Long-term cost effectiveness analysis of Ideglira vs. basal-bolus insulin regimen in type 2 diabetes mellitus in Spain

1. Miriam Prades
Outcomes'10, Universidad Jaime I, Castellón, Spain
2. Luis Lizán
Outcomes'10, Universidad Jaime I, Castellón, Spain
3. Barnaby Hunt
Ossian Health Economics and Communications, Switzerland
4. Antonio Ramírez de Arellano
HEOR Europe, Novo Nordisk, Madrid, Spain

INTRODUCTION

- Patients with type 2 diabetes mellitus (T2DM) receive stepwise progressive therapeutic schemes throughout the trajectory of their disease, as treatments eventually lose their effectiveness as their condition worsens [1].
- Glucagon-like peptide-1 (GLP-1) receptor agonists (RA), such as liraglutide (Lira), are usually added to metformine, when it fails adequate glycemic control [1].
- Oral antidiabetic combinations eventually lose effectiveness in controlling blood glucose in long-run T2DM patients, thus insulinization becomes unavoidable [1].
- Basal insulin, such as degludec (IDeg) or glargine (IGlar), is the next therapeutic option for its high glycemic reduction power, and rapid insulin boluses, such as insulin aspart (IAsp) can be added at meals if basal control is insufficient. Premixed insulins are also an option [2,3].
- However, insulin therapy is associated to a series of drawbacks such as higher risk of mild and severe hypoglycemic events and more difficult weight control on one side [4], and worse patient convenience associated to multiple injected administration and self-monitoring blood glucose (SMBG) [5].
- IDegLira is the first product to combine a basal insulin (IDeg) and a GLP-1 RA, liraglutide (Lira), for the treatment of T2DM [6,7,8], combining a low hypoglycemia risk, good weight control and patient convenience (injected administration and SMBG just once a day).

OBJETIVE

- To compare the long-term cost-effectiveness of IDegLira and basal-bolus insulin as two alternative insulin intensification therapies in patients with type 2 diabetes (T2DM) 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 [9,10,11] was used to simulate the long-term (lifetime up to 50 years) outcomes of treating T2DM patients with IDegLira vs. IGlar+3xIAsp.

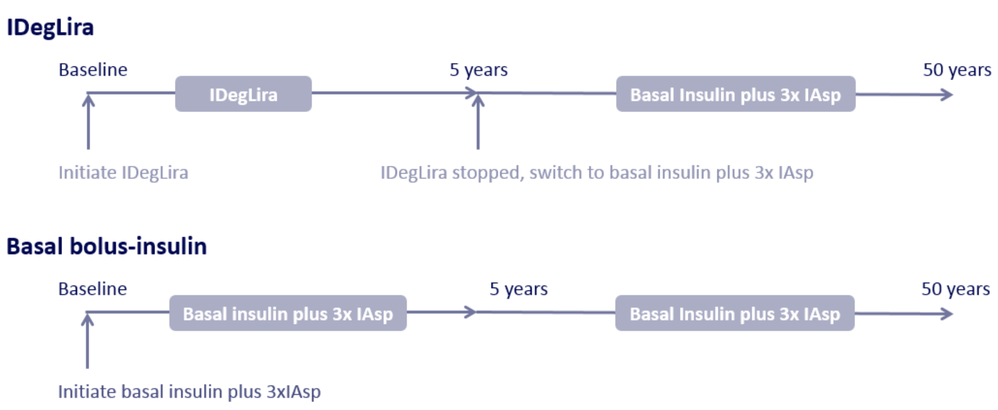
Patients' characteristics

- An hypothetical cohort of 1,000 T2DM patients.
- Baseline characteristics of patients were based on patients receiving IDegLira in the DUAL II trial [8].

Treatment

- First 5 years: patients were treated with either IDegLira or IGlar+3xIAsp **(Fig. 1)**.
- Following years: it was assumed that glycemic control with IDegLira failed and patients were switched to a basal-bolus insulin regimen with IDeg once daily intensified by IAsp thrice a day with meals **(Fig. 1)**. Patients in IGlar+3xIAsp arm continued with the same treatment regimen.

