



Medtronic

Clinical Programs

Medtronic Coronary Stents



**ENDEAVOR® DES
DRIVER®/INTEGRITY® BMS**

December 2010

*All studies were conducted with the Driver stent.

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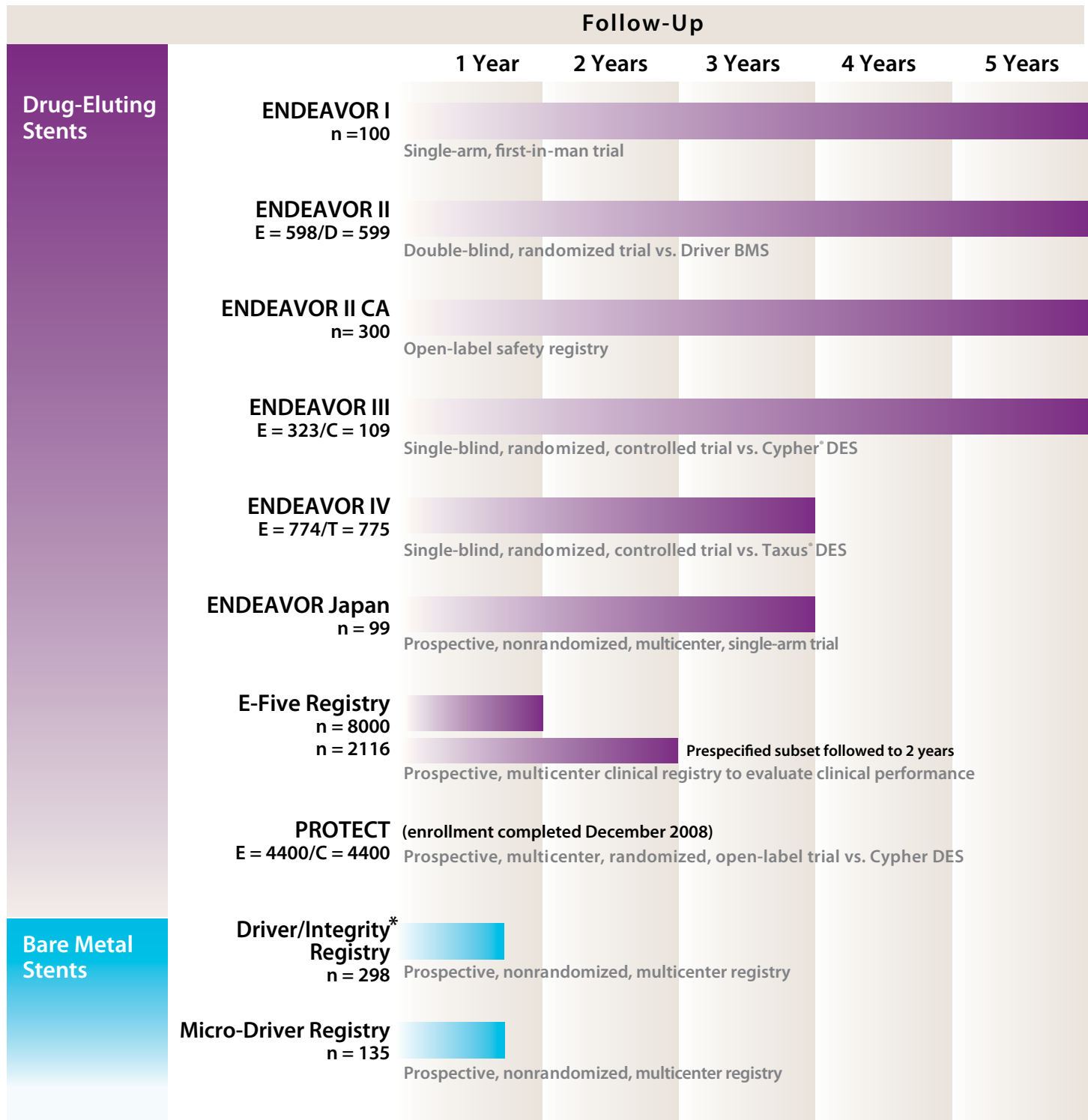
Bare Metal Stents

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*E I-E IV data analysed at the same data coordinating center and by the same core laboratories.

[†]All studies were conducted with the Driver stent.

Comprehensive and Robust Clinical Programs



*All studies were conducted with the Driver stent.

