

ORIGINAL ARTICLE

Evaluating the long-term cost-effectiveness of fixed-ratio combination insulin degludec/liraglutide (IDegLira) for type 2 diabetes in Spain based on real-world clinical evidence

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Aim: To evaluate the long-term cost-effectiveness of fixed-ratio combination insulin degludec/liraglutide (IDegLira) versus comparator regimens for type 2 diabetes in Spain, based on real-world evidence.

Materials and methods: Clinical data were taken from the European Xultophy Treatment Retrospective Audit (EXTRA) real-world evidence study in which patients failing to meet glycaemic targets were switched to IDegLira. Baseline regimens (prior to IDegLira treatment) were categorized as: multiple daily insulin injections (MDI; 28%); glucagon-like peptide-1 (GLP-1) receptor agonists in combination with insulin (24%); basal insulin (19%); GLP-1 receptor agonists (10%); and non-injectable medications (19%). The IQVIA CORE Diabetes Model was used to project long-term outcomes for patients switching to IDegLira or continuing their baseline regimens (excluding non-injectable regimens). Costs were accounted from a Spanish National Health System perspective. Future costs and clinical benefits were discounted at 3% annually and sensitivity analyses were performed.

Results: IDegLira was projected to reduce the incidence of diabetes-related complications and improve quality-adjusted life expectancy versus all four comparators. IDegLira reduced direct medical costs versus GLP-1 receptor agonists in combination with insulin, and versus GLP-1 receptor agonist therapy, and was therefore considered dominant (cost saving while improving outcomes). IDegLira was found to be cost-effective versus MDI and basal insulin with incremental cost-effectiveness ratios of EUR 3013 per quality-adjusted life-year (QALY) gained and EUR 6890 per QALY gained, respectively.

Conclusions: Long-term projections based on real-world evidence indicated that IDegLira is likely to improve clinical outcomes and reduce costs or be cost-effective compared with other injectable regimens in people with type 2 diabetes in Spain.

KEYWORDS

cost, cost-effectiveness, IDegLira, insulin, real-world evidence, Spain, type 2 diabetes

1 | INTRODUCTION

Glucagon-like peptide-1 (GLP-1) receptor agonists administered in combination with basal insulin therapy have been shown to address several of the defects seen in the pathophysiology of type 2 diabetes.¹

The combination of insulin degludec (100 units/mL) and liraglutide (3.6 mg/mL), termed IDegLira (Xultophy[®]), was approved in 2014 for the treatment of type 2 diabetes inadequately controlled with oral glucose-lowering agents alone or in combination with a GLP-1 receptor agonist or basal insulin (European indication).² In randomized

TABLE 1 Baseline characteristics of each of the four sub-groups based on the EXTRA study: Effectiveness analysis set

	MDI	Basal insulin	GLP-1 receptor agonist	GLP-1 receptor agonist in combination with insulin
Age, years	63.8 (11.2)	61.4 (10.7)	61.6 (9.3)	61.0 (10.1)
Duration of diabetes, years	16.3 (7.7)	12.4 (7.1)	11.0 (5.1)	14.1 (8.0)
HbA1c	67 (16)	67 (17)	70 (14)	67 (14)
Mmol/Mol	8.31 (1.46)	8.29 (1.55)	8.55 (1.25)	8.25 (1.27)
%				
Systolic blood pressure, mmHg	139.3 (19.1)	146.4 (21.9)	143.0 (20.2)	144.4 (18.7)
Total cholesterol, mmol/L	4.1 (0.9)	5.0 (1.7)	5.6 (1.1)	5.0 (1.3)
HDL cholesterol, mmol/L	1.3 (0.6)	1.2 (0.4)	1.2 (0.4)	1.1 (0.3)
LDL cholesterol, mmol/L	2.2 (0.9)	2.4 (1.1)	3.3 (1.5)	2.8 (1.1)
Triglycerides, mmol/L	2.2 (1.3)	2.7 (1.7)	3.0 (0.8)	2.7 (1.4)
BMI, kg/m ²	35.7 (6.4)	33.7 (6.8)	37.4 (5.8)	35.4 (6.1)

Abbreviations: BMI, body mass index; GLP-1, glucagon-like peptide 1; HbA1c, glycated haemoglobin; MDI, multiple daily insulin injections. Values are means (SD).

