AstraZeneca

Clinical Study Report Synopsis

Drug Substance	Not Applicable
Study Code	D3560L00071
Edition Number	1
Date	12 January 2011

OPtimal Type 2 dIabetes Management Including benchmarking and Standard trEatment.

"OPTIMISE Study"

Study dates: First subject enrolled: 6 March 2008
Last subject last visit: 1 February 2010

Phase of development: Not Applicable

This study was performed in compliance with Good Clinical Practice, including the archiving of essential documents.

Study centre(s)

477 physicians centres in 6 countries

Publications

None at the time of writing this report.

Objectives and criteria for evaluation

Table S1 Primary and secondary objectives and outcome variables

Objectives	Outcome variables
Primary	**Primary**
Demonstrate that the use of benchmarking improves quality of patient care, in particular the control of diabetes, lipids and blood pressure, by determining the percentage of patients in the benchmarking group achieving pre-set targets for HbA1c, LDL-cholesterol and Systolic Blood Pressure versus control group (non-benchmarking group) after 12 months of follow-up.	SBP target (<130 mmHg or <125 mmHg for patients with known proteinuria) HbA1c target (<7%) LDL-c target (<100 mg/dL or <70 mg/dL for patients with diabetes and CHD)
Secondary	**Secondary**
Demonstrate that the use of benchmarking improves quality of patient care, in particular the control of diabetes, lipids and blood pressure, by determining the percentage of patients achieving pre-set targets for HbA1c, glycaemia, LDL-cholesterol and Systolic Blood Pressure values after 12 months of follow-up versus baseline. Demonstrate that the use of benchmarking improves quality of patient care, in particular the control of diabetes, lipids and blood pressure, by determining the percentage improvement in HbA1c, glycaemia, LDL-cholesterol and Systolic Blood Pressure values after 12 months of follow-up versus baseline. To follow up evolution markers of preventive screening; retinopathy, neuropathy, dietary counselling, microalbuminuria, smoking habits, BMI, physical activity. To measure the physical activity of a diabetic population in a primary care setting by means of a four point scale as well as on the basis of the number of steps and the distance walked per day by using a step counter (optional).	HR, DBP, SBP SBP % change between baseline and Month 12 SBP class: Excellent (<130 mmHg), borderline (>=130 mmHg and <140 mmHg), too high (>=140 mmHg) HbA1c HbA1c % change between baseline and Month 12 HbA1c class: Excellent (<=7%), borderline (>7% and <=7.5%), too high (>7.5%) TC, LDL-c, HDL-c, triglycerides LDL-c % change between baseline and Month 12 LDL-c class: Excellent (<80 mg/dL), borderline (>=80 mg/dL and <100 mg/dL), too high (>=100 mg/dL) Glycaemia Glycaemia target (<110 mg/dL) Glycaemia class: Normal (<110 mg/dL), borderline (>=110 mg/dL and <125 mg/dL), diabetes (>=125 mg/dL) Total-c class: Excellent (<175 mg/dL), good (>=175 mg/dL and <250 mg/dL), too high (>=250 mg/dL) HDL-c class: Excellent (>50 mg/dL), good (<=50 mg/dL and >40 mg/dL), too low (<40 mg/dL) Triglycerides class: Excellent (<150 mg/dL), good (>=150 mg/dL and <200 mg/dL), too high (>=200 mg/dL) Age and sex (Month 0), weight, waist circumference Albuminuria recorded at Month 0 and at Month 12 Foot examination (yes, no)

Objectives	Outcome variables
	Ophthalmological examination (yes, no)
	Needs assessment for aspirine (yes, no), and in case of yes, indication for aspirine
	Smoking (yes, no, ex) and number of cigarettes smoked
	Dietary advice (yes, no, and if yes by whom)
	Physical Exercise, recorded on a 4 point ordinal scale
	Daily number of steps, recorded using a step counter, for the periods between successive visits

Study design

This study was designed to observe the effect of benchmarking on the quality of patients care in a population of adult patients with type 2 diabetes. Patients were recruited by their general practitioners or treating physician (investigators). Baseline assessments (demographic data, vital signs, medical history, medication taken and blood sample for laboratory analysis) were performed on the first visit (Month 0, baseline). Follow-up data, including blood sampling, were collected after approximately 4 months (Visit 2), 8 months (Visit 3), and 12 months (Visit 4). All blood samples were analysed by a central laboratory for lipids, glycaemia, and microalbuminuria.

Investigators were randomly allocated to a benchmarking or to a control group in a 1:1 ratio in Belgium and to a 3:1 ratio (benchmarking group: control group), in the other countries. Feedback on each patient's risk factors was provided to all investigators. Additionally, investigators of the benchmarking group received information on the level of control of cardiovascular risk for their patients anonymously compared with their colleagues.

Target subject population and sample size

This study included patients of at least 18 years of age, suffering from diabetes type 2, on insulin or not, excluding diabetes type 1 and gestational diabetes.

Planned subjects: 4000 patients
Analysed subjects: 3996 patients

Investigational product and comparator(s): dosage, mode of administration and batch numbers

Not Applicable

Duration of treatment

Each patient was followed for 12 months and was to attended 4 visits: Visit 1 (baseline, Month 0), Visit 2 (approximately 4 month after Visit 1), Visit 3 (approximately 8 months after Visit 1), and Visit 4 (approximately 12 months after Visit 1)

Statistical methods

The analysis was performed on the basis of the evaluable patient set that consists of all subjects who fulfilled the inclusion criteria. Comparison of the two treatment groups was performed using mixed or repeated measures models.

