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The FREEDOM Trial: Clinical and Angiographic Profile at Study Entry

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Abstract

Background—The optimal revascularization strategy for diabetic patients with multivessel coronary artery disease (MVD) remains uncertain for lack of an adequately powered, randomized trial. The FREEDOM trial was designed to compare contemporary coronary artery bypass grafting (CABG) to percutaneous coronary intervention (PCI) with drug-eluting stents in diabetic patients with MVD against a background of optimal medical therapy.

Methods—A total of 1900 diabetic subjects with MVD were randomized to PCI or CABG worldwide from April 2005–March 2010. FREEDOM is a superiority trial with a mean follow-up of 4.37 years (minimum 2 years) and 80% power to detect a 27.0% relative reduction. We present the baseline characteristics of patients screened and randomized, and provide a comparison with other MVD trials involving diabetic patients.

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Clinical Trial Registration #:NCT00086450

Results—The randomized cohort was 63.1 ± 9.1 years old and 29% female with median diabetes duration 10.2 ± 8.9 years. Most (83%) had three-vessel disease and on average took 5.5 ± 1.7 vascular medications, with 32% on insulin therapy. Nearly all had hypertension and/or dyslipidemia and 26% had a prior myocardial infarction. Mean HbA1C was 7.8 ± 1.7 mg/dl, 29% had low-density lipoprotein < 70 mg/dl and mean systolic blood pressure was 134 ± 20 mmHg. The mean SYNTAX score was 26.2 with a symmetric distribution. FREEDOM trial subjects have baseline characteristics similar to those of contemporary multivessel and diabetes trial cohorts.

Conclusions—The FREEDOM trial has successfully recruited a high-risk diabetic MVD cohort. Follow-up efforts include aggressive monitoring to optimize background risk factor control. FREEDOM will contribute significantly to the PCI vs. CABG debate in diabetic subjects with MVD.

INTRODUCTION

Diabetes is increasingly prevalent worldwide and is an important risk factor for coronary artery disease and atherothrombotic events.¹ Many diabetic patients require coronary revascularization. Therefore, defining the most suitable approach, coronary bypass grafting (CABG) or percutaneous intervention (PCI), is central to the optimal care of these patients.

An analysis of the Balloon Angioplasty Revascularization Investigation (BARI)² study, a randomized trial comparing balloon angioplasty with CABG in patients with multi-vessel coronary artery disease (CAD), showed increased mortality among the subgroup of diabetic patients randomized to angioplasty. Similar results in the EAST (Emory Angioplasty versus Surgery) and CABRI (Coronary Angioplasty versus Bypass Revascularization Investigation) trials led to guidelines recommending CABG as the preferred approach to revascularization over angioplasty in diabetic patients with multivessel coronary disease (MVD)³. On the other hand reports regarding diabetic sub-groups from the Duke registry, the ARTS (Arterial Revascularization Study), ERACI (Argentine randomized trial of angioplasty vs. Surgery), SOS (Stent or Surgery) and MASS (Medicine, Angioplasty or Surgery) trials showed comparable mortality rates for the two strategies and the AWESOME (Angina with Extremely Serious Operative Mortality Evaluation) trial even showed that PCI may in fact fare better than bypass surgery.⁴⁻⁹

Since these studies were reported, there have been immense technological advances in PCI, including most prominently, the evolution of stents and adjunctive drug therapy, which are now central to most PCI procedures¹⁰. These changes call into question the applicability of the earlier trial results to current practice. However, to date, definitive guidance based on randomized trial data is lacking, especially for diabetic subjects, who have comprised less than a quarter of the patients randomized in these studies. To address the need for compelling data, the randomized FREEDOM trial was designed to compare a strategy of CABG to a strategy of PCI with drug-eluting stents (DES) in diabetic patients with MVD using PCI.

The aims of this report are to: 1) Describe the baseline characteristics of subjects in the trial and 2) compare the baseline profile of the FREEDOM trial cohort with that of cohorts from other trials with multivessel and/or diabetic patients.

