SUPPLEMENTARY DATA

Supplementary Table 1. Countries participating in the trial.

Country	Number of participants	Percentage of total study population
Argentina	30	4.4
Finland	39	5.7
Hungary	43	6.3
India	122	17.8
Israel	81	11.8
Malaysia	55	8.0
Mexico	40	5.8
Norway	25	3.6
Republic of Macedonia	71	10.3
Russian Federation	62	9.0
Serbia and Montenegro	33	4.8
South Africa	40	5.8
Taiwan	15	2.2
UK	31	4.5

Supplementary Table 2. Inclusion criteria.

1	Informed consent obtained before any trial related activities. (Trial related activities were defined as any procedure that would not have been performed during standard management of the subject).
2	Male or female ≥18 years of age.
3	Type 2 diabetes mellitus (diagnosed clinically) for ≥6 months.
4	Current treatment: OAD(s) alone, basal insulin alone or the combination of OAD(s) and basal insulin. Allowed OADs (alone or in combination with basal insulin) were metformin, insulin secretagogues (SUs or glinides), pioglitazone with unchanged dosing for at least 3 months prior to Visit 1 with the minimum doses stated: Metformin: alone or in combination (including fixed combination) 1500 mg daily, or maximum tolerated dose (at least 1000 mg daily) Insulin secretagogues (SU or glinide): minimum half of the daily maximal dose according to local labeling Pioglitazone: minimum half of the daily maximal dose according to local labeling or maximum tolerated dose.
5	HbA_{1c}: OAD-only users with HbA_{1c} 7.0–11.0% (both inclusive), basal insulin ± OADs users with HbA_{1c} 7.0–10.0% (both inclusive) by central laboratory analysis.
6	BMI ≤40.0 kg/m^2.
7	Ability and willingness to adhere to the protocol including performance of SMPG profiles according to the protocol.

HbA_{1c}=glycated hemoglobin. OAD=oral antidiabetic drug. SMPG=self-measured plasma glucose. SU=sulphonylurea.

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Supplementary Table 3. Exclusion criteria.

1	Use within the last 3 months prior to Visit 1 of: GLP-1 receptor agonists (exenatide, liraglutide), rosiglitazone, DPP-4 inhibitors, α-glucosidase-inhibitors.
2	Anticipated change in concomitant medication known to interfere significantly with glucose metabolism, such as systemic corticosteroids, beta blockers, monoamine oxidase inhibitors.
3	CVD within the last 6 months prior to Visit 1, defined as: stroke; decompensated heart failure New York Heart Association (NYHA) class III or IV; myocardial infarction; unstable angina pectoris; or coronary arterial bypass graft or angioplasty.
4	Uncontrolled treated/untreated severe hypertension (systolic blood pressure [BP] >180 mmHg or diastolic BP >100 mmHg).
5	Impaired liver function, defined as alanine aminotransferase (ALAT) ≥2.5 times upper limit of normal (one retest analyzed at the central laboratory within a week of receipt of the result was permitted with the result of the last sample being conclusive).
6	Impaired renal function defined as serum creatinine of ≥125 μmol/L (≥1.4 mg/dL) for males and ≥110 μmol/L (≥1.3 mg/dL) for females or according to local label for metformin use. One retest within 1 week of receipt of the result was permitted with the result of the last sample being conclusive.
7	Recurrent severe hypoglycemia (>1 severe hypoglycemic event during last 12 months), or hypoglycemic unawareness as judged by the investigator or hospitalization for diabetic ketoacidosis during the previous 6 months.
8	Proliferative retinopathy or maculopathy requiring treatment according to the investigator.
9	Pregnancy, breast-feeding, the intention of becoming pregnant or not using adequate contraceptive measures according to local requirements. (For the UK, adequate contraceptive measures were defined as established use of oral, injected, or implanted hormonal methods of contraception, sterilization, intrauterine device or intrauterine system, or consistent use of barrier methods.)
10	Cancer and medical history of cancer hereof (except basal-cell skin cancer and squamous-cell skin cancer).
11	Any clinically significant disease or disorder, except for conditions associated with type 2 diabetes, which in the investigator's opinion could have interfered with the results of the trial.
12	Mental incapacity, psychiatric disorder, unwillingness or language barriers precluding adequate understanding or cooperation, including subjects unable to read or write.
13	Previous participation in this trial. Participation was defined as randomized. Rescreening of screening failures was allowed only once within the limits of the recruitment period.
14	Known or suspected allergy to any of the trial products or related products.
15	Receipt of any investigational drug within 1 month prior to Visit 1.
16	Donation of blood or participation in other trials within 1 month prior to Visit 1.
17	Known or suspected abuse of alcohol, narcotics, or illicit drugs.

