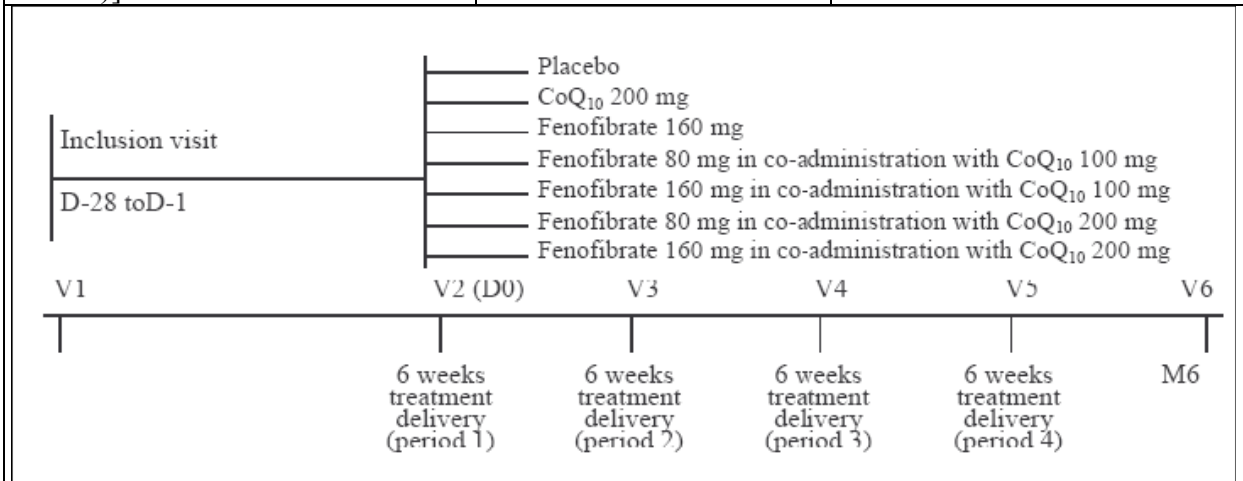


These results are supplied for informational purposes only. Some clinical studies may include information not contained in the approved prescribing information. Please refer to the full prescribing information for additional information.

Proprietary Drug Name: [Product Name/Trade Name may vary by country or area (e.g. Tricor [®] in the U.S., Lipanthyl [®] in the EU)]	Generic Drug Name: Fenofibrate	Condition: Type 2 Diabetes
Name of Sponsor/Company: Fournier Laboratories Ireland Ltd.		
Title of Study: A randomised, double-blind, placebo-controlled study assessing the effect of fenofibrate, coenzyme Q10 and their co-administration on ventricular diastolic function in patients with type 2 diabetes Protocol No.: CFEN0205		
Investigator(s): Prof. G.F. Watts, Royal Perth Hospital, Perth WA 6000, Australia.		
Study Center(s): 3 centers in Australia – Royal Perth Hospital, – Fremantle Hospital, – Sir Charles Gairdner Hospital.		
Publication (Reference): None		
Study Period: 29 MAY 2003 (First Subject First Visit) – 06 SEPT 2004 (Last Subject Last Visit)	Phase of Development: II	
Objectives: The primary objective was to assess the effects of the co-administration of fenofibrate and coenzyme (Co) Q10, as compared with products given alone at the highest dose and placebo, on ventricular diastolic function assessed by echocardiography in patients with type 2 diabetes mellitus (T2DM). The secondary objectives were: - to explore the effect of the co-administration of fenofibrate and CoQ10 on systemic arterial compliance and blood pressure, on biological markers of oxidative stress, inflammation, and left ventricle (LV) dysfunction (aminoterminal pro-B-type natriuretic peptide [NT pro-BNP]). - to evaluate the general tolerability and safety of the treatments.		
Methodology: This study was a multicenter, randomized, double-blind, placebo-controlled, parallel-group efficacy trial in patients with T2DM. Patients were included in the study at V1 and were randomized at V2 to 1 of the 7 following treatment groups.		

These results are supplied for informational purposes only. Some clinical studies may include information not contained in the approved prescribing information. Please refer to the full prescribing information for additional information.

Proprietary Drug Name: [Product Name/Trade Name may vary by country or area (e.g. Tricor® in the U.S., Lipanthyl® in the EU)]	Generic Drug Name: Fenofibrate	Condition: Type 2 Diabetes
---	--	--------------------------------------



Number of Subjects (Planned, Consented, Randomized and Analyzed):
 The initial sample size was of 224 patients completing the study. Following the Protocol Amendment No. 4, this was reduced to 112 patients.
 Included: 278 patients, randomized: 128 patients, treated: 126 patients, completed: 115 patients.

Diagnosis and Main Criteria for Inclusion:
 Men and women with T2DM aged 40 to 79 years with HbA_{1c} < 9% and evidence of LV diastolic dysfunction (LVDD) assessed by echocardiography, in absence of significant LV systolic dysfunction (Ejection Fraction ≥ 50%).
 Main exclusion criteria: creatinine > 130 μmol/L, known hepatic dysfunction and/or alanine aminotransferase (ALT)/aspartate aminotransferase (AST) > 2 times the upper limit of normal (ULN), creatine kinase (CK) > 3 times the ULN.

Test Product, Dose and Mode of Administration:

- 80 mg fenofibrate (= 1 x 80 mg tablet) + 100 mg CoQ₁₀ (= 2 x 50 mg capsules): F80/C100 group,
- 160 mg fenofibrate (= 2 x 80 mg tablets) + 100 mg CoQ₁₀ (= 2 x 50 mg capsules): F160/C100 group,
- 80 mg fenofibrate (= 1 x 80 mg tablet) + 200 mg CoQ₁₀ (= 4 x 50 mg capsules): F80/C200 group,
- 160 mg fenofibrate (= 2 x 80 mg tablets) + 200 mg CoQ₁₀ (= 4 x 50 mg capsules): F160/C200 group.

