BRISTOL-MYERS SQUIBB COMPANY

ARIPIPRAZOLE

Final Clinical Study Report for Study CN138489

SYNOPTIC REPORT

A 16-Week, Multicenter, Randomized, Open-Label Study to Assess the Effects of Aripiprazole Versus Other Atypical Antipsychotics in the Treatment of Schizophrenic Patients with Metabolic Syndrome

Indication:	Metabolic Syndrome
Phase:	4
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THIS STUDY WAS CONDUCTED IN ACCORDANCE WITH GOOD CLINICAL PRACTICE

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SYNOPSIS

Final Clinical Study Report for Study CN138489

TITLE OF STUDY: A 16-Week, Multicenter, Randomized, Open-label Study to Assess the Effects of Aripiprazole Versus Other Atypical Antipsychotics in the Treatment of Schizophrenic Patients with Metabolic Syndrome.

PURPOSE: The primary objective of the study was to compare aripiprazole to the comparator drugs (olanzapine, quetiapine, and risperidone) on mean percent changes from baseline in fasting non-high density lipoprotein (HDL) cholesterol levels in schizophrenic patients who presented with metabolic syndrome. Following one of the company's regular reviews of all studies within the development program, a strategic decision was made to terminate the study because of slow patient accrual. The patients who were randomized at the time of study termination and who had started the 16-week treatment phase of the protocol could continue the study as per protocol until completion.

NUMBER OF PATIENTS: Two hundred fifty-eight patients were planned for study; 52 patients were randomized to treatment, and 51 patients (26 control group; 25 aripiprazole group) were treated before the study was terminated.

DISPOSITION, DEMOGRAPHICS AND OTHER PERTINENT BASELINE CHARACTERISTICS:

Patient disposition and demographic characteristics are presented in Table 1 and Table 2, respectively.

Table 1: Patient Disposition - Enrolled Patients

	Number of Patients (%)		
Patient Status	**Control**	**Aripiprazole**	**Total**
Enrolled			125
Baseline Failures			73
Randomized	26	26	52
Discontinued from treatment phase	2 (7.7)	3 (11.5)	5 (9.6)
Adverse Event	0	1 (3.8)	1 (1.9)
Subject Withdrew Consent	1 (3.8)	0	1 (1.9)
Lost to Follow up	1 (3.8)	0	1 (1.9)
Subject No Longer Meets Study Criteria	0	1 (3.8)	1 (1.9)
Other known Cause	0	1 (3.8)	1 (1.9)
Completed Treatment Phase	24 (92.3)	23 (88.5)	47 (90.4)

Table 2: Demographic Characteristics-Randomized Sample

	Control N=26	Aripiprazole N=26	Total N=52
Age(yrs)			
Mean	40.7	43.9	42.3
Min-Max	22-56	26-62	22-62
Gender N (%)			
Male	13 (50.0)	15 (57.7)	28 (53.8)
Female	13 (50.0)	11 (42.3)	24 (46.2)
Weight (kg)			
Mean	89.1	91.6	90.3
Min-Max	57-132	67-152	57-152
BMI (kg/m^2)			
Mean	31.45	31.31	31.38
Min-Max	19.0-42.8	25.1-49.1	19.0-49.1
BMI Category N (%)			
< 30 Kg/m^2	7 (26.9)	13 (50.0)	20 (38.5)
≥ 30 Kg/m^2	19 (73.1)	13 (50.0)	32 (61.5)
Waist Circumference (cm)			
Mean	107.1	107.1	107.1
Min-Max	90-136	91-134	90-136
Waist Circumference Category N (%)			
≤ 102 cm for Men/ ≤ 88 cm for Women	1 (3.8)	2 (7.7)	3 (5.8)
> 102 cm for Men/ > 88 cm for Women	25 (96.2)	24 (92.3)	49 (94.2)

SUMMARY OF SAFETY RESULTS: There were no deaths or serious adverse events (SAEs) during the study. One patient (randomized to the aripiprazole group) was discontinued from the study due to an AE (worsening of paranoia). One randomized patient who did not receive study drug developed T-wave abnormality on electrocardiogram ([ECG], was withdrawn from the study to undergo cardiologic assessment, and was not included in the safety analysis. The overall safety profile is presented in Table 3.

Table 3: Overall Safety Summary - Safety Sample

	No. of Patients (%)	
	Control N = 26	**Aripiprazole N = 25**
Deaths	0	0
SAEs	0	0
AEs leading to discontinuation	0	1 (4.0)
With ≥ 1 AE	8 (30.8)	11 (44.0)

The most frequently reported AEs (i.e., occurring in more than 1 patient) in the aripiprazole group were headache (4 patients; 16.0%), anxiety, insomnia and nausea (3 patients each; 12.0%), and rash (2 patients; 8.0%). None of these events was reported in the control group. The AE of increased blood cholesterol was reported by 2 patients (7.7%) in the control group and none in the aripiprazole group. One patient in the control group (on olanzapine) had a P-wave abnormality on ECG that was considered to be not related to study medication, and the patient continued in the study.

Other Results: The mean percent change from baseline in non-HDL cholesterol at 16 weeks of treatment (last observation carried forward [LOCF] data set) was 10.06 in the control group and -2.36 in the aripiprazole group (treatment difference: -11.28; 95% CI -19.14, -2.66).

The number of patients with metabolic syndrome according to the Adult Treatment Panel III (ATP-III-A) criteria at the end of treatment was 22 of 26 (84.6%) in the control group and 16 of 25 (64.0%) in the aripiprazole group (LOCF) (ratio of metabolic syndrome rates [aripiprazole/control group] = 0.76; 95% CI 0.54, 1.06).

Other secondary objectives were not analyzed because the study was terminated early and there were insufficient data to draw meaningful conclusions.

CONCLUSIONS:

- Aripiprazole treatment was well tolerated in patients with metabolic syndrome.
- The aripiprazole group had a decrease in non-HDL cholesterol mean percent change from baseline, 11.28 points less than the control group.

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