ENDEAVOR I

Single-arm trial

Trial size: 100 patients (100 actual)

Single *de novo* native coronary artery lesions (Type A–B2)

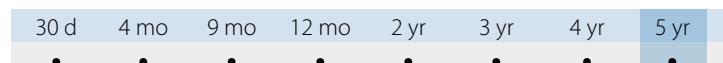
Reference vessel diameter: 3.0–3.5 mm

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



FOLLOW-UP/MACE ASSESSMENT

ANGIO/IVUS FOLLOW-UP

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/Integrity* stent: n = 600 patients (599 actual)

Single *de novo* native coronary artery lesions (Type A–C)

Reference vessel diameter: 2.25–3.5 mm*

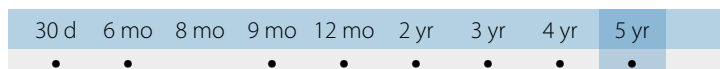
Lesion length: 14–27 mm

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



FOLLOW-UP/MACE ASSESSMENT

ANGIO FOLLOW-UP: n = first 600

IVUS FOLLOW-UP: n = first 300

Primary endpoint: TVF (cardiac death, MI, TVR) at 9 months

Antiplatelet therapy for ≥3 months

	Endeavor	Driver/ Integrity*	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	—

	Endeavor	Driver Integrity*	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	—

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

*All studies were conducted with the Driver stent.

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

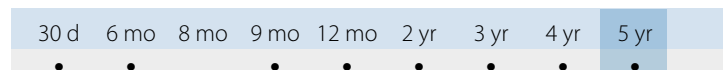
Lesion length: 14–27 mm

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



FOLLOW-UP/MACE ASSESSMENT

ANGIO FOLLOW-UP: n = first 150 patients

IVUS FOLLOW-UP: n = first 100 patients and for patients receiving >1 stent

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
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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
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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

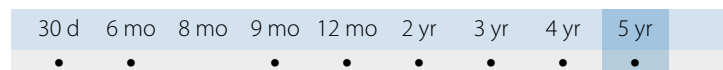
Reference vessel diameter: 2.5–3.5 mm

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



FOLLOW-UP/MACE ASSESSMENT

ANGIO/IVUS FOLLOW-UP

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)

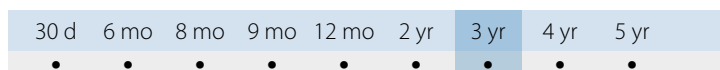
Reference vessel diameter: 2.5–3.5 mm

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



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

	Endeavor	Taxus	p-Value
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

	Endeavor	Taxus	p-Value
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

	Endeavor	Taxus	p-Value
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.

	Endeavor	Taxus	p-Value
Diabetics			
	n = 224	n = 218	
Clinical Follow-Up (36 mo)			
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)

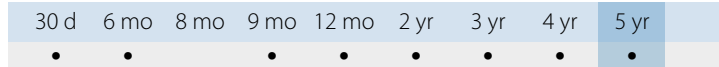
Sample size: 2728 patients

Endeavor stent: n = 2132

Control Driver/Integrity† stent: n = 596

Single *de novo* native coronary artery lesions (Type A–C)

Principal investigator: Laura Mauri, MD



FOLLOW-UP/MACE ASSESSMENT

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

	Endeavor	Driver/ Integrity†
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/ Integrity† 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)

Stent Thrombosis Clinical Follow-Up at 1 Yr[§]	ARC Def/Prob (%)
On DAPT	
at 30 days	0.3 (n = 2007)
at 6 mo	0.3 (n = 1499)
at 12 mo	0.4 (n = 790)
Off DAPT	
at 30 days	0 (n = 1544)
at 6 mo	0.4 (n = 469)
at 12 mo	0.2 (n = 1246)

Important Safety Subsets*

Diabetics	Endeavor	Driver/ Integrity†	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

† All studies were conducted with the Driver stent.

‡ Driver/Integrity 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.

