COST-EFFECTIVENESS OF INSULIN GLARGINE 300 UNITS/ML (GLA-300) VS INSULIN DEGLUDEC 100 UNITS/ML (IDEG) IN T2D

DANIEL R. MURPHY[1], XUETING YU[1], MARIE FOURNIER[2], TIMOTHY M. KLEIN[1], TAO FAN[3], SINEM PERK[1], RON PREBLICK[3], FANG LIZ ZHOU[3]

[1]MEDICAL DECISION MODELING INC., INDIANAPOLIS, IN, USA; [2]SANOFI, CHILLY-MAZARIN, FRANCE; [3]SANOFI US, INC., BRIDGEWATER, NJ, USA

BACKGROUND

- According to the Centers for Disease Control and Prevention, 29.1 million people in the US (equivalent to 9.3% of the population) had diabetes in 2014.[1]
- People with type 2 diabetes (T2D) not adequately controlled on metformin and additional oral medications may benefit from initiating basal insulin; this approach is supported by the American Diabetes Association (ADA) and American Association of Clinical Endocrinologists (AACE) 2017 recommendations.[2,3]
- Recently, novel second-generation basal insulin analogues have been approved, and evidence supporting their efficacy and safety continues to emerge.[4,5]
  - The novel insulin analogues insulin glargine 300 units/mL (Gla-300) and insulin degludec were approved in the US in 2015.
- A recent network meta-analysis (NMA) estimated the relative clinical efficacy of Gla-300 against that for insulin degludec 100 units/mL (IDeg) and other insulins.[6]
  - The NMA showed that Gla-300 was associated with a numerically lower, although not statistically significant, risk of hypoglycaemia compared with IDeg.

OBJECTIVE

- This study evaluated cost-effectiveness for Gla-300 and IDeg from a US payer perspective.

METHODS

Study Design

- This modelling study was performed using the IMS Core Diabetes Model V8.5,[7] which simulates clinical outcomes and costs for cohorts of patients with diabetes.

Cohort Definition

- The initial simulated cohort consisted of 2 subgroups of patients with T2D corresponding to the patient characteristics for the EDITION II and EDITION III trials for Gla-300:
  - the first subgroup consisted of patients previously treated with basal insulin plus a non-insulin antidiabetes treatment
  - the second subgroup consisted of patients initially adding basal insulin to a non-insulin antidiabetes treatment (i.e. insulin-naive patients)
  - patients previously treated with basal insulin and insulin-naive patients represented 52% and 48% of the cohort, respectively.
- The simulated cohort consisted of patients with an average age of 62 years; mean duration of diabetes was 10 years in this cohort.
- The gender and ethnic makeup of the cohort was 52% male; 60% were Non-Hispanic White, 24% Non-Hispanic Black, 7% Hispanic, 6% Asian, and 3% Native American.
- Mean glycated haemoglobin A_{1c} (A1C) for the cohort was 8.3%.
- The initial clinical and complications profile reflected data for a typical cohort of this age group and T2D duration.

Model Inputs

- Unless specified, base case model inputs utilized default values from the IMS Core Diabetes Model; a list of inputs for these major parameters in the base case analysis is presented in **Table 1**.

Treatment Efficacy

- Treatment efficacy, measured as reduction in A1C and reduction in hypoglycaemia rates, was estimated using data from the NMA for a cohort corresponding to EDITION II and EDITION III patients.[6]
  - A1C: the NMA estimated an A1C reduction of –1.00% for Gla-300 and –0.98% for IDeg over 24 weeks.
  - hypoglycaemia: event rates were estimated for NSHEs and SHEs typically requiring medical assistance.
    - Gla-300 was estimated to be associated with 2.5 SHEs per 100 patient-years; for IDeg, 4 SHEs per 100 patient-years.
    - Gla-300 was estimated to be associated with 446 NSHEs; for IDeg, 555 NSHEs per 100 patient-years.

Dosage

- The mean Gla-300 dosage used in this analysis was a weighted average of the dosages from the EDITION II and EDITION III trials.[12,13]
- The mean IDeg dosage was estimated from trial data against insulin glargine.[14-18]
- Using these data, a dosage ratio between insulin glargine and IDeg of 0.9367 was estimated; this dosage ratio was applied to the EDITION II and EDITION III insulin glargine dosages to estimate the IDeg dosage for these populations.

