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Asenapine in the Treatment of Older Adults with Bipolar Disorder

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Abstract

Objective—In spite of growing numbers of elderly there are few treatment studies on late-life bipolar disorder (BD). This was a 12-week prospective, open-label trial to assess efficacy and tolerability of adjunct asenapine in non-demented elderly (≥ 60 years) with sub-optimal previous response to BD treatments.

Methods—Asenapine was initiated at 5 mg/day and titrated as tolerated. Effects on global psychopathology were measured with Clinical Global Impression, Bipolar version (CGI-BP) and the Brief Psychiatric Rating Scale (BPRS). Mood polarity severity was measured with the Hamilton Depression Rating Scale (HAM-D), Montgomery Asberg Depression Rating Scale (MADRS) and Young Mania Rating Scale (YMRS). Other outcomes included the WHO-Disability Assessment Schedule II (WHO-DAS II).

Results—Fifteen individuals were enrolled (mean age 68.6, SD 6.12), 53% female, 73% Caucasian, 13% African-American, 7% Asian). There were 4/15 (27%) individuals who prematurely terminated study while 11/15 (73%) completed study. There were significant improvements from baseline on BPRS ($P<.05$), on CGI overall ($P<.01$), and on CGI mania ($P<.05$) and depression ($P<.01$) sub-scales. Mean dose of asenapine was 11.2 (SD 6.2) mg/day. The most common reported side effects were gastrointestinal discomfort ($n=5$, 33%), restlessness ($n=2$, 13%), tremors ($n=2$, 13%), cognitive difficulties ($n=2$, 13%), and sluggishness ($n=2$, 13%).

Conclusions—Elders with BD had global improvements on asenapine. Most reported adverse effects were mild and transient, but adverse effects prompted drug discontinuation in just over one-quarter of patients. While risks vs. benefits in older people must always be carefully considered, asenapine may be a treatment consideration for some non-demented geriatric BD patients.

Keywords

bipolar disorder; elderly; geriatric; manic depressive disorder; antipsychotic medications; mood stabilizers

Introduction

Bipolar disorder (BD) in older adults has gained increasing attention due to the growing proportion of elderly individuals (Jeste *et al.*, 1999; CDC, 2003; Depp *et al.*, 2004; Depp *et al.*, 2006; Sajatovic and Blow, 2007). In the United States, of the 6 million American adults with BD, roughly 1 million are over the age of 60 years (U.S. Census Bureau, 2010; NIMH, 2010).

Elderly people with BD are often functionally impaired even with relatively modest symptom levels (Bartels *et al.*, 2000; Depp *et al.*, 2006; Sajatovic and Blow, 2007), have less severe manic symptoms than younger individuals (Kessing, 2006; Oostervink *et al.*, 2009), and may be more likely to have mixed presentations (Depp *et al.*, 2004). A continuing unmet need is the identification of agents that are generally well tolerated and effective in later life BD (Aziz *et al.*, 2006; Sajatovic and Blow, 2007). Traditional mood stabilizing agents such

as valproate and lithium are used in the management of later life BD (Aziz *et al.*, 2006). However, side effects reduce tolerability and failure to fully respond is common (Al Jurdi *et al.*, 2008). Additionally, there is a growing awareness that use of combination medication therapy is an important clinical and research topic, which has not been well studied. It is critical that combination therapies that are safe and beneficial in older adults with BD be evaluated (Aziz *et al.*, 2006; Geddes *et al.*, 2010).