METHODS

Trial Design

The FREEDOM trial was designed as a two-armed superiority trial to assess the effectiveness of multi-vessel PCI with DESs relative to CABG in preventing the composite endpoint of all cause mortality, non-fatal MI or stroke at a mean follow-up of 4.37 years (Fig 1). Minimum follow-up on all subjects is 2 years. The design of the FREEDOM trial has been presented previously¹¹. Briefly, FREEDOM recruited adult subjects with diabetes (type I or II) that met American Diabetes Association criteria. Trial eligibility required baseline values greater than 126 mg/dl for fasting glucose and >200 mg/dl for random glucose, or for patients to be undergoing pharmacological or non-pharmacological treatments for diabetes. In addition, patients were required to have MVD, defined as angiographically confirmed MVD (>70% lesions in 2 major epicardial vessels and in 2 separate coronary artery territories). All patients had an indication for revascularization based upon anginal symptoms or objective evidence of myocardial ischemia. Broadly, FREEDOM excluded subjects with prior CABG or valve surgery, left main disease, ST-elevation myocardial infarction (STEMI) in the past 72 hours or prior PCI in past 6 months. Institutional review boards at all participating sites approved the protocol and patients provided written informed consent. No extramural funding was used to support this work. The authors are solely responsible for the design and conduct of this study; all study analyses, the drafting and editing of the paper and its final contents.

Statistical Methods

Descriptive statistics are presented as mean± standard deviation and median for continuous variables and frequency with percentage for categorical variables. Baseline characteristics of enrolled and eligible non-enrolled patients were compared using a Fisher exact test for categorical variables, the Wilcoxon rank sum test for continuous variables with a skewed distribution, and Student's t-test for other continuous variables. A p-value less than 0.05 was considered significant. All analyses were conducting using SAS version 9.2 (Statistical Analysis System, SAS Institute, Inc., Cary, NC).

Changes in trial design since publication of design manuscript

Upon recommendation by the independent Data and Safety Monitoring Committee, sample size was changed from 2,058 to 1,900 subjects. Trial duration was changed from 6.75 to 7.0 yrs. The recruitment period was extended from 4.25 to 5.0 yrs. Minimum follow-up was changed from 2.5 yrs to 2.0 yrs. Average follow-up has increased from 4.07 yrs to 4.37 yrs. Assuming 4-year rate of the primary outcome measure to be 21.5% in the trial arm with a higher event rate, with 1% crossover rate and 1% loss to follow-up rate, and up to 3 interim looks at the data, a sample size of 1,900 provides 80% power to detect a relative reduction in the rate of the primary endpoint as low as 27.0% (4.65% absolute rate difference).

Baseline Measurement

Cardiovascular risk factors (blood pressure, lipid panel, HbA1c, renal function) and anthropometric measures were carried out for all subjects using standardized methodology.

All patients screened for eligibility for the FREEDOM Trial underwent coronary angiography and the studies from eligible subjects were submitted to an independent angiographic core laboratory for assessment.

Disease-specific health status was assessed using the Seattle Angina Questionnaire (SAQ), a 19 item instrument that yields five measures of health status related to coronary artery disease; scores range from 0 to 100, with higher scores indicating fewer symptoms and better health status^{12,13}. The EuroSCORE¹⁴ was calculated using data available from the medical history close to the time of randomization. The Syntax score¹⁵ was performed by the independent angiographic core laboratory from the baseline angiogram, and all angiographic data such as LVEF and the presence vs. absence of a chronic total occlusion (CTO) are based on core laboratory determination¹⁶. The Duke jeopardy score was calculated using the method described by Califf et al.¹⁷

RESULTS

Patient recruitment

A total of 32,966 patients were screened, of whom 3309 (10%) subjects met clinical and angiographic inclusion criteria and 1900 (57% consent rate) were randomized at 140 sites worldwide between April 2005 and March 2010. Table 1 compares randomized subjects to those who were eligible for randomization but not randomized and those who were ineligible. The enrolled cohort is representative with respect to gender but was slightly younger (mean 63.1 vs. 64.4 years), more often Hispanic, and less often Asian than the eligible, non-consenting patients.

