number QID (CPS-TPS) Positive Cases</th>
<th>Number of Specimens Flipped at Cut-off</th>
<th>Proportion of Samples Flipped</th>
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</thead>
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<tr>
<td>ESCC</td>
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<td>170</td>
<td>123</td>
<td>28</td>
<td>45</td>
<td>36.6</td>
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<tr>
<td>UC</td>
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<td>186</td>
<td>113</td>
<td>58</td>
<td>57</td>
<td>46.3</td>
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<tr>
<td>GC/CES</td>
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<td>164</td>
<td>184</td>
<td>16</td>
<td>110</td>
<td>55.0</td>
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<tr>
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<td>303</td>
<td>280</td>
<td>13</td>
<td>4.3</td>
</tr>
<tr>
<td>HNSCC</td>
<td>≥20</td>
<td>303</td>
<td>156</td>
<td>26</td>
<td>130</td>
<td>83.3</td>
</tr>
</tbody>
</table>

Abstract 82 Figure 1 SQ3370 is a novel approach that decreases adverse drug exposure and achieves robust injected and non-injected anti-tumor responses

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Background Cancer immunotherapies are dependent on endogenous biomarker expression and other biological factors that often result in varying response rates across tumor types and benefit only a subset of patients. Conversely, conventional cytotoxic, the first-line treatment against solid tumors, are effective in a large patient population, but lack specificity, and often result in dose-limiting systemic toxicity. Here, we present SQ3370, a modular approach that activates doxorubicin (Dox) directly at the tumor site with reduced toxicity and potentially activates an immune response against tumor. The technology is independent of biomarkers, enzymatic activity, pH or oxygen levels and is hence expected to be effective in a wider group of patients. SQ3370 consists of a local intratumoral injection of a produrg-capturing biomaterial (SQL70) followed by 5 daily infusions of SQP33, an attenuated produg of Dox. Complementary click chemistry groups in both components allow active Dox release at the tumor site (figure 1). SQP33 prodrug is ~82-fold less cytotoxic than Dox in vitro. We safely administered SQ3370 in dogs at 8.95-times the veterinary clinical dose of Dox, thus widening the therapeutic window, and showed minimal side effects including cardiotoxicity and immunosuppression. We hypothesize that releasing Dox at a local site with SQ3370 may also promote immune activation against the tumor. We evaluated this in a dual-tumor model of syngeneic MC38 tumors.

Methods Immunocompetent mice were inoculated with MC38 tumor cells in two subcutaneous flanks. One tumor was intramuscularly injected with the biomaterial, SQL70. SQP33 produrg, control Dox, or saline was administered intravenously as per treatment schedule (figure 2A). Tumors harvested from a subset of mice at 2 weeks were assessed for immune biomarkers.

Results In mice bearing two tumors, SQ3370 significantly increased overall survival and the anti-tumor response against injected tumors (figure 2B,C). Surprisingly, SQ3370 also induced regression of the non-injected tumors (figure 2D). Assessment of tumor-infiltrating immune cells showed an increase in CD3+, CD4+, and CD8+ T cells and a decrease in tumor size from initial measurement. Curves stopped when a mouse died, or its tumor volume reached 2000 mm³.

Abstract 82 Figure 2 Systemic anti-tumor response and improved survival

Immunocompetent C57Bl/6 mice were inoculated with mouse MC38 tumors. Tumors were implanted on Day 0. Treatments started on Day 7 with local injection of SQL70 biomaterial at ‘injected’ tumor, followed by systemic administration of saline, Dox, or SQP33 produrg (A). Median overall survival (B) was significantly higher with SQ3370 as compared to Dox, as determined by Logrank test. Injected tumor response (C) was also significantly better with SQ3370, as assessed by corrected t tests, and non-injected tumors (D) showed a favorable response only with SQ3370. Injected-tumor growth curves show mean ± SEM, and growth curves for non-injected tumors show the percentage change in tumor size from initial measurement. Curves stopped when a mouse died, or its tumor volume reached 2000 mm³.
in regulatory T cells in both injected and non-injected lesions (figure 3). The T-cell response correlated with the anti-tumor efficacy data, supporting the immune activation hypothesis.

