

Medical Treatment after Endovascular Therapy (Focus on STOP-IC Study)

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Disclosure Statement of Financial Interest

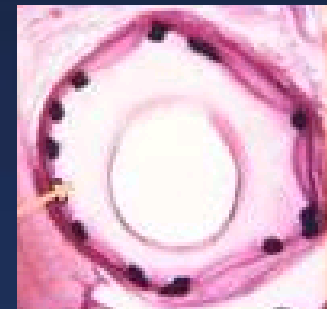
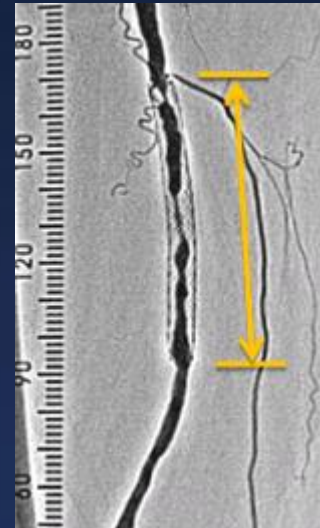
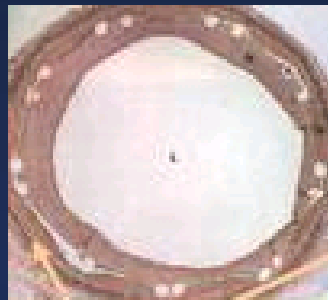
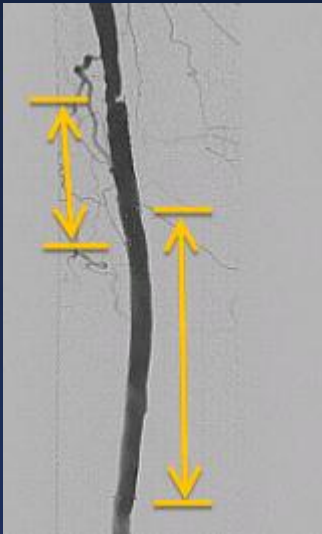
- I, (Hiroyoshi Yokoi) DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation



Background

- Although endovascular treatment (EVT) of femoropopliteal (FP) lesions is associated with a >95% initial technical success rate and low procedural mortality, late clinical failure, especially angiographic restenosis, remains a critically important concern with high restenosis rate.

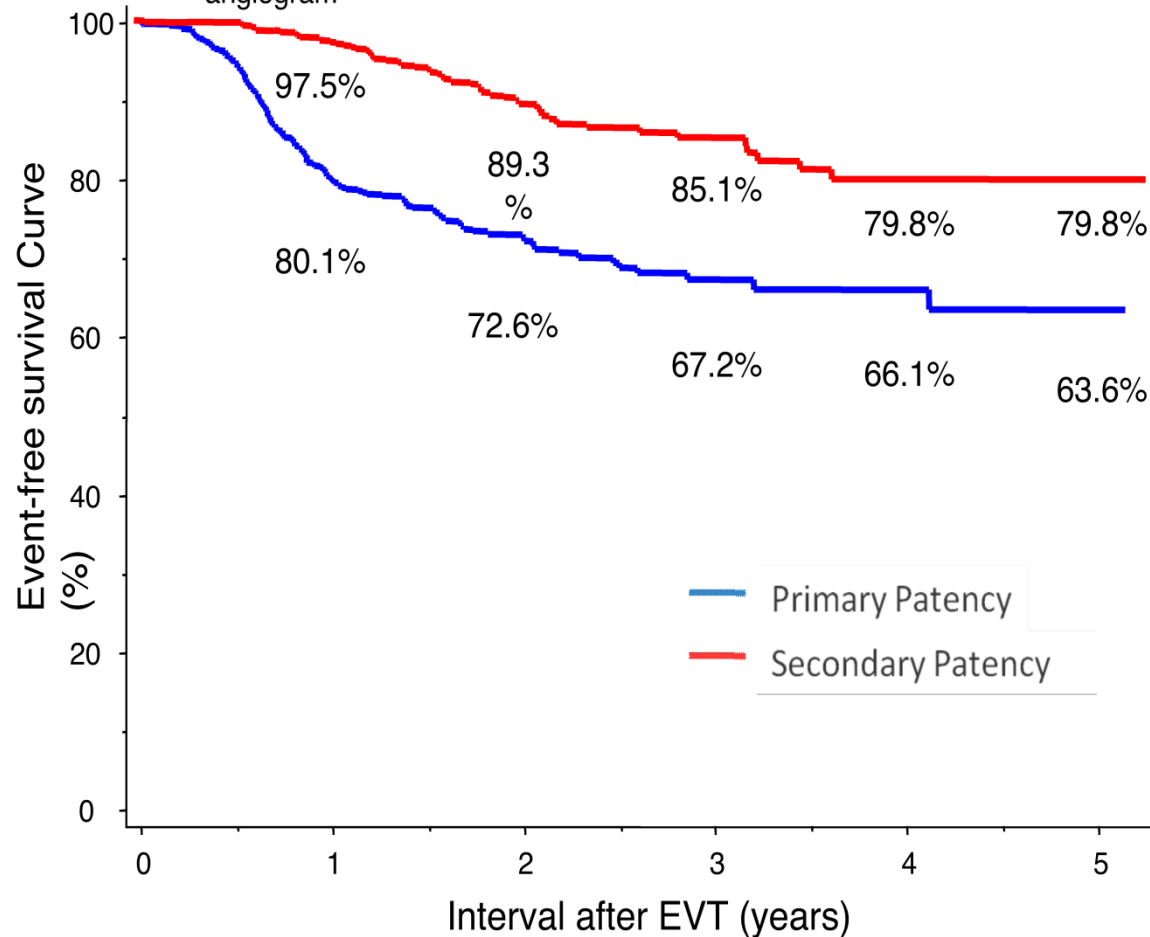
TASC II



Mid-Term Clinical Outcome and Predictors of Vessel Patency after Femoropopliteal stenting with Self-Expanding Nitinol Stent (n=511)

Primary Patency and Secondary Patency Rate after Femoropopliteal Stenting

Primary patency : PSVR > 2.4 by duplex or >50% stenosis by angiogram



Multivariate Analysis of predictors for Stent Restenosis in patients with SFA disease

Variables	HR	95% CI	P value
Female	1.82	1.33 – 2.49	0.0002
ABI<0.6	1.71	1.25 – 2.31	0.0007
TASC-II C/D	1.98	1.38 – 2.85	0.0002
Stent Fracture	2.20	1.41 – 3.43	0.0005
Cilostazol (-)	1.87	1.37 – 2.54	<0.0001

Multifaceted Effects of Cilostazol

Reduced Restenosis after implantation of coronary artery stents
(Circulation, Nov 2005; 112: 2826 - 2832.)

