

# The long-term cost-effectiveness of insulin iicodec versus once-daily basal insulin analogs in Italy

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## Aim

- The present study aimed to evaluate the long-term cost-effectiveness of once-weekly insulin iicodec versus once-daily basal insulin analogs that currently hold majority market share in Italy in insulin-naïve patients with type 2 diabetes, based on the results of the ONWARDS clinical trial program.

## Introduction

- More than 3.6 million people were estimated to be affected by diabetes in Italy in 2024, with diabetes-related healthcare expenditure exceeding EUR 10 billion.<sup>1</sup>
- Type 2 diabetes (T2D) accounts for more than 90% of diabetes cases.<sup>2</sup>
- Improvements in physiological parameters such as glycated hemoglobin (HbA1c), blood pressure and body mass index (BMI) has been shown to reduce the risk of costly long-term diabetes-related complications in landmark studies, and is recommended in the latest guidelines published by the European Association for Study of Diabetes (EASD).<sup>3</sup>
- Due to the progressive nature of T2D, insulin therapies are often eventually required following treatment with oral and other injectable antidiabetic medications.<sup>3</sup>
- For example, daily basal insulin injections (while remaining a cornerstone of T2D management) can impose a considerable burden on patients' quality of life, with people often citing fear of injections as a reason for delaying timely treatment intensification.<sup>4</sup>
- Iicodec is a novel once-weekly basal insulin associated with superior improvements in HbA1c versus once-daily insulins glargine U100, degludec, and a mix of degludec, glargine U100 and glargine U300 in the ONWARDS 1, 3 and 5 clinical trials, respectively.<sup>5,6,7</sup>
- Based on these consistent clinical benefits, the present study evaluated the long-term cost-effectiveness of iicodec for treating insulin-naïve people with T2D in Italy.

## Methods

- Outcomes were projected over patient lifetimes using the published and validated PRIME T2D Model.<sup>8</sup>
- ONWARDS 1, 3 and 5 informed baseline characteristics and treatment effects in the comparisons of iicodec with glargine U100, degludec, and the mix of once-daily basal insulins, respectively (Tables 1 and 2).
- Modeled patients received iicodec or a comparator basal insulin for 4 years before intensifying with the addition of bolus insulin, with differences in treatment effects maintained until intensification.
- A quality-of-life benefit associated with once-weekly versus once-daily injection (0.0389) was taken from a published time-trade-off study and applied in the iicodec arm until intensification.<sup>9</sup>
- Costs and utilities were taken from published sources, with costs expressed in euros (EUR) from the perspective of the Italian National Health Service.

**Table 1:** Baseline cohort characteristics applied in the analyses, capturing insulin-naïve patients

Parameter	ONWARDS 1	ONWARDS 3	ONWARDS 5
Age, years	59.0 (10.0)	58.1 (10.0)	59.3 (10.5)
Duration of diabetes, years	11.5 (6.7)	11.3 (6.6)	11.9 (7.3)
Proportion male, %	56.7	62.8	57.3
Proportion smokers, %	17.2	14.3	18.3
HbA1c, %	8.5 (1.0)	8.5 (1.1)	8.9 (1.6)
SBP, mmHg	131.6 (14.2)	128.9 (15.1)	131.2 (15.0)
BMI, kg/m <sup>2</sup>	30.1 (4.9)	29.6 (5.1)	32.8 (7.0)
HDL cholesterol, mmol/L	1.2 (0.3)	1.1 (0.3)	1.1 (0.3)
LDL cholesterol, mmol/L	2.3 (0.9)	2.2 (0.9)	2.2 (1.0)
eGFR, mL/min/1.73 m <sup>2</sup>	85.5 (18.9)	90.8 (18.9)	88.1 (20.7)

BMI, body mass index; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure. Values are means (standard deviations).

