Selinexor, Daratumumab, and Dexamethasone in Patients with Relapsed/Refractory Multiple Myeloma (MM)

**Selinexor: First-in-Class, Oral Selective Inhibitor of Nuclear Export (SINE)**

Selinexor (IAP090) is a oral nuclear export protein inhibitor: - Tumor suppressor proteins (TSPs, e.g., p53, Bax, NOXA), downregulate cell cycle arrest and apoptosis.\(^\text{1,2}\)
- Oncoproteins: XPO1 is overexpressed in MM: high XPO1 levels enable cancer cells to escape TSP-mediated cell cycle arrest and apoptosis.\(^\text{3}\)

**Background: Daratumumab and Selinexor Activity in Heavily-Treated MM**

**Daratumumab and Selinexor Single Agent Activity in Heavily-Treated MM**

**STORM: Daratumumab + Dexamethasone Refractory to Dara, PI, and IMiD**

**STOMP SdD Arm Study Design**

**Patient Characteristics and DLTs**

**Eligibility at January 3, 2020:**
- MM stage: rel/ref MM in PI or IMiD in ≥2 lines of therapy
- 18–75 years of age
- NCI performance status of 0–2
- Measurable disease by D90
- LVEF (left ventricular ejection fraction) >50%
- Pretreatment cardiac or neurologic history of grade 2 or 3 toxicity
- Other IMiD/PI exposure <3 months prior to study
d

**Median Age, Years (range):**
- 66 (18–80)

**Median Time from Diagnosis to SdD Treatment, Years:**
- 0.6 (0–14.1)

**Median Prior Regimens (range):**
- 3 (2–7)
- 30 (15–100) cycles of prior IMiD therapy
- 33 (0–60) cycles of prior PI therapy
- 23 (0–30) regimens of prior IMiD therapy
- 16 (0–30) regimens of prior PI therapy
- 11 (0–20) regimens of prior SdD therapy

**Selinexor, Daratumumab, and Dexamethasone in Patients with Relapsed/Refractory Multiple Myeloma (MM)**

**Key Results and Conclusion**

Once Weekly Selinexor with Daratumumab/Dexamethasone is Highly Active, Produces Deep and Durable Responses in Patients with RRMM Who Were Heavily Pretreated

- **RP2D was established as selinexor 100 mg once weekly (QW), daratumumab 16 mg/kg (per label), and dexamethasone 40 mg QW**
- **ORR and CBR were 73% and 87% respectively in daratumumab-naïve patients**
- **Median progression-free survival was 12.5 months in all patients who had median of 3 prior therapies**
- **Common treatment-related AEs with SdD were thrombocytopenia, anemia, neutropenia, nausea, dysgeusia, anorexia, and fatigue**

**Treatment-Related Adverse Events in ≥10% Patients (RP2D Patients)**

**Selinexor-Daratumumab-Dex: Efficacy**

<table>
<thead>
<tr>
<th>Category</th>
<th>N(^*)</th>
<th>ORR (%)</th>
<th>VGPR (%)</th>
<th>PR (%)</th>
<th>CBR (%)</th>
<th>MR (%)</th>
<th>SD (%)</th>
<th>PD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All</strong></td>
<td>8510</td>
<td>26.2%</td>
<td>9.1%</td>
<td>14.7%</td>
<td>30.3%</td>
<td>13.5%</td>
<td>15.9%</td>
<td>4.7%</td>
</tr>
<tr>
<td><strong>Daratumumab</strong></td>
<td>30</td>
<td>22.7%</td>
<td>9.1%</td>
<td>12.8%</td>
<td>38.4%</td>
<td>13.3%</td>
<td>16.7%</td>
<td>3.3%</td>
</tr>
<tr>
<td><strong>RP2D</strong></td>
<td>29</td>
<td>20.6%</td>
<td>10.3%</td>
<td>17.9%</td>
<td>48.3%</td>
<td>14.1%</td>
<td>13.8%</td>
<td>3.3%</td>
</tr>
</tbody>
</table>

Note: *patients prior to disease follow-up, **patients pre-protocol for ≥3 previous lines of therapy for MM, including an IMiD and an PI, and a PI and an IMiD, respectively.

**Figure 2: Waterfall Plot: Deep reductions in Disease Burden (n=32)**

**Once weekly Selinexor with Daratumumab/Dexamethasone is highly active, produces deep and durable responses in patients with RRMM who were heavily pretreated.**

**Abbreviations:**
- CBR: clinical benefit rate
- MR: minimal response
- ORR: overall response rate
- PD: progressive disease
- PR: partial response
- SD: stable disease
- VGPR: very good partial response

**Limiting Toxicity**

- No treatment-related AE or SAE leading to death were reported
- No severe infection or ≥3 organ system toxicity (≥3OS) was observed
- No second malignancies or ≥2 organ system toxicity (≥2OS) or any grade 5 toxicity was reported
- No treatment-related deaths were reported
- No major bleeding events (except for GI bleed) were reported
- No hospitalization for grade ≥3 fatigue was reported
- No grade ≥3 neurotoxicity was reported
- No grade ≥3 sensory or peripheral neuropathy was reported
- No grade ≥3 hypercalcemia was reported
- No grade ≥3 pulmonary embolism was reported
- No grade ≥3 pancreatitis was reported
- No grade ≥3 cholecystitis was reported
- No grade ≥3 atrial fibrillation was reported
- No grade ≥3 deep vein thrombosis was reported
- No grade ≥3 pulmonary embolism was reported

**Once weekly Selinexor with Daratumumab/Dexamethasone is highly active, produces deep and durable responses in patients with RRMM who were heavily pretreated.**

- **RP2D was established as selinexor 100 mg once weekly (QW), daratumumab 16 mg/kg (per label), and dexamethasone 40 mg QW.**
- **ORR and CBR were 73% and 87% respectively in daratumumab-naïve patients.**
- **Median progression-free survival was 12.5 months in all patients who had median of 3 prior therapies.**
- **Common treatment-related AEs with SdD were thrombocytopenia, anemia, neutropenia, nausea, dysgeusia, anorexia, and fatigue.**

**Acknowledgments:**

This study was supported by Karyophycin Therapeutics, Inc. and Neovii Biotech.