The treatments were taken orally, once daily, with breakfast.

These results are supplied for informational purposes only. Some clinical studies may include information not contained in the approved prescribing information. Please refer to the full prescribing information for additional information.

Proprietary Drug Name: [Product Name/Trade Name may vary by country or area (e.g. Tricor [®] in the U.S., Lipanthyl [®] in the EU)]	Generic Drug Name: Fenofibrate	Condition: Type 2 Diabetes
---	--	--------------------------------------

Duration of Treatment:
24 weeks

Reference Therapy, Dose and Mode of Administration:

- Placebo (F0/C0 group),
- 200 mg CoQ10 (= 4 x 50 mg capsules): F0/C200 group,
- 160 mg fenofibrate (= 2 x 80 mg tablets): F160/C0 group.

Same dosing regimen and clinical batch numbers as for test products.

Criteria for Evaluation:

Efficacy
Primary Criterion: ratio of early transmitral diastolic filling velocity to myocardial peak velocity during early diastole (E/E' ratio).

Main Secondary Criteria:

- Classification of patients according to the severity of LVDD.
 Patients were classified within the following groups based on Doppler parameters: **(1) normal (Grade 0)**, **(2) abnormal (Grade 1a)**: mild diastolic dysfunction with an abnormal relaxation pattern, but with a normal E/E' ratio and a normal response to Valsalva (i.e. < 40% change in E/A ratio on Valsalva compared to the pre-Valsalva E/A ratio), **(3) abnormal (Grade 1b)**: mild diastolic dysfunction with an abnormal relaxation pattern, but with abnormal E/E' ratio or an abnormal response to Valsalva (i.e. ≥ 40% change in E/A ratio on Valsalva compared to the pre-Valsalva E/A ratio), **(4) pseudonormalisation (Grade 2)** - moderate diastolic dysfunction, **(5) restriction to filling (Grade 3)**: severe diastolic dysfunction unlikely to be seen in the presence of normal LV systolic function with E/A > 2 and DT < 150 ms. Elevated LV filling pressure is usually associated with E/E' > 15.
- Additional echocardiographic data including: left atrial (LA) and right atrial (RA) volumes indexed or not to body surface area (BSA), left and right sizes (normal, mildly dilated, moderately dilated, severely dilated), left ventricular end diastolic and end systolic dimensions indexed or not to BSA, left ventricular end diastolic and end systolic volumes indexed or not to BSA, LV mass indexed or not to BSA, LV ejection fraction, pulmonary vein Doppler parameters including S/D ratio, pulmonary vein (PV) 'A' reversal velocity, PV 'A' reversal duration, PV 'A' reversal duration – Mitral 'A' wave duration, isovolumic relaxation time (IVRT), tissue Doppler E'/A' ratio, PA systolic pressure, severity of mitral regurgitation (none, trivial, mild, mild to moderate, moderately severe and severe).
- CR 2000 data including capacitive or large artery compliance C1, oscillatory or small artery compliance C2, systemic vascular resistance, total vascular impedance.
- Sphygmocor data including central pulse wave velocity and Central Augmentation Index.

These results are supplied for informational purposes only. Some clinical studies may include information not contained in the approved prescribing information. Please refer to the full prescribing information for additional information.

Proprietary Drug Name: [Product Name/Trade Name may vary by country or area (e.g. Tricor [®] in the U.S., Lipanthyl [®] in the EU)]	Generic Drug Name: Fenofibrate	Condition: Type 2 Diabetes
---	--	--------------------------------------

- Ambulatory arterial blood pressure.
- NT-pro-BNP.
- Inhibitory kappa Beta protein (IkB), inducible nitric oxide synthase (iNOS), fibrinogen.
- Alpha-tocopherol, gamma-tocopherol, 20-hydroxyecosatetraenoic acid (20-HETE), Advanced Glycosylation Endproducts (AGEs).
- Standard lipid parameters: total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), TC/HDL-C, apolipoproteins and non esterified fatty acids [NEFA]).
- CoQ10 levels in plasma and monocytes.

Safety

General safety: adverse events (AEs), vital signs (systolic blood pressure [SBP], diastolic blood pressure [DBP] and heart rate), laboratory tests: fasting glucose, HbA1c, creatinine, ALT, AST, CK, total bilirubin, uric acid, alkaline phosphatase, hematology parameters, urinalysis: creatinine, albumin, total protein.

Statistical Methods:

Efficacy

Due to a smaller sample size than originally planned, co-administration groups were pooled by fenofibrate dose, i.e. F80/C100 group + F160/C100 group resulted in the F*/C100 group and F80/C200 group + F160/C200 group resulted in the F*/C200 group.

Descriptive Analysis: mean, SD, median, first quartile (Q1), third quartile (Q3), min, max for quantitative variables, n and percentage (%) by category for qualitative variables. Descriptive statistics were provided for the 7 treatment groups: (F0/C0, F0/C200, F160/C0, F80/C100, F160/C100, F80/C200 and F160/C200) and for the 5 treatment groups (F0/C0, F0/C200, F160/C0, F*/C100 and F*/C200).

Primary Statistical Analysis

This was performed on FAS and PPS.

The “Multiple Comparison with the Best” (MCB) or the “Multiple Comparison to the Worst” (MCW) procedure were used to identify the best treatment arm with regard to the E/E’ ratio and test which ones amongst the others differ significantly from it. This approach was supported by a global analysis of LVDD evolution. The MCB procedure was used to compare the 5 treatment groups: F0/C0, F0/C200, F160/C0, F*/C100, F*/C200.

