Pharmacotherapy IV: Liraglutide for Chronic Weight Management

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Disclosures

Faculty

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Relationships with commercial interests:

- Speakers Bureau/ Honoraria: Novo Nordisk, Valeant

Objectives

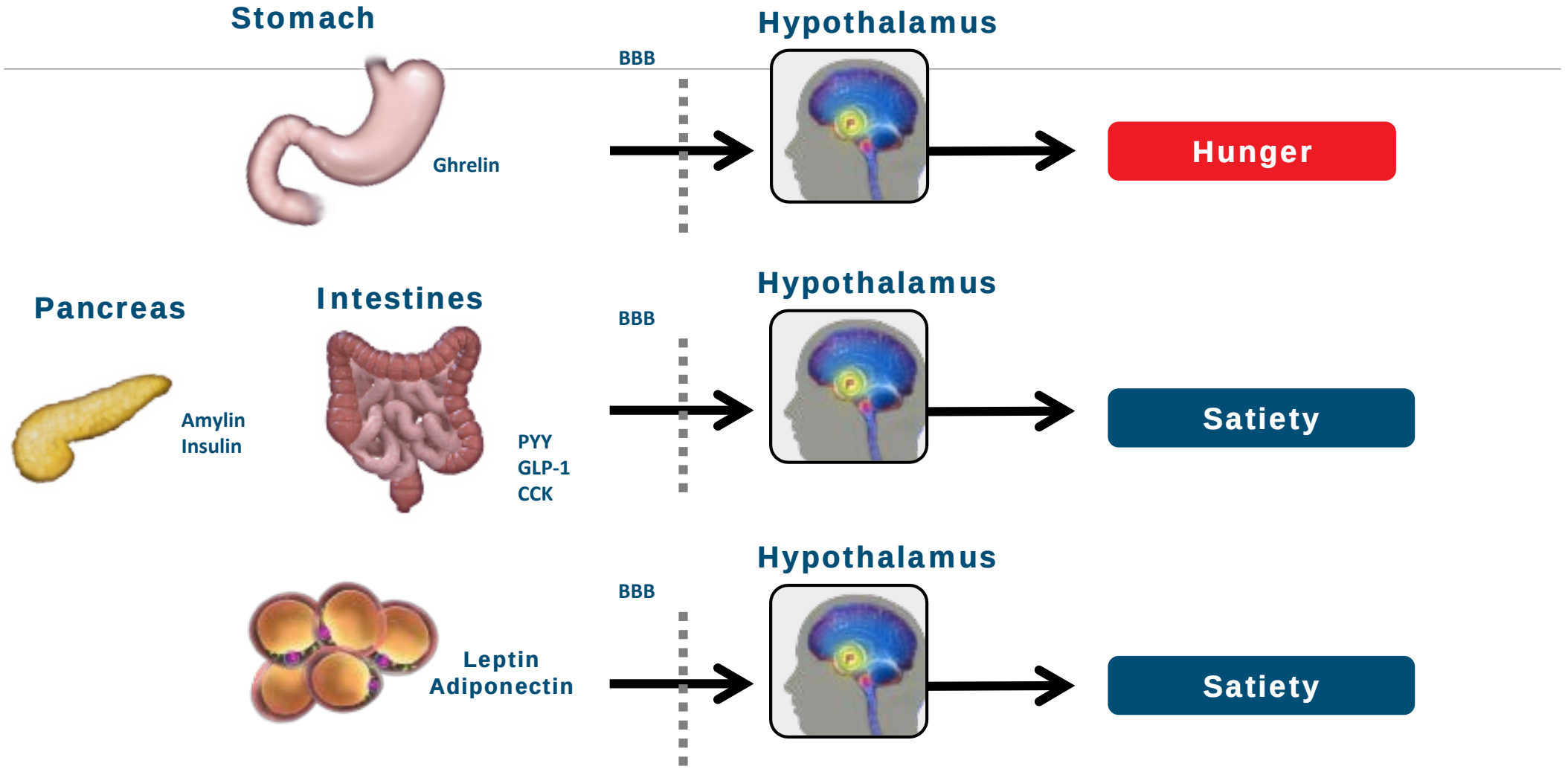
Role of GLP-1 in appetite regulation

Clinical trials of Liraglutide (Saxenda®) in weight management

