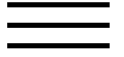


Liraglutide once a day versus exenatide twice a day for type 2 diabetes: a 26-week randomised, parallel-group, multinational, open-label trial (LEAD-6.

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Liraglutide once a day versus exenatide twice a day for type 2 diabetes: a 26-week randomised, parallel-group, multinational, open-label trial (LEAD-6)

Prof John B Buse MD ^a ... for the LEAD-6 Study Group

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Summary

Background

Unlike most antihyperglycaemic drugs, glucagon-like peptide-1 (GLP-1) receptor agonists have a glucose-dependent action and promote weight loss. We compared the efficacy and safety of liraglutide, a human GLP-1 analogue, with exenatide, an exendin-based GLP-1 receptor agonist.

Methods

Adults with inadequately controlled type 2 diabetes on maximally tolerated doses of metformin, sulphonylurea, or both, were stratified by previous oral antidiabetic therapy and randomly assigned to receive additional liraglutide 1.8 mg once a day (n=233) or exenatide 10 µg twice a day (n=231) in a 26-week open-label, parallel-group, multinational (15 countries) study. The primary outcome was change in glycosylated haemoglobin (HbA_{1c}). Efficacy analyses were by intention to treat. The trial is registered with [ClinicalTrials.gov](https://clinicaltrials.gov), number [NCT00518882](https://clinicaltrials.gov/ct2/show/study/NCT00518882).

Findings

Mean baseline HbA_{1c} for the study population was 8.2%. Liraglutide reduced mean HbA_{1c} significantly more than did exenatide (8.12% [SE 0.08] *vs* 8.79% [0.08]; estimated treatment difference -0.67; 95% CI -0.47 to -0.87; *p*<0.0001) and more patients achieved a HbA_{1c} value of less than 7% (54% *vs* 43%, respectively; odds ratio 2.02; 95% CI 1.31 to 3.11; *p*=0.0015). Liraglutide reduced mean fasting plasma glucose more than did exenatide (1.61 mmol/L [SE 0.20] *vs* 0.60 mmol/L [0.20]; estimated treatment difference 1.01 mmol/L; 95% CI 0.37 to 1.65; *p*<0.0001) but postprandial glucose control was less effective after breakfast and dinner. Both drugs promoted similar weight losses (liraglutide 3.24 kg *vs* exenatide 2.87 kg). Both drugs were well tolerated, but nausea was less persistent (estimated treatment rate ratio 0.448, *p*<0.0001) and minor hypoglycaemia less frequent with liraglutide than with exenatide (1.93 *vs* 2.60 events per patient per year; rate ratio 0.55; 95% CI 0.34 to 0.88; *p*=0.0131; 25.5% *vs* 33.6% had minor hypoglycaemia). Two patients taking both exenatide and a sulphonylurea had a major hypoglycaemic episode.

Interpretation

Liraglutide once a day provided significantly greater improvements in glycaemic control than did exenatide twice a day, and was generally better tolerated. The results suggest that liraglutide might be a treatment option for type 2 diabetes, especially when weight loss and risk of hypoglycaemia are major considerations.

Funding

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