Demographic Characteristics

The mean age of the FREEDOM trial sample was 63.1 ± 9.1 years with over half of the subjects being white males (Table I). Seven hundred and four (37%) subjects were enrolled from North America, 520 (27%) from South America, 480 (25%) from Europe and 196 from Australasia (11%).

Clinical Presentation

In keeping with the inclusion criteria, 31% of subjects in FREEDOM had recent (>72 hours) acute coronary syndromes with normalizing biomarkers of myocardial ischemia upon trial enrollment, and the rest had stable coronary disease with anginal symptoms and/or inducible ischemia with stress testing (Table II). The overall mean angina frequency score on the Seattle Angina Questionnaire (SAQ) was 71, indicating mild angina (angina on a weekly basis), and 23% of patients had no angina at baseline (angina frequency score of 100). The mean (SAQ) physical limitations score was 69 indicating mild limitations, and mean SAQ quality of life score was 48 (fair). SAQ results indicate that physical limitation and angina frequency are mild to moderate (means of 69 and 71 out of 100 with 100 indicating better health), and angina stability and quality of life being on an average lower (mean 43 and 48, respectively.) Out of the 69% with stable disease, approximately 41% underwent ischemia testing. Seventy five percent subjects were found to have moderate or severe ischemia.

More than 95% of subjects had type-2 diabetes. Complications associated with longstanding diabetes were relatively frequent (18%, table III); 85% had hypertension, 84% from hyperlipidemia and 55% of subjects had tobacco exposure. One-quarter (26%) of subjects had a prior MI, 3% had a prior stroke and 11% had known peripheral arterial disease. Less than 1% (11 subjects) had a PCI between 6 and 12 months before enrollment in the trial (Table III).

Physical Exam and Laboratory evaluations

Mean duration of diabetes was 10.2 ± 8.9 years. At baseline, the mean HbA1C was $7.8 \pm 1.7\%$, LDL was 92.7 ± 36.3 mg/dl and systolic BP was 133.7 ± 19.8 mmHg. At baseline 36% of FREEDOM subjects had a HbA1C $< 7\%$, 62% had a LDL < 100 mg/dl, 19% had a systolic blood pressure of < 120 mmHg, 53% had a diastolic blood pressure of < 80 mmHg for, and 16% were current smokers (Table IV). Almost half (42%) of subjects were obese based on body mass index, 59% met the abnormal waist circumference criterion, 48% had a triglyceride level > 150 mg/dl and 75% had a low HDL.

Medications

Participants in the FREEDOM trial were taking an average of 1.5 ± 0.8 medications for diabetes (range 0–5) and 5.5 ± 1.7 medications (range 0–11) daily for secondary prevention.. At baseline 93% were receiving antiplatelet therapy, 88% anti-anginal agents, 86% lipid-lowering agents and 78% a renin-angiotensin system inhibiting agent. In terms of diabetes treatments, 32% of subjects were being treated with insulin, 56% were receiving biguanides, 44% sulfonylureas and 8% were receiving thiazolidinediones (Table V).

Baseline Angiographic Findings

Triple vessel disease was present in 83% of subjects in FREEDOM, with a mean of 5.7 ± 2.2 lesions (of $> 50\%$ diameter stenosis) per patient and a mean total burden of disease (total length of all lesions) of 77.6 ± 33.5 mm. Left main disease was an exclusion criterion. Almost all (99%) subjects had LAD involvement. The target lesion was located in the proximal LAD for 14%. Mean left ventricular ejection fraction (LVEF) was $66.2 \pm 11.3\%$, with only 1% of subjects having LVEF $< 35\%$. Among all 11,226 lesions, 6% were total occlusions, 22% were bifurcation lesions, 21% were calcific lesions and 46% were ACC/AHA grade C lesions. The mean Duke jeopardy score was high at 9.3 (Table VI).¹⁷