Secondary Efficacy Analysis

These results are supplied for informational purposes only. Some clinical studies may include information not contained in the approved prescribing information. Please refer to the full prescribing information for additional information.

Proprietary Drug Name: [Product Name/Trade Name may vary by country or area (e.g. Tricor [®] in the U.S., Lipanthyl [®] in the EU)]	Generic Drug Name: Fenofibrate	Condition: Type 2 Diabetes
---	--	--------------------------------------

The global evolution of LVDD was assessed by shift tables presenting the frequency distribution of the following categories of patients: “normal (Grade 0)”, “abnormal (Grade 1a)”, “abnormal (Grade 1b)”, “pseudonormalisation (Grade 2)”, “restriction to filling (Grade 3)” at baseline versus the end of the study for the 7 and the 5 treatment groups. Furthermore, the number of regressors, progressors and unchanged patients with regard to LVDD were tabulated by treatment group. The F*/C100 and F*/C200 groups were compared to the F0/C0 group, the F0/C200 group and the F160/C0 group using Chi-square or Fisher’s Exact tests. This analysis was done on FAS and PPS and repeated excluding patients with moderate LVDD at baseline.

Other Secondary Efficacy Variables

The MCB or MCW procedures were also performed on the main echocardiography criteria, the CR 2000 data, the Sphygmocor data, the ambulatory blood pressure monitoring data except heart rate, on NT pro-BNP and the oxidative stress markers.

The safety analysis, conducted on FAS, included summary statistics of blood chemistry and hematology parameters, incidence of abnormal values, number of AEs, number and % of patients who experienced AEs, descriptive statistics of vital signs and anthropometric measurements.

Summary

Demographic and Other Baseline Characteristics

Demographic and anthropometric characteristics and vital signs of FAS patients are summarized below:

Women / Men (n[%])	Age (years)	Weight (kg)	BMI (kg/m ²)	Heart rate (bpm)	Sitting SBP (mmHg)	Sitting DBP (mmHg)
44 (34.9%) / 82 (65.1%)	63.5 (7.7)	86.2 (14.4)	29.6 (5.0)	71.2 (9.6)	130.7 (16.3)	73.5 (10.0)

59 FAS patients (46.8%) were shown to have ECG abnormalities. In 5 of them, the abnormality was clinically significant.

84.1% of the women were post-menopausal. Median time since T2DM diagnosis was 5.0 years (between 0.2 and 32.8 years) and 66.7% of the patients (84/126) were using antidiabetic drugs. Mean and associated SD values of glucose concentration and HbA1c at baseline were 7.50 (1.91) mmol/L and 6.60% (0.90%), respectively.

The primary efficacy criterion (E/E’ ratio) at baseline in FAS is summarized below (n, mean (SD) median):

F0/C0	F0/C200	F160/C0	F80/C100	F160/C100	F80/C200	F160/C200	Total
-------	---------	---------	----------	-----------	----------	-----------	-------

These results are supplied for informational purposes only. Some clinical studies may include information not contained in the approved prescribing information. Please refer to the full prescribing information for additional information.

Proprietary Drug Name: [Product Name/Trade Name may vary by country or area (e.g. Tricor [®] in the U.S., Lipanthyl [®] in the EU)]			Generic Drug Name: Fenofibrate			Condition: Type 2 Diabetes	
(N = 20)	(N = 16)	(N = 18)	(N = 20)	(N = 16)	(N = 18)	(N = 18)	(N=126)
20	16	18	20	16	18	18	126
7.69 (1.18)	7.75 (1.91)	7.90 (1.73)	7.20 (1.33)	7.62 (1.85)	7.90 (1.90)	7.88 (1.87)	7.70 (1.66)
7.50	7.45	7.61	7.04	6.84	7.84	7.67	7.46

Mean and median values of E/E' ratio were within normal range (< 8.0).

The other main echography criteria are summarized below (n, mean (SD) median):

E/E' lateral ratio	E/A ratio	E/A ratio Valsalva	E' septal velocity (cm/s)	E' lateral velocity (cm/s)	IVRT (ms)	DT (ms)	E/Vp
126	126	126	126	126	126	126	126
6.08 (1.53)	0.84 (0.21)	0.82 (0.19)	8.56 (1.33)	11.0 (2.08)	107.9 (9.11)	222.0 (30.9)	1.58 (0.28)
5.80	0.82	0.80	8.33	10.9	106.9	220.6	1.55

At baseline, LVDD was moderate in 11.9% of the patients. The mean and associated SD values for the E/E' septal ratio were 9.86 (1.25) in the patients with moderate LVDD and 7.41 (1.49) in those with mild LVDD.

E/E' lateral ratio, E/A ratio and E/Vp at baseline were greater in the patients with moderate LVDD than in those with mild LVDD: 7.34 (1.93) versus 5.91 (1.39) for E/E' lateral ratio, 1.01 (0.45) versus 0.82 (0.13) for E/A ratio and 1.93 (0.36) versus 1.53 (0.23) for E/Vp.

Heart rate and blood pressure over the day-time period and over the night-time period are summarized below (n, mean (SD) median):

Day-time period				Night-time period			
Heart rate (bpm)	Mean arterial blood pressure (mmHg)	Mean SBP (mmHg)	Mean DBP (mmHg)	Heart rate (bpm)	Mean arterial blood pressure (mmHg)	Mean SBP (mmHg)	Mean DBP (mmHg)
111	111	111	111	108	108	108	108
77.0 (10.3)	95.8 (8.04)	131.7 (10.1)	76.7 (7.93)	67.0 (7.93)	83.3 (8.29)	117.0 (11.4)	64.6 (7.64)
77.7	95.9	130.8	76.8	66.0	82.7	115.4	65.3

Mean and median blood pressure over the day-time period were close to normal. Blood pressure was abnormal but non clinically significant in 13.8% of the patients and abnormal and clinically significant in 21.6% of the patients.