Clinical use of Liraglutide (Saxenda®) in weight management

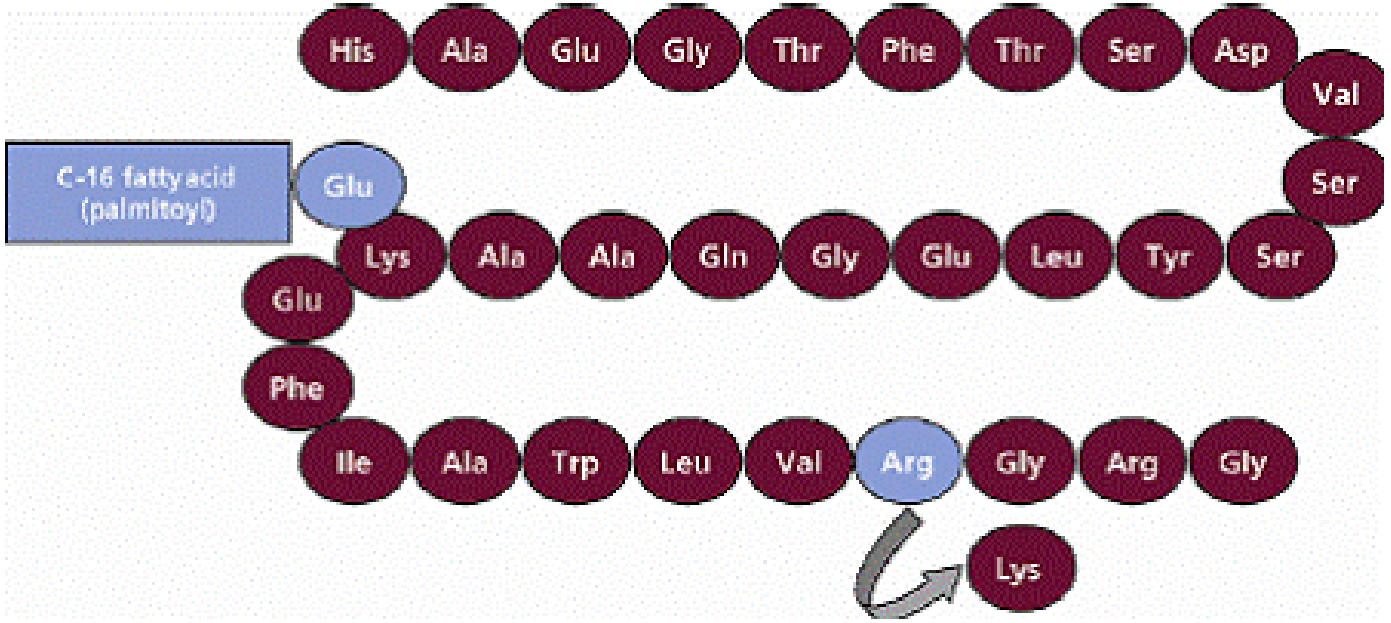
- Indications
- Contraindications
- Cautions
- Dosing
- Side Effects
- Follow up

Multiple hormones play a key role in hunger and satiety



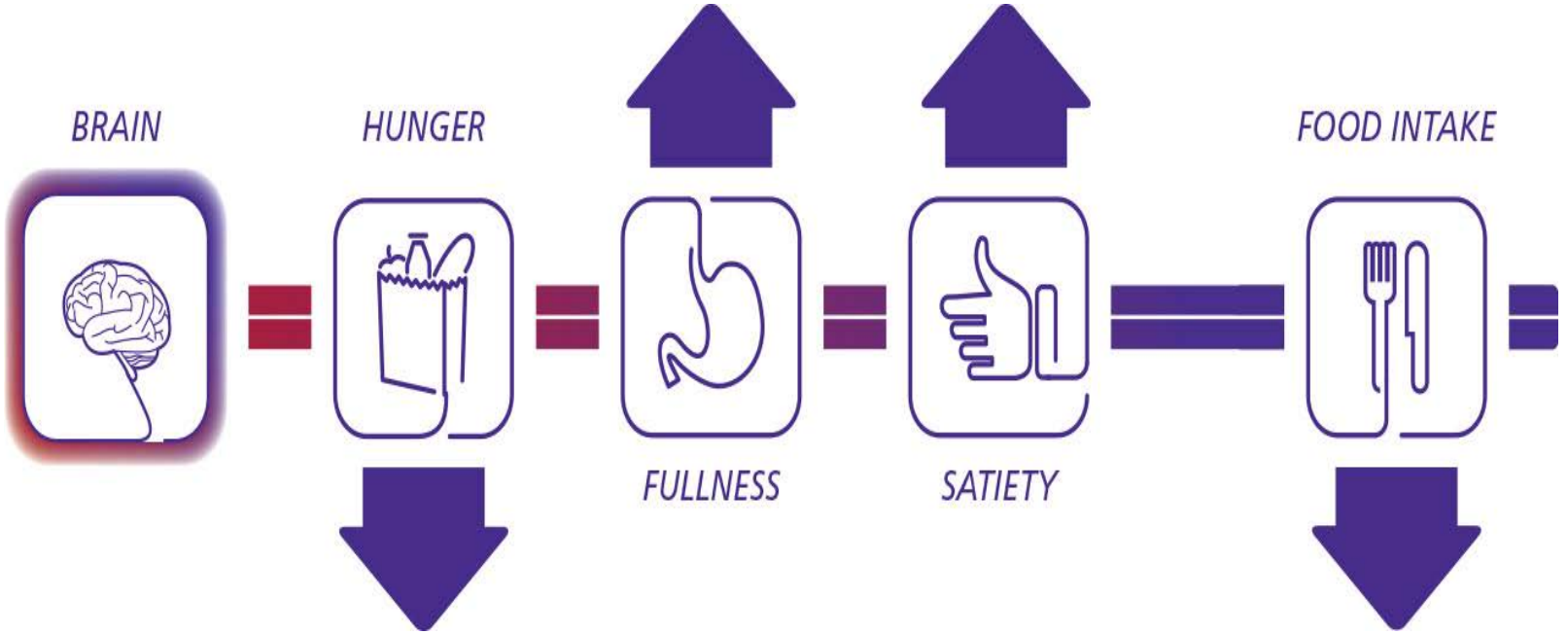
BBB, blood-brain barrier; CCK, cholecystokinin; GLP-1, glucagon-like peptide-1; PYY, peptide YY .
Suzuki K et al. *Exp Diabetes Res.* 2012;2012:824305.