Subject population

A total of 477 centres participated to the study from 6 countries, 293 were allocated to the benchmarking group and 184 to the control group. The database contained data for 4027 patients. Of these patients 31 were not included in the analysis set due to not fulfilling inclusion/exclusion criteria. Of the patients of the Evaluable Analysis Set 508 discontinued the study prematurely.

Summary of results

Of the 4027 patients who participated to the study, 3996 were included in the analysis set at baseline, 2493 in the benchmarking group and 1503 in the control group. These patients were enrolled by 368 investigators, of which 229 were assigned to the benchmarking group and 139 to the control group. Of the 3996 patients, 2178 were enrolled in Belgium, 797 in Greece, 208 in Luxembourg, 188 in Portugal, 311 in Spain, and 314 in the UK. The mean age of the patients was 66 years, with about 92% of the patients aged 50 years or more, and 37% aged 70 years or more. The sex ratio was 55% male, 45% female. On average, diabetes was diagnosed 8.1 years before inclusion in the study.

Family diabetes and family history of premature heart disease were respectively reported for 57% and 23% of the patients. The most frequently reported pathologies in medical history were arterial hypertension (78%), coronary heart disease (19%), peripheral vascular disease (10%), and known proteinuria (9%). Prior to treatment, total cholesterol was too high (≥250 mg/dL) for 49% of the patients with a recording before first drug treatment and SBP was too high (≥140 mg/dL) for 95% of the patients with a recording before first drug treatment.

At baseline, SBP target was reached by 27% of the patients in both groups. After 12 months of follow-up the frequency reaching SBP target in the benchmarking group increased significantly (40%, $p<0.001$). In the control group, less patients achieved the SBP target (30%, benchmarking versus control: $p<0.001$). Accordingly, the frequency of patients with SBP considered excellent, increased in the benchmarking group but not in the control group (Benchmarking: from 27% to 40%, Control: from 28% to 31%).

About half of the patients were on target for HbA_{1c} at baseline (benchmarking: 49%, control: 55%). After 12 months of follow-up the frequency of patients achieving the HbA_{1c} target increased from 49% to 59% in the benchmarking group and increased from 55% to 62% in the control group. The change between baseline and Month 12 in the frequency of patients reaching HbA_{1c} target in the benchmarking group was statistically significant ($p<0.001$). After 12 months of follow-up the difference between the 2 groups was not statistically significant.

A significant increase in the frequency of patients reaching LDL-c target was observed between baseline and Month 12 in the benchmarking group (from 41% to 54%, $p<0.001$).

The increase observed in the control group was smaller (from 41% to 50%). The number of patients reaching target at Month 12 was statistically significantly different in the 2 groups (p=0.006).

An increase is also observed in the frequency of patients reaching the mixed LDL-c target (<80 mg/dL for Belgium and <100 mg/dL for the other countries). In the benchmarking group the frequency increased from 49% to 63% (p<0.001), while in the control group the increase observed was smaller (from 48% to 57%). The probability of reaching this target at Month 12 was statistically significantly different in the 2 groups (p=0.002).

The frequency of patients achieving all three targets increased more in the benchmarking group than in the control group (from 5.2% to 12.5% versus from 5.7% to 8.1%). The probability of reaching all three targets at Month 12 was statistically significantly different in the 2 groups (p<0.001). When considering the mixed LDL-c target (<80 mg/dL for Belgium and <100mg/dL for the other countries), the frequency of patients achieving all three targets also increased more in the benchmarking group than in the control group (from 5.0% to 10.9% versus from 3.8% to 5.8%). The probability of reaching all three targets at Month 12 was also statistically significantly different in the 2 groups (p<0.001).

Of the hygiene and life style parameters, an improvement over time, but without statistically significant difference between groups was observed in physical activity. No marked difference was observed in the change in smoking status and in dietary advice between the two study groups.

Throughout the study diabetes treatment was prescribed to over 92% of the patients, antihypertensives to over 96% of the patients with hypertension, and lipid lowering medications to over 64 % of the patients. Generally, not much change over time was observed in the frequency of patients using these medications except for aspirin (47% at baseline to 56% at Month 12 in the benchmarking group and 47% to 57% in the control group), and lipid lowering medications (68% at baseline to 76% at Month 12 in the benchmarking group and 64% to 70% in the control group).

Little change over time was observed in the frequency of patients reaching the glycaemia target and no notable difference was observed between the study groups. About 40% of the patients in both groups had a HDL-c value considered excellent (>50 mg/dL) at Month 0. Overall, no marked differences were observed in the evolution over time between the benchmarking and the control group. After 12 months of follow-up the frequency of patients having a HDL-c considered excellent increased to about 44%. Mean total cholesterol slightly decreased in the two groups between Month 0 and Month 12. At Month 12, the mean difference from baseline was -10.0 mg/dL in the benchmarking group and -6.5 mg/dL in the control group. Triglycerides improved slightly in the benchmarking group but became slightly worse in the control group. No significant changes over time in albuminuria were observed between the groups.

Based on the European data the average SCORE risk decreased from 5.41 at Month 0 to 5.02 at Month 12 in the benchmarking group but did not decrease in the control group.

Summary of pharmacokinetic results

Not Applicable

Summary of pharmacodynamic results

Not Applicable

Summary of pharmacokinetic/pharmacodynamic relationships

Not Applicable

Summary of pharmacogenetic results

Not Applicable

Summary of safety results

As no investigational products were supplied for this study, no pro-active safety data collection was done. Safety events occurring during the study were to be reported as required by post-marketing pharmacovigilance regulations and were not recorded in the CRF.