Antiplatelet activity

Cilostazol

In vitro inhibition of vascular smooth muscle cells

Antithrombotic activity

Decreases triglycerides

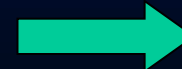
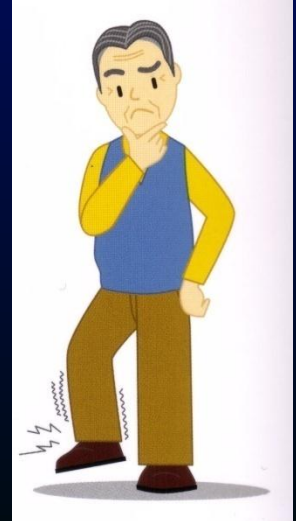
Mildly increases heart rate

Increases HDL-C

Produces vasodilation

Increases blood flow

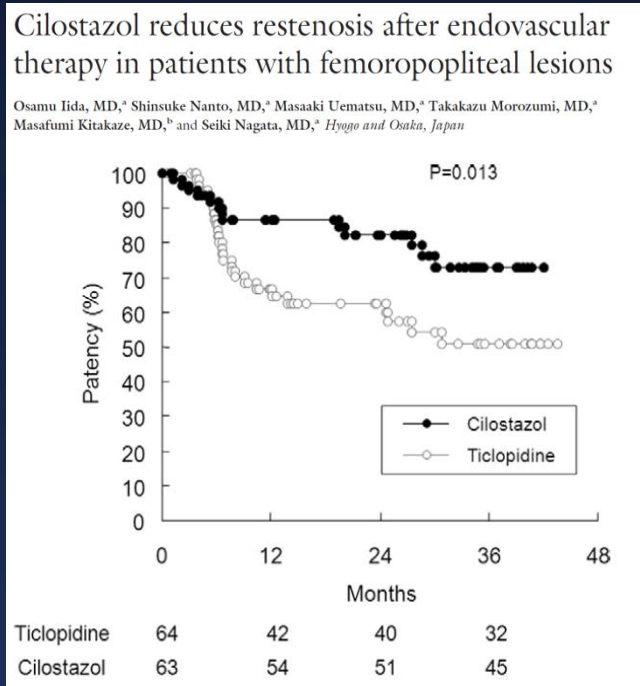
Improved of symptoms and walking distance (Circulation.1998;98:678-68)



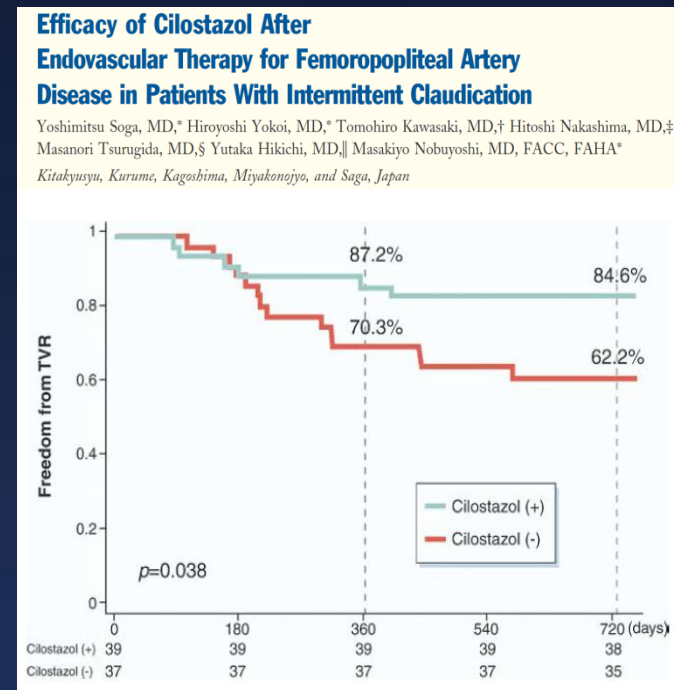


Background

Recently, cilostazol therapy after EVT for FP lesions has been shown to improve clinical outcome. However, it is unknown whether it reduces angiographic restenosis after EVT.



J Vasc Surg. 2008;48:144-9.



J Am Coll Cardiol. 2009;53:48-53.



