Supplementary Online Content

Lind M, Polonsky W, Hirsch IB, et al. Effect of continuous glucose monitoring vs conventional therapy on glycemic control among patients with type 1 diabetes treated with multiple daily insulin injections: the GOLD randomized clinical trial. *JAMA*. doi:10.1001/jama.2016.19976

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Randomization

The study had a randomized two cross-over arms design (effectively randomizing each subject to which out of two treatment to start the study with). Block randomization was used, with variable block size and stratified by study site, i.e. each site had its' own separate block sequence. Block sizes were randomly varied between 1+1 (1 position per arm) or 2+2 (two positions per arm) within each site's block sequence. The order of arm assignment positions within each one block was random.

The study used an externally managed web-based randomization tool. Arm assignment was revealed one subject at a time upon completing randomization of each subject. There were no means to preview the block schema or the next position within a block.

eTable 1. Adherence for CGM Treatment Group (Safety Population)

Variable	CGM (DexCom G4) (n=161)
Patients with CGM Data available in Study	
No	13 (8.1%)
Yes	148 (91.9%)
Total Adherence in Study (while Using CGM)	87.8 (13.4) 92.8 (16.7; 98.2) n=148
Adherence before Week 2 (CGM used in Period 1) or Week 43 (CGM used in Period 2)	91.9 (11.7) 95.1 (0.2; 99.8) n=144
Adherence before Week 4 (CGM used in Period 1) or Week 47 (CGM used in Period 2)	91.8 (13.0) 95.9 (1.5; 98.9) n=144
Adherence before Week 13 (CGM used in Period 1) or Week 56 (CGM used in Period 2)	88.9 (14.5) 94.6 (19.7; 105.1) n=142
Adherence before Week 26 (CGM used in Period 1) or Week 69 (CGM used in Period 2)	86.5 (16.7) 92.6 (6.8; 98.6) n=140

For categorical variables n (%) is presented.

For continuous variables Mean (SD) / Median (Min; Max) n= is presented.

Only patients using CGM for at least one day during last 30 days before a specific visit are included in this summary.

Adherence to CGM sensor usage is defined as percent of total time on CGM in-between the visits and in total. The total time in-between the visits was set to maximum of 30 days.

eTable 2. Difference Between FAS Population and Excluded Patients With Respect to Baseline Data (All Patients)

Variable	Excluded from FAS Population (n=19)	FAS Population (n=142)	p-value
Age at Inclusion visit	37.2 (17.3)	44.6 (12.7)	0.024
Sex			
Male	8 (42.1%)	80 (56.3%)	
Female	11 (57.9%)	62 (43.7%)	0.35
Race			
Black	0 (0.0%)	1 (0.7%)	
White (Caucasian, including Middle East & North Africa)	19 (100.0%)	141 (99.3%)	1.00
Ethnicity			
Not Hispanic or Latino	19 (100.0%)	142 (100.0%)	1.00
Weight (kg) at Randomization visit	77.7 (14.1)	82.2 (16.0)	0.25
BMI (kg/m2) at Randomization visit	27.0 (4.1)	27.1 (4.5)	0.96
HbA1c (NGSP, %) at Inclusion visit	9.55 (1.22)	8.71 (0.84)	0.0005
HbA1c (NGSP, %) at Randomization visit	9.36 (1.23)	8.47 (0.86) n=141	0.0003
Years from Diabetes Onset to Inclusion visit	23.8 (13.7)	22.2 (11.8)	0.59
Smoking at Inclusion visit			
Current	4 (21.1%)	17 (12.0%)	
Previous	4 (21.1%)	32 (22.5%)	
Never	11 (57.9%)	93 (65.5%)	0.34
Insulin and Metformin at Randomization visit			
Base Insulin Type			
Insulatard (NPH-Insulin)	0 (0.0%)	3 (2.1%)	
Glargine	14 (73.7%)	112 (78.9%)	
Detemir	2 (10.5%)	20 (14.1%)	
Degludec	3 (15.8%)	7 (4.9%)	0.28
Meal Insulin Type			
Lispro	7 (36.8%)	53 (37.3%)	
Aspart	10 (52.6%)	80 (56.3%)	
Glulisine	1 (5.3%)	7 (4.9%)	
Insulin regular human	1 (5.3%)	2 (1.4%)	0.71
Total daily meal Insulin dose (units)	25.8 (16.0)	27.5 (13.4)	0.61
Total daily base Insulin dose (units)	28.2 (11.0)	30.3 (13.8)	0.54
Total daily Insulin dose (units)	54.0 (25.3)	57.8 (23.2)	0.52

