Medtronic

Clinical Programs

Medtronic Coronary Stent Systems

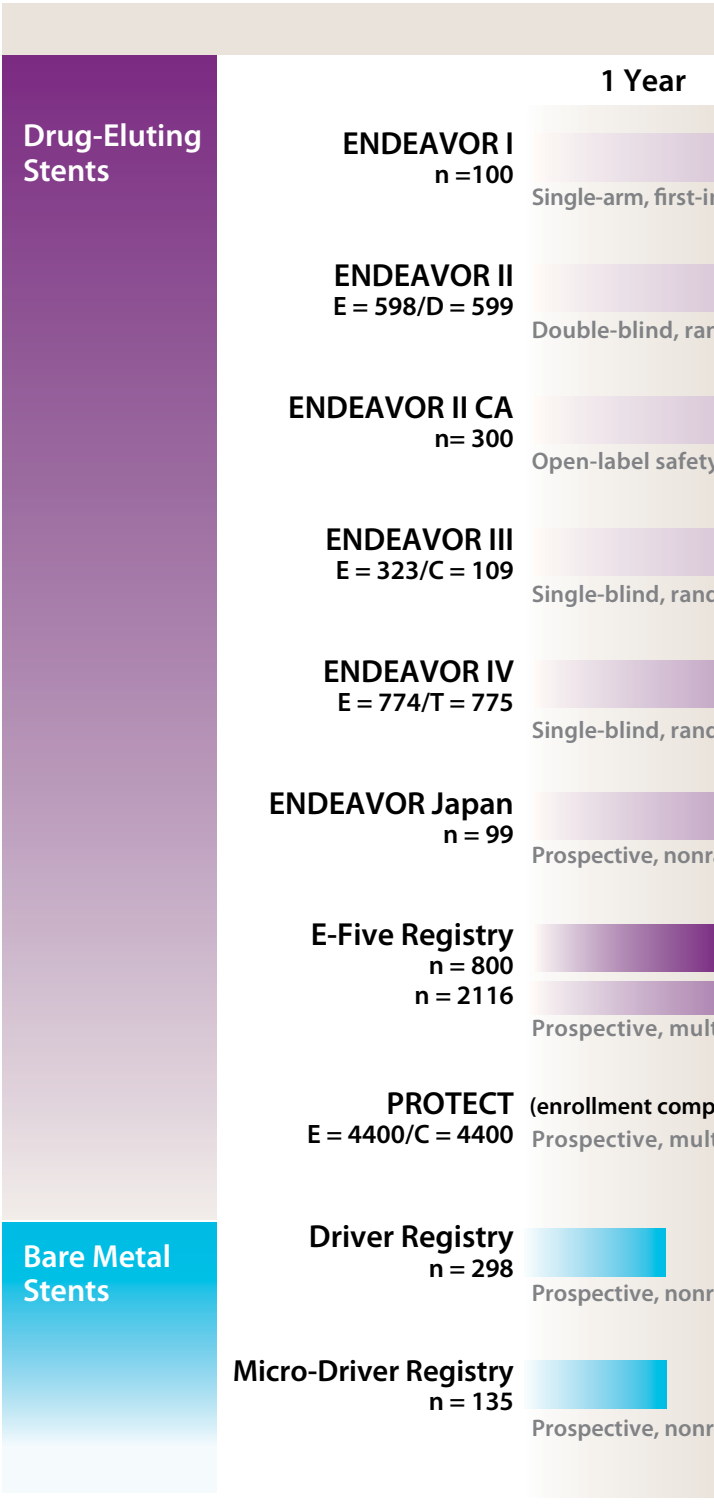
ENDEAVOR® DES
DRIVER® BMS

July 2010

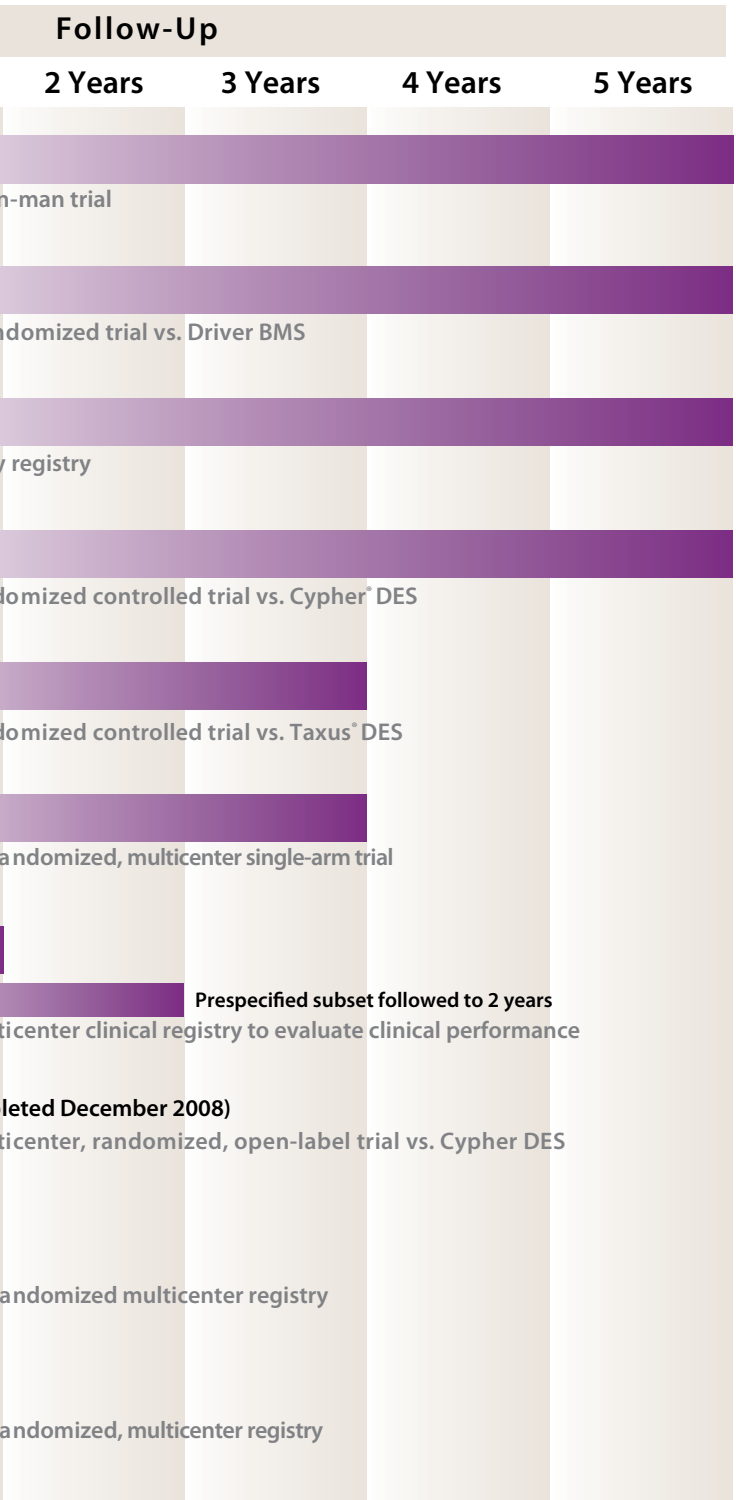
Contents

*E I–E IV data analyzed at the same data coordinating center and by the same core laboratories.

Comprehensive and Robust

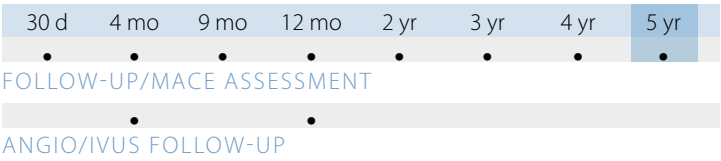


Clinical Programs



ENDEAVOR I

Single-arm trial
Trial size: 100 patients (100 actual)
Single *de novo* native coronary artery lesions (Type A–B2)
Reference vessel diameter: 3.0–3.5 mm
Lesion length: <15 mm
Stent sizes: 3.0–3.5 mm x 18 mm
Principal investigator: **Prof. Ian Meredith, MD, PhD, FACC, FRACP**
8 sites: Australia and New Zealand



Primary endpoints: MACE at 30 days and late loss* (QCA) at 4 months
Antiplatelet therapy for ≥3 months

Patient Demographics and Lesion Characteristics	n = 100
Male gender (%)	79.0
Diabetes mellitus (%)	16.0
B2/C lesions (%)	49.0
Lesion location: LAD (%)	43.0

Acute Performance Results	n = 100
Device success (%)	100
Lesion success (%)	100
Procedure success (%)	100

Baseline Characteristics	n = 100
Reference vessel diameter (RVD) (mm)	2.96
Average lesion length (mm)	10.94

Postprocedure MLD	n = 100
In-stent MLD (mm)	2.84 ±0.35
In-segment MLD (mm)	2.52 ±0.42