**STOP
IC**

**Sufficient Treatment Of
Peripheral Intervention by Cilostazol**

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Hiroyoshi Yokoi

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and

STOP-IC Investigators



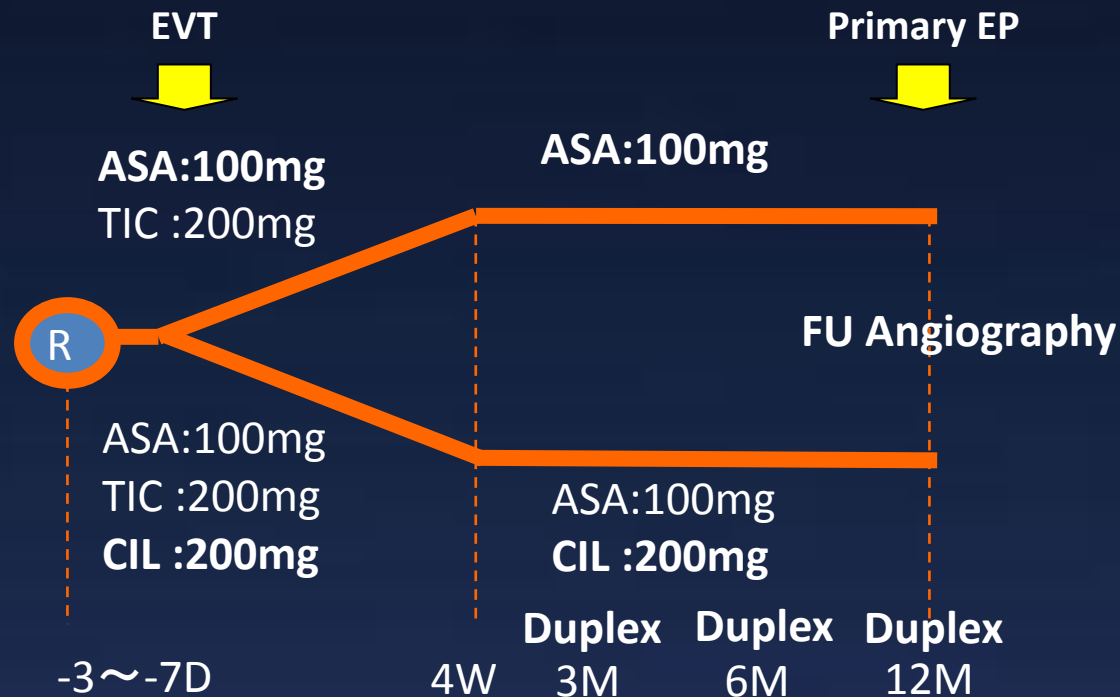
Objective

To investigate whether cilostazol reduces the binary restenosis after EVT for *de novo* FP lesions by angiographic follow-up



Methods

Study Design: Prospective, multicenter (17 cardiovascular centers), open-label trial



Duration of patients entry

2009/1 ~ 2011/6

R:Randomization

ASA: aspirin

TIC: ticlopidine

CIL: cilostazol

Participants Centers of STOP-IC



Kansai Rosai HP 69



Omihachiman Com. Med. Center 6



Tokeidai Memorial HP 5



Hyogo College of Med. HP 8



Kishiwada Tokushukai HP 19



Sendai Kousei HP 21



Kokura Memorial HP 56



Shinonoi General HP 1



Kikuna Memorial HP 4



Shin Koga HP 5



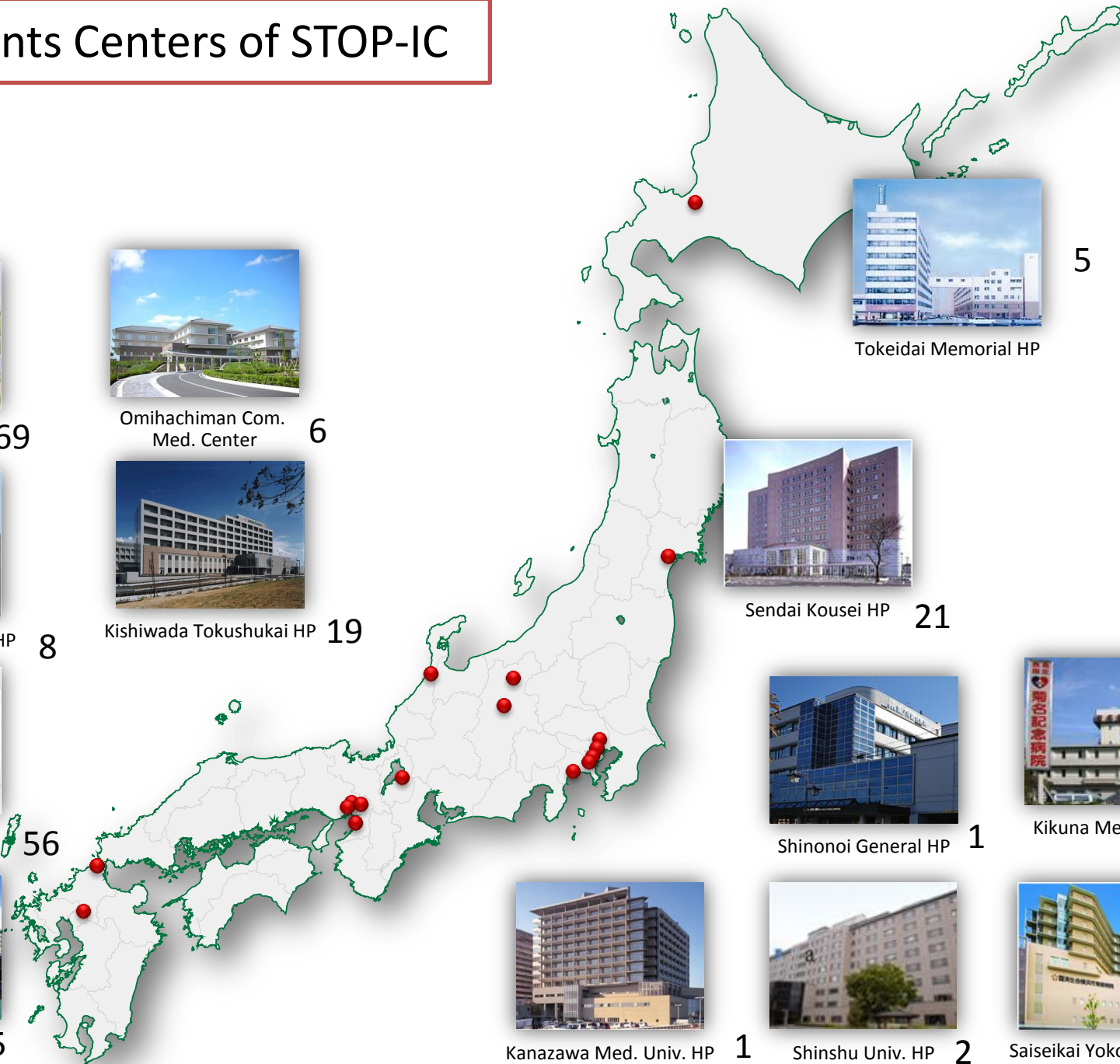
Kanazawa Med. Univ. HP 1



Shinshu Univ. HP 2



Saiseikai Yokohama-city Eastern HP 3





Methods

- Inclusion criteria
 - Written informed consent.
 - Symptomatic leg ischemia defined as Rutherford classification 2-4 patients with femoro-Popliteal *de novo* lesion presenting > 50% stenosis
Available for angiographic follow-up at 12 months
- Exclusion criteria
 - life expectancy of less than 2 year
 - Symptom due to acute onset leg ischemia.