CVD=cardiovascular disease. DPP-4=dipeptidyl peptidase-4. GLP=glucagon-like peptide.

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Supplementary Table 4. Titration algorithm.

Mean pre-breakfast plasma glucose*		**Dose adjustment of IDeg or IGlar**
mmol/L	mg/dL	
<3.1[†]	<56[†]	Decrease by 4 U[‡]
3.1–3.8[†]	56–69[†]	Decrease by 2 U[§]
3.9–<5.0	70–<90	No adjustment
5.0–<7.0	90–<126	Increase by 2 U
7.0–<8.0	126–<144	Increase by 4 U
8.0–<9.0	144–<162	Increase by 6 U
≥9·0	≥162	Increase by 8 U

*Mean from the 3 consecutive days prior to the site visit or telephone contact. [†]Unless there was an obvious explanation for the low value (eg, a missed meal). [‡]For a dose of >45 U, a 10% dose reduction was recommended. [§]For a dose of >45 U, a 5% dose reduction was recommended.
IDeg=insulin degludec. IGlar=insulin glargine.
Insulin doses were individually titrated once a week throughout the trial (by clinic or telephone contacts). Investigators based their decision to adjust doses on the average pre-breakfast SMPG and other available data, such as additional measurements of plasma glucose, hypoglycemic episodes, and lifestyle changes. A blinded titration committee (Novo Nordisk A/S) reviewed deviations weekly. Medically qualified Novo Nordisk employees, also blinded, visited sites for discussions about general issues on titration. SMPG was measured using a plasma-calibrated blood glucose meter (Abbott Diabetes Care, Illinois, USA).

Supplementary Table 5. Sensitivity analyses of the primary endpoint.

Analysis	**Estimated treatment difference** (IDeg OD Flex - IGlar OD)
Per-protocol*	0.06 [–0.09 to 0.22]
Simple model[†]	0.03 [–0.13 to 0.19]
Repeated measurements model[‡]	0.06 [–0.09 to 0.20]

*The change from baseline in the response after 26 weeks of treatment was analyzed using an ANOVA method with treatment, region, sex, and antidiabetic treatment at screening as fixed effects, and age and baseline as covariates. [†]Change from baseline in the response after 26 weeks of treatment was analyzed using an ANOVA method (FAS) with treatment as fixed effect, and baseline response as covariate. [‡]HbA_{1c} (%) records available at scheduled time points after randomization were jointly analyzed in a linear mixed model (FAS) with an unstructured residual covariance matrix, and with treatment, time, interaction between treatment and time, region, anti-diabetic treatment at screening, and sex as fixed effects, and age and baseline HbA_{1c} (%) as covariates. FAS=full analysis set. HbA_{1c}=glycated hemoglobin. IDeg=insulin degludec. IGlar=insulin glargine. OD=once daily.

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Supplementary Table 6. Nocturnal confirmed hypoglycemic episodes by weekday.

	IDeg OD Flex (n=230)				**IGlar OD** (n=229)				**IDeg OD** (n=226)		
	n	**%**	**rate**		**n**	**%**	**rate**		**n**	**%**	**rate**
Total	31	13.5	0.63		49	21.4	0.75		24	10.6	0.56
Mon	10	4.3	0.86		14	6.1	1.13		6	2.7	0.54
Tues	13	5.7	1.05		15	6.6	1.06		9	4.0	0.60
Weds	6	2.6	0.53		13	5.7	0.86		10	4.4	0.87
Thurs	9	3.9	0.66		5	2.2	0.40		5	2.2	0.47
Fri	7	3.0	0.53		6	2.6	0.46		8	3.5	0.67
Sat	4	1.7	0.33		6	2.6	0.60		5	2.2	0.33
Sun	6	2.6	0.46		11	4.8	0.73		6	2.7	0.40

Hypoglycemic episodes occurring on or after the first day of exposure to treatment and no later than 7 days after the last day of treatment. Nocturnal confirmed hypoglycemia=confirmed hypoglycemia with an onset between 00:01 h and 05:59 h (inclusive). IDeg=insulin degludec. IGlar=insulin glargine. n=number of participants; %=percentage of all randomized participants in treatment group. rate=unadjusted event rate (episodes/patient year of exposure for the weekday). Data are from a post-hoc analysis.