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)** [12].

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

	IDegLira	Basal-bolus
Changes from baseline		
HbA1c [mean (SD)]	−1.66 (0.96)	−1.33 (0.96)*
Systolic blood pressure (mmHg) [mean (SD)]	−6.86 (13.20)	−0.93 (13.20)*
Total cholesterol (mg/dL) [mean (SD)]	−10.13 (30.28)	1.50 (30.28)*
HDL cholesterol (mg/dL) [mean (SD)]	0.52 (6.79)	0.79 (6.79)
LDL cholesterol (mg/dL) [mean (SD)]	−6.85 (23.83)	0.08 (23.83)*
Triglycerides (mg/dL) [mean (SD)]	−25.74 (103.71)	3.82 (103.71)*
Body mass index (kg/m2) [mean (SD)]	−1.04 (1.34)	1.38 (1.34)*
Event rate		
Severe hypoglycaemia [events per 100 patient/year]	0.84	2.85
Non-severe hypoglycaemia[events per 100 patient/year]	125.05	794.63*

*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 IDegLira arm 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+3xIAsp were €5.09 and €4.98, 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 in also the IDegLira arm for the basal insulin treatment and the use of 4 SMBG tests a day was assumed giving a total cost of €4.98/day.
- 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 [9].

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 0.18 LYs and 0.36 QALYs compared to IGlar+3xIAsp **(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 0.5 years longer than with IGlar+3xIAsp.

Long-term costs

- The mean direct medical cost per patient with IDegLira was €671 less than with IGlar+3xIAsp **(Table 2)**. Even though the acquisition cost of IDegLira over the first 5 years was higher than comparator (€26,428 vs. €25,696), this was entirely offset by avoiding diabetes-related complications.
- Further cost savings were associated to avoided treatment of diabetes-related complications (IDegLira: €26,458 vs. IGlar+3xIAsp: €27,871), particularly chronic heart failure and myocardial infarction.

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-bolus (Mean)	Difference
LYs	14.35	14.17	0.18
QALYs	9.17	8.81	0.36
Discounted direct costs (€)	54,078	54,748	−671
ICER (€/LY)			Dominant
ICUR (€/QALY)			Dominant

Sensitivity analysis

- The majority of variables tested in the OWSA gave dominant ICER and ICUR for IDegLira and when this was not the case ICUR still remained beneath the cost-effectiveness threshold commonly accepted for Spain (€30,000/QALY).
- In PSA, the majority of the simulations fell into the dominant quadrant **(Fig. 2)**, and the 98.3% 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.**

