SUPPLEMENTARY DATA

Supplementary Table 1. Study inclusion and exclusion criteria

Inclusion criteria included:
• Adults (≥ 18 years old) with type 2 diabetes (World Health Organization criteria)
• Duration of diabetes ≥1 year
• Receiving basal insulin (NPH [isophane], insulin detemir or insulin glargine) and from 0 to 3 OAMs for ≥90 days prior to the study. Doses of oral antihyperglycemic medications (OAMs) were required to be stable for ≥90 days prior to Visit 1 (at least 1 of the OAMs ≥half the maximum daily dose allowed by local regulations or at the maximally tolerated dose).
• HbA1c ≤9.0% (75 mmol/mol)
• Body Mass Index ≤45.0 kg/m^2
Exclusion criteria included:
• Use of a routine regimen of insulin glargine twice daily in the past 90 days or routine use of prandial (rapid-acting) insulin therapy (outside of pregnancy) anytime in the past 6 months (except for short-term), Use of rosiglitazone, pramlintide, glucagon-like peptide-1 receptor agonist or weight-loss medications within 90 days prior to screening
• Use of niacin preparations as a lipid-lowering medication or bile acid sequestrants within 90 days prior to Visit 1
• Use of lipid-lowering medication at a dose that was not stable within 90 days prior to screening
• Any episodes of severe hypoglycemia, diabetic ketoacidosis or hyperglycemic hyperosmolar nonketotic coma within 6 months prior to Visit 1
• New York Heart Association Class III or IV cardiac disease
• History of renal transplantation
• Current renal dialysis
• Serum creatinine ≥2 mg/dL (177 µmol/L)
• Obvious clinical signs of liver disease (excluding non-alcoholic fatty liver disease)
• Acute or chronic hepatitis
• Non-alcoholic steatohepatitis
• Elevated liver enzyme measurements
o total bilirubin ≥2x upper limit of normal (ULN)
o Alanine aminotransferase (ALT) >2.5x ULN
o Aspartate aminotransferase (AST) >2.5x ULN)
• Fasting triglycerides >400 mg/dL
• Active or untreated malignancy
• In remission from clinically significant malignancy (other than basal cell or squamous cell skin cancer) for <5 years
• Increased risk for new or recurrent cancer in the opinion of the investigator
• Blood transfusion or severe blood loss within 3 months prior to Visit 1
• Hemoglobin abnormality known to interfere with measurement of HbA1c
• A known hypersensitivity or allergy to study insulins or their excipients.

SUPPLEMENTARY DATA

Supplementary Table 2. List of Investigators by Country

Czech Republic: Dagmar Bartaskova, Petra Horanska, Sarka Kopecka, Lea Raclavska

Germany: Susanne Höltz, Gerhard Klausmann, Frank Schaper, Simon Vidal, Hubert Wübbolding.

Greece: Iakovos Avramidis, Georgios Chaliotis, Kalliopi Kotsa

Israel: Michaela Garber**,** Adiv Goldhaber, Naim Shehadeh, Julio Wainstein,

Romania: Gheorghe Ghise, Amorin Remus Popa, Georgeta Vacaru, Mihaela Vlaiculescu

Russia: Svetlana Ivanova, Svetlana Mustafina, Natalia Zhavoronkova

Spain: Luis Ciprés Casasnovas, Esteban Jodar Gimeno, Mercedes Codina Marcet, Alejandro López Suárez, Carlos Trescoli Serrano

United States: Angela Adelizzi, Marie Albert, Royal Anspach, Timothy Bailey, Bruce Barker, Philip Behn, Thomas Blevins, Bradley Block, John Buse, Rafael Canadas, Anna Chang, A. Jay Cohen, Lisa Cohen, Richard Dobrusin, Rachel Espiritu, Daniel Honeycutt, Andrew Kim, Eric Klein, Gregory Ledger, Peter Levins, Robert Lipetz, Hiralal Maheshwari, Wilfred McKenzie, Francisco Miranda, Paul Norwood, Kerem Ozer, John Chip Reed, Angel Comulada Rivera, Helena Rodbard, Julio Rosenstock, John Rubino, Luis Ruiz-Rivera, Gerald Shockey, Robert Silver, Larry Stonesifer, Danny Sugimoto, Ralph Wade, Alan Wynne

