

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: None

ACTIVE INGREDIENT: None

Study No: NIS-NES-DUM-2009/1 (NCT00824031)

Epidemiological study to assess treatment adherence of bipolar patients in Spain. Adherence study
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Developmental phase: Epidemiological Study

Study Completion Date: 09 Oct 2009

Date of Report: 31 Jul 2010

OBJECTIVES:

Main Objective

To increase the knowledge about adherence to treatment in patients diagnosed with bipolar disorder in the scope of the real-life practice at the ambulatory setting.

Secondary Objectives

- To estimate the degree of treatment adherence in bipolar disorder.
- To describe patients diagnosed with bipolar disorder based on their degree of adherence to the treatment prescribed at the time of the study.
- To determinate those variables related to poor adherence to treatment in real-life practice in patients diagnosed with bipolar disorder.

METHODS:

The ADHERENCE study is a national, multicentre, observational, cross-sectional study. Patients were included from July to October 2009. Investigators were asked to make up part of the sample with potentially non-adherent patients. The identification of these patients was made using their disease history. Those with at least one relapse episode within a year of the start of the study were considered potentially non-adherent. Patients also had to be treated with at least one oral antipsychotic. Measurement of adherence was done using the Morisky-Green Test, the DAI-10 Scale and the Clinician Rating Scale (CRS). Clinical status was measured by means of CGI-BP-M, YMRS and MADRS scales, whereas functioning was assessed with the FAST scale.

Method of statistical analysis

Due to the study design, variables were presented by descriptive statistics. Categorical data were reported as frequencies and proportions. Continuous data were reported as means and standard deviations. When appropriate, alternative descriptive statistics, such as quartile ranges and medians with ranges, for categorical and continuous data respectively, were reported.

Model creation and selection was based on *a priori* clinical and biological considerations. The significance level was 5% for keeping independent predictors in the models. Statistical analyses were performed in SAS[®] statistical software system (SAS Institute, Inc., Cary, NC, USA).

RESULTS:

A total of 303 patients were included from 31 different sites. 135 (44.5%) patients were potentially adherent to treatment, whereas 168 (55.5%) were potentially non-adherent. The mean age of patients was 46.0 years old and 60% of them were female. A total of 229 (75.6%) patients had type I BD diagnosis, being maniac was the most common polarity at first mood episode (43.6%). Nevertheless, the most common last reported mood episode was depression (38.1%).

Table 1. Socio-demographic data

	Potentially adherent	Potentially non-adherent	Total
Female, N (%)	79 (58.52%)	102 (60.71%)	181 (59.74%)
Age, N; Mean (SD)	135; 46.2 (12.17)	168; 45.8 (12.02)	303; 46.0 (12.07)
Working Status, N (%)			
Active	48(36.09%)	56(33.94%)	104(34.90%)
Unemployed	20(15.04%)	23(13.94%)	43(14.43%)
Student	3(2.26%)	2(1.21%)	5(1.68%)
House wife	15(11.28%)	22(13.33%)	37(12.42%)
Retired	18(13.53%)	14(8.48%)	32(10.74%)
Permanent incapacity	22(16.54%)	31(18.79%)	53(17.79%)
Temporary incapacity	4(3.01%)	14(8.48%)	18(6.04%)
Never worked	3(2.26%)	3(1.82%)	6(2.01%)
Education			
Less than primary	5(3.70%)	11(6.55%)	16(5.28%)
Primary	22(16.30%)	32(19.05%)	54(17.82%)
Secondary (1 st grade)	33(24.44%)	37(22.02%)	70(23.10%)
Secondary (2 nd grade)	43(31.85%)	52(30.95%)	95(31.35%)
University	32(23.70%)	36(21.43%)	68(22.44%)
Co-habitation, N (%)	110(81.48%)	142(84.52%)	252(83.17%)
Place of residence, N (%)			
Rural	15(11.11%)	22(13.10%)	37(12.21%)
Urban small	28(20.74%)	41(24.40%)	69(22.77%)
Urban mean	45(33.33%)	66(39.29%)	111(36.63%)
Urban large	47(34.81%)	39(23.21%)	86(28.38%)

