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

An international, randomised, parallel-group, multinational, open-label trial (LEAD-6).
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\textsubscript{1c}). Efficacy analyses were by intention to treat. The trial is registered with ClinicalTrials.gov, number NCT00518882.

Findings
Mean baseline HbA\textsubscript{1c} for the study population was 8.2%. Liraglutide reduced mean HbA\textsubscript{1c} significantly more than did exenatide (−1.12% [SE 0.08] vs −0.79% [0.08]; estimated treatment difference −0.33; 95% CI −0.47 to −0.18; p<0.0001) and more patients achieved a HbA\textsubscript{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 −1.37 to −0.65; 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
Novo Nordisk A/S.
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, the presented content analysis is psycholinguistic in its basis, thus the suspension is determined.

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