When and how to stop etanercept after successful treatment of patients with juvenile idiopathic arthritis


Published in:
Annals of the Rheumatic Diseases

DOI:
10.1136/ard.2008.101030

Citation for published version (APA):
When and how to stop etanercept after successful treatment of patients with juvenile idiopathic arthritis

F H M Prince, M Twilt, S C M Simon, et al.

Ann Rheum Dis 2009 68: 1228-1229
doi: 10.1136/ard.2008.101030

Updated information and services can be found at:
http://ard.bmj.com/content/68/7/1228.full.html

These include:

References
This article cites 9 articles, 4 of which can be accessed free at:
http://ard.bmj.com/content/68/7/1228.full.html#ref-list-1

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To order reprints of this article go to:
http://ard.bmj.com/cgi/reprintform

To subscribe to Annals of the Rheumatic Diseases go to:
http://ard.bmj.com/subscriptions
When and how to stop etanercept after successful treatment of patients with juvenile idiopathic arthritis

Currently, little is known about when or how to stop etanercept in patients with juvenile idiopathic arthritis (JIA) when a good clinical response is reached, and therefore no guidelines are available.1 We evaluated the disease course of patients with JIA who discontinued etanercept because of a sustained good clinical response.

This study is embedded in the Arthritis and Biologicals in Children (ABC) project, a prospective ongoing multicentre, observational study that includes all Dutch patients with JIA who used etanercept since 1999.2,3 We selected all patients who discontinued etanercept because of sustained good clinical response determined by the treating doctor. The outcome measures to assess disease activity consisted of the JIA core set of six response variables.4 To evaluate the disease course we used the criteria for inactive disease on medication (IDM) or off medication (ID) and the criteria for clinical remission on medication (CRM) or off medication (CR) by Wallace.5,6 We defined erythrocyte sedimentation rate (ESR) values under 16 mm/h as normal and stated that a doctor’s overall assessment score below 10 mm on a visual analogue scale (VAS) indicated no disease activity.7 Differences were tested with the Mann–Whitney U test using level of significance p<0.05.

In all, 19 patients on the ABC register discontinued etanercept because of a sustained good clinical response. Most data on these patients were prospectively collected in the register, more detailed data on disease activity after etanercept discontinuation were collected retrospectively.

Characteristics and disease course of each individual patient are shown in table 1.

After discontinuation 10 patients (53%) retained remission over a median of 0.8 years (interquartile range (IQR) 0.5 to 2.8). They used etanercept longer (3.5 vs 2.1 years, p = 0.21) and showed a longer median period of CRM (1.5 vs 0 years, p = 0.004) compared to the nine patients who experienced flares. None of the juvenile arthritis psoriatica patients had psoriatic lesions and the enthesis-related arthritis patient had no enthesis. At last observation 4 of the 10 had reached the criteria for CR.

Four out of five patients who discontinued etanercept without tapering experienced flares. In total nine patients developed a disease flare within a median of 0.7 years (IQR 0.1 to 1.1) after discontinuation of etanercept. All eight patients who resumed etanercept use after experiencing flares reacted promptly to treatment.

This explorative study shows some important indicators for successful discontinuation of etanercept: prolonged CRM and careful tapering of etanercept. Rheumatoid factor positivity seems to be negatively related with sustained remission. This is all inline with data from rheumatoid arthritis treatment.9,10 We suggest that patients with JIA should meet the criteria of CRM for at least 1.5 years before considering discontinuation of etanercept, and then taper it carefully.

It is reassuring that patients regained effectiveness of etanercept after experiencing flares. A promising result is that four out of five patients with systemic JIA retained ID after discontinuation of etanercept. This last finding indicates that etanercept can be successful in systemic JIA, as we previously showed in results from our ABC register in which the same percentages of patients with systemic JIA meet the criteria of CRM compared to other subtypes after prolonged treatment.7

F H M Prince,1 M Twilt,1,2 S C M Simon,3 M A J van Rossum,3 W Armbrust,3 E P A H Hoppenreijis,3 S Kamphuis,5 M van Santen-Hoeuff,6 Y Koopman-Keemink,7 N M Wulffraat,8 R ten Cate,2 L W A van Suijlekom-Smit1