Primary Endpoint (30 days)	n = 100
MACE (%)	1.0

Clinical Follow-Up	12 mo n = 99	24 mo n = 99	36 mo n = 98	48 mo n = 97	60 mo n = 97
MACE (%)	2.0	3.0	6.1	7.2	7.2
Death (all)	0	1.0	3.1	4.1	4.1
Cardiac death	0	0	0	0	0
MI (all)	1.0	1.0	1.0	1.0	1.0
Q-wave	0	0	0	0	0
Non-Q-wave	1.0	1.0	1.0	1.0	1.0
TLR	2.0	2.0	3.1	3.1	3.1
TVF (%)	2.0	4.0	5.1	5.2	5.2
TVR (non-TL) (%)	0	2.0	2.0	2.1	2.0
Thrombosis (ARC def/prob) (%)	1.0	1.0	1.0	1.0	1.0
Late (>30 days)	0	0	0	0	0

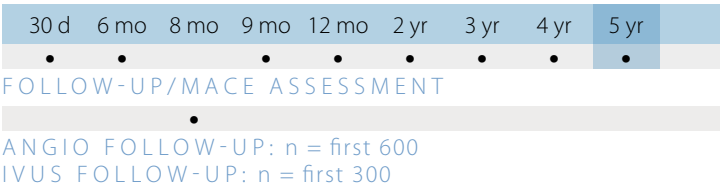
*Late lumen loss

Angiographic Follow-Up	4 mo n = 98	12 mo n = 92
Binary restenosis rate (%)		
In-stent	2.0	4.3
In-segment	3.1	5.4
Minimum luminal diameter (mm)		
In-stent	2.52	2.26
In-segment	2.29	2.08
Late loss (mm)		
In-stent	0.32	0.58
In-segment	0.22	0.43
Diameter stenosis (%)		
In-stent	14.4	21.75
In-segment	22.4	28.0

IVUS Follow-Up	4 mo n = 94	12 mo n = 86
Late incomplete apposition (%)	0	0
NIH volume (mm^3)	6.1	14.2

ENDEAVOR II

Randomized, double-blind trial
Trial size: 1200 patients (1197 actual)
Endeavor stent: n = 600 patients (598 actual)
Control Driver stent: n = 600 patients (599 actual)
Single *de novo* native coronary artery lesions (Type A–C)
Reference vessel diameter: 2.25–3.5 mm*
Lesion length: 14–27 mm
Stent sizes: 2.25–3.5 mm x 18–30 mm (8/9 mm bailout)
Principal investigators: **Jean Fajadet, MD; Rick Kuntz, MD, MSc; William Wijns, MD, PhD**
72 sites: Europe, Asia-Pacific, Israel, Australia and New Zealand



Primary endpoint: TVF (cardiac death, MI, TVR) at 9 months
Antiplatelet therapy for ≥3 months

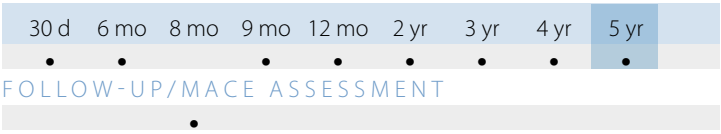
	Endeavor	Driver	*p*-Value
Patient Demographics and Lesion Characteristics	**n = 598**	**n = 599**	
Male gender (%)	77.2	75.3	NS
Diabetes mellitus (%)	18.2	22.2	NS
B2/C lesions (%)	78.5	79.0	NS
Lesion location: LAD (%)	43.2	47.5	NS
Acute Performance Results	**n = 598**	**n = 599**	
Device success (%)	98.8	99.2	NS
Lesion success (%)	99.7	100	NS
Procedure success (%)	96.5	96.4	NS
Baseline Characteristics	**n = 598**	**n = 599**	
Reference vessel diameter (RVD) (mm)	2.73	2.76	NS
Average lesion length (mm)	14.04	14.38	NS
Postprocedure MLD	**n = 598**	**n = 599**	
In-stent MLD (mm)	2.59	2.61	NS
In-segment MLD (mm)	2.21	2.24	NS
Clinical Follow-Up (9 mo)	**n = 592**	**n = 592**	
TVF (%)	7.9	15.0	<0.001
Clinical Follow-Up (12 mo)	**n = 590**	**n = 590**	
MACE (%)	8.8	15.6	<0.001
Death	1.4	0.7	NS
MI (all)	2.7	3.9	NS
Q-wave	0.3	0.8	NS
Non-Q-wave	2.4	3.1	NS
TLR	5.9	13.1	<0.001
TVF (%)	10.0	16.6	<0.001
TVR (non-TL) (%)	2.0	2.5	NS
Thrombosis (ARC def/prob) (%)	0.7	1.2	NS
Late (>30 days)	0.2	0	—

p-Values for outcome differences are not adjusted for multiple comparisons.
*2.25 mm not available for sale in USA.

	Endeavor	Driver	*p*-Value
Clinical Follow-Up (24 mo)	**n = 588**	**n = 588**	
MACE (%)	9.9	18.0	<0.001
Death	2.0	2.2	NS
MI (all)	2.9	3.9	NS
Q-wave	0.3	0.9	NS
Non-Q-wave	2.6	3.1	NS
TLR	6.5	14.1	<0.001
TVF (%)	11.1	19.7	<0.001
TVR (non-TL) (%)	2.4	4.1	NS
Thrombosis (ARC def/prob) (%)	0.8	1.2	NS
Late (>30 days)	0.1	0	—
Clinical Follow-Up (36 mo)	**n = 585**	**n = 587**	
MACE (%)	12.1	20.6	<0.001
Death	3.6	4.4	NS
MI (all)	3.2	4.3	NS
Q-wave	0.3	1.0	NS
Non-Q-wave	2.9	3.2	NS
TLR	7.2	14.7	<0.001
TVF (%)	12.6	21.3	<0.001
TVR (non-TL) (%)	2.9	4.8	NS
Thrombosis (ARC def/prob) (%)	0.8	1.2	NS
Late (>30 days)	0.1	0	—
Clinical Follow-Up (48 mo)	**n = 583**	**n = 584**	
MACE (%)	13.4	22.1	<0.001
Death (all)	5.0	5.1	NS
Cardiac	2.4	2.6	NS
MI (all)	3.3	4.5	NS
Q-wave	0.3	1.0	NS
Non-Q-wave	2.9	3.4	NS
TLR	7.2	15.8	<0.001
TVF (%)	13.6	22.6	<0.001
TVR (non-TL) (%)	3.4	5.3	NS
Thrombosis (ARC def/prob) (%)	0.8	1.2	NS
Late (>30 days)	0.1	0	—
Clinical Follow-Up (60 mo)	**n = 577**	**n = 582**	
MACE (%)	15.4	24.6	<0.001
Death	6.2	7.6	NS
MI (all)	3.8	4.8	NS
Q-wave	0.3	1.2	NS
Non-Q-wave	3.5	3.6	NS
TLR	7.5	16.3	<0.001
TVF (%)	15.4	24.4	<0.001
TVR (non-TL) (%)	—	—	—
Thrombosis (ARC def/prob) (%)	0.9	1.2	0.29
Late (>30 days)	0.2	0.2	1.00
Angiographic Follow-Up (8 mo)	**n = 264**	**n = 265**	
Binary restenosis rate (%)			
In-stent	9.5	33.2	<0.001
In-segment	13.3	34.7	<0.001
Minimum luminal diameter (mm)			
In-stent	1.99	1.62	<0.001
In-segment	1.86	1.56	<0.001
Late loss (mm)			
In-stent	0.62	1.03	<0.001
In-segment	0.36	0.72	<0.001
Diameter stenosis (%)			
In-stent	27.9	42.2	<0.001
In-segment	32.7	44.3	<0.001
IVUS Follow-Up (8 mo)	**n = 114**	**n = 104**	
Late incomplete apposition (%)	0	0	—

ENDEAVOR II CA

Single-arm, multicenter registry
Trial size: 300 patients (296 actual, 297 lesions treated)
Single *de novo* native coronary artery lesions
Reference vessel diameter: 2.25–3.5 mm
Lesion length: 14–27 mm
Stent sizes: 2.25–3.5 mm x 18–30 mm (8/9 mm bailout)
Direct stenting for lesions ≤20 mm per investigator discretion
Principal investigators: **Jean Fajadet, MD; William Wijns, MD, PhD**
15 sites: Europe



Primary endpoint: MACE at 30 days
Antiplatelet therapy for ≥3 months

Patient Demographics and Lesion Characteristics	n = 296
Male gender (%)	75.0
Diabetes mellitus (%)	25.8
B2/C lesions (%)	74.4
Lesion location: LAD (%)	50.5

Acute Performance Results	n = 296
Device success (%)	98.3
Lesion success (%)	99.7
Procedure success (%)	94.9

Baseline Characteristics	n = 296
Reference vessel diameter (RVD) (mm)	2.63
Average lesion length (mm)	16.49

