Evaluating the Effectiveness of Switching to Insulin Degludec from Other Basal Insulins in a Real-World Canadian Population with Type 1 or Type 2 Diabetes: The CAN-TREAT Study

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SUPPLEMENTARY MATERIAL

Statistical analysis

Paired *t*-tests were also conducted for the change from baseline to 6 ± 3 months after insulin degludec (degludec) initiation in fasting plasma glucose (FPG), mean daily insulin dose (basal, prandial and total) and body weight. Least-square means estimates for change from baseline in glycated haemoglobin (HbA_{1c}) to 6 months after degludec initiation were reported and include associated 95% confidence intervals (CIs) and *p*-values. To obtain the analogous unadjusted estimate of least-square means, the analogous analysis of variance (ANOVA) model was generated where the only independent variable was the baseline HbA_{1c} value. McNemar's test was used to compare the change in proportion of patients attaining HbA_{1c} targets (<7.0%, <7.5% or <8.0%) from baseline to 6 ± 3 months after degludec initiation. The change in rate of hypoglycaemic episodes was analysed using a negative binomial model in which rate differences were analysed using an identity link function, and rate ratios were analysed using a log link function.

Table S1. Participation feasibility questionnaire

Questions
1. How many type 1 and type 2 diabetes patients do you see (per month)?
2. How frequently do you see your type 1 and type 2 patients treated with basal insulin?
3. How many of those did you prescribe degludec to, and how many started this drug at least 6 months ago?
4. Have you ever been involved in any type of clinical research or non-interventional study?
5. Would you be interested in taking part in a retrospective chart review looking at the treatment of diabetes with degludec and its outcomes?

Degludec, insulin degludec

Table S2. List of investigators, research ethics boards/institutional review boards

Site no.	Investigator name and address	Name of research ethics board/institutional review board	Reference no.
101	Dr Tharsan Sivakumar Sivakumar Medicine Professional Corporation (Institute of Diabetes & Endocrinology), Scarborough, ON, Canada	Advarra, Aurora, ON, Canada	IRB00000971
102	Dr Sorin Beca My Endo Diabetes & Endocrinology, Markham, ON, Canada	Advarra, Aurora, ON, Canada	IRB00000971
103	Dr Joanne Frances Liutkus Dr. Liutkus' office, Cambridge, ON, Canada	Advarra, Aurora, ON, Canada	IRB00000971
104	Dr James Robin Conway Canadian Centre for Research on Diabetes, Smiths Falls, ON, Canada	Advarra, Aurora, ON, Canada	IRB00000971
105	Dr John Sigalas Dr Sigalas' office, Scarborough, ON, Canada	Advarra, Aurora, ON, Canada	IRB00000971
106	Dr Farrukh Khan Dr Khan's office, Scarborough, ON, Canada	Advarra, Aurora, ON, Canada	IRB00000971
107	Dr Lionel Hindler Shubenacadie Medical Centre, Shubenacadie, NS, Canada	Advarra, Aurora, ON, Canada	IRB00000971
108	Dr Basel Bari Markham HealthPlex Medical Centre, Markham, ON, Canada	Advarra, Aurora, ON, Canada	IRB00000971
109	Dr Liviu Danescu L. Danescu Medicine Professional Corporation, Guelph, ON, Canada	Advarra, Aurora, ON, Canada	IRB00000971
110	Dr Donald Breton Clinique Médicale Angus/Pavillon Sherbrooke, Montreal, QC, Canada	Advarra, Aurora, ON, Canada	IRB00000971
111	Dr Deborah Zwicker Dr Zwicker's office, Sydney, NS, Canada	Advarra, Aurora, ON, Canada	IRB00000971
112	Dr Adam White	Advarra, Aurora, ON, Canada	IRB00000971