A novel treatment option for clinicians challenged with treating the older adult with BD is the atypical antipsychotic medication, asenapine. Asenapine is effective and well tolerated in BD mixed-age adults (McIntyre *et al.*, 2009; McIntyre *et al.*, 2009a; Calabrese *et al.*, 2010; McIntyre *et al.*, 2010) and is U.S. FDA-approved as a monotherapy or adjunct for acute manic or mixed episodes in type I BD. In younger patients with BD mania and mixed states, asenapine appears to have only modest propensity to cause weight gain, metabolic effects and extrapyramidal symptoms (EPS) (Weber *et al.*, 2009). Cardiac effects appear minimal (Chapel *et al.*, 2009) and the sub-lingual route of administration may be helpful for those who may have difficulty swallowing pills. Baruch and colleagues (Baruch *et al.*, 2013) recently noted positive findings in a first report of asenapine in elderly (mean age 67.7 years) individuals with type I acute BD mania. There are no studies with asenapine in older adults that have specifically targeted individuals with functional impairment due to BD—a key concern for real-world patients and families. To further assess asenapine treatment effects and tolerability in elderly with BD we conducted a prospective, 12-week trial of asenapine therapy in non-demented elderly with previous sub-optimal functional response to current BD treatments.

Methods

Overview

Older adults (≥ 60 years) with type I or type II BD who had previous suboptimal functional response to prescribed BD treatments received 12 weeks of open-label, adjunct asenapine. We assessed change from baseline in global psychopathology, mood polarity severity, functional and general health status, cognition, reported and observed side effects, and extrapyramidal symptoms.

Participants

Participants were recruited from clinical and community settings such as senior centers and senior housing using institutional review board (IRB) approved advertisements. Inclusion criteria included having type I or type II BD by DSM-IV criteria confirmed on the Mini Neuropsychiatric Interview (MINI; Sheehan *et al.*, 1998), being age ≥ 60, and having sub-optimal response to current psychotropic management defined by at least one of the following: a.) Behaviors and symptoms of irritability, agitation, mood lability that diminished ability to interact with others; and/or b.) Diminished ability to take care of basic personal needs due to symptoms of BD.

Exclusion criteria included having a history of intolerance or resistance to asenapine, clinical diagnosis of dementia or Mini-Mental State Examination (MMSE) score of < 24 (Folstein *et*

al., 1975), history of TIA, stroke or MI within the past 12 months, medical illness as underlying etiology of BD, unstable medical condition including prolonged QT interval, which could affect the outcome of the study or the subject's safety, DSM-IV substance dependence (except nicotine or caffeine) within the past 3 months, rapid cycling BD defined as 4 or more discrete mood episodes within the previous 12 months and individuals at high risk for suicide.

All participants provided written informed consent. Participants were informed that while asenapine is FDA-approved for BD, there are possible risks (which were specifically noted) and that there was no assurance that asenapine would help their specific situation. Participants were also informed that the study was funded by an investigator-initiated research grant to the study PI.

Measures

All individuals were assessed at baseline and followed up at 1, 2, 4, 8 and 12 (end of study) week time points during the trial. Individuals who terminated prematurely (before 12 weeks) completed end of study assessments at the time of study termination. All measures were conducted at all follow-up time points except that laboratory testing, EKG and patient satisfaction were only assessed at baseline, 4 and 12 week time points. Cognitive testing and CIRS-G were only assessed at baseline and 12 weeks, and the WHO-DAS and SF-12 were not assessed at 1 week.

Global psychopathology—Overall psychiatric illness severity was measured with the Brief Psychiatric Rating Scale (BPRS; Overall and Gorham, 1962), and the Clinical Global Impression, Bipolar version (CGI-BP; Spearing *et al.*, 1997).

Bipolarity Severity—Manic symptoms were measured with the Young Mania Rating Scale (YMRS; Young *et al.*, 1978). Depressive symptoms were measured with the Montgomery Asberg Depression Rating Scale (MADRS; Montgomery and Asberg, 1979) and the 17-item Hamilton Depression Rating Scale (HAM-D; Hamilton, 1960).

Functioning and general health status—Functional and general health status was measured with the WHO-Disability Assessment Schedule II (WHO-DAS II; Epping-Jordan and Ustun, 2000) and MOS Short Form General Health Survey (SF-12; Ware *et al.*, 1996). Medical comorbidity was evaluated with the Cumulative Illness Rating Scale (CIRS-G; Linn *et al.*, 1968; Miller *et al.*, 1992). Treatment satisfaction was assessed with a self-rated Likert-type scale.