**Table 2:** Treatment effects applied in the analyses from ONWARDS 1, ONWARDS 3, and ONWARDS 5

Parameter	Iicodec	Glargine U100	Iicodec	Degludec	Iicodec	Once-daily basal insulins mix
HbA1c, %	<b>-1.6 (1.3)</b>	<b>-1.4 (1.1)</b>	<b>-1.6 (0.9)</b>	<b>-1.4 (0.9)</b>	<b>-1.7 (2.1)</b>	<b>-1.3 (2.8)</b>
Systolic blood pressure, mmHg	-1.8 (12.2)	-1.7 (12.2)	-0.3 (11.2)	-0.8 (11.2)	-0.5 (13.5)	-1.4 (13.3)
Body mass index, kg/m <sup>2</sup>	0.8 (1.8)	0.7 (2.0)	1.0 (1.4)	0.8 (1.7)	0.9 (3.0)	0.6 (4.0)
High-density lipoprotein cholesterol, mmol/L	0.03 (0.22)	0.02 (0.22)	0.05 (0.17)	0.03 (0.17)	<b>0.03 (0.23)</b>	<b>-0.03 (0.46)</b>
Low-density lipoprotein cholesterol, mmol/L	-0.06 (0.66)	-0.01 (0.66)	0.01 (0.68)	0.03 (0.68)	-0.02 (0.9)	0.04 (1.4)
Severe hypoglycemia, events per patient-year	0.002	0.006	0.000	0.012	0.000	0.009
Non-severe hypoglycemia, events per patient-year	0.294	0.155	0.310	0.134	0.186	0.136

HbA1c, glycated hemoglobin. **Bold** indicates statistically significant difference between iicodec and the comparator (glargine U100 in ONWARDS 1, degludec in ONWARDS 3, mix of once-daily basal insulins in ONWARDS 5) when using a significance level of 5%. Values are means (standard deviations).