Liraglutide



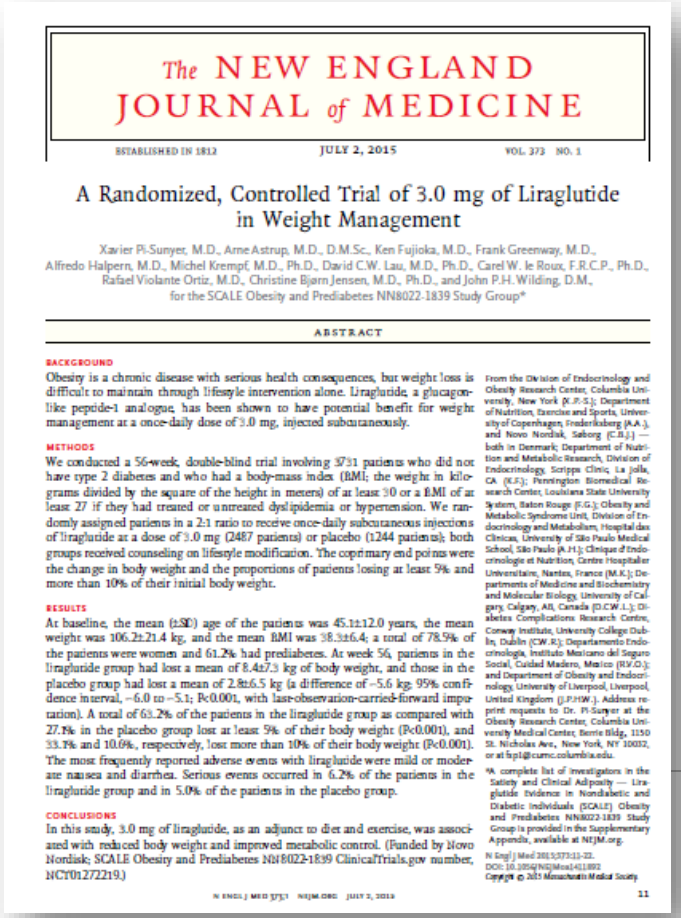
GLP-1 is a physiological regulator of appetite and food intake

Like natural GLP-1, liraglutide activates specific areas in the brain involved in the regulation of appetite and food intake[*†]



Liraglutide reduced hunger, increased fullness and satiety, and decreased food intake, compared to placebo.[†]

[*]Clinical significance has not been established.



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A Randomized, Controlled Trial of 3.0 mg of Liraglutide in Weight Management

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ABSTRACT

BACKGROUND

Obesity is a chronic disease with serious health consequences, but weight loss is difficult to maintain through lifestyle intervention alone. Liraglutide, a glucagon-like peptide-1 analogue, has been shown to have potential benefit for weight management at a once-daily dose of 3.0 mg, injected subcutaneously.

METHODS

We conducted a 56-week, double-blind trial involving 3731 patients who did not have type 2 diabetes and who had a body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) of at least 30 or a BMI of at least 27 if they had treated or untreated dyslipidemia or hypertension. We randomly assigned patients in a 2:1 ratio to receive once-daily subcutaneous injections of liraglutide at a dose of 3.0 mg (2487 patients) or placebo (1244 patients); both groups received counseling on lifestyle modification. The coprimary end points were the change in body weight and the proportions of patients losing at least 5% and more than 10% of their initial body weight.