Costs

- The cost per unit for Gla-300 was set at $0.222; this cost represents the dosage-adjusted parity price for insulin glargine based on dosage for all patients in the EDITION trials.
- The cost of IDeg was set to $0.2959 per unit.
- Insulin costs were based on the wholesale acquisition cost from Red Book Online (2015).
- Yearly insulin costs per patient were estimated as $6,043 for Gla-300 and $6,718 for IDeg.
- The cost per event for hypoglycaemia was set to $1,561 for SHEs and $13.65 for NSHEs.[19,20]
- Costs were adjusted for inflation to 2015 US dollar values (US Dept. of Labor 2015).

Utilities

- Utilities to estimate patient quality adjusted life years (QALYs) for multiple comorbidities were applied using the minimum utility approach.[8,9]
- A disutility was applied for each SHE.[7] For NSHEs, the method of diminishing marginal disutility was used.[10]

MODEL ANALYSES

- Base case:
  - a cohort of 1,000 patients was simulated
  - the simulation time-horizon was set to 50 years
  - clinical and economic discount rates were set at 3%.[7]
- One-way sensitivity analyses: a series of one-way sensitivity simulations were performed by varying parameters ± 10% from their base case values (treatment efficacy, drug costs, hypoglycaemia costs, non-hypoglycaemia medical costs).
- Probabilistic sensitivity analysis (PSA):
  - the direct medical costs for complications were varied in a range of ± 10% using a uniform distribution
  - treatment efficacies were varied based on the 95% confidence intervals determined from the NMA[6]
  - patient baseline clinical data variation was based on the standard deviation/error of the model inputs in **Table 1**
  - for both treatment efficacy and baseline clinical data, samples were drawn from a normal distribution.

Table 1. Model Inputs.

Parameters	Base Case Input	Data Source
Patient demographics		CORE V8.5 Defaults (IMS Health Incorporated, 2016)[7]
Start age, mean (SD), years	62.2 (6.9)	
Duration of diabetes, years	10	
Proportion male, %	52.3	
Clinical values		
A1C, mean (SD), %	8.30 (1.10)	
Systolic blood pressure, mean (SD), mmHg	139.2 (15.8)	
Diastolic blood pressure, mean (SD), mmHg	80 (0)	
Body mass index, mean (SD), kg/m^2	32.1 (5.6)	
Estimated glomerular filtration rate, mean (SD), mL/min/1.73 m^2	77.5 (0)	
Haemoglobin, mean (SD), g/dL	14.5 (0)	
Proportion smoker	0.13	
Treatment efficacy (A1C reduction), %		Freemantle, et al., 2016[6]
Gla-300	–1.00	
IDeg	–0.98	
Hypoglycaemia (events per 100 patient-years), n		
Gla-300 SHEs	2.5	
Gla-300 NSHEs	446	
IDeg SHEs	4	
IDeg NSHEs	555	
Quality of life utilities		CORE V8.5 Defaults (IMS Health Incorporated, 2016);[7] Dale, et al., 2008;[8] Fu and Kattan, 2008;[9] Lauridsen et al., 2014[10]
T2D with no complications	0.814	
Disutility myocardial infarction event	–0.129	
Disutility stroke event	–0.181	
Microalbuminuria	0.814	
Gross proteinuria	0.814	
Haemodialysis	0.604	
Peritoneal dialysis	0.612	
Renal transplant	0.75	
Neuropathy	0.63	
Disutility for NSHE	Diminishing approach[10]	
Disutility for SHE	–0.0118	
Medical costs, $		CORE V8.5 Defaults (IMS Health Incorporated, 2016)[7]
Statins	61	
Aspirin	30	
Acetylcholinesterase inhibitor	62	
Screening for microalbuminuria	23	
Screening for gross proteinuria	36	
Myocardial infarction (first year)	53,226	
Myocardial infarction (≥ second year)	4,847	
Stroke (first year)	18,005	
Stroke (≥ second year)	1,834	
Stroke death within 30 days	18,005	
Haemodialysis costs first year	32,105	
Annual costs haemodialysis (≥ second year)	23,157	
Peritoneal dialysis costs (first year)	37,798	
Annual costs peritoneal dialysis (≥ second year)	34,042	
Renal transplant costs (first year)	28,678	
Annual costs renal transplant (≥ second year)	14,677	
Neuropathy (first year)	4,668	
Neuropathy (≥ second year)	1,275	
NSHE	13.65	
SHE	1,561	
Insulin costs and dosages, $		First Databank, Inc., 2015;[11] Freemantle, et al., 2016;[6] Yki-Järvinen, et al., 2014;[12] Bolli, et al., 2015[13]
Gla-300 cost per unit	0.2220	
IDeg cost per unit	0.2959	
Gla-300 estimated cost per year	6,043	
IDeg estimated cost per year	6,718	
Discount rates, %		CORE V8.5 Defaults (IMS Health Incorporated, 2016)[7]
Discount clinical	3	
Discount costs	3	

NSHE, non-severe hypoglycaemia events; SD, standard deviation; SHE, severe hypoglycaemia events.