## Results

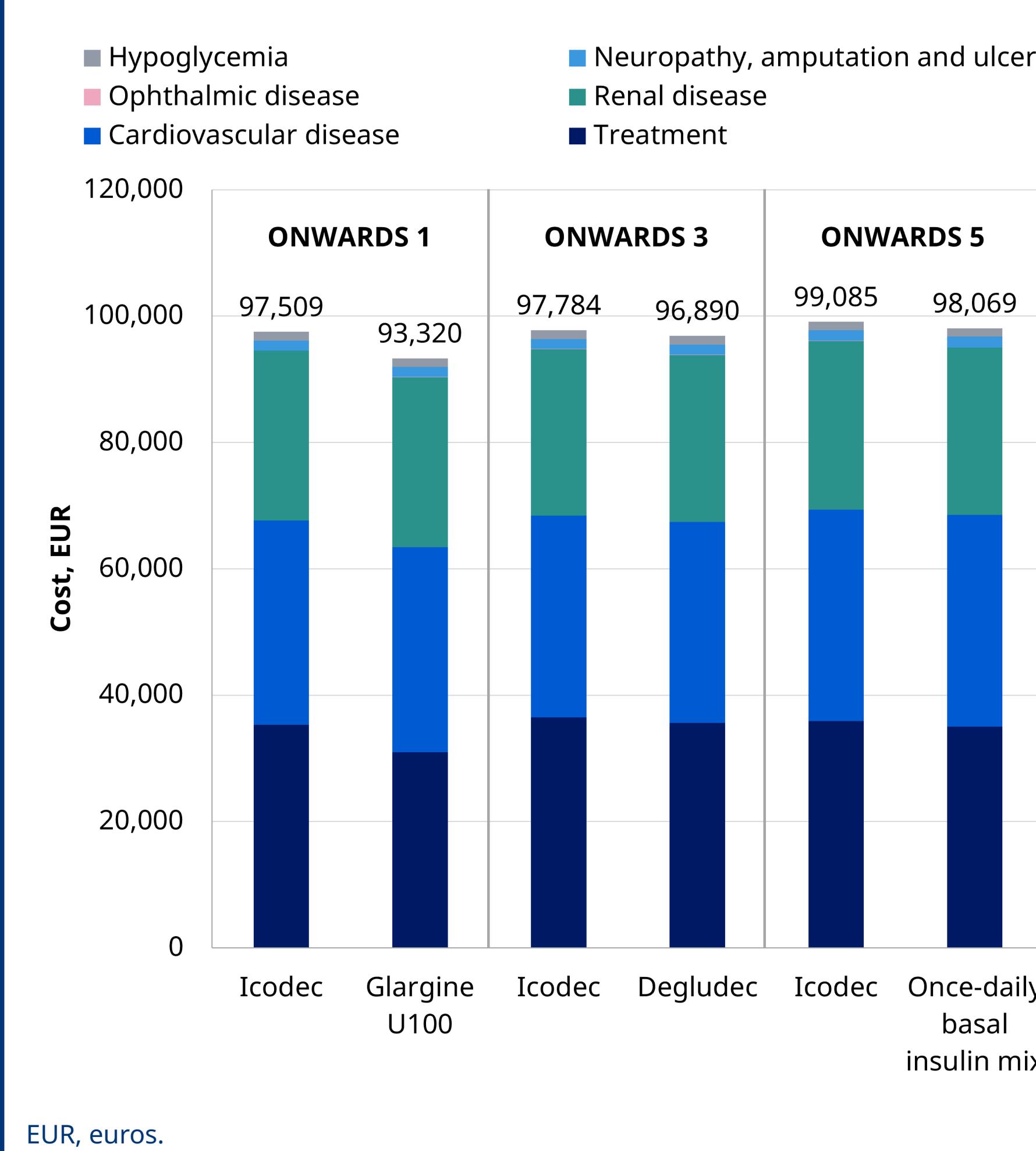
- Iicodec was associated with improved life expectancy of 0.02 years versus both glargine U100 and degludec (based on ONWARDS 1 and ONWARDS 3, respectively), and 0.14 years versus the mix of once-daily basal insulins in ONWARDS 5 (Table 3).
- Quality-adjusted life expectancy was improved with iicodec by 0.16 quality-adjusted life years (QALYs) versus glargine U100 and degludec, and 0.26 QALYs versus the mix of once-daily insulins (Table 3).
- Direct costs were projected to be higher with iicodec, with increased treatment costs partially offset by avoidance of diabetes-related complications (Figure 1).
- Iicodec was associated with incremental cost-effectiveness ratios of EUR 25,623 per QALY gained, EUR 5,438 per QALY gained, and EUR 3,940 per QALY gained versus glargine U100, degludec, and the mix of once-daily insulins, respectively (Table 3).
- The key driver of clinical benefits with iicodec in all three comparisons was reduced injection frequency.
- Probabilistic sensitivity analysis showed that results were robust to variations in input parameters (Figure 2).