	Vancouver Endocrinology Associates, Vancouver, BC, Canada		
113	Dr Jean Garon Clinique Medigo-Endocrinologie, Gatineau, QC, Canada	Advarra, Aurora, ON, Canada	IRB00000971
114	Dr Yves Robitaille Centre de Médecine Métabolique de Lanaudière, Terrebonne, QC, Canada	Advarra, Aurora, ON, Canada	IRB00000971
115	Dr Marie-Andrée Corbeil Bureau Dr M.A.Corbeil, St-Jean-sur-Richelieu, QC, Canada	Advarra, Aurora, ON, Canada	IRB00000971
116	Dr Joseph Shaban 11811 Tecumseh Road E, Tecumseh, ON, Canada	Advarra, Aurora, ON, Canada	IRB00000971
117	Dr Luis Noronha Diabetes Heart Research Centre, Toronto, ON, Canada	Advarra, Aurora, ON, Canada	IRB00000971
118	Dr Jeffrey Winterstein 8882- 170th Street, Edmonton, Canada	Health Research Ethics Board of Alberta, Community Health Committee, Edmonton, AB, Canada	IRB00001209
119	Dr George M. Tsoukas Applied Medical Informatics Research Inc. (A.M.I.R.), Montreal, QC, Canada	Advarra, Aurora, ON, Canada	IRB00000971
120	Dr George O. Tsoukas Applied Medical Informatics Research Inc. (A.M.I.R.), Montreal, QC, Canada	Advarra, Aurora, ON, Canada	IRB00000971
121	Dr Michael Tsoukas Applied Medical Informatics Research Inc. (A.M.I.R.), Montreal, QC, Canada	Advarra, Aurora, ON, Canada	IRB00000971
122	Dr Alexandro Zarruk West Island Metabolic Unit, Pierrefonds, QC, Canada	Advarra, Aurora, ON, Canada	IRB00000971
123	Dr Richard Dumas Centre de recherches cliniques de Laval, Laval, QC, Canada	Advarra, Aurora, ON, Canada	IRB00000971
124	Dr John MacFadyen Orillia Internal Medicine Associates Inc., Orillia, ON, Canada	Advarra, Aurora, ON, Canada	IRB00000971

125	Dr Stewart Harris Western University-Centre for Studies in Family Medicine, London, ON, Canada	Western Research, London, ON, Canada	IRB00000940
126	Dr Sylvie Bertrand Clinique Médicale Angus, Montreal, QC, Canada	Advarra, Aurora, ON, Canada	IRB00000971
127	Dr Buki Ajala LMC Healthcare, Calgary, AB, Canada	Health Research Ethics Board of Alberta, Community Health Committee, Edmonton, AB, Canada	IRB00001209
128	Dr Harpreet Bajaj LMC Healthcare, Brampton, ON, Canada	Advarra, Aurora, ON, Canada	IRB00000971
129	Dr Tina Kader LMC Healthcare, Montreal, QC, Canada	Advarra, Aurora, ON, Canada	IRB00000971
130	Dr Hasnain Khandwala LMC Healthcare, Etobicoke, ON, Canada	Advarra, Aurora, ON, Canada	IRB00000971
131	Dr Patricia Peticca LMC Healthcare, Nepean, ON, Canada	Advarra, Aurora, ON, Canada	IRB00000971
132	Dr Stuart Ross LMC Healthcare, Calgary, AB, Canada	Health Research Ethics Board of Alberta, Community Health Committee, Edmonton, AB, Canada	IRB00001209
133	Dr Nouhad Saliba LMC Healthcare, Ville Saint-Laurent, QC, Canada	Advarra, Aurora, ON, Canada	IRB00000971
134	Dr Robert Schlosser LMC Healthcare, Concord, ON, Canada	Advarra, Aurora, ON, Canada	IRB00000971
135	Dr Oren Steen LMC Healthcare, Toronto, ON, Canada	Advarra, Aurora, ON, Canada	IRB00000971
136	Dr David Twum-Barima LMC Healthcare, Oakville, ON, Canada	Advarra, Aurora, ON, Canada	IRB00000971
137	Dr Barna Tugwell Nova Scotia Health Authority/QE II Health Sciences Centre, Halifax, NS, Canada	Nova Scotia Health Authority Research Ethics Board, Centre for Clinical Research, Halifax, NS, Canada	IRB00010873
138	Dr Irene Hramiak St. Joseph’s Health Care London, London, ON, Canada	Western Research, London, ON, Canada	IRB00000940

Table S3. Reasons for screening failure

Reason	***N* (%)**
Patients who were excluded from the analysis	41 (6.1)
Patient records failed minimum data requirement	29 (4.3)
Patient did not switch to degludec ≤6 months prior to date of informed consent obtained	5 (0.7)
<6 months' basal insulin before switch	3 (0.4)
Initiated degludec as part of a clinical trial	2 (0.3)
SCII ≤6 months before switch	2 (0.3)
No medical visit after switch	1 (0.1)

Degludec, insulin degludec; *N*, number of patients*; SCII*, subcutaneous insulin infusion.

