

# Efficacy and safety of liraglutide 3.0 mg in individuals with overweight or obesity and type 2 diabetes (T2D) treated with basal insulin: the SCALE Insulin trial

WT GARVEY,<sup>1</sup> AL BIRKENFELD,<sup>2</sup> D DICKER,<sup>3</sup> G MINGRONE,<sup>4</sup> SD PEDERSEN,<sup>5</sup> A SATYLGANOVA,<sup>6</sup> D SKOVGAARD,<sup>6</sup> D SUGIMOTO,<sup>7</sup> N ZEUTHEN,<sup>6</sup> O MOSENZON<sup>8</sup>

<sup>1</sup>Department of Nutrition Sciences, University of Alabama at Birmingham and the Birmingham VA Medical Center, Birmingham, AL, USA; <sup>2</sup>Universitätsklinikum Carl Gustav Carus an der Technischen Universität Dresden, Dresden, Germany; <sup>3</sup>Internal Medicine D Hasharon Hospital, Rabin Medical Center, Petah Tikva, Sackler School of Medicine Tel Aviv University, Israel; <sup>4</sup>Department of Internal Medicine, Catholic University, Rome, Italy and Department of Diabetes, King's College London, United Kingdom; <sup>5</sup>C-endo Diabetes & Endocrinology Clinic, Calgary, AB, Canada; <sup>6</sup>Novo Nordisk A/S, Soeborg, Denmark; <sup>7</sup>Cedar Crosse Research Center, Chicago, IL, USA; <sup>8</sup>Hadassah Hebrew University Hospital, Jerusalem, Israel

**Introduction:** Liraglutide 3.0 mg is approved for weight management in adults with and without T2D. Liraglutide up to 1.8 mg has been used in combination with insulin for treatment of T2D, but combination of a 3.0 mg dose with insulin has previously not been investigated.

**Methods:** The 56-week double-blind SCALE insulin trial randomised individuals with T2D with overweight or obesity (BMI  $\geq 27$  kg/m<sup>2</sup>) to liraglutide 3.0 mg or placebo, both as adjunct to intensive behaviour therapy (IBT). All study participants were on stable treatment with basal insulin and up to 2 oral antidiabetic drugs. Primary endpoints were mean change in body weight (%), and proportion with weight loss (WL)  $\geq 5\%$  at week 56, using all observed values regardless of week 56 treatment status, and a jump-to-reference multiple imputation approach to missing data, based on values from placebo group.

**Results:** Mean baseline characteristics at randomisation (n=198) for liraglutide 3.0 mg included: 55.9 years of age, 54.5% females, 101 kg, BMI 35.9 kg/m<sup>2</sup>, diabetes duration 11.4 years and HbA<sub>1c</sub> 7.9%. Corresponding placebo values (n=198) were: 57.6 years, 50.0% females, 99 kg, BMI 35.3 kg/m<sup>2</sup>, 12.8 years, and HbA<sub>1c</sub> 8.0%. Of those randomised, 195 were exposed to liraglutide 3.0 mg and 197 to placebo, with 166 (83.8%) and 168 (84.8%) still on drug at 56 weeks. Respective mean weight change at week 56 was -5.85% and -1.53%, respectively, estimated treatment difference (ETD) -4.32 ( $p < 0.0001$ ). WL  $\geq 5\%$  was observed in 51.80% participants on liraglutide and 23.98% on placebo, odds ratio (OR) 3.41 ( $p < 0.0001$ ). Respective values for  $>10\%$  WL were 22.77% and 6.55%, OR 4.21,  $p < 0.0001$  (other efficacy outcomes in table). HbA<sub>1c</sub> reduction was greater with liraglutide than placebo (-1.09 vs. -0.55%,  $p < 0.0001$ ), and there were respective changes in insulin dose of +2.8U and +17.8U from a baseline mean (both groups) of 38U (ETD -15U,  $p < 0.0001$ ). Documented hypoglycaemia (on-drug) occurred at respective rates of 7.42 and 9.38 events/subject-year with liraglutide 3.0 mg and placebo, with 3 and 2 severe events in each group respectively. Adverse event incidence was similar for liraglutide 3.0 mg and placebo, except gastrointestinal events (liraglutide 3.0 mg, 62.1%; placebo, 46.7%).

**Conclusion:** In insulin-treated T2D, liraglutide 3.0 mg was superior to placebo with respect to mean and categorical weight loss, as well as improvements in glycaemic control without increasing the risk of hypoglycaemia. No new safety or tolerability issues were observed.

Endpoint at 56 weeks	Liraglutide 3.0 mg	Placebo	Treatment difference
Change in weight (%)	-5.85	-1.53	ETD: -4.32 $p < 0.0001$
WL $\geq 5\%$ (%)	51.80	23.98	OR: 3.41 $p < 0.0001$
WL $>10\%$ (%)	22.77	6.55	OR: 4.21 $p < 0.0001$
Change in waist circumference (cm)	-5.28	-2.56	ETD: -2.71 $p < 0.0001$
Change in HbA <sub>1c</sub> (%)	-1.09	-0.55	ETD: -0.53 $p < 0.0001$
Change in heart rate (beats/min)	1.35	-0.16	ETD: 1.51 $p = 0.084$
Change in systolic blood pressure (mmHg)	-5.62	-1.62	ETD: -3.98 $p = 0.0014$
Change in diastolic blood pressure (mmHg)	-2.34	-0.94	ETD: -1.40 $p = 0.091$
Change in SF-36 Physical function score	2.68	2.28	ETD: 0.39 NS
Change in IWQoL-Lite CT Physical function score	8.20	5.74	ETD: 2.46 NS