Supplementary Table 7. Summary of adverse events.

	IDeg OD Flex (n=230)				**IDeg OD** (n=226)				**IGlar OD** (n=229)		
	n (%)	**E**	**rate**		**n (%)**	**E**	**rate**		**n (%)**	**E**	**rate**
AEs	122 (53)	428	4.0		128 (57)	411	3.9		128 (56)	405	3.8
SAEs	6 (3)	9	0.08		8 (4)	11	0.11		4 (2)	4	0.04
AEs possibly or probably related to investigational product											
	25 (11)	36	0.3		20 (9)	26	0.2		19 (8)	24	0.2

Table shows treatment-emergent adverse events (adverse events occurring on or after the first day of exposure to treatment and no later than 7 days after the last day of treatment). Data are from the safety analysis set. AE=adverse event. E=number of events. IDeg=insulin degludec. IGlar=insulin glargine. n=number of participants with events. OD=once daily. rate=events/patient year of exposure. SAE=serious adverse event. %=proportion of participants with events.

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Three SAEs were reported (for three participants in the IDeg OD group) that were considered as possibly or probably related to investigational product by the investigator: colon cancer and two cases of severe hypoglycemia. The case of colon cancer was considered by the investigator to be possibly related to trial product (based on recent publications discussing the relationship between IGlar and cancer), but unlikely related to investigational product by the sponsor (considering the potential association of diabetes with colon cancer).

Supplementary Table 8. Adverse events occurring with a frequency of ≥5%.

	IDeg OD Flex (n=230)				**IDeg OD** (n=226)				**IGlar OD** (n=229)		
AE	**n (%)**	**E**	**rate**		**n (%)**	**E**	**rate**		**n (%)**	**E**	**rate**
Nasopharyngitis	23 (10)	28	0.3		20 (9)	28	0.3		18 (8)	21	0.2
URI	20 (9)	21	0.2		11(5)	14	0.1		20 (9)	27	0.3
Dizziness	3 (1)	3	0.03		3 (1)	3	0.03		12 (5)	13	0.1
Headache	16 (7)	25	0.2		16 (7)	18	0.2		9 (4)	12	0.1
Diarrhea	10 (4)	12	0.1		14 (6)	17	0.2		10 (4)	11	0.1
Back pain	12 (5)	13	0.1		9 (4)	9	0.1		6 (3)	9	0.1

Treatment-emergent adverse events (adverse events occurring on or after the first day of exposure to treatment and no later than 7 days after the last day of treatment) reported by ≥5% of participants in any one treatment group. Data are from the safety analysis set. AE=adverse event. E=number of events. IDeg=insulin degludec. IGlar=insulin glargine. n=number of participants with events. OD=once daily. rate=events/patient year of exposure. URI=upper respiratory tract infection. %=proportion of participants with events.

Supplementary Table 9. Antibodies cross-reacting to human insulin (% B/T) in participants treated with insulin prior to the study.

	Baseline				**End of follow-up***		
	n	**mean (SD)**	**median (min; max)**		**n**	**mean (SD)**	**median (min; max)**
IDeg OD Flex	98	7.6 (16.4)	0·0 (0.0; 72.0)		91	8.0 (16.9)	1.0 (–1.0; 71.0)
IDeg OD	95	7.4 (14.5)	1.0 (0.0; 68.0)		89	7.7 (16.0)	1.0 (0.0; 72.0)
IGlar OD	95	7.4 (13.7)	1.0 (–1.0; 68.0)		88	7.1 (13.1)	1.0 (–1.0; 65.0)

*End of follow-up was week 27 (ie, 1 week after the end of the treatment period to allow washout).
% B/T=percentage bound/total radioactivity. IDeg=insulin degludec. IGlar=insulin glargine. OD=once daily.

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Supplementary Table 10. Antibodies cross-reacting to human insulin (% B/T) in participants who were insulin naïve prior to the study.