These results are supplied for informational purposes only. Some clinical studies may include information not contained in the approved prescribing information. Please refer to the full prescribing information for additional information.

Proprietary Drug Name: [Product Name/Trade Name may vary by country or area (e.g. Tricor [®] in the U.S., Lipanthyl [®] in the EU)]	Generic Drug Name: Fenofibrate	Condition: Type 2 Diabetes
---	--	--------------------------------------

Data of NT pro-BNP, oxidative stress markers and inflammation markers at baseline are summarized below (n, mean (SD) median):

NT pro-BNP (pg/mL)	Oxidative stress markers				Inflammation markers				
	20-HETE (pmol/L)	AGEs	Alphatocopherol (μmol/L)	Gammatocopherol (μmol/L)	IκB/b-actin x 1E04	iNOS/b-actin x 1E08	IκB/b-actin x 1E04 Stimulate _{da}	iNOS/b-actin x 1E08 Stimulate _{da}	Fibrinogen (g/L)
126	109	116	123	123	118	118	118	118	126
65.0 (71.7)	258 (340)	4.80 (7.97)	39.3 (12.8)	3.41 (1.37)	7.24 (21.6)	6186 (64001)	9.58 (11.1)	382 (2684)	3.49 (0.73)
39.3	184	3.39	38.3	3.31	3.09	5.81	6.64	24.2	3.40

^a monocytes were stimulated with 1 μg/mL of LPS for 6 hours.

Except for alpha-tocopherol, gamma-tocopherol and fibrinogen, individual values were highly variable.

Data of main lipids and lipoproteins at baseline are summarized below (n, mean (SD) median):

HDL-C (mmol/L)	LDL-C (mmol/L)	TC (mmol/L)	TG (mmol/L)	ApoAI (g/L)	ApoAII (g/L)	ApoB (g/L)	ApoCIII (mg/L)	NEFA (mmol/L)
126	126	126	126	126	126	126	126	126
1.30 (0.35)	2.50 (0.84)	4.57 (0.92)	1.70 (0.82)	1.43 (0.27)	0.32 (0.05)	0.93 (0.21)	126.4 (34.6)	0.45 (0.24)
1.20	2.40	4.50	1.50	1.40	0.32	0.94	124.4	0.42

According to NCEP-ATP III, mean and median HDL-C values were within the low risk range (> 1.03 mmol/L), mean and median LDL-C values were within the optimal range (< 2.58 mmol/L) and mean and median TG values were within normal range (< 1.71 mmol/L) as 57% of the patients were on statin therapy at baseline and during the trial.

Efficacy Results

The results of the analyses performed on the 5 treatment groups as defined in the statistical section are presented below.

Main Analysis on the Primary Efficacy Criterion

The results of the analysis of the E/E' septal ratio data in FAS are summarized below (mean (SD) median):

E/E' septal ratio-FAS	F0/C0 (N=20)	F0/C200 (N=16)	F160/C0 (N=18)	F*/C100 (N=36)	F*/C200 (N=36)
n	20	16	18	36	35
Baseline	7.69 (1.18) 7.50	7.75 (1.91) 7.45	7.90 (1.73) 7.61	7.39 (1.57) 6.92	7.97 (1.82) 7.77
V6	7.61 (1.48) 7.61	8.33 (2.08) 7.69	8.56 (1.23) 8.36	7.84 (1.66) 7.25	8.63 (1.92) 8.24

These results are supplied for informational purposes only. Some clinical studies may include information not contained in the approved prescribing information. Please refer to the full prescribing information for additional information.

Proprietary Drug Name: [Product Name/Trade Name may vary by country or area (e.g. Tricor [®] in the U.S., Lipanthyl [®] in the EU)]		Generic Drug Name: Fenofibrate		Condition: Type 2 Diabetes	
Absolute change from baseline at V6	-0.09 (1.09) 0.12	0.57 (1.28) 0.30	0.67 (1.10) 0.49	0.45 (1.10) 0.29	0.66 (1.08) 0.42
% change from baseline at V6	-0.8 (15.6) 1.4	8.8 (20.0) 4.5	11.2 (18.1) 6.1	7.4 (15.8) 4.7	9.5 (14.8) 5.4
LS-Mean (SE) ^a p ^c	7.63 (0.24) ^b	8.30 (0.27) 0.0884	8.42 (0.25) 0.0381	8.11 (0.18) 0.1746	8.43 (0.18) 0.0166

Conclusion: Observed best response = F0/C0 - Set of best groups = F0/C0 F0/C200 F*/C100

^a of V6 values, ^b group associated with the best response according to the MCB procedure, ^c provided by the comparison to the group associated with the best response.

The changes of E/E' septal ratio with F160/C0 and F*/C200 should not be considered as clinically relevant as the actual changes were less than 1 unit.

These results are supplied for informational purposes only. Some clinical studies may include information not contained in the approved prescribing information. Please refer to the full prescribing information for additional information.

Proprietary Drug Name: [Product Name/Trade Name may vary by country or area (e.g. Tricor® in the U.S., Lipanthyl® in the EU)]	Generic Drug Name: Fenofibrate	Condition: Type 2 Diabetes
---	--	--------------------------------------

Complementary Analyses on the Primary Criterion

The PPS analysis confirmed the FAS analysis. The analyses performed excluding patients with moderate LVDD at baseline provided also similar results.