RESULTS

At baseline, the mean (±SD) age of the patients was 45.1±12.0 years, the mean weight was 106.2±21.4 kg, and the mean BMI was 38.3±6.4; a total of 78.5% of the patients were women and 61.2% had prediabetes. At week 56, patients in the liraglutide group had lost a mean of 8.4±7.3 kg of body weight, and those in the placebo group had lost a mean of 2.8±6.5 kg (a difference of −5.6 kg; 95% confidence interval, −6.0 to −5.1; P<0.001, with last-observation-carried-forward imputation). A total of 63.2% of the patients in the liraglutide group as compared with 27.1% in the placebo group lost at least 5% of their body weight (P<0.001), and 33.1% and 10.0%, respectively, lost more than 10% of their body weight (P<0.001). The most frequently reported adverse events with liraglutide were mild or moderate nausea and diarrhea. Serious events occurred in 6.2% of the patients in the liraglutide group and in 5.0% of the patients in the placebo group.

CONCLUSIONS

In this study, 3.0 mg of liraglutide, as an adjunct to diet and exercise, was associated with reduced body weight and improved metabolic control. (Funded by Novo Nordisk; SCALE Obesity and Prediabetes NN8022-1839 ClinicalTrials.gov number, NCT01272219.)

From the Division of Endocrinology and Obesity Research Center, Columbia University, New York (X.P.-S.); Department of Nutrition, Exercise and Sports, University of Copenhagen, Frederiksberg (A.A.), and Novo Nordisk, Søborg (C.B.J.) — both in Denmark; Department of Nutrition and Metabolic Research, Division of Endocrinology, Scripps Clinic, La Jolla, CA (K.F.); Pennington Biomedical Research Center, Louisiana State University System, Baton Rouge (F.G.); Obesity and Metabolic Syndrome Unit, Division of Endocrinology and Metabolism, Hospital das Clínicas, University of São Paulo Medical School, São Paulo (A.H.); Clinique d'Endocrinologie et Nutrition, Centre Hospitalier Universitaire, Nantes, France (M.K.); Departments of Medicine and Biochemistry and Molecular Biology, University of Calgary, Calgary, AB, Canada (D.C.W.L.); Diabetes Complications Research Centre, Conway Institute, University College Dublin, Dublin (C.W.R.); Departamento Endocrinología, Instituto Mexicano del Seguro Social, Ciudad Madero, Mexico (R.V.O.); and Department of Obesity and Endocrinology, University of Liverpool, Liverpool, United Kingdom (J.P.H.W.). Address reprint requests to Dr. Pi-Sunyer at the Obesity Research Center, Columbia University Medical Center, Berrie Bldg., 1150 St. Nicholas Ave., New York, NY 10032, or at fxp1@cumc.columbia.edu.

*A complete list of investigators in the Safety and Clinical Adiposity — Liraglutide Evidence in Nondiabetic and Diabetic Individuals (SCALE) Obesity and Prediabetes NN8022-1839 Study Group is provided in the Supplementary Appendix, available at NEJM.org.

