Medication Adherence and Discontinuation in Patients with Bipolar Disorder
Who Initiated a Long-Acting Injectable Antipsychotic Versus Those Who Changed to a Different Oral Antipsychotic Monotherapy

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Objective

To examine medication adherence and discontinuation in patients with bipolar disorder who initiated an LAI versus those who changed to a different oral antipsychotic monotherapy.

Methods

Retrospective cohort study using the Truven MarketScan® Commercial and Medicaid Databases

Patient identification:

- Patients with bipolar disorder (1 inpatient claim or 2 outpatient claims with ICD-9-CM code: 296.0x, 296.1x, 296.4x, 296.6x, 296.7x, 296.8x) (existing or newly diagnosed) between 01/01/2012 to 06/30/2015
- LAI cohort
  - Initiated an LAI during the ID period (01/01/2013 to 06/30/2014)
  - Index date: first LAI use
  - No index LAI use 1 year prior to the index date (use of a different LAI was allowed)
- Oral cohort
  - Patients with bipolar disorder who did not initiate an LAI and changed to a different oral antipsychotic monotherapy
  - Index date: date of change
- Additional inclusion criteria
  - Bipolar disorder diagnosis prior to index date
  - 1-year pre-index (baseline) continuous enrollment
  - 1-year post-index continuous enrollment
- Exclusion criteria
  - ≤ 17 years old on index date
  - Patients followed for variable period until discontinuement or study end
- Medication adherence reported as proportion of days covered (PDC) during the 1-year post-index period
  - PDC = number of days when index medication was available / 365 days
- Discontinuation defined as switch or gap of ≥60 days

Statistical analysis:

- A general linear regression model used to estimate medication adherence
- A Kaplan-Meier Curve and a Cox regression model used to estimate the time to discontinuation and risk of discontinuation
- All models adjusted for patient demographic and clinical characteristics, baseline medication, and baseline emergency department (ED) visits or hospitalizations

Results

- 1,672 (84.9%) LAI initiators and 9,672 (85.3%) oral monotherapy users were identified (Figure 1).
- Compared with oral users, LAI initiators were younger (mean [SD] LAI vs. oral: 43.8 [13.9] vs. 51.3 [13.4]), and a higher percentage of them were female (83.3% vs. 42.1%) (Table 1).
- LAI initiators had higher psychiatric comorbidities and somatic comorbid disease burden than users, and more ED or inpatient utilization during the baseline period (Table 1).
- Adjusting for covariates, LAI initiators had better medication adherence than oral users (adjusted PDC mean: 0.50 vs. 0.45; p<0.001) (Figure 2).
- Median time to discontinue index LAI was 149 days vs. 96 days for the oral cohort (p=0.001) (Figure 2).
- Oral users had higher risks than LAI initiators to discontinue their index treatment (hazard ratio: 1.19; p=0.001) (Table 2).

Figure 1: Patient Identification

1,672 LAI initiators and 9,672 oral monotherapy users with at least two index claims or two outpatient claims for bipolar disorder from 01/01/2012 to 06/30/2015

Table 2: Multivariable Results: Risk of Discontinuation and Adjusted Medication Adherence (PDC) Estimates

| Risk of discontinuation (in the entire follow-up period) |
|-----------------|-----------------|-----------------|-----------------|-----------------|
|                  | All              | Oral LAI         | Monotherapy     | Other LAI        |
| p-value          | 0.041            | 0.001            | 0.036           | 0.001           |
| Index treatment  | n/a              | n/a              | n/a             | n/a             |
| PDC estimate     | n/a              | n/a              | n/a             | n/a             |
| 1-year follow-up | n/a              | n/a              | n/a             | n/a             |
| PDC estimate     | n/a              | n/a              | n/a             | n/a             |

Addition of any oral antipsychotic medication (n=1,672)

- 1,495.8 (17.9) PDC (95% CI: 1,486.7 - 1,505.0) in the 1-year follow-up period
- 1,495.0 (9.4) PDC (95% CI: 1,485.2 - 1,494.9) in the 1-year follow-up period

Table 1: Demographics

<table>
<thead>
<tr>
<th>Demographics</th>
<th>LAI N=1,672</th>
<th>Oral N=9,672</th>
<th>All N=11,344</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, mean (SD)</td>
<td>38.1 (13.3)</td>
<td>38.1 (13.4)</td>
<td>38.1 (13.4)</td>
<td>0.120</td>
</tr>
<tr>
<td>Female, %</td>
<td>1,382 (82.3)</td>
<td>5,080 (52.6)</td>
<td>6,462 (56.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Medication adherence, %</td>
<td>842 (50.4)</td>
<td>8,791 (88.7)</td>
<td>9,633 (84.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Charlson comorbidity index,</td>
<td>1.9 (4.0)</td>
<td>2.1 (4.2)</td>
<td>2.0 (4.2)</td>
<td>0.726</td>
</tr>
<tr>
<td>Somatic comorbidities, %</td>
<td>1.53 (6.1)</td>
<td>6.63 (10.4)</td>
<td>5.64 (9.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anxiety</td>
<td>83 (4.7)</td>
<td>640 (6.8)</td>
<td>523 (4.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Depression</td>
<td>134 (7.2)</td>
<td>840 (8.6)</td>
<td>574 (4.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Personal disorder</td>
<td>136 (7.4)</td>
<td>859 (9.1)</td>
<td>595 (5.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>7 (0.4%)</td>
<td>3 (0.0%)</td>
<td>0.036</td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Limitations

- Clinical differences unmeasurable in this database may have been responsible for the choice of LAI vs. oral antipsychotics, and these differences may be responsible for some of the adherence advantages observed.
- Results may not be generalizable to uninsured patient populations.

Conclusions

- Patients with bipolar disorder initiating LAIs had better medication adherence and lower discontinuation risk than patients who changed to a different oral antipsychotic monotherapy.
- Payers and clinicians treating patients with bipolar disorder should consider LAIs as treatment options for patients with known or suspected poor adherence.

References