Introduction

• Renal impairment (RI) occurs in 20% to 40% of newly diagnosed patients (pts) with multiple myeloma (MM) and is associated with poor prognosis1,2.
• Pts with MM who relapse on or become refractory to treatment (Tx) experience shortened overall survival (OS)3.
• Pomalidomide + low-dose dexamethasone (POM + LDex) is approved for the Tx of relapsed/refractory MM (RRMM) in pts who have had Tx failure with lenalidomide (LEN) and/or bortezomib (BORT)4.
• In clinical trials, POM + LDex demonstrated safety and efficacy in pts with RRMM (MM-010)5,6, as well as extended progression-free survival (PFS) and OS vs high-dose dexamethasone (MM-003) or POM alone (MM-002)7.
• This pooled analysis examined the efficacy and safety of POM + LDex in pts with RRMM with and without moderate RI who were enrolled across POM clinical studies.

Methods

Exclusion Criteria

- Age ≥ 18 yrs with documented RRMM
- ≥ 2 prior therapies including ≥ 2 cycles of LEN or BORT, alone or in combination
- Documented disease progression during or within 60 days of last Tx
- Refractoriness to LEN and BORT (or intolerant of BORT) was allowed (MM-002) or required (MM-003 and MM-010)

Exclusion Criteria

- Absolute neutrophil count < 1000/uL (MM-002, MM-003) or < 800/uL (MM-010)
- Platelet count < 75,000/uL (< 30,000/uL for pts with ≥ 50% plasma cells of nucleated bone marrow cells)
- Creatinine clearance (CrCl) < 45 mL/min (MM-003 and MM-010) or serum creatinine ≥ 3.0 mg/dL (MM-002)
- Peripheral neuropathy (PN) grade (Gr) ≥ 2

Assessments

- Pts were grouped by RI status (with moderate RI [CrCl ≥ 30 to < 60 mL/min] and without RI [CrCl ≥ 60 mL/min]) and assessed for safety and efficacy
- Overall response rate (ORR) was assessed based on International Myeloma Working Group (IMWG) criteria10
- Adverse event (AE) severity was graded according to the National Cancer Institute Toxicity Criteria for Adverse Events (NCI-CTCAE)

Results

Patient and Disease Characteristics

- 93% of pts with moderate RI and 73% of pts without RI were analyzed (Table 1)
- Pts with moderate RI were older vs pts without RI (median age of 70 vs 65 yrs)
- Pts with moderate RI had more advanced disease vs pts without RI
- Median time since diagnosis was 5.3 yrs for both pts subgroups

Table 1. Patient and Disease Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>With Moderate RI</th>
<th>Without Moderate RI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs (range)</td>
<td>70.3 (34-84)</td>
<td>65.2 (34-80)</td>
</tr>
<tr>
<td>ECOG, %</td>
<td>4.2 (0-10)</td>
<td>9.1 (0-30)</td>
</tr>
<tr>
<td>ISS, %</td>
<td>4.1 (0-10)</td>
<td>3.6 (0-10)</td>
</tr>
<tr>
<td>Percentage of plasma cells</td>
<td>51.9 (30-72)</td>
<td>50.2 (30-75)</td>
</tr>
<tr>
<td>% w/ bone lesions</td>
<td>78.1 (60-100)</td>
<td>75.8 (60-100)</td>
</tr>
<tr>
<td>% w/ lytic lesions</td>
<td>58.1 (0-100)</td>
<td>65.7 (0-100)</td>
</tr>
<tr>
<td>% w/ hypercalcemia</td>
<td>6.9 (0-30)</td>
<td>13.2 (0-30)</td>
</tr>
<tr>
<td>% w/ hypocalcemia</td>
<td>0 (0-10)</td>
<td>17.8 (0-30)</td>
</tr>
<tr>
<td>% w/ renal impairment</td>
<td>51.1 (30-72)</td>
<td>50.2 (30-75)</td>
</tr>
</tbody>
</table>

Table 2. Treatment

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>With Moderate RI</th>
<th>Without Moderate RI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median average dose (mg/day) (range), mos</td>
<td>4.0 (1.6-4.2)</td>
<td>4.0 (1.6-4.2)</td>
</tr>
<tr>
<td>Median Tx duration</td>
<td>4.0 (1.6-4.2)</td>
<td>4.0 (1.6-4.2)</td>
</tr>
</tbody>
</table>

Safety

- Safety profile of POM + LDex was similar across pt subgroups
- The most common Gr 3/4 AEs were hematologic (Table 4)
- Rates of Gr 3/4 AEs were similar in pts with and without moderate RI
  - Neutropenia: 46.7% vs 46.9%
  - Anemia: 35.8% vs 35.9%
  - Infections: 24.4% vs 24.5%
  - Thrombocytopenia: 20.7% vs 20.8%
  - Neutropenia: 2.7% vs 5.4%
  - Anemia: 0% vs 0%
  - Infections: 5.3% vs 5.3%
  - Thrombocytopenia: 0% vs 0%
  - Frequency of Gr 3/4 deep vein thrombosis/pulmonary embolism or PN was ≤ 2.5% in both subgroups

Table 3. Efficacy Outcomes

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>With Moderate RI</th>
<th>Without Moderate RI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall response rate (ORR; 95% CI), mos</td>
<td>6.8 (2.8-10.7)</td>
<td>6.9 (2.8-10.8)</td>
</tr>
<tr>
<td>Median PFS (95% CI), mos</td>
<td>10.5 (8.1-12.0)</td>
<td>10.6 (8.2-12.1)</td>
</tr>
<tr>
<td>Median DOR (95% CI), mos</td>
<td>4.0 (3.3-4.8)</td>
<td>4.0 (3.3-4.8)</td>
</tr>
<tr>
<td>Median TTP (95% CI), mos</td>
<td>6.9 (5.3-8.5)</td>
<td>7.0 (5.4-8.6)</td>
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</table>

DISCLOSURES

D.S.S. reports speakers bureau for Celgene, Amgen, Takeda, Merck, Novartis; K.C.W. reports consultancy and honoraria from Celgene, Millennium, Amgen, Bristol-Myers Squibb; X.Y., K.H., L.S., M.H.Z. report employment and equity ownership for Celgene; A.P. reports board for Celgene, Janssen, Takeda, Novartis, Amgen, honoraria and served as a member on an entity’s board of directors or advisory committee for Celgene; P.M. reports advisory membership on an entity’s board of directors or advisory committee, research funding from Celgene Canada; J.S.M. reports consultancy and honoraria from MedTech Media (Hair Gurus, PhD and Peter Simon, PhD and printing support from MedTech Media, sponsored by Celgene Corporation.

Conclusions

- This pooled analysis of 3 RRMM trials provides the opportunity to compare the comprehensive safety and efficacy of POM + LDex in pts with and without moderate RI
- ORR, PFS, TTP, DOR, and tolerability following Tx with POM + LDex appeared to be independent of the presence or absence of moderate RI
- Pts with moderate RI had shorter OS vs pts without RI, consistent with increased risk of mortality previously reported for this pt population
- Results support use of POM + LDex at approved dosing as a standard of care in RRMM for pts with or without moderate RI

References


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