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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Introduction

- Bipolar disorder, a chronic, recurring mood disorder, affects approximately 2.6% (5.7 million) of the adult population in the US.[1]
- Medication non-adherence is associated with greater risks of relapse and repeated hospitalizations.[2-4]
- Long-acting injectable antipsychotics (LAIs) were developed to improve medication adherence and have been increasingly used either as monotherapy or as adjunctive therapy to mood stabilizers for patients with bipolar disorder.[5]
- Risperidone LAI is the only LAI antipsychotic approved by the FDA for the maintenance treatment of bipolar disorder in the US. However, other LAIs are used off-label for the treatment of bipolar disorder.[6]

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.

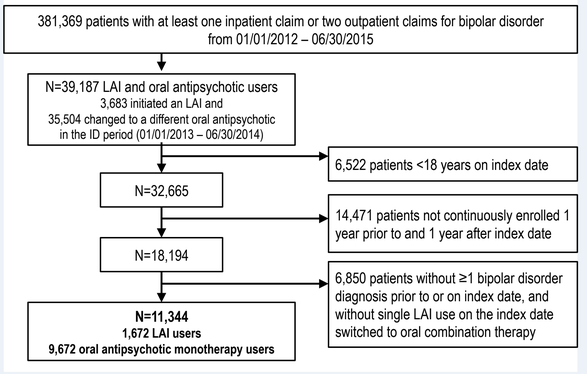
Methods

- 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 and 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 disenrollment 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 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 (14.7%) 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: 36.1 (13.3) vs. 39.1 (13.4)], and a higher percentage of them were female (83.3% vs. 42.1%) (Table 1).
- LAI initiators had higher psychiatric comorbid and somatic comorbid disease burden than oral 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) (Table 2).
- Median time to discontinue index LAI was 149 days vs. 99 days for the oral cohort (p<0.001) (Figure 2).
- Oral users had higher risks than LAI initiators to discontinue their index treatments (hazard ratio: 1.19; p<0.001) (Table 2).

Figure 1. Patient Identification



Results (cont'd)

Table 1: Patient Characteristics

	LAIs N=1,672; 14.7%	Oral Monotherapy N=9,672; 85.3%	All N=11,344	*P* Value
Demographics				
Age in years, mean (SD)	36.1 (13.3)	39.1 (13.4)	38.6 (13.4)	<0.001
Female, n (%)	1,392 (83.3)	4,068 (42.1)	5,460 (48.1)	<0.001
Medicaid enrollees, n (%)	842 (50.4)	6,570 (67.9)	7,412 (65.3)	<0.001
Comorbidities				
Charlson comorbidity index, mean (SD)	1.2 (1.8)	1.1 (1.8)	1.1 (1.8)	0.062
No. chronic conditions, mean (SD)	4.0 (2.3)	4.0 (2.2)	4.0 (2.2)	0.706
Psychiatric comorbidities, n (%)	1,531 (91.6)	8,063 (83.4)	9,594 (84.6)	<0.001
Depression	918 (54.9)	5,569 (57.6)	6,487 (57.2)	0.041
Anxiety	830 (49.6)	5,403 (55.9)	6,233 (54.9)	<0.001
Personality disorder	346 (20.7)	1,074 (11.1)	1,420 (12.5)	<0.001
Substance abuse disorders	1,005 (60.1)	4,504 (46.6)	5,509 (48.6)	<0.001
Schizophrenia	1,127 (67.4)	1,613 (16.7)	2,740 (24.2)	<0.001
Somatic comorbidities[a], n (%)	948 (56.7)	4,959 (51.3)	5,907 (52.1)	<0.001
Baseline[b] medication and healthcare service use				
Use of any oral antipsychotic medication, n (%)	1,465 (87.6)	9,672 (100.0)	11,137 (98.2)	n/a
Any use of selected psychiatric medications[c], n (%)	1,406 (84.1)	9,091 (94.0)	10,497 (92.5)	<0.001
Somatic medications, n (%)	770 (46.1)	4,706 (48.7)	5,476 (48.3)	0.049
Any inpatient hospitalization or ED visit, n (%)	1,363 (81.5)	6,634 (68.6)	7,997 (70.5)	<0.001

[a] Obesity, diabetes mellitus, hyperlipidemia, hypertension. [b] One year prior to the index date. [c] Antidepressant, anti-anxiety medications, sedatives or hypnotics.

Figure 2. Time to Discontinuation of Index Treatment

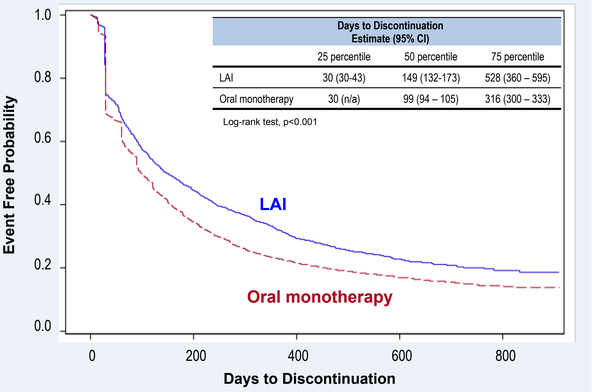


Table 2: Multivariate[a] Results: Risk of Discontinuation and Adjusted Medication Adherence (PDC) Estimates

	Risk of discontinuation of index treatment in the entire follow-up period[b]		Index treatment PDC in the 1-year follow-up period[c,d]	
	HR (95% CI)	*P* Value	Estimate (95% CI)	*P* Value
Oral monotherapy (Ref: LAI)	1.19 (1.12 – 1.28)	<0.001	-0.045 (-0.068 – -0.022)	<0.001

[a] Adjusted for age groups, gender, race (White vs. non-White), Charlson comorbidity index, number of chronic conditions, any baseline inpatient hospitalization or ED visit, depression, anxiety, schizophrenia, any baseline psychiatric medication use, and any baseline somatic medication use.
[b] Cox regression model.
[c] General linear regression model.
[d] Adjusted mean (95% CI) PDC of index treatment in 1-year follow-up period: mono oral antipsychotic 0.453 (0.445 – 0.461); LAI 0.498 (0.477 – 0.519).

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.

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Disclosures: Greene is an employee of Otsuka Pharmaceutical Development and Commercialization, Inc., Princeton, NJ. Chang, Yan, and Broder are employees of Partnership for Health Analytic Research, LLC, Beverly Hills, CA. Touya is an employee of Lundbeck, Deerfield, IL. Funding for the study and this poster was received from Otsuka Pharmaceutical Development and Commercialization, Inc. and Lundbeck.

International Society for Pharmacoeconomics and Outcomes Research, May 20-24, 2017, Boston, MA, USA

Research was conducted by Partnership for Health Analytic Research, LLC.