Long-term cost effectiveness analysis of Ideglira vs GLP-1 added to basal insulin as intensification therapies in type 2 diabetes mellitus in Spain

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INTRODUCTION

- Current guidelines for the treatment of type 2 diabetes mellitus (T2DM) recommend choosing antidiabetics that control bodyweight and reduce the risk of hypoglycemia as well as they control glycemia [1].
- Liraglutide (Lira) is an analogue of the glucagon-like peptide-1 (GLP-1) that has shown HbA1c reductions between 0.8 and 1.5%, weight reduction and low hypoglycemia rates in T2DM patients uncontrolled with other oral antidiabetics both in clinical trials [2,3,4,5,6] and real-world setting [7].
- Insulin degludec (IDeg) is a long-acting insulin analogue non-inferior to insulin glargine (IGlar) in terms of long-term glycemic control in T2DM, with statistically significantly lower rates of hypoglycemia [8,9].
- Limitations related to weight gain and hypoglycemia exist, however, with the use of basal insulin regimens, while issues on the efficacy of GLP-1 analogues when used alone have also arisen [10].
- A fixed-ratio combination of IDeg and Lira (IDegLira) has been developed as a once-daily subcutaneous injection, which has shown to be effective and well tolerated and seems to counterbalance limitations of its individual components [11,12,13].

OBJETIVE

- To compare the long-term clinical and costs outcomes associated with IDegLira versus GLP-1 added to basal insulin in T2DM patients uncontrolled on basal insulin from the perspective of the Spanish National Health System (NHS).

METHODS

Model description and time horizon

- The IMS Health CORE model [14,15,16] was used to simulate the long-term (lifetime up to 50 years) outcomes of treating T2DM patients with IDegLira vs. IGlar+Lira.

Patients' characteristics

- An hypothetical cohort of 1,000 T2DM patients.
- Baseline characteristics of patients were based on patients receiving IDegLira in the DUAL II trial [13].

Treatment

- First 5 years: patients were treated with either IDegLira or IGlar+Lira **(Fig. 1)**.
- Following years: it was assumed that glycemic control failed and both treatment arms were switched to a basal-bolus insulin regimen with either IDeg or IGlar once daily intensified by insulin aspart (IAsp) thrice a day with meals **(Fig. 1)**.

Figure 1. **Treatments duration over time horizon**

Treatment efficacy and safety

- Fist year: due to the lack of head-to-head data for IDegLira, efficacy and safety were estimated by indirect comparison by means of a pooled analysis of patient-level data from patients treated with IDegLira or basal insulin plus Lira from Novo Nordisk CT databases **(Table 1)** [17].

Table 1. **Treatment effects for the first year of the simulation in uncontrolled patients on basal insulin.**

Changes from baseline	IDegLira	Basal-bolus
Changes from baseline		
HbA1c [mean (SD)]	−1.66 (0.96)	−1.32 (0.96)*
Systolic blood pressure (mmHg) [mean (SD)]	−6.86 (13.20)	−4.67 (13.20)
Total cholesterol (mg/dL) [mean (SD)]	−10.13 (30.28)	−12.66 (30.28)
HDL cholesterol (mg/dL) [mean (SD)]	0.52 (6.79)	−0.77 (6.79)
LDL cholesterol (mg/dL) [mean (SD)]	−6.85 (23.83)	−9.07 (23.83)
Triglycerides (mg/dL) [mean (SD)]	−25.74 (103.71)	−18.99 (103.71)
Body mass index (kg/m2) [mean (SD)]	−1.04 (1.34)	−1.29 (1.34)
Event rate		
Severe hypoglycemia [events per 100 patient/year]	0.84	0.00
Non-severe hypoglycemia[events per 100 patient/year]	125.05	124.46

*Statistically significant difference; SD: standard deviation

- Years 1-to-5: Benefits in terms of HbA1c and weight were assumed to persist while patients receive initial therapies and were annulled after treatment switching. Blood pressure and serum lipids effects followed the natural progression algorithms built into the CORE Diabetes Model.
- Following years: HbA1c and weight benefits in both arms were replaced with those associated with basal-bolus insulin regimen.

Resource use, costs and perspective

- Costs (in €, 2013) were computed from the perspective of the Spanish NHS.
- Pharmacy, diabetes-related complications and concomitant patient management costs were included.
- Spanish pharmacy discounted ex-factory cost per day with IDegLira and IGlar+Lira were €5.09 and €5.83, respectively, which included the cost of medication plus metformin 1,500mg/day, needles (1 and 2/day, respectively), and one self-monitoring blood glucose (SMBG) strip and lancet test per day.
- After therapy intensification, the cost of IGlar was assumed for the basal insulin treatment and the use of 4 SMBG tests a day was assumed giving a total cost of €4.98/day for both arms.
- Patient management was assumed to be the same in both treatment arms and included concomitant medications (aspirin, statins and angiotensin-converting enzyme (ACE) inhibitors), screening for renal disease, retinopathy and diabetic foot complications, and post-complication management.
- The cost of diabetes-related complications in the year of event and during the years of follow-up were identified through literature reviews and searches of Spanish diagnosis-related groups.