continued eTable 2. Difference Between FAS Population and Excluded Patients With Respect to Baseline Data (All Patients)

Variable	Excluded from FAS Population (n=19)	FAS Population (n=142)	p-value
Number of insulin injections	4.32 (1.06)	4.82 (0.96)	0.037
Median (range)	4.00 (1.00; 6.00)	5.00 (1.00; 8.00)	
Number of insulin injections (categories)			
<3 injections	1 (5.3%)	3 (2.1%)	
>=3 injections	18 (94.7%)	139 (97.9%)	0.80
Metformin used	0 (0.0%)	2 (1.4%)	1.00
Other glucose lowering medication used			
No	19 (100.0%)	142 (100.0%)	1.00
Glucose data at Run-in visit (Measured by CGM During 2 Weeks)			
Mean Glucose Level (mg/dL)	214.3 (35.6) n=17	194.1 (31.3) n=132	0.015
Mean Amplitude Glycaemic Excursions (MAGE) (mg/dL)	187.7 (37.5) n=17	181.8 (30.3) n=132	0.47
SD of Glucose Levels (mg/dL)	81.2 (15.6) n=17	78.7 (12.9) n=132	0.47
Percent of Time with Low Glucose Levels below 54 mg/dl [3.0 mmol/l]	1.55 (2.39) 0.49 (0.00; 7.47) n=17	2.18 (2.40) 1.28 (0.00; 12.33) n=132	0.31
Percent of Time with Low Glucose Levels below 70 mg/dl [3.9 mmol/l]	3.33 (3.99) 2.10 (0.00; 12.18) n=17	5.31 (4.27) 4.61 (0.00; 19.97) n=132	0.072
Percent of Time with High Glucose Levels above 180 mg/dl [10.0 mmol/l]	57.4 (14.8) n=17	47.7 (13.9) n=132	0.0085
Percent of Time with High Glucose Levels above 250 mg/dl [13.9 mmol/l]	31.3 (14.8) n=17	22.5 (11.4) n=132	0.0048
Percent of Time with Euglycaemic Levels 99-180 mg/dl [5.5-10.0 mmol/l]	26.5 (10.3) n=17	30.5 (12.3) n=132	0.20
Percent of Time with Euglycaemic Levels 70-180 mg/dl [3.9-10.0 mmol/l]	32.8 (13.4) n=17	38.7 (15.7) n=132	0.14
Medical History at Inclusion visit			
Previous laser photocoagulation of the retina	6 (31.6%)	28 (19.7%)	0.37
Previous myocardial infarction	1 (5.3%)	3 (2.1%)	0.80
Previous stroke	1 (5.3%)	2 (1.4%)	0.63
Previous bypass-graft	0 (0.0%)	1 (0.7%)	1.00
Previous PCI	1 (5.3%)	2 (1.4%)	0.63
Previous amputation	0 (0.0%)	1 (0.7%)	1.00
Previous diabetic foot (or leg) ulcer	0 (0.0%)	6 (4.2%)	0.93
Current diabetic foot (or leg) ulcer	0 (0.0%)	3 (2.1%)	1.00

continued eTable 2. Difference Between FAS Population and Excluded Patients With Respect to Baseline Data (All Patients)