controlled trials (RCTs), IDegLira has been shown to result in superior glycaemic control, significant weight loss and lower risk of hypoglycaemia compared with basal insulin and basal-bolus insulin regimens.^{3,4} Similarly, IDegLira has been shown to offer improved glycaemic control versus a GLP-1 receptor agonist regimen and versus the combination of GLP-1 receptor agonists with insulin (indirectly, not in a fixed ratio combination).^{5,6} In addition to the valuable data provided by RCTs, real-world evidence providing insights into effectiveness and safety in routine clinical practice is playing an increasingly important role in healthcare decision-making.⁷ The first large, multi-country real-world evidence on IDegLira was recently published by Price et al⁸ from the European Xultophy Treatment Retrospective Audit (EXTRA) study. EXTRA was a multicentre, retrospective chart review in 611 adults with type 2 diabetes, who started IDegLira ≥6 months before data collection. After 6 months of IDegLira treatment, significant reductions in glycated haemoglobin (HbA1c) were observed in the overall population (−10 mmol/mol [−0.9%]; $P < 0.0001$) and in all subgroups defined by prior therapy. Improved glycaemic control was accompanied by a significant reduction in mean body weight (−0.7 kg; $P = 0.0127$) and an 82% reduction in hypoglycaemia rates (rate ratio 0.18; $P < 0.0001$).

Diabetes represents a serious healthcare challenge in Spain, where Soriguer et al⁹ reported an overall national prevalence of diabetes mellitus of 13.8% (95% confidence interval [CI] 12.8, 14.7) from the di@bet.es Study. Mata-Cases et al¹⁰ reported an average annual cost per patient over EUR 3110, suggesting that annual healthcare expenditure on type 2 diabetes may be approximately EUR 10 bn. The need for the efficient allocation of healthcare resources and effective management of type 2 diabetes to minimize the risk of costly complications is clear. Health economic analyses based on real-world evidence provide valuable information in addition to evaluations based on RCTs, and have an important role to play in informing decision-making regarding treatment allocation. The aim of the present study was to evaluate the long-term cost-effectiveness of IDegLira versus continuing other treatment regimens (GLP-1 receptor agonists, insulin plus GLP-1 receptor agonists, basal insulin therapy or multiple daily insulin injections [MDI]) in the Spanish setting, based on real-world evidence from the EXTRA study. In line with the approved indication for IDegLira in the European Union ("to improve glycaemic control in combination with oral glucose-lowering medicinal products when these alone or combined with a GLP-1 receptor agonist or basal insulin do not provide adequate glycaemic control"), IDegLira was not compared directly with oral antidiabetic medications in the present analysis.

TABLE 2 Treatment effects in each of the four subgroups based on data from the EXTRA study 6 months after initiation of fixed-ratio combination insulin degludec/liraglutide (IDegLira): Effectiveness analysis set

	MDI	Basal insulin	GLP-1 receptor agonist	GLP-1 receptor agonist in combination with insulin
HbA1c	−0.71 (0.10) / −7.8 (1.1) ^a	−0.94 (0.14) / −10.3 (1.5) ^a	−1.01 (0.17) / −11.0 (1.9) ^a	−0.60 (0.09) ^a / −6.6 (1.0) ^a
Mmol/Mol				
%				
Systolic blood pressure, mmHg	−1.4 (0.7)	−4.60 (2.50)	−2.00 (4.49)	−3.40 (2.14)
Total cholesterol, mmol/L	+0.1 (0.2)	−0.2 (0.3)	−0.7 (0.4)	−0.7 (0.4)
HDL cholesterol, mmol/L	−0.1 (0.1)	0.0 (0)	+0.1 (0.1)	+0 (0)
LDL cholesterol, mmol/L	+0.3 (0.2)	0 (0.3)	−0.4 (0.2)	−0.6 (0.3)
Triglycerides, mmol/L	−0.7 (0.5)	−1.1 (0.5)	−1.0 (0.4)	−1.3 (0.3)
BMI, kg/m ²	−0.81 (0.14) ^a	−0.05 (0.23)	+0.29 (0.49)	−0.05 (0.14)

Abbreviations: BMI, body mass index; GLP-1, glucagon-like peptide 1; HbA1c, glycated haemoglobin; MDI, multiple daily insulin injections. Values are means (SD).

^aStatistically significant difference at 95% confidence level.

