SUPPLEMENTARY DATA

List of Harmony 8 Principal Investigators

A Adetola, CW Ahn, D Anjani, L Akright, NS Andrawis, S Ansari, HC Arbañil Huamán, A Arif, V Aroda, AE Badat, TW Bauch, MV Bernardo, JA Betts, A Bhargava, JLC Borges, CR Bratcher, AP Brockmyre, LJ Burgess, RJ Buynak, LA Camacho Cosavalente, R Canadas, GC Canas, MR Castillo Gamarra, SA Chandatreya, C-T Chang, RS Cherlin, JH Cho, YW Cho, DS Choi, CJS Chrisman, TA Christensen, DD Collins, CN Corder, CA Cure, TD Daniel, K Darzy, T Davis, C De la Cuesta, RE De La Rosa, L de Teresa, RG DeGarmo, LB Delos Santos, MK Denopol, KM Derwahl, NR Deshpande, D Dewan, MJ DiGiovanna, LA Distiller, SG Dorfman, HJ Downey, HD Durrence, M El Shahawy, GC Ellis, J Eris, DP Escalante, H Fernandez-Miro, MA Fulat, GS Funk, N Gabra, JD Gabriel, M Gani, M Gerstman, C Gilfillan, L Gnudi, A Goldfein, LM Gonzales Bravo, MD Gonzalez, RJ Graf, D Grant, E Grineva, JL Gross, SD Grubb, Y Handelsman, M Hanefeld, I Harman-Boehm, AF Harris, CY Hayashida, CB Herring, KS Hoffman, R Hootkins, MA Ibraheem, A Iranmanesh, NA Jaffrani, MV Jali, A Jamal, CA Jimeno, C Jones, SW Jones, D Katselnik, IA Khan, GA Ledger, M Lee, S Lerman, C Lloyd Turney, JP Lopez-Jaramillo, AA Luna Figueroa, HA Makan, V Marasaev, EE Martin, RE Martinez, SO Mayeda, RK Mayfield, T McCarren, KW Min, OR Minuchin, DJ Molter, JO Navarro, GE Newman, TT Nguyen, AE Nolasco, PC Norwood Jr, JE Pappas, SR Phatak, P Pillai, SJ Powell, C Ragland, G Ramamurthy, JCH Reed III, M Rendell, DH Rodriguez, CT Romney, RD Rosen, PD Rosenblit, JG Rothman, SS Samudrala, S Sathyanarayana, PJ Sebastian, J Septimus, SS Shaikh, P Shamanna, JA Shapiro, CW Sofley Jr, JE Solís Villanueva, AR Sosale, A Soto González, DA Streja, RA Sy, S Teniola, TM Thorp, R Tidman, K-J Tien, E van Nieuwenhuizen, RD Wade, J Wainstein, GR Weiner, TB Wiegmann, T Williams, J Wing, J Wood, DLB Ygpuara Ma, H Ypanqui Lozno, LHT Zapata Rincón.

SUPPLEMENTARY DATA

Supplementary Table 1. *Summary of change from baseline in HbA1c (%) and fasting plasma glucose (mmol/L) at week 26 by renal impairment status in intent-to-treat population using a last observation carried forward analysis*

