Outcomes at week 56 in individuals losing ≥4% weight at week 16 on liraglutide 3.0 mg: SCALE IBT

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Background

- The SCALE IBT trial demonstrated superiority of liraglutide 3.0 mg for weight reduction versus placebo as an adjunct to intensive behavior therapy (IBT) after 56 weeks of treatment (–7.5% vs. –4.0%; estimated treatment difference –3.4% [95% CI: –5.3; –1.6], p=0.0003).[1]
- The United States Food and Drug Administration (FDA) prescribing information for liraglutide 3.0 mg defines a stopping rule for individuals achieving <4% body weight reduction after 16 weeks' treatment.[2]
- This *post hoc* analysis explored the effect of intervention in the subgroup of liraglutide-treated individuals categorized as early responders (ERs).
  - This subgroup corresponded to individuals who would have been eligible to continue treatment after 16 weeks in a real-world clinical setting.

Methods

- The 56-week SCALE IBT trial (ClinicalTrials.gov: NCT02963935) randomized adults with obesity (BMI ≥30 kg/m²) and without diabetes to liraglutide 3.0 mg or placebo as an adjunct to a program of IBT, including physical activity (escalating up to 250 min/week), hypocaloric diet (1200–1800 kcal/day) and 23 behavior counseling sessions, delivered on the visit schedule recommended by the Centers for Medicare and Medicaid Services.
- Data are presented for ERs (≥4% weight loss at week 16) and early non-responders (ENRs; <4% weight loss at week 16) after 56 weeks of treatment with liraglutide 3.0 mg.
  - Individuals who withdrew from the trial before 16 weeks were classified as non-responders.
- Efficacy outcomes are estimated means or proportions based on the intention-to-treat principle (missing values were handled using a jump-to-reference multiple imputation model). Safety outcomes are based on observed data.
- Data presented for the two subsets are for descriptive purposes only. As data are not placebo-adjusted, any differences in outcomes between ERs and ENRs should be interpreted with caution.

Results

Efficacy

- The baseline characteristics of ERs and ENRs for liraglutide 3.0 mg-treated individuals are presented in Table 1.
- At week 16, 76.1% of randomized individuals had achieved ≥4% weight loss and were classified as ERs.
- At week 56, mean observed weight loss in the ER subgroup was 9.4% (Figure 1a).
- At week 56, 72.7%, 38.6% and 22.8% of ERs achieved weight loss of ≥5%, >10% and >15%, respectively (Figure 1b).
- In general, improvements in waist circumference, glycemic parameters, cardiometabolic markers and patient-reported physical function were observed in ERs (Table 2).

Table 1: Baseline demographics and individual disposition

	Liraglutide 3.0 mg (n=142)	
	Early non-responders (n=34)	Early responders (n=108)
Sex, female, n [%]	27 [79.4]	92 [85.2]
Age, years	41.6 (10.6)	46.7 (11.6)
Body weight, lbs	249.3 (52.2)	236.1 (47.2)
Body weight, kgs	113.1 (23.7)	107.1 (21.4)
BMI, kg/m²	40.7 (7.9)	38.9 (6.4)
HbA_{1c}, %	5.6 (0.3)	5.5 (0.4)
SBP, mmHg	121 (16)	127 (15)
DBP, mmHg	76 (10)	81 (9)

Data are mean (±SD) unless otherwise stated. BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure; SD, standard deviation.

