Liraglutide is Moderately Superior To Exenatide In Improving Glycemic Control In Patients With Type-2 Diabetes.

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June 27, 2018 – Liraglutide therapy was moderately superior in improving glycemic control in type-2 diabetes patients compared with exenatide, although both treatments significantly lowered their glucose levels, a phase 3, randomized study reported.

John B. Buse, MD, with the University of North Carolina, School of Medicine at Chapel Hill reported the findings of a multinational, head-to-head comparison study in the November 7th, 2012 issue of the journal *The Lancet*.

Glucagon-**l**ike **p**eptide-**1** (GLP-1) is a naturally occurring hormone that is responsible for increased secretion of insulin and promoting insulin sensitivity. This mechanism is particularly relevant immediately after a meal when levels of glucose in the body are elevated. GLP-1 is susceptible to protease degradation in healthy individuals and patients with type 2- diabetes. Synthetic GLP-1 receptor agonists serve as a treatment option for type 2-diabetes because they mimic GLP-1 activity and are resistant to degradation by proteases.

Liraglutide (Victoza) and exenatide (Bydureon) are two GLP-1 receptor agonists that have been approved as antihyperglycemic drugs for patients with type-2 diabetes. In this open-label study, researchers compared the safety and efficacy of liraglutide and exenatide treatment in the reduction of HbA_{1c} levels – an indicator of long-term blood glucose levels.

The patients analyzed in this study had sub-optimum glycemic control despite lifestyle changes and use or oral antihyperglycemic drugs such as metformin, sulfonylurea, pioglitazone or a combination thereof.

A total of 911 patients were randomly assigned in a 1:1 ratio to receive injections of either liraglutide, once-daily (1.8mg; n=450) or exenatide, once-weekly (2mg; n=461) for 26 weeks. Liraglutide dosage was gradually increased from 0.6mg/day to 1.8mg/day within 4 weeks after which the patients continued to receive 1.8mg/day.

The randomization was also stratified based on sulfonylurea treatment, levels of HbA_{1c} and the country.

The primary end-point of the study was change in HbA_{1c} levels at week 26 compared to their baseline measurement.

The number of patients achieving normal HbA1c levels (< 7%), weight changes, safety, tolerability, fasting serum glucose concentrations, blood pressure, serum lipid concentrations, and patient-reported outcomes served as secondary endpoints.

Patients in both the groups exhibited a clinically relevant reduction in HbA_{1c} levels. The reachers reported the decrease as percent (%) least-squares mean change.

At 26 weeks, change in HbA_{1c} levels were greater in liraglutide group (-1·48%, standard error SE 0·05) than in the exenatide group (–1·28%, SE 0·05), although the treatment difference did not meet the statistical

non-inferiority criteria. Also, irrespective of the body mass index, patients in the liraglutide group lost more weight (-3.57 %, SE 0.18) compared with the exenatide group (-2.68 %, SE 0.18). All the stratified groups showed comparable results.

In the liraglutide group, 60 % of the patients achieved normal HbA_{1c} levels by 26 weeks compared with 53% in exenatide group. Similar results were observed in fasting serum glucose levels.

Reduction in blood pressure and serum lipid concentrations were reported in both groups. However, no significant difference was observed between the two groups.

A larger number of patients reported adverse events in the liraglutide group (68%) than in the exenatide group (61%). The most common adverse events reported were nausea, diarrhea, and vomiting.

Dr. Buse and colleagues concluded, "The differences noted between the clinical efficacy of liraglutide once daily and exenatide once weekly at the doses tested, together with frequency and method of injection, can be used by clinicians in shared decision making for treatment of patients with type 2 diabetes uncontrolled by oral anti hyperglycaemic drugs."

The study is registered with Clinicaltrials.gov - NCT01029886

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Buse JB, Nauck M, Forst T, et. al. **Exenatide once weekly versus liraglutide once daily in patients with type 2 diabetes (DURATION-6): a randomised, open-label study**. *Lancet*. 2013 Jan; 381(9861):117-124.