Table 2. Disease data

	Potentially adherent	Potentially non- adherent	Total
Bipolar Disorder I, N (%)	104(77.04%)	125(74.40%)	229(75.58%)
Years from diagnosis, N; Mean (SD)	135; 13.16 (10.27)	168; 12.19 (9.52)	303; 12.62 (9.86)
Polarity first episode, N (%)			
Mania	61(45.19%)	71(42.26%)	132(43.56%)
Hypomania	16(11.85%)	20(11.90%)	36(11.88%)
Depression	53(39.26%)	69(41.07%)	122(40.26%)
Mixed	3(2.22%)	8(4.76%)	11(3.63%)
No other specified	2(1.48%)	0(0.00%)	2(0.66%)
Severity of first episode, N (%)			
Mild	5(3.73%)	9(5.42%)	14(4.67%)
Moderate	46(34.33%)	53(31.93%)	99(33.00%)
Severe, without psychotic symptoms	35(26.12%)	46(27.71%)	81(27.00%)
Severe, with psychotic symptoms	48(35.82%)	58(34.94%)	106(35.33%)
Polarity of relapses, N (%)			
Mania	97(71.85%)	120(71.43%)	217(71.62%)
Hypomania	80(59.26%)	81(48.21%)	161(53.14%)
Depression	115(85.19%)	151(89.88%)	266(87.79%)
Mixed	34(25.19%)	48(28.57%)	82(27.06%)
No other specified	6(4.44%)	2(1.19%)	8(2.64%)

At the study start 12 (4.0%) patients were taking only one medication for BD, whereas 88 (29.0%), 103 (34.0%) and 100 (33.0%) were taking 2, 3 and 4 or more medications for BD respectively.

Table 3. Number of drugs taken by patients at the time of visit

	Potentially adherent	Potentially non- adherent	Total
Number of current treatments - total, N (%)			
1	5 (3.70%)	4 (2.38%)	9(2.97%)
2	31 (22.96%)	34 (20.24%)	65(21.45%)
3	40 (29.63%)	51 (30.36%)	91(30.03%)
≥4	59 (43.71%)	79 (47.02%)	138(45.54%)
Number of current treatments – bipolar disorder, N (%)			
1	6(4.44%)	6(3.57%)	12(3.96%)
2	41(30.37%)	47(27.98%)	88(29.04%)
3	48(35.56%)	55(32.74%)	103(33.99%)
≥4	40(29.63%)	60(35.71%)	100(33.01%)
Number of other current treatments, N (%)			
Ninguno	94(69.63%)	108(64.29%)	202(66.67%)
1	28(20.74%)	41(24.40%)	69(22.77%)
2	5(3.70%)	10(5.95%)	15(4.95%)
3	4(2.96%)	5(2.98%)	9(2.97%)
≥4	4(2.96%)	4(2.38%)	8(2.64%)

According to the adherence and compliance scales (putting together the three scales), there were 211 patients (69.6%) that could be classified as not completely adherent to treatment.

Table 4. Overall adherence assessment

	N	Percentage	CI (95%)
Good adherence	92	30.4%	(25.2%,35.5%)
Poor adherence	211	69.6%	(64.5%,74.8%)
Total	303	100%	

Regarding the Morisky-Green Test, 203 (67.0%) patients reported to having non-optimal drug compliance; that means not answering the four questions asked positively. Of these, a 62.6% were previously classified as potentially non-adherent and a 37.4% as potentially adherent.

