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Targeted Therapies in RA: Real World Comparative Effectiveness Research

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Targeted Therapies in RA: Real World Comparative Effectiveness Research

Leslie R. Harrold, MD MPH
Associate Professor of Medicine
Structure of TNF Antagonists Currently Approved in US

- **Etanercept** (Enbrel®)
  - Receptor
  - IgG1 Fc
  - Recombinant receptor/Fc fusion protein

- **Infliximab** (Remicade®)
  - Fab
  - IgG1 Fc
  - Recombinant human/mouse chimeric IgG1

- **Adalimumab** (Humira®)
  - IgG1 Fc
  - Recombinant human IgG1

- **Certolizumab pegol** (Cimzia®)
  - 1 Fab’
  - No Fc
  - Recombinant humanized PEGylated IgG1 Fab’ fragment

- **Golimumab** (Simponi®)

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**Full Monoclonal Antibody**

Fc: fragment, crystallizable; Ig: immunoglobulin.
Abatacept Selectively Modulates Co-stimulation via CD80/86:CD28 Pathway
Comparative Effectiveness of Abatacept versus Anti-TNF agents in the Treatment of Biologic Naïve Rheumatoid Arthritis Patient Using the CORRONA Registry

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CORRONA

Consortium of Rheumatology Researchers of North America (CORRONA)

• Gathers information on arthritis, comorbidities, functional status, medications, adverse events and outcomes from both patients and providers

• Includes over 100 practice sites
• 37 states across the US
• 80% private practice and 20% academic

[Map of the United States showing 74 private sites and 22 academic sites]
The objective of this study was to compare the effectiveness of abatacept to anti-TNFs using the following:

- Change in disease activity based on the Clinical Disease Activity Index (CDAI)
- Achievement of remission based on the CDAI
METHODS

- **Study setting:** The Consortium of Rheumatology Researchers of North America (CORRONA) registry is a prospective observational cohort of >20,000 RA patients

- **Study Population:**
  - Visits between 2/20/02 and 12/14/09
  - Biologic naïve
  - Not in remission at baseline
  - Follow-up visit 1 year after initiation.
  - Patients who initiated abatacept or an anti-TNF were identified
  - Anti-TNF initiators were matched to abatacept initiators (3 to 4:1 match) based on age, disease duration, use of methotrexate at time of initiation, initiation time frame (at or prior to index visit) and baseline CDAI
METHODS

- **Outcomes**: Comparative effectiveness was examined by comparing abatacept initiators to anti-TNF initiators 1 year after initiation on the following:
  - Treatment response based on change in CDAI
  - Achievement of remission based on the CDAI

- **Analyses**:
  - Three analytic approaches were used
  - Intention to treat (ITT): all initiators were included in these analyses
  - Nonresponder imputation: nonresponse was imputed for those who discontinued for reasons other than toxicity and last response if due to toxicity
  - Completers analysis: included only those who remained on drug
  - Regression models were performed to adjust for clustering by physician and by matched clusters as well baseline differences.
Table 1. Baseline characteristics of abatacept and matched anti-TNF initiators

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Abatacept initiators N=36</th>
<th>Anti-TNF initiators N=139</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female (%)</td>
<td>81</td>
<td>78</td>
<td>0.81</td>
</tr>
<tr>
<td>Age (in years)</td>
<td>66</td>
<td>65</td>
<td>0.41</td>
</tr>
<tr>
<td>Private insurance (%)</td>
<td>71</td>
<td>71</td>
<td>1.00</td>
</tr>
<tr>
<td>Medicaid (%)</td>
<td>6</td>
<td>7</td>
<td>1.00</td>
</tr>
<tr>
<td>Medicare (%)</td>
<td>65</td>
<td>55</td>
<td>0.41</td>
</tr>
<tr>
<td>No insurance (%)</td>
<td>3</td>
<td>1</td>
<td>0.42</td>
</tr>
<tr>
<td>Disabled (%)</td>
<td>3</td>
<td>13</td>
<td>0.19</td>
</tr>
<tr>
<td>Duration of RA (mean years, ±SD)</td>
<td>11.5 (10.1)</td>
<td>10.6 (8.6)</td>
<td>0.65</td>
</tr>
<tr>
<td>CDAI (mean, ±SD)</td>
<td>16.5 (11.0)</td>
<td>18.0 (10.0)</td>
<td>0.44</td>
</tr>
<tr>
<td>Tender joint count (mean, ±SD)</td>
<td>4.7 (5.9)</td>
<td>5.1 (5.0)</td>
<td>0.72</td>
</tr>
<tr>
<td>Swollen joint count (mean, ±SD)</td>
<td>5.8 (4.4)</td>
<td>6.0 (4.6)</td>
<td>0.86</td>
</tr>
<tr>
<td>Physician global (mean, ±SD)</td>
<td>24.9 (18.3)</td>
<td>32.3 (19.0)</td>
<td>0.04</td>
</tr>
<tr>
<td>Patient global (mean, ±SD)</td>
<td>34.7 (20.2)</td>
<td>37.0 (24.9)</td>
<td>0.60</td>
</tr>
<tr>
<td>Morning stiffness RA (mean hours, ±SD)</td>
<td>1.1 (1.6)</td>
<td>1.3 (1.8)</td>
<td>0.46</td>
</tr>
<tr>
<td>ESR (mean mmHg, ±SD)</td>
<td>22.6 (11.6)</td>
<td>28.4 (25.9)</td>
<td>0.49</td>
</tr>
<tr>
<td>Prior number of DMARDs (mean, ±SD)</td>
<td>1.2 (0.9)</td>
<td>1.2 (1.2)</td>
<td>0.73</td>
</tr>
<tr>
<td>Current methotrexate use (%)</td>
<td>71</td>
<td>72</td>
<td>1.00</td>
</tr>
</tbody>
</table>
Table 2. Comparison of response based on change in CDAI in abatacept (ABA) initiators as compared to anti TNF initiators

