Drug product:	tesaglitazar tablets 0.25, 0.5, 0.75 and 1 mg	**SYNOPSIS**	
Drug substance(s):	AZ 242 (tesaglitazar)		
Document No.:	SH-SBD-0013 (D6160L00001)		
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Date:	9 June 2006		

A randomised, double-blind, multicentre, placebo-controlled study to evaluate the efficacy, dose-response and safety of tesaglitazar therapy in Japanese subjects with type 2 Diabetes

International co-ordinating investigator

Study centre(s)

This study was conducted at 34 centres in Japan.

Publications

None at the time of writing this report.

Study dates		**Phase of development**
First patient enrolled	14 May 2004	Therapeutic exploratory (II)
Last patient completed	17 October 2005	

Objectives

The primary objective of this study was to investigate the dose-response relationship of tesaglitazar in patients[1] with type 2 diabetes. The dose-response was analysed by the assessment of the effects of each of four doses of tesaglitazar (0.25, 0.5, 0.75 and 1 mg) to placebo with respect to fasting plasma glucose (FPG) after 12 weeks of randomised treatment.

The secondary objectives of this study were as follows:

[1] In this report the wording "patient (s)" is used instead of "subject (s)" written in the protocol.

1. To compare the effects of tesaglitazar with that of placebo on the following fasting lipid parameters: triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C), non high-density lipoprotein cholesterol (non-HDL-C), total cholesterol (TC), apolipoproteins (Apo A-I, Apo B and Apo C-III), and free fatty acids (FFA).

2. To compare the effects of tesaglitazar with that of placebo on glucose and insulin values during an oral glucose tolerance test (OGTT).

3. To compare the effects of tesaglitazar with that of placebo on the reduction of insulin and HbA1c levels.

4. To compare the effects of tesaglitazar with that of placebo on the proportion of FPG responders (i.e. patients with a decrease in FPG ≥30 mg/dL). In addition, the proportion of patients in each group who achieved FPG ≤140 mg/dL and ≤126 mg/dL was described.

5. To compare the effects of tesaglitazar with that of placebo on the proportion of HDL-C responders (i.e. patients with an increase in HDL-C ≥5%) and TG responders (i.e. patients with a decrease in TG ≥15%).

6. To compare the effects of tesaglitazar with that of placebo on the changes from baseline in waist/hip ratio[1].

7. To evaluate the pharmacokinetics of tesaglitazar.

8. To assess the safety and tolerability of tesaglitazar compared to placebo.

Study design

This was a randomised, double-blind, multicentre, placebo-controlled, parallel group, clinical study to show the dose response and further assess the efficacy, safety and pharmacokinetics of tesaglitazar in comparison to placebo in patients with type 2 diabetes.

Target patient population and sample size

Japanese males and females with type 2 diabetes aged between 30 and 80 years.

Fifty evaluable patients each in 5 groups (tesaglitazar 0.25, 0.5, 0.75 or 1 mg or placebo), i.e., 250 patients in total.

[1] In this report, "weight" is evaluated as a safety variable and therefore deleted from this bullet point, although it was included here in the protocol.

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

Tesaglitazar 0.25, 0.5, 0.75 or 1 mg tablet (batch numbers: H 1466-03-01-01, H 1434-05-01-01 and H 1434-05-01-02, H 1707-01-01-01, and H 1467-04-01-01, respectively) or matching placebo tablet (batch number: H 1428-05-01-01), orally once daily.

Duration of treatment

Run-in (4 weeks) and Treatment (12 weeks)

Criteria for evaluation (main variables)

Efficacy and pharmacokinetics

- Primary variable:
  - Change from baseline in FPG at Week 12
- Secondary variables:
  - Change from baseline in fasting TG, HDL-C, LDL-C, VLDL-C, non HDL-C, TC, Apo A-I, Apo B, Apo C-III, FFA, HbA1c and insulin
  - Post-glucose challenge plasma glucose and insulin at 120 minutes
  - Percentage of FPG responders (i.e. the percentage of patients with a decrease in FPG from baseline of ≥30 mg/dL and the percentage of patients achieving FPG ≤140 mg/dL and ≤126 mg/dL)
  - Percentage of HDL-C and TG responders (i.e. the percentage of patients with an increase in HDL-C from baseline of ≥5% and a decrease in TG from baseline of ≥15%)
  - Change from baseline in waist/hip ratio[1]
  - Plasma tesaglitazar concentrations and population pharmacokinetic parameters

Safety

The safety variables were adverse events (AEs), changes in clinical laboratory tests, vital signs, weight[1], physical examinations and electrocardiograms (ECG).