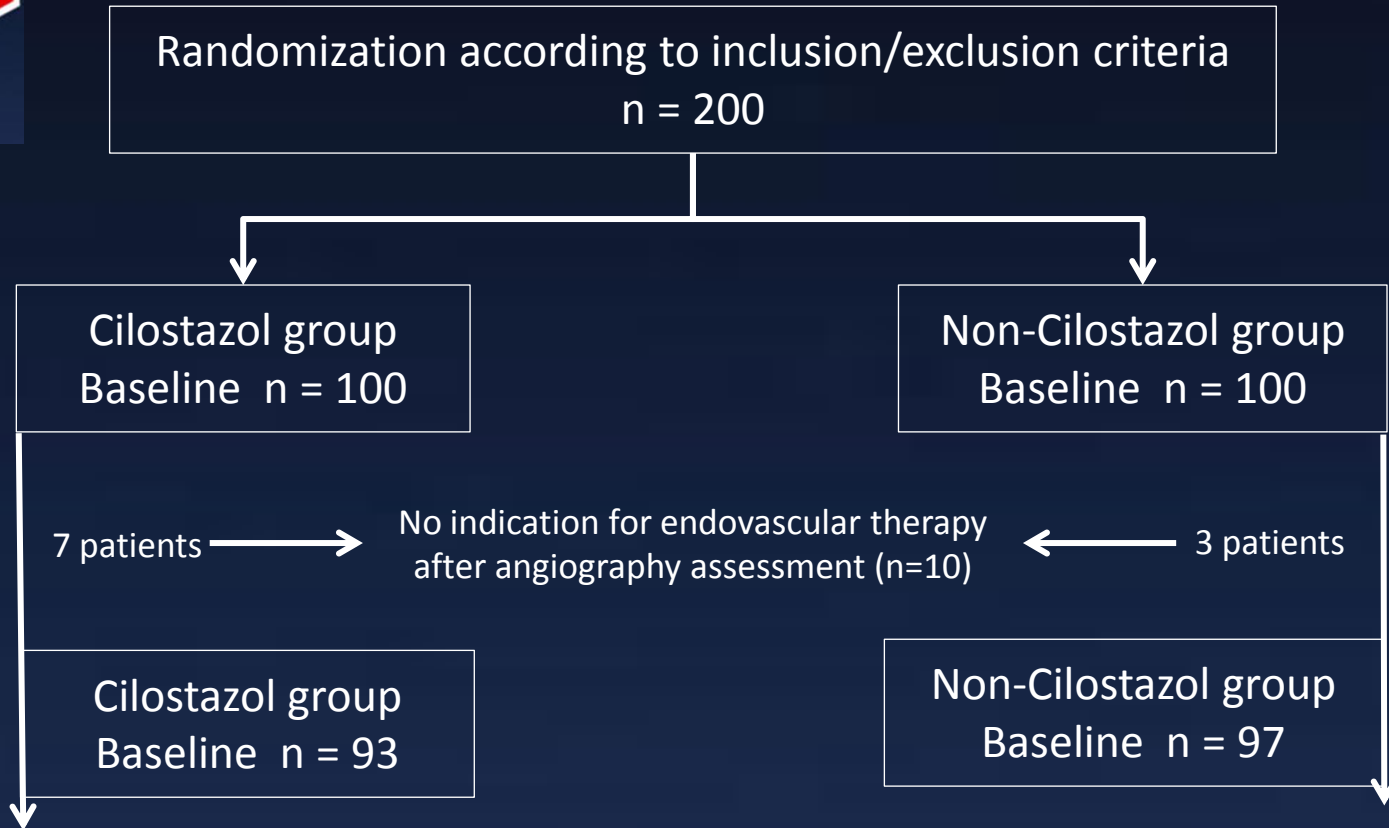


Methods

- Primary endpoint
 - 12 months angiographic restenosis rate
(Defined as %DS>50%) evaluated by independent Core Laboratory
- Secondary endpoint
 - 12 months restenosis rate assessed by angiographic or duplex (PSVR<2.5)
 - Target lesion revascularization (TLR)
 - Incidence of death, major amputation and surgical conversion



12 months Angiography follow-up chart





Baseline Patient Characteristics

	Cilostazol group N=93	Non-Cilostazol group N=97	All N=190	P value
Age-yrs	72±9	73±8	72±9	0.5
Male gender-no. (%)	69% (64)	68.0% (66)	68.4% (130)	0.9
Body mass index	22 ± 3	22 ± 3	22 ± 3	0.8
Hypertension-no. (%)	81% (75)	81% (78)	81% (153)	0.9
Dislipidemia-no. (%)	43% (40)	51% (49)	47% (89)	0.3
Statin treatment-no. (%)	29% (27)	40% (39)	35% (66)	0.1
Diabetes mellitus-no. (%)	57% (53)	55% (53)	56% (106)	0.7
Glycosylated hemoglobin at baseline-%	6.4 ± 1.7	6.2 ± 1.1	6.3 ± 1.4	0.4
History of Smoking-no. (%)	45% (42)	48% (46)	47% (88)	0.7
End stage renal disease on dialysis-no. (%)	16% (15)	16% (15)	16% (30)	0.9
Coronary artery disease-no. (%)	38% (35)	40% (38)	39% (73)	0.8
Cerebrovascular disease-no. (%)	24% (22)	20% (19)	22% (41)	0.5
Rutherford classification-no. (%)				
2	24% (22)	29% (28)	27% (50)	0.4
3	67% (62)	58% (55)	63% (117)	
4	9% (8)	13% (12)	11% (20)	
Absolute claudication distance (ACD)	98 (50 - 133)	76 (50 - 101)	80 (50 - 115)	0.5
Baseline ankle brachial index ABPI	0.72 ± 0.16	0.66 ± 0.13	0.69 ± 0.15	0.008