Postprocedure MLD	n = 297
In-stent MLD (mm)	2.56
In-segment MLD (mm)	2.24

Primary Endpoint (30 days)	n = 296
MACE (%)	5.4

Clinical Follow-Up (9 mo)	n = 293
MACE (%)	10.6
Death	0.7
MI (all)	5.1
Q-wave	0.3
Non-Q-wave	4.8
TLR	5.1
Emergent CABG	0.3
TVF (%)	13.0
TVR (non-TL) (%)	4.1
Thrombosis (all) (%)	0
Late (>30 days)	0

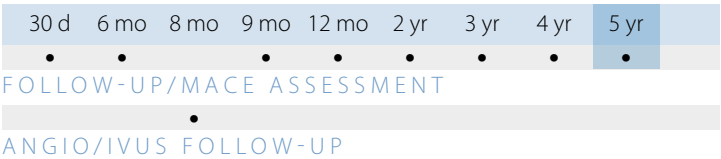
Clinical Follow-Up	12 mo n = 293	24 mo n = 292	36 mo n = 290	48 mo n = 287	60 mo n = 287
MACE (%)	12.3	12.7	13.8	15.3	17.8
Death	0.7	1.4	2.1	3.8	5.9
MI (all)	5.5	5.8	6.2	6.6	7.0
Q-wave	0.3	0.3	0.3	0.3	0.7
Non-Q-wave	5.1	5.5	5.9	6.3	6.6
TLR	6.5	7.2	7.2	7.3	7.3
Emergent CABG	0.3	0.3	1.4	1.4	0.3
TVF (%)	15.7	16.1	17.6	19.2	21.6
TVR (non-TL) (%)	5.8	5.8	6.9	8.4	9.8
Thrombosis (ARC def/prob) (%)	0	0	0	0	0
Early (0–30 days)	0	0	0	0	0
Late (31–360 days)	0	0	0	0	0
Very late (361–1825 days)	0	0	0	0	0

Angiographic Follow-Up (8 mo)	n = 117
Binary restenosis rate (%)	
In-stent	15.4
In-segment	17.1
Minimum luminal diameter (mm)	
In-stent	1.92
In-segment	1.81
Late loss (mm)	
In-stent	0.58
In-segment	0.39
Diameter stenosis (%)	
In-stent	27.7
In-segment	31.9

IVUS Follow-Up (8 mo)	n = 42
Late incomplete apposition (%)	0

ENDEAVOR III

Randomized, single-blind, prospective trial
Sample size: 436 patients (436 actual)
Endeavor stent: n = 327 patients (323 actual)
Control Cypher® stent: n = 109 patients (113 actual)
Single *de novo* native coronary artery lesions
Reference vessel diameter: 2.5–3.5 mm
Lesion length: 14–27 mm
Stent sizes: 2.5–3.5 mm x 18–30 mm (8/9 mm bailout)
Principal investigator: **Martin B. Leon, MD**
29 sites: USA



Primary endpoint: in-segment late lumen loss by QCA at 8 months
Antiplatelet therapy for ≥3 months

	Endeavor	Cypher	*p*-Value
Patient Demographics and Lesion Characteristics	**n = 323**	**n = 113**	
Male gender (%)	65.3	81.4	0.001
Diabetes mellitus (%)	29.7	28.3	NS
B2/C lesions (%)	67.2	56.6	NS
Lesion location: LAD (%)	41.2	39.8	NS
Acute Performance Results	**n = 323**	**n = 113**	
Device success (%)	98.8	94.7	0.02
Lesion success (%)	100	99.1	NS
Procedure success (%)	99.4	91.2	0.01
Baseline Characteristics	**n = 323**	**n = 113**	
Reference vessel diameter (RVD) (mm)	2.75	2.79	NS
Average lesion length (mm)	14.98	14.95	NS
Postprocedure MLD	**n = 323**	**n = 113**	
In-stent MLD (mm)	2.67	2.67	NS
In-segment MLD (mm)	2.27	2.28	NS
Clinical Follow-Up (9 mo)	**n = 321**	**n = 113**	
MACE (%)	7.5	7.1	NS
Death	0.6	0	NS
MI (all)	0.6	3.5	0.04
Q-wave	0	0	—
Non-Q-wave	0.6	3.5	0.04
TLR	6.2	3.5	NS
TVF (%)	11.8	11.5	NS
TVR (non-TL) (%)	5.9	5.3	NS
Thrombosis (ARC def/prob) (%)	0.3	0	1.00
Late (>30 days)	0.3	0	1.00
Clinical Follow-Up (12 mo)	**n = 320**	**n = 112**	
MACE (%)	7.8	8.0	NS
Death	0.6	0.9	NS
MI (all)	0.6	3.6	0.04
Q-wave	0	0	—
Non-Q-wave	0.6	3.6	0.04
TLR	6.6	3.6	NS
TVF (%)	12.8	11.6	NS
TVR (non-TL) (%)	6.6	5.4	NS
Thrombosis (ARC def/prob) (%)	0.3	0	NS
Late (>30 days)	0.3	0	NS

p-Values for outcome differences are not adjusted for multiple comparisons.

	Endeavor	Cypher	*p*-Value
Clinical Follow-Up (24 mo)	**n = 323**	**n = 113**	
MACE (%)	9.2	11.6	NS
Death	1.6	4.5	NS
MI (all)	0.6	3.6	0.04
Q-wave	0	0	—
Non-Q-wave	0.6	3.6	0.04
TLR	7.0	4.5	NS
TVF (%)	14.2	13.4	NS
TVR (non-TL) (%)	8.3	6.3	NS
Thrombosis (ARC def/prob) (%)	0.3	0	NS
Very late (366–730 days)	0	0	NS
Clinical Follow-Up (36 mo)	**n = 304**	**n = 110**	
MACE (%)	11.5	14.5	NS
Death	3.3	7.3	NS
MI (all)	0.6	4.5	0.01
Q-wave	0	0.9	NS
Non-Q-wave	0.6	3.6	0.04
TLR	7.6	4.5	NS
TVF (%)	16.1	14.5	NS
TVR (non-TL) (%)	9.5	7.3	NS
Thrombosis (ARC def/prob) (%)	0.3	0.9	—
Very late (366–1095 days)	0	0.9	0.46
Clinical Follow-Up (48 mo)	**n = 307**	**n = 110**	
MACE (%)	12.7	19.1	0.11
Death	4.2	10.0	0.03
MI (all)	1.0	4.5	0.33
Q-wave	0.3	0.9	0.46
Non-Q-wave	0.7	3.6	0.04
TLR	7.8	6.4	0.83
TVF (%)	15.6	16.4	1.00
TVR (non-TL) (%)	10.1	7.3	0.45
Thrombosis (ARC def/prob) (%)	0.7	0.9	1.00
Very late (366–1460 days)	0.3	0.9	0.45
Clinical Follow-Up (60 mo)	**n = 323**	**n = 113**	
MACE (%)	14.0	22.2	0.05
Death	5.2	13.0	0.02
MI (all)	1.0	4.6	0.03
Q-wave	0.3	0.9	0.45
Non-Q-wave	0.7	3.7	0.04
TLR	8.1	6.5	0.68
TVF (%)	17.9	18.5	0.89
TVR (non-TL) (%)	11.4	8.3	0.47
Thrombosis (ARC def/prob) (%)	0.7	0.9	1.00
Very late (366–1800 days)	0.3	0.9	0.45
Angiographic Follow-Up (8 mo)	**n = 277**	**n = 94**	
Binary restenosis rate (%)			
In-stent	9.7	2.1	0.01
In-segment	12.3	4.3	0.03
Minimum luminal diameter (mm)			
In-stent	2.06	2.52	<0.001
In-segment	1.91	2.16	<0.001
Late loss (mm)			
In-stent	0.62	0.15	<0.001
In-segment	0.36	0.13	<0.001
Diameter stenosis (%)			
In-stent	24.9	11.0	<0.001
In-segment	30.4	23.9	<0.001
IVUS Follow-Up (8 mo)	**n = 189**	**n = 68**	
Late incomplete apposition (%)	0.5	5.9	0.02

ENDEAVOR IV

Randomized, single-blind, prospective trial
Trial size: 1548 patients (1548 actual)
Endeavor stent: n = 774 patients (773 actual)
Control Taxus® stent: n = 774 patients (775 actual)
Single *de novo* native coronary artery lesions (Type A–C)
Reference vessel diameter: 2.5–3.5 mm
Lesion length: ≤27 mm
Stent sizes: 2.5–3.5 mm x 18–30 mm (8/9 mm bailout)
Principal investigator: **Martin B. Leon, MD**
80 sites: USA

