

Summary of Results for Targeting Beta-cell Failure in Lean Patients With Type 2 Diabetes (Lean-DM; #ISRCTN85605342)

Background

Type 2 diabetes (T2D) is characterized by insulin resistance (IR) and dysregulated insulin secretion. Glucagon-like peptide-1 receptor agonist liraglutide promotes insulin secretion, whereas thiazolidinedione-pioglitazone decreases IR.

Objectives

This study aimed to compare the efficacies of increasing insulin secretion vs decreasing IR strategies for improving myocardial perfusion, energetics, and function in T2D via an open-label randomized crossover trial.

Methods

Forty-one patients with T2D (age 63 years [95% CI: 59-68 years], 27 [66%] male, body mass index 27.8 kg/m² [95% CI: 26.1-29.5 kg/m²]) without cardiovascular disease were randomized to liraglutide or pioglitazone for a 16-week treatment followed by an 8-week washout and a further 16-week treatment with the second trial drug. Participants underwent rest and dobutamine stress ³¹phosphorus magnetic resonance spectroscopy and cardiovascular magnetic resonance for measuring the myocardial energetics index phosphocreatine to adenosine triphosphate ratio, myocardial perfusion (rest, dobutamine stress myocardial blood flow, and myocardial perfusion reserve), left ventricular (LV) volumes, systolic and diastolic function (mitral in-flow E/A ratio), before and after treatment. The 6-minute walk-test was used for functional assessments.

Results

Pioglitazone treatment resulted in significant increases in LV mass (96 g [95% CI: 68-105 g] to 105 g [95% CI: 74-115 g]; $P = 0.003$) and mitral-inflow E/A ratio (1.04 [95% CI: 0.62-1.21] to 1.34 [95% CI: 0.70-1.54]; $P = 0.008$), and a significant reduction in LV concentricity index (0.79 mg/mL [95% CI: 0.61-0.85 mg/mL] to 0.73 mg/mL [95% CI: 0.56-0.79 mg/mL]; $P = 0.04$). Liraglutide treatment increased stress myocardial blood flow (1.62 mL/g/min [95% CI: 1.19-1.75 mL/g/min] to 2.08 mL/g/min [95% CI: 1.57-2.24 mL/g/min]; $P = 0.01$) and myocardial perfusion reserve (2.40 [95% CI: 1.55-2.68] to 2.90 [95% CI: 1.83-3.18]; $P = 0.01$). Liraglutide treatment also significantly increased the rest (1.47 [95% CI: 1.17-1.58] to 1.94 [95% CI: 1.52-2.08]; $P = 0.00002$) and stress phosphocreatine to adenosine triphosphate ratio (1.32 [95% CI: 1.05-1.42] to 1.58 [95% CI: 1.19-1.71]; $P = 0.004$) and 6-minute walk distance (488 m [95% CI: 458-518 m] to 521 m [95% CI: 481-561 m]; $P = 0.009$).

Conclusions

Liraglutide treatment resulted in improved myocardial perfusion, energetics, and 6-minute walk distance in patients with T2D, whereas pioglitazone showed no effect on these parameters (Lean-DM [Targeting Beta-cell Failure in Lean Patients With Type 2 Diabetes]; NCT04657939).

Citation: Chowdhary A, Thirunavukarasu S, Joseph T, Jex N, Kotha S, Giannoudi M, Procter H, Cash L, Akkaya S, Broadbent D, Xue H, Swoboda P, Valkovič L, Kellman P, Plein S, Rider OJ, Neubauer S, Greenwood JP, Levelt E. Liraglutide Improves Myocardial Perfusion and Energetics and Exercise Tolerance in Patients With Type 2 Diabetes. *J Am Coll Cardiol*. 2024 Aug 6;84(6):540-557. doi: 10.1016/j.jacc.2024.04.064. PMID: 39084829; PMCID: PMC11296502.