Baseline Lesion Characteristics

	Cilostazol group N=93	Non-Cilostazol group N=97	All N=190	P value
TASC II classification-no. (%)				1.0
A	37% (34)	34% (32)	35% (66)	
B	21% (19)	22% (21)	21% (40)	
C	25% (23)	27% (25)	25% (48)	
D	17% (16)	17% (16)	17% (32)	
Length of target lesion-mm	130 ± 89	124 ± 82	127 ± 86	0.8
Reference vessel diameter (mm)				
Proximal	5.4 ± 1.4	5.3 ± 1.3	5.3 ± 1.4	0.9
Distal	4.9 ± 1.0	5.0 ± 1.0	4.9 ± 1.0	0.5
Degree of stenosis pre intervention(%)	82 ± 21	81 ± 20	81 ± 20	1.0
Occlusion-no of patients (%)	39% (37)	35% (33)	37% (70)	0.6
MLD pre intervention-mm	1.4	1.6	1.5	0.8
ALD pre intervention-mm	1.4	1.7	1.6	0.6
Plaque area before intervention-mm ²	63	81	70.3	0.3
Lesion calcification-%	47% (25)	51% (22)	49% (47)	0.8
Number of below the knee run-off (%)				0.4
0	4% (4)	1% (1)	3% (5)	
1	31% (28)	35% (32)	33% (60)	
2	40% (36)	35% (32)	37% (68)	
3	24% (22)	29% (27)	27% (49)	

MLD: Minimum lumen diameter, ALD: Average lumen diameter



Baseline Procedural Characteristics

	Cilostazol group N=93	Non-Cilostazol group N=97	All N=190	P value
Stent implantation-no. (%)	89% (82)	90% (85)	89% (167)	0.9
Stent length (mm)	167±94	154±86	161±90	0.8
Number of stent implantation				0.2
1	45% (37)	41% (35)	43% (72)	
2	24% (20)	37% (31)	31% (51)	
3	31% (25)	22% (19)	26% (44)	
Diameter of post dilation balloon-mm				0.1
4	18% (16)	11% (10)	14% (26)	
5	46% (42)	60% (56)	53% (98)	
6	36% (33)	29% (27)	33% (60)	
Degree of stenosis post intervention-%	20	22	21	1.0
MLD post intervention-mm	3.8	3.7	3.7	0.7
ALD post intervention-mm	11.4	11.3	11.4	0.7
SD /proximal RD ratio	1.4	1.3	1.3	0.7
SD /distal RD ratio	1.5	1.4	1.5	0.6
Procedure related complication-no. (%)	2.2% (2)	3.1% (3)	2.7% (5)	1.0
Distal embolization-no. (%)	1.6% (1)	1.6% (1)	1.6% (2)	1.0
Puncture site complication-no. (%)	1.1% (1)	2.1% (2)	1.6% (3)	1.0

MLD: Minimum lumen diameter, ALD: Average lumen diameter

Stent: SMART stent, SD: Stent diameter, RD: Reference diameter



12-month Angiography Follow-up

Randomization according to inclusion/exclusion criteria
n = 200

No indication for endovascular therapy after
angiography assessment

Cilostazol group
Baseline n = 93

Non-cilostazol group
Baseline n = 97

7 patients → Death before 12-month follow-up (n=11) ← 4 patients

- Pneumonia 2
- Sepsis 1
- Lung cancer 1
- Myocardial infarction 2
- Unknown 1

- Pneumonia 2
- Myocardial infarction 1
- Multiple organ failure 1

86 patients → Eligible 12-month FU ← 93 patients

11 patients → Lost to 12-month follow-up angiography (n=28) ← 17 patients

12-month FU
Angiography
n=75 /86 (87%)

12-month FU
Angiography
151/179 (84%)

12-month FU
Angiography
n=76/93 (82%)



Representative case

-Follow up angiogram@12 months-

Lesion background: lesion length > 15cm, CTO, DM (+)

EVT procedure: S.M.A.R.T. stent 7.0*100mm*2



Cilostazol (+)

