Lenalidomide maintains remissions in persons with multiple myeloma intolerant to thalidomide

Guillermo J Ruiz-Delgado,* Guillermo J Ruiz-Argüelles*

RESUMEN

Antecedentes: la lenalidomida es un modificador de la respuesta inmune que ha mostrado utilidad en el tratamiento de pacientes con mieloma múltiple. Su indicación se ha limitado en México por el costo alto. El tratamiento óptimo del mieloma múltiple en México es la inducción a la remisión con talidomida-dexametasona seguida de trasplante de células hematopoyéticas autólogas y, posteriormente, mantenimiento con inmunomodulación.

Objetivo: analizar si la introducción tardía de lenalidomida en el tratamiento de pacientes con mieloma múltiple es útil como parte del tratamiento de mantenimiento.

Material y métodos: se trataron ocho pacientes consecutivos con mieloma múltiple con talidomida-dexametasona hasta inducir la remisión parcial o completa. Posteriormente, cuatro de ellos recibieron quimioterapia a dosis altas (melfalán 200 mg/m²) rescatada con trasplante de células hematopoyéticas autólogas y todos recibieron tratamiento de mantenimiento con talidomida, 100 mg/día. A la aparición de síntomas de intolerancia a la talidomida, a los ocho pacientes se les cambió a lenalidomida, 25 mg/día.

Resultados: en todos los pacientes se mantuvo la remisión de la enfermedad y en dos se abatió aún más la magnitud de la paraproteinemia; en todos desaparecieron los datos de intolerancia a la talidomida.

Conclusión: la introducción tardía de la lenalidomida al armamento terapéutico del mieloma múltiple se asocia con resultados favorables y disminuye los costos cuando se compara con la indicación temprana de este fármaco.

Palabras clave: lenalidomida, talidomida, mieloma múltiple.

ABSTRACT

Background: The most recommended therapy-approach in patients with multiple (MM) myeloma in México is induction with thalidomide and dexametasona (Thal/Dex) followed by autologous hematopoietic stem cell transplantation, followed by Thal maintenance; however, the toxicity of Thal develops eventually in most patients with MM. Lenalidomide (Len) is an expensive drug.

Material and methods: In a single institution in México, patients with MM intolerant to Thal were switched to Len during maintenance therapy. Eight of twelve subjects with MM who were able to defray the cost of Len were switched from Thal to Len as remission maintenance after developing peripheral neuropathy.

Results: Amount of monoclonal protein when Len was started dropped or remained stable. One subject had amyloidosis-related nephrotic syndrome; the amount of urinary albumin dropped following Len therapy. Side-effects of Thal remained stable or improved, as judged subjectively by the patients.

Conclusions: A delay in the introduction of Len in the treatment of patients with MM results in lower costs.

Key words: Lenalidomide, talidomide, multiple myeloma.


Correspondence: Guillermo J. Ruiz-Argüelles MD, FACCP, FRCP (Glasg). Clínica Ruiz. Centro de Hematología y Medicina Interna. 8B Sur 3710 Puebla 72530, Pue. Mexico. E-mail: gruiz1@clinicaruiz.com

Received: april 2011. Accepted: may 2011.

in persons with relapsed or refractory MM in phase-1 and phase-2 studies. Two large phase-3 studies showed Len combined with dexamethasone was superior to dexamethasone only in persons with relapsed or refractory MM receiving 1 or more prior therapies.3-5

Len is an expensive drug in Mexico; Thal is considerably cheaper and dexamethasone is also inexpensive.6,7,8 Accordingly, the current recommendation for initial therapy of MM in Mexico is Thal/dexamethasone (Thal/Dex)7 followed by AHCT in appropriate subjects.9 Posttransplant maintenance with Thal is a reasonable option in Mexico1,6,7,8 but most people become intolerant to Thal because of peripheral neuropathy or other side-effects.9,10

PATIENTS AND METHODS

Eight persons with MM diagnosed at the Centro de Hematología y Medicina Interna de Puebla were included in the study. All subjects provided informed consent before participating in the study. Table 1 shows some characteristics of the subjects; persons with light chain myeloma had positive urine immunofixation. Thal was given by mouth at a dose of 100 mg/d. Dexamethasone was given by mouth at a dose of 36-40 mg once weekly. Aspirin 100 mg/d was given to prevent thrombosis. All subjects received Thal/Dex until achieving a complete remission or a very good partial remission. Subjects were offered an AHCT; 4 subjects chose this therapy. After achieving a remission or having the AHCT, per protocol, all patients were given Thal by mouth at a dose of 100 mg/d. When patients developed Thal-induced peripheral neuropathy they were offered Len, 25 mg/d by mouth given 21 d of 28 d cycles.