	Albiglutide (N=246)			Sitagliptin (N=240)		
	Mild	**Moderate**	**Severe**	**Mild**	**Moderate**	**Severe**
HbA1c (%) [mmol/mol]						
Number of patients[1]	125	98	19	122	99	15
Number (%) of values carried forward	17 (13.6)	21 (21.4)	2 (10.5)	15 (12.3)	37 (37.4)	6 (40.0)
Baseline – mean (SD)	7.96 (0.804) [63.49 (8.79)]	8.26 (0.922) [66.77 (10.08)]	8.05 (0.746) [64.47 (8.15)]	8.16 (0.894) [65.68 (9.77)]	8.28 (0.927) [66.99 (10.13)]	8.32 (0.922) [67.42 (10.08)]
Week 26 – mean (SD)	7.23 (0.887) [55.51 (9.696)]	7.37 (1.144) [57.04 (12.505)]	6.97 (1.103) [52.67 (12.057)]	7.50 (1.066) [57.46 (11.65)]	7.91 (1.413) [62.94 (15.45)]	7.67 (1.261) [60.32 (13.78)]
Change from Baseline – mean (SD)	-0.72 (0.807) [-7.87 (8.82)]	-0.88 (0.998) -9.62 ([10.91)]	-1.08 (0.914) [-11.81 (9.99)]	-0.66 (0.879) [-7.21 (9.61)]	-0.37 (1.325) [-4.04 (14.48)]	-0.65 (1.239) [-7.11 (13.54)]
Model-adjusted change from Baseline[2]						
LS mean (SE)	-0.80 (0.087)	-0.83 (0.097)	-1.08 (0.221)	-0.67 (0.087)	-0.31 (0.097)	-0.61 (0.249)
95% CI	(-0.97, -0.63)	(-1.03, -0.64)	(-1.52, -0.65)	(-0.84, -0.50)	(-0.50, -0.12)	(-1.10, -0.12)
Difference from sitagliptin[2]						
Difference of LS means	-0.13	-0.53	-0.47			
95% CI	(-0.37, 0.11)	(-0.80, -0.26)	(-1.12, 0.18)			
Fasting Plasma Glucose (mmol/L)						
Number of patients[1]	126	99	19	124	99	17
Number (%) of values carried forward	18 (14.3)	24 (24.2)	2 (10.5)	17 (13.7)	37 (37.4)	9 (52.9)
Baseline – mean (SD)	8.78 (2.380)	9.58 (3.967)	9.82 (3.668)	8.59 (2.246)	9.85 (3.335)	9.24 (3.305)
Week 26 – mean (SD)	7.59 (2.205)	8.10 (4.045)	7.04 (2.421)	8.32 (2.843)	9.83 (3.930)	8.39 (3.668)
Change from Baseline – mean (SD)	-1.19 (2.239)	-1.48 (3.834)	-2.78 (3.349)	-0.27 (2.746)	-0.02 (4.031)	-0.85 (3.101)
Model-adjusted change from Baseline[2]						
LS mean (SE)	-1.41 (0.257)	-1.24 (0.289)	-2.45 (0.659)	-0.58 (0.260)	0.36 (0.291)	-0.89 (0.696)
95% CI	(-1.92, -0.91)	(-1.81, -0.67)	(-3.74, -1.15)	(-1.09, -0.07)	(-0.21, 0.93)	(-2.25, 0.48)
Difference from sitagliptin[2]						
Difference of LS means	-0.83	-1.60	-1.56			
95% CI	(-1.54, -0.12)	(-2.40, -0.81)	(-3.44, 0.31)			

CI = confidence interval; HbA_{1c} = glycosylated hemoglobin; ITT = intent to treat; LOCF = last observation carried forward; LS = least squares; SD = standard deviation; SE = standard error.

Note: This analysis used the LOCF method for missing postbaseline HbA_{1c} or FPG values, as applicable. The HbA_{1c} or FPG values obtained after hyperglycemia rescue were treated as missing and replaced with prerescue values.

1. Number of patients with a value at Baseline and at the specified visit.

2. Based on analysis of covariance (ANCOVA): Change = treatment + baseline HbA_{1c} + renal impairment + prior myocardial infarction history + age category + region + treatment*renal impairment. The difference of least squares means (albiglutide - sitagliptin) is from ANCOVA model. The p-value for the interaction term was above 0.05.

SUPPLEMENTARY DATA

Supplementary Table 2. *Conditions for dose titration or hyperglycemia rescue*

Time Interval on Treatment	Dose Titration	Hyperglycemia Rescue
≥Day 1 and <Week 2	No titration	No rescue
≥Week 2 and <Week 4	No titration	A single FPG ≥280 mg/dL*
Week 4	A single FPG ≥250 mg/dL* and HbA_{1c} unchanged or increased from Baseline	A single FPG ≥280 mg/dL*
>Week 4 and <Week 12	A single FPG ≥250 mg/dL[1] and HbA_{1c} unchanged or increased from Baseline	A single FPG ≥250 mg/dL* AND previous titration for ≥4 weeks
≥Week 12 and <Week 26	HbA_{1c} ≥7.0% and ≤0.5% reduction from Baseline	HbA_{1c} ≥8.5% and ≤0.5% reduction from Baseline AND previous titration for ≥4 weeks
≥Week 26 and <Week 48	HbA_{1c} ≥7.0%	HbA_{1c} ≥8.5% AND previous titration for ≥4 weeks
≥Week 48 and <Week 52	No titration	HbA_{1c} ≥8.0% AND previous titration for ≥4 weeks

* Confirmed by a second sample drawn within 7 days and analyzed by the central laboratory.

SUPPLEMENTARY DATA

Supplementary Table 3. *Concomitant medications flagged by the investigators as hyperglycemic rescue medication.*
Note: Rescue medication was provided at the discretion of the investigator. The protocol indicated to the investigators that the preferred postrescue add-on treatment was insulin and that other medications could be added at the investigator's discretion. The addition of other GLP-1R agonists was prohibited, and the addition of a TZD was discouraged.