Table S4. Prevalence of diabetes complications and comorbidities at baseline in patients with T1D or T2D

Diabetes complications	**T1D (*N*=275)**	**T2D (*N*=351)**
Sensory-motor neuropathy	40 (15.0)	63 (18.2)
Diabetic retinopathy	67 (25.1)	62 (17.9)
Renal insufficiency	17 (6.4)	55 (15.9)
Mild	3 (1.1)	18 (5.2)
Moderate	6 (2.2)	17 (4.9)
Severe	3 (1.1)	9 (2.6)
Unknown	5 (1.9)	11 (3.2)
Comorbidities*		
None	88 (33.0)	43 (12.4)
Coronary heart disease	16 (6.0)	63 (18.2)
Myocardial infarction	6 (2.2)	24 (6.9)
Reperfusion/revascularization procedure	7 (2.6)	35 (10.1)
Other	3 (1.1)	1 (0.3)
Missing	0	3 (0.9)
Stroke	4 (1.5)	10 (2.9)
Peripheral vascular disease	6 (2.2)	12 (3.5)
Hypertension	83 (31.1)	219 (63.1)
Dyslipidaemia	122 (45.7)	253 (72.9)
Other	51 (19.1)	70 (20.2)
Missing	0	0
Unknown	8 (2.9)	4 (1.1)

N, number of patients; *T1D,* type 1 diabetes; *T2D,* type 2 diabetes.

Notes: Data are *n* (%).

* Percentages were calculated for patients with known comorbidities (i.e. by excluding ‘unknown’ values from the denominator).

Table S5. Proportion of patients from the total population achieving HbA_{1c} targets at baseline and 6 ± 3 months after initiating degludec

T1D			
Baseline HbA_{1c}	Month 6 ≥7.0%	Month 6 <7.0%	Difference
<7.0%	12 (4.4)	22 (8.0)	*p*=0.063
≥7.0%	204 (74.2)	23 (8.4)	
	Month 6 ≥7.5%	Month 6 <7.5%	
<7.5%	20 (7.3)	57 (20.7)	*p*=0.096
≥7.5%	152 (55.3)	32 (11.6)	
	Month 6 ≥8.0%	Month 6 <8.0%	
<8.0%	19 (6.9)	94 (34.2)	*p*<0.001
≥8.0%	102 (37.1)	46 (16.7)	
T2D			
Baseline HbA_{1c}	Month 6 ≥7.0%	Month 6 <7.0%	Difference
<7.0%	17 (4.8)	25 (7.1)	*p*<0.001
≥7.0%	250 (71.2)	50 (14.2)	
	Month 6 ≥7.5%	Month 6 <7.5%	
<7.5%	25 (7.1)	62 (17.7)	*p*<0.001
≥7.5%	185 (52.7)	70 (19.9)	
	Month 6 ≥8.0%	Month 6 <8.0%	
<8.0%	23 (6.6)	136 (38.7)	*p*<0.001
≥8.0%	107 (30.5)	76 (21.7)	

HbA_{1c}, glycated haemoglobin*; degludec,* insulin degludec; *T1D,* type 1 diabetes; *T2D,* type 2 diabetes.

Notes: *p*-value corresponding to the comparison between baseline and 6-months in each study population (T1D and T2D) using McNemars' Test. Only patients with known HbA_{1c} at baseline and 6 ± 3 months after degludec initiation were eligible for *p*-value calculation.

