A Randomized Phase 2 Study of Pomalidomide/Dexamethasone With or Without Elotuzumab in Patients With Relapsed/Refractory Multiple Myeloma

**Background**

Multiple myeloma

- Multiple myeloma (MM) is the second most prevalent blood cancer after non-Hodgkin lymphoma, representing 10% of all hematologic malignancies. In the US, ~30,330 new cases and 12,650 deaths were predicted for 2016.
- The incidence of MM increases with age; median age at onset in the US is 68 years, and the median age at death is 70–71 years (men and women).
- MM is a malignant neoplasm of plasma cells, caused by the expansion of a single clone of abnormal terminally differentiated B cells (plasma cells).
- These cells produce a monoclonal immunoglobulin (M protein) and replace the normal bone marrow, leading to the destruction of bone and marrow failure.
- The current standard of care for the treatment of relapsed/refractory multiple myeloma (RRMM) predominantly includes combination therapies based on proteasome inhibitors (PSis; eg, bortezomib, carfilzomib, ixazomib), immunomodulatory drugs (IMiDs; eg, lenalidomide, carfilzomib, pomalidomide), or combinations of both.
- Patients can become refractory to PSIs and IMiDs over time, highlighting an unmet need.
- In the absence of a cure, current therapies can only slow disease progression, prolong survival, and minimize symptoms.

Elotuzumab

- Elotuzumab is a humanized IgG1 immunostimulatory monoclonal antibody targeted against signaling lymphocytic activation molecule F7 (SLAMF7), a glycoprotein expressed on ~95% of myeloma cells and normal killer cells but not on normal tissue.
- Elotuzumab works via a dual mechanism of action, both by directly activating natural killer cells and by mediating antibody-dependent cell-mediated cytotoxicity (ADCC) via the CD16 pathway, to cause targeted myeloma cell death (Figure 1).

ELOQUENT-3 study design

- ELOQUENT-3 (NCT02654132) is a Phase 2, multicenter, randomized, open-label study to evaluate the efficacy and safety of elotuzumab plus pomalidomide and dexamethasone, compared with pomalidomide and dexamethasone alone (Figure 3).
- Eligible patients are required to have RRMM and ≥2 prior lines of therapy that include >2 consecutive cycles of lenalidomide and a PI, alone or in combination (Table 1).

Objectives

**Primary**

- PFS

**Secondary**

- Objective response rates
- Overall survival

**Rationale**

- Previous studies have demonstrated the safety of combining elotuzumab with the IMiDs thalidomide and lenalidomide.
- Since lenalidomide and pomalidomide are in the same class of drugs, and have a similar mechanism of action and safety profile, elotuzumab plus pomalidomide and dexamethasone is expected to elicit a similar safety profile as elotuzumab plus lenalidomide and dexamethasone.
- To show treatment benefit in patients who have progressed following prior IMiD therapy, versus pomalidomide and dexamethasone alone.

**References**


**Study sites and dates**

- 46 international study sites in 11 countries (Figure 4)
- Estimated enrollment: 121
- Study start date: March 2016
- Final data collection date for primary outcome measure: May 2017
- Estimated study completion date: November 2018

**Table 1. Key inclusion and exclusion criteria**

<table>
<thead>
<tr>
<th>Inclusion</th>
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<tr>
<td>≥18 years of age</td>
<td>Active plasma cell leukemia</td>
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<tr>
<td>≥2 prior lines of therapy including &gt;2</td>
<td>Prior treatment with pomalidomide</td>
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<td>consecutive cycles of lenalidomide and a PI, alone or in combination</td>
<td>Documented refractory MM or RRMM</td>
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<td>Fails treatment with a PI and lenalidomide in one of the following ways:</td>
<td>Grade &gt;2 peripheral neuropathy</td>
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<tr>
<td>1. Refractory to PI and lenalidomide, and to last treatment</td>
<td>Creatinine clearance &lt;45 mL/min</td>
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<td>2. Relapsed and refractory; achieved at least partial response to previous treatment with a PI or lenalidomide, or both, but progressed within 6 months and refractory to last treatment</td>
<td>Unable to tolerate thromboembolic prophylaxis while on study</td>
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<td>Measureable disease at screening</td>
<td>Prior autologous stem cell transplantation within 12 weeks</td>
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**ECOG performance status =2**

**ECOG Eastern Cooperative Oncology Group**

**Figure 3. ELOQUENT-3 study design**

**Figure 4. Study sites for ELOQUENT-3 (NCT02654132)**

**References**


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Elotuzumab was developed in partnership between Bristol-Myers Squibb and AbbVie Biotherapeutics. Elotuzumab is approved for use in the United States in combination with lenalidomide and dexamethasone in patients with multiple myeloma who have received ≥3 prior therapies, and for use in Europe in combination with lenalidomide/dexamethasone in adult patients with multiple myeloma who have received at least 1 prior therapy.

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