Cognitive Functioning—Cognitive testing included the Hopkins Verbal Learning Test (HVLT; Brandt and Benedict, 2001), Mattis Dementia Rating Scale (DRS; Mattis, 2004), Stroop (Halstead, 1947; Reitan and Wolfson, 1993), and Trails A and B assessments (Trenerry *et al.*, 1989).

Safety Assessments—Safety assessments included 12-lead EKG, serum electrolytes, renal thyroid, liver and metabolic functions as well as CBC with differential. Levels of B12 and folate were assessed at baseline only. Adverse effects were evaluated with the

standardized UKU (Lingjaerde *et al.*, 1987), the Simpson Angus Scale (SAS; Simpson and Angus, 1970), and the Barnes Akathisia Rating Scale (BARS; Barnes, 1989). Additional safety physical parameters included body mass index (BMI), vital signs and spontaneous report of adverse events which were assessed at every visit.

Treatment

Study Drug—Asenapine was initiated at 5 mg once a day and increased as tolerated to a maximum of 20 mg/day. Mean daily dose of asenapine was 11.2 mg (SD 6.2) with range 5 to 25 mg/day.

Concurrent mood stabilizing medications—Current maintenance medication treatments for BD were continued for subjects maintained on these medications with no change in dosage for a minimum of 30 days (60 days for lamotrigine). Mood stabilizer serum levels were not assessed. Antidepressant medications at stable doses for at least the last 30 days were continued as were maintenance hypnotic drugs prescribed for chronic insomnia. Initiation of concurrent antipsychotic medications was not permitted during the course of the study. There were two individuals on antipsychotic medications at study start. One individual had risperidone tapered and then discontinued over a 2-week period while another individual remained on low-dose quetiapine at bedtime for sleep. Other than the study agent, no new psychotropic medications were permitted during the study.

Data analysis

We used a modified “intent-to-treat” analysis that included all enrolled individuals who took at least a single dose of study drug regardless of their eventual retention in the study.

Adverse events were defined as increases of 2 points on UKU or a score of 3 on any one item (Meyers *et al.*, 2009). Descriptive statistics were calculated for baseline characteristics. Using paired t-tests, we performed a pre/post analysis of changes in outcomes from baseline to last visit on asenapine therapy. When 12-week data were unavailable, the final visit was based on the last date the subject followed protocol (and was known to be taking asenapine).

Results

Enrollment and Baseline Characteristics

A total of 17 individuals were screened for the study with two individuals failing study screen (one due to not having bipolar disorder and one due to having a history of stroke within the past 12 months). Group means of clinical characteristics of the 15 individuals eventually enrolled are illustrated in Table 1. Table 2 illustrates participant-specific details on baseline clinical status including comorbidity and concomitant medications.

Drop-outs

There were 4 individuals who dropped out prematurely, three due to adverse events and one lost to follow-up. At study endpoint one individual had elevated liver function possibly related to the study drug which resolved with drug discontinuation. Three individuals had severe adverse effects which caused them to be discontinued from study: mixed depressive/manic symptoms (n=1), recurrence of suicidal ideation in the context of tooth abscess (n=1),

and reported dizziness/refusal to take additional mood stabilizer after taking a single dose of asenapine in an individual with euphoric mania (n=1). Only one of these more severe adverse effects (mixed manic emergence) appeared to be a possible medication effect.

Therapeutic Response

Table 3 notes mean changes in global psychopathology and functional outcomes. There were significant improvements in change from baseline on BPRS ($P<.05$), on CGI overall ($P<.01$), and on CGI mania ($P<.05$) and depression ($P<.01$) sub-scales. There was no significant improvement in either mental health or physical health domains of the SF-12 and no significant change in WHODAS-II subscales. There was no significant change in DRS, HVLT-R, Stroop, or Trails cognitive assessments.