30 d	6 mo	8 mo	9 mo	12 mo	2 yr	3 yr	4 yr	5 yr
•	•	•	•	•	•	•	•	•

FOLLOW-UP/MACE ASSESSMENT

•	

ANGIO/IVUS FOLLOW-UP

Primary endpoint: TVF at 9 months
Antiplatelet therapy for ≥6 months

	Endeavor	Taxus	*p*-Value
Patient Demographics and Lesion Characteristics	**n = 773**	**n = 775**	
Male gender (%)	66.9	68.5	NS
Diabetes mellitus (%)	31.2	30.5	NS
B2/C lesions (%)	69.6	70.9	NS
Lesion location: LAD (%)	42.2	41.5	0.791
Acute Performance Results	**n = 773**	**n = 775**	
Device success (%)	97.3	97.9	NS
Lesion success (%)	99.6	99.2	NS
Procedure success (%)	98.7	96.8	0.02
Baseline Characteristics	**n = 773**	**n = 775**	
Reference vessel diameter (RVD) (mm)	2.73	2.70	NS
Average lesion length (mm)	13.41	13.80	NS
Postprocedure MLD	**n = 770**	**n = 772**	
In-stent MLD (mm)	2.62	2.61	NS
In-segment MLD (mm)	2.22	2.19	NS
Primary Endpoint (9 mo)	**n = 758**	**n = 749**	
TVF (%)	6.6	7.2	NS
Clinical Follow-Up (12 mo)	**n = 754**	**n = 751**	
MACE (%)	6.5	6.7	0.92
Death	1.1	1.1	1.0
Cardiac death	0.5	0.5	1.0
MI (all)	1.6	2.7	0.16
Q-wave	0.3	0.1	1.0
Non-Q-wave	1.3	2.5	0.095
Cardiac death and MI	2.1	3.2	0.20
TLR	4.5	3.2	0.23
TVF (%)	7.7	9.6	0.20
TVR (non-TL) (%)	2.5	4.3	0.07
Thrombosis (ARC def/prob) (%)	0.9	0.1	NS
Early (0–30 days)	0.4	0.1	0.62
Late (31–360 days)	0.5	0	0.12

p-Values for outcome differences are not adjusted for multiple comparisons.

	Endeavor	Taxus	*p*-Value
Clinical Follow-Up (24 mo)	**n = 742**	**n = 739**	
MACE (%)	9.8	10.0	0.93
Death	3.1	2.6	0.64
Cardiac death	1.5	1.2	0.82
MI (all)	2.0	4.1	0.02
Q-wave	0.4	0.5	0.73
Non-Q-wave	1.6	3.5	0.02
Cardiac death and MI	3.4	5.1	0.09
TLR	5.9	4.6	0.29
TVF (%)	11.1	13.1	0.23
TVR (non-TL) (%)	4.2	5.8	0.15
Thrombosis (ARC def/prob) (%)	1.1	0.9	1.00
Early (0–30 days)	0.4	0.1	0.62
Late (31–360 days)	0.5	0	0.12
Very late (361–730 days)	0.1	0.8	0.07
Clinical Follow-Up (36 mo)	**n = 734**	**n = 733**	
MACE (%)	11.4	13.8	0.21
Death	4.0	4.5	0.70
Cardiac death	1.6	2.3	0.45
MI (all)	2.2	4.9	0.01
Q-wave	0.4	0.7	0.73
Non-Q-wave	1.8	4.2	0.01
Cardiac death and MI	3.7	7.1	0.01
TLR	6.5	6.0	0.75
TVF (%)	12.4	16.1	0.05
TVR (non-TL) (%)	4.8	6.8	0.12
Thrombosis (ARC def/prob) (%)	1.1	1.6	0.50
Early (0–30 days)	0.4	0.1	0.62
Late (31–360 days)	0.5	0.0	0.12
Very late (361–1095 days)	0.1	1.5	0.01
Angiographic Follow-Up (8 mo)	**n = 144**	**n = 135**	
Binary restenosis rate (%)			
In-stent	13.3	6.7	NS
In-segment	15.3	10.4	NS
Minimum luminal diameter (mm)			
In-stent	1.95	2.25	<0.001
In-segment	1.80	1.98	0.008
Late loss (mm)			
In-stent	0.67	0.42	<0.001
In-segment	0.36	0.23	0.02
Diameter stenosis (%)			
In-stent	26.41	16.09	<0.001
In-segment	32.28	26.61	0.004
IVUS Follow-Up (8 mo)	**n = 106**	**n = 95**	
Late incomplete apposition (%)	0.9	3.2	NS

Note: ENDEAVOR IV was not specifically powered or designed to evaluate this subset. The Endeavor stent is not specifically indicated for use in diabetics.

Diabetics	Endeavor	Taxus	*p*-Value
Clinical Follow-Up (36 mo)	**n = 224**	**n = 218**	
Cardiac death and MI (%)	2.7	7.3	0.03
TLR (%)	9.8	8.7	0.74
TVF (%)	15.6	21.6	0.11

ENDEAVOR Pooled Safety Analysis*

ENDEAVOR I, E II, E II CA, E III, E IV and E pK
KM cumulative incidence of safety endpoints to 1880 days (*post hoc* analysis)
Sample size: 2728 patients
Endeavor stent: n = 2132 (n = 1005 at 1800 days)
Control Driver stent: n = 596 (n = 445 at 1800 days)
Single *de novo* native coronary artery lesions (Type A–C)
Principal investigator: **Laura Mauri, MD**

30 d	6 mo	8 mo	9 mo	12 mo	2 yr	3 yr	4 yr	5 yr
•	•		•	•	•	•	•	•

FOLLOW-UP/MACE ASSESSMENT

Antiplatelet therapy for ≥3 months in all trials except E IV (antiplatelet therapy for ≥6 months)

	Endeavor	Driver†
Patient Demographics and Lesion Characteristics	**n = 2132**	**n = 596**
Male gender (%)	71.5	75.3
Diabetes mellitus (%)	26.1	22.2
B2/C lesions (%)	71.3	79.0
Baseline Characteristics	**n = 2132**	**n = 596**
Reference vessel diameter (RVD) (mm)	2.73	2.76
Average lesion length (mm)	14.16	14.38
Dual Antiplatelet Therapy Usage‡		
1 yr (%)	38.8	29.0
2 yr (%)	31.0	13.5
3 yr (%)	23.7	9.1
4 yr (%)	7.9	9.2
5 yr (%)	7.5	8.6

Clinical Follow-Up (60 mo) Cumulative Incidence	Endeavor n = 2132	Driver n = 596	Difference (95% CI)
MACE (%)	14.3	24.3	-10.02 (-14.36, -5.68)
Death	6.1	7.6	-1.55 (-4.30, 1.19)
Cardiac death	2.2	3.7	-1.51 (-3.42, 0.41)
MI (all)	3.2	4.8	-1.56 (-3.81, 0.68)
Cardiac death and MI	5.2	8.4	-3.25 (-6.09, -0.40)
TLR	7.0	16.5	-9.49 (-13.31, -5.67)
TVF (%)	16.0	24.2	-8.29 (-12.77, -3.81)
TVR (%)	12.6	20.2	-7.6 (-11.82, -3.38)
Thrombosis (ARC def/prob) (%)			
Early/late (0–360 days)	0.6	1.4	-0.73 (-1.73, 0.27)
Very late (361–1800 days)	0.2	0.4	-0.19 (-0.80, 0.43)
Cumulative to 1800 days	0.8	1.7	-0.92 (-2.23, 0.40)

Important Safety Subsets*

Diabetics	Endeavor	Driver	Difference (95% CI)
Clinical Follow-Up (60 mo) Cumulative Incidence	**n = 555**	**n = 132**	
Death (%)	5.45	14.74	-9.29 (-16.69, -1.90)
Cardiac death	1.87	8.76	-6.90 (-12.78, -1.01)
MI (%)	2.61	4.59	-1.98 (-6.78, 2.82)
Cardiac death and MI (%)	4.09	13.26	-9.17 (-16.33, -2.01)
Thrombosis (protocol) (%)	0.54	2.27	-1.73 (-4.96, 1.50)
Thrombosis (ARC def/prob) (%)	1.11	3.07	-1.96 (-5.79, 1.86)

Small Vessels RVD ≤2.5 mm

Clinical Follow-Up (60 mo) Cumulative Incidence	n = 725	n = 190	
Death (%)	6.13	7.98	-1.86 (-6.79, 3.07)
Cardiac death	2.74	5.35	-2.61 (-6.59, 1.37)
MI (%)	2.29	6.39	-4.10 (-8.42, 0.21)
Cardiac death and MI (%)	4.87	11.68	-6.81 (-12.40, -1.21)
Thrombosis (protocol) (%)	0.28	2.63	-2.36 (-5.03, 0.32)
Thrombosis (ARC def/prob) (%)	0.42	3.71	-3.29 (-6.46, -0.12)

Long Lesions ≥20 mm

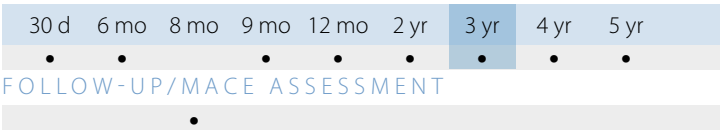
Clinical Follow-Up (60 mo) Cumulative Incidence	n = 324	n = 91	
Death (%)	4.93	13.64	-8.71 (-17.02, -0.40)
Cardiac death	2.04	4.76	-2.71 (-8.14, 2.71)
MI (%)	5.08	15.62	-10.54 (-19.87, -1.21)
Cardiac death and MI (%)	6.78	20.2	-13.42 (-23.53, -3.31)
Thrombosis (protocol) (%)	0	3.51	-3.51 (-7.94, 0.92)
Thrombosis (ARC def/prob) (%)	0.8	4.65	-3.84 (-9.09, 1.40)

Note: The ENDEAVOR pooled safety analysis was not specifically powered or designed to evaluate these subsets. The Endeavor stent is not specifically indicated for use in RVD <2.25 mm or lesion lengths >27 mm.