Abstract 82 Figure 3 Tumor-infiltrating immune cells in both tumors Tumor samples were stained with antibodies and analyzed by multicolor flow cytometry. Dead cells were excluded from analysis. Results show mean ± SEM (n = 3–5 per group) as a percentage of total or marker-gated (CD4 or CD8) cells obtained from the tumor sample. Statistical significance was assessed using a corrected t test.

Conclusions SQ3370 is a proof of concept example for a novel modular approach that addresses limitations of current immuno- and cytotoxic therapies for patients with solid tumors. Local release of Dox with SQ3370 expands the therapeutic window of Dox, minimizes toxicities and leads to a robust anti-tumor response that potentially also causes immune activation against the tumors.

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Ethics Approval This study, project number: SQI-FFS-ON-20181119_04_v4, was approved by the Institutional Animal Care and Use Committee (IACUC) of the vendor, following the guidance of Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC), accreditation number 001516.

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Abstract 83 Figure 1 Kaplan-Meier survival estimates between groups with different ALC at the start date of pembrolizumab and at 6 weeks after initiation of pembrolizumab. There is a statistically significant difference in OS between patients with ALC < 1.4 and patients with ALC ≥ 1.4 at 6 weeks after initiation of pembrolizumab (p = 0.046), but not at the start of treatment (p = 0.095).

Abstract 83 Figure 2 Kaplan-Meier survival estimates between groups with different ANC/ALC at the start date of pembrolizumab and at 6 weeks after initiation of pembrolizumab. There is a statistically significant difference in OS between patients with ANC/ALC < 5 and patients with ANC/ALC ≥ 5, both at the start date of pembrolizumab (p = 0.003) and at 6 weeks after initiation of pembrolizumab (p = 0.028).

Acknowledgements

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Background Pembrolizumab is an anti-programmed cell death protein 1 (PD-1) antibody used for the treatment of advanced non-small cell lung carcinoma (NSCLC). Systemic inflammation has long been associated with poor outcomes in many types of solid tumors. Peripheral blood biomarkers such as absolute lymphocyte count (ALC) and absolute neutrophil count to absolute lymphocyte count ratio (ANC/ALC) serve as surrogate markers of inflammation. The aim of this study is to investigate ALC and ANC/ALC in patients with advanced NSCLC receiving pembrolizumab and determine if there is a correlation between these biomarkers and overall survival (OS).

Methods A total of 240 patients with advanced NSCLC treated with pembrolizumab at Northwell Health hospital centers were included. The ALC and ANC/ALC were examined at initiation of pembrolizumab and after 6 weeks on treatment. The prognostic role of these peripheral blood biomarkers on OS were examined with Kaplan-Meier curves and a multivariable cox regression analysis.

Results Of the 240 patients, the majority were male (52%), with a median age of 67 years (interquartile range [IQR] 59–73 years), had a diagnosis of adenocarcinoma (76%), with stage IV disease (82%). PD-L1 expression was >50% in 44% of the patients. The median time on treatment with pembrolizumab was 5.7 months [IQR: 2.7–12.5]. The median ALC and ANC/ALC were significantly lower at 6 weeks of pembrolizumab compared to the start date of treatment (1.38 vs. 1.4, p<0.001) and (3.6 vs. 4.6, p<0.001) respectively. An ALC greater than 1.4 was associated with an increased OS (figure 1), at 6 weeks after initiation of pembrolizumab (p = 0.046), but not at the start of treatment (p = 0.095). An ANC/ALC less than 5 was associated with improved OS (figure 2), both at initiation of pembrolizumab (p = 0.003) and at 6 weeks after initiation of treatment (p = 0.028). Likewise, after adjusting for potential cofounders with a multivariate analysis (table 1), a baseline ANC/ALC of 5 or higher had a significantly increased risk of death (hazards ratio (HR)=1.84; 95% confidence interval (CI), 1.21–2.79; p = 0.004), compared with patients with a lower ratio.

Conclusions High ALC at time of diagnosis as well as low ANC/ALC at baseline and at 6 weeks on treatment correlated with an increased OS in patients with advanced NSCLC treated with pembrolizumab. These findings represent a readily available predictive biomarker for oncologists and may help with risk stratification and strategizing treatment plans.