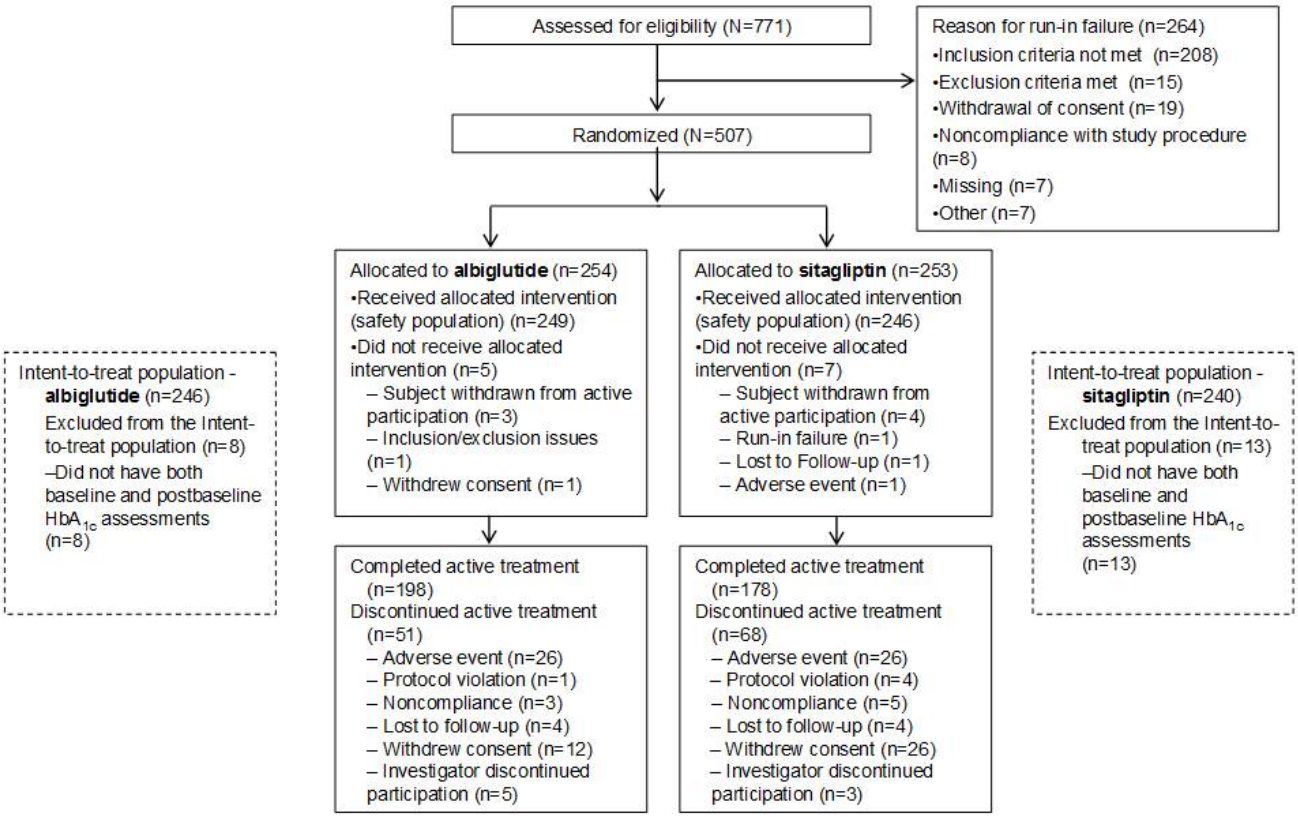
	Albiglutide (N=249) n (%)	**Sitagliptin (N=246) n (%)**
Patients with any rescue medications	45 (18.1)	67 (27.2)
Metformin		
Metformin	10 (4.0)	10 (4.1)
Metformin hydrochloride	1 (0.4)	3 (1.2)
Insulin		
Insulin aspart	1 (0.4)	0
Insulin detemir	1 (0.4)	5 (2.0)
Insulin glargine	5 (2.0)	12 (4.9)
Insulin human	6 (2.4)	7 (2.8)
Insulin human injection, isophane	3 (1.2)	7 (2.8)
Insulin isophane, human biosynthetic	1 (0.4)	1 (0.4)
Insulin lispro	0	1 (0.4)
Insulin NOS	4 (1.6)	1 (0.4)
Pioglitazone		
Pioglitazone hydrochloride	1 (0.4)	4 (1.6)
Glimepiride	6 (2.4)	8 (3.3)
Gliclazide	3 (1.2)	6 (2.4)
Glibenclamide	2 (0.8)	6 (2.4)
Glipizide	1 (0.4)	3 (1.2)
Acarbose	1 (0.4)	2 (0.8)
Isophane insulin	1 (0.4)	2 (0.8)
Rosiglitazone maleate	2 (0.8)	0
Glucomet (NOS)	0	1 (0.4)
Diabeta (NOS)	1 (0.4)	0
Liraglutide	1 (0.4)	0
Voglibose	1 (0.4)	0

NOS = not otherwise specified.