RESULTS

Base Case

- The base case results from the simulation are presented in **Table 2**.
- Gla-300 dominated IDeg with both an effectiveness advantage of 0.035 QALYs (7.677 QALYs vs 7.642 QALYs, respectively) gained from the better A1C efficacy and reduced hypoglycaemia, and a lifetime cost saving of $8,998 ($162,288 vs $171,286 for Gla-300 vs IDeg, respectively).

Table 2. Base Case Analysis Summary Results.

	Gla-300	IDeg
Life expectancy, years	12.024	12.015
Undiscounted life expectancy, years	16.483	16.470
Quality-adjusted life expectancy, years	7.677	7.642
Undiscounted quality-adjusted life expectancy, years	10.426	10.378
Combined costs, $	162,288	171,286
Incremental cost per incremental QALY, $	–257,074	

One-Way Sensitivity Analyses

- The results from this one-way sensitivity analysis are shown in **Figure 1**.
- A 10% change in either direction for any single variable did not change the ICER dominance for Gla-300 vs IDeg.

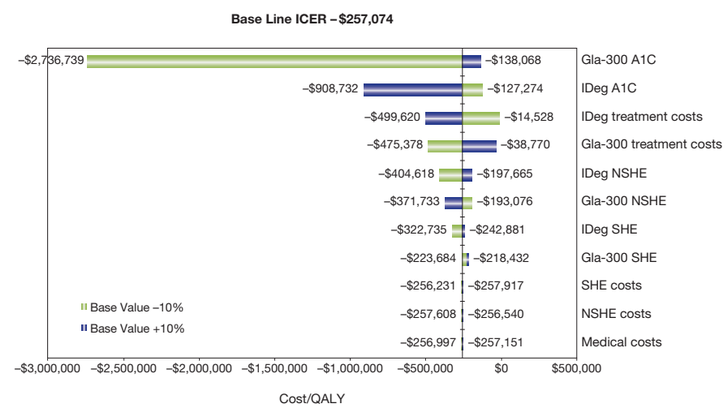
Probabilistic Sensitivity Analysis

- Results from the PSA for the base case scenario are shown in **Figure 2**, which shows the joint incremental total costs and QALYs for 1,000 groups of 1,000 patients.
- Incremental total costs from the PSA ranged from $15,033 (favouring IDeg) to –$26,885 (favouring Gla-300).
- Incremental QALYs ranged from 0.622 (favouring Gla-300) to –0.507 (favouring IDeg).
- Gla-300 was estimated to be less costly in 95.4% of the cases and more effective in 60.1% of the cases.
- IDeg was estimated to be both less costly and more effective in 1 case (0.1% of cases).
- Gla-300 was estimated to be both less costly and more effective in 556 cases (55.6% of cases).