**Table 3:** Cost-effectiveness outcomes

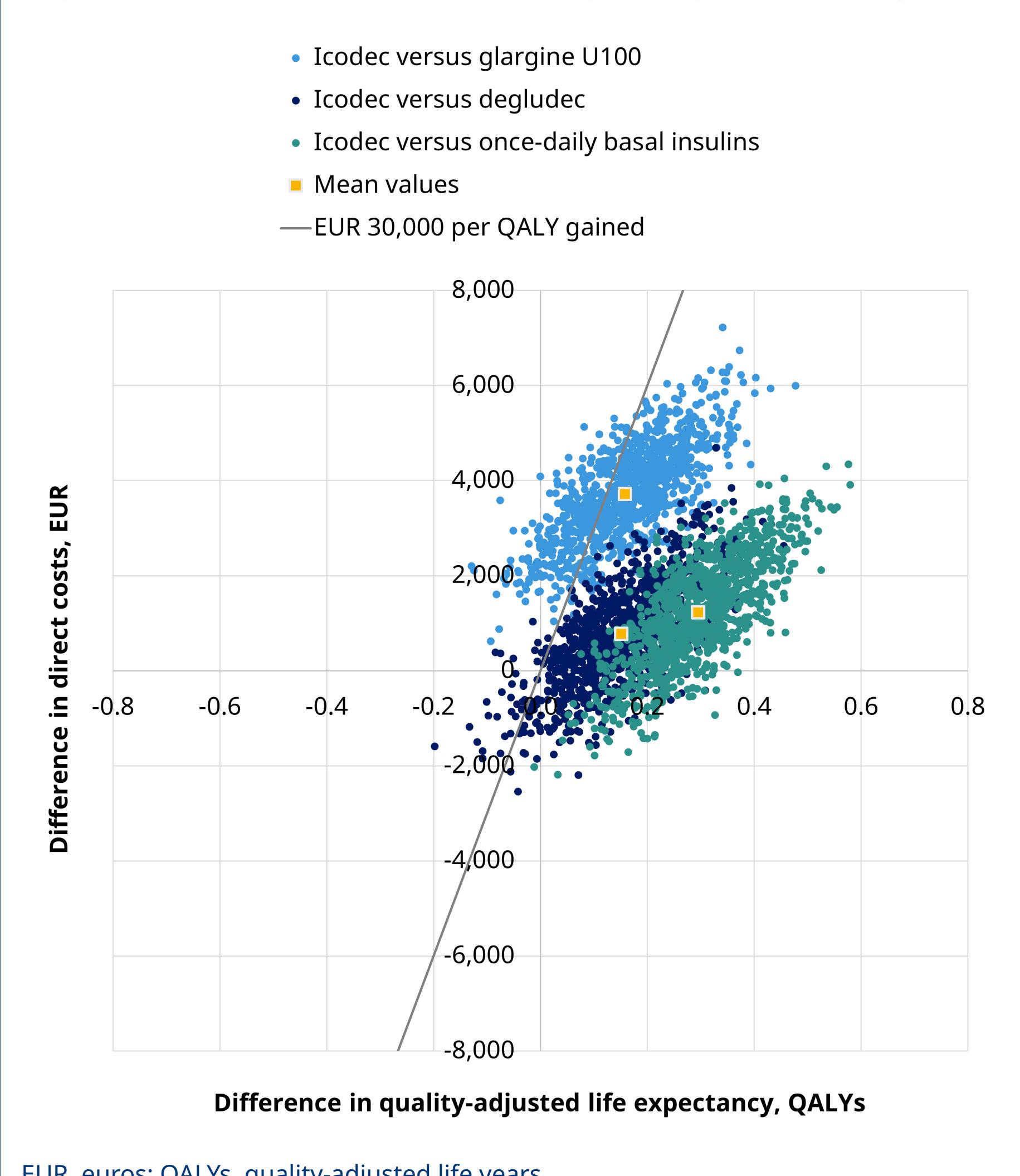
Health outcome	Iicodec versus glargine U100	Iicodec versus degludec	Iicodec versus once-daily basal insulins
Difference in LE, years	+0.02	+0.02	+0.14
Difference in QALE, QALYs	+0.16	+0.16	+0.26
Difference in costs, EUR	+4,190	+893	+1,017
ICER, EUR per QALY gained	25,623	5,438	3,940

EUR, euros; ICER, incremental cost-effectiveness ratio; LE, life expectancy; QALE, quality-adjusted life expectancy; QALY, quality-adjusted life year. Values are means.

**Figure 1:** Direct costs over patient lifetimes



**Figure 2:** Probabilistic sensitivity analysis scatterplot



## Discussion

- The once-weekly administration of iicodec has the significant potential to mitigate concerns regarding high injection frequency, helping to overcome the inertia that can lead to delayed insulin initiation.<sup>3,4</sup>
- A utility benefit relating to this reduced administration burden and significant benefits in HbA1c observed in ONWARDS 1, 3 and 5 were likely key drivers of cost-effectiveness outcomes.
- The quality-of-life impact of injection frequency represents the most conservative value from a recent publication evaluating patient preferences for once-weekly versus once-daily insulin injections in T2D, with the smallest value chosen in lieu of Italy-specific data.<sup>9</sup>
- Projecting long-term outcomes from short-term clinical trial data involves recognized uncertainty associated with all long-term modeling studies in T2D, but in the absence of long-term clinical data, modeling provides the best available evidence for supporting decision making for novel interventions.
- The environmental impact of a reduced treatment administration burden was not captured in the present analysis, but treatment of iicodec with FlexTouch® has been associated with reduced carbon emissions and plastic use compared with insulins administered once daily or multiple times daily.<sup>10</sup>

## Conclusion

- Based on the results of ONWARDS 1, 3 and 5 and a willingness-to-pay threshold of EUR 25,000–40,000 per QALY gained, the present study has projected that once-weekly insulin iicodec represents a highly cost-effective treatment option versus once-daily insulins for insulin-naïve people with T2D in Italy.
- These findings should be considered by prescribing physicians and healthcare payers when evaluating insulin therapies as potential treatment options, particularly given the simplified treatment regimen of iicodec.