Overall Survival of Triple Class Refractory, Penta-Exposed Multiple Myeloma (MM) Patients Treated with Selinexor Plus Dexamethasone or Conventional Care: A Combined Analysis of the STORM and Mammoth Studies

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Background

- Despite dramatic successes in novel drug approvals, almost all MM patients (pts) eventually progress to relapsed refractory MM (RRMM)
- Patients whose disease becomes triple class refractory (TCR, i.e. refractory to an IMiD, PI and CD8 mAbs) have survival measured in months (mos)3
- Selinexor is a selective inhibitor of nuclear export (SINE™) compound which blocks exportin 1 (XPO1). XPO1 is overexpressed in MM cells and essential for MM cell survival
- In the STORM study, selinexor (S) was used in combination with low-dose dexamethasone (Sd) and demonstrated anti-tumor activity in TCR, penta-exposed (TCR-PI, i.e. exposed to lenalidomide, pomalidomide, bortezomib, carfilzomib and daratumumab) MM4,5
- In the retrospective MAMMOTH study, we reported the outcomes of pts with RRMM after they become refractory to a CD8 mAb, including a subset of pts whose disease was documented to be TCR
- Lack of benchmark for outcomes in the TCR-PE population has been a concern

Objective

To compare therapeutic outcomes of similar cohorts of patients treated with Sd in STORM and patients receiving other therapeutics and included in MAMMOTH.

Methods

- Primary endpoint was overall survival (OS) calculated from the time of initiation of next line of therapy after MM reached TCR-PE status until death or censored at last follow-up
- From STORM, we included all patients who received Sd as the first line therapy after their disease reached TCR-PE status (n=64)
- Dataset from MAMMOTH was interrogated to identify all patients matching STORM patients

MAMMOTH Inclusion Criteria

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Removed</th>
<th>Remaining</th>
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<tbody>
<tr>
<td>Initial population</td>
<td></td>
<td>275</td>
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<tr>
<td>Patients receiving therapy after becoming refractory to daratumumab.</td>
<td>26</td>
<td>249</td>
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<tr>
<td>Patients not treated with selinexor in subsequent line</td>
<td>14</td>
<td>235</td>
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<tr>
<td>Patients treated with bortezomib, carfilzomib, lenalidomide, pomalidomide and daratumumab and with MM refractory to at least 1 PI, 1 IMID and daratumumab. Prior therapy with an alkylating agent and/or corticosteroid required. Receiving subsequent therapy</td>
<td>107</td>
<td>128</td>
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Conclusions

- Despite inherent limitations in comparison of trial enrollees vs. real world patients, this analysis suggests improved OS with Sd vs conventional care in patients with TCR-PE RRMM treated in the academic setting
- Prognosis for these patients remains poor and underscores the need for therapeutic advancements

References