Utilities

- The additive CORE Default Method was applied, which implies taking the lowest utility associated with existing complications and subtracting utilities for events that occur in that year, estimating annual utility scores for each simulated patient [14].

Discounting

- A yearly discount rate of 3% in costs and utilities was applied.

Outcomes

- The lifetime (50 years) outcomes estimated (1,000 simulations) by the model were: life years (LY), quality-adjusted life years (QALY), cumulative incidence of diabetes-related complications, time to onset of diabetes-related complications and costs, incremental cost-effectiveness ratio (ICER) and incremental cost-utility ratio (ICUR).

Sensitivity analysis

- One-way sensitivity analysis (OWSA) tested the impact on ICER and ICUR of the main model variables.
- Probabilistic sensitivity analysis (PSA) was also performed. Cohort characteristics, treatment effects, complication costs and utilities were sampled from distributions and 1,000 cohorts of 1,000 patients were simulated using a second order Monte Carlo approach.

RESULTS

Long-term effectiveness

- IDegLira was associated with an improvement of 0.06 LYS and 0.07 QALYs compared to IGlar+Lira **(Table 2)**, resulting from a reduced incidence of diabetes-related complications.
- IDegLira was associated with a delayed onset of micro- and macrovascular complications, with a mean time 0.3 years longer than with IGlar+Lira.

Long-term costs

- The mean direct medical cost per patient with IDegLira was €1,729 less than with IGlar+Lira **(Table 2)**, due mainly to the lower acquisition cost of IDegLira over the first 5 years (€26,422 vs. €27,501).
- Further cost savings were associated to avoided treatment of diabetes-related complications (IDegLira: €15,646 vs. IGlar+Lira: €16,307), particularly ulcer and neuropathy complications.

Long-term cost-effectiveness

- IDegLira was dominant over IGlar+Lira as it was more effective and less costly **(Table 2)**.

Table 2. **Long-term cost-effectiveness results.**

	IDegLira (Mean)	Basal insulin plus liraglutide (Mean)	Difference
LYs	14.34	14.28	0.06
QALYs	9.25	9.18	0.07
Discounted direct costs (€)	53,984	55,713	-1,729
ICER (€/LY)			Dominant
ICUR (€/QALY)			Dominant

Sensitivity analysis

- All variables tested in the OWSA gave dominant ICER and ICUR for IDegLira except for insulin daily dose that resulted in an ICUR of €3,553/QALY, which can be considered cost-effective for Spain (commonly accepted threshold €30,000/QALY).
- In PSA, the majority of the simulations fell into the dominant quadrant **(Fig. 2)**, and the 75.4% of the simulation was cost-effective with a willingness-to-pay threshold of €30,000/QALY **(Fig. 3)**.

Figure 2. **Cost-effectiveness scatterplot from the probabilistic sensitivity analyses.**

