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First study with liraglutide in an adolescent population with obesity: a phase 1, randomized, double-blind, placebo-controlled trial to assess safety, tolerability and pharmacokinetics of liraglutide in adolescents aged 12 to 17 years

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Childhood obesity is associated with increased risk of developing various diseases at a later age. Only orlistat is currently approved for weight management in the USA for adolescents aged ≥ 12 years. This trial (NCT01789086) assessed the safety, tolerability, and PK of liraglutide at doses up to 3.0 mg in adolescents (12–17 years) with obesity (BMI $\geq 95^{\text{th}}$ percentile for age and gender, and BMI corresponding to ≥ 30 kg/m² for adults). The trial was conducted as part of the liraglutide 3.0 mg regulatory agreements with the FDA and EMA.

In total, 21 subjects (67% female; mean age, 14.9 years; body weight, 106 kg (79–164 kg); BMI, 36.2 kg/m²; BMI Z-score, 3.2; all Tanner stages 3–5) were randomized 2:1, liraglutide:placebo, for 5–6 weeks. Liraglutide (or placebo) was administered by dose-escalation starting at 0.6 mg/day followed by weekly 0.6 mg dose escalations (as tolerated) to a maximum of 3.0 mg.

With liraglutide, 77% of the possibly or probably treatment-related AEs were gastrointestinal disorders (mainly abdominal pain, nausea, vomiting and diarrhea). Most events were mild, with no pattern in timing/duration. No serious AEs were reported. There were 12 hypoglycemic episodes with liraglutide (1 episode leading to a postponed dose escalation with a maximum attained dose of 2.4 mg in 1 subject) vs 2 with placebo; no episodes were severe and most occurred with liraglutide escalation doses of 0.6 mg and 1.2 mg.

There were no clinically significant changes in laboratory parameters (except for increased lipase in two subjects [transient in one]), physical examination or ECG. No anti-liraglutide antibodies were detected. Resting pulse was numerically increased with liraglutide compared to placebo (mean change from baseline: 6 vs 1 beat/minute, respectively). The clinical significance of this is unknown. In a joint analysis with data from adults with obesity, sex was a relevant PK covariate, as observed for adults (estimated exposure ratio between male and females was 0.77 [0.65;0.92]_{90%CI}). Lower exposure was also observed with higher body weight. After covariate adjustment, the exposure ratio for adolescents vs adults was 1.10 [0.93;1.31]_{90%CI}; considered not clinically relevant. Overall, the PK parameters at steady state were similar between obese adolescents and adults.

No significant treatment effect was observed with liraglutide on BMI Z-score, body weight (-0.70 [-4.24;2.84] kg), fasting plasma glucose, HbA_{1c} and serum insulin after 5–6 weeks treatment.

In adolescents with obesity, liraglutide appeared to be well tolerated, with similar safety, tolerability and PK properties as observed in adults with obesity. A 3.0 mg dose resulted in similar exposure in both adult and adolescent subjects. Findings of this trial suggest that the dosing regimen approved for weight management in adults may be appropriate for use in adolescents. This will be further investigated in a safety and efficacy trial.