	Baseline				End of follow-up*		
	n	**mean (SD)**	**median (min; max)**		**n**	**mean (SD)**	**median (min; max)**
IDeg OD Flex	132	1.3 (7.3)	0.0 (–1.0; 5.0)		118	1.8 (6.7)	0.0 (–1.0; 56.0)
IDeg OD	131	1.3 (6.0)	0.0 (–1·0; 48.0)		121	3.2 (11.3)	0·0 (–1.0; 71.0)
IGlar OD	134	0.5 (1.8)	0.0 (–1.0; 14·0)		122	3.5 (11.7)	0.0 (–1.0; 70.0)

*End of follow-up was week 27 (ie, 1 week after the end of the treatment period to allow washout).
% B/T=percentage bound/total radioactivity. IDeg=insulin degludec. IGlar=insulin glargine. OD=once daily.

Supplementary Table 11. Principal Investigators.

Argentina	Laura Elena Maffei, Daniel Prudente Sandin, Jorge Horacio Alvariñas, Luis de Loredo
Finland	Jorma Lahtela, Vesa Järveläinen, Päivi Korhonen, Markku Savolainen, Merja Laine, Tina Hellsten, Anne-Mari Helkkula.
Hungary	Albert Szocs, Tibor Hidvegi, Marietta Baranyai
India	Sunil M. Jain, Nihal Thomas, Harish Kumar, A. Ramachandran, Bipin Kumar Sethi, Nalini Shah, Subhankar Chowdhury, Debasish Maji, Nikhil Tandon, Anil Bhansali
Israel	Ilana Harman-Boehm, Itamar Raz, Hilla Knobler, Julio Wainstein, Ilan Shimon, Victor Vishlitzky, Mark Niven, Eddy Karnieli
Malaysia	Wan Mohamad Wan Bebakar, Zanariah Hussein, Malik Mumtaz, Nor Azmi Kamaruddin, Chan Siew Pheng
Mexico	Pedro Alberto García-Hernández, Israel Olvera-Alvarez
Norway	Kåre I. Birkeland, Christian Fossum, Hans Olav Høivik, Aleksandra Debowska, Paal Norheim, Ephrem Thanendran Mariampillai
Republic of Macedonia	Cedomir Dimitrovski.
Russian Federation	Marina Shestakova, Alexander Yurievich Maiorov, Alsou Gafurovna Zalevskaya, Natalia V. Vorokhobina, Irina Askoldovna Egorova, Irina Yurievna Demidova, Farida Vadutovna Valeeva, Marina Fedorovna Kalashnikova
Serbia and Montenegro	Nebojsa Lalic, Dragan Micic, Miroslava Zamaklar
South Africa	Deepak Ramjee Lakha, S Pillay, Essack Aziz Mitha
Taiwan	Lee-Ming Chuang, Larry Ho, Yi-Jen Hung
UK	Steve Atkin, Roy Harper, Carol McKinnon, John McKnight, Gerry Rayman, Stephen Bain