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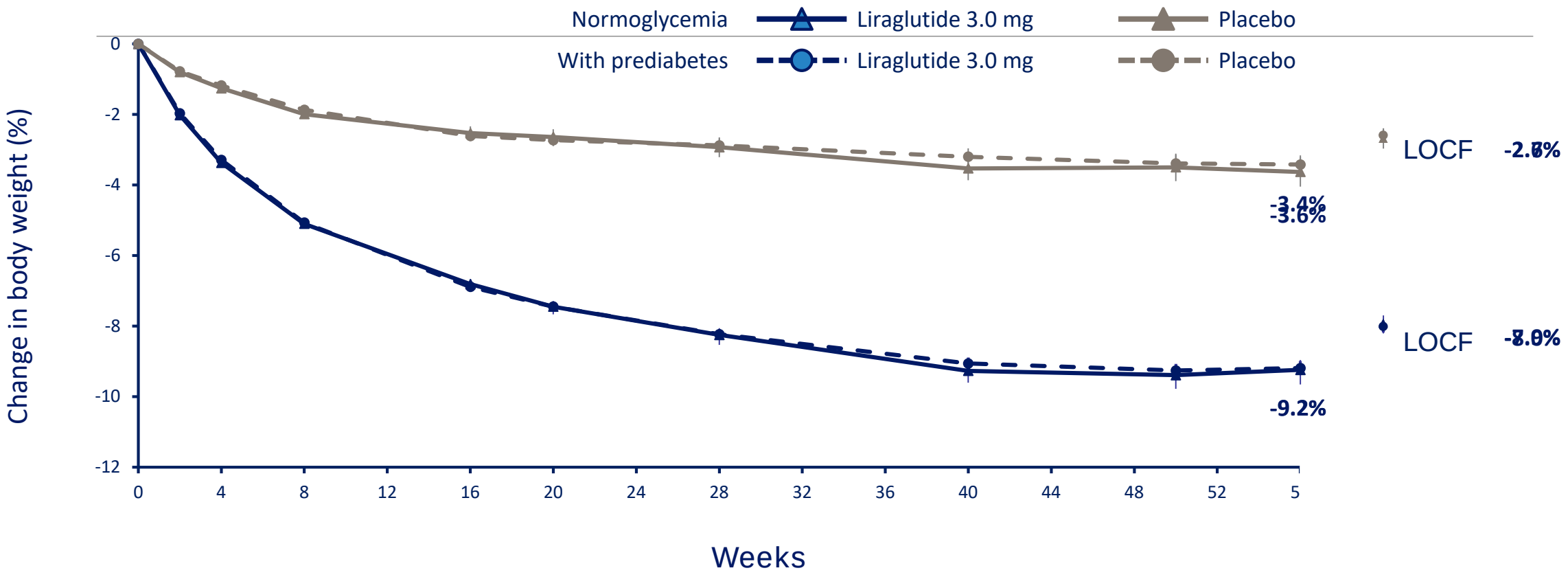
A Randomized Controlled Trial of 3.0 mg of Liraglutide in Weight Management

PI-SUNYER X, ASTRUP A, FUJIOKA K, GREENWAY F, HALPERN A, KREMPF M, LAU DCW, LE ROUX CW, VIOLANTE R, JENSEN CB AND WILDING JPH ON BEHALF OF THE SCALE OBESITY AND PREDIABETES NN8022-1839 STUDY GROUP

Mean change in body weight (%)

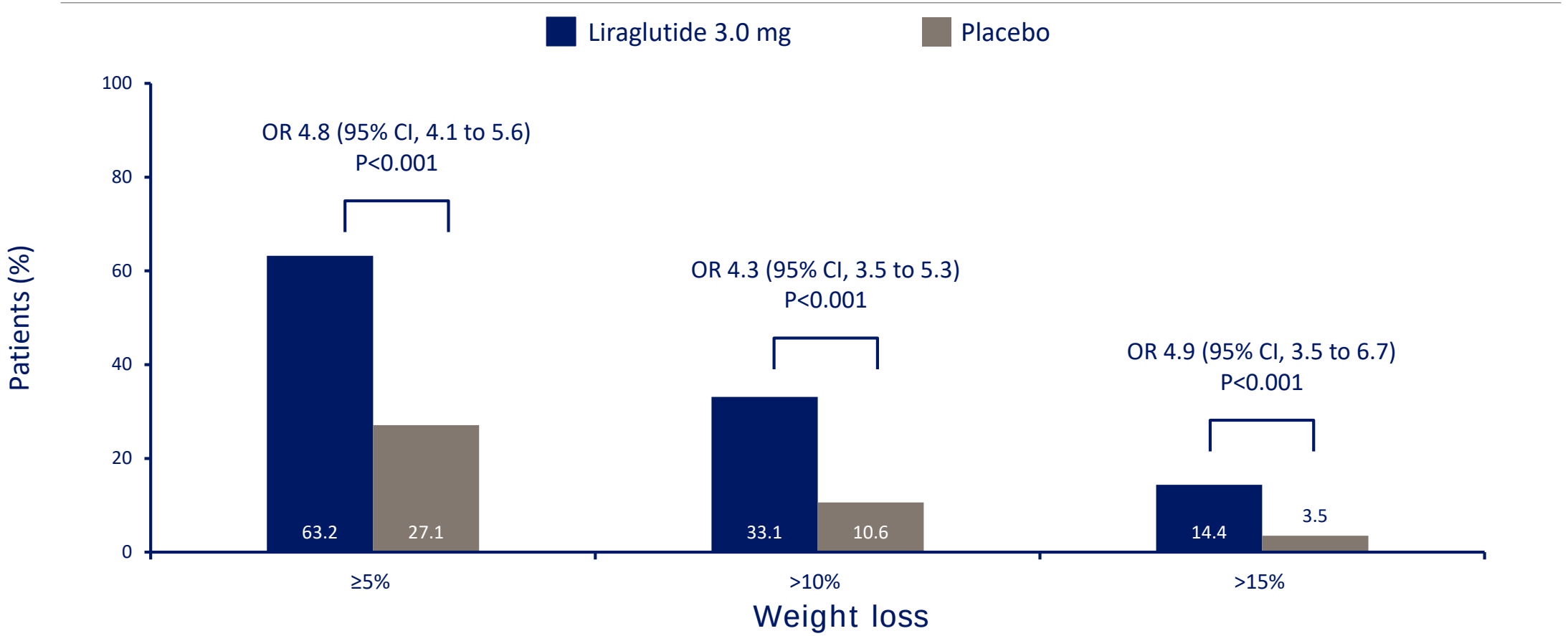
By prediabetes status: 0–56 weeks



Data are observed means with standard error bars, and the symbols at the right represent the 56-week weight change using LOCF imputation