SUPPLEMENTARY DATA

Supplementary Table 3. Insulin initiation and dose adjustment

A. Initiation of bedtime dosing of study basal insulin

Entry basal insulin regimen	Study basal insulin initiation
once-daily pre-study insulin dose	Initiated insulin peglispro or insulin glargine at the same dose at bedtime on the night of Visit 3
twice-daily insulin detemir or NPH insulin	Received 80% of the total daily insulin dose as the initial dose of study insulin at bedtime on the night of Visit 3
pre-study morning-only basal insulin	Converted to bedtime administration as follows: 50% of the prescribed study insulin dose at the site the morning of Visit 3 and the remaining 50% at bedtime on the night of Visit 3. Thereafter, these patients continued the full prescribed study insulin dose on the night following Visit 3.

B. Treat to Target Algorithm*

Median Fasting Blood Glucose (from SMBG) Days 5, 6, and 7 since the last insulin dose increment	Change in Study Basal Insulin Dose
101- 120 mg/dL	2 Unit increase
121 – 140 mg/dL	4 Unit increase
141-180 mg/dL	6 Unit increase
Greater than 180 mg/dL	8 Unit increase
If any SMBG value during the preceding week was ≤70 mg/dL	No dose increase
If multiple episodes of hypoglycemia with SMBG ≤70 mg/dL were recorded, if severe hypoglycemia (requiring assistance) occurred, or if any SMBG value was ≤54 mg/dL in the preceding week	Dose decreases of 2 to 4 Units based on investigator's judgment

Abbreviation: FBG = fasting blood glucose, SMBG = self-monitored blood glucose
*Treat-to-target FBG was ≤100 mg/dL

SUPPLEMENTARY DATA

Supplementary Table 4. Lipid and Hepatic Criteria for Study Insulin Discontinuation

Lipid and Hepatic Criteria for Study Insulin Discontinuation
Fasting triglyceride level >600 mg/dL
ALT or AST >8x ULN
ALT or AST >5x ULN for >2 weeks
ALT or AST >3x ULN and total bilirubin level >2x ULN or prothrombin time >1.5x ULN
ALT or AST >3x ULN with the appearance of fatigue, nausea, vomiting, right upper quadrant pain or tenderness, fever, rash, and/or eosinophilia (>5%)

Abbreviation: ALT = alanine aminotransferase, AST = aspartate aminotransferase, SMBG = self-monitored blood glucose, ULN = upper limit of normal