Table 5. Morisky-Green Scale Results

	Potentially adherent	Potentially non-adherent	Total
Questionnaire, N (%)			
Question 1 = No	80(59.26%)	88(52.38%)	168(55.45%)
Question 2 = Yes	111(82.22%)	120(71.43%)	231(76.24%)
Question 3 = No	120(88.89%)	115(68.45%)	235(77.56%)
Question 4 = No	94(69.63%)	70(41.67%)	164(54.13%)
Patient assessment, N (%)			
Good adherence (No-Yes-No-No)	59(43.70%)	41(24.40%)	100(33.00%)
Poor adherence (other responses)	76(56.30%)	127(75.60%)	203(67.00%)

Regarding the DAI-10 Scale, an 86.1% of patients had a positive subjective attitude to medication (positive result of the scale) although the mean scores were 6.3 ± 4.1 and 3.7 ± 5.1 for potentially adherent and non-adherent respectively.

Table 6. DAI-10 Scale Results

	Potentially adherent	Potentially non-adherent	Total
Total Score			
N	135	168	303
Mean	6.27	3.68	4.83
SD	4.06	5.12	4.84
CI 95%	(5.58,6.96)	(2.90,4.46)	(4.28,5.38)
Subjective attitude, N (%)			
Positive (score>0)	125(92.59%)	136(80.95%)	261(86.14%)
Negative (score<0)	10(7.41%)	32(19.05%)	42(13.86%)

Finally, regarding the CRS, the mean score was 5.3 ± 1.7 with no big differences between potentially adherent and non-adherent groups.

Table 7. Clinician Rating Scale (CRS) Results

	Potentially adherent	Potentially non-adherent	Total
Total Score			
N	135	168	303
Mean	5.61	5.11	5.33
SD	1.56	1.74	1.68
CI 95%	(5.34,5.87)	(4.85,5.38)	(5.14,5.52)
Subjective attitude, N (%)			
Positive (score 5-7)	116(85.93%)	119(70.83%)	235(77.56%)
Negative (score1-4)	19(14.07%)	49(29.17%)	68(22.44%)

Mean YMRS score was 3.0 ± 4.6 in adherent and 6.8 ± 7.9 in non-adherent patients ($p < 0.0001$), whereas the mean MADRS score was 6.3 ± 7.2 and 9.3 ± 8.4 in adherent and non-adherent patients respectively ($p = 0.0046$). No differences regarding CGI-BP-M mean scores were found between both groups ($p = 0.3951$). Regarding FAST scale, the mean score in adherent patients was significantly ($p < 0.0001$) lower (17.8 ± 16.7) (better functioning) than in non-adherent patients (27.3 ± 17.5).

Table 8. Psychometric results on adherent and non-adherent patients

	Good adherence	Poor adherence	p-value
YMRS			
N	86	196	<0.0001
Mean	3.01	6.85	
SD	4.59	7.86	
CI 95%	(2.03,3.99)	(5.74,7.96)	
MADRS			
N	88	182	0.0046
Mean	6.27	9.27	
SD	7.25	8.45	
CI 95%	(4.74,7.81)	(8.04,10.51)	
CGI-BP-M (Depression)			
N	90	209	0.0040
Mean	1.71	2.14	
SD	1.03	1.24	
CI 95%	(1.50,1.93)	(1.97,2.31)	
CGI-BP-M (Mania)			
N	91	208	<0.0001
Mean	1.48	2.05	
SD	0.99	1.33	
CI 95%	(1.28,1.69)	(1.87,2.23)	
CGI-BP-M (General)			
N	91	205	0.3951
Mean	2.59	2.74	
SD	1.25	1.37	
CI 95%	(2.33,2.85)	(2.55,2.93)	
FAST Scale			
N	84	190	<0.0001
Mean	17.81	27.32	
SD	16.69	17.54	
CI 95%	(14.19,21.43)	(24.81,29.83)	
Disease Insight			
Mean	3.82	5.75	<0.0001
SD	1.73	2.99	
CI 95%	(3.46,4.17)	(5.35,6.16)	