Variable	Excluded from FAS Population (n=19)	FAS Population (n=142)	p-value
Average number of experienced hypoglycaemia per week during the last two months (not based on blood glucose values, but subjective estimation) at Inclusion visit	1.58 (0.83) 2.00 (0.00; 3.00) n=17	2.13 (1.90) 2.00 (0.00; 12.00) n=134	0.23
Number of severe hypoglycaemias past year	0.368 (0.684) 0.000 (0.000; 2.000)	0.071 (0.351) 0.000 (0.000; 3.000) n=141	0.014
Number of severe hypoglycaemias past 5 years	1.789 (3.190) 0.000 (0.000; 10.000)	0.596 (2.197) 0.000 (0.000; 20.000) n=141	0.045
Questionnaires at Run-in visit			
Treatment Satisfaction Total Scale (DTSQs)	25.9 (5.4) 25.0 (14.0; 34.0)	25.2 (5.9) 26.0 (4.0; 36.0) n=141	0.61
WHO-5 Well-Being Index	64.8 (16.1) 68.0 (20.0; 84.0)	59.9 (17.5) 64.0 (12.0; 100.0) n=141	0.25
Hypoglycaemic Fear Scale Behaviour/Avoidance	2.15 (0.70) 2.20 (1.00; 3.40)	1.92 (0.58) 1.90 (0.60; 3.70) n=141	0.12
Hypoglycaemic Fear Scale (SWE-HFS) Worry	1.336 (0.850) 1.231 (0.154; 3.077)	0.845 (0.674) 0.769 (0.000; 3.615) n=140	0.0054
Problem Areas in Diabetes (SWE-PAID-20) Total Scale	28.9 (21.9) 22.5 (3.8; 72.5)	25.6 (17.2) 22.5 (0.0; 83.8) n=141	0.46
Hypoglycaemic Confidence Questionnaire (HCQ) Total Scale	3.25 (0.54) 3.38 (2.44; 4.00)	3.24 (0.48) 3.22 (2.11; 4.00) n=137	0.91

For categorical variables n (%) is presented.
For continuous variables Mean (SD) / n= is presented for normally distributed variables and Mean (SD), Median (Range) for not normally distributed variables.
For comparison between groups Fisher´s Exact test (lowest 1-sided p-value multiplied by 2) was used for dichotomous variables and the Mantel-Haenszel Chi Square test was used for ordered categorical variables and Chi Square test was used for non-ordered categorical variables and the Fisher´s Non Parametric Permutation Test was used for continuous variables.
Severe hypoglycaemic events are defined as unconsciousness due to hypoglycaemia or need of assistance from another person to resolve the hypoglycaemia.

eTable 3. Descriptive Data for Secondary Endpoints (FAS Population)

