OR33-01: Liraglutide for Weight Management in Pubertal Adolescents with Obesity: A Randomized Controlled Trial

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Background: Pediatric obesity is a chronic disease with rising prevalence and limited treatment options; first-line intervention is lifestyle therapy, which is typically unsuccessful.[1] Liraglutide (3.0 mg) as an adjunct to lifestyle therapy has provided weight loss and improved cardiometabolic risk factors in adults.[2] Here we report the results of liraglutide 3.0 mg in adolescents with obesity who failed to respond to lifestyle therapy.

Methods: A multinational, randomized, double-blind trial (NCT02918279) with a 12-wk run-in of lifestyle therapy, 4-8-wk dose escalation, 52-wk maintenance period and 26-wk follow-up off trial drug. Adolescents aged 12-<18 years with obesity, stable weight and suboptimal response to lifestyle therapy alone were randomized 1:1 to once-daily subcutaneous liraglutide 3.0 mg (or maximum tolerated dose) or placebo (PBO), both as an adjunct to lifestyle therapy. Randomization was stratified by pubertal and glycemic (normal vs prediabetes/type 2 diabetes) status. Primary endpoint was change in BMI standard deviation score (SDS)[3] from wk 0 to 56.

Results: Of 125 adolescents randomized to liraglutide 3.0 mg and 126 to PBO, 101 and 100 completed treatment at wk 56, respectively; 99 in each arm completed the trial at wk 82. 40.6% were male; mean age 14.5 years; mean BMI 35.6 kg/m2; mean BMI SDS 3.17. Liraglutide 3.0 mg was superior to PBO for change in BMI SDS at wk 56 (estimated treatment difference [ETD] -0.22; 95% CI -0.37, -0.08; p=0.0022). In the liraglutide 3.0 mg vs PBO arm, 43.25% vs 18.73% (p=0.0002) and 26.08% vs 8.11% (p=0.0006) of adolescents had ≥5% and ≥10% reduction in baseline BMI at wk 56, respectively. A significant difference in change in BMI was seen for liraglutide 3.0 mg vs PBO: ETD -4.64%; 95% CI -7.14, -2.14; p=0.0003. A significant reduction in waist circumference with liraglutide 3.0 mg was shown at wk 56 (p=0.0126). Greater weight regain/rebound in BMI SDS at wk 82 was seen for liraglutide 3.0 mg vs PBO after drug discontinuation (ETD 0.15; 95% CI 0.07, 0.23; p=0.0002). There were no significant differences in blood pressure, fasting lipids, fasting plasma glucose or HbA1c at wk 56. No unexpected safety concerns and no severe hypoglycemia were reported. During treatment (0-56 wks), more adolescents in the liraglutide 3.0 mg (64.8%) vs PBO arm (36.5%) reported gastrointestinal adverse events (AEs), and 3 vs 5 adolescents, respectively, reported serious AEs. Mental health questionnaire results were similar in both arms at wk 56. No effect on growth or pubertal development was found.

Conclusions: This trial demonstrates clinically meaningful[4] weight loss in adolescents with obesity treated with liraglutide 3.0 mg as an adjunct to lifestyle therapy. The safety profile was similar to that observed in adults.

1. Ryder et al *Obesity* 2018;26:951. 2. Pi-Sunyer et al *N Engl J Med* 2015;373:11. 3. EMA doc. ref. EMEA/402888/2008. 4. Grossman et al JAMA 2017;317:2417.