Secondary Efficacy Analyses

Global Evolution of LVDD

The results are presented below:

Evolution of LVDD	F0/C0 (N=20)	F0/C200 (N=16)	F160/C0 (N=18)	F*/C100 (N=36)	F*/C200 (N=36)
n	20	16	18	36	35
Progressor	0	0	1 (5.6%)	1 (2.8%)	4 (11.4%)
Regressor	4 (20.0%)	2 (12.5%)	3 (16.7%)	5 (13.9%)	3 (8.6%)
Unchanged	16 (80.0%)	14 (87.5%)	14 (77.8%)	30 (83.3%)	28 (80.0%)

The comparisons of the F*/C100 and F*/C200 groups with each of the other groups using the Fischer's Exact test did not reach statistical significance. The PPS analysis provided similar results.

Other Echocardiography Criteria

Mean and median changes in other echography criteria were minor and variable across treatment groups, not indicative of an improvement in the left ventricular function with the fenofibrate / CoQ10 co-administrations. The only favorable trend to be noted with the co-administrations was a slight increase in the E/A ratio: +5.7% with F*/C100, +6.7% with F*/C200, compared to +2.6% with F0/C200, +3.4% with F160/C0 and +1.3% with F0/C0.

Small and Large Vessel Compliance using CR 2000

No trends to improvement with the co-administrations were observed in large vessel compliance, small artery compliance, systemic vascular resistance and total vascular impedance.

Sphygmocor Data

Changes in central pulse wave velocity and Central Augmentation Index (AG/PP) were highly variable. No trends to differences between groups were observed in both parameters.

Ambulatory Blood Pressure and Heart Rate

The results of the analysis of mean arterial blood pressure data (mmHg) over the day-time period and over the nighttime period in FAS are summarized below (mean (SD)):

These results are supplied for informational purposes only. Some clinical studies may include information not contained in the approved prescribing information. Please refer to the full prescribing information for additional information.

Proprietary Drug Name: [Product Name/Trade Name may vary by country or area (e.g. Tricor [®] in the U.S., Lipanthyl [®] in the EU)]	Generic Drug Name: Fenofibrate	Condition: Type 2 Diabetes
---	--	--------------------------------------

Mean arterial blood pressure	Day-time period					Night-time period				
	F0/C0	F0/C20	F160/C0	F*/C10	F*/C20	F0/C0	F0/C20	F160/C0	F*/C10	F*/C20
	(N=20)	(N=16)	(N=18)	(N=36)	(N=36)	(N=20)	(N=16)	(N=18)	(N=36)	(N=36)
n	15	9	15	25	30	15	8	16	24	29
Baseline	95.8 (6.92)	96.6 (7.07)	97.0 (6.36)	97.6 (8.16)	93.8 (8.46)	82.4 (6.79)	85.5 (14.1)	85.8 (8.96)	84.8 (7.89)	81.8 (7.90)
V6	96.1 (10.5)	96.5 (8.67)	96.0 (6.59)	95.2 (7.98)	92.7 (6.96)	83.8 (8.30)	88.1 (11.5)	84.8 (9.03)	82.7 (8.38)	78.7 (6.75)
Absolute change from baseline at V6	0.32 (6.85)	-0.07 (5.90)	-1.03 (6.13)	-2.41 (4.50)	-1.09 (5.32)	1.39 (6.57)	2.58 (4.87)	-1.06 (7.88)	-2.09 (6.57)	-3.13 (6.88)
% change from baseline at V6	0.3 (7.0)	-0.0 (6.0)	-0.9 (6.2)	-2.4 (4.4)	-0.9 (5.6)	1.8 (7.8)	3.6 (6.2)	-0.9 (9.4)	-2.2 (7.9)	-3.4 (8.0)
LS-Mean (SE) ^a	96.2 (1.37)	96.0 (1.78)	95.1 (1.38)	93.9 (1.07)^b	94.3 (0.98)	84.7 (1.59)	86.9 (2.18)	83.4 (1.55)	82.0 (1.26)	79.9 (1.15)^b
p ^c	0.2369	0.3140	0.4886		0.7364	0.0298	0.0090	0.1165	0.3148	

^aof V6 values, ^bgroup associated with the best response according to the MCB procedure, ^cprovided by the comparison to the group associated with the best response.

Mean arterial blood pressure recorded over the night-time period decreased by 3.4% at end of treatment from baseline in the F*/C200 group. This group, associated with the best response, was significantly different from the F0/C0 group and the F0/C200 group. Changes in day-time recordings were smaller, the group associated with the best response (F*/C100 group) was not statistically different from any of the other groups.

These results are supplied for informational purposes only. Some clinical studies may include information not contained in the approved prescribing information. Please refer to the full prescribing information for additional information.

Proprietary Drug Name: [Product Name/Trade Name may vary by country or area (e.g. Tricor [®] in the U.S., Lipanthyl [®] in the EU)]	Generic Drug Name: Fenofibrate	Condition: Type 2 Diabetes
---	--	--------------------------------------

The results of the analysis of SBP data over the day-time period and over the night-time period in FAS are summarized below (mean (SD)):

