Adenosine Receptor Blockade with Ciforadenant ± Atezolizumab in Advanced Metastatic Castration Resistant Prostate Cancer (mCRPC)

Fong L1, Chu M2, George S1, Hughes B3, Carthon B4, Merchant J1, Harshman L1, Munneke P5, Kwei L6, Hotson A7, Mobasher M8, Miller R9

1USC Comprehensive Cancer Center, Los Angeles CA, 2Vince Cancer Institute, Louisville KY, 3Roswell Park Cancer Institute, Buffalo NY, 4Vincicancer Hospital, Belgrade Serbia, 5Weill Cornell Institute, Atlanta GA, 6Sidney Comprehensive Cancer Center, Miami FL, 7Dana-Farber Cancer Institute, Boston MA, 8Corvus Pharmaceuticals, Burlingame CA

**ADENOSINE INHIBITS ANTI-TUMOR IMMUNITY**

- **Cancer cell**
- **Resistant Prostate**
- **Anti-CD73 antibody**
- **CPI-006**
- **CD39**
- **CD73**
- **CD39**
- **AMP**
- **ATP**
- **CIFORADENANT**
- **A2AR antagonist**
- **A2BR antagonist**
- **TCR**
- **Dendritic cell**
- **Myeloid Cell / Macrophage**
- **NK Cell**
- **Decreased tumor antigen cross presentaton**
- **Decreased proliferation**
- **Increased CTLA-4 and PD-1 expression**
- **Decreased IL-2 production**

**IMMUNE CORRELATES WITH Tx & RESPONSE**

**Maximum % Change in SLD**

- PSA (Best % change). Changes > +100% labelled as X
- * Patient continuing on treatment as of Feb 2020

**CONCLUSIONS**

- Ciforadenant ± atezolizumab treatment was well tolerated.
- Ciforadenant demonstrated anti-tumor activity in heavily pretreated mCRPC patients as monotherapy and in combination with atezolizumab.
- Confirmed DCR (established with ≥2 scans) = 20% + additional pts with unconfirmed SD continuing on treatment.
- Tumor regression occurs in 11/35 pts, including 2 treated with monotherapy.
- Expression of CD73, an anti-tumor mechanism that produces adenosine, correlates with expression of a recently described Adenosine Gene Signature, supporting the potential relevance of adenosine in prostate cancer.
- Cytokine changes after treatment consistent with an immune response.

**TREATMENT EMERGENT ADVERSE EVENTS**

<table>
<thead>
<tr>
<th>Event</th>
<th>Ciforadenant (n=11)</th>
<th>Ciforadenant + Atezolizumab (n=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Grade</td>
<td>Any Grade</td>
<td></td>
</tr>
<tr>
<td>Grade 1/4</td>
<td>Grade 1/4</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Anemia</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pruritus</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Back pain</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Chills</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Myalgia</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Rash</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

At least 5% of any grade in any treatment

**DURATION OF TREATMENT**

- **Pre Treatment**
- **Post Treatment**

**THERAPEUTIC RESPONSE**

- **PSA (Best % change). Changes > +100% labelled as X**
- * Patient continuing on treatment as of Feb 2020

**PATIENT CHARACTERISTICS**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age (years)</td>
<td>68.0</td>
</tr>
<tr>
<td>Median Prior Treatments</td>
<td>3.0 (IQR: 1-6)</td>
</tr>
<tr>
<td>Androgen blockade</td>
<td>13/35 (37%)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>1/35 (3%)</td>
</tr>
<tr>
<td>Androgen blockade and chemotherapy</td>
<td>21/35 (60%)</td>
</tr>
<tr>
<td>Metastasis burden:</td>
<td></td>
</tr>
<tr>
<td>Node only</td>
<td>13/35 (37%)</td>
</tr>
<tr>
<td>Visceral only</td>
<td>3/35 (9%)</td>
</tr>
<tr>
<td>Node and Bone</td>
<td>4/35 (11%)</td>
</tr>
<tr>
<td>Bone and/or node and visceral</td>
<td>15/35 (43%)</td>
</tr>
</tbody>
</table>

**Eligibility**

- Measurable disease
- Progressive disease on prior therapy
- Failed up to 5 prior therapies
- No selection for PD-L1 expression
- Treated until disease progression or toxicity

**PROTOCOL DESIGN SUMMARY**

- **Metastatic Castration-Resistant Prostate Cancer (n=35)**
  - Ciforadenant Monotherapy (n=11)
  - Ciforadenant + Atezolizumab (n=24)
  - Treatment Started: Dec 2016 to Dec 2017
  - Last Dose: Oct 2017 to Dec 2017
  - Median age: 68.0 years (IQR: 62.0-74.3)
  - Median prior treatments: 3.0 (IQR: 1-6)
  - Androgen blockade: 13/35 (37%)
  - Chemotherapy: 1/35 (3%)
  - Androgen blockade and chemotherapy: 21/35 (60%)
  - Metastasis burden:
    - Node only: 13/35 (37%)
    - Visceral only: 3/35 (9%)
    - Node and Bone: 4/35 (11%)
    - Bone and/or node and visceral: 15/35 (43%)
    - Prior PD-L1 Exposure:
      - Naive: 33/35 (94%)
      - Resistant/refractory: 1/35 (3%)
      - Missing: 1/35 (3%)

**TREATMENT EMA**

- **Maximum % Change in SLD**
  - PSA (Best % change). Changes > +100% labelled as X
  - * Patient continuing on treatment as of Feb 2020

**DIFFERENCES IN IMMUNE CORRELATES WITH TX & RESPONSE**

- **CD73 (NT5E NanoString)**
  - Fold Change in Serum TNF-α
  - Pre Treatment: 0.0
  - Post Treatment: 10000
  - p = 0.004

- **Adenosine Signature (AdenoSig) Expression**
  - Pre Treatment: 0
  - Post Treatment: 1000
  - p = 0.0002

**IMMUNE CORRELATES WITH Tx & RESPONSE**

- **Ciforadenant**
  - Fold Change in Serum TNF-α
  - Pre Treatment: 0
  - Post Treatment: 10000
  - p = 0.004

- **Ciforadenant + Atezolizumab**
  - Fold Change in Serum TNF-α
  - Pre Treatment: 0
  - Post Treatment: 10000
  - p = 0.0002

**PSA Result**

- **PD**
- **SD**
- **PR**
- **Ongoing**

**CONCLUSIONS**

- Ciforadenant ± atezolizumab treatment was well tolerated.
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**Patient followup continues. Updated results planned for 2020 ASCO Annual Meeting**