2 | MATERIALS AND METHODS

2.1 | Modelling approach

Long-term projections of costs and clinical outcomes based on data from the EXTRA study were made using the IQVIA CORE Diabetes Model Version 8.5+ (IQVIA, Basel, Switzerland), a previously published and validated model of type 2 diabetes.^{11–13} The model is a non-product-specific diabetes policy analysis tool, capable of performing real-time simulations taking different treatment regimens into account. It was used to project life expectancy, quality-adjusted life expectancy, complication rates, time to onset of complications and direct costs for 1000 iterations of individual cohorts, each of 1000 simulated patients. For the base-case and one-way sensitivity analysis, first order Monte Carlo simulations were run (also known as random walk or microsimulations), with probabilistic sensitivity analysis, including sampling of patients' baseline characteristics, treatment effects, probabilities, costs and utilities from distributions in the model, presented separately. Cost-effectiveness was evaluated by calculating incremental cost-effectiveness ratios (ICERs) where appropriate. Probabilistic sensitivity analysis was performed to generate cost-effectiveness scatter plots and acceptability curves to evaluate uncertainty around the base case outcomes. A time horizon of 50 years was used for the base-case analyses. Future costs and clinical benefits were discounted at 3% per annum, in line with published guidance for Spain.¹⁴

2.2 | Simulated cohort and treatment effects

Cohort characteristics and treatment effects were derived from the pre-treatment subgroups of the effectiveness analysis set in the EXTRA study, which included all patients in the full analysis set who continued IDegLira for at least 6 months after initiation.¹⁵ Baseline regimens (prior to IDegLira treatment) were categorized as: MDI (28%); GLP-1 receptor agonists in combination with insulin (24%); basal insulin (19%); GLP-1 receptor agonists (10%); and non-injectable medications (19%), all with or without oral antidiabetic medications. The modelling analysis compared IDegLira with the four subgroups corresponding to post-intensification regimens after failure on non-injectable therapy, specifically MDI, basal insulin, GLP-1 receptor agonists and GLP-1 receptor agonists in combination with insulin. In the MDI group, 72% of patients were on basal-bolus therapy, with 14% on premixed insulin, 10% on a bolus insulin regimen and 4% on a combination of premixed with either basal or bolus insulin. In the GLP-1 receptor agonist group, 72% of patients were on liraglutide and 28% were on dulaglutide. Liraglutide was also the dominant baseline treatment in the subgroup GLP-1 receptor agonist in combination with insulin, in which 89% of patients were taking liraglutide ($n = 108$) and 11% were taking other GLP-1 receptor agonists (exenatide, $n = 10$; exenatide once weekly, $n = 6$; lixisenatide, $n = 1$; dulaglutide, $n = 16$), and the most common insulin regimen was basal insulin (67%) followed by basal-bolus therapy (24%), with the remainder on bolus insulin, premixed insulin or a premixed insulin combination (9%).

Based on pre-study therapy, four simulation cohorts were generated for the modelling analysis, each of which corresponded to a subgroup in the EXTRA study (Table 1). The effect of IDegLira on clinical

risk factors after 6 months was applied in the modelling analysis (in line with the primary endpoint in the EXTRA study), and was compared with continuing the baseline therapy (assuming no further changes in risk factors whilst on the same therapy; Table 2). Changes in hypoglycaemia rates were conservatively not included in the base-case analysis (but were investigated in sensitivity analyses) as rates were consistently low and not anticipated to notably influence cost-effectiveness outcomes. All treatments were assumed to be continued for 5 years in the modelling analysis, before intensification to therapy equivalent to the MDI subgroup (assumed to be basal-bolus therapy for most patients) in line with previously published economic evaluations of IDegLira.^{16,17} No further intensification steps were modelled. Treatment effects on HbA1c and body mass index (BMI) were assumed to persist for the 5 years of IDegLira therapy, before reverting back to baseline levels at intensification (making it the same in both the IDegLira and comparator arms). Long-term progression of systolic blood pressure was modelled based on the UK Prospective Diabetes Study (UKPDS) data in all treatment

TABLE 3 Long-term cost-effectiveness outcomes

	IDegLira	Comparator	Difference
IDegLira vs MDI			
Discounted life expectancy, years	11.00 (0.17)	10.86 (0.17)	+0.14
Discounted quality-adjusted life expectancy, QALYs	6.51 (0.10)	6.37 (0.11)	+0.14
Discounted direct costs, EUR	58 304 (1659)	57 889 (1654)	+415
ICER	EUR 3013 per QALY gained		
IDegLira vs basal insulin			
Discounted life expectancy, years	12.11 (0.19)	11.82 (0.18)	+0.28
Discounted quality-adjusted life expectancy, QALYs	7.41 (0.12)	7.17 (0.11)	+0.25
Discounted direct costs, EUR	56 682 (1559)	54 975 (1608)	+1707
ICER	EUR 6890 per QALY gained		
IDegLira vs GLP-1 receptor agonists			
Discounted life expectancy, years	12.13 (0.18)	11.70 (0.17)	+0.43
Discounted quality-adjusted life expectancy, QALYs	7.18 (0.11)	6.85 (0.10)	+0.33
Discounted direct costs, EUR	58 681 (1636)	61 981 (1689)	–3300
ICER	IDegLira dominant		
IDegLira versus GLP-1 receptor agonists in combination with insulin			
Discounted life expectancy, years	11.41 (0.18)	11.13 (0.18)	+0.27
Discounted quality-adjusted life expectancy, QALYs	6.86 (0.11)	6.63 (0.12)	+0.22
Discounted direct costs, EUR	57 219 (1481)	60 961 (1602)	–3742
ICER	IDegLira dominant		

