Liraglutide 1.2 mg vs. sitagliptin 100 mg as add-on to metformin treatment for type 2 diabetes mellitus: short-term cost-per-controlled-patient in Italy

1. **Antonio Ramirez de Arellano**
Novo Nordisk, Madrid, Spain
2. **Roberta Montagnoli**
Novo Nordisk, Rome, Italy
3. **Maria Giovanna Ferrario**
Outcomes'10, Castellón, Spain
4. **Luis Lizán**
Universidad Jaume I, Castellón, Spain

Abstract

Objective: To estimate the short-term cost per controlled patient with type 2 diabetes mellitus (T2DM) with liraglutide 1.2mg/day vs. sitagliptin 100mg/day in Italy. **Methods**: A composite endpoint defined as "HbA_{1c}<7% AND no weight gain AND no hypoglycemia" was adopted to describe the controlled T2DM patient. The percentage of patients achieving this composite endpoint at 26 and 52 weeks with liraglutide and sitagliptin, as well as that of patients switching at 52 weeks from sitagliptin to liraglutide up to 78 weeks was considered. Treatment cost was calculated from the perspective of the Italian National Health System over a 26-, 52- and 78- time horizon. The cost-effectiveness primary outcome was the cost per patient achieving the composite endpoint. **Results**: Despite the daily cost ratio of 2.30 between liraglutide and sitagliptin, at 26-week liraglutide resulted in a lower cost per controlled patient, both with efficacy data extracted from the clinical trial data (€1,460 vs. €1,820) and from a meta-analysis of available liraglutide trials (€1,593 vs. €2,234). At 52 weeks, liraglutide cost per controlled patient is also slightly lower than with sitagliptin (€2,627 vs. €2,649). At 78 weeks, in patients who have switched from sitagliptin to liraglutide at 52 weeks, the cost per controlled patient is lower than that of the patient controlled with 78 weeks of sitagliptin treatment (€2,889 vs. €3,970). **Conclusions**: These results indicate that, due to higher effectiveness, liraglutide at 1.2mg/day is associated to better cost-effectiveness than sitagliptin 100mg/day at 26 and 52 weeks. Moreover, switching patients from sitagliptin to liraglutide results in a clinical benefit that lowers the cost per controlled patient with respect to 78-weeks of sitagliptin treatment.

Introduction

- Diabetes mellitus is a multifactorial metabolic disorder which is characterized by chronic hyperglycemia with modification of carbohydrate, fat and protein metabolism.[1]
- The prevalence of diabetes in Italy is currently 4.9% in the adult population[2] (almost 3 million people), of which about 90% have type 2 diabetes mellitus (T2D).[3] The direct costs of diabetes in Italy are estimated to be €9 billion, representing 9% of the total expenditure of the National Health System, and 50% of the cost is due to hospitalizations.[3]
- The key to successfully treating T2D includes maintaining glycemic control, minimizing the risk of hypoglycemia, controlling cardiovascular risk factors and reducing or controlling body weight,[4] thus reducing the risk of complications.
- The new generation of antidiabetic drugs, namely glucagon-like peptide-1 (GLP-1) receptor agonists, (e.g. liraglutide), and dipeptidyl-peptidase-4 inhibitors (DPP-4is) (e.g. sitagliptin), are associated with improved glycemic control and weight loss (DPP-4is are weight-neutral), thereby meeting some of the complex needs of patients with T2D.[5]
- The efficacy of liraglutide (1.2 mg and 1.8 mg/day) vs. sitagliptin as add-on treatment to metformin has been assessed in the parallel-group, open-label LIRA-DPP-4 clinical trial.[6,7,8] Results showed that significantly more patients in both liraglutide treatment groups, compared to those in the sitagliptin group, reached the composite endpoint: Hb_{A1c}<7% without hypoglycemia and without weight gain.[9]
- The aim of the present analysis is to evaluate the short-term cost-per-controlled-patient in Italy of liraglutide 1.2 mg/day vs. sitagliptin 100 mg/day.

Methods

Cost-effectiveness outcomes

- "Cost-per-controlled-patient" was defined as the cost of a patient achieving the composite endpoint "reaching a glycemic target of HbA_{1c} <7% without hypoglycemia and without weight gain" over the considered time horizon.

Treatment cohorts and time horizons

- Liraglutide (1.2 mg/day) vs. sitagliptin (100 mg/day) at 26 and 52 weeks, and sitagliptin switched to liraglutide at 52 vs. sitagliptin at 78 weeks.

Efficacy data

- Clinical efficacy data: from the LIRA-DPP-4 head-to-head liraglutide vs. sitagliptin randomized clinical trial (RCT), and a meta-analysis (MA) of RCTs of liraglutide vs. different comparators (Figure 1).

