Biologic Treatment Persistence, Switching, and Restart Patterns in US Managed Care Patients Treated for Psoriasis (PsO)

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Abstract

Objective: Etanercept (ETN), adalimumab (ADA), and ustekinumab (UST) are FDA approved for moderate to severe plaque PsO, and infliximab (INF) for severe only. Due to differences in clinical response and tolerability in individual patients, switching, discontinuation, and restarting biologics is common. This study explored treatment patterns in PsO with ETN, ADA, INF and UST.

Methods: The IMS LifeLink Health Plan Claims Database was used to identify adults with PsO (18-63 years) with a claim for ETN, ADA, INF, or UST between Jan 1, 2008 and Dec 31, 2010. The first preceded by ≥6-months of enrolment defined the index date and biologic. Patients without a claim for the same biologic in the 6-months pre-index were classified as “new”, otherwise they were classified as “continuing”. Patients were followed for 360 days post-index. Patients were "persistent" if they continued on their index biologic until the end of the follow-up period without a ≥45-day gap or a claim for another biologic; "switchers" if they had claims for another biologic; “restarting” if they had a ≥45-day gap and a subsequent claim for the index drug; otherwise they were categorized as “discontinuers”.

Results: Of the 6,073 “new” and “continuing” patients meeting inclusion criteria, 57% were male with a mean age of 45.5 years (SD 11.0). The index biologic was ETN in 64.4% of patients, ADA in 30.9%, INF in 2.8%, and UST in 1.9%. Persistence was greatest in UST (49%), followed by INF (46%), and both ETN and ADA (38%). Restart of index drug was seen most in ETN (21%), followed by ADA (17%), UST (15%), and INF (13%). Switch rates for ETN, ADA, INF, and UST patients were 12%, 9%, 7%, and 3% respectively. Discontinuation rates were somewhat lower for ETN (29%) than for, ADA (35%), INF (34%), and UST (33%).

Conclusions: Less than half of patients who were either “new” or “continuing” on therapy were fully persistent on treatment for the entire year, although almost one fifth of patients who had a gap in therapy restarted the same treatment before the end of the year. Switching was relatively uncommon. Over 95% of patients were taking self-injected TNF-blockers, suggesting these are the mainstay of biologic treatment in this population. Unobserved patient or physician characteristics may have led to the choice of other agents. Considering the chronic nature of PsO, more research is needed to understand the reasons for the relatively low persistence and high discontinuation rates in this population.
Introduction

- Biologics (including tumor necrosis factor [TNF] inhibitors) are approved for the treatment of moderate to severe plaque psoriasis (infliximab for severe plaque psoriasis only)\textsuperscript{1–4}
- Rates of persistence to TNF therapies are lower in patients with psoriasis compared with patients with other rheumatic diseases
  - One-year persistence rates ranged from 22 – 36\%\textsuperscript{4} for psoriasis vs. 45 – 57\%\textsuperscript{5} and 69% – 89% for rheumatoid arthritis\textsuperscript{6}
- There are no clear clinical guidelines for treatment options after discontinuing TNF therapy, yet data suggest that treatment with a second TNF inhibitor may be effective after inadequate response with the first\textsuperscript{7}
- The objective of this analysis was to characterize treatment patterns of etanercept, adalimumab, infliximab, and ustekinumab

1. Enbrel\textsuperscript{®} (etanercept) Prescribing Information, 2011.
2. Humira\textsuperscript{®} (adalimumab) Prescribing Information, 2011.
3. Remicade\textsuperscript{®} (infliximab) Prescribing Information, 2011.
4. Stelara \textsuperscript{®} (ustekinumab) Prescribing Information, 2013.
Methods

Study Design

- Retrospective observational cohort study of administrative data for commercially-insured persons from the IMS LifeLink® Health Plan Claims Database.
  - The LifeLink database contains fully-adjudicated medical and pharmacy claims for over 70 million patients from over 80 health plans in the United States.
    - Includes inpatient and outpatient diagnoses and procedures, and retail and mail order prescriptions.
    - Representative of the national, commercially-insured population (age, gender, type of health plan).
    - Mean enrollment time = 2 years.
- Only health plans submitting data for all members are included, ensuring complete data capture.
Methods - Patients

