Outcomes in early responders achieving ≥5% weight loss at 16 weeks with liraglutide 3.0 mg as an adjunct to intensive behaviour therapy (IBT) in individuals with obesity in the SCALE IBT trial

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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 behaviour therapy (IBT) after 56 weeks of treatment (–7.5% vs. –4.0%; estimated treatment difference –3.5% [95% CI: –5.3; –1.6], p=0.0003).[1]
- The European Medicines Agency (EMA) prescribing information for liraglutide 3.0 mg defines a stopping rule for individuals achieving <5% body weight reduction after 16 weeks' treatment.[2]
- This *post hoc* analysis explored the effect of intervention in the subgroup of liraglutide-treated individuals categorised 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) randomised adults with obesity (BMI ≥30 kg/m^2) 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 behaviour counselling sessions, delivered on the visit schedule recommended by the Centers for Medicare and Medicaid Services.
- Data are presented for ERs (≥5% weight loss at week 16) and early non-responders (ENRs; <5% 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

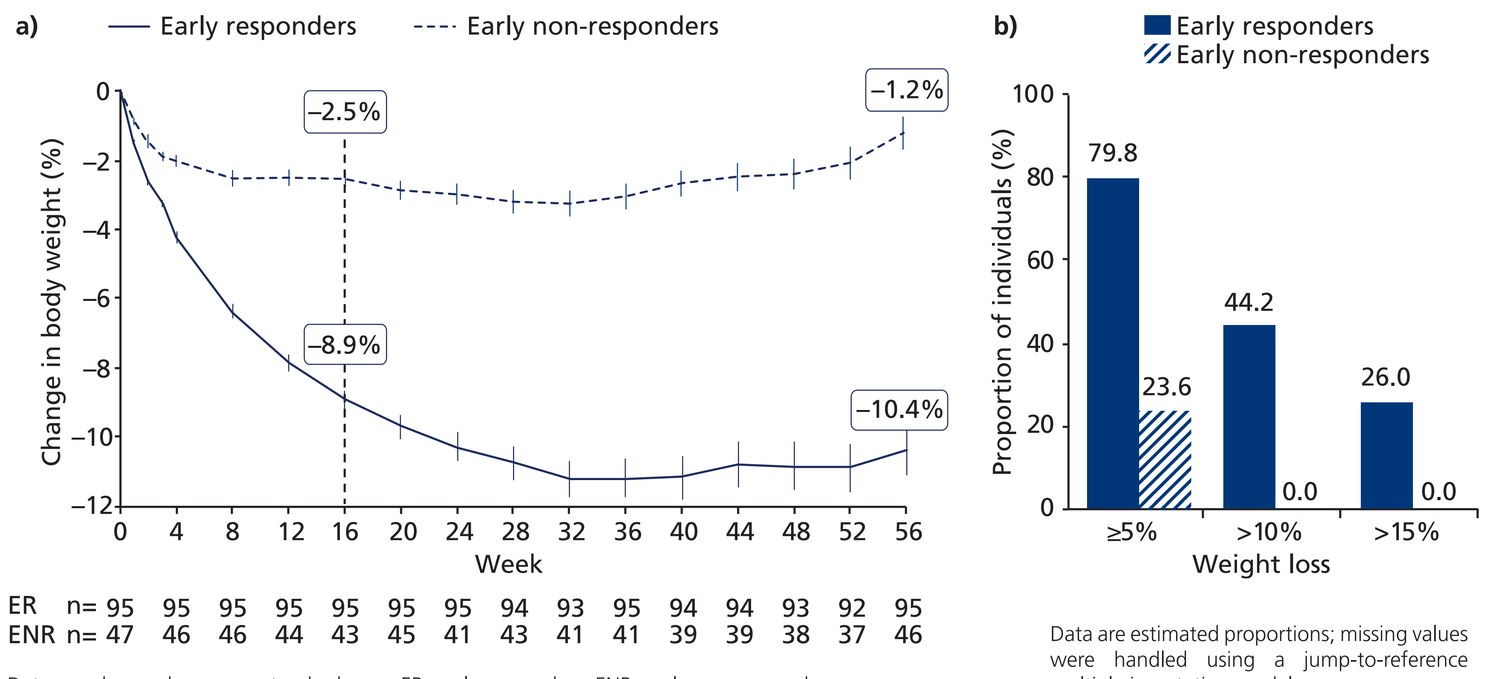
- The baseline characteristics of ERs and ENRs for liraglutide 3.0 mg-treated individuals are presented in Table 1.
- At week 16, 66.9% of randomised individuals had achieved ≥5% weight loss and were classified as ERs.
- At week 56, mean observed weight loss in the ER subgroup was 10.4% (Figure 1a).
- At week 56, 79.8%, 44.2% and 26.0% of ERs achieved weight loss of ≥5%, >10% and >15%, respectively (Figure 1b).