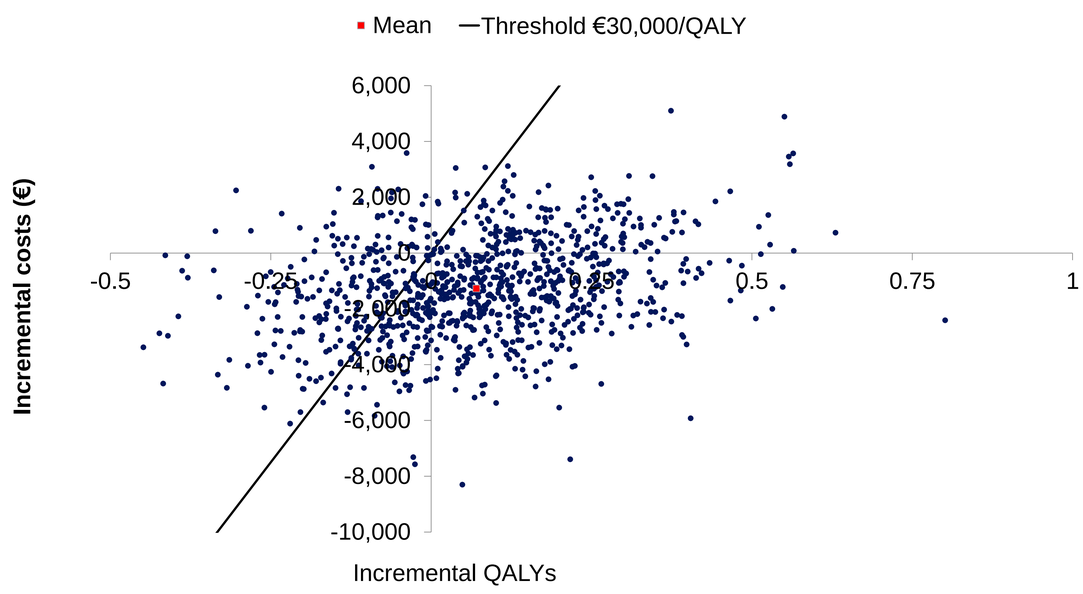
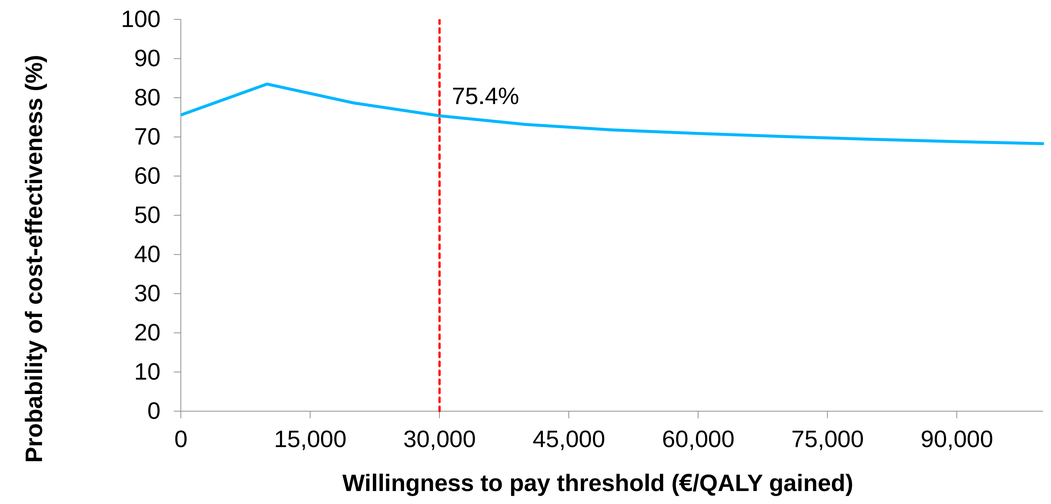


Figure 3. **Cost-effectiveness acceptability curve from the probabilistic sensitivity analysis.**



CONCLUSION

IDegLira is a less costly and more effective alternative for the treatment of patients with T2DM uncontrolled on basal insulin compared with GLP-1 added to basal insulin (IGlar+Lira), from the perspective of the National Health System in Spain.

REFERENCES

1. AACE/ACE. Endocr Pract. 2015;21(4):e1-10; 2. Marre M et al.; LEAD-1 SU Study Group. Diabet Med. 2009;26:268–78; 3. Nauck M, et al. Diabetes Care. 2009;32:84–90.Rodbard HW, et al. Lancet Diabetes Endocrinol. 2014;2(1):30-7; 4. Garber A, et al. Lancet; 5. Zinman B et al., LEAD-4 Study Investigators. Diabetes Care; 6. Russell-Jones D, et al. Diabetologia. 2009;52:2046–55; 7. Mezquita-Raya P, et al. Diabetes Ther. 2015; 6 (2):173-85; 8. NICE advice [ESNM25] Available at https://www.nice.org.uk/advice/esnm25/chapter/key-points-from-the-evidence. Accessed September 2015; 9. Zinman B, et al. Diabetes Care. 2012;35(12):2464-71; 10. Aroda VR, et al. Diabetes Metab Res Rev.2011;27(6):528-42; 11. Greig SL, et al. Drugs. 2015;75(13):1523-34; 12. Gough SC, et al.; NN9068-3697 (DUAL-I) trial investigators. Lancet Diabetes Endocrinol. 2014;2(11):885-93; 13. Buse JB, et al.; NN9068-3912 (DUAL-II) Trial Investigators. Diabetes Care. 2014;37(11):2926-33; 14. Palmer AJ, et al. Curr Med Res Opin 2004;20(Suppl): S5–26; 15. McEwan P, et al. Value Health. 2014;17(6):714-24; 16. Palmer AJ, et al. Curr Med Res Opin. 2004;20 Suppl 1:S27-40; 17. Freemantle et al. Diabetes Ther. 2015 Dec;6(4):573-91.