• Inclusion criteria
  – At least 1 claim for etanercept, adalimumab, infliximab, or ustekinumab from 1 Jan 2008 until 31 December 2010, and at least 180 days of enrollment in the health plan before the claim
    • The first claim meeting this criterion defines the index date and index agent
  – Age 18 – 63 years at index
  – A diagnosis of psoriasis (ICD-9: 696.0x) 180 prior to, or 30 days following the index date
    • Data were also collected from patients with (ICD-9) rheumatoid arthritis (714.0x), psoriatic arthritis (696.0x), and ankylosing spondylitis (720.0x), but these data are not included
  – Continuously enrolled in the insurance plan for 360 days following the index date

• Exclusion criteria
  – Patients with >1 claim for a biologic therapy of interest on the index date
  – A diagnosis (ICD-09) of juvenile idiopathic arthritis (714.3x), non-Hodgkin’s lymphoma (200.xx and 202.xx), chronic lymphocytic leukemia (204.1.x), ulcerative colitis (556.xx), or Crohn’s disease (555.xx) ≥180 days prior to and 360 days following the index date
Methods

Definitions

• **Index date**: first observed claim for etanercept, adalimumab, infliximab, or ustekinumab

• **Patient categories**
  
  – **New**: patients without a claim for the index biologic within the 180 days prior to the index date
  
  – **Continuing**: patients with a claim for the index biologic in the 180 days prior to the index date
  
  – **Persistent**: patients who continued on treatment for 12 months following the index date, with any gap in treatment <45 days
  
  – **Restarted**: patients with a ≥45 day gap in treatment with a subsequent claim for the same initial biologic therapy within 12 months following the index date
  
  – **Discontinued**: patients with a ≥45 day gap in treatment without a subsequent claim for any biologic therapy for 12 months following the index date
  
  – **Switched**: patients with a claim for a different biologic therapy within 12 months of the index date
Methods

Statistical Analysis

• Cohorts were stratified by index drug and treatment status (e.g., New or Continuing)

• Descriptive statistics were calculated for the overall population and by treatment status groups

• Outcomes:
  – Persistence, discontinuation, restarting, and switching rates
  – Time on index therapy
Results

*Treatment Distribution*

- Of the 6,073 patients with psoriasis, 56% were classified as New, and 44% were classified as Continuing

<table>
<thead>
<tr>
<th>Treatment</th>
<th>New, n (%)</th>
<th>Continuing, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etanercept (N=3,913)</td>
<td>1,740 (44.5)</td>
<td>2,173 (55.5)</td>
</tr>
<tr>
<td>Adalimumab (N=1,874)</td>
<td>1,458 (77.8)</td>
<td>416 (22.2)</td>
</tr>
<tr>
<td>Infliximab (N=170)</td>
<td>93 (54.7)</td>
<td>77 (45.3)</td>
</tr>
<tr>
<td>Ustekinumab (N=116)</td>
<td>96 (82.8)</td>
<td>20 (17.2)</td>
</tr>
</tbody>
</table>
### Results - Demographic Characteristics by Index Therapy

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Etanercept (N=3,913)</th>
<th>Adalimumab (N=1,874)</th>
<th>Infliximab (N=170)</th>
<th>Ustekinumab (N=116)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>45.7 (10.9)</td>
<td>45.0 (11.3)</td>
<td>45.4 (11.0)</td>
<td>46.7 (10.5)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>2,273 (58.1)</td>
<td>1,028 (54.9)</td>
<td>100 (58.8)</td>
<td>65 (56.0)</td>
</tr>
<tr>
<td>Payer Type, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Commercial Plan</td>
<td>3,484 (89.0)</td>
<td>1,619 (86.4)</td>
<td>147 (86.5)</td>
<td>93 (80.2)</td>
</tr>
<tr>
<td>Medicaid</td>
<td>36 (0.9)</td>
<td>21 (1.1)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Medicare Risk</td>
<td>6 (0.2)</td>
<td>6 (0.3)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Self-insured</td>
<td>341 (8.7)</td>
<td>192 (10.2)</td>
<td>21 (12.4)</td>
<td>19 (16.4)</td>
</tr>
<tr>
<td>Unknown</td>
<td>46 (1.2)</td>
<td>36 (1.9)</td>
<td>2 (1.2)</td>
<td>4 (3.4)</td>
</tr>
<tr>
<td>Plan type, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consumer-directed Healthcare Product</td>
<td>31 (0.8)</td>
<td>30 (1.6)</td>
<td>0 (0.0)</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>Health Maintenance Organization</td>
<td>668 (17.1)</td>
<td>244 (13.0)</td>
<td>19 (11.2)</td>
<td>10 (8.6)</td>
</tr>
<tr>
<td>Indemnity Plan</td>
<td>81 (2.1)</td>
<td>33 (1.8)</td>
<td>3 (1.8)</td>
<td>0 (0.0)</td>
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<tr>
<td>Point of Service</td>
<td>541 (13.8)</td>
<td>189 (10.1)</td>
<td>12 (7.1)</td>
<td>2 (1.7)</td>
</tr>
<tr>
<td>Preferred Provider Organization</td>
<td>2,527 (64.6)</td>
<td>1,337 (71.3)</td>
<td>132 (77.6)</td>
<td>99 (85.3)</td>
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<tr>
<td>Unknown</td>
<td>65 (1.7)</td>
<td>41 (2.2)</td>
<td>4 (2.4)</td>
<td>4 (3.4)</td>
</tr>
</tbody>
</table>
# Results