STRENGTHS AND LIMITATIONS

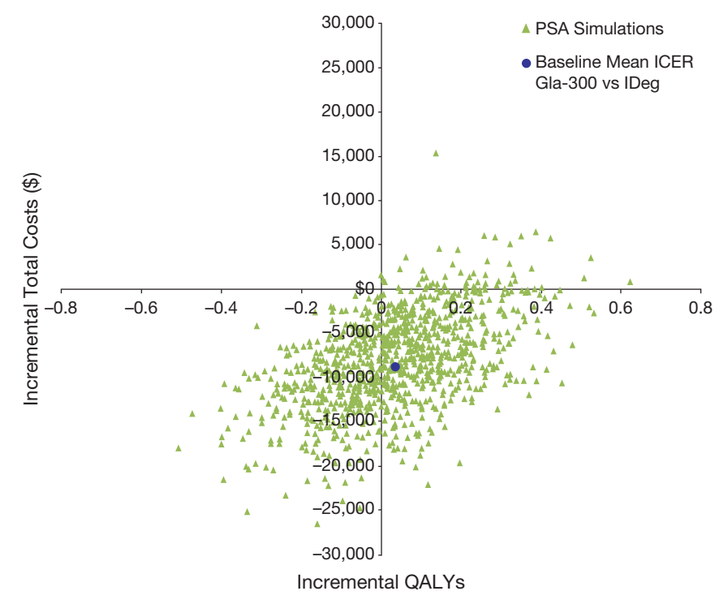
- In this analysis, we showed a dominant ICER for Gla-300 in the base case scenario, as well as in one-way and probabilistic sensitivity analyses; this was demonstrated over a wide range of estimates.
- Limitations of this study include the fact that treatment efficacy and hypoglycaemia rates may not be reflective of real-world data; we also note that trial definition of NSHE is based typically on blood glucose readings, which may or may not be reflective of the actual need for (and expense of) medical assistance in a real-world setting.
- Another limitation of this analysis is that long-term projections of incremental patient outcomes are based solely on the A1C efficacy and hypoglycaemia rates estimated by NMA.
- The sensitivity analyses did not include changes to patient clinical parameters such as cardiovascular variables and estimated glomerular filtration rate, which would also impact complication risk in patients with T2D.

Figure 1. One-Way Sensitivity Analysis Tornado Diagram.



ICER, incremental cost-effectiveness ratio.

Figure 2. Probabilistic Sensitivity Analyses Plots.



CONCLUSIONS

- Gla-300 provided a dominant cost-effectiveness profile vs IDeg primarily due to lower treatment- and hypoglycaemia-related medical costs and higher QALYs from fewer hypoglycaemia events, though real-world data are needed to confirm this finding.

REFERENCES

1. Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2014. Available from: www.cdc.gov/diabetes/pubs/statsreport14/national-diabetes-report-web.pdf. Accessed April 12, 2016.
2. American Diabetes Association. Standards of Medical Care in Diabetes – 2017. Available from: http://professional.diabetes.org/sites/professional.diabetes.org/files/media/dc_40_s1_final.pdf. Accessed April 12, 2017.
3. The American Association of Clinical Endocrinologists and American College of Endocrinology. Available from: www.aace.com/sites/all/files/diabetes-algorithm-executive-summary.pdf. Accessed January 30, 2017.
4. Russell-Jones D, et al. Nutr Metab Cardiovasc Dis. 2015;25:898-905.
5. Clements JN, Bello L. Am J Health Syst Pharm. 2016;73:359-66.
6. Freemantle N, et al. Diabetes. 2016;65(Suppl. 1):A566.
7. IMS Health Incorporated. Available from: www.core-diabetes.com/login.asp. Accessed January 2016.
8. Dale W, et al. Med Decis Making. 2008;28:102-12.
9. Fu AZ, Kattan MW. Med Care. 2008;46:984-90.
10. Lauridsen JT, et al. Qual Life Res. 2014;23:2645-50.
11. First Databank, Inc. FDB MedKnowledge. Available from: www.fdbhealth.com. Accessed February 2015.
12. Yki-Järvinen H, et al. Diabetes Care. 2014;37:3235-43.
13. Bolli GB, et al. Diabetes Obes Metab. 2015;17:386-94.
14. Garber AJ, et al. Lancet. 2012; 379:1498-507.
15. Gough SC, et al. Diabetes Care. 2013;36:2536-42.
16. Zinman B, et al. Diabetes Care. 2012;35:2464-71.
17. Zinman B, et al. Lancet Diabetes Endocrinol. 2013;1:123-31.
18. Meneghini L, et al. Diabetes Care. 2013;36:858-64.
19. Curkendall SM, et al. JCOM. 2011;18:455-62.
20. Brod M, et al. Value Health. 2011;14: 665-71.

ACKNOWLEDGEMENTS AND DISCLOSURES

This poster was presented previously at the 77th Scientific Sessions of the American Diabetes Association (ADA); 9–13 June 2017; San Diego, CA, USA, 1323-P. This study was funded by Sanofi US, Inc. The authors received writing/editorial support in the preparation of this poster provided by Yunyu Huang, PhD, of Excerpta Medica, funded by Sanofi US, Inc.

Murphy, Yu, Klein, and Perk are employees of Medical Decision Modeling Inc., under contract with Sanofi US, Inc. Fournier is an employee of Sanofi Global. Fan, Preblick, and Zhou are employees of Sanofi US, Inc. and stockholders of Sanofi.

Email address for presenting author: drm@mdm-inc.com