Is Tocilizumab an Effective Option for Treatment of Refractory Uveitis Associated with Juvenile Idiopathic Arthritis?

CHRISTOPH TAPPEINER, CARSTEN HEINZ, GERD GANSER and ARND HEILIGENHAUS

J Rheumatol 2012;39;1294-1295
http://www.jrheum.org/content/39/6/1294.2

1. Sign up for TOCs and other alerts
   http://www.jrheum.org/alerts

2. Information on Subscriptions
   http://jrheum.com/faq

3. Information on permissions/orders of reprints
   http://jrheum.com/reprints_permissions

The Journal of Rheumatology is a monthly international serial edited by Earl D. Silverman featuring research articles on clinical subjects from scientists working in rheumatology and related fields.
Is Tocilizumab an Effective Option for Treatment of Refractory Uveitis Associated with Juvenile Idiopathic Arthritis?

To the Editor:

Anti-interleukin 6 receptor (anti-IL-6R) antibodies have been effective in experimental models of autoimmune arthritis, encephalomyelitis, and also uveitis. Tocilizumab (TCZ; RoActemra®, Hoffmann-La Roche, Basel, Switzerland), a fully humanized anti-IL-6R antibody, has been approved for the treatment of rheumatoid arthritis. Efficacy has also been shown for systemic-onset juvenile idiopathic arthritis (JIA) and vasculitis. To date, however, no reports have appeared concerning its efficacy in JIA-associated uveitis.

In about one-third of JIA patients with uveitis, eye inflammation runs a severe course and vision-threatening complications develop, and immunosuppressive treatment is required. Because some patients do not respond properly to the widely used disease-modifying antirheumatic drugs (DMARD), including tumor necrosis factor-α (TNF-α) inhibitors, there is a significant need for alternative treatment options. We describe our initial experience with TCZ for treatment of JIA-associated uveitis at a tertiary uveitis and pediatric rheumatology referral center.

Three adult patients (mean age 18.3 yrs) with JIA-associated chronic anterior uveitis (mean duration 8 yrs, range 4–13) with insidious onset of flare and the presence of vision-threatening complications (Table 1) were treated with intravenous TCZ 8 mg/kg body weight at 4-weekly intervals. Written informed consent was obtained from patients for off-label use of TCZ. In all patients the disease had been refractory to high dosages of topical corticosteroids and systemic immunosuppression. Dosages were within generally used ranges, e.g., for methotrexate (MTX) 15 mg/m², azathioprine (AZA) 2 mg/kg body weight, adalimumab (ADA) 40 mg biweekly, etanercept (ETA) 0.8 mg/kg body weight weekly, abatacept (ABA) 10 mg/kg body weight monthly.

In about one-third of JIA patients with uveitis, eye inflammation runs a severe course and vision-threatening complications develop, and immunosuppressive treatment is required. Because some patients do not respond properly to the widely used disease-modifying antirheumatic drugs (DMARD), including tumor necrosis factor-α (TNF-α) inhibitors, there is a significant need for alternative treatment options. We describe our initial experience with TCZ for treatment of JIA-associated uveitis at a tertiary uveitis and pediatric rheumatology referral center.

Three adult patients (mean age 18.3 yrs) with JIA-associated chronic anterior uveitis (mean duration 8 yrs, range 4–13) with insidious onset of flare and the presence of vision-threatening complications (Table 1) were treated with intravenous TCZ 8 mg/kg body weight at 4-weekly intervals. Written informed consent was obtained from patients for off-label use of TCZ. In all patients the disease had been refractory to high dosages of topical corticosteroids and systemic immunosuppression. Dosages were within generally used ranges, e.g., for methotrexate (MTX) 15 mg/m², azathioprine (AZA) 2 mg/kg body weight, adalimumab (ADA) 40 mg biweekly, etanercept (ETA) 0.8 mg/kg body weight weekly, abatacept (ABA) 10 mg/kg body weight monthly.

TCZ treatment achieved suppression of uveitis in 2 of 3 patients in whom disease had been refractory to previous DMARD, including at least 1 TNF-α inhibitor. In our cases, all medication was used at conventional doses. Whether further dose escalation (e.g., adalimumab at once-weekly intervals) would have been more effective is unclear.