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[1] In this report, "weight" is evaluated as a safety variable and therefore moved it from "Efficacy and pharmacokinetics" to "Safety" in the "Criteria for evaluation (main variables)" , although it was included in "Efficacy and pharmacokinetics" in the protocol.

Statistical methods

All analyses of efficacy variables were made using Full Analysis Set (FAS). The analysis of FPG was also performed using Per Protocol Set (PPS). Patients who had taken at least one dose of the randomised investigational product and their post-randomisation data available were included in safety analysis set.

The changes from baseline in log (FPG) at Week 12 were analysed based on ANOVA (Analysis of Variance) model including treatment group and previous treatment status as fixed effects.

Patient population

A total of 537 patients were enrolled in the study and 258 out of them were randomised to each treatment group; 51 to tesaglitazar 0.25 mg, 51 to tesaglitazar 0.5 mg, 52 to tesaglitazar 0.75 mg, 51 to tesaglitazar 1 mg and 53 to placebo. Forty four (17.1%) out of the randomised patients discontinued the study during the randomised treatment period. The overall percentage of patients who discontinued the study ranged from 5.9% for tesaglitazar 0.5 mg group to 24.5% for placebo group. The major reason for discontinuation was discontinuation due to prespecified laboratory test criteria (reported as AEs) for tesaglitazar groups and development of study-specified discontinuation for placebo group. There was no dose-related increase in AEs leading to discontinuation for tesaglitazar doses of 0.25 mg to 1 mg.
A total of 257 patients were included in the safety analysis set and FAS, 253 in PPS, and 191 in restricted PPS. The number of patients included in the pharmacokinetic analysis was 203.

Demographic and baseline characteristics of randomised patients are presented in Table S1.

Table S1 Patient population and disposition

		Placebo	tesaglitazar				
			0.25 mg	0.5 mg	0.75 mg	1 mg	**Total**
Population							
N randomised		53	51	51	52	51	205
Demographic characteristics							
Sex (n and %)	Male	36 (67.9)	34 (66.7)	38 (74.5)	43 (82.7)	38 (74.5)	153 (74.6)
	Female	17 (32.1)	17 (33.3)	13 (25.5)	9 (17.3)	13 (25.5)	52 (25.4)
Age (years)	Mean (SD)	61.4 (8.9)	62.8 (8.1)	63.4 (9.1)	61.4 (9.4)	60.8 (7.5)	62.1 (8.6)
	Range	46-77	36-78	35-79	41-79	47-77	35-79
BMI (kg/m^2)	Mean (SD)	23.89 (2.67)	24.18 (3.06)	24.29 (2.86)	24.90 (2.91)	24.53 (3.17)	24.48 (2.99)
	Range	18.9-29.8	18.1-30.8	18.3-31.3	17.9-30.4	16.1-31.0	16.1-31.3
Waist to hip ratio	Mean (SD)	0.886 (0.073)	0.893 (0.069)	0.898 (0.057)	0.902 (0.060)	0.897 (0.063)	0.898 (0.062)
	Range	0.71-1.08	0.68-1.02	0.76-1.04	0.77-1.02	0.68-1.04	0.68-1.04

		Placebo	tesaglitazar				
			0.25 mg	0.5 mg	0.75 mg	1 mg	**Total**
Baseline characteristics[a]							
Mean (SD) FPG (mg/dL)		171.1 (29.3)	168.0 (33.2)	166.5 (30.1)	175.5 (32.1)	166.8 (27.7)	169.2 (30.9)
Mean (SD) HbA1c (%)		7.45 (0.84)	7.50 (1.03)	7.41 (0.89)	7.64 (1.08)	7.42 (0.88)	7.49 (0.97)
Mean (SD) TG (mg/dL)		131.9 (86.9)	137.9 (65.5)	135.5 (77.1)	140.2 (88.4)	173.6 (107.1)	146.8 (86.7)
Mean (SD) HDL-C (mg/dL)		52.9 (11.6)	54.6 (13.4)	52.7 (11.3)	55.3 (13.0)	49.2 (12.1)	53.0 (12.6)
Disposition							
N (%) of patients who	Completed	40 (75.5)	44 (86.3)	48 (94.1)	40 (76.9)	42 (82.4)	214 (82.9)
	discontinued	13 (24.5)	7 (13.7)	3 (5.9)	12 (23.1)	9 (17.6)	44 (17.1)
N analysed for safety[b]		53	50	51	52	51	257
N analysed for efficacy (FAS)		53	50	51	52	51	257
N analysed for efficacy (PPS)		51	50	51	51	50	253
N analysed for pharmacokinetics		0	50	51	51	51	203

[a] Baseline: For FPG and TG, mean of the last two measured values before the start of the randomised treatment. For HbA1c and HDL-C, the last measured value before the start of the randomised treatment.

