Bortezomib, Ascorbic Acid and Melphalan (BAM) Therapy for Patients with Newly Diagnosed Multiple Myeloma: An Effective and Well-Tolerated Frontline Regimen

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INTRODUCTION

It has been shown that combination of treatment for cancer patients are more effective than any single agent alone. Extensive research has shown that the combination of bortezomib, ascorbic acid (AA) or vitamin C, and melphalan is a promising approach in the treatment of newly diagnosed multiple myeloma (MM). This comodity, consisting of a 28-day cycle for a maximum of 8 cycles, was investigated in a phase I study.

INCLUSION/EXCLUSION CRITERIA

• Primary endpoints:
  - To assess the objective response rate (ORR) for the combined treatment of bortezomib, AA, and melphalan (BAM)
  - To assess the overall survival of the patients

• Secondary endpoints:
  - To assess the progression-free survival

TREATMENT SCHEMA

Treatment consisted of a 28-day cycle for a maximum of 8 cycles.

• Oral ascorbic acid at a dose of 1g and oral melphalan at 0.1 mg/kg were both administered in the evening on days 1-4 of each cycle.

RESULTS

Table 1. Patient Demographics

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Median Age (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/Female</td>
<td>70 (range: 50-90)</td>
</tr>
</tbody>
</table>

Table 2. Patient Responses

| Disease Status | Complete Response (CR) (n=35) | Very Good Partial Response (VGPR) (n=23) | Partial Response (PR) (n=12) | Minor Response (MR) (n=4) | Stable Disease (SD) (n=2) | Progression Disease (PD) (n=3) |

Table 3. Patient Status

<table>
<thead>
<tr>
<th>Patient Status</th>
<th>Active on BAM</th>
<th>Maintenance (BAM) Phase</th>
<th>Expired</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Status</td>
<td>4</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

ADVERSE EVENTS

No patients were evaluable for safety:

• 17 (40%) patients experienced grade 3 or greater side effects

Table 4. Patient Survival

<table>
<thead>
<tr>
<th>Patient Survival</th>
<th>Median Survival (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evaluable for Efficacy</td>
<td>13 (range: 0.4 - 3.5)</td>
</tr>
<tr>
<td>Overall Survival</td>
<td>15 (range: 1-21+)</td>
</tr>
</tbody>
</table>

ENDPOINTS

• Primary endpoints:
  - To assess the overall response rate (ORR), complete response rate (CR), and very good partial response (VGPR)
  - To assess the overall survival (OS) and time to progression (TTP)
  - To assess the safety and tolerability of BAM therapy for patients with MM

• Secondary endpoints:
  - To assess the progression-free survival and overall survival
  - To assess time to disease progression among patients who continue on maintenance treatment with bortezomib.

SUMMARY

Bortezomib, Ascorbic Acid and Melphan (BAM) Therapy for Patients with Newly Diagnosed Multiple Myeloma: An Effective and Well-Tolerated Frontline Regimen

- An NIH- and steroid-free regimen with an excellent response rate (overall - 74%, CR - 16%, VGPR - 10%, PR - 35%, MR - 35%)
- Well-tolerated with few significant AEs reported
- AEs were predictable and manageable
- Infrequently reported is grade 2 neuropathy and most cases of peripheral neuropathy resolved