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Efficacy and safety of liraglutide vs. placebo in children and adolescents with type 2 diabetes: the ellipse randomised trial results

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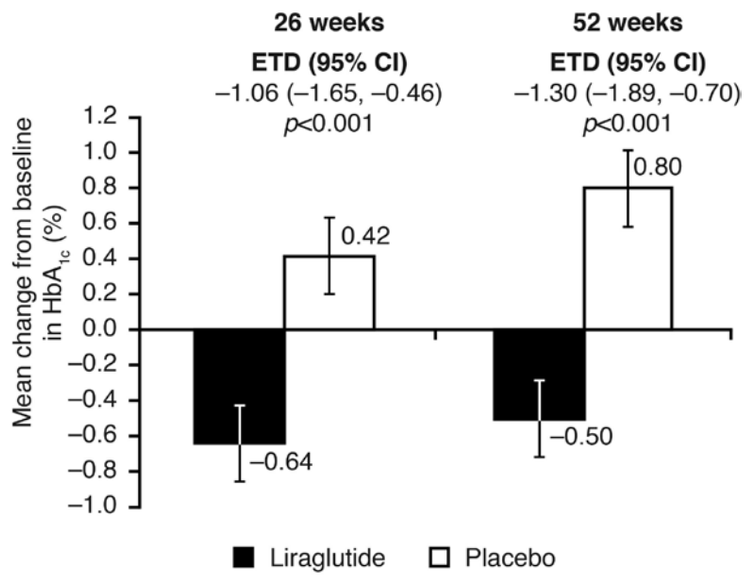
Background and aims: Despite the T2D burden in children and adolescents, metformin and insulin are the only agents currently approved for this age group. The ellipse trial assessed the efficacy and safety of liraglutide vs. placebo when added to metformin, with or without basal insulin, as a new treatment option for youth with T2D.

Materials and methods: In ellipse, children aged 10 to <17 years were randomised 1:1 to liraglutide up to 1.8 mg/day (or max. tolerated dose) or placebo for a 26-week, double-blind period, followed by a 26-week open label extension for additional data collection (total 52 weeks). Inclusion criteria: BMI >85th percentile of the general age- and gender-matched population; HbA_{1c} ≥7.0% and ≤11% if diet- and exercise-treated or ≥6.5% and ≤11% if treated with metformin and/or basal insulin. Primary endpoint: HbA_{1c} change from baseline at 26 weeks. Secondary endpoints included change in fasting plasma glucose (FPG). Safety was assessed throughout the trial.

Results: Of 135 children randomised, 134 were exposed to treatment (liraglutide 66; placebo 68). Mean age: 14.6 yrs (SD: 1.7 yrs; range: 10.0–16.9 yrs; 30% aged 10–14 yrs), 62% were female. Demographics were similar in both groups. At 26 weeks (primary endpoint), HbA_{1c} decreased from 7.87% to 7.13% with liraglutide and increased from 7.69% to 8.19% with placebo (estimated treatment difference [ETD]: –1.06%; 95% CI 1.65, 0.46; p<0.001; **Figure**). Similarly, after 52 weeks, HbA_{1c} decreased with liraglutide and increased with placebo (ETD: –1.30%; 95% CI 1.89, –0.70; p<0.001; **Figure**). Liraglutide also decreased FPG at 26 and 52 weeks (–1.1 and –1.0 mmol/L, respectively) versus increases with placebo (+0.8 and +0.8 mmol/L respectively). The percentage of children who reported an adverse event (AE) was similar in both groups (84.8% vs. 80.9% with liraglutide vs. placebo, respectively). Gastrointestinal AEs were more frequent with liraglutide (33.3%) than placebo (13.2%).

Conclusion: Liraglutide at doses up to 1.8 mg/day (when added to metformin ± basal insulin) offers a new, efficacious and durable treatment option, with an acceptable safety profile, for children and adolescents with T2D in need of improved glycaemic control.

Figure. Mean change from baseline in HbA_{1c}, estimate from primary analysis



Error bars represent standard error. ETD, estimated treatment difference

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