[b] Number of patients who took at least 1 dose of study treatment and had at least 1 data point after dosing

N=Number of patients

Overall the baseline demographic characteristics of the study population for age, gender, BMI, and waist/hip ratio were similar across the treatment groups except for a higher proportion (82.7%) of male in tesaglitazar 0.75 mg group, compared with that (66.7% to 74.5%) in the other treatment groups. Despite negligible differences in the mean age among the treatment groups, the proportion of <65 years old (68.6%) in tesaglitazar 1 mg group was higher than that (45.1% to 57.7%) in the other treatment groups. In each treatment group around 70% of patients had previously received drug therapy for type 2 diabetes. The baseline characteristics of the study population for glycaemic and lipid parameters were approximately similar across the treatment groups except for higher value in the mean TG level (173.6 mg/dL) in tesaglitazar 1 mg group, compared with that (131.9 mg/dL to 140.2 mg/dL) in the other treatment groups.

Efficacy results

Results of the analysis of the change from baseline in FPG at Week12 are shown in Table S2.

Table S2 Analysis of change from baseline to Week 12 (LOCF) in FPG (FAS)

Statistics	**Placebo**	**tesaglitazar**			
		0.25 mg	**0.5 mg**	**0.75 mg**	**1 mg**
N	53	50	51	52	51
Baseline[a]					
Mean (SD)	171.1 (29.3)	167.6 (33.5)	166.5 (30.1)	175.5 (32.1)	166.8 (27.7)
Week 12 (LOCF)					
Mean (SD)	178.3 (42.0)	155.8 (31.8)	147.2 (29.6)	152.2 (45.0)	141.4 (33.0)
Change from baseline					

Statistics	Placebo	tesaglitazar			
		0.25 mg	0.5 mg	0.75 mg	1 mg
Mean (SD)	7.3 (37.6)	-11.8 (22.0)	-19.3 (31.7)	-23.3 (36.0)	-25.4 (24.1)
% Change from baseline					
Mean (SD)	5.01 (21.45)	-6.29 (12.67)	-10.25 (18.18)	-13.16 (18.19)	-15.08 (14.03)
ANCOVA[b] (vs Placebo)					
Estimate (%)	NA	-10.4	-14.9	-16.8	-19.2
95% CI (%)	NA	-16.1, -4.4	-20.3, -9.2	-22.0, -11.2	-24.3, -13.8
p-value	NA	0.0010	<.0001	<.0001	<.0001
ANOVA[c] (vs Placebo)					
Estimate (%)	NA	-10.0	-14.4	-17.2	-18.7
95% CI (%)	NA	-15.8, -3.8	-19.9, -8.5	-22.5, -11.5	-24.0, -13.1
p-value	NA	0.0022	<.0001	<.0001	<.0001

a Baseline: Mean of the last two measured values before the start of the randomised treatment.
b Based on ANCOVA model including baseline as a covariate and treatment group and previous diabetic therapy as fixed effects.
c Based on ANOVA model including treatment group and previous diabetic therapy as fixed effects.

Tesaglitazar 0.25, 0.5, 0.75 and 1 mg produced a dose-dependent reduction in FPG from 10.4% to 19.2% relative to placebo from baseline to Week 12 (LOCF). The reduction from baseline to Week 12 (LOCF) in FPG was statistically significant for all doses of tesaglitazar compared with placebo ($p<0.0001$ for tesaglitazar 0.5, 0.75 and 1 mg, and $p=0.0010$ for tesaglitazar 0.25 mg). Additional analysis using the PPS as well as restricted PPS (PPS excluding patients who had FPG measurements performed at the study sites) confirmed the primary analysis based on FAS. Overall, tesaglitazar showed a similar reduction in FGP for both drug naïve and drug savvy patients.
A dose-dependent increase in the proportion of patients who achieved ≥30 mg/dL reduction in FPG, who achieved FPG ≤140 mg/dL and who achieved FPG ≤126 mg/dL was observed with tesaglitazar.