<table>
<thead>
<tr>
<th></th>
<th>Intention to Treat*</th>
<th>Completers analysis*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean change in CDAI in abatacept vs. anti-TNF initiators</td>
<td>-6.51 vs. -7.89</td>
<td>-8.25 vs. -9.28</td>
</tr>
<tr>
<td>Adjusted difference</td>
<td>0.81 (-2.54 to 4.15)</td>
<td>-0.70 (-4.41 to 3.01)</td>
</tr>
</tbody>
</table>

*Not statistically significant: models adjusted for clustering by physician, matched clusters and baseline CDAI
Table 3. Comparison of CDAI remission in abatacept (ABA) initiators as compared to anti-TNF initiators

<table>
<thead>
<tr>
<th></th>
<th>Intention to Treat</th>
<th>Nonresponder imputation</th>
<th>Completers analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remission (%)</td>
<td>36 vs 25</td>
<td>36 vs 19</td>
<td>45 vs 27</td>
</tr>
<tr>
<td>Adjusted likelihood of remission</td>
<td>1.62 (0.63-4.17)</td>
<td>2.21 (0.80-6.12)</td>
<td>1.87 (0.68-5.18)</td>
</tr>
</tbody>
</table>
CONCLUSIONS

• Among this small sample of RA patients in a real-world setting, treatment with abatacept was not associated with any differences in response or remission rates from those seen with anti-TNFs based on mean change in CDAI and achievement of CDAI remission.

• This study suggests similar effectiveness of abatacept and anti-TNFs in biologic naïve RA patients.

• Further research with a larger sample size is needed to confirm these findings.
Clinical Trials: Investigator Initiated Teriparatide for Joint Erosions in RA

• Randomized, controlled, 12-month open-label study of teriparatide in patients with RA and T-scores between -1.0 and -2.5 who have joint erosions
  – Subjects will be randomized to receive:
    • Teriparatide + TNF antagonist
    • TNF antagonist alone.

• Hypothesis: Combination of teriparatide + TNF antagonist will be much more effective at retarding erosion progression in RA then a TNF antagonist alone and may allow for healing of erosions
  – Joint erosion scores will be significantly improved at study completion in patients taking teriparatide
  – Teriparatide will significantly increase
  – RA disease activity measures will remain stable during the study year

• Conducted at UMass Memorial Medical Center & Brigham and Women’s Hospital
• Funded by a grant from Lilly
Clinical Trials: Sponsored Multi-center

Rheumatoid Arthritis

• Tocilizumab (anti-IL-6R mAB) - Hoffmann-La Roche Inc.
  – Randomized, Double-blind, Parallel Group Study of the Safety, Disease Remission and Prevention of Structural Joint Damage During Treatment with Tocilizumab, as a Monotherapy and in Combination with MTX, Vs. MTX in Patients with Early Moderate to Severe RA (Hoffmann-La Roche Inc. - WA19926)

Ankylosing Spondylitis

• SAR153191 (anti-IL-6R mAB) - Sanofi-Aventis
  – Randomized, Double-blind, Placebo-controlled, Dose Ranging Study to Evaluate Efficacy and Safety of SAR153191 in Patients with AS (ALIGN)
  – Uncontrolled Extension Study Evaluating the Long Term Safety and Efficacy of SAR153191 in Patients with AS (SUSTAIN)

Osteoarthritis

• Hymovis™ (Hyluronic acid) - Fidia Farmaceutici S.p.A.
  – Parallel, Double-blind, Blinded Evaluator, Randomized, Placebo-controlled, Study to Evaluate the Safety and Effectiveness of a New Viscoelastic Hydrogel (Hymovis™) in the Treatment of Knee OA with an Open-label Extension