As noted in Table 2, the majority of participants had at least moderate to severe depression at baseline, while a smaller proportion had mild mania or hypomania severity at baseline. Among individuals with at least mild mania or hypomania symptoms (YMRS ≥ 12), there was significant improvement in YMRS scores ($p<.01$). Among individuals with at least mild depression (HAMD ≥ 8 , MADRS ≥ 16), there was a trend for significant improvement on MADRS ($p=.06$) and HAMD ($p=.01$) scores.

Tolerability

The most common spontaneously reported side effects among BD elders on asenapine included gastrointestinal discomfort (n=5, 33%), restlessness (n=2, 13%), tremors (n=2, 13%), cognitive difficulties (n=2, 13%), and sluggishness/sedation (n=2, 13%). Most side effects were tolerable for patients and did not lead to study termination. Over the course of 78 patient visits, the most common adverse events captured by the UKU were reduced duration of sleep (N=27, 35%), reduced salivation (N=24, 31%), tension/inner unrest (N=24, 31%), fatigue (N=22, 29%), increased dream activity (N=21, 27%), depression (N=17, 22%), difficulty concentrating (N=14, 18%), akathisia (N=9, 12%), weight gain (N=7, 9%), and sedation (N=7, 9%). There was no significant change from baseline on SAS or BARS scales and no significant change in BMI, glucose, total cholesterol or triglycerides. No individuals had significant changes on EKG.

With respect to the orally-dissolving formulation, some individuals noted that they preferred sub-lingual tablets to swallowing pills, while others found the taste of the quick-dissolve tablets to be mildly unpleasant. No individuals were unable to tolerate the sub-lingual tablets because of bad taste or inconvenience.

Patient satisfaction and asenapine continuation post-study

Seven of eleven participants who completed the study (63%) felt that they benefited a great deal/a lot from asenapine while four (36%) felt they either did not benefit or benefited only somewhat. Among study completers, six (55%) stated that they would continue to take asenapine after the study concluded.

Discussion

To the best of our knowledge there is only one previous report that has specifically investigated asenapine therapy in older adults with BD, a prospective analysis on inpatient BD elders with acute mania (Baruch *et al.*, 2013). In the study by Baruch and colleagues (2013), 11 highly symptomatic BD elders (mean baseline YMRS = 33.5) had significant antimanic response and good tolerability. In this prospective, uncontrolled trial of 15 outpatient non-demented elders with BD we observed global psychiatric symptom improvement on asenapine, although functional status did not improve. Consistent with the report by Baruch and colleagues (2013) we noted significant reduction in YMRS scores in BD elders who had manic or hypomanic symptoms at baseline. Our sample also included BD elders who were depressed. Depressed individuals had improvement on HAMD that was significant, while change on MADRS did not quite reach statistical significance ($P=.07$). Cognition did not change with asenapine therapy, although individuals with cognitive impairment consistent with a dementia diagnosis were specifically excluded from study participation.

Asenapine dosing in this elderly sample was 11.2 mg/day, which is substantially lower than the 20 mg/day dosing used in the acute mania geriatric bipolar study by Baruch and colleagues (2013), but is in the 11–13 mg/day dose range used in an asenapine adjunct treatment study involving mixed age manic adults (Szegedi *et al.*, 2012). While most reported adverse effects were mild and transient, adverse effects prompted drug discontinuation in just over one-quarter of patients. This is similar to a prospective multi-site clinical trial involving BD elderly outpatients which had a dropout rate of 33% (Sajatovic *et al.*, 2011).