Mean SBP (mmHg)	Day-time period					Night-time period				
	F0/C0 (N=20)	F0/C200 (N=16)	F160/C0 (N=18)	F*/C100 (N=36)	F*/C200 (N=36)	F0/C0 (N=20)	F0/C200 (N=16)	F160/C0 (N=18)	F*/C100 (N=36)	F*/C200 (N=36)
n	15	9	15	25	30	15	8	16	24	29
Baseline	130.3 (6.06)	132.0 (8.71)	134.3 (10.1)	133.1 (9.94)	129.6 (11.6)	114.6 (7.86)	118.4 (19.3)	121.0 (12.8)	117.8 (9.56)	116.4 (11.9)
V6	130.5 (11.1)	133.5 (11.6)	134.3 (10.9)	131.7 (9.21)	128.4 (9.50)	116.5 (10.1)	123.2 (14.8)	119.9 (13.8)	115.7 (10.4)	111.8 (9.32)
Absolute change from baseline at V6	0.23 (9.48)	1.57 (7.53)	-0.01 (9.25)	-1.41 (6.80)	-1.17 (6.91)	1.89 (7.80)	4.76 (8.63)	-1.13 (11.4)	-2.08 (9.34)	-4.58 (7.96)
% change from baseline at V6	0.2 (7.2)	1.2 (5.7)	0.2 (6.7)	-0.9 (5.0)	-0.6 (5.4)	1.7 (6.8)	4.8 (8.0)	-0.6 (9.9)	-1.5 (8.0)	-3.6 (6.6)
LS-Mean (SE) ^a	131.5 (1.88)	133.3 (2.43)	132.4 (1.89)	130.7 (1.46)	129.9 (1.34) ^b	118.4 (2.10)	122.6 (2.87)	117.6 (2.05)	115.5 (1.66)	112.5 (1.51) ^b
p ^c	0.5026	0.2391	0.3316	0.6900	-	0.0407	0.0041	0.0756	0.2610	-

^a of V6 values, ^b group associated with the best response according to the MCB procedure, ^c provided by the comparison to the group associated with the best response.

SBP recorded over the night-time period decreased by 3.6% at end of treatment from baseline in the F*/C200 group. This group, associated with the best response, was significantly different from the F0/C0 group and the F0/C200 group. Changes in day-time recordings during the study were minor.

The results of the analysis of DBP data over the day-time period and over the night-time period in FAS are summarized below (mean (SD)).

These results are supplied for informational purposes only. Some clinical studies may include information not contained in the approved prescribing information. Please refer to the full prescribing information for additional information.

Proprietary Drug Name: [Product Name/Trade Name may vary by country or area (e.g. Tricor [®] in the U.S., Lipanthyl [®] in the EU)]	Generic Drug Name: Fenofibrate	Condition: Type 2 Diabetes
---	--	--------------------------------------

Mean DBP (mmHg)	Day-time period					Night-time period				
	F0/C0	F0/C200	F160/C0	F*/C100	F*/C200	F0/C0	F0/C200	F160/C0	F*/C100	F*/C200
	(N=20)	(N=16)	(N=18)	(N=36)	(N=36)	(N=20)	(N=16)	(N=18)	(N=36)	(N=36)
n	15	9	15	25	30	15	8	16	24	29
Baseline	77.9 (9.63)	78.2 (5.14)	76.2 (6.29)	78.3 (7.28)	75.2 (8.33)	65.1 (8.59)	65.9 (9.69)	66.0 (8.18)	65.9 (7.45)	63.4 (7.36)
V6	78.5 (11.6)	78.1 (7.64)	75.3 (6.77)	76.0 (7.74)	73.7 (7.41)	65.8 (10.0)	68.5 (7.86)	65.0 (7.52)	64.1 (7.43)	60.4 (6.70)
Absolute change from baseline at V6	0.65 (5.37)	-0.17 (5.80)	-0.90 (4.96)	-2.30 (4.19)	-1.55 (4.32)	0.71 (5.59)	2.59 (4.50)	-1.04 (6.45)	-1.83 (6.12)	-3.02 (6.68)
% change from baseline at V6	0.8 (6.6)	-0.2 (7.3)	-1.0 (6.3)	-2.9 (5.2)	-1.8 (5.5)	1.1 (8.3)	4.5 (7.4)	-1.0 (9.8)	-2.3 (9.9)	-4.2 (10.0)
LS-Mean (SE) ^a	77.7 (1.20)	76.9 (1.55)	75.9 (1.20)	74.8 (0.93)^b	75.2 (0.86)	65.8 (1.45)	67.9 (1.99)	64.3 (1.41)	63.5 (1.15)	61.5 (1.05)^b
p ^c	0.0893	0.2607	0.4792	-	0.7461	0.0309	0.0081	0.1582	0.2813	-

^aof V6 values, ^bgroup associated with the best response according to the MCB procedure, ^cprovided by the comparison to the group associated with the best response.

Mean DBP recorded over the night-time period decreased by 4.2% at end of treatment from baseline in the F*/C200 group. This group, associated with the best response, was significantly different from the F0/C0 group and the F0/C200 group. Changes in mean DBP over the day-time period were smaller. The group associated with the best response was the F*/C100 group with -2.9%. This group was not statistically different from any of the other groups. Regarding heart rate, the most meaningful change was a mean decrease of 6.4% in overnight recordings at end of treatment from baseline in the F*/C200 group.

Laboratory Efficacy Assessments

NT pro-BNP, Oxidative Stress Markers and Inflammation Markers

These results are supplied for informational purposes only. Some clinical studies may include information not contained in the approved prescribing information. Please refer to the full prescribing information for additional information.

Proprietary Drug Name: [Product Name/Trade Name may vary by country or area (e.g. Tricor [®] in the U.S., Lipanthyl [®] in the EU)]	Generic Drug Name: Fenofibrate	Condition: Type 2 Diabetes
---	--	--------------------------------------

Changes in NT pro-BNP were highly variable and tended to increase with all treatments. Changes were not consistent among oxidative stress markers. Alpha-tocopherol decreased in the F160/C0 group (median: -12.6%), the F*/C100 group (median: -12.4%) and the F*/C200 group (median: -6.1%) and remained unchanged in the other groups.