There were 1857 subjects with a calculable EuroSCORE and 1887 subjects with a calculable SYNTAX score. The EuroSCORE distribution was highly positively skewed and has a median of 1.9 (interquartile range, 1.3 to 3.1) for FREEDOM subjects (Fig. 2). The EuroSCORE was significantly higher for black and non-Hispanic subjects, for those with longer diabetes duration, and those with 3VD. The Syntax score distribution was symmetric with a mean of 26.2 ± 8.6 and median of 26.0 (interquartile range, 20.0 to 31.5) (Fig. 3). The SYNTAX score was also significantly higher for black and non-Hispanic subjects and not surprisingly for those with CTOs and 3VD. There were 395 subjects (20.9%) with a high SYNTAX score (> 32), 839 (44.0%) with an intermediate score (22–32) and 662 (35.1%) with a low score (< 22)¹⁸. The observed tertiles of the SYNTAX score in the FREEDOM cohort were 22 and 29.

FREEDOM cohort compared to other trial cohorts

We compared the baseline clinical and angiographic characteristics of subjects enrolled in the FREEDOM trial with those from other published contemporary studies such as Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2-D), Coronary Artery Revascularization in Diabetes (CARDia), SYnergy between percutaneous coronary intervention with TAXus and cardiac surgery (SYNTAX) and the Bypass Angioplasty Revascularization Investigation (BARI) as a historical comparator (Table VII and Fig. 4–5). The BARI 2-D trial randomized 2,368 diabetic patients with stable documented coronary disease or myocardial ischemia to early or deferred revascularization in the presence of aggressive medical therapy with either insulin sensitizing or insulin providing agents. CARDia studied 510 diabetic subjects with multi-vessel coronary disease and compared the strategies of PCI with DES versus CABG. SYNTAX evaluated 1800 subjects with left main or MVD, of which 452 had medically treated diabetes. This trial, like FREEDOM, compared PCI with DES to CABG. The clinical profiles of the patients in these studies conducted worldwide are remarkably similar to each other and to the FREEDOM cohort. FREEDOM stands out in having the largest proportion of patients with 3-vessel disease. Compared with the BARI trial, which randomly assigned 1,829 subjects (456 diabetic subjects) to PCI versus CABG in the 1980s, the FREEDOM cohort had a significantly lower LDL (93 mg/dl versus 140mg/dl in BARI), and the prevalence of hypertension and hyperlipidemia in FREEDOM were almost double that of the BARI trial.

DISCUSSION

Over the last decade, the advent of DES, vast improvements in adjunctive medical therapies, significant advances in operative techniques (total arterial revascularization, off-pump surgery, minimally invasive robotic surgery) and better peri-operative care, has rekindled the revascularization debate regarding the optimal strategy for coronary revascularization in diabetic patients. Recent large studies such the VA-CARDS and the CARDIA trial¹⁹ were terminated before complete recruitment of the target sample size and were therefore unable or underpowered to provide a definitive answer. The FREEDOM trial has recruited an adequate sample size to provide a definitive answer with regard to superiority of one revascularization strategy over another with 80% power to detect a 27.0% relative reduction in the primary endpoint attributable to the superior strategy. The trial will report its primary outcome of the composite (earliest occurring of) death, non-fatal MI and non-fatal stroke at mean 4.37 years of follow-up in 2012.

Only 3309 subjects out of the screened 32,966 (10%), subjects met angiographic eligibility criteria for FREEDOM (Table I). While this posed a great challenge for recruitment, we believe that this “low” incidence of multi-vessel disease in diabetic subjects is a result of successes in medical therapy, such as increasing use of statin and renin-angiotensin system (RAS) inhibitor therapies. The FREEDOM trial cohort is notable for the high prevalence of multiple cardiovascular risk factors such as hypertension, obesity and dyslipidemia in addition to long-standing diabetes. With enrollment criteria including a history of having suffered an acute coronary syndrome or having inducible ischemia, and the fact that 83% subjects enrolled in FREEDOM have 3 vessel disease and 99% have LAD involvement,