	CGM (DexCom G4)	Conventional therapy
Hypoglycaemic Fear Scale (SWE-HFS) Worry	0.80 (0.68) 0.7 (0.0-3.8) n=139	0.81 (0.67) 0.6 (0.0-3.4) n=141
Problem Areas in Diabetes (SWE-PAID-20) scale	22.62 (14.89) 21.3 (0.0-63.8) n=140	24.25 (17.18) 23.8 (0.0-78.8) n=141
Percentage of Time with Low Glucose Levels (Measured by CGM During 2 Weeks) below 54 mg/dl [3.0 mmol/l]	0.79 (1.23) 0.4 (0.0-10.5) n=123	1.89 (2.12) 1.1 (0.0-9.5) n=125
Percentage of Time with Low Glucose Levels (Measured by CGM During 2 Weeks) below 70 mg/dl [3.9 mmol/l]	2.79 (2.97) 2.2 (0.0-20.4) n=123	4.79 (4.03) 3.5 (0.0-17.3) n=125
Percentage of Time with High Glucose Levels (Measured by CGM During 2 Weeks) above 180 mg/dl [10.0 mmol/l]	44.90 (15.68) 46.1 (9.0-81.5) n=123	46.98 (14.01) 46.0 (19.4-81.0) n=125
Percentage of Time with High Glucose Levels (Measured by CGM During 2 Weeks) above 250 mg/dl [13.9 mmol/l]	18.48 (12.28) 16.8 (1.3-55.3) n=123	21.92 (12.39) 18.7 (2.1-59.6) n=125
Percentage of Time with Euglycaemic Levels (Measured by CGM During 2 Weeks) 99-180 mg/dl [5.5-10.0 mmol/l]	34.69 (11.76) 34.5 (7.9-60.0) n=123	31.85 (9.85) 33.1 (8.2-53.0) n=125
Percentage of Time with Euglycaemic Levels (Measured by CGM During 2 Weeks) 70-180 mg/dl [3.9-10.0 mmol/l]	42.28 (14.95) 41.7 (8.0-73.8) n=123	39.81 (12.56) 41.0 (8.4-65.2) n=125
Percentage of Patients Reducing their HbA1c by 0.5% (5 mmol/mol) (LOCF)	105 (73.9%)	78 (56.5%)
Percentage of Patients Reducing their HbA1c by 1% (10 mmol/mol) (LOCF)	46 (32.4%)	14 (10.1%)
Occurrence of Severe Hypoglycaemic Events	1 (0.7%)	5 (3.5%)
Measurements per Day between Weeks 4-26 (from Weeks 1-4 if Missing) (LOCF)	2.75 (1.39) 2.4 (0.4-10.1) n=139	3.66 (2.30) 3.5 (0.2-14.8) n=139
Mean (SD), Median (Range) and n are presented for continuous variables and n (%) for categorical variables.		

eTable 4. Adverse Events, by System Organ Class and Preferred Term (Safety Population)

System Organ Class (SOC) Preferred Term (PT)	CGM (DexCom G4) (n=156)		Conventional therapy (n=151)	
	Events	Patients with Events n (%)	Events	Patients with Events n (%)
Any AE	**137**	**77 (49.4%)**	**122**	**67 (44.4%)**
Blood and lymphatic system disorders			**1**	**1 (0.7%)**
Anaemia			1	1 (0.7%)
Cardiac disorders	**1**	**1 (0.6%)**		
Palpitations	1	1 (0.6%)		
Ear and labyrinth disorders	**1**	**1 (0.6%)**	**1**	**1 (0.7%)**
Vertigo	1	1 (0.6%)	1	1 (0.7%)
Eye disorders	**5**	**5 (3.2%)**	**1**	**1 (0.7%)**
Cataract	1	1 (0.6%)		
Eye inflammation	1	1 (0.6%)		
Macular degeneration			1	1 (0.7%)
Macular oedema	1	1 (0.6%)		
Retinal detachment	1	1 (0.6%)		
Retinopathy	1	1 (0.6%)		
Gastrointestinal disorders	**3**	**3 (1.9%)**	**6**	**6 (4.0%)**
Abdominal pain upper	1	1 (0.6%)	1	1 (0.7%)
Diarrhoea			2	2 (1.3%)
Dyspepsia			1	1 (0.7%)
Gastritis	1	1 (0.6%)		
Toothache	1	1 (0.6%)		
Vomiting			2	2 (1.3%)
General disorders and administration site conditions	**13**	**10 (6.4%)**	**8**	**8 (5.3%)**
Application site pruritus	1	1 (0.6%)	1	1 (0.7%)
Application site rash	2	1 (0.6%)		
Chest pain	4	2 (1.3%)		
Device issue	1	1 (0.6%)		
Fatigue	1	1 (0.6%)	2	2 (1.3%)
Hernia			1	1 (0.7%)
Inflammation	1	1 (0.6%)	1	1 (0.7%)
Oedema peripheral			1	1 (0.7%)
Pyrexia	2	2 (1.3%)	2	2 (1.3%)
Thirst	1	1 (0.6%)		
Immune system disorders	**2**	**2 (1.3%)**		
Allergy to arthropod bite	1	1 (0.6%)		

continued eTable 4. Adverse Events, by System Organ Class and Preferred Term (Safety Population)