Gamma-tocopherol increased in the F0/C200 group (median: +23.5%) and remained roughly unchanged in the F*/C100 and F*/C200 groups. Changes in 20-HETE were highly variable, a decreasing trend was observed in the F160/C0 group (median: -16.6%), not in the F*/C100 and F*/C200 groups. AGEs tended to increase in the F160/C0 group (median: +35.8%), in the F*/C100 group (median: +20.4%) and in the F*/C200 group (median: +6.7%). No improvement in inflammatory markers was observed with the co-administrations. Changes in IκB/b-actin and iNOS/b-actin were highly variable, making it difficult to observe differences between treatments. F160/C0, F*/C100 and F*/C200 were associated with the same reduction in fibrinogen (medians: -0.30 g/L).

Lipids and Apolipoproteins

The mean and associated SD and median % change in main lipids and apolipoproteins are presented below:

	F0/C0	F0/C200	F160/C0	F80/C100	F160/C100	F80/C200	F160/C200
	(N=20)	(N=16)	(N=18)	(N=20)	(N=16)	(N=18)	(N=18)
	20	16	18	20	16	17	18
TG	24.8 (65.9) 14.9	1.63 (39.0) -5.3	-20.8 (37.8) -31.9	-23.1 (23.7) -24.3	-23.7 (18.3) -31.0	-13.2 (29.7) -16.7	-29.5 (29.6) -30.8
TC	1.6 (19.3) 3.3	2.1 (13.1) 0.00	-4.0 (11.8) -6.6	-11.3 (10.5) -12.0	-7.0(10.2) -8.1	-2.9 (10.6) -5.0	-8.8 (13.3) -9.9
LDL-C	2.3 (35.0) -3.6	7.3 (20.7) 3.9	0.8 (27.1) -6.1	-11.2 (18.1) -7.4	0.3 (21.1) -7.9	2.8 (29.1) -4.8	-2.3 (22.4) -3.7
HDL-C	-1.1 (6.3) 0.0	-0.7 (10.6) 0.0	7.0 (11.6) 7.7	4.3 (11.6) 0.0	-1.1 (10.8) 0.0	3.1 (11.4) 0.0	-1.7 (13.2) 0.0
ApoAI	3.8 (9.5) 5.6	1.4 (8.4) 1.9	9.0 (11.5) 7.6	5.0 (10.6) 7.2	3.5 (10.2) 1.7	6.8 (12.7) 2.7	4.5 (13.1) 5.1
ApoAII	1.6 (8.8) 1.5	-0.8 (19.8) -4.1	22.6 (19.6) 23.1	15.5 (14.0) 15.9	21.5 (22.5) 25.5	12.8 (19.4) 10.0	23.2 (19.1) 25.4
ApoB	1.7 (24.0) 3.0	1.4 (16.0) -0.4	-8.4 (12.8) -8.8	-11.1 (18.8) -12.8	-9.3 (17.0) -12.5	-7.5 (13.6) -2.9	-13.6 (13.5) -13.7
ApoCIII	4.2 (18.0) 0.2	1.8 (16.2) -1.4	-21.0 (16.0) -21.0	-14.8 (13.5) -17.6	-18.4 (12.5) -23.4	-10.5 (18.7) -12.1	-21.6 (15.5) -22.8

Based on medians, the TG-reducing effect of 160 mg fenofibrate was not changed by CoQ10. Similarly, the reduction in ApoCIII and the increase in ApoAII with fenofibrate were unchanged by CoQ10. HDL-C and ApoAI increased by 7.0% and 9.0% with F160/C0 and remained unchanged with the co-administrations. The reduction in TC, LDL-C and ApoB were mild in this population with only minimal anomalies at baseline. Changes in NEFA were variable.

These results are supplied for informational purposes only. Some clinical studies may include information not contained in the approved prescribing information. Please refer to the full prescribing information for additional information.

Proprietary Drug Name: [Product Name/Trade Name may vary by country or area (e.g. Tricor [®] in the U.S., Lipanthyl [®] in the EU)]	Generic Drug Name: Fenofibrate	Condition: Type 2 Diabetes
---	--	--------------------------------------

CoQ₁₀ Concentrations in Plasma and in Monocytes

Mean and associated SD of concentrations at baseline and at V6 are presented below.

	F0/C0	F0/C200	F160/C0	F80/C100	F160/C100	F80/C200	F160/C200
	(N=20)	(N=16)	(N=18)	(N=20)	(N=16)	(N=18)	(N=18)
Concentrations of CoQ ₁₀ in plasma (nmol/L)							
n	20	16	18	19	15	18	18
Baseline	7.74 (5.07)	9.32 (4.90)	9.27 (6.00)	9.58 (6.47)	9.64 (7.32)	8.60 (5.91)	7.46 (4.56)
V6	7.36 (5.19)	38.1 (25.2)	8.85 (4.74)	29.1 (21.7)	24.8 (12.9)	27.6 (29.8)	27.2 (16.0)
Concentrations of CoQ ₁₀ in monocytes (pmol/mg of proteins)							
n	19	15	18	18	13	17	18
Baseline	112.8 (34.9)	128.8 (41.2)	109.4 (23.3)	115.9 (31.9)	111.7 (21.6)	114.7 (28.2)	115.5 (32.7)
V6	126.7 (73.2)	156.6 (50.4)	106.1 (24.2)	124.6 (23.5)	133.2 (33.2)	136.3 (39.5)	140.8 (27.8)

In the 5 groups who received CoQ₁₀, concentrations of CoQ₁₀ in plasma and in monocytes were clearly higher at V6 than at baseline. At V6, the concentrations were slightly lower in the F80/C200 and F160/C200 groups than in the F0/C200 group in both plasma and monocytes. In plasma, there were no meaningful differences between the co-administrations with 100 mg CoQ₁₀ and the co-administrations with 200 mg, while in monocytes, the concentrations were slightly higher with F160/C200 than with the other co-administrations.