Note: Only concomitant antihyperglycemia medications that were indicated by the investigator as being used for hyperglycemia rescue were included in this summary. At each level of summarization, a patient was counted once if the patient reported 1 or more medications. Medications are coded using World Health Organization Drug Dictionary. Concomitant hyperglycemia rescue medications were those taken at any time on or after the day of the first dose of study medication and within 56 days after the last dose of study medication.

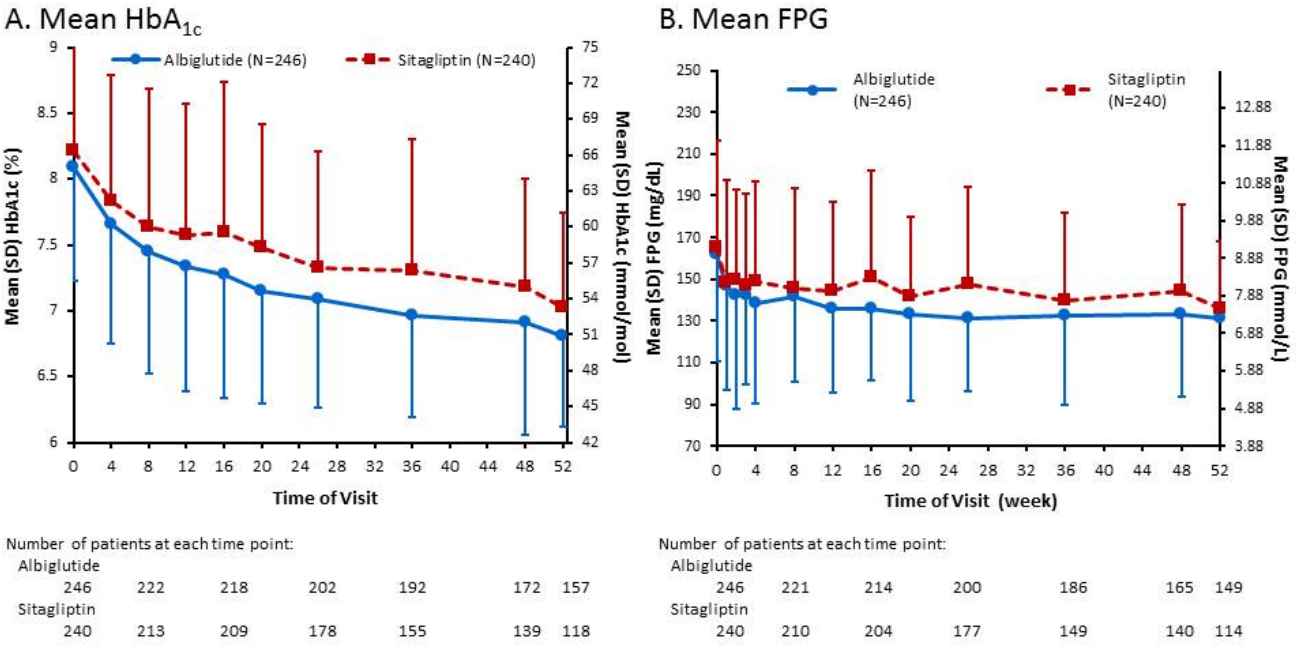
SUPPLEMENTARY DATA

Supplementary Figure 1. Flow diagram of patient disposition



SUPPLEMENTARY DATA

Supplementary Figure 2. Summary of efficacy data at week 52 in safety population using an observed cases analysis and excluding patients who received hyperglycemia rescue.
Note: the number of patients at each time point represents the number of patients who have not received rescue medication, not the number of patients remaining in the study.



Number of patients at each time point:

Albiglutide	246	222	218	202	192	172	157
Sitagliptin	240	213	209	178	155	139	118

Number of patients at each time point:

Albiglutide	246	221	214	200	186	165	149
Sitagliptin	240	210	204	177	149	140	114