Categorical weight loss

At week 56



Weight loss with Liraglutide

in conjunction with reduced calorie diet and increased PA

~2/3 of patients lost >5% initial body weight

~1/3 of patients lost >10% initial body weight

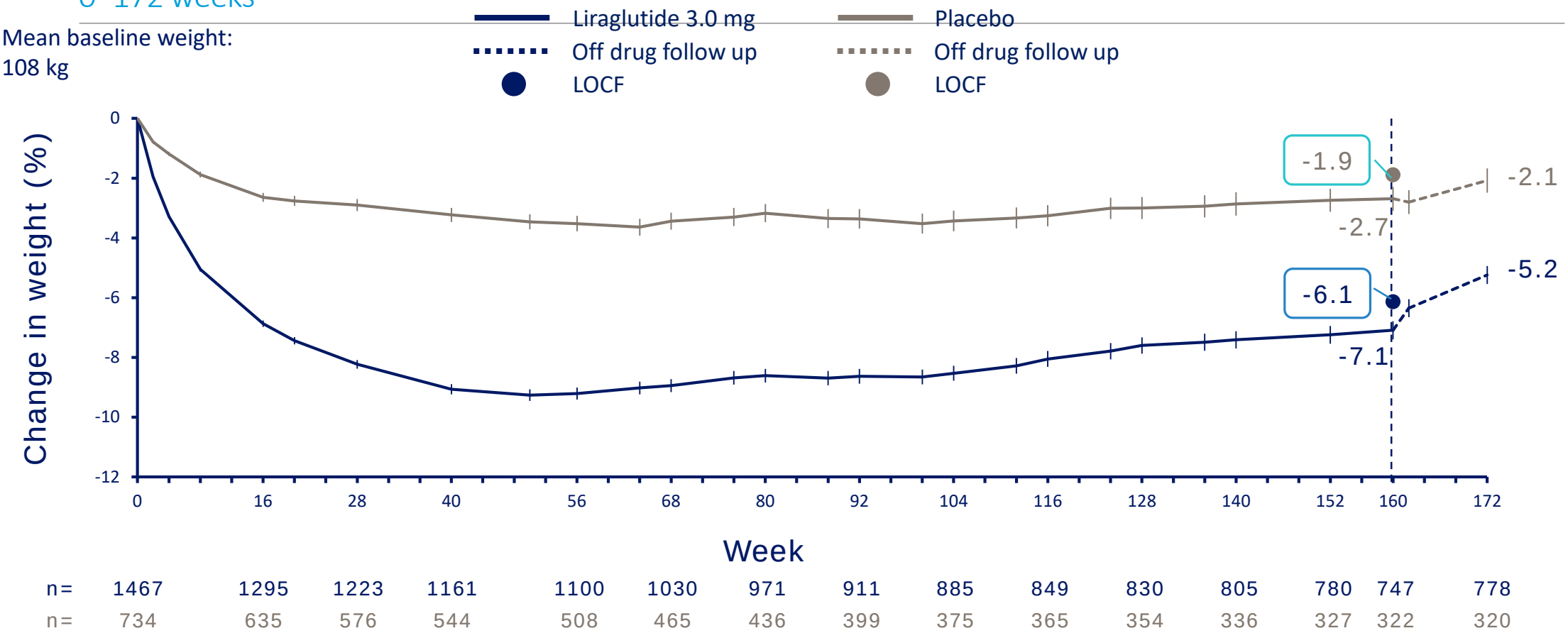
~15% of patients lost >15% initial body weight

Pi-Sunyer *et al. NEJM* 2015;373:11-22

Mean change in body weight (%)

0–172 weeks

Mean baseline weight:
108 kg



Liraglutide indication

Liraglutide is indicated as an adjunct to a reduced calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of:

- **≥30 kg/m^2 or greater (obese), or**
- **≥27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbidity (e.g., hypertension, type 2 diabetes, or dyslipidemia) and who have failed a previous weight management intervention**

Liraglutide contraindications

Personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2)