The price of IDegLira in Spain has not been approved by the Ministry of Health at the time of publication. Abbreviations: BOT, basal only therapy; EUR, 2016 Euros; GLP-1, glucagon-like peptide 1; ICER, incremental cost-effectiveness ratio; MDI, multiple daily insulin injections; QALY, quality-adjusted life-year.

arms, and serum lipid levels were modelled based on data from the Framingham Heart Study.¹¹

2.3 | Costs and quality-of-life utilities

Costs were expressed in 2016 Euros (EUR) from a Spanish national healthcare payer perspective. Pharmacy costs were estimated based on wholesale acquisition costs and medication use reported in the EXTRA study for each of the subgroups (before and after initiation of IDegLira). Annual treatment costs include all anti-diabetes medications, needles for injection and self-monitoring of blood glucose test strips (Table S1). In certain subgroups, a proportion of patients received prandial insulin therapy concomitant to IDegLira, and this was captured in the estimates of annual treatment costs (using the cost of insulin aspart). In the MDI subgroup, ~33% of patients took prandial insulin after the initiation of IDegLira; in the basal insulin subgroup this value was 3% and in the GLP-1 receptor agonist in combination with insulin group it was 16%.

Costs associated with diabetes-related complications were derived from a literature review and searches of Spanish diagnosis-related group data.^{18–20} Costs were inflated to 2016 EUR values if required using the Spanish consumer price index for health.²¹ Quality-of-life utilities associated with type 2 diabetes and its complications were taken from published sources, and are consistent with previously published cost-effectiveness analyses.^{22–25}

2.4 | Sensitivity analyses

For each of the four subgroup comparisons, one-way and probabilistic sensitivity analyses were carried out to identify the key variables influencing costs and clinical outcomes. One-way sensitivity analysis

included varying the time horizon (between 10 and 50 years), varying discount rates (between 0 and 5%), and abolishing between-treatment differences in individual risk factors (HbA1c, systolic blood pressure, serum lipids and BMI). To investigate the role of HbA1c as a driver of cost-effectiveness, sensitivity analyses were performed in which the HbA1c benefit was maintained (not abolished) after treatment intensification, the UKPDS Outcomes Model progression equation for HbA1c was applied for both treatments, and change from baseline in HbA1c was varied between the upper and lower 95% CIs from the EXTRA Study. Other sensitivity analyses included applying only statistically significant differences between treatments, including hypoglycaemia rates from the EXTRA study, maintaining the BMI difference between treatments after intensification, varying the time of treatment intensification between 3 and 7 years, simulating no treatment intensification, varying the costs of diabetes-related complications by $\pm 10\%$, applying the costs of NPH insulin for insulin glargine U100, using defined daily doses of therapies in the comparator arms, and modelling the risk of diabetes-related complications using the UKPDS Outcomes Model 2 risk equations in the IQVIA CORE Diabetes Model.

3 | RESULTS

3.1 | IDegLira versus MDI

Model projections indicated that improved glycaemic control with IDegLira led to fewer diabetes-related complications than MDI therapy over patients' lifetimes (Figures S1 and S2). This led to an improvement in quality-adjusted life expectancy of 0.14 quality-adjusted life-years (QALYs) with IDegLira versus MDI (Table 3). A similar survival benefit was observed with IDegLira over MDI

