

SUPPLEMENTARY DATA

Supplementary Table 1. Cumulative Incidence of Lower Extremity Outcomes, by Assigned Glycemic Control Strategy, Intention-To-Treat Analysis.

	Patients with Normal ABI at Study Entry (N=1479)		P-Value
	IS (N=735)	IP (N=744)	
Peripheral Arterial Disease*	124 (16.9%)	179 (24.1%)	<.001
Incident Low ABI	121 (16.5%)	169 (22.7%)	0.001
Lower Extremity Revascularization	8 (1.1%)	17 (2.6%)	0.07
Lower Extremity Amputation	1 (0.1%)	12 (1.6%)	0.002
	Patients with Low ABI at Study Entry (N=430)		P-Value
	IS (N=207)	IP (N=223)	
Lower Extremity Revascularization	14 (6.7%)	17 (7.7%)	0.69
Lower Extremity Amputation	7 (3.4%)	16 (7.2%)	0.08
Revascularization and/or Amputation	19 (9.2%)	25 (11.2%)	0.48

IS =Insulin Sensitizing Assignment; IP = Insulin Providing Assignment

*Patients are classified as an incident case of peripheral arterial disease if any of the following occur: i) ABI < 0.9 with a decrease of 0.1 from baseline, ii) lower extremity revascularization, iii) lower extremity amputation

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Supplementary Table 2. Baseline Characteristics of Participants in Per Protocol Analysis (N=942).

	IP (N=643)	IS (N=299)	P-Value
Age at study entry, mean, sd	61.8, 8.7	62.3, 9.2	0.4413
Male, %	71.7	75.9	0.1738
Black, %	14.5	12.4	0.3869
BMI, mean, sd	31.4, 5.6	30.6, 5.2	0.0385
Current Smoker, %	10.7	10	0.7395
Total cholesterol mg/dl, mean, sd	171.1, 39.4	164.6, 39.1	0.0211
LDL mg/dl, mean, sd	97.3, 31.3	93.7, 31.7	0.1144
HDL mg/dl, mean, sd	38.4, 10.2	37.2, 9.1	0.0648
Triglyceride mg/dl, mean, sd	184.8, 154.6	171.1, 113.3	0.1283
Systolic BP average, mean, sd	130.2, 19.1	130.3, 19.4	0.9599
Diastolic BP average, mean, sd	74.7, 10.7	76.2, 10.4	0.0436
Duration of DM, mean, sd	10.3, 8.2	6.6, 6.7	<.0001
On insulin at study entry, %	28.1	5	<.0001
HbA1c %, mean, sd	7.8, 1.6	7.0, 1.3	<.0001
ACR mg/g, mean, sd	125.9, 468.5	38.4, 122.9	<.0001
Albuminuria categories, %			
No albuminuria	72	79.5	0.0022
Micro albuminuria	20.7	18.7	
Macro albuminuria	7.3	1.8	
ABI, mean, sd	1.09, 0.1	1.10, 0.1	0.2684

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Supplementary Table 3. Cumulative Incidence of Lower Extremity Outcomes, by Glycemic Control Strategy, Per Protocol Analysis (N=942).

	IS (N=299)	IP (N=643)	P-Value
Peripheral Arterial Disease*	37 (12.4%)	167 (26.0%)	<.001
Incident Low ABI	36 (12.0%)	158 (24.6%)	<.001
Lower Extremity Revascularization	3 (1.0%)	15 (2.3%)	0.16
Lower Extremity Amputation	0 (0.0%)	12 (1.9%)	0.002

*Patients are classified as an incident case of peripheral arterial disease if any of the following occur: i) ABI < 0.9 with a decrease of 0.1 from baseline, ii) lower extremity revascularization, iii) lower extremity amputation

Supplementary Table 4. Effects of Glycemic Control Strategy on Lower Extremity Outcomes, Per Protocol Analysis (N=942).

Outcome	# Events	Unadjusted			Adjusted for in-trial HbA1c		
		HR	95% CI	P-Value	HR	95% CI	P-Value
Peripheral Arterial Disease	204	0.44	0.31, 0.62	<.001	0.54	0.37, 0.79	0.002
Incident Low ABI	194	0.44	0.31, 0.63	<.001	0.54	0.37, 0.80	0.002
Lower Extremity Revascularization	18	0.43	0.12, 1.48	0.18	0.70	0.18, 2.63	0.59
Lower Extremity Amputation	12	**	**	**	**	**	**

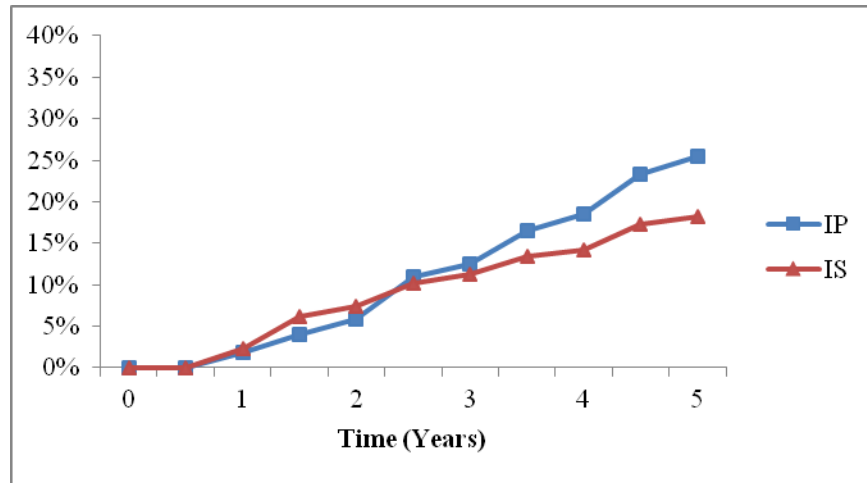
HR = Hazard Ratio; 95% CI = 95% confidence interval

*Hazard Ratios are for IS arm vs. IP arm (reference group)

**Hazard Ratio cannot be estimated for amputation because, in per-protocol analysis, all amputation events occurred in IP arm and there are no amputation events in IS arm

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Supplementary Figure 1. Cumulative Incidence of Peripheral Arterial Disease Among Patients Not On Insulin at Baseline, by Assigned Glycemic Control Strategy.



Supplementary Figure 2. Cumulative Incidence of Peripheral Arterial Disease Among Patients On Insulin at Baseline, by Assigned Glycemic Control Strategy.