Prospective, nonrandomized, multicenter, single-arm trial

Trial size: 99 patients (99 actual)

Single *de novo* native coronary artery lesions (Type A–C)

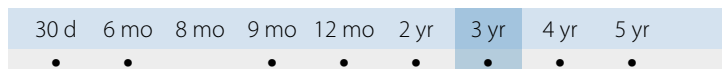
Reference vessel diameter: 2.25–3.5 mm

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



FOLLOW-UP/MACE ASSESSMENT

ANGIO/IVUS FOLLOW-UP: n = 99

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, multicentre 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

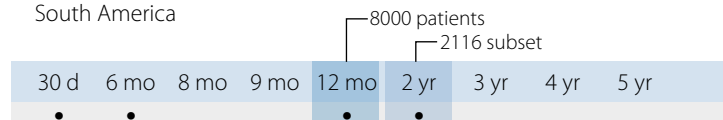
Stent sizes: 2.25–4.0 mm x 8/9–30 mm

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 \pm 11.06	62.1 \pm 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 \pm 0.47
Average lesion length (mm)	18.51 \pm 10.61

Procedure Characteristics	n = 10,339 Lesions
Total stent length (mm)	23.48 \pm 12.21
Stent:lesion length (mm)	1.36 \pm 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	0.1
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)[†]

Stent Thrombosis Clinical Follow-Up at 1 Yr	ARC Def/Prob (%)
On DAPT	
at 30 days	0.4 (n = 6661)
at 6 mo	0.3 (n = 6325)
at 12 mo	0.2 (n = 4870)
Off DAPT	
at 30 days	0.3 (n = 1554)
at 6 mo	0.5 (n = 1863)
at 12 mo	0.2 (n = 2314)

Diabetics Clinical Follow-Up	30 days n = 3586	12 mo n = 3402
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 (RVD ≤ 2.75 mm) Clinical Follow-Up	30 days n = 3586	12 mo n = 3402
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 Vessels (>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

[†]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. 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 RVD < 2.25 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.

Prospective, randomized, multicenter, open-label trial

Trial size: 8800 patients (8749 actual; enrollment completed

December 2008)

Endeavor stent: n = 4400 patients

Cypher stent: n = 4400 patients

All-comers, single and multiple coronary artery lesions; no limitations on number of lesions/vessels

Principal investigators: **Edoardo Camenzind, MD (Switzerland)**

Prof. Philippe Gabriel Steg (France)

William Wijns, MD, PhD (Belgium)

196 sites: worldwide

**FOLLOW-UP**

Primary endpoint: composite of ARC definite/probable stent thrombosis at 3 years

Secondary endpoints: total death/large MI, total death/nonfatal MI, cardiac death/large MI, cardiac death/nonfatal MI at 3 years

Open label: antiplatelet therapy for 3–12 months

Patient Demographics and Lesion Characteristics (%)		n = 8749
Age (yr)		62.2 ±10.6
Male gender (%)		76.3
BMI (kg/M ²)		27.8 ±4.5
Diabetes mellitus (%)		27.7
IDDM		6.9
Hypertension		63.8
Hyperlipidemia		62.2
Current smoker		25.0
Premature CAD in 1° relative		34.4
Prior MI		20.5
Prior PCI		12.5
Prior CABG		4.8
Silent ischemia		6.4
Stable angina		48.8
Unstable angina		18.8
Recent MI		25.9
Acute MI (within 72 hr)		14.4
B2/C lesions (%)		54.8
Lesion location: LAD (%)		46.6

Lesion Characteristics (%)		n = 8749
Left anterior descending		46.6
Left circumflex		22.7
Right coronary artery		29.6
Left main		0.8
Bypass graft		0.3
<i>De novo</i>		98.2
B2/C2 lesions		54.8
In-stent restenosis		1.0
TIMI flow 2–3		85.0
Chronic total occlusion		2.8
Bifurcation		16.4
Thrombus		7.8
Complex patients		78.3

Procedure Characteristics	n = 8749 12,328 Lesions
Multiple vessels treated (%)	18.9
Multiple lesions treated (%)	30.2
No lesions treated (%)	0.8
Prestent balloon dilatation (%)	68.5
Lesions treated per patient (%)	1.39 ±0.71
No. of stents per patient (%)	1.61 ±0.98
No. of stents per lesion (%)	1.14 ±0.47
RVD (mm)	3.0 ±0.5
MLD (mm)	0.5 ±0.4
Preprocedure diameter stenosis (%)	82.8 ±12.9
Lesion length (mm)	17.7 ±9.2
Postprocedure diameter stenosis (%)	2.1 ±9.7

Prospective, nonrandomized, multicenter registry

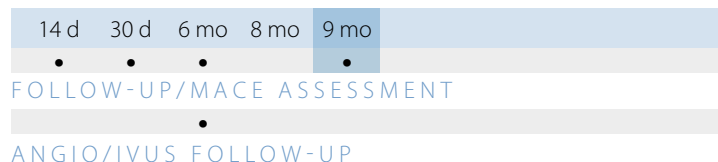
Trial size: 298 patients (298 actual)

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



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

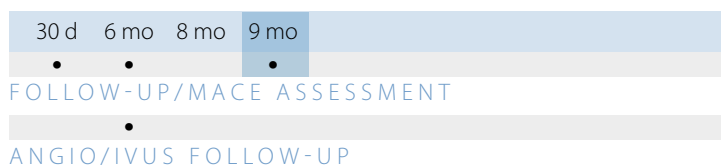
Trial size: 135 patients (135 actual, one nonevaluable)

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



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 $\geq 50\%$ 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 $\geq 70\%$ (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

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

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), 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.