there can be no doubt that this is a cohort at very high risk for future cardiovascular events. Challenges in achieving near-complete revascularization in subjects with a mean aggregate lesion length of 78 mm and high myocardial jeopardy scores add to the complexity of the FREEDOM patient cohort. The EuroSCORE calculation is skewed with a low median score, probably due to the fact that FREEDOM, by virtue of its design, either excludes subjects with significant co-morbidities or does not fully capture data related to previous cardiac surgery, critical pre-operative state, pulmonary hypertension, active endocarditis and other complications related to thoracic surgery (components of the EuroSCORE). The SYNTAX score, being an anatomical angiographic score, is very normally distributed, with almost 45% subjects having scores in what is considered the intermediate range (22–32). Subjects with such scores and concomitant diabetes have been the subject of recent interesting speculation regarding the relative efficacy of PCI versus CABG.

In comparing the baseline characteristics of FREEDOM with recent landmark studies such as CARDia¹⁹, BARI-2D^{20, 21}, and SYNTAX²² (Fig. 4, Table VII), it becomes evident that our subjects are comparable in terms of the clinical and angiographic characteristics, as are the rates of use of evidence-based medications for secondary prevention of atherosclerotic disease. In aggregate, these studies are markedly different from the historical BARI trial, with twice as much hypertension and hyperlipidemia noted in the recent trials.

The FREEDOM trial is unique in many ways. FREEDOM is the largest randomized trial of MVD treatments dedicated to diabetic subjects only. The mean values for blood pressure, lipids (LDL) and HbA1C upon entry into the trial are relatively favorable, and these risk factors are being aggressively targeted in the trial. From the inception of the trial, the importance of achieving optimal medical therapy in both arms has been emphasized. We firmly believe that in the post COURAGE²³ and BARI-2D world, there is no place for evaluating revascularization strategies with sub-optimal medical therapy. The trial has fostered teamwork, coordination and communication between the cardiologist, interventionalist, cardiac surgeon and the diabetologist. We have taken special effort from the initiation of the trial to ensure an adequate multi-ethnic representation and equitable recruitment from sites in North and South Americas, Europe and Australasia.

The baseline data from the FREEDOM trial establish that the trial has successfully recruited a high-risk diabetic multi-vessel coronary disease cohort to test the optimal revascularization strategy. FREEDOM will contribute towards a definitive answer to the twodecade long debate regarding the merits of PCI vs. CABG for diabetic patients with multivessel disease. Simultaneously, it will also serve as a rich database to generate additional hypotheses regarding the role of optimal medical therapy in the management of these complex subjects for the reduction of long-term macro-vascular events.

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Figure 1.
FREEDOM Trial Design

Figure 2.
EuroSCORE Distribution for FREEDOM Subjects at Randomization (N=1857)

Figure 3.
Syntax Score Distribution for FREEDOM Subjects at Randomization (N=1887)

Figure 4.
Comparison of Contemporary Trials

Figure 5.
Comparison of Evidence-Based Medication Use Across Trials

Table I

Baseline Characteristics for N=32966 Patients Screened for FREEDOM Trial Eligibility

Characteristic	Ineligible	Eligible		p-value ***
		Not Enrolled	Enrolled	
N	29657	1409	1900	
Mean Age at Screening, yr	65.2 ± 10.8	64.4 ± 9.6	63.1 ± 9.1	<0.0001
Male	64.7 ± 10.5	63.7 ± 9.4	62.6 ± 9.0	0.005
Female	66.2 ± 11.2	66.4 ± 9.7	64.4 ± 9.2	0.002
Male	67.7%	72.8%	71.4%	0.38
Did not meet angiographic Inclusion Criteria *	85.6%	NA	NA	NA
Clinical Exclusion Present	57.7%	NA	NA	NA
Prior cardiac surgery or planned cardiac surgery **	32 %	NA	NA	NA
Race/Ethnicity				<.0001
White, Non-Hispanic		69.6%	51.3%	
Black or African American, Non-Hispanic		4.7%	2.7%	
Asian, Non-Hispanic		13.3%	9.7%	
Other, Non-Hispanic		4.3%	1.8%	
Hispanic		8.2%	34.5%	
Planned Management Strategy				
PCI		51.8%	50%	NA
CABG		33.6%	50%	
Medical therapy alone		5.8%		
Unknown		8.8%		

* Subjects needed to have multi-vessel CAD defined as critical (70%) lesions in at least two major epicardial vessels. Angiographic characteristics needed to be amenable to both PCI/DES and CABG. Left main disease, in-stent restenosis and >1 chronic total occlusion were excluded.

