Volume 374, Issue 9683, 4â€“10 July 2009, Pages 39-47

Articles

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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https://doi.org/10.1016/S0140-6736(09)60659-0

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 1Â·8 mg once a day (n=233) or exenatide 10 Î¼g 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, number NCT00518882.

Findings

Mean baseline HbA_{1c} for the study population was 8Â·2%. Liraglutide reduced mean HbA_{1c} significantly more than did exenatide (â^'1Â·12% [SE 0Â·08] *vs* â^'0Â·79% [0Â·08]; estimated treatment difference â^'0Â·33; 95% CI â^'0Â·47 to â^'0Â·18; p<0Â·0001) and more patients achieved a HbA_{1c} value of less than 7% (54% *vs* 43%, respectively; odds ratio 2Â·02; 95% CI 1Â·31 to 3Â·11; p=0Â·0015). Liraglutide reduced mean fasting plasma glucose more than did exenatide (â^'1Â·61 mmol/L [SE 0Â·20] *vs* â^'0Â·60 mmol/L [0Â·20]; estimated treatment difference â^'1Â·01 mmol/L; 95% CI â^'1Â·37 to â^'0Â·65; p<0Â·0001) but postprandial glucose control was less effective after breakfast and dinner. Both drugs promoted similar weight losses (liraglutide â^'3Â·24 kg *vs* exenatide â^'2Â·87 kg). Both drugs were well tolerated, but nausea was less persistent (estimated treatment rate ratio 0Â·448, p<0Â·0001) and minor hypoglycaemia less frequent with liraglutide than with exenatide (1Â·93 *vs* 2Â·60 events per patient per year; rate ratio 0Â·55; 95% CI 0Â·34 to 0Â·88; p=0Â·0131; 25Â·5% *vs* 33Â·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.

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