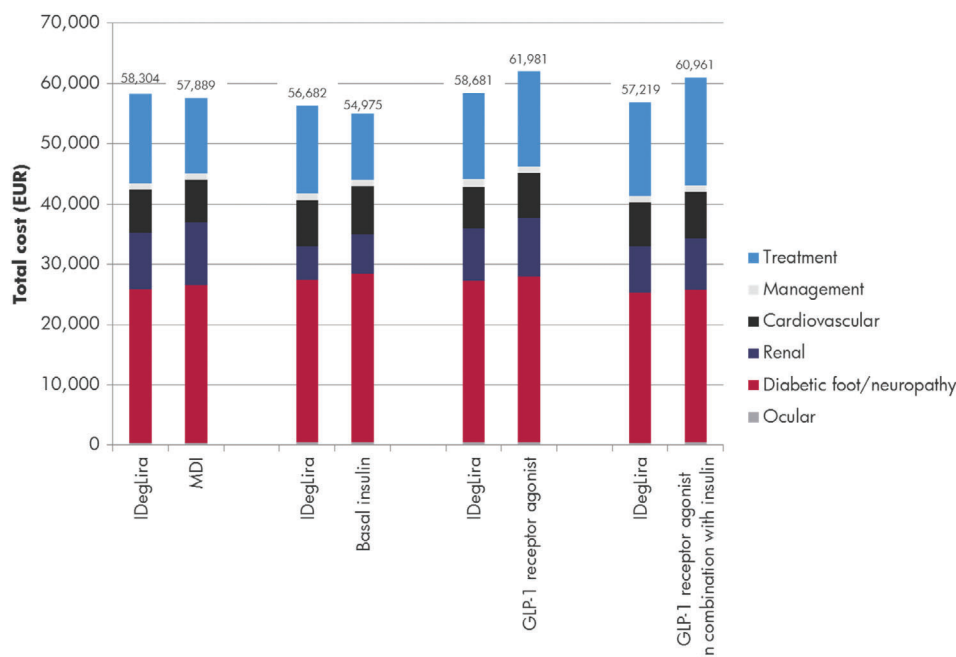


FIGURE 1 Breakdown of direct costs by cost category. Costs were categorized as treatment costs (costs associated with diabetes therapy), management costs (associated with routine care) and complication costs (associated with cardiovascular, renal, diabetic foot or neuropathy, or ocular complications). The price of IDegLira in Spain has not been approved by the Ministry of Health at the time of publication. EUR, 2016 Euros; GLP-1, glucagon-like peptide-1; IDegLira, fixed-ratio combination insulin degludec/liraglutide; MDI, multiple daily insulin injections

(0.14 years). Lifetime costs were higher by EUR 418 on IDegLira than on MDI therapy (EUR 58 304 vs 57 889), with higher pharmacy costs in the IDegLira arm partly offset by the reduced costs of diabetes-related complications (Figure 1). IDegLira was associated with an ICER of EUR 3013 per QALY gained versus MDI.

3.2 | GLP-1 receptor agonist in combination with insulin

IDegLira was also projected to improve clinical outcomes in the comparison with GLP-1 receptor agonists in combination with insulin regimens. Benefits in terms of glycaemic control with IDegLira were associated with fewer diabetes-related complications and improvements in quality-adjusted life expectancy (by 0.22 QALYs) and life expectancy (0.27 years) versus GLP-1 receptor agonists in combination with insulin (Table 3, Figures S1 and S2). Mean total costs were lower with IDegLira by approximately EUR 3742 per patient, as a result of reduced complication costs and lower pharmacy costs versus continuing GLP-1 receptor agonists in combination with insulin therapy. As a result, IDegLira was considered

dominant to GLP-1 receptor agonists in combination with insulin (cost and life saving) over patient lifetimes (therefore no ICER is presented).

3.3 | Basal insulin

The clinical benefits with IDegLira were more marked in comparison with basal insulin therapy. Reduced complication rates and a delayed onset of most diabetes-related complications meant that IDegLira was associated with an improvement in quality-adjusted life expectancy of 0.25 QALYs versus basal insulin (Table 3, Figures S1 and S2). IDegLira was also associated with an improvement in life expectancy (0.28 years) over basal insulin. Higher pharmacy costs with IDegLira resulted in total direct costs being EUR 1707 higher than for basal insulin on average, despite lower diabetes-related complication costs. IDegLira was associated with an ICER of EUR 6890 per QALY gained versus basal insulin.

3.4 | GLP-1 receptor agonist therapy

In the comparison with GLP-1 receptor agonist therapy, improved glycaemic control with IDegLira was also projected to lead to benefits in

