Long-Term Outcome of Tocilizumab for Patients With Giant Cell Arteritis: Results From Part 2 of a Randomized Controlled Phase 3 Trial

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for the GiACTA Investigators

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Note: The entire presentation will be made available to qualified providers on medically.roche.com: https://bit.ly/32q93PS
Disclosures

- JH Stone: research grants from Roche/Genentech and Xencor; consulting fees from Chugai, Roche/Genentech, and Xencor
- M Bao: employee of Genentech
- J Han: employee of Genentech
- M Aringer: consulting fees and speakers bureaus for Roche and Chugai
- D Blockmans: consulting fees from Roche
- E Brouwer: nothing to disclose
- MC Cid: regional principal investigator in GiACTA trial, sponsored by Roche
- B Dasgupta: consulting fees from Roche, GSK, and Sanofi Aventis
- J Rech: nothing to disclose
- C Salvarani: nothing to disclose
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- SH Unizony: research funding from Roche/Genentech; consulting fees from Kiniksa, Sanofi, and GSK
GiACTA Part 2: Purposes

• Evaluate long-term safety of TCZ-treated GCA patients

• Explore maintenance of efficacy after TCZ discontinuation

• Gain insight into the long-term steroid-sparing effect of TCZ

GCA, giant cell arteritis; TCZ, tocilizumab.
GiACTA Part 1: Randomized

**Part 1**
52 Weeks Double-Blind*1,2

- SC placebo + 26-week GC taper (n = 50)
- SC placebo + 52-week GC taper (n = 50)
- SC TCZ 162 mg QW + 26-week GC taper (n = 100)
- SC TCZ 162 mg Q2W + 26-week GC taper (n = 50)

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**Baseline**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Duration</th>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>SC placebo + 26-week GC taper</td>
<td>26 weeks</td>
<td>50</td>
</tr>
<tr>
<td>SC placebo + 52-week GC taper</td>
<td>52 weeks</td>
<td>50</td>
</tr>
<tr>
<td>SC TCZ 162 mg QW + 26-week GC taper</td>
<td>26 weeks</td>
<td>100</td>
</tr>
<tr>
<td>SC TCZ 162 mg Q2W + 26-week GC taper</td>
<td>26 weeks</td>
<td>50</td>
</tr>
</tbody>
</table>

GC, glucocorticoid; QW, every week; Q2W, every 2 weeks; SC, subcutaneous.

*Prednisone ≤30 vs >30 mg/day.

GiACTA Part 2: Not Randomized

Part 1
52 Weeks Double-Blind*  

Different categories at end of part 1:
- In remission, no treatment
- In remission, on treatment
- Recently active, on treatment

Baseline
- SC placebo + 26-week GC taper (n = 50)
- SC placebo + 52-week GC taper (n = 50)
- SC TCZ 162 mg QW + 26-week GC taper (n = 100)
- SC TCZ 162 mg Q2W + 26-week GC taper (n = 50)

Week 52

*Prednisone ≤30 vs >30 mg/day.

GiACTA Part 2: Not Randomized

Part 1
52 Weeks Double-Blind*1,2

Baseline
- SC placebo + 26-week GC taper (n = 50)
- SC placebo + 52-week GC taper (n = 50)
- SC TCZ 162 mg QW + 26-week GC taper (n = 100)
- SC TCZ 162 mg Q2W + 26-week GC taper (n = 50)

Week 52
- Blinded injections stopped at week 52
- Original blinding maintained

Part 2
104 Weeks Long-Term Follow-Up

Week 156
- Treatment at investigator’s discretion

*Prednisone ≤30 vs >30 mg/day.

197 of 215 (92%) completed Part 2
Time to Flare After Remission: Part 1 and Part 2

Kaplan-Meier plot of time to first flare over 3 years (part 1 and part 2)

Patients, n
PBO+Pred-26 (n = 50)
PBO+Pred-52 (n = 51)
TCZ-QW+Pred-26 (n = 100)
TCZ-Q2W+Pred-26 (n = 49)

Patients never in remission were censored at day 1. Patients who withdrew were censored from the time of withdrawal. Dashed line indicates start of part 2.
The Lowest Cumulative GC Doses Over 3 Years Were Observed in the TCZ-QW Group

<table>
<thead>
<tr>
<th>Group</th>
<th>Median Cumulative GC Dose, mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>PBO+Pred-26 (n = 50)</td>
<td>5277 mg</td>
</tr>
<tr>
<td>PBO+Pred-52 (n = 51)</td>
<td>5323 mg</td>
</tr>
<tr>
<td>TCZ-QW+Pred-26 (n = 100)</td>
<td>2647 mg</td>
</tr>
<tr>
<td>TCZ-Q2W+Pred-26 (n = 49)</td>
<td>3948 mg</td>
</tr>
</tbody>
</table>
Original Assignment to TCZ Corresponded With Maintenance of Treatment-Free Remission

<table>
<thead>
<tr>
<th>In Clinical Remission at Week 52</th>
<th>PBO+Pred-26 n = 33</th>
<th>PBO+Pred-52 n = 34</th>
<th>TCZ QW+Pred-26 n = 81</th>
<th>TCZ Q2W +Pred-26 n = 36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maintained clinical remission in part 2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>18</td>
<td>20</td>
<td>38</td>
<td>13</td>
</tr>
<tr>
<td>Treatment-free</td>
<td>7/18 (39%)</td>
<td>10/20 (50%)</td>
<td>25/38 (66%)</td>
<td>8/13 (62%)</td>
</tr>
<tr>
<td></td>
<td>17/38 (45%)</td>
<td></td>
<td>33/51 (65%)</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>Regardless of treatment; included patients in part 2 for >1.75 years.
At week 52

Entered GiACTA Part 2
n = 85

At week 52

In clinical remission
n = 81 (95%)

At week 52

In clinical remission on no treatment
n = 59 (73%)

Another 2 years

Maintained clinical remission on no treatment
n = 25 (42%)
Context: What Happened When Prednisone Was Stopped?