Table S6. Reasons for initiating degludec in patients with T1D and T2D

	T1D (*N*=275)	T2D (*N*=351)
Not at glycaemic target	174 (68.8)	248 (73.4)
Hypoglycaemia	135 (53.4)	111 (32.8)
Severe*	12 (8.9)	6 (5.4)
Non-severe*	116 (85.9)	91 (82.0)
Nocturnal*	58 (43.0)	48 (43.2)
Hypoglycaemia unawareness	20 (7.9)	12 (3.6)
Multiple risk factors for hypoglycaemia	19 (7.5)	30 (8.9)
Basal insulin dose >80 units/day	5 (2.0)	40 (11.8)
Twice-daily basal insulin dosing	33 (13.0)	38 (11.2)
FBG variability	112 (44.3)	83 (24.6)
Need for flexible time of dosing	49 (19.4)	61 (18.0)
Device issue	1 (0.4)	3 (0.9)
Other	9 (3.6)	13 (3.8)
Unknown	22 (8.0)	13 (3.7)

FBG, fasting blood glucose; *degludec,* insulin degludec ; *N*, number of patients; *T1D*, type 1 diabetes; *T2D,* type 2 diabetes.

Notes: Data are *n* (percentage) of patients out of the total number of patients with known reasons. Reasons were not mutually exclusive and multiple reasons could be selected for each patient.

* Data are *n* (percentage) of patients out of the total number of patients with a reason of hypoglycaemia.

Table S7. Reasons for discontinuing degludec in patients with T1D and T2D

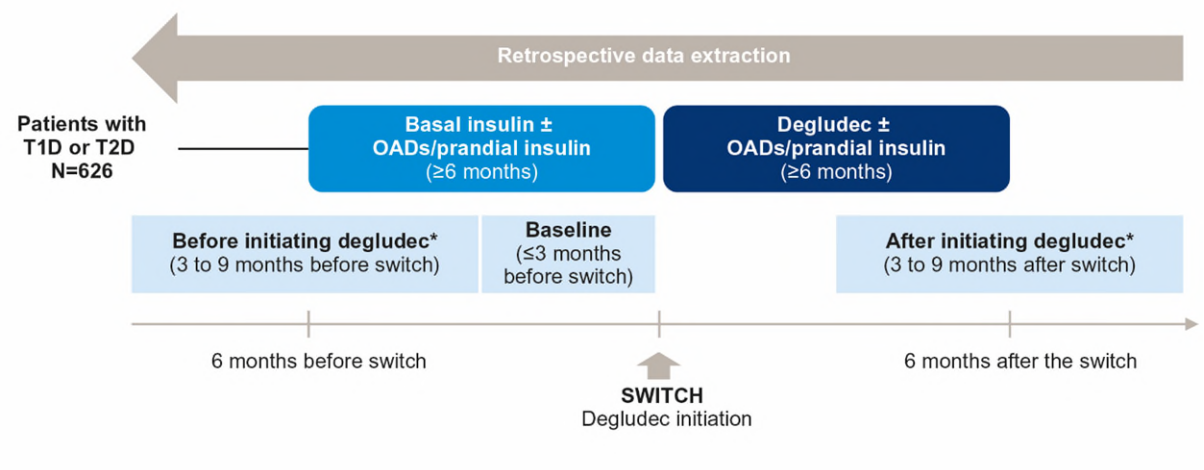
	T1D (*N*=275)	T2D (*N*=351)
Cost	0 (0.0)	2 (66.7)
Device issue	1 (50.0)	0 (0.0)
Other*	1 (50.0)	1 (33.3)
Unknown	3 (60.0)	0 (0.0)

Degludec, *insulin degludec; N*, number of patients; *T1D*, type 1 diabetes; *T2D*, type 2 diabetes.

Notes: Data are percentage of patients who discontinued degludec. Proportions were calculated as a percentage of known reasons for discontinuing degludec.

*One patient with T1D switched their degludec treatment to their original insulin glargine 300 units/mL; 1 patient with T2D discontinued degludec due to the occurrence of diarrhoea.

Fig. S1. Trial design.



*Time periods are correct for all endpoints with the exception of hypoglycaemia events, for which data were collected over specific 6-month periods (before initiating degludec: 6 to 0 months prior to baseline; after initiating degludec: 0–6 months after baseline).

Degludec, insulin degludec; *N*, number of patients; *OAD*, oral antidiabetic drug; *T1D*, type 1 diabetes; *T2D*, type 2 diabetes.