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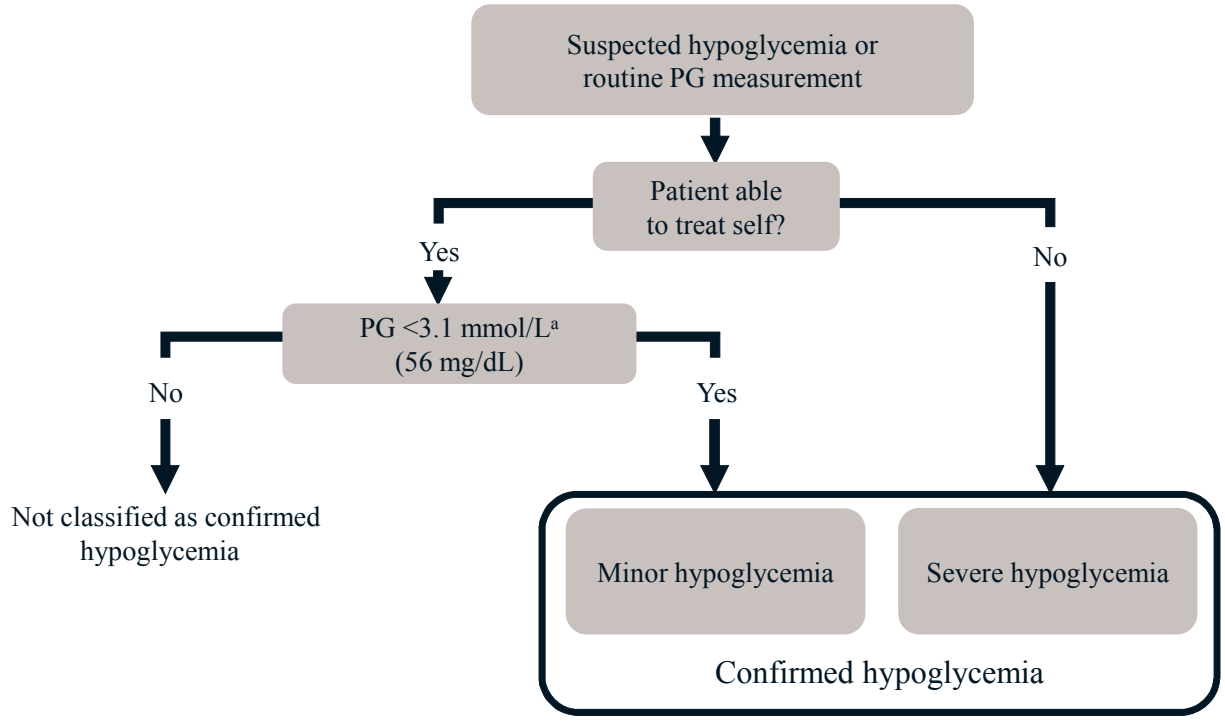
Supplementary Figure 1. Definition of confirmed hypoglycemia.



[a] with or without symptoms; severe episodes did not need to be confirmed by a PG value <3.1 mmol/L. PG=plasma glucose.