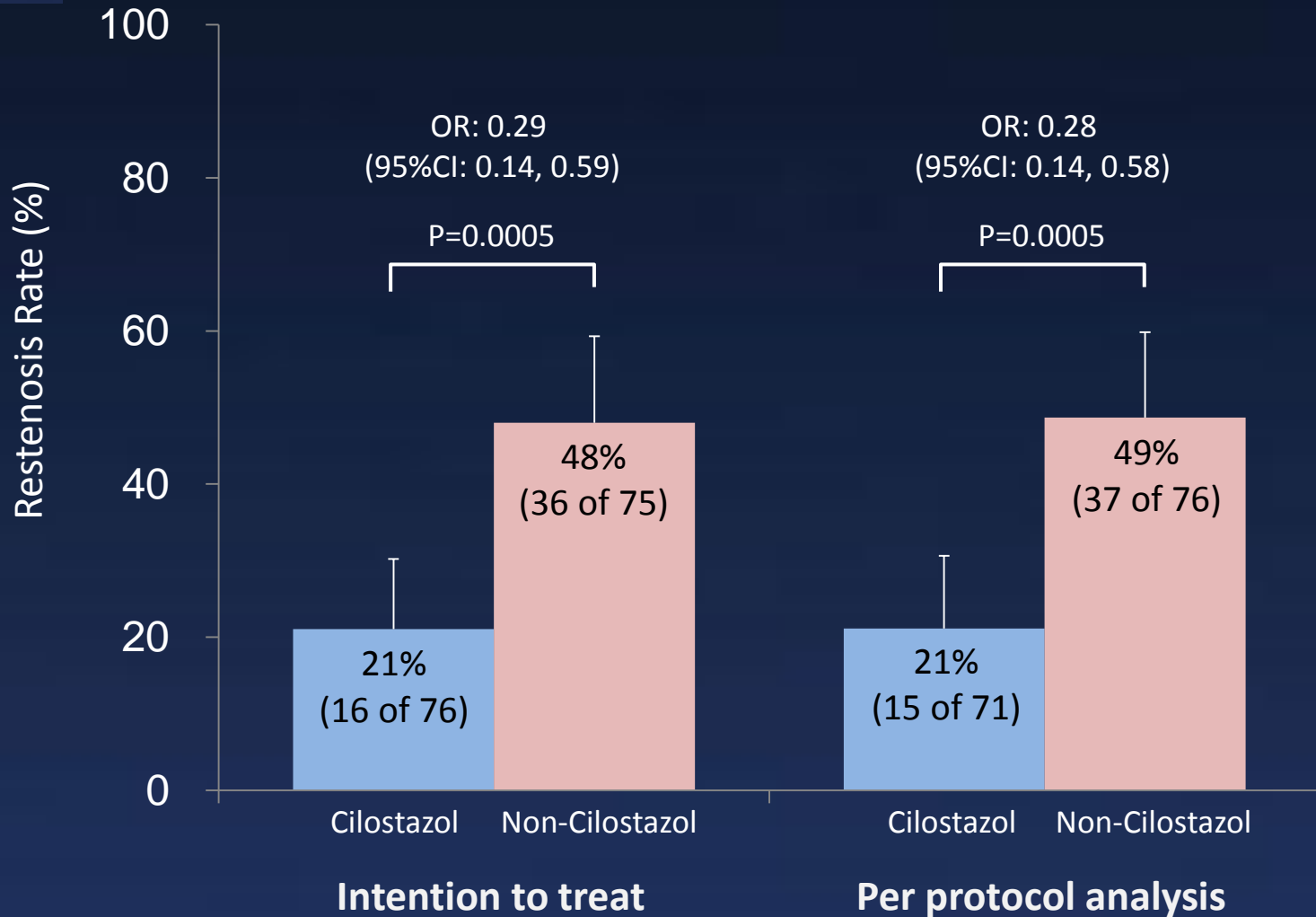


Cilostazol (-)



Results

Primary Endpoint (12 months angiographic restenosis)





12-month Angiography Follow-up

Randomization according to inclusion/exclusion criteria
n = 200

No indication for endovascular therapy after
angiography assessment

Cilostazol group
Baseline n = 93

Non-cilostazol group
Baseline n = 97

7 patients → Death before 12-month follow-up (n=11) ← 4 patients

- Pneumonia 2
- Sepsis 1
- Lung cancer 1
- Myocardial infarctio 2
- Unknown 1

- Pneumonia 2
- Myocardial infarction 1
- Multiple organ failure 1

86 patients → Eligible 12-month FU ← 93 patients

4 patients → Lost to 12-month follow-up
angiography or duplex (n=10) ← 6 patients

12-month FU
Angiography or duplex
N=82 /86 (95%)

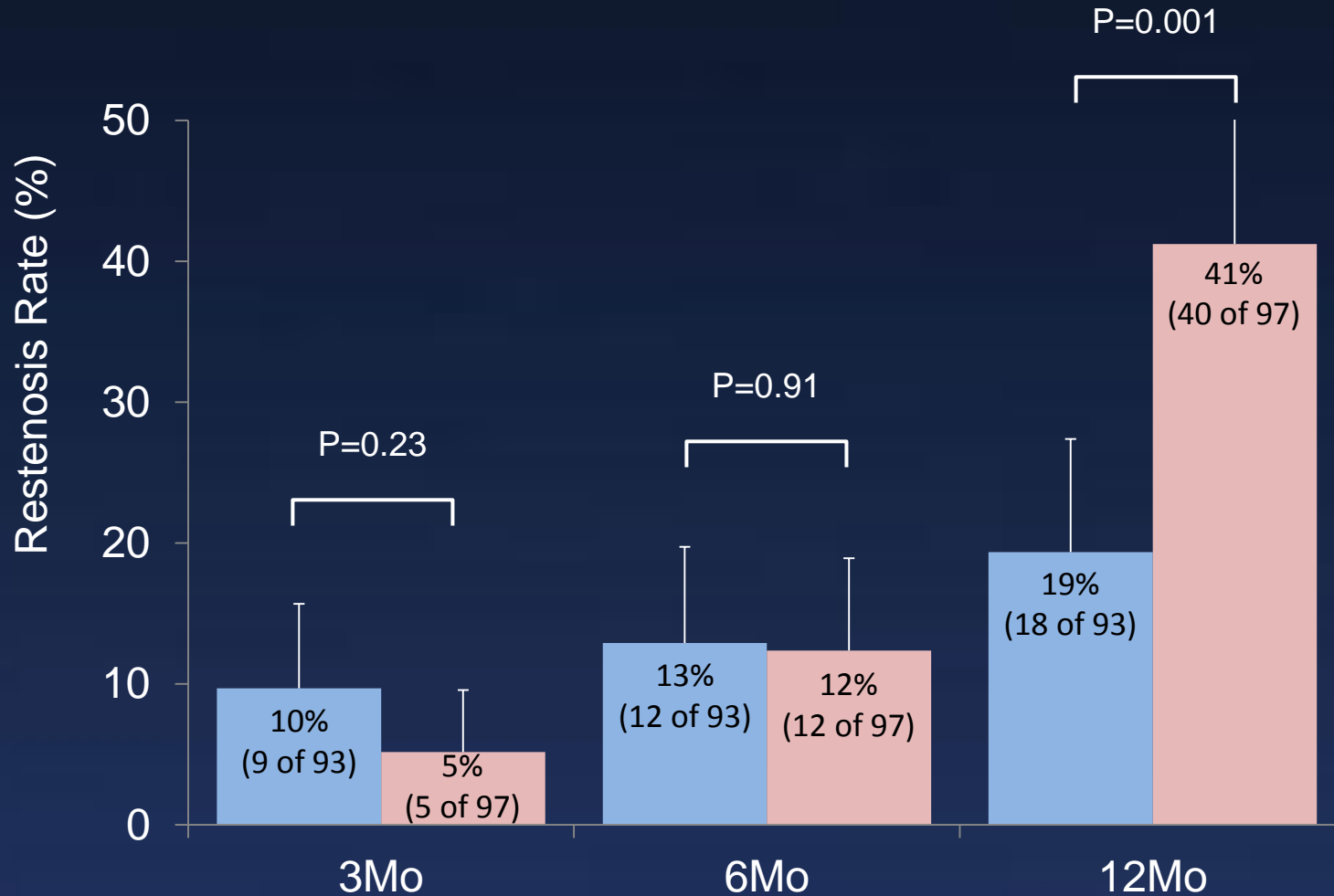
12-month FU
Angiography or duplex
169/179 (94%)

