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Brief Report

Safety and efficacy of lobeglitazone monotherapy in patients with type 2 diabetes mellitus over 52 weeks: An open-label extension study

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ABSTRACT

We aimed to assess the safety and efficacy of lobeglitazone in patients with type 2 diabetes over 52 weeks through 28-week extension study. Clinical benefits in terms of glycemic and lipid control were maintained for 52 weeks. Lobeglitazone showed a favorable balance of efficacy and safety during the extension study.

1. Introduction

Thiazolidinediones (TZDs) are antihyperglycemic agents that reduce insulin resistance in liver and peripheral tissues [1]. In several studies [2–5], it has been documented that TZDs have long-term benefits in glycemic control by augmenting insulin sensitivity and preserving β-cell function. Moreover, TZDs activate peroxisome proliferator-activated receptor (PPAR)-γ,

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leading to a favorable change in atherosclerotic markers including lipid profile [6,7]. However, the use of TZDs has rapidly decreased because of various safety concerns, and nowadays, accounting for less than 5% of the prescriptions of oral AHAs [8].

Lobeglitazone (CKD-501; Chong Kun Dang pharmaceutical Corp., Korea) is a novel PPAR-γ agonist containing the TZD motif (Supplementary Fig. 1). It was approved by Korean FDA in 2013. It has been documented [9] that a 24-week monotherapy with lobeglitazone significantly improved glycemic control and showed a positive effect on lipid profile compared with placebo in patients with type 2 diabetes. In contrast to other TZDs, lobeglitazone is mainly excreted in feces, thereby reducing the concern about the risk of bladder cancer. As an extension of the 24-week study, this 28-week study was conducted to assess the safety and efficacy of lobeglitazone.

2. Methods

This multicenter, randomized, controlled, parallel-group, 52-week study consisted of a 24-week, double-blinded study followed by a 28-week, open-labeled extension study. Details of the 24-week study design have been previously reported [9].

Eligible patients were randomized at a 2:1 ratio to receive either lobeglitazone 0.5 mg ($n = 115$) or matching placebo ($n = 58$) and entered a 24-week study. After completing the study, the participants who were randomly assigned to receive lobeglitazone at baseline maintained the treatment for the entire 52 weeks (group M) whereas patients with placebo were switched to lobeglitazone 0.5 mg during the extension (group S). Rescue medication (metformin) was introduced when fasting plasma glucose (FPG) were >200 mg/dL at week 28 or 40.

The primary endpoint was the change in glycated hemoglobin (HbA1c) from baseline to week 52. A p-value <0.05 was considered statistically significant. Details of the study protocol and statistical analysis are summarized in Supplementary File.

3. Results

3.1. *Baseline characteristics*

Of the 144 patients who completed the 24-week study, 94 (group M; $n = 65$ vs. group S; $n = 29$) entered the extension study, of which 88 (93.6%) completed the 52-week treatment (Supplementary Fig. 2). Demographics and baseline characteristics were generally well matched between the groups

Table 1 – Effects on glycemic parameters including markers of insulin resistance and β-cell function in ITT population.

	Group M ($n = 64$)		Group S ($n = 29$)		p-Value[b]
	Mean (SD)	p-Value[a]	Mean (SD)	p-Value[a]	
HbA1c (%)					
Baseline	7.79 (0.83)		8.00 (0.68)		
Week 24	7.26 (1.25)	<0.001*	8.01 (0.94)	0.957	0.005*
Week 52	7.30 (1.29)		7.48 (0.94)		
Change from baseline	−0.50 (1.14)	<0.001*	−0.52 (0.81)	0.002*	0.904
Change from week 24			−0.53 (0.74)	< 0.001*	
FPG (mg/dL)					
Baseline	150.0 (38.0)		149.7 (32.8)		
Week 24	131.8 (40.5)	< 0.001*	143.2 (27.0)	0.252	0.128
Week 52	136.5 (41.7)		135.0 (31.3)		
Change from baseline	−13.5 (40.2)	0.009*	−14.8 (32.5)	0.021*	0.878
Change from week 24			−8.2 (25.6)	0.096	
HOMA-IR					
Baseline	3.6 (2.3)		3.6 (1.6)		
Week 24	3.0 (1.9)	0.004*	3.3 (1.7)	0.318	0.351
Week 52	3.0 (1.7)		2.7 (1.0)		
Change from baseline	−0.55 (2.2)	0.045*	−0.82 (1.7)	0.012*	0.559
Change from week 24			−0.53 (1.5)	0.066	
HOMA-β					
Baseline	44.5 (24.2)		44.4 (18.0)		
Week 24	59.5 (37.5)	<0.001*	43.5 (18.0)	0.713	<0.001*
Week 52	56.8 (38.3)		47.1 (19.1)		
Change from baseline	12.3 (32.8)	0.004*	2.7 (15.5)	0.359	0.058
Change from week 24			3.6 (13.0)	0.149	

FPG, fasting plasma glucose; HOMA-IR, homeostasis model assessment of insulin resistance; HOMA-β, homeostasis model assessment of β-cell function.
Data are shown as means (SD).
[a] Differences from baseline at each time point were assessed using paired t-test.
[b] Treatment group differences were analyzed using Student's t-test or ANCOVA.
* p-Value <0.05 was considered statistically significant.