1 Department of Paediatrics/Paediatric Rheumatology, Erasmus MC Sophia Children’s Hospital, Rotterdam, The Netherlands; 2 Department of Paediatrics/Paediatric Rheumatology, Leiden University Medical Centre, The Netherlands; 3 Department of Paediatrics/Paediatric Rheumatology, Emma Children’s Hospital AMC and Jan van Breemen Institute, Amsterdam, The Netherlands; 4 Department of Paediatrics/Paediatric Rheumatology, Beatrix Children’s Hospital, University Medical Centre Groningen, The Netherlands; 5 Department of Paediatrics/Paediatric Rheumatology, University Nijmegen Medical Centre Radboud, The Netherlands; 6 Department of Internal Medicine, subdivision Rheumatology, Maastricht University Medical Centre, The Netherlands; 7 Department of Paediatrics, Hagaziekenhuis Juliana Children’s Hospital, Den Haag, The Netherlands; 8 Department of Paediatrics/Paediatric Rheumatology, Utrecht MC Wilhelmina Children’s Hospital, The Netherlands

Correspondence to: F H M Prince, Department of Paediatrics, Sp 1546, Erasmus MC Sophia Children’s Hospital, PO Box 2060, 3000 CB Rotterdam, The Netherlands; f.prince@erasusmc.nl

Acknowledgements: We thank the Dutch Board of Health Insurances for funding the ABC project and Wyeth International for funding the development and maintenance of the web-based ABC register.

Competing interests: Wyeth International financially supported (unconditionally) the development and maintenance of the web-based ABC register.

Ethics approval: Ethics approval was obtained.