12-month FU
Angiography or duplex
N=87/93 (94%)



Results

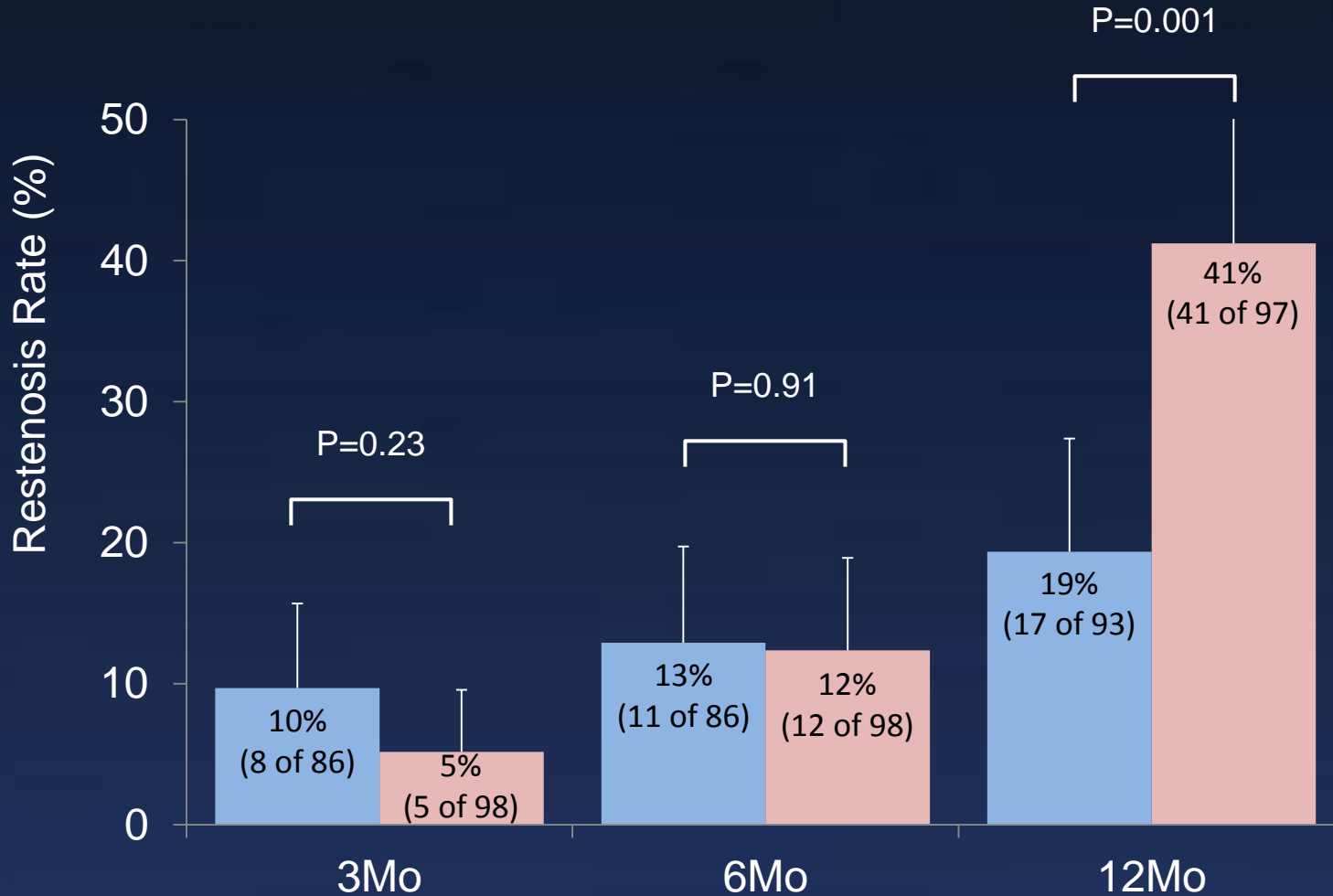
Secondary endpoint (12 months restenosis assessed by angiography or duplex, *intention to treat analysis*)





Results

Secondary endpoint (12 months restenosis assessed by angiography or duplex, *per protocol analysis*)