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.

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Integrity Indications for Use

The Integrity 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 2.25–4.0 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 or proper placement of a stent or stent delivery system

Warnings/Precautions

- The long-term effects of stents and the risks associated with lifelong carrying of these implants are unknown. This lack of knowledge should be considered in making a risk/benefit assessment for the patient prior to implantation.
- The Integrity Coronary Stent Systems are provided sterile, for one procedure only. Do not resterilize. Use by the "Use by" date noted on the package.
 - Only physicians who have received appropriate training should perform implantation of the stent. Use of an Integrity Coronary Stent System requires advanced coronary angioplasty technical skills. The instructions will give technical guidance, but do not obviate the need for formal training in the use of the device.
 - Patients allergic to cobalt alloy may suffer an allergic reaction to this implant.
 - Do not remove the stent from the stent delivery system; the stent cannot be removed and placed on another balloon catheter for deployment.
 - Do not try to straighten a kinked shaft or hypotube. Straightening a kinked metal shaft may result in breakage of the shaft. If the device is kinked, it should not be used.
 - Significant amounts of air in the balloon may cause uneven expansion of the stent and difficulty in deployment of the stent. Do not pre-inflate balloon prior to stent deployment. Use balloon preparation technique described within this instructional material.
 - The Integrity Coronary Stent Systems do not provide for distal dye injections or pressure measurements through the guidewire lumen.
 - Expansion of the stent should not be undertaken if the stent is not appropriately positioned in the vessel. If the position of the stent is not optimal, it should not be expanded.
 - Incomplete deployment of the stent (i.e., stent not fully expanded) may cause procedural complications resulting in patient injury.
 - Advancement of an Integrity Coronary Stent System through a previously stented segment may cause procedural complications resulting in patient injury.
 - Placement of the stent has the potential to compromise sidebranch patency.
 - Administer appropriate anticoagulant/antiplatelet and coronary artery vasodilator therapy according to current medical guidelines and manufacturer's instructions.

- Caution must be taken when using ancillary equipment, such as intravascular ultrasound catheters, to avoid dislodgement or deformation of the stent.
- 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 cobalt alloy stent (Medtronic Integrity Coronary Stent) in combination with a stainless steel alloy stent (Boston Scientific Liberté® Coronary Stent) do not suggest an increased risk of *in vivo* corrosion.
- When using two wires, care should be taken when introducing, torquing and removing one or both guidewires to avoid entanglement. It is recommended that one guidewire be completely withdrawn from the patient before removing any additional equipment.
- Stent placement should only be performed at hospitals where emergency coronary artery bypass graft surgery can be readily performed.
- Judicious selection of patient 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.
- 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.

Potential Adverse Events

The following complications may be associated with the use of coronary stenting devices or PTCA:

- Acute myocardial infarction
- Allergic reaction to contrast medium/stent material/medications
- Arrhythmias (including ventricular fibrillation and ventricular tachycardia)
- Arteriovenous fistula
- Bleeding complications
- Cardiac tamponade
- Cerebrovascular accident/stroke
- Death
- Dissection of coronary artery
- Drug reactions
- Embolization (air, stent, tissue or thrombotic)
- Emergency coronary artery bypass graft surgery (CABG)
- Endocarditis
- Failure to deliver the stent
- Stent deformation, collapse or fracture
- Hematoma
- Hemorrhage requiring transfusion
- Injury of the coronary artery
- Myocardial ischemia/infarction
- Pain and tenderness at the insertion site
- Perforation
- Peripheral Ischemia
- Peripheral nerve injury
- Pseudoaneurysm (coronary/femoral/radial)
- Pyrogenic reaction
- Restenosis of the dilated artery or stented segment
- Sepsis/infection
- Short-term hemodynamic deterioration (hypotension/hypertension)
- Stent thrombosis or occlusion
- Total occlusion of coronary artery
- Unstable angina
- Vascular thrombosis
- Vessel dissection/perforation/spasm

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

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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.

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