TABLE 4 Cost-effectiveness outcomes for selected sensitivity analyses

	Quality-adjusted life expectancy, QALYs			Direct costs, EUR			ICER, EUR per QALY gained
	IDegLira	Comparator	Difference	IDegLira	Comparator	Difference	
IDegLira vs MDI							
<i>Base case</i>	6.51	6.37	+0.14	58 304	57 889	+415	3013
HbA1c difference abolished	6.39	6.37	+0.02	60 036	57 889	+2147	133 371
BMI difference abolished	6.48	6.37	+0.11	58 200	57 889	+311	2940
Hypoglycaemia included	6.50	6.36	+0.14	58 304	57 889	+415	2906
Statistically significant differences only	6.54	6.37	+0.17	58 456	57 889	+567	3361
NPH insulin costs applied	6.51	6.37	+0.14	57 779	57 063	+716	5201
IDegLira vs basal insulin							
<i>Base case</i>	7.41	7.17	+0.25	56 682	54 975	+1707	6890
HbA1c difference abolished	7.23	7.17	+0.06	58 534	54 975	+3559	56 945
BMI difference abolished	7.41	7.17	+0.25	56 702	54 975	+1727	6989
Hypoglycaemia included	7.40	7.16	+0.25	56 682	54 975	+1707	6901
Statistically significant differences only	7.35	7.17	+0.19	56 685	54 975	+1710	9118
NPH insulin costs applied	7.41	7.17	+0.25	56 083	53 979	+2104	8494
IDegLira vs GLP-1 receptor agonists							
<i>Base case</i>	7.18	6.85	+0.33	58 681	61 981	-3300	IDegLira dominant
HbA1c difference abolished	6.95	6.85	+0.10	60 769	61 981	-1213	IDegLira dominant
BMI difference abolished	7.18	6.83	+0.35	58 681	61 862	-3181	IDegLira dominant
Hypoglycaemia included	7.17	6.83	+0.33	58 681	61 981	-3300	IDegLira dominant
Statistically significant differences only	7.06	6.83	+0.23	58 128	61 862	-3734	IDegLira dominant
NPH insulin costs applied	7.18	6.85	+0.33	58 083	61 412	-3329	IDegLira dominant
IDegLira vs GLP-1 receptor agonists in combination with insulin							
<i>Base case</i>	6.86	6.63	+0.22	57 219	60 961	-3742	IDegLira dominant
HbA1c difference abolished	6.74	6.63	+0.11	58 719	60 961	-2241	IDegLira dominant
BMI difference abolished	6.86	6.63	+0.22	57 200	60 961	-3760	IDegLira dominant
Hypoglycaemia included	6.84	6.61	+0.23	57 219	60 961	-3742	IDegLira dominant
Statistically significant differences only	6.75	6.63	+0.11	57 147	60 961	-3813	IDegLira dominant
NPH insulin costs applied	6.86	6.63	+0.22	56 664	60 015	-3351	IDegLira dominant

The price of IDegLira in Spain has not been approved by the Ministry of Health at the time of publication. Abbreviations: BMI, body mass index; EUR, 2016 Euros; GLP-1, glucagon-like peptide 1; HbA1c, glycated haemoglobin; ICER, incremental cost-effectiveness ratio; MDI, multiple daily insulin injections.

clinical outcomes. Greater reductions in diabetes-related complication rates were observed with IDegLira versus GLP-1 receptor agonists than in either of the comparisons with insulin regimens (basal or MDI), leading to an improvement in quality-adjusted life expectancy of 0.33 QALYs with IDegLira (Table 3, Figures S1 and S2). The survival benefit projected for IDegLira was 0.43 years per patient over GLP-1 receptor agonist therapy. Pharmacy costs and complication costs were lower with IDegLira than with GLP-1 receptor agonists and, over patients' lifetimes, this led to a saving of approximately EUR 3300 per patient with IDegLira in direct medical costs. IDegLira was dominant to GLP-1 receptor agonist therapy (cost and life saving) over patient lifetimes (therefore no ICER is presented).

3.5 | Sensitivity analyses

Sensitivity analyses showed that the HbA1c benefits associated with IDegLira were a key driver of cost-effectiveness in all four scenarios (Table 4). In the comparison with MDI, abolishing the HbA1c benefit associated with IDegLira produced an ICER of approximately EUR 133 371 per QALY gained, as IDegLira was associated with only modest benefits in terms of quality-adjusted life expectancy relative to the base case. Similarly, in the comparison with basal insulin,

abolishing the HbA1c benefit with IDegLira led to an ICER of EUR 56 945 per QALY gained. In all other sensitivity analyses versus MDI and basal insulin, IDegLira remained cost-effective (Tables S2 and S4). In the comparisons with GLP-1 receptor agonists and GLP-1 receptor agonists in combination with insulin, IDegLira remained dominant in all sensitivity analyses (Tables S3 and S5). Probabilistic sensitivity analysis showed that, assuming a willingness to pay of EUR 30 000 per QALY gained, the probabilities that IDegLira would be considered cost-effective were: 58.6% versus MDI; 59.6% versus basal insulin; 76.6% versus GLP-1 receptor agonists; and 74.0% versus GLP-1 receptor agonists in combination with insulin therapy (Figure 2, Figure S4).

