Use of Liraglutide in the Real World and Impact at 36 Months on Metabolic Control, Weight, Lipid Profile, Blood Pressure, Heart Rate, and Renal Function

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ABSTRACT

Purpose: An observational retrospective study was conducted by 2 diabetes clinics in Italy to assess patterns of use and long-term effectiveness of liraglutide on established and emerging parameters.

Methods: Data from 261 patients with type 2 diabetes who started treatment with liraglutide between 2010 and 2014 were collected. Hierarchical linear regression models were applied to assess trends over time of clinical parameters. Factors associated with higher likelihood of dropout were identified through multivariate logistic analysis.

Findings: Liraglutide was initiated as a switch in 42.5% of patients and as an add-on in 49.8%; in 7.7% of the patients initiation of liraglutide was associated with a reduction in the number of pharmacologic agents. A statistically significant reduction after 36 months was found for the following parameters (mean change [95% CIs]): glycosylated hemoglobin (HbA_{1c}; –1.01% [1.34% to –0.68%]), fasting blood glucose (–27.5 [–40.6 to –14.4] mg/dL), weight (–2.9 [–4.5 to –1.3] kg), body mass index (–1.13 [–1.76 to –0.50] kg/m^2), waist circumference (–1.74 [–3.85 to –0.37] cm), and LDL-C (–24.7 [–36.67 to –12.8] mg/dL). Improvements in systolic (–3.5 mm Hg) and diastolic (–2.3 mm Hg) blood pressures were observed at 24 months. Albuminuria was reduced by –16.6 mg/L during 36 months, although statistical significance was not reached. Glomerular filtration rate and heart rate were unchanged. Reductions in HbA_{1c} between –0.6% and –1.3% were obtained in specific subgroups. Treatment was effective also in patients with >20 years of diabetes duration, although the likelihood of dropout was 6% higher for each additional year of disease duration (RR = 1.06; 95% CI, 1.01–1.12). The likelihood of dropout was almost four times higher for subjects treated with insulin (RR = 3.82; 95% CI, 1.22–11.96) and more than twice for those treated with sulfonylureas (RR = 2.39; 95% CI, 1.16–4.94) compared with patients not treated with these agents.

Implications: Liraglutide used in routine clinical conditions maintains its effectiveness on metabolic control and weight after 3 years. Improvements in terms of metabolic control were found when liraglutide was used as both switch and add-on treatment. In addition, improvements were sustained when

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liraglutide replaced sulfonylureas or insulin. Diabetes duration had no impact on drug efficacy. Long-term benefits relative to blood pressure and LDL-C were also found, which could not be entirely explained by antihypertensive/lipid-lowering treatment intensification. No major effect on renal parameters was documented. Diabetes duration and some concomitant treatments were associated with a higher likelihood of liraglutide discontinuation. These data can contribute to improve appropriateness and cost-effectiveness profile of liraglutide. (*Clin Ther.* 2017;39:159–169)

Key words: effectiveness, liraglutide, real world, type 2 diabetes.

INTRODUCTION

Among the new available therapies for type 2 diabetes (T2D), liraglutide represents an attractive option due to its efficacy on glycosylated hemoglobin (HbA_{1c}) and weight, associated with a low risk of hypoglycemia and cardiovascular tolerability. Liraglutide belongs to the class of glucagon-like polypeptide receptor agonists (GLP-1 RAs), and in head-to-head comparisons, it emerged as one of the GLP-1 RAs determining the largest reduction in HbA_{1c} and weight, with a low frequency of adverse reactions.[1] However, after 6 years from the publication of the first LEAD studies,[2] further research is still required to clarify some aspects of the therapy with liraglutide. In particular, key open questions can be represented by (1) the long-term effectiveness of liraglutide when used in real-world settings on patients with T2D and in specific subgroups (eg, patients with very longstanding diabetes or patients treated with different antihyperglycemic agents before or in combination with liraglutide); (2) the impact of liraglutide on additional clinical parameters, that is, not only blood pressure and lipid profile, but also new emerging parameters such as heart rate (HR) and renal function; and (3) how to improve the cost-effectiveness profile of treatment.

In the absence of large observational postmarketing studies, several small observational studies provide information on the long-term effect of liraglutide. Two studies on the effectiveness and safety profile of liraglutide at 1 year were conducted in Italy (481 subjects) and in Belgium (245 subjects). Both studies documented that the use of liraglutide in real-world settings was associated with good metabolic response and weight loss and with additional improvements in systolic blood pressure and lipid profile.[3,4] Another Italian study (205 subjects) documented a persistent reduction of ~1% in HbA_{1c} after 24 months.[5] A 36-month follow-up was taken into consideration by a Spanish multicenter study of 753 patients, further confirming long-term benefits on glycemic control, weight, blood pressure, and lipid profile.[6]

Relative to the additional effects of liraglutide, a series of network meta-analyses conducted by Sun F et al[7–9] took into account data from 16 to 35 randomized clinical trials (RCTs) to assess the impact of GLP-1 RAs on blood pressure and HR, lipid profile, and waist circumference (WC). They found that GLP-1 RAs were associated with a modest reduction of blood pressure; a slight increase in HR; modest reductions in LDL-C, total cholesterol, and triglycerides but no significant improvement in HDL-C. Furthermore, some GLP-1 RAs, especially liraglutide at doses of 1.8 and 1.2 mg daily, were associated with a significant reduction in WC.[7–9]

Moreover, with data from animal studies, recent small human observational studies are indicating improvements in renal outcomes (estimated glomerular filtration rate [eGFR] and microalbuminuria) after a prolonged treatment with liraglutide.[10]

Regarding the cost-effectiveness of liraglutide, a study documented that adherence and persistence to this agent are associated with improved HbA_{1c} outcomes and lower medical costs versus liraglutide discontinuation.[11] Therefore, identification of patients more likely to be adherent and persistent is important to improve the cost-effectiveness of therapy.

The aim of this study was to assess patterns of use of liraglutide, its effectiveness on established and emerging parameters after 36 months, and to explore factors associated with liraglutide discontinuation.

PATIENTS AND METHODS

This is an observational retrospective study based on clinical data stored in the electronic medical records of 2 diabetes outpatient clinics in Italy. Data of all consecutive patients who have been treated with liraglutide under routine clinical practice conditions were retrospectively evaluated. Data on age; sex; diabetes duration; HbA_{1c}; fasting blood glucose