RESULTS

Eight of twelve subjects able to defray the cost of the drug were switched from Thal to Len as remission maintenance after developing peripheral neuropathy. Important features are indicated in Table 1. Amount of monoclonal protein when Len was started dropped (2 cases) or remained stable (6 cases). One subject (number three) had amyloidosis-related nephrotic syndrome; the amount of urinary albumin dropped from 4 g to 2 g following Len therapy. Len was given for 2-14 mo. Side-effects of Thal remained stable or improved, as judged subjectively by the patients. The initial dose of Len was switched to a 14 d schedule every 28 d in cases of myelosuppression.

DISCUSSION

The use of novel drugs in MM has challenged the practice of high-dose therapy AHCT.6,10 Since the use of novel therapies in MM results in substantially higher costs, the debate about the role of AHCT is different in countries with restricted economies.6 In developing countries, AHCT is cheaper than the use of novel anti-MM drugs.6,7,8 Accordingly, the use of Len as initial therapy for people with MM in these countries is difficult.

Currently, the most recommended therapy-approach in Mexico is induction with Thal/Dex followed by AHCT followed by Thal maintenance.7 The toxicity of Thal, which develops eventually in most patients with MM,

Table 1. Salient features of the eight persons with multiple myeloma included in the study. * amyloid patient. F = female, M = male, AHCT = Autologous hematopoietic stem cell transplantation. 2 indicates that two autografts were done.

<table>
<thead>
<tr>
<th>Case</th>
<th>1</th>
<th>2</th>
<th>3 *</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>55</td>
<td>63</td>
<td>53</td>
<td>54</td>
<td>54</td>
<td>73</td>
<td>68</td>
<td>81</td>
</tr>
<tr>
<td>Sex</td>
<td>F</td>
<td>M</td>
<td>M</td>
<td>F</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>F</td>
</tr>
<tr>
<td>Paraprotein</td>
<td>IgA kappa</td>
<td>Lambda</td>
<td>IgA lambda</td>
<td>IgG kappa</td>
<td>IgG kappa</td>
<td>Kappa</td>
<td>IgG kappa</td>
<td>IgG kappa</td>
</tr>
<tr>
<td>M spike at diagnosis (gr/dl)</td>
<td>3.8</td>
<td>0.0</td>
<td>1.1</td>
<td>4.6</td>
<td>1.1</td>
<td>0.0</td>
<td>6.3</td>
<td>2.8</td>
</tr>
<tr>
<td>AHCT</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes (2)</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>M spike at starting lenalidomide (gr/dl)</td>
<td>1.4</td>
<td>0.0</td>
<td>0.0</td>
<td>0.7</td>
<td>0.7</td>
<td>0.0</td>
<td>0.3</td>
<td>1.5</td>
</tr>
<tr>
<td>Last M spike (gr/dl)</td>
<td>0.6</td>
<td>0.0</td>
<td>0.0</td>
<td>0.6</td>
<td>0.6</td>
<td>0.0</td>
<td>0.3</td>
<td>1.5</td>
</tr>
<tr>
<td>Time since diagnosis, months</td>
<td>92</td>
<td>42</td>
<td>100</td>
<td>33</td>
<td>108</td>
<td>16</td>
<td>56</td>
<td>222</td>
</tr>
<tr>
<td>Time since starting lenalidomide, months</td>
<td>14</td>
<td>11</td>
<td>12</td>
<td>2</td>
<td>2</td>
<td>10</td>
<td>4</td>
<td>2</td>
</tr>
</tbody>
</table>
Lenalidomide maintains remissions in persons with multiple myeloma intolerant to thalidomide

results in either stopping or switching to Dex. This small study shows that Len can be effectively and safely used instead of Thal. A delay in the introduction of Len in the treatment of patients with MM results in lower costs. Additional studies are needed to define if the use of Len in this setting is appropriate.

Acknowledgements
The authors are most grateful to Robert P. GALE MD, PhD for criticism and editing of the manuscript.

REFERENCES