Our study had a number of limitations including small size, uncontrolled design, inclusion of individuals with both depressive and manic symptoms, use of concomitant medications, and the fact that concomitant mood stabilizer levels were not assessed. However, since this is the first available data on asenapine that includes outpatient and depressed elders, findings may still be helpful to clinicians treating the growing proportion of older adults with BD who need care and who may not be responsive to previously available therapies. While the findings in depressive symptoms are interesting, the small sample and even smaller group of individuals with significant depression preclude any conclusion on effects of asenapine in geriatric BD depression. Larger studies that specifically enroll elders with BD depression are needed to evaluate this issue.

In conclusion, while risks vs. benefits in older people must always be carefully considered, asenapine may be a treatment consideration for some non-demented geriatric BD patients who have poor response to previous BD treatments.

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Key points

- In spite of changing global demographics that project rapidly growing numbers of older adults, there are few treatment studies specific to late-life bipolar disorder (BD).
- This 12-week prospective, open-label trial assessed efficacy and tolerability effects of adjunct asenapine in 15 non-demented elderly (≥ 60 years) ambulatory patients with suboptimal response to previous BD treatments.
- Older non-demented elders (mean age 68.6, SD 6.12) with BD had global psychopathology improvement on asenapine (mean dose 11.2, SD 6.2, mg/day), but no significant change in functional status. Most reported adverse effects were mild and transient, but adverse effects prompted drug discontinuation in just over one-quarter of patients.
- Although risks vs. benefits in older people must always be carefully considered, asenapine may be a treatment consideration for some non-demented geriatric BD patients.

Table 1

Clinical Characteristics of Bipolar, Non-demented Older Adults on Asenapine

Variable	Value
Age in years Mean (SD)	68.6 (6.1)
Range	60–80
Gender N (%)	
Male	7 (46.7)
Female	8 (53.3)
Race N (%)	
White	11 (73.3)
Black	2 (13.3)
Asian	1 (6.7)
Other	1 (6.7)
Hispanic ethnicity N (%)	1 (6.7)
Education in years Mean (SD)	13.1 (1.6)
Range	10–16
Living Alone N (%)	6 (40.0)
Marital Status N (%)	
Single, never married	1 (6.7)
Married	4 (26.7)
Separated	1 (6.7)
Divorced	8 (53.3)
Widowed	1 (6.7)
BMI Mean (SD)	31.0 (5.3)
Range	23.1–43.2
Type of Bipolarity N (%)	
Type I	13 (86.7)
Type II	2 (13.3)
Duration of BD illness in years	
Mean, SD	30.5 (19.0)
Range (Median)	5–60 (33)
Past suicide attempt N (%)	3 (20.0)
MMSE Mean (SD)	28.3 (2.1)
Range	24–30
CIRS-G cumulative score Mean (SD)	6.5 (2.5)
Range	2–13

Variable	Value
Concomitant maintenance BD treatment N (%)	
Lithium	3 (20)
Any Anticonvulsant	5 (33.3)
Antidepressant	6 (40.0)

MMSE: Mini-Mental State Examination

CIRS-G: Cumulative Illness Rating Scale for Geriatrics

Table 2

Baseline clinical status and asenapine treatment response/tolerability among older adults with BD