SUPPLEMENTARY DATA

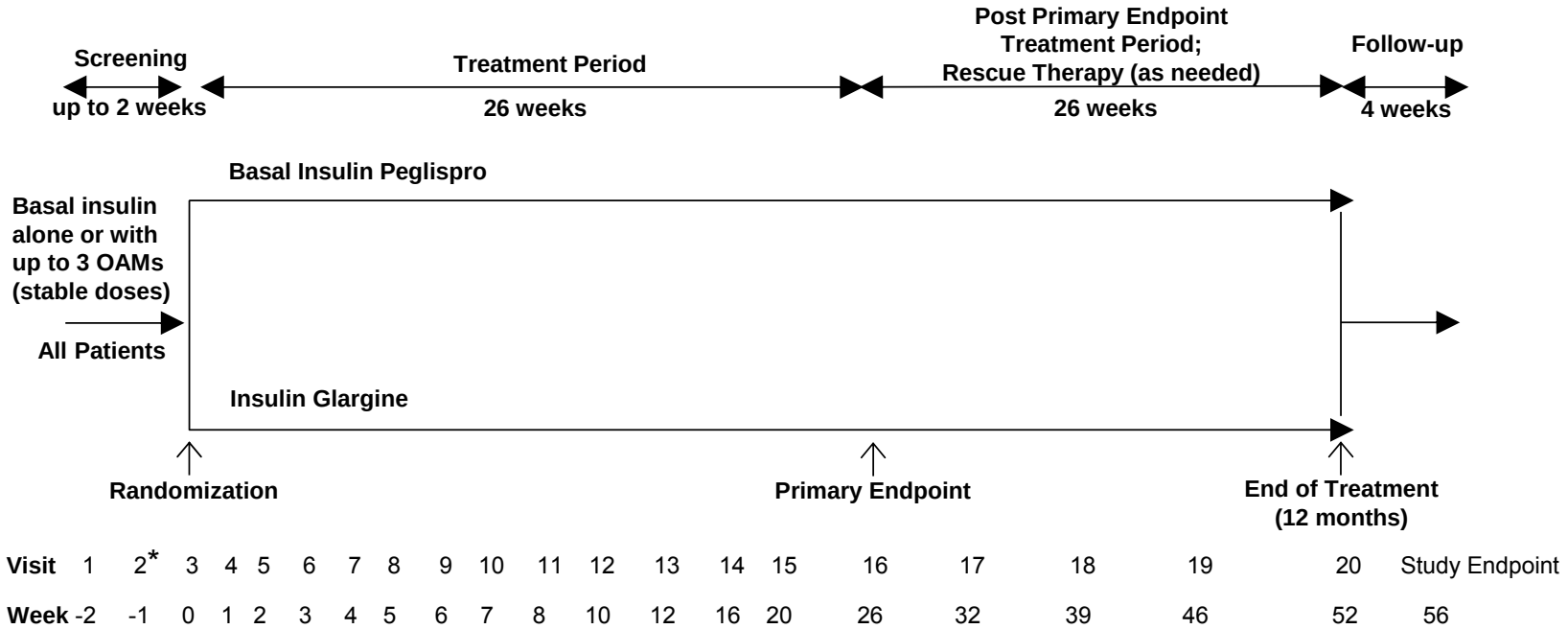
Supplementary Table 5. Percent of Patients Experiencing Treatment-Emergent Adverse Events and Serious Adverse Events from Randomization to the End of the Study

	Treatment-Emergent Adverse Events			Serious Adverse Events		
System Organ Class Preferred Term	**GL N=159**	**BIL N=305**	**P-value**	**GL N=159**	**BIL N=305**	**P-value**
Patients with ≥1 event	67.3	73.4	0.19	13.8	11.8	0.56
Blood and lymphatic system disorders	3.8	1.3	0.10	0	0	--
Cardiac disorders	8.8	4.6	0.10	6.9	2.3	0.02
Congenital, familial and genetic disorders	0.6	0	0.34	0	0	--
Ear and labyrinth disorders	3.8	3.6	>0.99	0	0	--
Endocrine disorders	1.3	1.3	>0.99	0	0	--
Eye disorders	2.5	5.2	0.23	0	0.3	>0.99
Gastrointestinal disorders	22.0	22.6	0.91	0	1.3	0.30
General disorders and administration site conditions	8.2	8.5	>0.99	0.6	1.3	0.67
Hepatobiliary disorders	1.9	3.0	0.76	0	0	--
Immune system disorders	1.3	2.0	0.72	0	0	--
Infections and infestations	40.3	42.6	0.69	1.3	2.3	0.73
Injury, poisoning and procedural complications	11.3	8.2	0.31	1.3	1.0	>0.99
Investigations	6.9	7.9	0.85	0	1.0	0.55
Metabolism and nutrition disorders	8.8	4.3	0.06	1.9*	0	0.04
Musculoskeletal and connective tissue disorders	23.3	21.0	0.64	0	0.7	0.55
Neoplasms benign, malignant and unspecified	3.1	3.0	>0.99	2.5	1.0	0.24
Nervous system disorders	15.1	15.4	>0.99	1.3	1.0	>0.99
Psychiatric disorders	4.4	5.2	0.82	0	0.3	>0.99
Renal and urinary disorders	4.4	4.3	>0.99	0	0.3	>0.99
Reproductive system and breast disorders	2.5	4.9	0.32	0.6	1.0	>0.99
Respiratory, thoracic and mediastinal disorders	14.5	10.5	0.23	0.6	1.0	>0.99
Skin and subcutaneous tissue disorders	6.3	12.5	0.04	0	0	--
Surgical and medical procedures	7.5	9.2	0.61	0	0	--
Vascular disorders	5.0	3.9	0.63	0.6	0.0	0.34