KM = Kaplan-Meier
CI = confidence interval
*ENDEAVOR pooled: E I 5 yr, E II 5 yr, E II CA 5 yr, E III 5 yr, E IV 3 yr and E pK 3 yr
†Driver arm existed in E II only.
‡DAPT usage based on case report forms. The optimal duration of dual antiplatelet therapy, specifically clopidogrel, is unknown and DES thrombosis may still occur despite continued therapy.

ENDEAVOR Japan

Prospective, nonrandomized, multicenter, single-arm trial
Trial size: 99 patients (99 actual)
Single *de novo* native coronary artery lesions (Type A–C)
Reference vessel diameter: 2.25–3.5 mm
Lesion length: 14–27 mm
Stent sizes: 2.25–3.5 mm x 18–30 mm (8/9 mm bailout)
Principal investigator: **Shigeru Saito, MD**
11 sites: Japan



Primary endpoint: TVF (cardiac death, MI, TVR) at 9 months
Antiplatelet therapy for 3 months (ticlopidine, aspirin)

Patient Demographics and Lesion Characteristics	n = 99
Male gender (%)	67.7
Diabetes mellitus (%)	38.4
B2/C lesions (%)	88.9
Lesion location: LAD (%)	39.4

Acute Performance Results	n = 99
Device success (%)	97.0
Lesion success (%)	100
Procedure success (%)	98.0

Baseline Characteristics	n = 99
Reference vessel diameter (RVD) (mm)	2.78
Average lesion length (mm)	13.90

Postprocedure MLD	n = 99
In-stent MLD (mm)	2.68
In-segment MLD (mm)	2.23

Clinical Follow-Up (9 mo)	n = 99
MACE (%)	5.1
Death	0
MI (all)	2.0
Q-wave	0
Non-Q-wave	2.0
TLR	3.0
TLR-CABG	0
TLR-PCI	3.0
Emergent CABG	0
TVF (%)	5.1
TVR (non-TL) (%)	0
Thrombosis (ARC def/prob) (%)	0

Clinical Follow-Up (12 mo)	n = 95
MACE (%)	7.4
Death	1.1
MI (all)	2.1
Q-wave	0
Non-Q-wave	2.1
TLR	4.2
Emergent CABG	0
TVF (%)	7.4
TVR (non-TL) (%)	0
Thrombosis (ARC def/prob) (%)	0

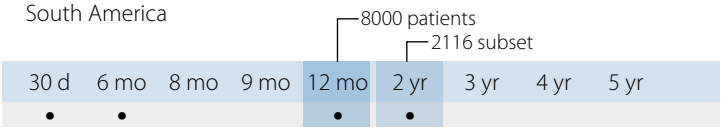
Clinical Follow-Up (24 mo)	n = 94
MACE (%)	9.8
Death	2.1
MI (all)	2.1
Q-wave	0
Non-Q-wave	2.1
TLR	5.3
Emergent CABG	0
TVF (%)	8.5
TVR (non-TL) (%)	0
Thrombosis (ARC def/prob) (%)	0

Clinical Follow-Up (36 mo)	n = 94
MACE (%)	10.6
Death	2.1
MI (all)	2.1
Q-wave	0
Non-Q-wave	2.1
TLR	5.3
TVF (%)	9.6
TVR (non-TL) (%)	1.1
Thrombosis (ARC def/prob) (%)	0

Angiographic Follow-Up (8 mo)	n = 98
Binary restenosis rate (%)	
In-stent	8.2
In-segment	8.2
Minimum luminal diameter (mm)	
In-stent	2.15
In-segment	2.00
Late loss (mm)	
In-stent	0.53
In-segment	0.23
Diameter stenosis (%)	
In-stent	23.7
In-segment	29.2

E-Five Registry

Prospective, multicenter registry
Trial size: 8000 patients (8314 actual) followed to 1 year
Prespecified subset: 2116 patients followed to 2 years
All-comers, single and multiple coronary artery lesions
Stent sizes: 2.25–4.0 mm x 8/9–30 mm
Principal investigators: **Chaim Lotan, MD**
Prof. Ian Meredith, MD, PhD, FACC, FRACP
Martin Rothman, MD
200 sites: Asia-Pacific, Europe, Israel, New Zealand and South America



FOLLOW-UP/MACE ASSESSMENT

Primary endpoint: MACE at 12 months
Antiplatelet therapy for ≥3 months

Patient Demographics and Lesion Characteristics	n = 8314	2 Yr Subset* n = 2116
Male gender (%)	76.7	77.3
Age (yr)	63.29 ±11.06	62.1 ±11.0
Diabetes mellitus (%)	32.7	30.1
B2/C lesions (%)	60.2	63.1
Bifurcation lesions (%)	16.5	16.3
Lesion location: LAD (%)	46.6	49.2

Baseline Characteristics	n = 8314
Reference vessel diameter (RVD) (mm)	2.93 ±0.47
Average lesion length (mm)	18.51 ±10.61

Procedure Characteristics	n = 10,339 Lesions
Total stent length (mm)	23.48 ±12.21
Stent:lesion length (mm)	1.36 ±0.69
Long lesions (>20 mm) (%)	3.04
Stent diameter (%)	
2.25 mm	6.9
2.5 mm	21.7
2.75 mm	16.1
3.0 mm	33.1
3.5 mm	17.9
4.0 mm	4.3

Clinical Follow-Up	30 days n = 8243	12 mo n = 7832	24 mo n = 2054
MACE (%)	1.6	7.5	8.5
Death	0.6	2.4	2.9
Cardiac death	0.6	1.7	1.5
MI (all)	0.9	1.6	1.5
Q-wave	0.2	0.4	0.3
Non-Q-wave	0.7	1.3	1.1
TLR	0.4	4.5	5.1
TVF (%)	1.6	7.2	7.9
TVR (non-TL) (%)	0	0.7	1.0
Thrombosis (ARC def/prob) (%)	0.8	1.0	0.7
Late (31–360 days)	—	0.3	0.1
Very late (366–730 days)	—	—	0.1

*Prespecified subset followed to 2 years.

Important Safety Subsets (from 8000-patient cohort)

Diabetics

Clinical Follow-Up	30 days n = 2698	12 mo n = 2563
MACE (%)	2.1	9.7
Death (all)	1.1	4.1
Cardiac death	0.9	2.7
MI (all)	1.0	1.8
Q-wave	0.2	0.5
Non-Q-wave	0.8	1.4
Cardiac death and MI	1.7	4.1
TLR	0.6	5.3
TVF (%)	1.9	8.7
TVR (non-TL) (%)	0.1	0.6
Thrombosis (all) (%)	1.2	1.6
Early (0–30 days)	1.2	1.3
Late (31–360 days)	—	0.3

Small Vessels (2.5 mm ≤2.75 mm)

Clinical Follow-Up	30 days n = 3503	12 mo n = 3336
MACE (%)	2.0	9.1
Death (all)	0.9	3.1
Cardiac death	0.8	2.3
MI (all)	1.0	1.8
Q-wave	0.2	0.4
Non-Q-wave	0.9	1.4
Cardiac death and MI	1.7	3.6
TLR	0.5	5.6
TVF (%)	2.0	8.8
TVR (non-TL) (%)	0.1	0.9
Thrombosis (all) (%)	1.1	1.5
Early (0–30 days)	1.1	1.1
Late (31–360 days)	—	0.4

Long Lesions (>20 mm)

Clinical Follow-Up	30 days n = 3586	12 mo n = 3402
MACE (%)	2.6	9.4
Death (all)	0.9	3.3
Cardiac death	0.8	2.3
MI (all)	1.6	2.4
Q-wave	0.4	0.5
Non-Q-wave	1.3	1.9
Cardiac death and MI	2.3	4.3
TLR	0.6	5.2
TVF (%)	2.6	8.9
TVR (non-TL) (%)	0.1	0.7
Thrombosis (all) (%)	1.1	1.5
Early (0–30 days)	1.1	1.2
Late (31–360 days)	—	0.3

Note: The E-Five registry was not specifically powered or designed to evaluate these subsets. The Endeavor stent is not specifically indicated for use in diabetics, RVD <2.5 mm or lesion lengths >27 mm.

