AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: N/A
ACTIVE INGREDIENT: N/A

Study No: NIS-CKR-DUM-2008/2
Retrospective survey for patients with hypertension and Diabetes Mellitus(CRYSTAL)

Developmental phase: Marketed

Study Completion Date: 2008-09-18

Date of Report: 2009-07-10

OBJECTIVES:

Primary objective

- ✓ Attainment rate to the target blood pressure in hypertension patients having Type 2 Diabetes mellitus during the follow-up period

Secondary objectives

- ✓ Analysis of the treatment durability of hypertension patients having Type 2 Diabetes mellitus and factors to affect the treatment durability
- ✓ Investigation on blood pressure lowering effect and used antihypertensive medications (including switch or addition of medicines) in treating hypertension patients having Type 2 Diabetes mellitus

METHODS:

This non-interventional observational study protocol was reviewed in accordance with the standard procedures of AstraZeneca.

This clinical study will collect basic clinical data on patients in order to assess attainment rate to target blood pressure and to find contributing factors in hypertension patients having Type 2 Diabetes mellitus.

This study will keep a record of the following data on patients selected through medical record review. (Record in e-CRFs.)

Patient enrollment: New patients (newly diagnosed patients or transferred patients after diagnosed in other center/department → patients first treated by the investigator) eligible for the inclusion/exclusion criteria and visited since January 1, 2006, will be enrolled in consecutive order.

RESULTS:

Baseline information

Demographics

Table 1 shows the summarized information about subject's demographics classified by gender, age, BMI.

As a result of survey on gender, 1,000 subjects (50.86%) were male, 966 subjects (49.14%) were female and the mean age was 58.69 ± 11.01 year-old. The most common group of age was '60~69' in 648 subjects (32.98%) followed by the age of '50~59' (626 subjects, 31.86%), the age of 'elder than 70' (305 subjects, 15.52%), the age of '40~49' (293 subjects, 14.91%) and so on. The average BMI was 25.16 ± 3.44 kg/m^2. The BMI of 524 subjects (31.21%) were lower than 23.5 kg/m^2, which was the most frequent group followed by the group of 25 ~ 27.5 kg/m^2 in 468 subjects (27.87%), and the group of 23.5~25 kg/m^2 in 358 subjects(21.32%).

Table 1. Demographics

		No. of subjects
		N (%)
Gender	Male	1000 (50.86)
	Female	966 (49.14)
Age	Mean ± SD (year)	58.69 ± 11.01
	Min-Max	17~94
	~29	19 (0.97)
	30 ~ 39	74 (3.77)
	40 ~ 49	293 (14.91)
	50 ~ 59	626 (31.86)
	60 ~ 69	648 (32.98)
	≥70	305 (15.52)
BMI	Mean ± SD (Kg/m^2)	25.16 ± 3.44
	Min-Max	15.41 ~ 48.30
	< 23.5 Kg/m^2	524 (31.21)
	23.5~<25 Kg/m^2	358 (21.32)
	25~27.5 Kg/m^2	468 (27.87)
	≥27.5 Kg/m^2	329 (19.59)

Missing(person): Age(1), BMI(287)

Medical History

The result of medical history and risk factors is summarized in Table 2.

Mean disease duration of diabetes mellitus (DM) was 7.10 ± 7.24 years and 1,034 subjects (52.59%) had the history of hypertension treatment. Among DM complication, Not Applicable was the most with 1,110 subjects (56.46%). Among total 1,045 subjects (53.15%) with Microvascular Disease, 440 subjects (22.38%) had Neurosis and 306 subjects (15.56%) had Retinopathy.

As a result of survey on risk factors, the most common risk factor was diabetes mellitus in 1,674 subjects(85.15%), followed by hypertension(1,413 subjects, 71.87%), old age in 1,076 subjects(54.73%), dislipidemia in 584 subjects(29.70%), cigarette smoking in 269 subjects(13.68%) and so on.

Table 2. Medical history and Risk Factors

		No. of subjects N(%)
DM duration	Mean ± SD (year)	7.10± 7.24
	Min-Max	0~39.00
DM Complication (Overlapped count)	Microvascular Disease	
	Retinopathy	306(15.56)
	Nephrosis	299(15.21)
	Neurosis	440(22.38)
	Macrovascular Disease	
	Cerebral infarction	85(4.32)
	Cardiac infarction	50(2.54)
	Angina	128(6.51)
	Peripheral vascular disease	64(3.26)
	Not Applicable	1110(56.46)
HT treatment history	Yes	1034(52.59)
	No	736(37.44)
	Unknown	196(9.97)
Risk Factor (Overlapped count)	Hypertension	1413(71.87)
	Cigarette smoking	269(13.68)
	Obesity (BMI_30)	125(6.36)
	Dislipidemia	584(29.70)
	Diabetes mellitus	1674(85.15)
	Microalbuminuria or estimated GFR_60 mL/min	251(12.77)
	Old age	1076(54.73)
	Family history of premature cardiovascular disease	136(6.92)
	NA	58(2.95)

Missing: DM duration(448 including unknown)

Follow Up(Treatment) Duration

The analysis of follow up(treatment) duration is summarized in Table 3.