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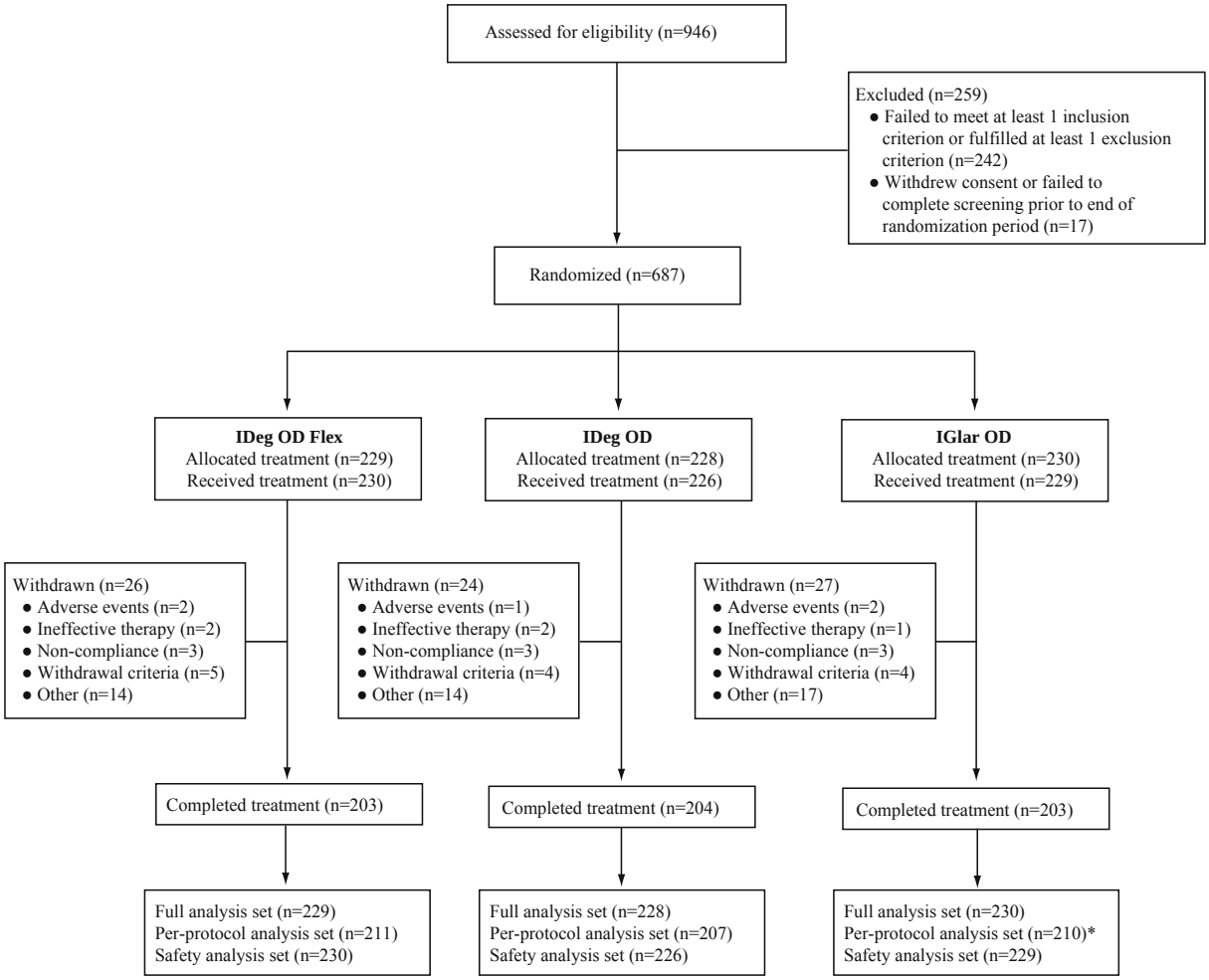
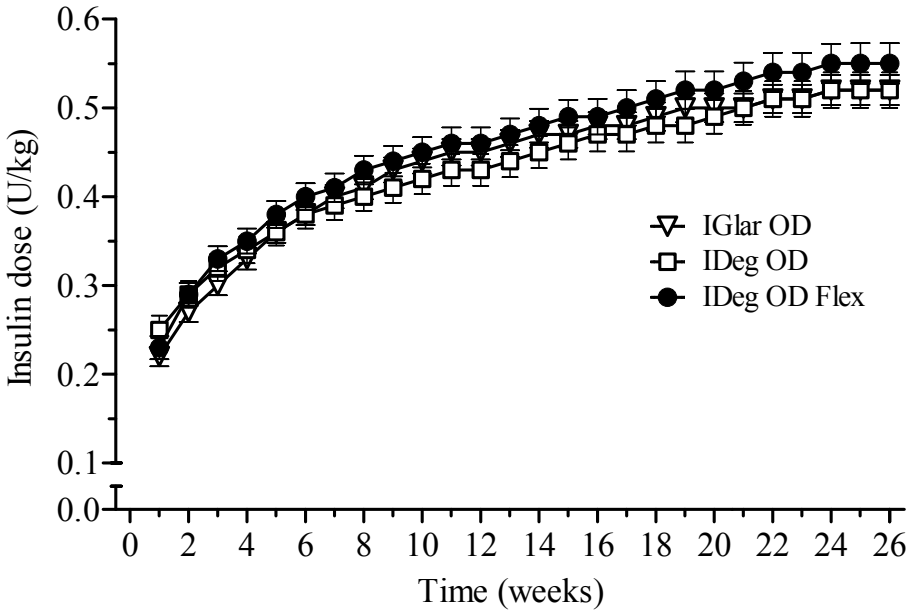
Supplementary Figure 2. Trial Profile.



Of the 687 randomized participants, two withdrew their consent before exposure to trial product (one subject in each of the IDeg OD Flex and IGlar OD groups). These subjects are included in the full analysis set for their respective treatment groups. Two subjects were randomized to IDeg OD but were treated according to the IDeg OD Flex regimen by mistake. Because the full analysis set was defined as all patients randomized to a particular treatment group (according to the intention-to-treat principle), these two subjects were included in the IDeg OD full analysis set. However, as subjects were to contribute to the statistical evaluation of safety 'as treated', they were included in the safety analysis set for the IDeg Flex group. *One patient was included in the per-protocol analysis set for IGlar OD by mistake; the patient received treatment with a DPP-4 inhibitor in violation of Exclusion Criteria #1 (Supplemental Table S3). IDeg=insulin degludec. IGlar=insulin glargine.

Supplementary Figure 3. Mean insulin dose over time (units/kg).



IDeg=insulin degludec. IGlar=insulin glargine. OD=once daily. Errors bars show standard error of the mean. Data are for the safety analysis set.