Rapid and Sustained Response to Tocilizumab in Patients with Polymyalgia Rheumatica Resistant or Intolerant to Glucocorticoids: A Multicenter Open-label Study

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To the Editor:

Polymyalgia rheumatica (PMR) is an inflammatory rheumatic disease affecting people aged 50 years or older. PMR usually improves with glucocorticoids (GC), with rapid resolution of symptoms in response to 15–20 mg/day prednisone. However, around half of the patients with PMR experience a flare of disease when GC are tapered or stopped, and these patients may require longterm GC treatment because of repeated relapses, leading to undesirable side effects. In addition, some patients with PMR have a partial response or do not respond to initial GC treatment. In this setting, alternative treatments, namely GC-sparing agents, are required. Methotrexate gave conflicting results in PMR while tumor necrosis factor-α inhibitors failed to prevent relapses in randomized controlled studies.

Data suggest that interleukin 6 (IL-6) contributes to the inflammatory process of PMR. Increased serum levels of IL-6 have been described in PMR and correlate with disease activity; the risk of recurrence/relapse of PMR is associated with persistent elevated IL-6 serum levels as well as with a genetic polymorphism of the IL-6 promoter gene; and reports described the efficacy of tocilizumab (TCZ), an anti-IL-6 receptor agent, in the treatment of giant cell arteritis (GCA). The clinical value of TCZ in isolated PMR is less well described. This prompted us to analyze the potential use of this biological agent in patients with isolated PMR who are refractory or intolerant to GC.

A call to observe all cases of patients with PMR who received at least 1 infusion of TCZ was sent to the members of the French specialist network Club Rhumatismes et Inflammation (including rheumatologists and specialists in internal medicine). Patients had to satisfy the Healey criteria for PMR and have pure or predominant PMR clinical features.

During a 24-month period (2013–2014), 7 cases were declared (Table 1). Included patients (4 men) had a mean age of 73.4 ± SD 7.9 and a mean duration of disease at time of TCZ initiation of 2.3 ± 1.6 years. They all had negative rheumatoid factor and anticyclic citrullinated peptide antibodies. The mean duration of GC treatment was 16.1 ± 9.2 months (range 1–48). Clinical features were pure PMR for 6 patients while 1 patient had PMR with biopsy-proven GCA, but without any related symptoms. Five patients had GC-refractory disease requiring a daily prednisone dosage of 20.7 ± 4.5 mg. Two patients had concomitant metabolic diseases (diabetes and metabolic syndrome), and TCZ was thus started shortly after GC initiation.

Table 1. Clinical features, therapy, and outcomes of 7 patients with isolated PMR treated with TCZ. CRP levels and GC dosage were given before initiating TCZ and after the last TCZ infusion.

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age, Yrs/Sex</th>
<th>Duration of GC Therapy before Initiating TCZ, Mos</th>
<th>Previous Drugs</th>
<th>Previous Drugs before TCZ</th>
<th>PMR-AS at the Start of TCZ</th>
<th>PMR-AS After TCZ, Last Assessment</th>
<th>CRP at the Start of TCZ, mg/l</th>
<th>CRP at TCZ, mg/l, Last Assessment</th>
<th>GC Dosage at the Start of TCZ, mg</th>
<th>GC Dosage after TCZ, Infusions, mg/l</th>
<th>No. TCZ Infusions</th>
<th>Followup Duration, Mos</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>65/M</td>
<td>20</td>
<td>MTX</td>
<td>MTX</td>
<td>41</td>
<td>23</td>
<td>30</td>
<td>5</td>
<td>15</td>
<td>0</td>
<td>19</td>
<td>20 TCZ ongoing</td>
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<tr>
<td>2</td>
<td>78/F</td>
<td>36</td>
<td>IFX, ADA</td>
<td>IFX</td>
<td>25</td>
<td>12</td>
<td>25</td>
<td>1</td>
<td>20</td>
<td>6</td>
<td>22</td>
<td>22 TCZ ongoing</td>
</tr>
<tr>
<td>3</td>
<td>80/M</td>
<td>1</td>
<td>MTX</td>
<td>MTX</td>
<td>37</td>
<td>1.5</td>
<td>100</td>
<td>5</td>
<td>25</td>
<td>0</td>
<td>2</td>
<td>20 TCZ stopped</td>
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<tr>
<td>4</td>
<td>74/M</td>
<td>4</td>
<td>MTX</td>
<td>MTX</td>
<td>40</td>
<td>1.5</td>
<td>119</td>
<td>5</td>
<td>25</td>
<td>0</td>
<td>3</td>
<td>20 TCZ stopped</td>
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<tr>
<td>5</td>
<td>71/F</td>
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<td>MTX, LFM</td>
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<td>26</td>
<td>7</td>
<td>50</td>
<td>7</td>
<td>20</td>
<td>2.5</td>
<td>21</td>
<td>25 TCZ stopped</td>
</tr>
<tr>
<td>6</td>
<td>84/F</td>
<td>3</td>
<td>MTX</td>
<td>MTX</td>
<td>26</td>
<td>4</td>
<td>40</td>
<td>5</td>
<td>25</td>
<td>5</td>
<td>2</td>
<td>25 TCZ stopped</td>
</tr>
<tr>
<td>7</td>
<td>62/M</td>
<td>48</td>
<td>MTX, ETA, ADA</td>
<td>MTX</td>
<td>24</td>
<td>2</td>
<td>2.9</td>
<td>2</td>
<td>15</td>
<td>4</td>
<td>4</td>
<td>4 TCZ ongoing</td>
</tr>
</tbody>
</table>

Mean ± SD 73.4 ± 7.9 16.1 ± 9.2 32.3 ± 7.8 7.0 ± 4.1 56.9 ± 24.1 4.2 ± 2.1 20.7 ± 4.5 2.5 ± 2.2 10.4 ± 6.6 19.4 ± 7.1

PMR: polymyalgia rheumatica; TCZ: tocilizumab; CRP: C-reactive protein; GC: glucocorticoids; PMR-AS: PMR activity score; M: male; F: female; MTX: methotrexate; IFX: infliximab; ADA: adalimumab; LFM: leflunomide; ETA: etanercept.
was necessary. Thus, future studies must clarify the indications, when to introduce it, the predictive factors for good response, and the duration of TCZ therapy in the management of PMR.

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REFERENCES

Figure 1. Changes in PMR-AS, CRP levels, and GC dosage (prednisone) following TCZ therapy in 7 patients with PMR. Since our series included patients with long duration of GC therapy (patients 1, 2, and 7) and patients with short GC treatment (patients 3, 4, 5, and 6), results are given separately for these 2 groups. The panel on the left shows patients for whom TCZ was introduced early after diagnosis (early initiation) and the panel on the right shows those with a late introduction of TCZ (late initiation). Assessments were performed just before the first infusion of TCZ and after the last TCZ infusion. PMR: polymyalgia rheumatica; PMR-AS: PMR activity score; CRP: C-reactive protein; GC: glucocorticoids; TCZ: tocilizumab.