System Organ Class (SOC) Preferred Term (PT)	CGM (DexCom G4) (n=156)		Conventional therapy (n=151)	
	Events	Patients with Events n (%)	Events	Patients with Events n (%)
Seasonal allergy	1	1 (0.6%)		
Infections and infestations	**64**	**47 (30.1%)**	**64**	**47 (31.1%)**
Bronchitis	1	1 (0.6%)		
Clostridial infection	1	1 (0.6%)		
Cystitis			1	1 (0.7%)
Ear infection	2	2 (1.3%)		
Gastroenteritis	4	4 (2.6%)	3	3 (2.0%)
Gastroenteritis viral			1	1 (0.7%)
Hand-foot-and-mouth disease			1	1 (0.7%)
Infection	2	2 (1.3%)		
Influenza	3	3 (1.9%)	1	1 (0.7%)
Localised infection	1	1 (0.6%)	1	1 (0.7%)
Nasopharyngitis	34	29 (18.6%)	46	37 (24.5%)
Oral candidiasis	1	1 (0.6%)		
Oral herpes	1	1 (0.6%)		
Otitis externa	1	1 (0.6%)	1	1 (0.7%)
Paronychia			1	1 (0.7%)
Pneumonia	2	2 (1.3%)	1	1 (0.7%)
Post procedural infection	1	1 (0.6%)		
Tonsillitis	2	2 (1.3%)		
Upper respiratory tract infection			2	2 (1.3%)
Urinary tract infection	8	6 (3.8%)	3	3 (2.0%)
Vaginal infection			1	1 (0.7%)
Vulvovaginal candidiasis			1	1 (0.7%)
Injury, poisoning and procedural complications	**4**	**4 (2.6%)**	**4**	**4 (2.6%)**
Fall	1	1 (0.6%)	1	1 (0.7%)
Hand fracture			1	1 (0.7%)
Intercepted drug dispensing error	1	1 (0.6%)		
Ligament sprain	1	1 (0.6%)		
Limb injury	1	1 (0.6%)		
Medication error			1	1 (0.7%)
Skeletal injury			1	1 (0.7%)
Metabolism and nutrition disorders	**1**	**1 (0.6%)**	**5**	**5 (3.3%)**
Hypoglycaemia	1	1 (0.6%)	5	5 (3.3%)

Continued eTable 4. Adverse Events, by System Organ Class and Preferred Term (Safety Population)

System Organ Class (SOC) Preferred Term (PT)	CGM (DexCom G4) (n=156)		Conventional therapy (n=151)	
	Events	Patients with Events n (%)	Events	Patients with Events n (%)
Musculoskeletal and connective tissue disorders	**5**	**5 (3.2%)**	**11**	**11 (7.3%)**
Arthralgia	1	1 (0.6%)	2	2 (1.3%)
Back pain	1	1 (0.6%)	2	2 (1.3%)
Bursitis	1	1 (0.6%)		
Exostosis	1	1 (0.6%)		
Groin pain			1	1 (0.7%)
Intervertebral disc protrusion			1	1 (0.7%)
Myalgia			1	1 (0.7%)
Myositis			1	1 (0.7%)
Neck pain			1	1 (0.7%)
Pain in extremity	1	1 (0.6%)	1	1 (0.7%)
Tendonitis			1	1 (0.7%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**3**	**2 (1.3%)**	**1**	**1 (0.7%)**
Breast cancer	3	2 (1.3%)		
Prostate cancer			1	1 (0.7%)
Nervous system disorders	**2**	**2 (1.3%)**	**2**	**2 (1.3%)**
Burning sensation			1	1 (0.7%)
Headache	1	1 (0.6%)		
Sciatica			1	1 (0.7%)
Sensory disturbance	1	1 (0.6%)		
Psychiatric disorders	**4**	**4 (2.6%)**	**1**	**1 (0.7%)**
Attention deficit/hyperactivity disorder	1	1 (0.6%)		
Depression	2	2 (1.3%)	1	1 (0.7%)
Stress	1	1 (0.6%)		
Reproductive system and breast disorders			**1**	**1 (0.7%)**
Benign prostatic hyperplasia			1	1 (0.7%)
Respiratory, thoracic and mediastinal disorders	**6**	**4 (2.6%)**	**3**	**3 (2.0%)**
Asthma	1	1 (0.6%)		
Cough	1	1 (0.6%)	1	1 (0.7%)
Dyspnoea	1	1 (0.6%)		
Nasal congestion	1	1 (0.6%)		
Oropharyngeal pain	1	1 (0.6%)	2	2 (1.3%)
Pleurisy	1	1 (0.6%)		