Safety:

As shown by the efficacy assessments, fenofibrate alone or in co-administration with CoQ₁₀ for 6 months in patients with T2DM did not modify unfavourably echocardiographic indices of heart function.

There were no deaths in this study.

AEs reported during the study are summarized by treatment group in the following table:

	F0/C0	F0/C200	F160/C0	F80/C100	F160/C100	F80/C200	F160/C200
	(N=20)	(N=16)	(N=18)	(N=20)	(N=16)	(N=18)	(N=18)
All AEs	16 (80.0%)	14 (87.5%)	17 (94.4%)	17 (85.0%)	13 (81.3%)	17 (94.4%)	12 (66.7%)
AEs related to study treatment	3 (15.0%)	7 (43.8%)	8 (44.4%)	7 (35.0%)	6 (37.5%)	8 (44.4%)	3 (16.7%)
All SAEs	1 (5.0%)	1 (6.3%)	0	2 (10.0%)	2 (12.5%)	2 (11.1%)	0
SAEs related to study treatment	0	0	0	0	1 (6.3%)	1 (5.6%)	0
AEs leading to premature withdrawal	0	1 (6.3%)	2 (11.1%)	2 (10.0%)	1 (6.3%)	2 (11.1%)	0

In 4 patients treated with fenofibrate, the AE leading to premature withdrawal was related to study treatment. This was increased transaminases in 1 patient and atrial fibrillation in 1 patient in the F160/C0 group, increased creatinine in 1 patient in the F80/C200 group, and epigastric

These results are supplied for informational purposes only. Some clinical studies may include information not contained in the approved prescribing information. Please refer to the full prescribing information for additional information.

Proprietary Drug Name: [Product Name/Trade Name may vary by country or area (e.g. Tricor [®] in the U.S., Lipanthyl [®] in the EU)]	Generic Drug Name: Fenofibrate	Condition: Type 2 Diabetes
---	--	--------------------------------------

pain (SAE) in 1 patient in the F160/C100 group. The other AEs leading to premature withdrawal, but not related to study treatment, included stress, diagnosis of breast cancer (SAE) and gastrointestinal symptoms. Besides epigastric pain, the other SAE considered as related to study treatment was worsening of angina pectoris in a patient in the F80/C200 group.

Abnormal investigations were the most frequent AEs considered as related to study treatment. They mainly consisted of increased glucose, increased creatinine, increased transaminases, and abnormal ambulatory blood pressure. AEs for increased glucose, mainly from home readings, were reported in 1 patient in the F0/C0 group, 1 patient in the F0/C200 group, 2 patients in the F160/C0 group, 1 patient in the F80/C100 group, 1 patient in the F80/C200 group, 3 patients in the F160/C100 group, and 2 patients in the F160/C200 group. However, mean and median changes in blood glucose were minor during the study.

AEs for increased creatinine were all reported in patients (n = 6) treated with fenofibrate: 1 patient in the F160/C0 group, 2 patients in the F80/C100 group, 1 patient in the F80/C200 group, and 2 patients in the F160/C200 group. All were considered as possibly related to study treatment. Abnormal values were between 1.0 and 1.4 times the upper limit of normal (ULN). AEs for increased transaminases were also all reported in patients (n = 3) treated with fenofibrate: 1 patient in the F160/C0 group and 2 patients in the F160/C200 group. The greatest increase, in the patient in the F160/C0 group, corresponded to values at 12.7 and 7.3 times the ULN for ALT and AST, respectively. In 2 of these 3 patients, the relationship with study treatment was considered as possible or probable.

Gastrointestinal symptoms considered as related to study treatment were reported by 1 to 4 patients in each active group. Abdominal pain was a reason for premature withdrawal of 1 patient in the F80/C100 group and of 1 patient in the F160/C100 group, irritable bowel syndrome, flatulence, abdominal pain and nausea were reasons for premature withdrawal of 1 patient in the F80/C200 group. One (1) patient in the F160/C0 group experienced myalgia, without increase in CK. In 3 patients, cardiac disorders were considered as related to study treatment. These AEs were atrial fibrillation in 1 patient in the F160/C0 group, worsening of angina pectoris in 1 patient and extrasystoles in 1 patient, both in the F80/C200 group.

Abnormal laboratory tests were rare. Three (3) patients, 1 patient in the F160/C0 group and 2 patients in the F160/C200 group were shown to have increased ALT from normal to > 3times the ULN. None of these patients were found to have increased total bilirubin. None of the patients were found to have increased CK to values > 5 times the ULN. Changes in hematology parameters included slight decreases in RBC and WBC in the 160 mg fenofibrate groups, in hemoglobin in all fenofibrate groups, and a slight increase in platelets in all active groups.

These results are supplied for informational purposes only. Some clinical studies may include information not contained in the approved prescribing information. Please refer to the full prescribing information for additional information.

Proprietary Drug Name: [Product Name/Trade Name may vary by country or area (e.g. Tricor [®] in the U.S., Lipanthyl [®] in the EU)]	Generic Drug Name: Fenofibrate	Condition: Type 2 Diabetes
---	--	--------------------------------------

These changes were without clinical relevance.

Concentrations of creatinine in urine tended to decrease in the 3 groups treated with 160 mg fenofibrate, but in a lesser extent with the co-administrations than with the monotherapy, and with F160/C200 than with F160/C100.

In none of the groups did urine protein concentrations increase. Albumin and albumin/creatinine ratio were higher at end of treatment than at baseline in the F0/C200 group, not in the other groups.

Body weight, BMI, BSA, waist circumference and hip circumference remained unchanged during the study.

Date of the report: 20 JUN 2007