** Prior bypass surgery or valvular surgery or valve surgery planned.

*** Test of significance for difference between enrolled patients and eligible but not enrolled patients

Table II

History of Presenting Illness

	Overall (N=1900)
HISTORY OF PRESENTING ILLNESS (Indication for coronary angiography)	
Stable coronary heart disease (1317 subjects)	69.3%
Acute Coronary Syndrome (ACS) (584 subjects)	30.7%
ST elevation MI (>72 hrs prior to admission)	20.2%
Non-ST elevation ACS (466 subjects)	79.8%
No recurrent/provocable ischemia	33.3%
Provocable ischemia only	23.4%
Spontaneous recurrent ischemia	41.3%
Refractory ischemia	1.9%

Table III**Past Medical and Surgical History (N=1900)**

	Overall
PAST MEDICAL HISTORY	
Diabetes Mellitus:	
Type I	4.5%
Type II	95.5%
Complications associated with diabetes *	18.0%
Diabetic foot ulcer	9.3%
Extremity amputation	3.8%
Diabetic retinopathy/blindness	39.4%
Diabetic nephropathy	32.7%
Diabetic neuropathy	54.5%
History of high blood pressure	84.8%
History of hyperlipidemia	83.7%
Prior myocardial infarction	25.6%
Prior stroke	3.2%
Peripheral arterial disease	11.2%
History of valvular heart disease	1.3%
History of arrhythmia	4.8%
If yes: Permanent Pacemaker Implanted	20.9%
AICD	0.0%
History of chronic renal insufficiency	6.8%
History of dialysis	0.4%
History of chronic obstructive pulmonary disease (COPD) or asthma	10.2%
Ever smoked	54.5%
If yes (n=91): Current smoker	28.8%
Ex-smoker (quit >12 months ago)	65.8%
History of gastrointestinal ulcer/bleed	4.7%
Aspirin daily for last 7 days or longer	71.7%
History of renal artery stenosis	0.5%
PAST SURGICAL HISTORY	
Prior PTCA (balloon angioplasty or atherectomy) within 12 months prior	0.6%
Prior PCI w/stent within the last 12 months	0.6%

* Percentages for the 5 diabetic complications are calculated based on the 343 subjects with complications

Table IV

Cardiovascular Risk Factor Profile of the FREEDOM Cohort *

Variable	Mean $\pm$ SD or %
LDL (mg/dl)	92.7 $\pm$ 36.6
LDL <100	62.4%
LDL <70	29.1%
HbA1c, %	7.8 $\pm$ 1.7
HbA1c (%)	
<7.0	36.0%
7.0%–8.0	25.4%
8.0	38.7%
SBP mmHg	133.8 $\pm$ 19.8
SBP (mmHg)	
<120	18.9%
120–140	43.0%
140	38.2%
DBP mmHg	76.0 $\pm$ 11.1
DBP (mmHg)	
<80	53.2%
80–90	33.1%
90	13.7%
Triglycerides (mg/dl)	177.9 $\pm$ 132.1 (148.0)
Triglycerides 150	48.0%
HDL (mg/dl)	39.2 $\pm$ 11.2
HDL 40 (men), 50 (women)	75.4%
Waist (cm)	102.6 $\pm$ 14.2
Waist 102 (men), 88 (women)	59.4%
Current Smoker, %	15.7%
Hemoglobin (g/dl)	13.6 $\pm$ 1.6
Creatinine (mg/dl)	1.1 $\pm$ 0.5
Presence of microalbuminuria (>30 mg/g)	40.3%

* N ranges from 1750 to 1899 for each measure.