Tesaglitazar 0.5, 0.75 and 1 mg reduced TG by 25.37, 20.00 and 42.00 mg/dL relative to placebo from baseline to Week 12 (LOCF), respectively. Tesaglitazar 0.75 and 1 mg increased HDL-C by 4.00 and 7.78 mg/dL relative to placebo from baseline to Week 12 (LOCF), respectively, and the mean changes from baseline were dose-dependent with all doses of tesaglitazar.
A dose-dependent increase in the proportion of HDL-C responders (increase ≥5%) and TG responders (decrease ≤ 15%) was observed with tesaglitazar.
Tesaglitazar 0.75 and 1 mg reduced non-HDL-C by 9.56 and 10.64 mg/dL relative to placebo from baseline to Week 12 (LOCF), respectively. Mean changes from baseline were dose-dependent with all doses of tesaglitazar.
Tesaglitazar 0.5, 0.75, and 1 mg reduced VLDL-C by 5.04, 4.32 and 7.16 mg/dL relative to placebo from baseline to Week 12 (LOCF), respectively, but the reduction was not dose-dependent.
In patients receiving tesaglitazar, no substantial changes relative to placebo from baseline to

Week 12 (LOCF), were observed in TC and LDL-C.
Tesaglitazar 0.75 and 1 mg reduced Apo B by 7.42 and 8.03 mg/dL relative to placebo from baseline to Week 12 (LOCF), respectively. Mean changes from baseline were dose-dependent with all doses of tesaglitazar. Tesaglitazar 0.5 and 1 mg produced reduction by 1.13 and 1.56 mg/dL, respectively, in Apo C-III relative to placebo from baseline to Week 12 (LOCF) but there were no substantial changes in 0.25 and 0.75 mg doses of tesaglitazar. Tesaglitazar produced no substantial changes in Apo A-I relative to placebo from baseline to Week 12 (LOCF).
On an OGGT, the glucose excursions in patients receiving tesaglitazer were lower at Week 12 than at baseline. Relative to placebo, reduction in glucose excursion at Week 12 from baseline was 31.49, 30.12 and 57.63 mg/dL with tesaglitazer 0.5, 0.75 and 1 mg, respectively. There were no obvious effects of tesaglitazar on the insulin excursions relative to placebo from baseline to Week 12.
All doses of tesaglitazar produced reduction in FFA and HbA1c relative to placebo from baseline to Week 12 (LOCF), but it was not dose-dependent. Tesaglitazar 1 mg reduced fasting insulin relative to placebo from baseline to Week 12 (LOCF). Mean changes in insulin from baseline to Week 12 (LOCF) were dose-dependent with tesaglitazar.
No substantial changes in mean waist/hip ratios were observed from baseline to Week 12 in tesaglitazar and placebo groups.

Pharmacokinetic results

A population pharmacokinetic analysis was performed to characterize the pharmacokinetic properties of tesaglitazar in Japanese patients with type 2 diabetes.

The pharmacokinetics of tesaglitazar was adequately described by a 1-compartment model with first-order absorption and elimination. Oral clearance (CL/F) was found to be positively correlated to renal function, assessed as creatinine clearance (CL_{CR}) calculated using the Cockroft-Gault formula (Cockroft and Gault, 1976). The mean population CL/F was estimated to 0.10 L/h and 0.079 L/h for males and females respectively (with a median CL_{CR} of 85 mL/min). The overall between-patient variability in CL/F was moderate (32%) and decreased to 24% after accounting for differences in renal fuction and gender. Other covariates tested (age, body weight, dose, creatinine, ALT, AST, albumin, ALP, bilirubin and smoking) showed no or minor effects on CL/F and V/F when differences in CL_{CR} and gender were accounted for. The median exposure of tesaglitazar (AUC dose adjusted to 1 mg) was 27.5 μmol·h/L in males and 35.8 μmol·h/L in females at Week 12.

The apparent volume of distribution (V/F) was 6.6 L. The median individual half-life at Week 12 was 57 h.

Safety results

Tesaglitazar was generally well tolerated at doses of 0.25 mg to 1 mg. The number of patients with AEs are presented in Table S3 by category and in Table S4 by the most common AEs.