Important Safety Subsets (from prespecified 2116-patient subset)

Diabetics

Clinical Follow-Up	12 mo n = 628	24 mo n = 614
MACE (%)	9.2	10.9
Death (all)	3.3	5.0
Cardiac death	2.2	2.6
MI (all)	1.4	1.6
Q-wave	0.2	0.2
Non-Q-wave	1.3	1.5
Cardiac death and MI	3.5	3.9
TLR	5.6	6.2
TVF (%)	8.6	9.6
TVR (non-TL) (%)	0.6	0.8
Thrombosis (ARC def/prob) (%)	0.8	0.8
Early (0–30 days)	0.8	0.8
Late (31–365 days)	0.0	0.0
Very late (366–730 days)	—	0.0

Small Vessels (2.5 mm ≤2.75 mm)

Clinical Follow-Up	12 mo n = 1207	24 mo n = 294
MACE (%)	9.1	10.2
Death (all)	3.6	4.4
Cardiac death	2.6	2.0
MI (all)	1.7	1.4
Q-wave	0.4	0.7
Non-Q-wave	1.3	1.7
Cardiac death and MI	4.1	3.1
TLR	5.0	5.4
TVF (%)	8.6	8.2
TVR (non-TL) (%)	0.7	0.7
Thrombosis (ARC def/prob) (%)	1.7	0.7
Early (0–30 days)	1.2	0.3
Late (31–365 days)	0.5	0.0
Very late (366–730 days)	—	0.3

Long Lesions (>20 mm)

Clinical Follow-Up	12 mo n = 956	24 mo n = 934
MACE (%)	7.2	9.1
Death (all)	2.2	3.4
Cardiac death	1.6	1.8
MI (all)	1.6	1.9
Q-wave	0.3	0.3
Non-Q-wave	1.3	1.6
Cardiac death and MI	3.0	3.5
TLR	4.4	4.8
TVF (%)	7.2	8.2
TVR (non-TL) (%)	0.7	1.0
Thrombosis (all) (%)	1.0	1.2
Early (0–30 days)	0.7	0.7
Late (31–360 days)	0.3	0.3
Very late (366–730 days)	—	0.1

Note: The E-Five registry was not specifically powered or designed to evaluate these subsets.

PROTECT

Prospective, multicenter, randomized, open-label trial
Trial size: 8800 patients (enrollment completed December 2008)
Endeavor stent: n = 4400 patients
Cypher stent: n = 4400 patients
All-comers, single and multiple coronary artery lesions
Principal investigators: **Edoardo Camenzind, MD (Switzerland)**
William O'Neill, MD (USA)
Prof. Patrick Serruys (The Netherlands)
Prof. Philippe Gabriel Steg (France)
William Wijns, MD, PhD (Belgium)
More than 200 international sites

30 d	6 mo	8 mo	9 mo	12 mo	2 yr	3 yr	4 yr	5 yr
•	•			•	•	•		

FOLLOW-UP

Primary endpoint: definite/probable stent thrombosis (ARC definition) to 3 years

Main secondary endpoint: composite endpoint of total death and number of patients with nonfatal myocardial infarctions at 3 years

Open label: antiplatelet therapy for 3–12 months

Driver Registry

Prospective, nonrandomized multicenter registry
Trial size: 298 patients (298 actual)
Single *de novo* or restenotic nonstented native coronary artery lesions (Type A–C)

Stent sizes: 3.0–4.0 mm x 9–18 mm

Principal investigator: **Michael H. Sketch Jr., MD, FACC**

23 sites: USA

	14 d	30 d	6 mo	8 mo	9 mo
FOLLOW-UP/MACE ASSESSMENT	•	•	•		•
ANGIO/IVUS FOLLOW-UP			•		

Primary endpoint: MACE at 6 months

Patient Demographics and Lesion Characteristics	n = 298
Male gender (%)	68.1
Diabetes mellitus (%)	27.6
B2/C lesions (%)	50.7
Lesion location: LAD (%)	45.1

Acute Performance Results	n = 298
Device success (%)	100
Lesion success (%)	100
Procedure success (%)	98.3

Baseline Characteristics	n = 298
Reference vessel diameter (RVD) (mm)	3.07 ±0.47
Average lesion length (mm)	11.04 ±4.24

Postprocedure MLD	n = 284
In-stent MLD (mm)	2.90 ±0.41
In-segment MLD (mm)	2.55 ±0.50

Clinical Follow-Up	180 days n = 298	270 days n = 298
MACE (%)	5.7	10.1
Death (all)	0.7	1.3
Cardiac death	0	0
MI (all)	1.7	1.7
Q-wave	0	0
Non-Q-wave	1.7	1.7
TLR	3.4	7.0
TVF (%)	6.7	9.7
TVR (%)	4.4	8.1
Thrombosis (all) (%)	0	0

Angiographic Follow-Up (9 mo)	n = 83
Binary restenosis rate (%)	
In-stent	15.7
In-segment	15.7
Minimum luminal diameter (mm)	
In-stent	1.99 ±0.62
In-segment	1.93 ±0.58
Late loss (mm)	
In-stent	0.94 ±0.54
In-segment	0.62 ±0.56
Diameter stenosis (%)	
In-stent	34.2 ±16.3
In-segment	36.1 ±15.0

Micro-Driver Registry

Prospective, nonrandomized, multicenter registry
Trial size: 135 patients (135 actual, one nonevaluable)
Single *de novo* native coronary artery lesions
Stent diameters: 2.25–2.75 mm x 8–24 mm
Principal investigator: **Michael H. Sketch Jr., MD, FACC**
17 sites: USA

30 d	6 mo	8 mo	9 mo
•	•		•
FOLLOW-UP/MACE ASSESSMENT			
	•		
ANGIO/IVUS FOLLOW-UP			

Primary endpoint: MACE at 30 days

Patient Demographics and Lesion Characteristics	n = 135
Male gender (%)	65.9
Diabetes mellitus (%)	31.9
B2/C lesions (%)	58.2
Lesion location: LAD (%)	26.1

Acute Performance Results	n = 134
Device success (%)	99.3
Lesion success (%)	100
Procedure success (%)	99.3

Baseline Characteristics	n = 134
Reference vessel diameter (RVD) (mm)	2.19
Average lesion length (mm)	9.60 ±3.97

Postprocedure Characteristics	0 days n = 134
MLD (mm)	
In-stent	2.16 ±0.27
In-segment	1.84 ±0.37
Diameter stenosis (%)	
In-stent	3.5 ±10.1
In-segment	18.5 ±8.9

Clinical Follow-Up	180 days n = 123	270 days n = 123
MACE (%)	13	19.5
Death (all)	0.8	0.8
Cardiac death	0.8	0.8
MI (all)	0.8	0.8
Q-wave	0	0
Non-Q-wave	0.8	0.8
TLR	11.4	17.9
Emergent CABG	0	0
TVF (%)	14.6	21.1
TVR (non-TL) (%)	3.3	4.9
Thrombosis (all) (%)	0	0

Angiographic Follow-Up (6 mo)	
Binary restenosis rate (%) (n = 109)	
In-stent	49.5
In-segment	53.2
Minimum luminal diameter (mm) (n = 109)	
In-stent	1.18 ±0.57
In-segment	1.12 ±0.53
Late loss (mm) (n = 108)	
In-stent	0.98 ±0.55
In-segment	0.71 ±0.55
Diameter stenosis (%) (n = 109)	
In-stent	46.4 ±24.5
In-segment	49.2 ±21.8

GLOSSARY

The following definitions and abbreviations were used throughout the ENDEAVOR clinical program.

Acute success

- Device success: attainment of <50% in-stent residual stenosis of the target lesion using only the assigned device
- Lesion success: attainment of <50% in-stent residual stenosis of the target lesion using any percutaneous method
- Procedure success: attainment of <50% in-stent residual stenosis of the target lesion and no in-hospital MACE
- Device-specific procedure success: device success and no in-hospital MACE. Device-specific procedure success is utilized to account for procedural successes/failures that are related to the implanted device.

Binary restenosis rate

Percent of patients with a follow-up percent diameter stenosis of ≥50% determined by QCA

Death

Divided into two categories:

- **Cardiac death** is defined as death due to any of the following:
  - Acute myocardial infarction
  - Cardiac perforation/pericardial tamponade
  - Arrhythmia or conduction abnormality
  - Stroke within 30 days of the procedure or stroke suspected of being related to the procedure
  - Death due to complication of the procedure, including bleeding, vascular repair, transfusion reaction or bypass surgery
  - Any death in which a cardiac cause cannot be excluded
- **Noncardiac death** is defined as a death not due to cardiac causes (as defined above).

Diabetes

A patient was considered to have a history of diabetes mellitus if he/she was taking insulin or oral antidiabetic agents or was on a modified diet to control diabetes mellitus. Patients who were taking both oral medications and insulin were considered to be insulin-dependent. Patients with a history of untreated diabetes mellitus (or diabetes mellitus treated with diet only) were classified as having noninsulin-dependent diabetes mellitus.