Part 1

- PBO+Pred-26 arm: Only 32% of patients did not flare over that year
  - Most who flared did so even before stopping prednisone completely

- PBO+Pred-52 arm: 51% of patients did not flare over that year
  - All who flared did so even before they stopped prednisone
**Part 2: What Treatments Had Patients Received Before Flare?**

Of the 89 patients who experienced flare in part 2, only 8 (9%) were receiving TCZ.

<table>
<thead>
<tr>
<th>In CR at Week 52</th>
<th>PBO+Pred-26 n = 33</th>
<th>PBO+Pred-52 n = 34</th>
<th>TCZ-QW+Pred-26 n = 81</th>
<th>TCZ-Q2W +Pred-26 n = 36</th>
<th>Total, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experienced ≥1 flare regardless of treatment(^a)</td>
<td>13</td>
<td>13</td>
<td>41</td>
<td>22</td>
<td>89</td>
</tr>
</tbody>
</table>

**Treatment received before first flare (patients who experienced flare)**

<table>
<thead>
<tr>
<th>Treatment-free, n (%)</th>
<th>2 (15)</th>
<th>4 (31)</th>
<th>24 (59)</th>
<th>17 (77)</th>
<th>47 (53)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GC only</td>
<td>10</td>
<td>6</td>
<td>13</td>
<td>4</td>
<td>33 (37)</td>
</tr>
<tr>
<td>TCZ only</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1 (1)</td>
</tr>
<tr>
<td>GC + TCZ</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>8 (9)</td>
</tr>
</tbody>
</table>

CR, clinical remission.

\(^a\)Includes patients who were in part 2 for >1.75 years.
### TCZ-Based Therapy Restored Clinical Remission After Flare

<table>
<thead>
<tr>
<th>Treatment for flare</th>
<th>PBO+Pred-26 n = 33</th>
<th>PBO+Pred-52 n = 34</th>
<th>TCZ-QW+Pred-26 n = 81</th>
<th>TCZ-Q2W +Pred-26 n = 36</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCZ only, n</td>
<td>2</td>
<td>0</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>Median time to remission</td>
<td>70 days</td>
<td>0</td>
<td>15.0 days</td>
<td>7.5 days</td>
</tr>
<tr>
<td>TCZ + GC, n</td>
<td>8</td>
<td>7</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>Median time to remission</td>
<td>8.0 days</td>
<td>8.0 days</td>
<td>8.5 days</td>
<td>18.0 days</td>
</tr>
<tr>
<td>GC only, n</td>
<td>4</td>
<td>5</td>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>Median time to remission</td>
<td>53.5 days</td>
<td>74.0 days</td>
<td>37.5 days</td>
<td>69.5 days</td>
</tr>
</tbody>
</table>

**n** = number of patients who entered part 2, were in CR at week 52, and started TCZ treatment at least 4 weeks after their last treatment.
Safety Over 3 Years: No New Safety Signals

<table>
<thead>
<tr>
<th></th>
<th>Part 1 + Part 2</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Never on TCZ</td>
<td>Ever on TCZ</td>
</tr>
<tr>
<td>Total patient-years</td>
<td>193.8</td>
<td>492.7</td>
</tr>
<tr>
<td>Events per 100 PY</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AEs</td>
<td>636.3</td>
<td>538.3</td>
</tr>
<tr>
<td>SAEs</td>
<td>23.2</td>
<td>25.4</td>
</tr>
<tr>
<td>Infection</td>
<td>121.8</td>
<td>120.2</td>
</tr>
<tr>
<td>Serious infection</td>
<td>4.6</td>
<td>3.5</td>
</tr>
<tr>
<td>Malignancy</td>
<td>2.1</td>
<td>1.8</td>
</tr>
<tr>
<td>GI perforation</td>
<td>0</td>
<td>0.2</td>
</tr>
<tr>
<td>Deaths, number of events</td>
<td>0</td>
<td>4</td>
</tr>
</tbody>
</table>

Ever on TCZ: all events that occurred after the first dose of TCZ are included. Never on TCZ: all events that occurred from the first study treatment date until the first TCZ dose or up to the last study date if no dose of TCZ was received are included.

AE, adverse event; GI, gastrointestinal; PY, patient-years; SAE, serious adverse event.
Conclusions

• 42% of patients in clinical remission and on no treatment after 1 year of weekly tocilizumab treatment maintained their treatment-free remission for another 2 years.

• Cumulative glucocorticoid exposure over 3 years was lower in patients originally assigned to tocilizumab.

• Restarting tocilizumab restored clinical remission.

• No new safety signals were observed in GCA patients treated with tocilizumab.

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