**CD68+ Tumor-Associated Myeloid Cells as the Target of Adenosine-Induced Gene Products and Predictor of Response to Adenosine Blockade with Ciforadenant (Cifo) in Renal Cell Cancer (RCC)**


Memorial Sloan Kettering Cancer Center, New York NY, Convex Pharmaceuticals, Burlington CA, Royal Brisbane Hospital, Brisbane Australia, Sylvester Comprehensive Cancer Center, Miami FL, KCSF Comprehensive Cancer Center, San Francisco CA, Cross Cancer Institute, Alberta Canada, Roswell Park Cancer Institute, Buffalo NY

**ADENOSINE INHIBITS ANTI-TUMOR IMMUNITY BY RECRUITMENT OF MYELOID CELLS**

- Adenosine in the tumor microenvironment reduces expression of gene products derived from myeloid cells which correlate with unfavorable prognoses in RCC
- Fang et al showed absence of an adenosine-induced gene signature in response to Adenosine-receptor blockade with Ciforadenant
- McKeown at al showed that an identical myeloid signature was associated with poor prognosis and poor response to pembrolizumab
- Issues at in ThalamicIDDLE at KCSF demonstrated shorter disease-free survival in myeloid adenosine signature (Adenosine-resistant) patients
- Adenosine genes include chemokines that signify through CD39 and CD73 to recruit myeloid and granulocytic cells via a transcriptional hyperactivation of myeloid receptors thought to mediate antitumor responses
- We define a refractory feature of the Adenosine (hyporesponsive CD68+ myeloid cells which further enhances the previously proposed (hyporesistency))

**PATIENT CHARACTERISTICS**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adenosine+ Responders</th>
<th>Adenosine- Responders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>64±14</td>
<td>65±15</td>
</tr>
<tr>
<td>Gender (M:F)</td>
<td>1:1</td>
<td>1:1</td>
</tr>
<tr>
<td>Tumor Stage</td>
<td>T1 or T2</td>
<td>T1 or T2</td>
</tr>
</tbody>
</table>

**ANTI-TUMOR ACTIVITY WITH CIFO + ATEZOLIZUMAB**

**PROTOCOL DESIGN SUMMARY**

**TREATMENT EMERGENT ADVERSE EVENTS**

<table>
<thead>
<tr>
<th>Event</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>25%</td>
<td>10%</td>
<td>5%</td>
<td>2%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>15%</td>
<td>20%</td>
<td>10%</td>
<td>5%</td>
</tr>
<tr>
<td>Anorexia</td>
<td>10%</td>
<td>5%</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Nausea</td>
<td>15%</td>
<td>3%</td>
<td>1%</td>
<td>0%</td>
</tr>
</tbody>
</table>

**PROGRESSION-FREE SURVIVAL**

**CONCLUSIONS**

- In these heavily pretreated patients with metastatic RCC, 45% of which had received >3 prior lines of therapy, including anti-angiogenic/cytokine therapy, adenosine blockade improved survival and disease control
- Adenosine blockade resulted in RCC patients with an unfavorable prognosis, but far more favorable outcomes in other tumors
- ARES1012 at 15 mg/kg + Adenosine+ has shown promising results in RCC and other malignancies
- Adenosine blockade results in RCC patients with an unfavorable prognosis, but far more favorable outcomes in other tumors
- CD68+ myeloid cells are a key target of adenosine and are comprised of granulocytic and myeloid subsets
- CD68+ myeloid cells may be a marker for metastatic tumor control and overall survival
- CD68+ myeloid cells are a key target of adenosine and are comprised of granulocytic and myeloid subsets
- CD68+ myeloid cells may be a marker for metastatic tumor control and overall survival
- CD68+ myeloid cells are a key target of adenosine and are comprised of granulocytic and myeloid subsets
- CD68+ myeloid cells may be a marker for metastatic tumor control and overall survival

**INFLITRATING CD68+ CELLS FURTHER ENRICHES FOR RESPONDERS**

**Figure 1a:** Graph showing the relationship between the percentage of infiltrating CD68+ cells and the response to Ciforadenant in RCC patients.
**Figure 2a:** Graph showing the correlation between the expression of CD68+ cells and the progression-free survival in RCC patients.
**Figure 3a:** Graph showing the association between the infiltration of CD68+ cells and the overall survival benefit in RCC patients.

For questions or comments, email Contact@Meskens.com