In-lesion measurement (also in-segment measurement)

Measurements either within the stented segment or within 5 mm proximal or distal to the stent edges

In-stent measurement

Measurements within the stented segment

Late lumen loss

Difference between the postprocedure minimal lumen diameter (MLD) and the follow-up angiography MLD

Major adverse cardiac events (MACE)

Composite of death, MI (Q-wave and non-Q-wave), emergent bypass surgery or TLR (repeat PTCA or CABG)

Myocardial infarction (MI)

A diagnosis of myocardial infarction is made when one of the following criteria is met:

- **Q-wave MI (QWMI):** QWMI requires one of the following criteria:
  - Chest pain or other acute symptoms consistent with myocardial ischemia and new pathological Q-waves in two or more contiguous ECG leads as determined by an ECG core laboratory or independent review of the CEC, in the absence of timely cardiac enzyme data

- New pathologic Q-waves in two or more contiguous ECG leads as determined by an ECG core laboratory or independent review of the CEC and elevation of cardiac enzymes. In the absence of ECG data, the CEC may adjudicate Q-wave MI based on the clinical scenario and appropriate cardiac enzyme data.

• **Non-Q-wave MI (NQWMI):** Elevated CK >2x the ULN with the presence of elevated CK-MB (any amount above the ULN) in the absence of new pathological Q-waves

Stent thrombosis (per protocol)

A diagnosis of stent thrombosis is made when one of the following criteria is met:

• Angiographic thrombus or subacute closure within the stented vessel at the time of the clinically driven angiographic restudy for documented ischemia (chest pain and ECG changes)
• Any death not attributed to a noncardiac cause within the first 30 days
• Late stent thrombosis is reported according to the following criteria:
  - **Definite late stent thrombosis:** MI >30 days after index and attributable to the target vessel, angiographic documentation (site-reported or by QCA) of thrombus or total occlusion at the target site, and freedom from interim revascularization of the target vessel
  - **Possible late stent thrombosis:** MI >30 days after index and attributable to the target vessel, no identifiable culprit lesion elsewhere, freedom from interim revascularization of the target lesion, and freedom from interim bypass grafting of the target vessel

Stent thrombosis (ARC, Academic Research Consortium)

1. Timing:

• Acute stent thrombosis*	0–24 hours poststent implantation
• Subacute stent thrombosis*	>24 hours to 30 days poststent implantation
• Late stent thrombosis†	>30 days to 1 year poststent implantation
• Very late stent thrombosis†	>1 year poststent implantation

2. Level of evidence:

• **Definite stent thrombosis:** considered to have occurred by either angiographic or pathologic confirmation
  - ***Angiographic confirmation of stent thrombosis:*** The presence of a thrombus originating in the stent or in the segment 5 mm proximal or distal to the stent **AND** at least one of the following criteria has been fulfilled within a 48-hour time window:
    1) Acute onset of ischemic symptoms at rest
    2) New ischemic ECG changes suggestive of acute ischemia
    3) Typical rise and fall in cardiac biomarkers (refer to definition of spontaneous MI)
  - ***Pathologic confirmation of stent thrombosis:*** evidence of recent thrombus within the stent determined at autopsy or via examination of tissue retrieved following thrombectomy
• **Probable stent thrombosis:** considered to have occurred after intracoronary stenting in the following cases:
  - Any unexplained death within the first 30 days
  - Irrespective of the time after the index procedure, any MI that is related to documented acute ischemia in the territory of the implanted stent without angiographic confirmation of stent thrombosis and in the absence of any other obvious cause
  • **Possible stent thrombosis:** considered to have occurred with any unexplained death from 30 days following intracoronary stenting until end of trial follow-up

3. Stent thrombosis after TLR: censored vs. *noncensored:*

Censoring stent thrombosis events that occur post-TLR performed for stent restenosis may be appropriate as the thrombosis may be related to the treatment chosen to treat restenosis (e.g., brachytherapy) rather than the

type of stent used in the index procedure. Alternatively, censoring stent thrombosis events that occur after TLR may bias results in favor of devices with higher restenosis risks. Therefore, stent thrombosis data presented in this review report both TLR-censored and TLR-uncensored rates as follows:

- **ARC definite + probable (TLR-censored):** adjudicated stent thrombosis meeting the definite or probable ARC definition with censoring of any definite or probable stent thrombosis events that may have occurred after a TLR
- **ARC definite + probable (TLR-uncensored):** adjudicated stent thrombosis meeting the definite or probable ARC definition, including any definite or probable stent thrombosis events that may have occurred after a TLR

The ARC definitions are available in the following publication: Cutlip DE, et al. Academic Research Consortium, Clinical endpoints in coronary stent trials: A case for standardized definitions. *Circulation.* 2007; 115:2344–2351.

Target lesion revascularization (TLR): any clinically driven repeat intervention of the target lesion by PCI or CABG of the target vessel. Clinically driven revascularizations are those in which the subject has a positive functional study, ischemic ECG changes at rest in a distribution consistent with the target vessel or ischemic symptoms. Revascularization of a target lesion with an in-lesion diameter stenosis ≥70% (by QCA) in the absence of the above-mentioned ischemic signs or symptoms is also considered clinically driven. In the absence of QCA data for relevant follow-up angiograms, the clinical need for revascularization is adjudicated using the presence or absence of ischemic signs and symptoms. Nonclinically driven repeat TLR are those in which the subject undergoes a nonemergent revascularization for a diameter stenosis <50% (by QCA). Nonemergent repeat TLR for a diameter stenosis <70% (by QCA) in subjects without either a positive functional study or angina are also considered nonclinically driven.

Target vessel failure (TVF): target vessel revascularization (defined below), Q- or non-Q-wave MI, or cardiac death that could not be clearly attributed to a vessel other than the target vessel. TVF includes any revascularization or adverse endpoint due to renarrowing of any portion of the target vessel and assumes that the entire vessel is vulnerable to late failures because of guide catheter or guidewire trauma or progression of disease remote from the treatment site.

Target vessel revascularization (TVR): any clinically driven (as defined for TLR) repeat percutaneous intervention of the target vessel or bypass surgery of the target vessel

*Acute or subacute can also be replaced by the term early stent thrombosis. Early stent thrombosis (0–30 days) is used in this document.

† Including "primary" as well as secondary late stent thrombosis; secondary late stent thrombosis is a stent thrombosis after a target lesion revascularization.

Driver Coronary Stent Systems

Intended Use

The Medtronic Driver Coronary Stent Systems are indicated for improving coronary luminal diameter in patients with symptomatic ischemic heart disease due to discrete *de novo* or restenotic lesions with reference vessel diameters of 3.0 mm to 4.0 mm and ≤30 mm in length using direct stenting or predilatation.

Contraindications

- Patients in whom antiplatelet and/or anticoagulation therapy is contraindicated.
- Patients who are judged to have a lesion that prevents complete inflation of an angioplasty balloon.

Warnings/Precautions

- Judicious selection of patients is necessary since the use of this device carries the associated risk of subacute thrombosis, vascular complications and/or bleeding events.
- Administration of appropriate anticoagulant, antiplatelet and coronary vasodilator therapy is critical to successful stent implantation and follow-up.
- Patients allergic to F-562 cobalt-chromium alloy may suffer an allergic reaction to this implant.
- Only physicians who have received appropriate training should perform implantation of the stent.
- Stent placement should only be performed at hospitals where emergency coronary artery bypass graft surgery can be readily performed.
- Subsequent restenosis may require repeat dilatation of the arterial segment containing the stent. The long-term outcome following repeat dilatation of endothelialized coronary stents is unknown at present.
- When multiple stents are required, stent materials should be of similar composition. Placing multiple stents of different materials in contact with each other may increase the potential for corrosion. Data obtained from *in vitro* corrosion tests using a F562 CoCr alloy stent (Medtronic Driver Coronary Stent) in combination with a 316L stainless steel alloy stent (Medtronic S7 Coronary Stent) do not suggest an increased risk of *in vivo* corrosion.
- If the physician encounters difficulty while trying to cross the lesion by direct stenting and determines the lesion to be uncrossable, this patient should be treated per predilatation practice. The stent (the same stent if undamaged) or a new stent of the same kind should then be advanced and deployed with predilatation.
- Implanting a stent may lead to dissection of the vessel distal and/or proximal to the stented portion and may cause acute closure of the vessel requiring additional intervention *(e.g.,* CABG, further dilatation, placement of additional stents or other).
- Outcomes (beyond 270 days) for this permanent implant are unknown at present.

Adverse Events

Potential adverse events that may be associated with the use of a coronary stent in native coronary arteries (including those listed in the Driver *Instructions for Use*) are death, myocardial infarction, emergency coronary artery bypass graft surgery (CABG), stent thrombosis, bleeding complications, stroke/cerebrovascular accidents, vascular complications, stent failures, acute myocardial infarction, myocardial ischemia, arrhythmias (including ventricular fibrillation and ventricular tachycardia dissection), distal emboli (air, tissue or thrombotic emboli), hemorrhage requiring transfusion, perforation, restenosis of stented segments, stent embolization, total occlusion of coronary artery, cardiac tamponade, femoral pseudoaneurysm, spasm, hypotension/hypertension, allergic reaction to drugs/contrast medium/stent material, peripheral ischemia, peripheral nerve injury, infection and pain at the insertion site, and hematoma.