Continued eTable 4. Adverse Events, by System Organ Class and Preferred Term (Safety Population)

System Organ Class (SOC) Preferred Term (PT)	CGM (DexCom G4) (n=156)		Conventional therapy (n=151)	
	Events	Patients with Events n (%)	Events	Patients with Events n (%)
Skin and subcutaneous tissue disorders	**14**	**9 (5.8%)**	**4**	**3 (2.0%)**
Dermatitis contact	1	1 (0.6%)	1	1 (0.7%)
Drug eruption	1	1 (0.6%)		
Eczema	1	1 (0.6%)		
Hidradenitis	1	1 (0.6%)		
Pruritus	1	1 (0.6%)		
Rash			1	1 (0.7%)
Skin reaction	1	1 (0.6%)		
Skin ulcer	8	3 (1.9%)	2	1 (0.7%)
Social circumstances	**1**	**1 (0.6%)**	**2**	**2 (1.3%)**
Abstains from alcohol			1	1 (0.7%)
Failed examinations	1	1 (0.6%)	1	1 (0.7%)
Surgical and medical procedures	**5**	**2 (1.3%)**	**6**	**2 (1.3%)**
Eye laser surgery	4	2 (1.3%)		
Hospitalisation			5	1 (0.7%)
Mass excision	1	1 (0.6%)		
Spinal decompression			1	1 (0.7%)
Vascular disorders	**3**	**3 (1.9%)**	**1**	**1 (0.7%)**
Deep vein thrombosis	1	1 (0.6%)		
Hypertension			1	1 (0.7%)
Hypotension	1	1 (0.6%)		
Thrombophlebitis	1	1 (0.6%)		

eTable 5. Serious Adverse Events, by System Organ Class and Preferred Term (Safety Population)

System Organ Class (SOC) Preferred Term (PT)	CGM (DexCom G4) (n=156)		Conventional therapy (n=151)	
	Events	Patients with Events n (%)	Events	Patients with Events n (%)
Any SAE	**9**	**7 (4.5%)**	**9**	**3 (2.0%)**
Eye disorders	**1**	**1 (0.6%)**		
Retinal detachment	1	1 (0.6%)		
Gastrointestinal disorders			**1**	**1 (0.7%)**
Diarrhoea			1	1 (0.7%)
General disorders and administration site conditions	**3**	**2 (1.3%)**		
Chest pain	3	2 (1.3%)		
Infections and infestations	**2**	**2 (1.3%)**		
Pneumonia	1	1 (0.6%)		
Post procedural infection	1	1 (0.6%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**3**	**2 (1.3%)**	**1**	**1 (0.7%)**
Breast cancer	3	2 (1.3%)		
Prostate cancer			1	1 (0.7%)
Psychiatric disorders			**1**	**1 (0.7%)**
Depression			1	1 (0.7%)
Social circumstances			**1**	**1 (0.7%)**
Abstains from alcohol			1	1 (0.7%)
Surgical and medical procedures			**5**	**1 (0.7%)**
Hospitalisation			5	1 (0.7%)