A long-term cost-effectiveness analysis of icodec used with the dosing guide app versus basal insulin analogs in the UK, based on a *post-hoc* analysis of the ONWARDS 5 clinical trial

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Aim

- This study aimed to evaluate the long-term cost-effectiveness of icodec versus three different once-daily basal insulin analogs in insulin-naïve patients with type 2 diabetes in the UK, based on a *post-hoc* analysis of the ONWARDS 5 trial.

Introduction

- Type 2 diabetes is a chronic metabolic disease that affected more than 4 million people in the UK in 2021, with diabetes-related healthcare expenditure estimated at GBP 10.7 billion in 2022.[1,2]
- Achieving glycemic control (alongside improvements in other risk factors) is associated with a reduced risk of costly long-term diabetes-related complications and is recommended in the latest guidelines published by the National Institute for Health and Care Excellence (NICE) and the European Association for Study of Diabetes (EASD).[3]
- A wide variety of modern treatments exist for type 2 diabetes, but insulin therapies are often eventually required to maintain blood glucose levels due to the progressive nature of the disease.[3]
- Traditional insulin regimens often require daily injections that can have a substantial impact on quality of life, with people often citing fear of injections as a reason for delaying timely treatment intensification.[4]
- Insulin icodec is the first basal insulin analog developed for once-weekly administration, and has demonstrated greater reductions in HbA_{1c} compared with a mix of three once-daily basal insulin analogs (degludec, glargine U100, and glargine U300) in the ONWARDS 5 trial.[5]
- In ONWARDS 5, icodec was used with a dosing guide app, which provided dose recommendations in accordance with standard clinical practice and icodec titration guidance.
- A *post-hoc* analysis of ONWARDS 5 was conducted to evaluate icodec against each of the three once-daily basal insulin analogs individually. Patients in the icodec arm of each comparison were matched to those in the comparator arm based on patient characteristics, with the caveat that smaller sample sizes in each subgroup lead to greater statistical variation and increased difficulty in detecting significant differences.

Methods

- Outcomes were projected over patients' lifetimes using the published and validated PRIME Type 2 Diabetes Model.[6]
- Baseline characteristics were sourced from the full population of ONWARDS 5, with comparison-specific treatment effects and insulin doses taken from the *post-hoc* analysis (Tables 1 and 2).
- Modeled patients received icodec or the comparator basal insulin for 4 years, before intensifying with the addition of bolus insulin. Treatment effects were applied in the first year and maintained until intensification, after which differences were abolished.
- A UK-specific disutility relating to once-daily versus once-weekly injection (–0.0389) was taken from a published time-trade-off study and applied until treatment intensification.[7]
- Prices used in the analysis were GBP 46.60 per 1,500 IU, GBP 34.75 per 1,500 IU and GBP 32.14 per 1,350 IU for degludec, glargine U100 and glargine U300, respectively. The icodec price (currently unkown) was assumed equal to the degludec price.

Table 1: Baseline cohort characteristics applied in the analysis, taken from all patients in the ONWARDS 5 trial

Parameter	Mean (standard deviation)
Age, years	59.3 (10.5)
Duration of diabetes, years	11.9 (7.3)
Proportion male, %	57.3
Proportion smokers, %	18.3
HbA_{1c}, %	8.9 (1.6)
SBP, mmHg	131.2 (15.0)
BMI, kg/m^2	32.8 (7.0)
HDL cholesterol, mmol/L	1.1 (0.3)
LDL cholesterol, mmol/L	2.2 (1.0)
eGFR, mL/min/1.73m^2	88.1 (20.7)

BMI, body mass index; eGFR, estimated glomerular filtration rate; HbA_{1c}, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure.

Table 2: Treatment effects applied in the analysis, taken from the ONWARDS 5 *post-hoc* analysis

Parameter	Icodec* (n=360)	Degludec (n=378)	Icodec* (n=99)	Glargine U100 (n=96)	Icodec* (n=83)	Glargine U300 (n=69)
HbA_{1c}, %	**–1.7 (1.5)**	**–1.3 (2.1)**	–1.6 (2.2)	–1.1 (2.6)	–1.7 (1.5)	–1.5 (1.4)
SBP, mmHg	–0.6 (13.3)	–1.8 (13.2)	–2.4 (15.1)	1.4 (15.1)	**1.9 (11.4)**	**–3.4 (11.3)**
BMI, kg/m^2	0.8 (2.7)	0.7 (3.1)	0.8 (3.1)	0.6 (3.7)	**1.0 (2.4)**	**–0.1 (2.7)**
HDL cholesterol, mmol/L	**0.02 (0.19)**	**–0.03 (0.38)**	0.03 (0.20)	–0.03 (0.29)	0.05 (0.18)	–0.01 (0.25)
LDL cholesterol, mmol/L	–0.04 (0.94)	0.02 (1.14)	0.01 (0.78)	0.19 (1.06)	0.00 (0.63)	–0.11 (0.65)
Severe hypoglycemia, events per patient-year	0.000	0.005	0.000	0.022	0.000	0.014
Non-severe hypoglycemia, events per patient-year	0.180	0.094	0.240	0.272	0.152	0.192

*With dosing guide app. BMI, body mass index; HbA_{1c}, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure.
Statistically significant difference at 95% confidence level.
Values are means (standard deviations).

Results

Clinical outcomes

- Icodec was associated with improved quality-adjusted life expectancy of 0.21, 0.28 and 0.11 quality-adjusted life years (QALYs) compared with degludec, glargine U100 and glargine U300, respectively (Table 3).
- The key driver of clinical benefits with icodec versus all three comparators was the utility benefit relating to reduced injection frequency with icodec.
- In addition, greater improvements in HbA_{1c} across all comparisons, systolic blood pressure compared with glargine U100, and lipid levels compared with degludec and glargine U100 contributed to improved quality-adjusted life expectancy with icodec (Table 2).