Table 1: Baseline demographics and individual disposition

	Liraglutide 3.0 mg (n=142)	
	Early non-responders (n=47)	Early responders (n=95)
Sex, female, n [%]	38 [80.9]	81 [85.3]
Age, years	43.4 (12.3)	46.4 (11.1)
Body weight, kg	111.8 (22.5)	106.9 (21.8)
BMI, kg/m^2	40.4 (7.4)	38.8 (6.4)
HbA_{1c}, %	5.6 (0.4)	5.5 (0.4)
SBP, mmHg	123.0 (17.0)	127.0 (14.0)
DBP, mmHg	78.0 (10.0)	81.0 (9.0)

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

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



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.

Key results

- In general, improvements in waist circumference, glycaemic parameters, cardiometabolic markers and patient-reported physical function were observed in ERs (Table 2).

Safety

- The proportion of ERs and ENRs reporting adverse events and serious adverse events was similar to that reported in the overall trial population.
- The most frequent adverse events were gastrointestinal events, reported by 74.7% in the ER subset and 63.8% in the ENR subset (Table 3).

Table 3: Summary of adverse events

	Liraglutide 3.0 mg (n=142)			
	Early non-responders (n=47)		Early responders (n=95)	
	n	(%)	n	(%)
Total adverse events	45	(95.7)	91	(95.8)
Serious adverse events	0	(0.0)	6	(6.3)
Gastrointestinal adverse events	30	(63.8)	71	(74.7)

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

Table 2: Estimated primary and secondary efficacy endpoints

	All randomised individuals		Early responders on-drug at week 56
	Early non-responders (n=47)	Early responders (n=95)	
Change in weight (%)	–1.3	–10.4	–11.4
Proportion with ≥5% weight loss (%)	23.6	79.8	87.9
Proportion with >10% weight loss (%)	0.0	44.2	49.0
Proportion with >15% weight loss (%)	0.0	26.0	29.6
Change in waist circumference (cm)	–3.1	–12.3	–13.0
Change in HbA_{1c} (% point)	–0.06	–0.21	–0.25
Change in heart rate (beats/min)	1.62	2.08	2.19
Change in systolic blood pressure (mmHg)	0.03	–3.32	–4.60
Change in diastolic blood pressure (mmHg)	0.93	–1.37	–2.12
Change in total cholesterol (mmol/L)	0.02	–0.02	–0.02
Change in LDL cholesterol (mmol/L)	–0.03	0.01	0.02
Change in HDL cholesterol (mmol/L)	0.03	0.08	0.08
Change in VLDL cholesterol (mmol/L)	0.02	–0.10	–0.12
Change in triglycerides (mmol/L)	0.00	–0.28	–0.32
Change in free fatty acids (mmol/L)	–0.07	–0.07	–0.09
Change in SF-36 Physical function score	2.53	3.93	4.20
Change in IWQoL-Lite CT Physical function score	12.0	13.9	15.6

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

Conclusion

- More than two-thirds 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 EMA prescribing information.
- Of these, the great majority continued on therapy to 56 weeks, achieving clinically meaningful reductions in body weight.

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