Efficacy and Safety of Abatacept, Adalimumab, and Etanercept in Pediatric Patients with Juvenile Idiopathic Arthritis

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I have no actual or potential conflicts of interest to disclose.
Objectives

1. Describe the efficacy of abatacept, adalimumab, and etanercept for the treatment of juvenile idiopathic arthritis based on the Physician’s Global Assessment

2. Evaluate reported adverse effects to determine the safety of abatacept, adalimumab, and etanercept

3. Propose future directions for the use of these agents, based on their comparative efficacy and tolerability
Monroe Carell Jr. Children’s Hospital at Vanderbilt

- Academic teaching and tertiary hospital
- 267 inpatient beds
- 15,000+ inpatient visits annually
- 330,000+ outpatient visits annually
Juvenile Idiopathic Arthritis (JIA)

- Heterogeneous group of several disease subtypes
- Characterized by the onset of arthritis prior to the age of 16 years
- Symptoms persist for more than 6 weeks
Classification of JIA

- **Oligoarticular**
  - One to four joints during the first six months

- **Polyarticular**
  - Five or more joints during the first six months

- **Systemic**
  - One or more joints with fever of at least two weeks that is daily for at least three days

Treatment of Oligoarticular JIA

**NSAID Monotherapy**
- Low disease activity

**Glucocorticoid Joint Injections**
- Moderate to high disease activity
- Any disease activity after 2 months of NSAID monotherapy

**Methotrexate (MTX)**
- High disease activity
- Moderate disease activity after multiple joint injections
- Low disease activity with poor prognostic features

**TNFα Inhibitor**
- High disease activity after 6 months MTX
- Moderate to high disease activity after 3 months MTX

Treatment of Polyarticular JIA

- **NSAID Monotherapy**
  - Low disease activity

- **Methotrexate**
  - Moderate to high disease activity
  - Low disease activity after 1 month of NSAID monotherapy

- **TNFα Inhibitor**
  - Moderate to high disease activity after 3 months of MTX
  - Low disease activity after 6 months of MTX

- **2nd TNFα Inhibitor or Abatacept**
  - Moderate to high disease activity after 4 months of TNFα inhibitor

Treatment of Systemic JIA

NSAID with Glucocorticoid Joint Injections

All patients

Disease activity after 1 month of NSAID with glucocorticoid joint injections

Methotrexate

Moderate to high disease activity after 3 months of MTX

TNFα inhibitor or Anakinra

Moderate to high disease activity after 4 months of TNFα inhibitor

Abatacept

## Current Body of Literature

<table>
<thead>
<tr>
<th>Study</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gartlehner G et al.</td>
<td>Adjusted indirect comparisons indicate no significant differences in efficacy between TNFα drugs</td>
</tr>
<tr>
<td>Horneff G et al.</td>
<td>Adalimumab, etanercept and tocilizumab showed comparable efficacy towards polyarticular JIA</td>
</tr>
<tr>
<td>Shepherd J et al.</td>
<td>Exploratory adjusted indirect comparison suggests that the four biologic DMARDs are similar</td>
</tr>
</tbody>
</table>
Study Objective

To assess the efficacy of abatacept, adalimumab, and etanercept in pediatric JIA patients through changes in the Physician’s Global Assessment (PGA)
Outcomes

**Primary**
- Efficacy of abatacept, adalimumab, and etanercept in pediatric JIA patients based on PGA

**Secondary**
- Change in:
  - Inflammatory markers
  - Joints with active disease
  - Joints with limitation of motion
  - Corticosteroid dose after initiation of therapy
  - Adverse effects
  - Adherence among patients who fill with Vanderbilt Specialty Pharmacy
  - Reason for discontinuation
Methods

Design

• IRB-approved, single-center, retrospective, chart review

Inclusion Criteria

• All pediatric JIA patients started on abatacept, adalimumab, or etanercept from December 1st, 2015 to August 31st, 2018

Exclusion Criteria

• No return to clinic visit within 4 to 6 months after initiation of biologic
• Age >18 years at time of initiation of biologic
• Primary diagnosis other than JIA for initiation of biologic
Physician’s Global Assessment

- Pain
- Active Joints
- Stiffness
- Inflammation
Study Population

Eligible JIA patients (n=233)

Excluded (n=94)
- Age > 18 years (9.6%)
- Started prior to study (16%)
- No return to clinic visit (69.1%)
- Primary diagnosis other than JIA (5.3%)