Table 3: Long-term cost-effectiveness outcomes

Comparison	**Difference in QALE** (QALYs)	**Difference in costs** (GBP)	**ICER** (GBP per QALY gained)
Icodec* versus degludec	+0.21	–1,093	**Icodec dominant**
Icodec* versus glargine U100	+0.28	+253	**904**
Icodec* versus glargine U300	+0.11	+690	**6,359**

*With dosing guide app. GBP, 2022 pounds sterling; ICER, incremental cost-effectivesness ratio; QALE, quality-adjusted life expectancy; QALYs, quality-adjusted life years.

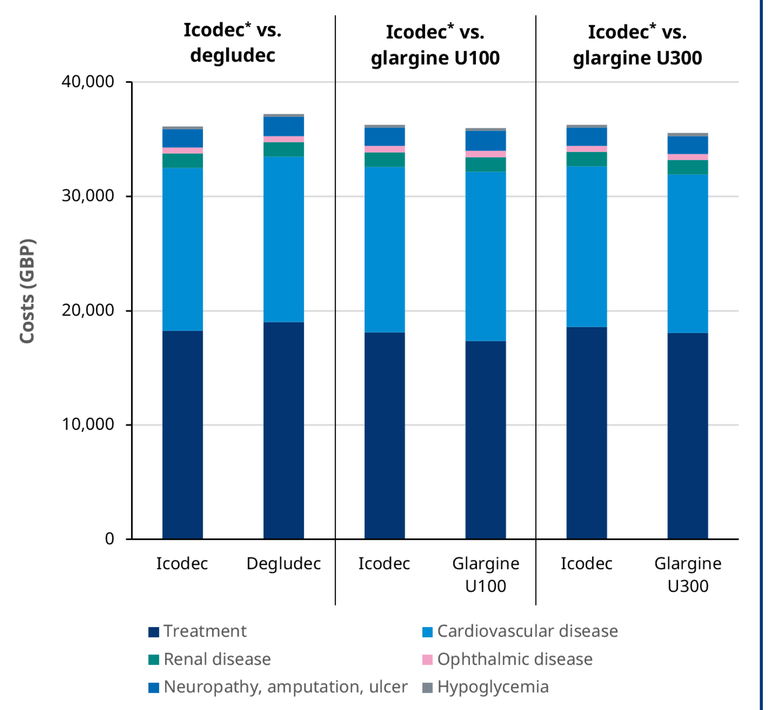
Cost outcomes

- Over the long term, with the price of icodec matched to degludec, direct costs for icodec were estimated to be GBP 1,093 lower versus degludec, and GBP 253 and GBP 690 higher versus glargine U100 and U300, respectively (Table 3).
- When compared with degludec, icodec was associated with lower treatment costs by GBP 792 per patient, mainly driven by cost savings from reduced consumables use (Figure 1).
- Additional cost savings arose from the avoidance of diabetes-related complications with icodec versus degludec, primarily from the reduced incidence of cardiovascular disease as well as neuropathy, amputation and ulcer with mean cost savings of GBP 219 and GBP 85 per patient, respectively (Figure 1).
- The higher treatment costs per patient with icodec compared with glargine U100 and U300 (by GBP 762 and GBP 498, respectively) were partially offset by cost savings from reduced consumables use and avoidance of diabetes-related complications (Figure 1).
- The largest cost savings resulted from reduced incidence of cardiovascular disease and neuropathy, amputation and ulcer (GBP 327 and GBP 128, respectively) with icodec versus glargine U100 and from avoidance of hypoglycemic events (GBP 29) with icodec versus glargine U300 (Figure 1).

Cost-effectiveness

- The results of the analysis showed that icodec was considered dominant versus degludec and associated with incremental cost-effectiveness ratios of GBP 904 and GBP 6,359 per QALY gained versus glargine U100 and U300, respectively, both of which fall below the UK willingness-to-pay threshold of GBP 20,000 per QALY gained (Table 3).

Figure 1: Direct costs over a patient's lifetime



*With dosing guide app. GBP, 2022 pounds sterling.

Discussion

- Icodec is the first insulin developed for once-weekly administration, with the potential to mitigate concerns around injection frequency that can lead to delayed insulin initiation, improve glycemic control over the short term and consequently lead to improved clinical outcomes over the long term.[3,4]
- The present study showed that icodec used with the dosing guide app was projected to be a cost-effective intervention compared with degludec, glargine U100 and glargine U300.
- The impact of reduced injection frequency on quality of life was a key driver of icodec being associated with improved quality-adjusted life expectancy across all comparisons.
- The results from the *post-hoc* analysis demonstrated the non-inferiority of icodec used with the dosing guide app compared with the other basal insulin analogs. However, these results should be interpreted with caution, especially when comparing icodec with glargine U100 and U300 given the very low number of patients in those treatment groups.
- For instance, the difference in the impact of the trial interventions on systolic blood pressure across the comparisons is very unlikely to be observed in clinical practice and might result from the low number of patients in the subgroups.
- Projecting long-term outcomes from short-term clinical trial data is associated with uncertainty in all long-term modeling studies in type 2 diabetes, but in the absence of long-term clinical data, modeling provides arguably the best available evidence for decision making for novel interventions.

Conclusion

- Icodec used with the dosing guide app was projected to be a cost-effective treatment compared with degludec, glargine U100 and glargine U300 in the UK, with utility benefits from reduced injection frequency a key driver of outcomes.

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References:
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