Table S3 Number (%) of patients who had at least 1 adverse event in any category, and total numbers of adverse events (safety analysis set)

Category of adverse event	Placebo		tesaglitazar									
			0.25 mg		0.5 mg		0.75 mg		1 mg		Total	
	(n=53)		(n=50)		(n=51)		(n=52)		(n=51)		(n=204)	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Number of patients[a]:												
Any adverse events	26	(49.1)	23	(46.0)	30	(58.8)	26	(50.0)	28	(54.9)	107	(52.5)
Serious adverse events leading to death	0		0		0		0		0		0	
Serious adverse events not leading to death	0		3	(6.0)	1	(2.0)	2	(3.8)	0		6	(2.9)
Discontinuations of study treatment due to adverse events	1	(1.9)	5	(10.0)	2	(3.9)	8	(15.4)	7	(13.7)	22	(10.8)
Drug-related adverse events	5	(9.4)	4	(8.0)	5	(9.8)	11	(21.2)	6	(11.8)	26	(12.7)
Other significant adverse events	0		0		0		0		0		0	
Total number of recorded:												
Any adverse events	42		41		50		42		45		178	
Serious adverse events leading to death	0		0		0		0		0		0	
Serious adverse events not leading to death	0		4		1		2		0		7	
Adverse events leadng to discontinuations	1		5		2		11		7		25	
Drug-related adverse events	9		5		7		12		7		31	
Other significant adverse events	0		0		0		0		0		0	

[a] Patients with multiple events in the same category are counted only once in that category. Patients with events in more than 1 category are counted once in each of those categories.

Table S4 Number (%) of patients with the most commonly reported adverse events, sorted by decreasing order of frequency as summarised over all treatment groups (safety analysis set)

Preferred Term	Placebo		tesaglitazar									
			0.25 mg		0.5 mg		0.75 mg		1 mg		Total	
	(n=53)		(n=50)		(n=51)		(n=52)		(n=51)		(n=204)	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
N (%) of patients with any adverse events[a]	26	(49.1)	23	(46.0)	30	(58.8)	26	(50.0)	28	(54.9)	107	(52.5)
NASOPHARYNGITIS	5	(9.4)	5	(10.0)	6	(11.8)	2	(3.8)	1	(2.0)	14	(6.9)
PHARYNGITIS	1	(1.9)	1	(2.0)	3	(5.9)	2	(3.8)	4	(7.8)	10	(4.9)
HAEMOGLOBIN DECREASED	0		2	(4.0)	1	(2.0)	4	(7.7)	2	(3.9)	9	(4.4)
BACK PAIN	2	(3.8)	2	(4.0)	1	(2.0)	2	(3.8)	0		5	(2.5)
BLOOD CREATININE INCREASED	0		1	(2.0)	0		2	(3.8)	2	(3.9)	5	(2.5)
BRONCHITIS ACUTE	0		1	(2.0)	0		1	(1.9)	3	(5.9)	5	(2.5)
ANAEMIA	1	(1.9)	1	(2.0)	0		1	(1.9)	2	(3.9)	4	(2.0)
ECZEMA	0		0		2	(3.9)	1	(1.9)	1	(2.0)	4	(2.0)
PHARYNGOLARYNGEAL PAIN	0		2	(4.0)	1	(2.0)	1	(1.9)	0		4	(2.0)

Preferred Term	Placebo		tesaglitazar									
			0.25 mg		0.5 mg		0.75 mg		1 mg		Total	
	(n=53)		(n=50)		(n=51)		(n=52)		(n=51)		(n=204)	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
ABDOMINAL PAIN UPPER	0		0		2	(3.9)	0		1	(2.0)	3	(1.5)
THIRST	1	(1.9)	0		2	(3.9)	1	(1.9)	0		3	(1.5)
HYPERGLYCAEMIA	0		0		0		2	(3.8)	0		2	(1.0)
INFLUENZA	1	(1.9)	0		0		0		2	(3.9)	2	(1.0)
MALAISE	1	(1.9)	0		0		0		2	(3.9)	2	(1.0)
MYALGIA	1	(1.9)	0		2	(3.9)	0		0		2	(1.0)
UPPER RESPIRATORY TRACT INFECTION	0		0		0		2	(3.8)	0		2	(1.0)

[a] Only those AEs with frequency >3% in any treatment group are shown.