Abbreviation: BIL = Basal insulin peglispro, GL = insulin glargine
N numbers reflect maximal sample size
*Hypoglycemia (n=2) and Hypovolemia (n=1)

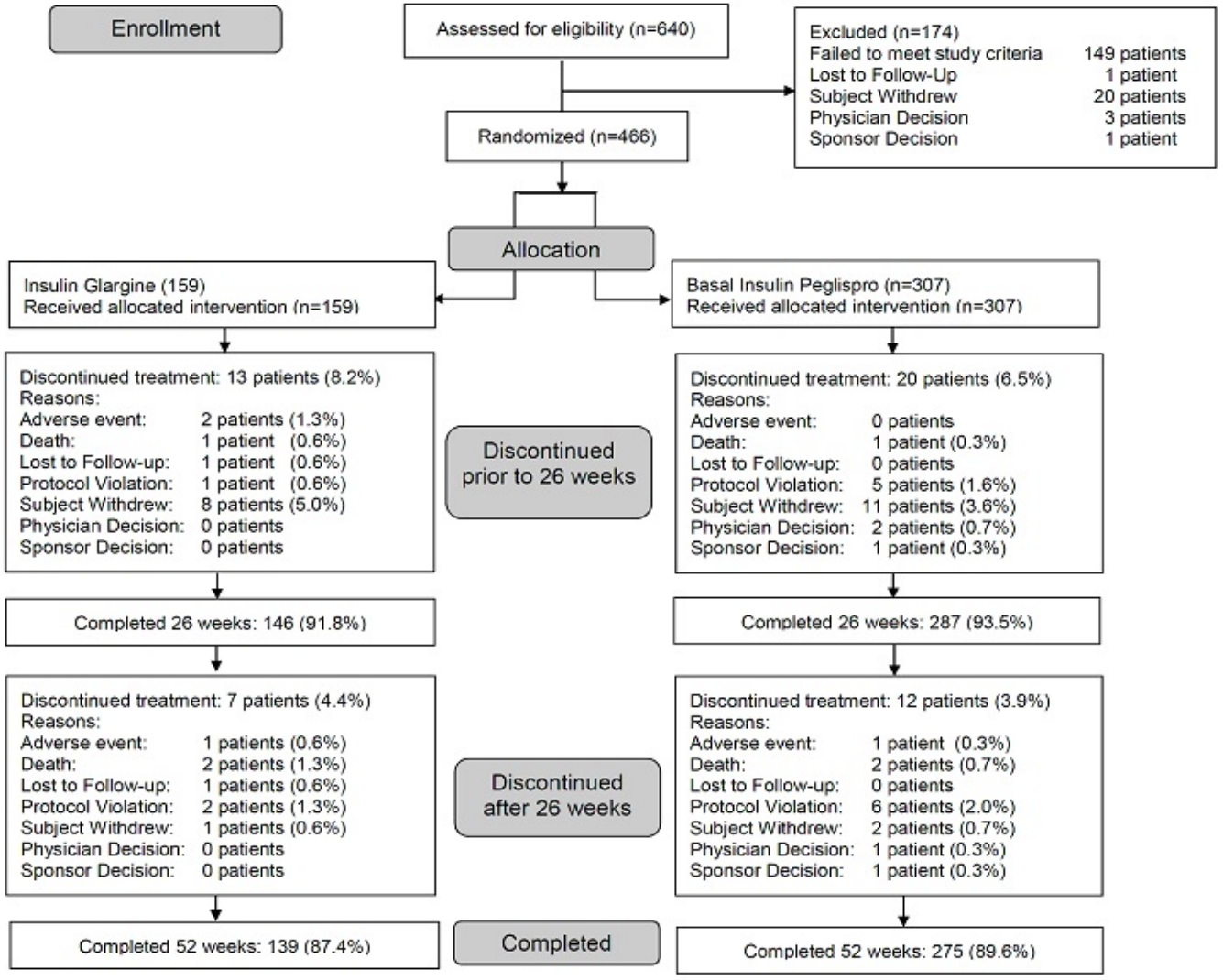
SUPPLEMENTARY DATA

**Supplementary Figure 1. Study Design. ***One-week pre-randomization period in between Visits 2 and 3. Abbreviations: OAM = oral antihyperglycemic medication.