Participant	Age	Sex	Comorbid medical conditions	Concomitant Medications	Asenapine Daily Dose	Baseline symptom ratings	Endpoint symptom ratings	Main Adverse Effects	Comments
01	65	M	Type 2 diabetes	Lithium	5 mg	YMRS: 3 HAM-D: 3 MADRS: 7	YMRS: 7 HAM-D: 8 MADRS: 11	Tremor	
02	76	F	Hypothyroidism Hypertension Hypertlipidemia	Lamotrigine Topiramate Venlafaxine Aspirin L-thyroxine Atorvastatin Benazepril	5 mg	YMRS: 1 HAM-D: 0 MADRS: 7	YMRS: 8 HAM-D: 12 MADRS: 24	Mixed mania switch leading to hospitalization	<ul style="list-style-type: none">Discontinued study prematurely
03	73	F	Hypertlipidemia Dermatitis/ Chronic allergies	Simvastatin Actonel Prednisone	20 mg	YMRS: 8, HAM-D: 18 MADRS: 33	YMRS: 9 HAM-D: 22 MADRS: 45	Suicidal ideation, Sedation	<ul style="list-style-type: none">Acute tooth infection (abscess) beginning in week 7 of studyDiscontinued study prematurely after 8 weeks due to suicidal ideation/lack of efficacy
04	63	M	Coronary Artery Disease Hypothyroidism	L-thyroxine Rosuvastatin	5 mg	YMRS: 8 HAM-D: 5 MADRS: 6	YMRS: 5 HAM-D: 4 MADRS: 1	Dizziness, Fatigue, Dry mouth	<ul style="list-style-type: none">Discontinued study after a single 5 mg dose of asenapine
05	62	F	Hypertension Osteoarthritis	Citalopram Ritalin Divalproex Trazadone for insomnia Metoprolol Triamterene- Hydrochlorothiazide	10 mg	YMRS: 4 HAM-D: 11 MADRS: 23	YMRS: 5 HAM-D: 15 MADRS: 22	GI discomfort	
06	77	M			20 mg	YMRS: 10 HAM-D: 5 MADRS: 7	YMRS: 2 HAM-D: 3 MADRS: 4	GI discomfort, Drooling	<ul style="list-style-type: none">Lost to follow-up after 8 weeks
07	73	F	Hypertension Hypertlipidemia	Citalopram Lisinopril Lovastatin Amlodipine	5 mg	YMRS: 6 HAM-D: 17 MADRS: 32	YMRS: 3 HAM-D: 5 MADRS: 3	Increased Liver Function Testing (LFT)	<ul style="list-style-type: none">Stopped asenapine at study end due to progressive LFT increaseIncreased LFT re-occurred with drug re-challenge post-study
08	70	M	Type 2 diabetes Osteoarthritis	Lamotrigine Metformin	10 mg	YMRS: 9 HAM-D: 11 MADRS: 12	YMRS: 0 HAM-D: 4 MADRS: 11	Headache, Restlessness	
09	68	F	Hypertension Asthma	Hydrochlorothiazide Diltiazam	10 mg	YMRS: 8 HAM-D: 24	YMRS: 4 HAM-D: 17	Increased appetite, Skin itching	

Participant	Age	Sex	Comorbid medical conditions	Concomitant Medications	Asenapine Daily Dose	Baseline symptom ratings	Endpoint symptom ratings	Main Adverse Effects	Comments
			Chronic lower back pain			MADR: 29	MADRS: 31		
10	62	F	Hypertension Gastroesophageal reflux disease Osteoarthritis	Lithium Lamotrigine Alprazolam for insomnia Clonidine Lisinopril Omeprazole Cyclobenzaprine	10 mg	YMRS: 4 HAM-D: 19 MADRS: 34	YMRS: 12 HAM-D: 12 MADRS: 23		On risperidone 3 mg/day at study entry. This was tapered and discontinued over a 2-week period.
11	64	F	Hyperlipidemia Hypertension Chronic obstructive pulmonary disease	Lithium, Sertraline Trazadone Alprazolam for insomnia Amlodipine Montelukast	10 mg	YMRS: 19 HAM-D: 19 MADRS: 22	YMRS: 12 HAM-D: 12 MADRS: 21	Tremor	
12	80	F	Hypertension Osteoarthritis Atrial fibrillation	Sertraline Nexium Lisinopril Actonel	7.5 mg	YMRS: 7 HAM-D: 21 MADRS: 27	YMRS: 4 HAM-D: 8 MADRS: 4	Episode of atrial fibrillation due to pericarditis that was treated /resolved with naproxyn and colchicine. The atrial fibrillation was not believed to be due to asenapine and the patient was continued on asenapine during and after the episode.	
13	68	M	Migraine Osteoarthritis Hypertension Coronary artery disease Gastroesophageal reflux disease	Quetiapine Lisinopril Propranolol Amlodipine Omeprazole	25 mg	YMRS: 15 HAM-D: 21 MADRS: 25	YMRS: 8 HAM-D: 1 MADRS: 5		
14	68	M	Coronary artery disease Hypertension Gastroesophageal reflux disease Chronic lower back pain	Topiramate Bupropion Gabapentin Atenolol Hydrochlorothiazide	10 mg	YMRS: 12 HAM-D: 10 MADRS: 9	YMRS: 4 HAM-D: 5 MADRS: 0	Difficulty concentrating, Fatigue	
15	60	M	Type 2 diabetes Sleep apnea	Escitalopram Metformin	15 mg	YMRS: 19 HAM-D: 22 MADRS: 26	YMRS: 12 HAM-D: 14 MADRS: 9	Dry mouth	