## Demographic Characteristics by Index Therapy (continued)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Etanercept (N=3,913)</th>
<th>Adalimumab (N=1,874)</th>
<th>Infliximab (N=170)</th>
<th>Ustekinumab (N=116)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Region, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td>781 (20.0)</td>
<td>360 (19.2)</td>
<td>20 (11.8)</td>
<td>14 (12.1)</td>
</tr>
<tr>
<td>Midwest</td>
<td>1,194 (30.5)</td>
<td>487 (26.0)</td>
<td>41 (24.1)</td>
<td>35 (30.2)</td>
</tr>
<tr>
<td>South</td>
<td>1,421 (36.3)</td>
<td>798 (42.6)</td>
<td>76 (44.7)</td>
<td>62 (53.4)</td>
</tr>
<tr>
<td>West</td>
<td>517 (13.2)</td>
<td>229 (12.2)</td>
<td>33 (19.4)</td>
<td>5 (4.3)</td>
</tr>
<tr>
<td>Prescriber Type, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>383 (9.8)</td>
<td>192 (10.2)</td>
<td>15 (8.8)</td>
<td>11 (9.5)</td>
</tr>
<tr>
<td>Internal Medicine</td>
<td>113 (2.9)</td>
<td>58 (3.1)</td>
<td>6 (3.5)</td>
<td>2 (1.7)</td>
</tr>
<tr>
<td>Dermatology</td>
<td>2,397 (61.3)</td>
<td>1,182 (63.1)</td>
<td>50 (29.4)</td>
<td>79 (68.1)</td>
</tr>
<tr>
<td>Rheumatology</td>
<td>30 (0.8)</td>
<td>27 (1.4)</td>
<td>40 (23.5)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Other</td>
<td>891 (22.8)</td>
<td>397 (21.2)</td>
<td>55 (32.4)</td>
<td>24 (20.7)</td>
</tr>
<tr>
<td>Unknown</td>
<td>99 (2.5)</td>
<td>18 (1.0)</td>
<td>4 (2.4)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>
Results - *Treatment Persistence, Discontinuation, and Switching in All Patients*

![Graph showing treatment persistence, discontinuation, and switching for various biologic medications in US managed care patients treated for psoriasis.](image-url)
Results

Time on Index Therapy

- Etanercept New (N=1,740)
- Adalimumab New (N=1,458)
- Infliximab New (N=93)
- Ustekinumab New (N=96)
- Etanercept Continuing (N=2,173)
- Adalimumab Continuing (N=416)
- Infliximab Continuing (N=77)
- Ustekinumab Continuing (N=20)
Conclusions

• After 12 months, fewer than half of patients with psoriasis had full-year treatment persistence
  – Treatment persistence was highest in patients treated with ustekinumab (49%), and lowest in patients treated with etanercept and adalimumab (38% each)
  – Restarting of initial treatment was highest in patients treated with etanercept (21%), and lowest in patients treated with infliximab (13%)
  – Discontinuation was highest in patients treated with adalimumab (35%), and lowest in patients treated with etanercept (29%)
  – Rates of switching between biologic therapies was low, ranging from 3% to 12%

• The overwhelming majority of patients were taking self-injected TNF inhibitors, suggesting that these are the treatments of choice for this population

• Further research is needed to understand the reasons and the implications of the high rates of discontinuation and the low rates of persistence
References


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