Abatacept (n=11)
Adalimumab (n=49)
Etanercept (n=79)
## Demographics

<table>
<thead>
<tr>
<th></th>
<th>Abatacept</th>
<th>Adalimumab</th>
<th>Etanercept</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years), median</strong></td>
<td>13.7</td>
<td>13.9</td>
<td>12.1</td>
</tr>
<tr>
<td><strong>Female, n (%)</strong></td>
<td>8 (73%)</td>
<td>36 (73%)</td>
<td>56 (71%)</td>
</tr>
<tr>
<td><strong>Caucasian, n (%)</strong></td>
<td>7 (64%)</td>
<td>38 (78%)</td>
<td>60 (76%)</td>
</tr>
<tr>
<td><strong>JIA type, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oligoarticular</td>
<td>5 (45%)</td>
<td>18 (37%)</td>
<td>33 (42%)</td>
</tr>
<tr>
<td>Polyrarticular</td>
<td>6 (55%)</td>
<td>30 (61%)</td>
<td>45 (57%)</td>
</tr>
<tr>
<td>Systemic</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td><strong>Duration of JIA, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 2 years</td>
<td>5 (45%)</td>
<td>25 (51%)</td>
<td>62 (78%)</td>
</tr>
<tr>
<td>≥ 2 years</td>
<td>6 (55%)</td>
<td>24 (49%)</td>
<td>17 (22%)</td>
</tr>
<tr>
<td><strong>Prior biologic, n (%)</strong></td>
<td>2 (18%)</td>
<td>23 (47%)</td>
<td>5 (6%)</td>
</tr>
<tr>
<td><strong>Time on therapy (days), median</strong></td>
<td>322</td>
<td>343</td>
<td>419</td>
</tr>
</tbody>
</table>
Primary Outcome: Change in PGA

![Bar chart showing frequency of 4-6 month change in PGA score for different drugs. The x-axis represents the change in PGA score, and the y-axis represents frequency. The bars are color-coded: purple for Etanercept, blue for Adalimumab, and light blue for Abatacept.](image-url)
Joints with Active Disease

![Chart showing frequency of joints with active disease between baseline and follow-up.](image-url)
# Adverse Events

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Abatacept</th>
<th>Adalimumab</th>
<th>Etanercept</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection site reactions/pain, n (%)</td>
<td>1 (9%)</td>
<td>15 (31%)</td>
<td>19 (24%)</td>
<td>0.31</td>
</tr>
<tr>
<td>Infections, n (%)</td>
<td>0 (0%)</td>
<td>2 (4%)</td>
<td>1 (1%)</td>
<td></td>
</tr>
<tr>
<td>None, n (%)</td>
<td>10 (91%)</td>
<td>33 (67%)</td>
<td>59 (75%)</td>
<td>0.26</td>
</tr>
</tbody>
</table>

*p-value < 0.05 indicates statistical significance
## Biologic Discontinuation

<table>
<thead>
<tr>
<th></th>
<th>Abatacept</th>
<th>Adalimumab</th>
<th>Etanercept</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biologic discontinued, n (%)</td>
<td>4 (36.4%)</td>
<td>6 (12.2%)</td>
<td>35 (44.3%)</td>
</tr>
<tr>
<td>Major side effect, n (%)</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
<td>3 (3.8%)</td>
</tr>
<tr>
<td>Non-compliance, n (%)</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
<td>6 (7.6%)</td>
</tr>
<tr>
<td><strong>No response to therapy, n (%)</strong></td>
<td>4 (36.4%)</td>
<td>4 (8.2%)</td>
<td>26 (32.9%)</td>
</tr>
<tr>
<td>Full course completed, n (%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>2 (2.5%)</td>
</tr>
<tr>
<td>Insurance change/mandate, n (%)</td>
<td>1 (9.1%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>
Limitations

• Retrospective, single-center analysis
• Low number of abatacept patients
• Large number of patients excluded based on time to follow up visit
• PGA scoring based on limited chart information
Conclusions

• Majority of patients saw an improvement in their PGA score
• Adverse events were similar across all three biologics
• Most common reason for biologic discontinuation was no response to therapy
Future Directions

• Change in adverse effects with adalimumab citrate free formulation
• Trends in future biologic use and prescribing practice
• Emphasis of PGA scoring in provider notes
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