4 | DISCUSSION

Based on the findings of the EXTRA study, the present modelling analysis provides evidence that IDegLira is likely to reduce the incidence of diabetes-related complications, improve quality-adjusted life expectancy and extend life expectancy versus four comparator regimens. In comparison with insulin regimens, IDegLira was found to be cost-effective, with ICERs of EUR 3013 per QALY gained versus MDI and EUR 6890 per QALY gained versus basal insulin. In comparison with

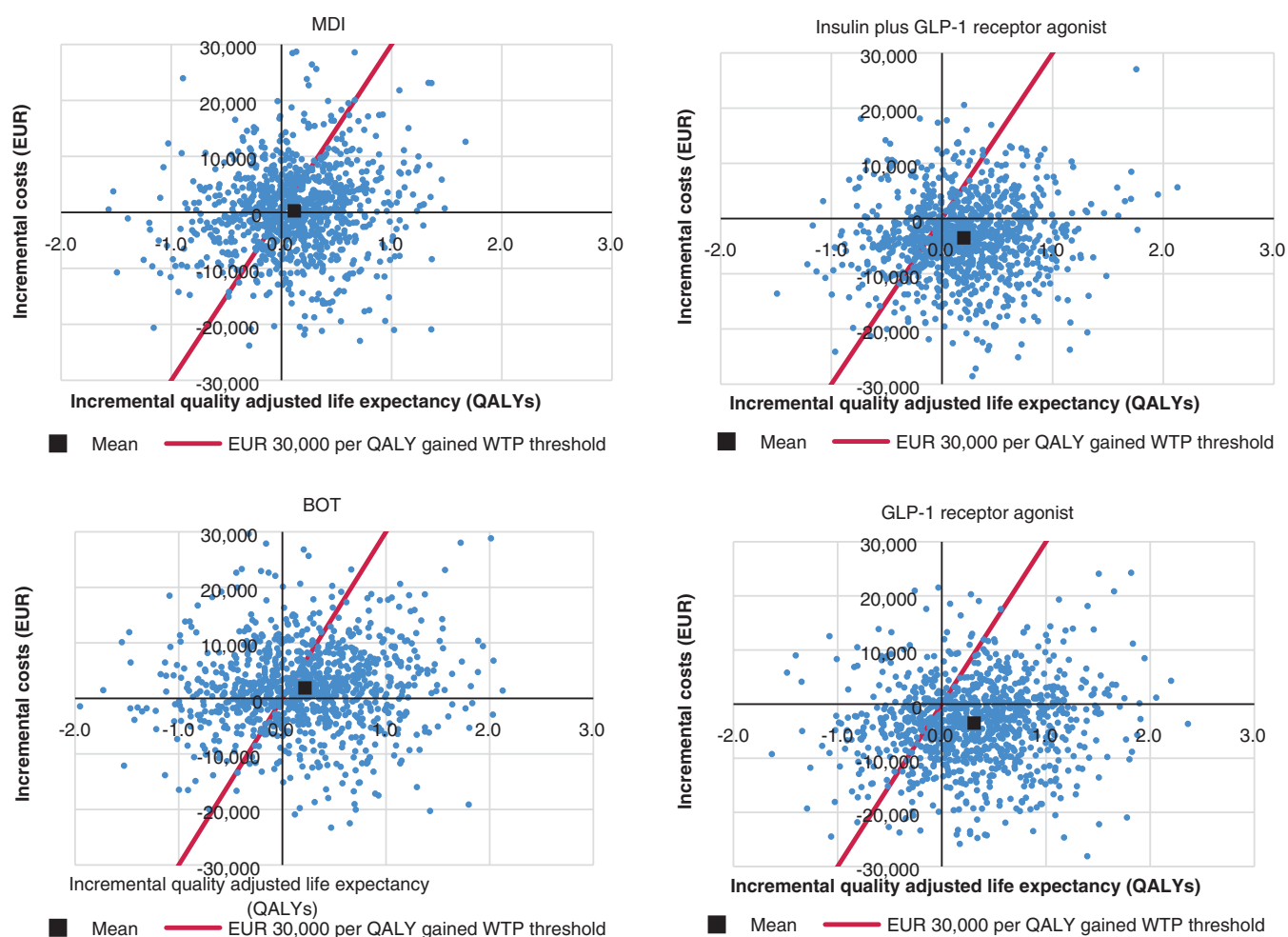


FIGURE 2 Probabilistic sensitivity analysis cost-effectiveness scatterplots for the four subgroups. The price of IDegLira in Spain has not been approved by the Ministry of Health at the time of publication. BOT, basal insulin (basal only therapy); GLP-1, glucagon-like peptide 1; MDI, multiple daily insulin injections; QALY, quality-adjusted life-year; WTP, willingness to pay

GLP-1 receptor agonist therapy and GLP-1 receptor agonists in combination with insulin regimens, IDegLira was projected to reduce direct medical costs for patients with type 2 diabetes in Spain. Sensitivity analysis showed that the improvement in HbA1c associated with IDegLira treatment was the key driver of improved outcomes.