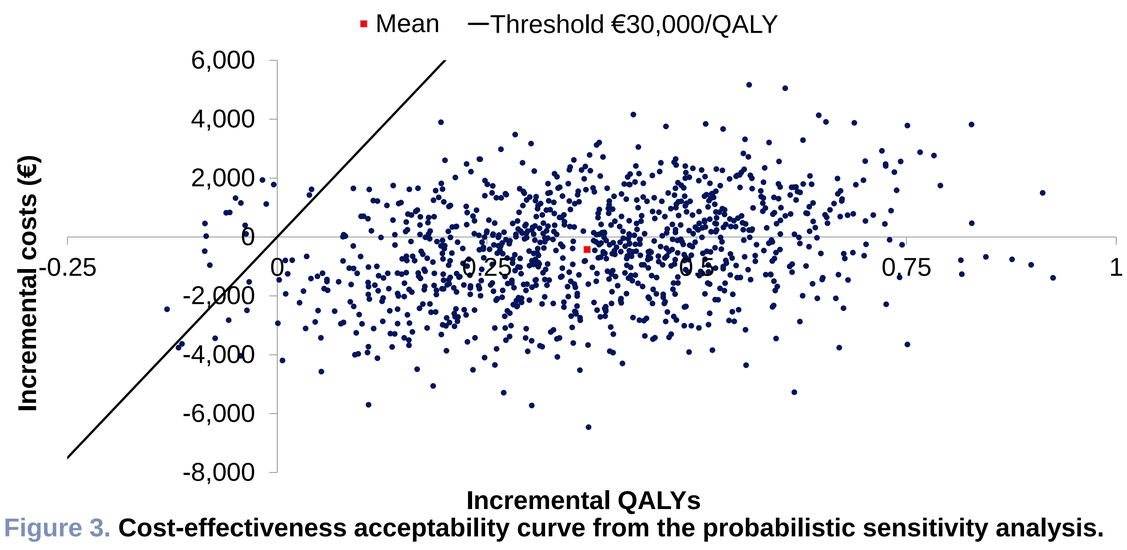
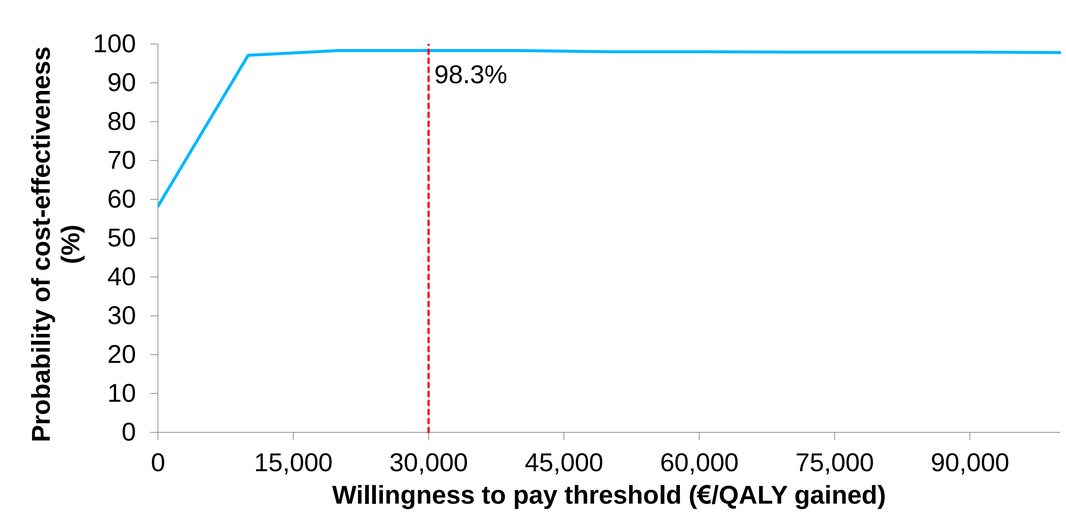


Figure 3. **Cost-effectiveness acceptability curve from the probabilistic sensitivity analysis.**



CONCLUSION

IDegLira is a less costly and more effective alternative for the treatment of patients with T2DM uncontrolled on basal insulin compared with basal-bolus insulin therapy in Spain.

REFERENCES

1. AACE/ACE. Endocr Pract. 2015;21(4):e1-10; 2. Rodbard HW, et al. Lancet Diabetes Endocrinol. 2014;2(1):30-7; 3. Vaag A, et al. Eur J Endocrinol 2012;166:159–70; 4. Zinman B, et al. Diabetes Care. 2012;35(12):2464-71; 5. Aronson R. Diabetes Technol Ther. 2012;14(8):741-7; 6. Greig SL, et al. Drugs. 2015;75(13):1523-34; 7. Gough SC, et al.; NN9068-3697 (DUAL-I) trial investigators. Lancet Diabetes Endocrinol. 2014;2(11):885-93; 8. Buse JB, et al.; NN9068-3912 (DUAL-II) Trial Investigators. Diabetes Care. 2014;37(11):2926-33; 9. Palmer AJ, et al. Curr Med Res Opin 2004;20(Suppl): S5–26; 10. McEwan P, et al; Value Health. 2014;17(6):714-24; 11. Palmer AJ, et al. Curr Med Res Opin. 2004;20 Suppl 1:S27-40; 12. Freemantle et al. Diabetes Ther. 2015 Dec;6(4):573-91.