Hypersensitivity to liraglutide or to any ingredient in the formulation

Pregnant and breastfeeding women

Liraglutide cautions

Severe renal impairment (GFR < 30)

Hepatic insufficiency

Prior pancreatitis

Unstable cardiovascular disease

Considerations in Diabetics

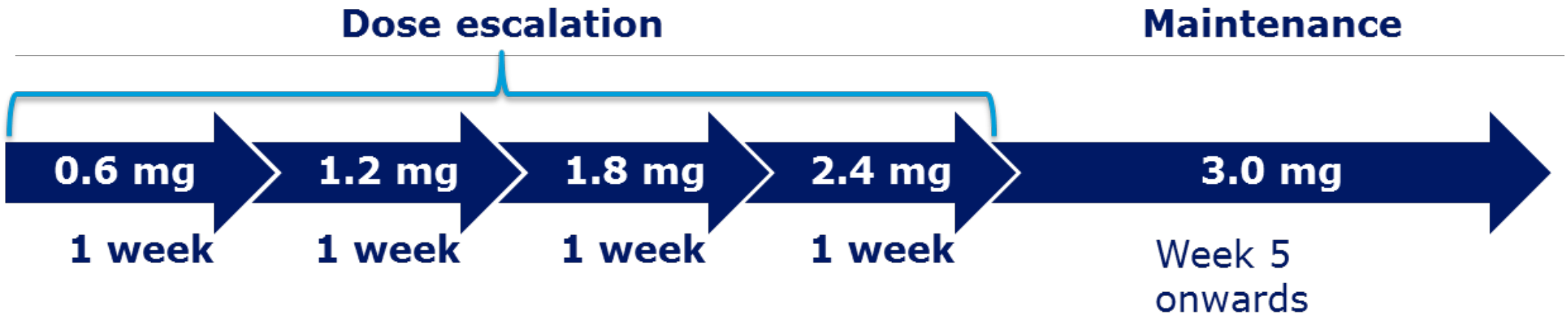
Stop DPP-IV inhibitors or other GLP-1 agonists

Reduce or discontinue insulin secretagogues

Recommendation against co-administration with insulin[1]

Saxenda® (liraglutide), Product Monograph, Novo Nordisk Canada Inc, June 2015

Dosage and administration



- The 0.6, 1.2, 1.8, and 2.4 mg doses are intended to reduce gastrointestinal symptoms during initial dose escalation
- If patients do not tolerate an increased dose during dose escalation, the dose escalation can be changed with a total delay of up to 7 days