Continuous variables are presented as mean $\pm$ standard deviation. Medians are presented in () after the standard deviation for skewed measures.

Table V**Baseline Medications (N=1900)**

	Overall
Medication	
Antiplatelet agent	
Aspirin	90.7%
Clopidogrel	23.9%
Ticlopidine	1.1%
Cilostazol	0.1%
Anti-anginal agent	
Beta blocker	75.3%
Calcium-channel antagonist	31.9%
Nitrate	39.4%
Lipid -lowering agent	
Statin	82.3%
Fibrate	4.8%
Other Cardiovascular Medications	
ACE inhibitor	64.3%
Angiotensin II antagonist	16.3%
ACE inhibitor or ARB	78.2%
Aldosterone antagonist	2.8%
Loop diuretics	10.3%
Thiazide diuretic	13.0%
Diabetes Medication	
Insulin	32.3%
Sulfonylurea	43.7%
Biguanides	55.8%
Alpha-glucosidase inhibitor	1.3%
Thiazolidinedione	8.2%
Rosiglitazone	4.7%
Pioglitazone	3.5%
NSAID	5.3%
PPI *	14.4%

ACE=angiotensin-converting enzyme; ARB=angiotensin II receptor blocker; NSAID=Nonsteroidal anti-inflammatory drug.

* PPI=Proton pump inhibitor; Total available N=369. PPI was added onto the data collection form in February, 2009

Table VI

Baseline Angiographic Profile for 1888 Subjects with a Centrally Interpreted Angiogram

Variable	Mean± SD or%	
No. of Diseased Vessels	1	0.1%
	2	16.6%
	3	83.3%
Location of disease	LAD	98.9%
	LCX	92.6%
	RCA	91.7%
Proximal LAD involvement (Target lesion=LAD located in proximal)		13.8%
# Lesions per patient		5.7 ± 2.2 (1888)
Extent of disease per patient (Total length of lesions, mm)		77.6 ± 33.8 (1888)
Duke Jeopardy Score		9.3 ± 3.1 (1874)
Left ventricular ejection fraction, %		66.2 ± 11.3 (1291)
Left ventricular ejection fraction	>50%	90.9%
	35%–50%	8.0%
	< 35%	1.1%

LAD=left anterior descending artery; LCX=left circumflex artery; RCA=right coronary artery DS=diameter stenosis

Table VIIComparison of Baseline Characteristics in Contemporary Trials.¹⁸

Variable	FREEDOM	BARI-2D	CARDia	BARI
Percentage or mean $\pm$ SD				
No. of subjects	1900	2368	510	1829
Duration of diabetes (yr)	10.2 $\pm$ 8.9	10.4 $\pm$ 8.7	10	N/A
LDL (mg/dl)	92.7 $\pm$ 36.3	92	75.66	140
Systolic BP (mmHg)	133.7 $\pm$ 19.8	131.7 $\pm$ 20	137 $\pm$ 19	130
Diastolic BP (mmHg)	76.0 $\pm$ 11.1	74.5 $\pm$ 11.2	73.5	76
Triglycerides (mg/dl)	177.9 $\pm$ 132.1	148	167.32	191
HDL (mg/dl)	39.2 $\pm$ 11.2	37	45.63	38.2
HbA1c (%)	7.8 $\pm$ 1.7	7.7 $\pm$ 1.6	7.9	N/A
Triglycerides > 150 mg/dl	48.0%	31%	N/A	N/A
Low HDL (mg/dl)	75.4%	72.4%	N/A	N/A
HbA1>7%	64.0%	58.3%	N/A	N/A
Chronic renal insufficiency	6.8%	N/A	4.7%	N/A
LV Ejection Fraction (%)	66.2 $\pm$ 11.3	N/A	59.5	57.3%

BP=blood pressure; LDL=low-density lipoprotein; HDL=high-density lipoprotein; LV=left ventricular; N/A: not available in published literature