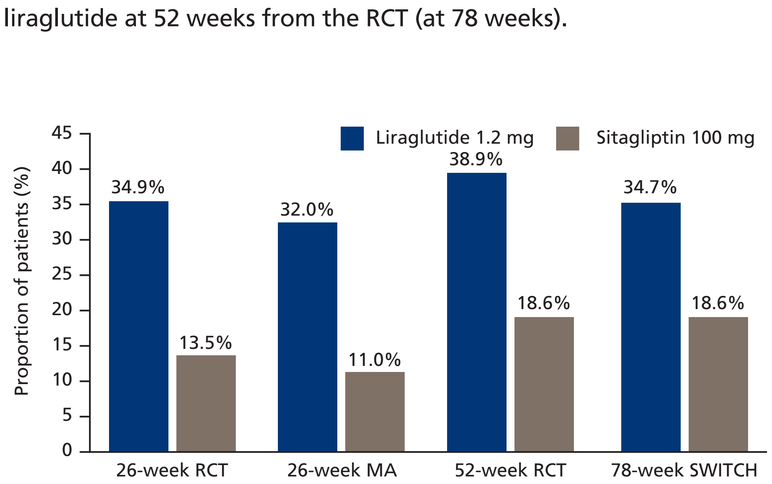
Costs

- Pharmacy costs of €2.80/day and €1.35/day were used for liraglutide 1.2 mg and sitagliptin 100 mg, respectively, expressed as ex-factory prices discounted by 5%.[10]

Sensitivity analysis

- The two key variables of the model were varied in a series of one-way sensitivity analyses (OWSA) to assess the impact on cost per patient achieving the endpoint: efficacy values (increased and decreased by 20% on the 26- and 78-week horizon, while on the 52-week horizon varied between the lower and upper limits of the 95% confidence interval) and daily treatment costs (increased and decreased by 5% with respect to the reference value, which represents realistic discounts that may be applied on antidiabetic drugs by the government or local administrations).

Figure 1 Proportion of patients reaching glycemic target of HbA_{1c} <7% without hypoglycemia and no weight gain at 26 weeks with either data from the LIRA-DPP-4 trial or the meta-analysis, at 52 weeks from the RCT, and after switching from sitagliptin to liraglutide at 52 weeks from the RCT (at 78 weeks).



MA, meta-analysis; RCT, randomized clinical trial.

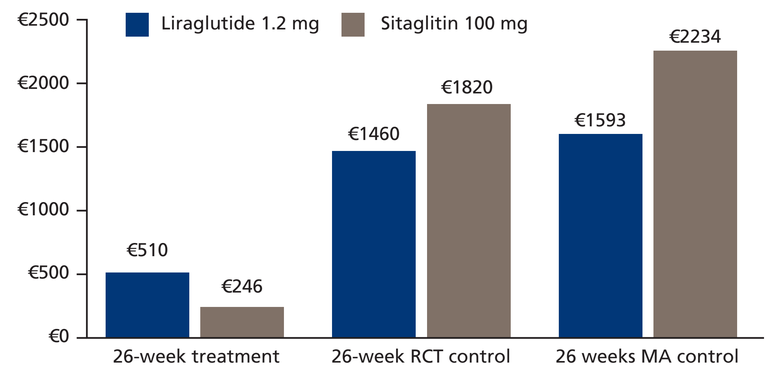
Results

- Although the daily acquisition cost for liraglutide 1.2 mg is 2.3 times higher than sitagliptin, the cost-per-controlled-patient after 26, 52 and 78 weeks with liraglutide 1.2 mg is lower than that with sitagliptin.

26-week

- The cost-per-controlled-patient after 26 weeks is lower for liraglutide than for sitagliptin, being the ratio 0.9 and 0.8, when using RCT and MA data, respectively (Figure 2).

Figure 2 Cost per treated patient (treatment) and cost-per-controlled-patient (control) with efficacy data from either the LIRA-DPP-4 (RCT) or the meta-analysis (MA) at 26 weeks.



MA, meta-analysis; RCT, randomized clinical trial.

52-week

- The higher efficacy shown by liraglutide over a 52-week treatment allows compensating the investment in pharmacy cost, resulting in a similar cost-per-controlled-patient for both treatments (cost ratio=0.99, Figure 3).