YMRS= Young Mania Rating Scale
HAM-D= Hamilton Depression Rating Scale
MADRS= Montgomery Asberg Depression Rating Scale

Table 3

Mean change from baseline in symptoms, functional status, abnormal movement, laboratory values and physical parameters among BD elders on asenapine

Variable	N	Baseline*	Endpoint*	Statistic
BPRS	15	35.1 (9.2)	28.6 (9.4)	t=2.39,df=14,p<0.05
CGI-BP Mean (SD)	15			
-Severity: Mania		2.7 (1.7)	1.9 (1.1)	t= 2.69,df=14,p<0.05
-Severity: Depression		3.6 (1.5)	1.7 (0.7)	t=5.80,df=14,p<0.01
-Severity: Overall		4.4 (1.0)	2.2 (1.0)	t=5.78,df=14,p<0.01
SF-12 Mean (SD)	15			
- Mental Score		38.7 (15.3)	43.1 (13.1)	t= -1.30,df=14,p=0.22
- Physical Score		46.8 (11.3)	46.4 (12.1)	t=0.16,df=14,p=0.88
WHO-DAS II (subscales)	15			
- Getting Around		4.3 (2.7)	4.7 (2.9)	t=-0.95,df=14,p=0.36
- Self Care		2.6 (1.3)	2.4 (0.7)	t=1.00,df=14, p=0.33
- Life Activities		9.1 (4.9)	7.1 (3.5)	t=2.05,df=14,p=0.06
- Understand/Communicate		3.6 (1.8)	3.1 (1.2)	t=1.39,df=14,p=0.19
- Participation in Society		4.3 (2.6)	3.8 (2.0)	t=1.24,df=14,p=0.24
- Getting Along with People		3.0 (1.5)	2.9 (1.9)	t=0.44,df=14,p=0.67
SAS Mean (SD)	15	0.4 (0.8)	0.5 (0.7)	t=-0.32, df=14,p=0.75
BAS Mean (SD)	15	0.0 (0.0)	0.1 (0.5)	t=-1.00,df=14,p=0.33
Physical Parameters:				
BMI Mean (SD)	15	31.0 (5.3)	31.3(5.3)	t=-0.86,df=14,p=0.40
Laboratory testing				
-Serum glucose	14	93.7 (19.7)	102.3 (27.5)	t=-0.83,df=13,p=0.42
-Total cholesterol	13	190.9 (44.7)	188.8 (27.2)	t=0.23,df=12,p=0.83
-Triglycerides	13	144.1 (87.6)	166.3 (100.4)	t=-0.93,df=12,p=0.37

* All values reported as mean (SD) pre/post comparison t-test comparison of baseline vs. value at last assessment that participant was known to be receiving asenapine

CGI-BP: Clinical Global Impression, Bipolar version

AIMS: Abnormal Involuntary Movement Scale

SAS: Simpson Angus Scale

BAS: Barnes Akathisia Scale

SF-12: Medical Outcomes Study Short Form General Health Survey

WHODAS-II: WHO-Disability Assessment Schedule II

BMI: Body Mass Index