Saxenda® (liraglutide), Product Monograph, Novo Nordisk Canada Inc, June 2015

CHECK PEN

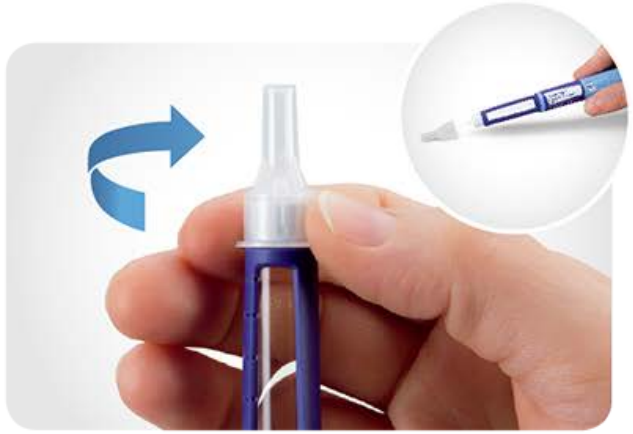
ATTACH A NEW NEEDLE

CHECK FLOW

Only check the Saxenda® flow before your first injection with each new pen

SELECT DOSE

INJECT DOSE



REMOVE NEEDLE

Side Effects

Nausea

Diarrhea

Constipation

Vomiting

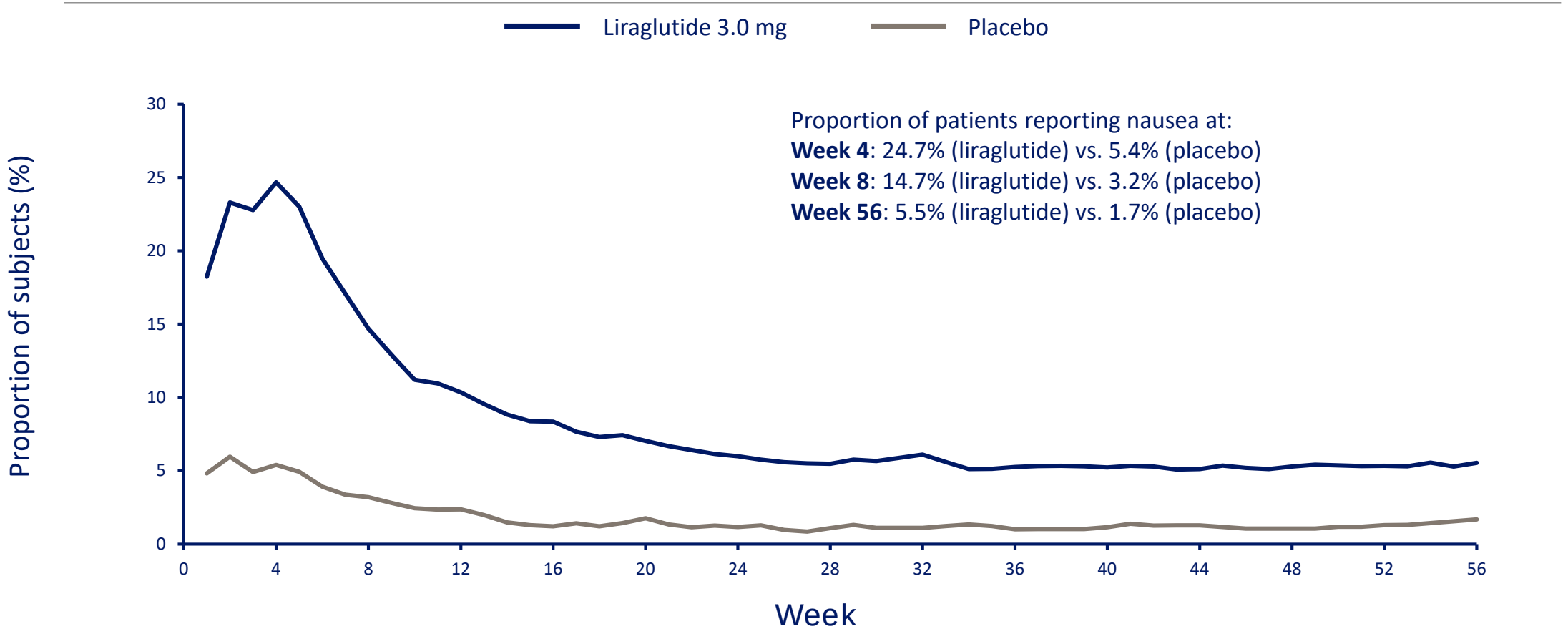
Dyspepsia

Dizziness

Dysgeusia

Proportion of subjects with nausea

0–56 weeks



Safety analysis set

Pi-Sunyer *et al. NEJM* 2015;373:11-22

Strategies to mitigate GI side effects

Delay dose escalation

Increase dose in smaller increments

Administer at bedtime

Submaximal dose

Change to a once weekly GLP-1 agonist[1]

[1]Trujillo JM *et al. Ther Adv Endocrinol Metab* 2015;6:19-28

Safety

Gallbladder disease

- Cholelithiasis: 2.2% Liraglutide vs. 0.8% placebo
- Cholecystitis: 0.8% Liraglutide vs. 0.4% placebo

Breast Neoplasms

- Breast cancer in 0.7% of Liraglutide treated women vs. 0.2% placebo treated
- Too few cases to determine if Liraglutide related
- Enhanced ascertainment

Follow up

Heart rate, blood pressure, weight

Glycemic control in diabetics

GI side effects

Effect on appetite

- meal skipping
- calorie intake
- protein intake (target 1 – 1.2 g / kg ideal body weight)

Stopping Rule

After 12 weeks at the maximum dose liraglutide should be stopped if body weight loss has not been >5%

Medication discontinuation

Weaning recommended

Based on the elimination half-life, patients should be advised to reinitiate liraglutide at 0.6 mg if more than 3 days have elapsed since the last liraglutide dose. This approach will mitigate any gastrointestinal symptoms associated with re-initiation of treatment.

SaxendaCare™

A FREE support program focused on small steps that help patients work towards their weight management goals—encourage your patients to enrol today!

Patients who enrol in SaxendaCare™ receive FREE access to a step-by-step support program designed to help them adhere to their therapy by:

- Getting them off to a good start on Saxenda® by learning how to inject, titrate and manage side effects
- Helping them build skills to make healthier choices and stay motivated

Benefits include:

Access to SaxendaCare™ Registered Nurses and Dietitians to provide support, answers to questions, and help with pen training

Tools and resources to help patients get started with Saxenda®

A website that includes education and tools on proper nutrition, physical activity and staying motivated

Weekly emails to guide patients along the way, keep them motivated and reinforce adherence

Encourage your Saxenda® patient to enrol by calling **1-844-SAX-ENDA** (1-844-729-3632) or by visiting **www.SaxendaCareCanada.ca**

Questions?