Please reference appropriate product *Instructions for Use* for a more detailed list of indications, warnings, precautions and potential adverse events.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.

For further information, please contact Medtronic at 888.283.7868 or consult Medtronic's website www.Medtronic.com.

Micro-Driver Coronary Stent Systems

Intended Use

The Medtronic Micro-Driver Coronary Stent Systems are indicated for improving coronary luminal diameter in patients with symptomatic ischemic heart disease due to discrete *de novo* lesions with reference vessel diameters of 2.25–2.75 mm and ≤21 mm in length. Outcome beyond 270 days for this permanent implant is unknown at present.

Contraindications

- Patients in whom antiplatelet and/or anticoagulation therapy is contraindicated.
- Patients who are judged to have a lesion that prevents complete inflation of an angioplasty balloon.

Warnings/Precautions

- Judicious selection of patients is necessary since the use of this device carries the associated risk of subacute thrombosis, vascular complications and/or bleeding events. Administration of appropriate anticoagulant, antiplatelet and coronary vasodilator therapy is critical to successful stent implantation and follow-up.
- Patients allergic to F-562 cobalt-chromium alloy (alloy components include cobalt, chromium, or nickel) may suffer an allergic reaction to this implant.
- Only physicians who have received appropriate training should perform implantation of the stent.
- Stent placement should only be performed at hospitals where emergency coronary artery bypass graft surgery can be readily performed.
- Subsequent restenosis may require repeat dilatation of the arterial segment containing the stent. The long-term outcome following repeat dilatation of endothelialized coronary stents is unknown at present.
- When multiple stents are required, stent materials should be of similar composition. Placing multiple stents of different materials in contact with each other may increase the potential for corrosion. Data obtained from *in vitro* corrosion tests using a F562 CoCr alloy stent (Medtronic Driver Coronary Stent) in combination with a 316L stainless steel alloy stent (Medtronic S7 Coronary Stent) do not suggest an increased risk of *in vivo* corrosion.

Adverse Events

Potential adverse events that may be associated with the use of a coronary stent in native coronary arteries in order of severity are death, emergency Coronary Artery Bypass Graft Surgery (CABG), stroke/cerebrovascular accidents, cardiac tamponade, stent thrombosis or occlusion, total occlusion of coronary artery, acute myocardial infarction, restenosis of stented segments, perforation, arrhythmias (including ventricular fibrillation and ventricular tachycardia), dissection, distal emboli (air, tissue or thrombotic emboli), stent embolization, hemorrhage requiring transfusion, femoral pseudoaneurysm, spasm, myocardial ischemia, hypotension/hypertension, allergic reaction to drugs/contrast medium/stent material, peripheral ischemia, peripheral nerve injury, infection and pain at the insertion site, and hematoma.

Please reference appropriate product *Instructions for Use* for a more detailed list of indications, warnings, precautions and potential adverse events.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.

Endeavor
Indications
The Endeavor® Sprint Zotarolimus-Eluting Coronary Stent Delivery System is indicated for improving coronary luminal diameter in patients with ischemic heart disease due to *de novo* lesions of length ≤27 mm in native coronary arteries with reference vessel diameters of ≥2.5 mm to ≤3.5 mm.

Contraindications
The Endeavor Zotarolimus-Eluting Coronary Stent System is contraindicated for use in:
• Patients with a known hypersensitivity to zotarolimus or structurally-related compounds • Patients with a known hypersensitivity to the cobalt-based alloy (cobalt, nickel, chromium, and molybdenum) • Patients with a known hypersensitivity to Phosphorylcholine polymer or its individual components.

Coronary artery stenting is contraindicated for use in:
• Patients with a known hypersensitivity or allergies to aspirin, heparin, clopidogrel or ticlopidine • Patients who cannot receive recommended antiplatelet and/or anticoagulation therapy • Patients who are judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the stent or stent delivery system.

Warnings
• Please ensure that the inner package has not been opened or damaged, as this indicates the sterile barrier has been breached • The use of this product carries the risks associated with coronary artery stenting, including subacute thrombosis, vascular complications, and/or bleeding events • This product should not be used in patients who are not likely to comply with the recommended antiplatelet therapy

Precautions
• Only physicians who have received adequate training should perform implantation of the stent • Stent placement should only be performed at hospitals where emergency coronary artery bypass graft surgery can be readily performed • Subsequent stent blockage may require repeat dilatation of the arterial segment containing the stent. The long-term outcome following repeat dilatation of endothelialized stents is not well characterized • Risks and benefits of the stent should be assessed for patients with history of severe reaction to contrast agents • Do not expose or wipe the product with organic solvents such as alcohol or detergents • Stent thrombosis is a low-frequency event that current drug-eluting stent (DES) clinical trials are not adequately powered to fully characterize. Stent thrombosis is frequently associated with myocardial infarction (MI) or death. Data from the ENDEAVOR randomized clinical trials have been prospectively evaluated and adjudicated using both the protocol definition of stent thrombosis and the definition developed by the Academic Research Consortium (ARC), and demonstrate specific patterns of stent thrombosis that vary depending on the definition used. In the ENDEAVOR clinical trials analyzed to date, the differences in the incidence of stent thrombosis observed with the Endeavor stent compared to bare metal stents have not been associated with an increased risk of cardiac death, MI, or all-cause mortality. Additional data from longer-term follow-up in the ENDEAVOR randomized clinical trials and analyses of DES-related stent thrombosis are expected and should be considered in making treatment decisions as data become available • When DES are used outside the specified *Indications for Use*, patient outcomes may differ from the results observed in the pivotal clinical trials • Compared to use within the specified *Indications for Use*, the use of DES in patients and lesions outside of the labeled indications, including more tortuous anatomy, may have an increased risk of adverse events, including stent thrombosis, stent embolization, MI, or death.

The safety and effectiveness of the Endeavor stent have not yet been established in the following patient populations:
• Women who are pregnant or lactating • Men intending to father children • Pediatric patients • Patients with vessel thrombus at the lesion site • Patients with coronary artery reference vessel diameters <2.5 mm or >3.5 mm • Patients with coronary artery lesions longer than 27 mm or requiring more than one Endeavor stent • Patients with lesions located in saphenous vein grafts, in the unprotected left main coronary artery, ostial lesions, or lesions located at a bifurcation • Patients with diffuse disease or poor flow distal to the identified lesions • Patients with multivessel disease • Patients with tortuous vessels in the region of the obstruction or proximal to the lesion • Patients with a recent acute myocardial infarction where there is evidence of thrombus or poor flow • Patients for longer than 48 months of follow-up • Patients with in-stent restenosis • Patients with moderate or severe calcification in the lesion or a chronic total occlusion • Patients with prior brachytherapy of the target lesion or the use of brachytherapy to treat in-stent restenosis in an Endeavor stent.

The safety and effectiveness of the Endeavor stent have not been established in the cerebral, carotid, or peripheral vasculature.

Potential Adverse Events
Other risks associated with using this device are those associated with percutaneous coronary diagnostic (including angiography and IVUS) and treatment procedures. These risks may include, but are not limited to • Abrupt vessel closure • Access site pain, hematoma or hemorrhage • Allergic reaction (to contrast, antiplatelet therapy, stent material, or drug and polymer coating) • Aneurysm, pseudoaneurysm, or arteriovenous fistula (AVF) • Arrhythmias • Balloon rupture • Cardiac tamponade • Coronary artery occlusion, perforation, rupture, or dissection • Coronary artery spasm • Death • Embolism (air, tissue, device, or thrombus) • Emergency surgery: peripheral vascular or coronary bypass • Failure to deliver the stent • Hemorrhage requiring transfusion • Hypotension/hypertension • Incomplete stent apposition • Infection or fever • Late or very late thrombosis • Myocardial infarction (MI) • Myocardial ischemia • Peripheral ischemia/peripheral nerve injury • Renal failure • Restenosis of the stented artery • Rupture of native or bypass graft • Shock/pulmonary edema • Stent deformation, collapse, or fracture • Stent migration • Stent misplacement • Stroke/transient ischemic attack • Thrombosis (acute and subacute) • Unstable angina • Ventricular fibrillation.

Adverse Events Related to Zotarolimus
Patients' exposure to zotarolimus is directly related to the total amount of stent length implanted. The actual side effects/complications that may be associated with the use of zotarolimus are not fully known. The adverse events that have been associated with the intravenous injection of zotarolimus in humans include • Anemia • Application site reaction • Diarrhea • Dry skin • Headache • Hematuria • Infection • Injection site reaction • Pain (abdominal, arthralgia, injection site) • Rash.

Please reference appropriate product *Indications for Use* for more information regarding indications, warnings, precautions and potential adverse events.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.

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