These findings are consistent with other published health economic analyses of IDegLira. Cost-effectiveness evaluations based on clinical trial data on IDegLira have shown that it is likely to improve clinical outcomes and be cost-effective versus several comparator regimens (basal insulin, basal-bolus insulin, and GLP-1 receptor agonists in combination with insulin) in patients with type 2 diabetes in the United States, the Netherlands, the Czech Republic, Sweden, the United Kingdom and Spain.^{17,26–30} Comparable health economic outcomes from the present study based on real-world evidence are reassuring, as they indicate that the benefits of IDegLira observed in RCTs translate to the real-world setting, and that similar improvements in long-term outcomes with IDegLira can be anticipated for patients in routine clinical practice.

The use of data from a single-arm study to model long-term outcomes can be considered a limitation of the analysis. Ideally, the modelling analysis would be based on several years of prospectively collected data from large-scale cohorts on IDegLira and multiple comparator regimens; however, this type of data is rarely available, particularly for modern interventions that are relatively new to the market. In the absence of such data, studies like EXTRA provide valuable information on the impact of therapy in the real-world setting and it is interesting to note that the results of the present evaluation were consistent with evaluations based on prospectively collected RCT data. A further criticism of the present analysis could be the use of short-term clinical data (6 months after IDegLira initiation in the EXTRA study) to inform long-term projections. However, in the absence of long-term data, projections using published and validated health economic models represent the best approach available for informing healthcare decision-making. As with any modelling study, particularly those in type 2 diabetes, simplifying assumptions were a necessary part of the analysis. In the present study, IDegLira was assumed to fit into the treatment algorithm at the same stage as basal insulin therapy, and was therefore compared directly with basal insulin therapy and treatment options adjacent to it in the algorithm. It was assumed that treatment with IDegLira and comparators was for a duration of 5 years before intensification to basal-bolus insulin therapy (in line with the treatment algorithm), assumed to be the same as MDI treatment in the present analysis. This duration of therapy was consistent with previously published economic evaluations of IDegLira, although long-term data supporting the durability of IDegLira therapy are not currently available.^{16,17} Importantly, in terms of cost-effectiveness, the present analysis balances the additional costs of therapy with the additional clinical benefits of therapy over the same 5-year duration. As a result, assumptions of shorter or longer treatment duration before intensification are likely to produce similar outcomes in terms of cost-effectiveness, provided the assumption that additional costs and clinical benefits are applied for an equal duration (i.e. costs are not applied for a shorter duration than clinical benefits) is maintained.

The EXTRA study provided evidence that IDegLira improves glycaemic control relative to a range of GLP-1 receptor agonist and

insulin regimens. In this health economic analysis for Spain, the benefits of IDegLira were projected to improve long-term clinical outcomes and be cost-saving or cost-effective for patients with type 2 diabetes previously treated with MDI, GLP-1 receptor agonists in combination with insulin, basal insulin or GLP-1 receptor agonist therapy.

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CONFLICT OF INTEREST

Pedro Mezquita Raya is a scientific collaborator with Novo Nordisk and has participated in advisory boards and clinical trials. Francisco Javier Ampudia Blasco has received research support and honoraria for advisory board and from Novo Nordisk. Barnaby Hunt is an employee of Ossian Health Economics and Communications. Ossian received consulting fees from Novo Nordisk to support the present analysis. Virginia Martin is a employee of Novo Nordisk Pharma SA. Brian Larsen Thorsted is an employee of Novo Nordisk A/S. Amaury Basse is an employee of Novo Nordisk Pharma Gulf FZ-LLC. Hermione Price has received lecture fees from conference travel and honoraria for advisory board or steering committee participation from Novo Nordisk.

AUTHOR CONTRIBUTIONS

The study was conceived and designed by all authors. Data were collected by Brian Larsen Thorsted and Amaury Basse. The analysis was performed by Barnaby Hunt. All others participated in preparation of the manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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