There were no appreciable differences of overall incidence of AEs among all treatment groups. The AEs profile was generally similar in all treatment groups except for haemoglobin decreased and serum creatinine increased of which incidence was higher in patients receiving tesaglitazar than in those receiving placebo. The most common AEs in patients receiving tesaglitazar were nasopharyngitis (6.9%), pharyngitis (4.9%) and haemoglobin decreased (4.4%). The discontinuation rate due to AEs was 10.8 % in patients receiving tesaglitazar without dose-related trends. The most common AEs leading to discontinuation were haemoglobin decreased fulfilling predefined criteria. Seven SAEs were reported in 6 patients receiving tesaglitazar but the incidence was not dose-related. Six SAEs other than gastric ulcer haemorrhage were judged not to be drug-related by the investigators. No deaths occurred during the randomised phase of the study.

Changes in haemoglobin, WBC, neutrophil, CK and serum creatinine from baseline to Week 12 are presented in Table S5.

Table S5 Changes in haemoglobin, WBC, neutrophil, CK and serum creatinine from baseline to Week 12

		Baseline			Week 12 (withdrawal)			Difference	
		n	Mean	SD	n	Mean	SD	Mean	SD
Haemoglobin	Placebo	53	14.85	1.59	52	14.87	1.58	0.02	0.66
(g/dL)	Tesaglitazar 0.25 mg	50	14.68	1.46	49	14.28	1.43	-0.40	0.82
	Tesaglitazar 0.5 mg	51	14.67	1.13	51	14.15	1.34	-0.51	0.72
	Tesaglitazar 0.75 mg	52	14.81	1.30	51	13.82	1.64	-0.99	0.99
	Tesaglitazar 1 mg	51	14.87	1.34	51	13.98	1.43	-0.89	0.77
WBC	Placebo	53	6273.6	1602.1	52	6311.5	1609.0	23.1	1222.9
(/μL)	Tesaglitazar 0.25 mg	50	5798.0	1272.9	49	5444.9	1187.3	-371.4	826.9
	Tesaglitazar 0.5 mg	51	5529.4	1302.4	51	5431.4	1438.4	-98.0	1285.8
	Tesaglitazar 0.75 mg	52	5701.9	1512.4	51	5445.1	1943.5	-292.9	1214.1

	Tesaglitazar 1 mg	51	6198.0	1749.9	51	5488.2	1449.1	-709.8	1292.3
Neutrophil	Placebo	53	3.86	1.31	52	3.92	1.29	0.04	1.26
(10^6/mL)	Tesaglitazar 0.25 mg	50	3.30	1.01	50	3.25	1.12	-0.05	0.93
	Tesaglitazar 0.5 mg	51	3.25	1.02	51	3.17	1.02	-0.07	1.16
	Tesaglitazar 0.75 mg	52	3.31	1.17	51	3.13	1.32	-0.21	1.06
	Tesaglitazar 1 mg	51	3.85	1.41	51	3.32	1.21	-0.53	1.23
CK	Placebo	53	101.8	60.6	52	108.3	70.8	6.8	50.8
(IU/L)	Tesaglitazar 0.25 mg	50	105.4	56.8	50	118.2	101.3	12.8	89.9
	Tesaglitazar 0.5 mg	51	97.5	43.4	51	110.5	66.4	13.0	50.8
	Tesaglitazar 0.75 mg	52	123.2	83.1	52	129.3	111.0	6.1	70.2
	Tesaglitazar 1 mg	51	107.3	45.7	51	146.2	83.0	38.9	75.9
Serum	Placebo	53	0.741	0.158	52	0.720	0.150	-0.017	0.061
creatinine	Tesaglitazar 0.25 mg	50	0.715	0.160	50	0.736	0.172	0.021	0.065
(mg/dL)	Tesaglitazar 0.5 mg	51	0.760	0.139	51	0.847	0.150	0.087	0.058
	Tesaglitazar 0.75 mg	52	0.746	0.146	52	0.855	0.206	0.109	0.104
	Tesaglitazar 1 mg	51	0.735	0.164	51	0.879	0.222	0.144	0.112

Treatment with tesaglitazar was associated with decrease in mean haemoglobin, WBC and neutrophil counts.
A small increase in mean CK was observed in tesaglitazar groups. No patients had an increase of CK >5 x UNL. Dose-dependent increase in mean serum creatinine levels was observed with tesaglitazar treatment. Two out of 27 patients with increased serum creatinine >30% from baseline developed microalbuminuria. In quantitative urinalysis, microalbuminuria was observed in 5 patients and persistent albuminuria in one patient receiving tesaglitazar. Tesaglitazar did not adversely affect hepatic biochemistry. Changes of mean values in pulse rate and blood pressure showed no treatment-related trends. No discernible effects of tesaglitazar on ECG overall evaluation were observed.