The average follow up(treatment) duration was 182.39±12.79 days in 1,574 subjects from visit1 to visit2 and 365.83±12.88 days in 1,922 subjects from visit2 to visit3

Table 3. Follow Up(Treatment) Duration

	N	Mean(day)	±SD	Min	Max
From Visit1 to Visit2	1574	182.39	± 12.79	151	215
From Visit2 to Visit3	1922	365.83	± 12.88	334	396

†paired t-test

Treatment status

Change of Blood Pressure

The analysis of change of blood pressure is summarized in Table 4.

Mean systolic blood pressure of 1,882 subjects at baseline was 138.15 ± 16.95 mmHg and mean diastolic blood pressure at baseline was 84.33 ± 12.59 mmHg. During follow up period these had decreased by 10.28 ± 18.26 mmHg and 6.37 ± 11.90 mmHg respectively. In follow up, mean syst

olic blood pressure was 127.88 ± 13.89 mmHg and the mean diastolic blood pressure was 77.96 ± 9.48 mmHg with statistical significance (p<.0001).

Table 4. Change of Blood Pressure

	N	Baseline	Follow Up	Difference	p-value †
		Mean±SD(mmHg)	Mean±SD(mmHg)	Mean±SD(mmHg)	
SBP	1882	138.15± 16.95	127.88± 13.89	-10.28± 18.26	<.0001
DBP	1882	84.33± 12.59	77.96± 9.48	-6.37± 11.90	<.0001

†paired t-test

Change of Lipid Profile

The mean LDL-C had decreased by 14.77 ± 47.81 mg/dL from 111.80 ± 43.06 mg/dL at baseline to 97.04 ± 30.25 mg/dL after follow up. The mean HDL-C of 973 subjects was 46.33 ± 12.16 mg/dL at baseline and 47.07 ± 10.89 mg/dL after follow up, so HDL-C had increased by 0.74 ± 9.90 mg/dL during follow up period. The mean TC of 1,060 subjects was 190.77 ± 63.24 mg/dL at baseline and 171.56 ± 39.29 mg/dL after follow up, which means mean TC had decreased by 19.21 ± 66.63 mg/dL. Mean TG of 1,008 subjects had decreased by 21.65 ± 115.28 mg/dL from 177.79 ± 124.64 mg/dL at baseline to 156.14 ± 98.48 mg/dL after follow up. All differences was statistically significant (p<.0001).

Change of HbA1C & Glucose level

The change of HbA1c and Glucose level is summarized and presented in Table 5.

As a result of comparison baseline and follow up, HbA1c, FPG, 2-hPPG has declined during follow up with statistical significance.

Table 5. Change of HbA1C & Glucose level

	N	Baseline	Follow Up	Difference	p-value†
		Mean±SD(mg/dL)	Mean±SD(mg/dL)	Mean±SD(mg/dL)	
HbA1c	1176	7.97 ± 1.77	7.46 ± 1.38	-0.51 ± 1.79	<.0001
FPG	1397	163.31 ± 79.62	143.96 ± 59.45	-19.35 ± 83.51	<.0001
2-hPPG	310	194.25 ± 68.45	182.99 ± 64.14	-11.26 ± 79.33	0.0130

†paired t-test

Blood Pressure

Rate of Reach to Target BP

The rate of reach to target BP(130/80 mmHg) is summarized in Table 6.

Total 562 subjects out of 1,887 subjects reached to target BP(130/80 mmHg) and the rate of reach to target BP was 29.78% (95%CI : 27.72~31.84).

Table 6. Rate of Reach to Target BP

	Reach(+)	[95% CI]		Reach(-)
	N(%)	lower	upper	N(%)
Target (130/80)	562(29.78)	27.72	31.84	1325(70.22)

Anti-hypertensive medications

Out of 1,767 subjects (89.88%) administered anti-hypertensive medications before follow up (treatment), 669 subjects (37.86%) administered ARB Mono, 167 subjects (9.45%) with ACEI and 152 subjects (8.60%) with CCB. After follow up, assessed for 1,773 subjects (92.25%), the

medication of ARB Mono for 652 subjects (36.77%) was the most frequently administered medication, but the number of subjects administered ARB Mono+CCB, 166 subjects (9.36%) was more than the number of subjects with CCB or ACEI monotherapy.

Concomitant Medication

The number of subjects with concomitant medication in visit1 was 1,120(56.97%). Aspirin was administered the most for 584 subjects (36.64%), followed by Statin for 547 subjects (34.22%), Other Antiplatelet for 200 subjects (12.55%) and so on. Among 1,179 subjects (61.34%) in last visit, Statin was the most frequently administered medication for 624 (35.80%), and it was followed by Aspirin for 599 subjects (34.37%), Other Antiplatelet for 251 subjects (14.40%), Others, Fibrate, Wafarin, etc.