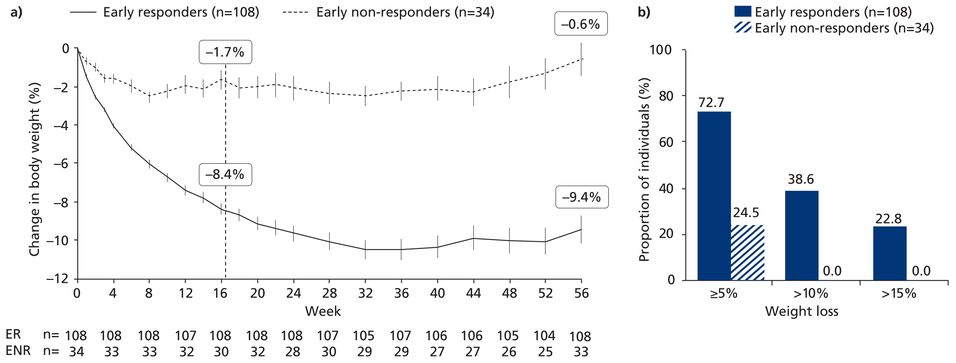
Table 2: Primary and secondary efficacy endpoints at week 56

	Liraglutide 3.0 mg (n=142)		
	Early non-responders (n=34)	Early responders (n=108)	Early responders on-drug (n=94)
Change in weight (%)	–0.8	–9.4	–10.6
Proportion with ≥5% weight loss (%)	24.5	72.7	81.5
Proportion with >10% weight loss (%)	0.0	38.6	43.6
Proportion with >15% weight loss (%)	0.0	22.8	26.4
Change in waist circumference (cm)	–2.2	–11.4	–12.3
Change in HbA_{1c} (% point)	–0.05	–0.20	–0.24
Change in heart rate (beats/min)	1.87	1.95	2.08
Change in systolic blood pressure (mmHg)	–1.27	–2.51	–4.09
Change in diastolic blood pressure (mmHg)	0.00	–0.80	–1.60
Change in total cholesterol (mg/dl)	–0.08	–0.08	–0.09
Change in LDL cholesterol (mg/dl)	–1.22	0.31	0.63
Change in HDL cholesterol (mg/dl)	0.91	2.74	3.07
Change in VLDL cholesterol (mg/dl)	–0.12	–3.10	–3.76
Change in triglycerides (mg/dl)	–4.36	–20.45	–24.67
Change in free fatty acids (mg/dl)	–1.28	–2.26	–2.68
Change in SF-36 Physical function score	2.00	3.93	4.15
Change in IWQOL-Lite CT Physical function score	12.21	13.57	15.38

Data are estimated means/proportions; missing values were handled using a jump-to-reference multiple imputation model. HDL, high-density lipoprotein; IWQOL-Lite CT, Impact of Weight on Quality of Life-Lite for Clinical Trials; LDL, low-density lipoprotein; SF-36, short form-36; VLDL, very low-density lipoprotein.

Figure 1: a) Change in body weight from baseline to week 56; b) Categorical weight loss at week 56

Key results



Data are observed means ± standard error. ER, early responders; ENR, early non-responders.

Data are estimated proportions; missing values were handled using a jump-to-reference multiple imputation model.

Safety

- The proportion of ERs and ENRs reporting adverse events was similar to that reported in the overall trial population.[1]
- The most frequent adverse events were gastrointestinal events, reported by 75.0% in the ER subset and 58.8% in the ENR subset (Table 3).

Table 3: Summary of adverse events

	Liraglutide 3.0 mg (n=142)			
	Early non-responders (n=34)		Early responders (n=108)	
	n	(%)	n	(%)
Total adverse events	32	94.1	104	96.3
Serious adverse events	0	0.0	6	5.6
Gastrointestinal adverse events	20	58.8	81	75.0

Safety analysis set. On-drug adverse events: adverse events with onset date no more than 14 days after any trial product administration.

Conclusion

- More than three quarters of individuals with obesity receiving liraglutide 3.0 mg as an adjunct to IBT were classified as responders at week 16 and were eligible for long-term treatment according to the FDA prescribing information.
- Of these, the great majority continued on therapy to 56 weeks, achieving clinically meaningful reductions in body weight.

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References: (**1**) Wadden *et al.* ENDO 2019, Poster SAT-099; (**2**) Food and Drug Administration, 2014. Saxenda® Prescribing information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/206321Orig1s000lbl.pdf