TCZ may represent a treatment option for otherwise refractory JIA-associated uveitis. Further prospective studies are needed to evaluate the efficacy of this new drug in comparison to other biologicals.

CHRISTOPH TAPPEINER, MD, FEBO, Department of Ophthalmology, Inselspital, University of Bern, Bern, Switzerland; CARSTEN HEINZ, MD, FEBO, Department of Ophthalmology, St. Franziskus Hospital, Münster, and University of Essen, Essen, Germany; GERD GANSER, MD, Department of Pediatric Rheumatology, St. Josef Stift, Sendenhorst.

Table 1. Adult patients with juvenile idiopathic arthritis (JIA)-associated uveitis were treated with tocilizumab when refractory to topical corticosteroids and systemic immunosuppression.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age/sex</th>
<th>ILAR Classification</th>
<th>HLA-B27/ANA/RF</th>
<th>JIA Diagnosis at Age, yrs</th>
<th>Uveitis Diagnosis at Age, yrs</th>
<th>Uveitis Type**</th>
<th>Involved Eyes</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>18 M</td>
<td>Oligoarthritis, ext.</td>
<td>Neg/pos/neg</td>
<td>4</td>
<td>5</td>
<td>Anterior</td>
<td>Both</td>
<td>Cataract, synechiae, glaucoma</td>
</tr>
<tr>
<td>2</td>
<td>18 F</td>
<td>Polyarthritis</td>
<td>Neg/pos/neg</td>
<td>11</td>
<td>11</td>
<td>Anterior</td>
<td>Both</td>
<td>Cataract, synechiae, macular edema, glaucoma</td>
</tr>
<tr>
<td>3</td>
<td>19 F</td>
<td>Polyarthritis</td>
<td>Neg/pos/neg</td>
<td>3</td>
<td>15</td>
<td>Anterior</td>
<td>Left</td>
<td>Cataract, synechiae, macular edema, glaucoma</td>
</tr>
</tbody>
</table>

* At time of starting tocilizumab therapy. ** Standardization of Uveitis Nomenclature classification. ANA: antinuclear antigen; RF: rheumatoid factor; ILAR: International League of Associations for Rheumatology.

Table 2. Response to treatment in adult patients with juvenile idiopathic arthritis (JIA)-associated uveitis treated with tocilizumab (TCZ) when refractory to topical corticosteroids and systemic immunosuppression. Dosages were within generally used ranges, e.g., for methotrexate (MTX) 15 mg/m², azathioprine (AZA) 2 mg/kg body weight, adalimumab (ADA) 40 mg biweekly, etanercept (ETA) 0.8 mg/kg body weight weekly, abatacept (ABA) 10 mg/kg body weight monthly.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Treatment Prior to TCZ</th>
<th>Uveitis Activity† After TCZ</th>
<th>Months Until Inactive</th>
<th>Sparing of Other Immunosuppressives After TCZ**</th>
<th>Steroid Eye Drops Before/ After TCZ (n = times daily)</th>
<th>Uveitis Recurrence (followup, mo)</th>
<th>Arthritis Activity†† Prior to TCZ</th>
<th>Arthritis Activity†† After TCZ</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PRED*, MTX*, ETA, ADA, ABA*</td>
<td>Active</td>
<td>—</td>
<td>No</td>
<td>5/7</td>
<td>Ongoing; 8</td>
<td>Yes</td>
<td>Improved</td>
</tr>
<tr>
<td>2</td>
<td>PRED*, MTX*, ETA, ADA*</td>
<td>Inactive</td>
<td>1</td>
<td>No</td>
<td>4/2</td>
<td>No; 12</td>
<td>Yes</td>
<td>Improved</td>
</tr>
<tr>
<td>3</td>
<td>PRED*, AZA*, MTX, ETA, ADA*</td>
<td>Inactive</td>
<td>1</td>
<td>No</td>
<td>3/1</td>
<td>No; 6</td>
<td>Yes</td>
<td>Improved</td>
</tr>
</tbody>
</table>

† Uveitis activity determined according to SUN criteria. †† Arthritis activity determined by PedACR30/50/70 criteria. Pred: prednisolone; SUN: Standardization of Uveitis Nomenclature.
REFERENCES