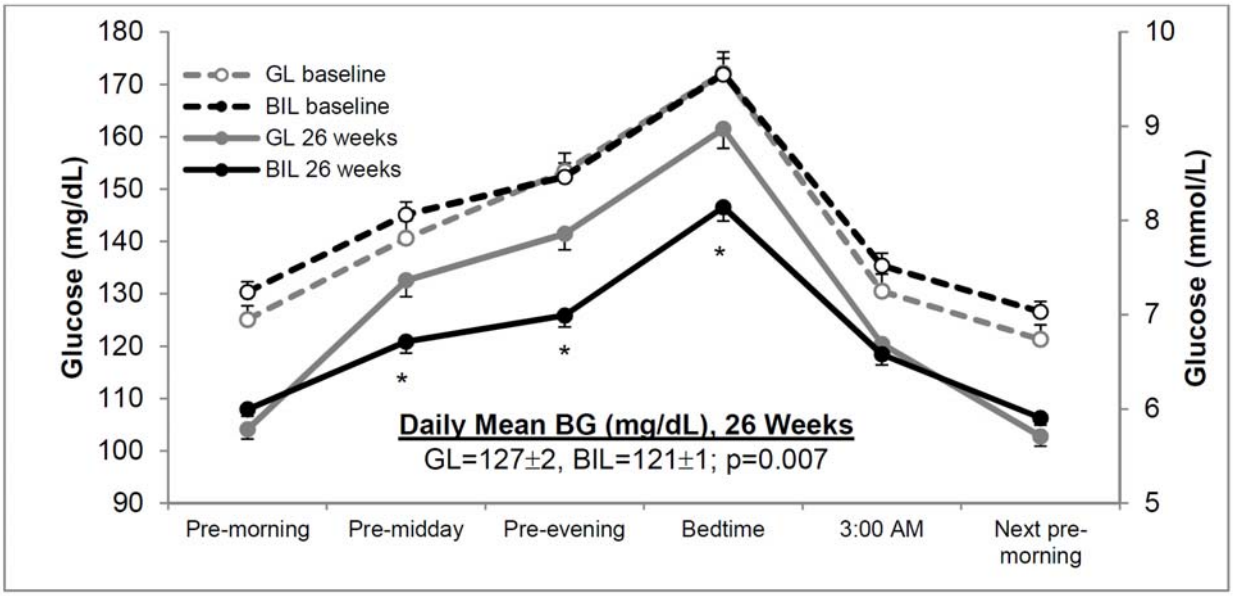
SUPPLEMENTARY DATA

Supplementary Figure 2. Participant Flow Diagram



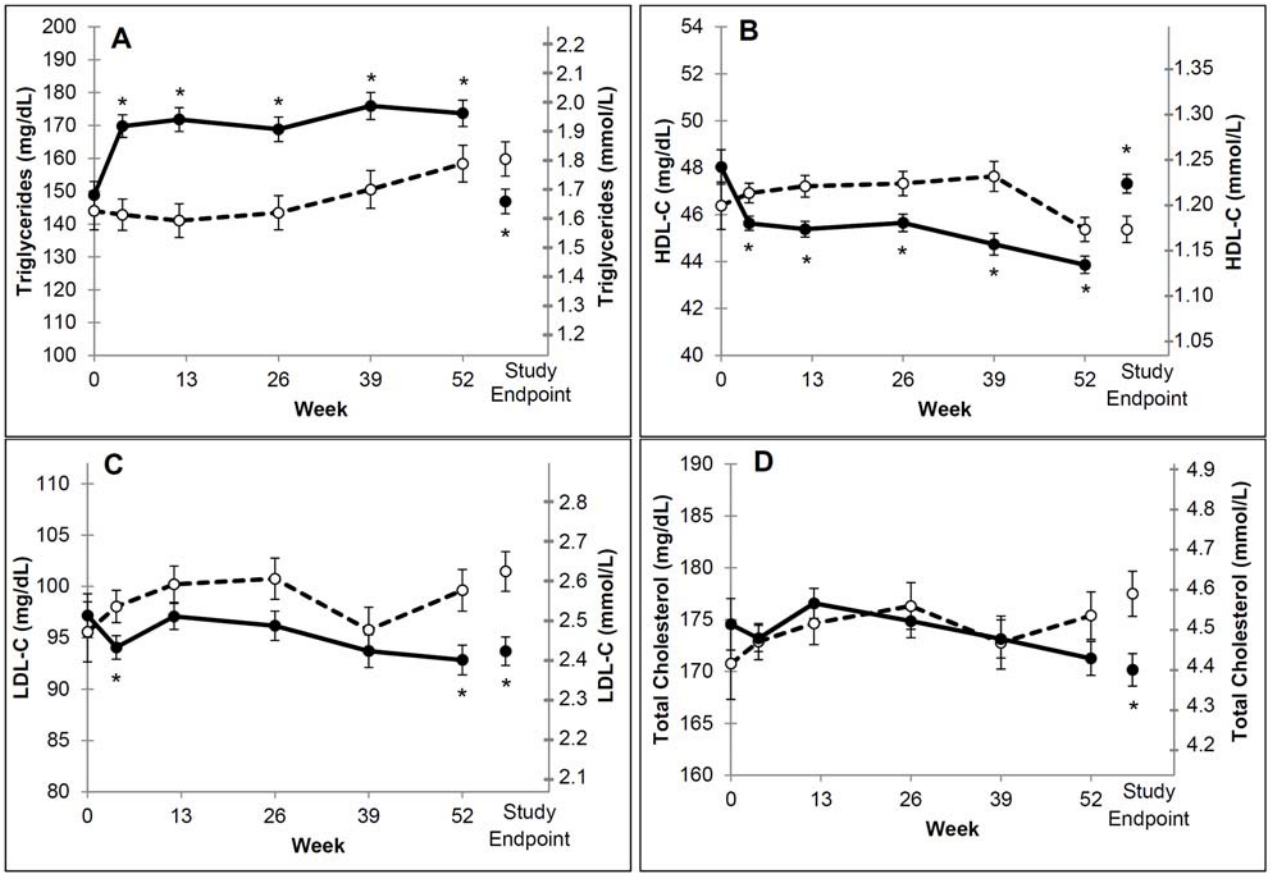
SUPPLEMENTARY DATA

Supplementary Figure 3. Six-point self-monitored blood glucose profile at 26 weeks Pre-morning = fasting (pre-morning meal); Pre-Midday = pre-mid-day meal; Pre-evening = preevening meal. Abbreviations: BIL = basal insulin peglispro, GL = insulin glargine. Data are least squares mean (LSM) ± standard error (SE). *p-values <0.05 for between treatment group comparisons.



SUPPLEMENTARY DATA

Supplementary Figure 4. Lipid Profile Over The Course of the Study. (A) Triglycerides. (B) High density lipoprotein cholesterol (HDL-C). (C) Low density lipoprotein cholesterol (LDL-C). (D) Total cholesterol. Closed circles with solid line = basal insulin lispro (BIL), open circles with dashed line = insulin glargine. Data are least squares mean (LSM) ± standard error (SE). Study endpoint indicates last visit completed including 4-week follow-up visit. *p<0.05 for between treatment group comparisons.



SUPPLEMENTARY DATA

Supplementary Figure 5. Alanine Aminotransferase (ALT) Over The Course of the Study. Closed circles with solid line = basal insulin lispro (BIL), open circles with dashed line = insulin glargine. Data are least squares mean (LSM) ± standard error (SE). Study endpoint indicates last visit completed including 4-week follow-up visit. *p<0.05 for between treatment group comparisons.