Accepted 22 September 2008


REFERENCES
<table>
<thead>
<tr>
<th>Patient</th>
<th>JIA subtype</th>
<th>Sex</th>
<th>Age at onset of JIA (years)</th>
<th>Disease duration at start of ETN (years)</th>
<th>Time on ETN therapy (years)</th>
<th>Tapering of ETN before stopping</th>
<th>IDM* (years)</th>
<th>CRM* (years)</th>
<th>ID* (years)</th>
<th>CR* (years)</th>
<th>Time to flare after stopping ETN (years)</th>
<th>Disease course and therapy after stopping ETN</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>sJIA</td>
<td>M</td>
<td>4.0</td>
<td>4.0</td>
<td>5.2</td>
<td>Y</td>
<td>2.4</td>
<td>1.9</td>
<td>1.6</td>
<td>0.6</td>
<td></td>
<td>Remission</td>
</tr>
<tr>
<td>2</td>
<td>sJIA</td>
<td>F</td>
<td>3.0</td>
<td>3.2</td>
<td>5.3</td>
<td>Y</td>
<td>2.6</td>
<td>2.1</td>
<td>0.8</td>
<td>0</td>
<td>0.76</td>
<td>Flare; restart NSAID and ETN</td>
</tr>
<tr>
<td>3</td>
<td>sJIA</td>
<td>M</td>
<td>9.0</td>
<td>2.8</td>
<td>3.7</td>
<td>Y</td>
<td>3.0</td>
<td>2.5</td>
<td>0.4</td>
<td>0</td>
<td></td>
<td>Remission</td>
</tr>
<tr>
<td>4</td>
<td>sJIA</td>
<td>M</td>
<td>5.2</td>
<td>11.5</td>
<td>5.1</td>
<td>Y</td>
<td>4.4</td>
<td>3.9</td>
<td>0.6</td>
<td>0</td>
<td></td>
<td>Remission</td>
</tr>
<tr>
<td>5</td>
<td>sJIA</td>
<td>M</td>
<td>5.5</td>
<td>5.2</td>
<td>6.5</td>
<td>Y</td>
<td>4.7</td>
<td>4.2</td>
<td>0.5</td>
<td>0</td>
<td></td>
<td>Remission</td>
</tr>
<tr>
<td>6</td>
<td>JIA RF+</td>
<td>F</td>
<td>11.2</td>
<td>4.8</td>
<td>0.6</td>
<td>N</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.25</td>
<td>Flare; restart NSAID, MTX and ETN</td>
</tr>
<tr>
<td>7</td>
<td>JIA RF+</td>
<td>F</td>
<td>14.0</td>
<td>2.0</td>
<td>1.1</td>
<td>N</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.18</td>
<td>Flare; restart ETN and continue MTX</td>
</tr>
<tr>
<td>8</td>
<td>JIA RF-</td>
<td>M</td>
<td>4.2</td>
<td>5.2</td>
<td>3.8</td>
<td>Y</td>
<td>0</td>
<td>0</td>
<td>1.3</td>
<td>0.3</td>
<td>2.25</td>
<td>Flare; hospitalisation, restart NSAID and prednisolone</td>
</tr>
<tr>
<td>9</td>
<td>JIA RF-</td>
<td>M</td>
<td>4.8</td>
<td>5.3</td>
<td>1.0</td>
<td>N</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.04</td>
<td>Flare; restart prednisolone and ETN</td>
</tr>
<tr>
<td>10</td>
<td>JIA RF-</td>
<td>F</td>
<td>7.5</td>
<td>0.3</td>
<td>2.4</td>
<td>Y</td>
<td>0.7</td>
<td>0.2</td>
<td>2.8</td>
<td>1.8</td>
<td></td>
<td>Remission</td>
</tr>
<tr>
<td>11</td>
<td>JIA RF-</td>
<td>F</td>
<td>10.0</td>
<td>1.6</td>
<td>2.1</td>
<td>Y</td>
<td>1.6</td>
<td>1.1</td>
<td>0.4</td>
<td>0</td>
<td></td>
<td>Remission</td>
</tr>
<tr>
<td>12</td>
<td>JIA RF-</td>
<td>F</td>
<td>5.0</td>
<td>11.1</td>
<td>3.6</td>
<td>Y</td>
<td>2.9</td>
<td>2.4</td>
<td>2.8</td>
<td>1.8</td>
<td></td>
<td>Remission</td>
</tr>
<tr>
<td>13</td>
<td>o.JIA ext</td>
<td>M</td>
<td>4.0</td>
<td>8.8</td>
<td>2.1</td>
<td>Y</td>
<td>0.3</td>
<td>0</td>
<td>0.1</td>
<td>0</td>
<td>0.05</td>
<td>Flare; restart NSAID and ETN</td>
</tr>
<tr>
<td>14</td>
<td>o.JIA ext</td>
<td>F</td>
<td>3.4</td>
<td>3.4</td>
<td>1.6</td>
<td>Y</td>
<td>0.8</td>
<td>0.3</td>
<td>4.5</td>
<td>3.5</td>
<td></td>
<td>Remission</td>
</tr>
<tr>
<td>15</td>
<td>o.JIA ext</td>
<td>F</td>
<td>8.1</td>
<td>1.4</td>
<td>1.7</td>
<td>N</td>
<td>1.4</td>
<td>0.9</td>
<td>1.0</td>
<td>0</td>
<td></td>
<td>Remission</td>
</tr>
<tr>
<td>16</td>
<td>PsJIA</td>
<td>F</td>
<td>13.1</td>
<td>0.4</td>
<td>2.5</td>
<td>N</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.62</td>
<td>Flare; hospitalisation, restart prednisolone, MTX and ETN</td>
</tr>
<tr>
<td>17</td>
<td>PsJIA</td>
<td>M</td>
<td>7.7</td>
<td>2.8</td>
<td>2.0</td>
<td>Y</td>
<td>0.8</td>
<td>0.3</td>
<td>0.5</td>
<td>0</td>
<td></td>
<td>Remission</td>
</tr>
<tr>
<td>18</td>
<td>PsJIA</td>
<td>M</td>
<td>9.9</td>
<td>4.6</td>
<td>1.6</td>
<td>Y</td>
<td>0.8</td>
<td>0.3</td>
<td>0</td>
<td>0</td>
<td>0.03</td>
<td>Flare; restart ETN</td>
</tr>
<tr>
<td>19</td>
<td>ERA</td>
<td>M</td>
<td>9.5</td>
<td>0.8</td>
<td>3.7</td>
<td>Y</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.68</td>
<td>Flare; restart NSAID and ETN</td>
</tr>
</tbody>
</table>

*According to the criteria of Wallace et al. CR, clinical remission off medication; CRM, clinical remission on etanercept medication; ERA, enthesitis-related arthritis; ETN, etanercept; ID, inactive disease off medication; IDM, inactive disease on etanercept medication; MTX, methotrexate; NSAID, non-steroidal anti-inflammatory drug; oJIA ext, oligoarticular extended JIA; pJIA RF+/−, polyarticular rheumatoid factor positive/negative JIA; PsJIA, juvenile arthritis psoriatica; sJIA, systemic JIA.