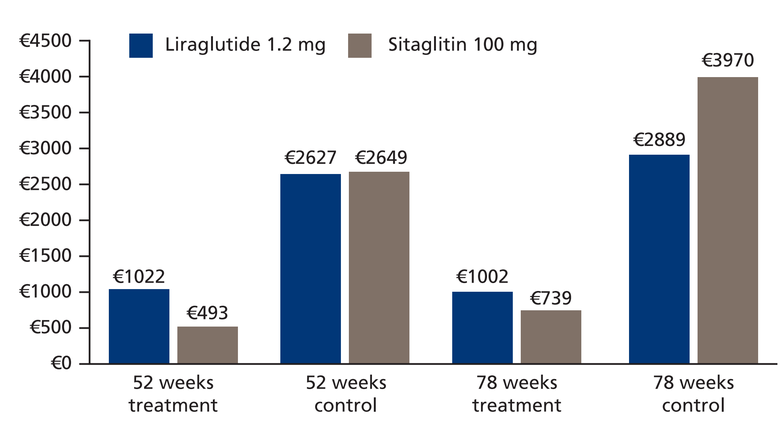
78-week

- The cost of a patient treated for 78 weeks with sitagliptin is lower than that of a patient switched from sitagliptin to liraglutide at week 52, due to the lower daily cost of sitagliptin (cost ratio over 78 weeks=1.36). However, the cost-per-controlled-patient is lower at 78 weeks for the sitagliptin-to-liraglutide switch arm (cost ratio over 78 weeks=0.72).

Sensitivity analysis

- At 26 weeks, when the efficacy outcome variable for either comparison arm is increased or decreased by 20%, liraglutide 1.2 mg always comes out as the most cost-effective treatment.
- At 52 weeks, either using the lower efficacy outcome for liraglutide 1.2 mg or the upper for sitagliptin results in a lower cost-per-controlled-patient for sitagliptin, while the reverse is strongly favorable to liraglutide.
- At 78 weeks, changing efficacy either in the 78-week sitagliptin arm or in the sitagliptin-to-liraglutide switch arm yields lower cost-per-controlled-patient for the switch cohort.

Figure 3 Cost per treated patient (treatment) and cost-per-controlled-patient (control) at 52 weeks and at 78 weeks after switching or not from sitagliptin to liraglutide 1.2 mg at week 52.



- Increasing or decreasing the daily treatment cost of either liraglutide 1.2 mg or sitagliptin by 5%, always results in lower cost-per-controlled-patient for liraglutide, except when either increasing liraglutide cost or decreasing sitagliptin cost by 5%. However, in this case, cost-per-controlled-patient variation is limited.

Limitations

- This estimation reduces the cost and benefit of treating T2D patients to the essential components of the efficacy and treatment cost of just one intervention, while, of course, clinical practice is much more complex. However, it is a simple and direct way to consider cost effectiveness in diabetes treatment.
- Adherence to the study medications was assumed to be 100% in both treatment groups, which is never achieved in clinical practice. However, a recently published observational study carried out in Italy reported a similar percentage of patients reaching the composite endpoint, indicating that, in the real world, liraglutide results should not differ very much from the estimated.

References

1. Rydén *et al. Eur Heart J* 2013;34:3035–87.
2. Istituto Nazionale di Statistica (ISTAT). Available at: www.istat.it/it/archivio/71090. Last accessed: Nov 2014.
3. Consorzio Mario Negri Sud. Available at: www.changingdiabetesbarometeritaly.com/pdf/documenti2011/Fact-and-figure-2011.pdf. Last accessed: Nov 2014.
4. Nathan *et al. Diabetes Care* 2006;29:1963–72.
5. Mezquita Raya *et al. Diabetes Ther* 2013;4:417–30.
6. Pratley *et al. Lancet* 2010;375:1447–56.
7. Pratley *et al. Int J Clin Pract* 2011;65:397–407.
8. Pratley *et al. Diabetes Care* 2012;35:1986–93.
9. Langer *et al. J Manag Care Pharm* 2013;19:237–46.
10. AIFA. Available at: www.agenziafarmaco.gov.it/it /content/tabelle-farmaci-di-classe-e-h-al-15102014. Last accessed: Nov 2014.

Conclusions

- Despite the higher acquisition cost (2.3 times higher for liraglutide 1.2 mg than for sitagliptin), the cost-per-controlled-patient (HbA_{1c} <7%, without hypoglycemia and no weight gain) of liraglutide 1.2 mg a day vs. sitagliptin 100 mg a day in Italy is lower at 26 weeks, both when estimates are based on the LIRA-DPP-4 results or a meta-analysis of 6 RCTs including LIRA-DPP-4, while it is very similar for both treatments at 52 weeks.
- Switching patients initially treated with sitagliptin, at week 52, to liraglutide 1.2 mg treatment yields a lower cost-per-controlled-patient at week 78. This indicates that sitagliptin-treated patients would obtain a health benefit from switching after 52 weeks to liraglutide, which would decrease the cost of control.

Scan here to view a PDF of this poster.

This analysis was sponsored by Novo Nordisk.
The authors take full responsibility for the content of the poster but are grateful to Watermeadow Medical (supported by Novo Nordisk) for poster development assistance.
Presented at the ISPOR 20th Annual International Meeting, 16–20 May 2015, Philadelphia, PA, USA.