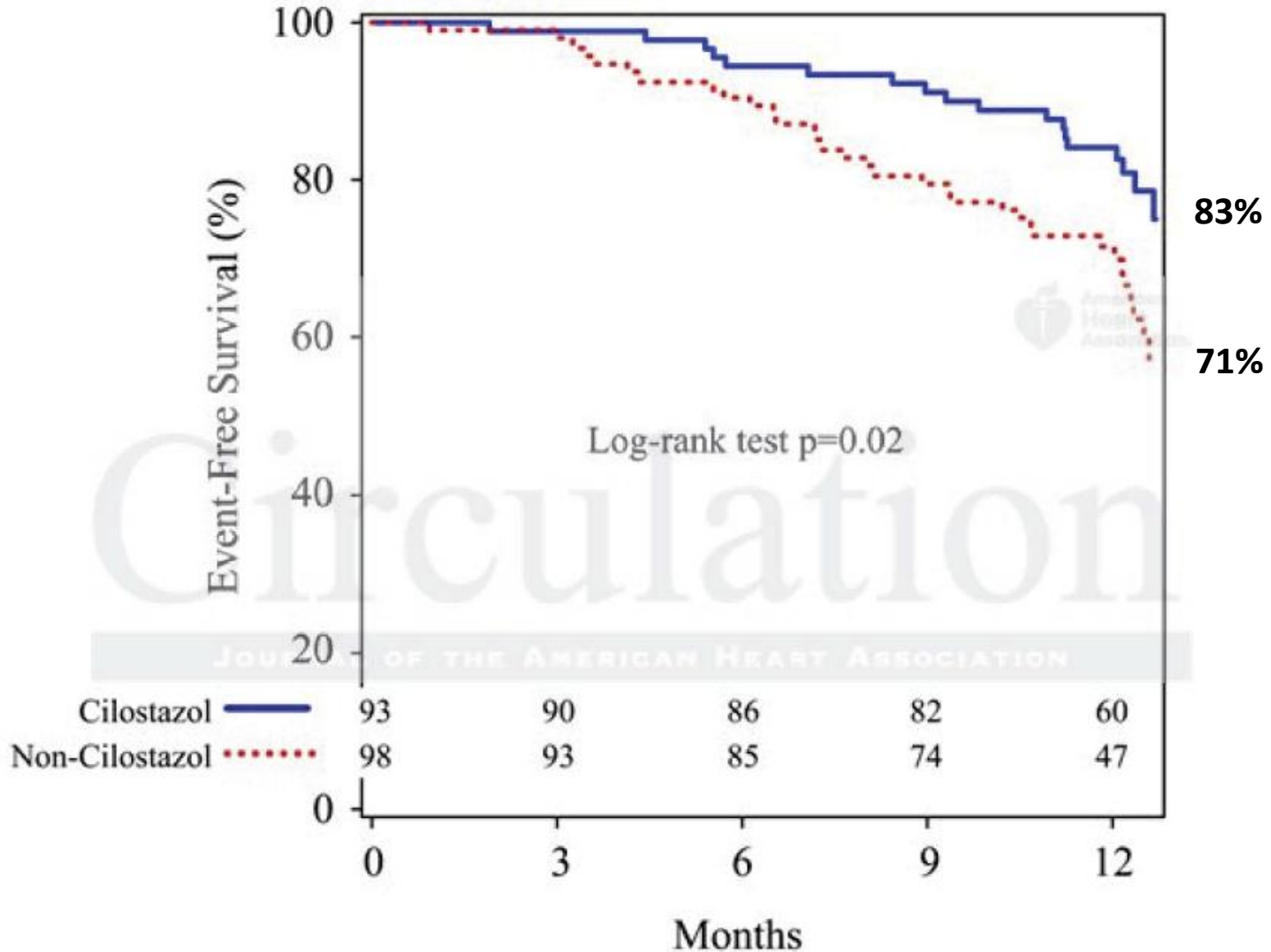


Results

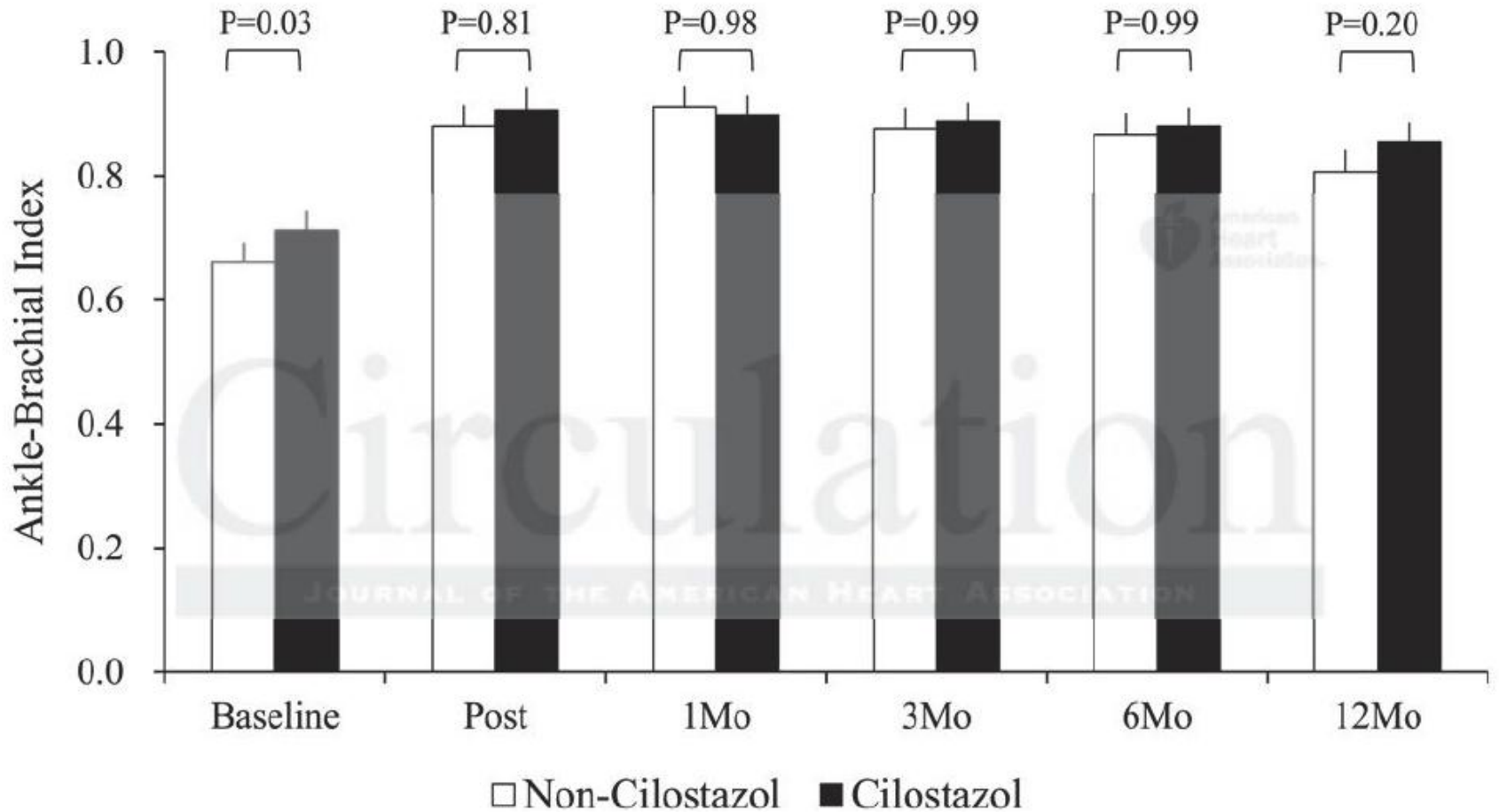
12 months FU Clinical Outcome Data

	Cilostazol group N=93	Non-Cilostazol group N=97	P value
TLR	17%	37%	0.004
Surgical bypass conversion	0%	0%	-
Stent fracture	17%	16%	0.90
Amputation	2.2% (2)	3.1% (3)	1.0
Death	4.6%	4.4%	1.0

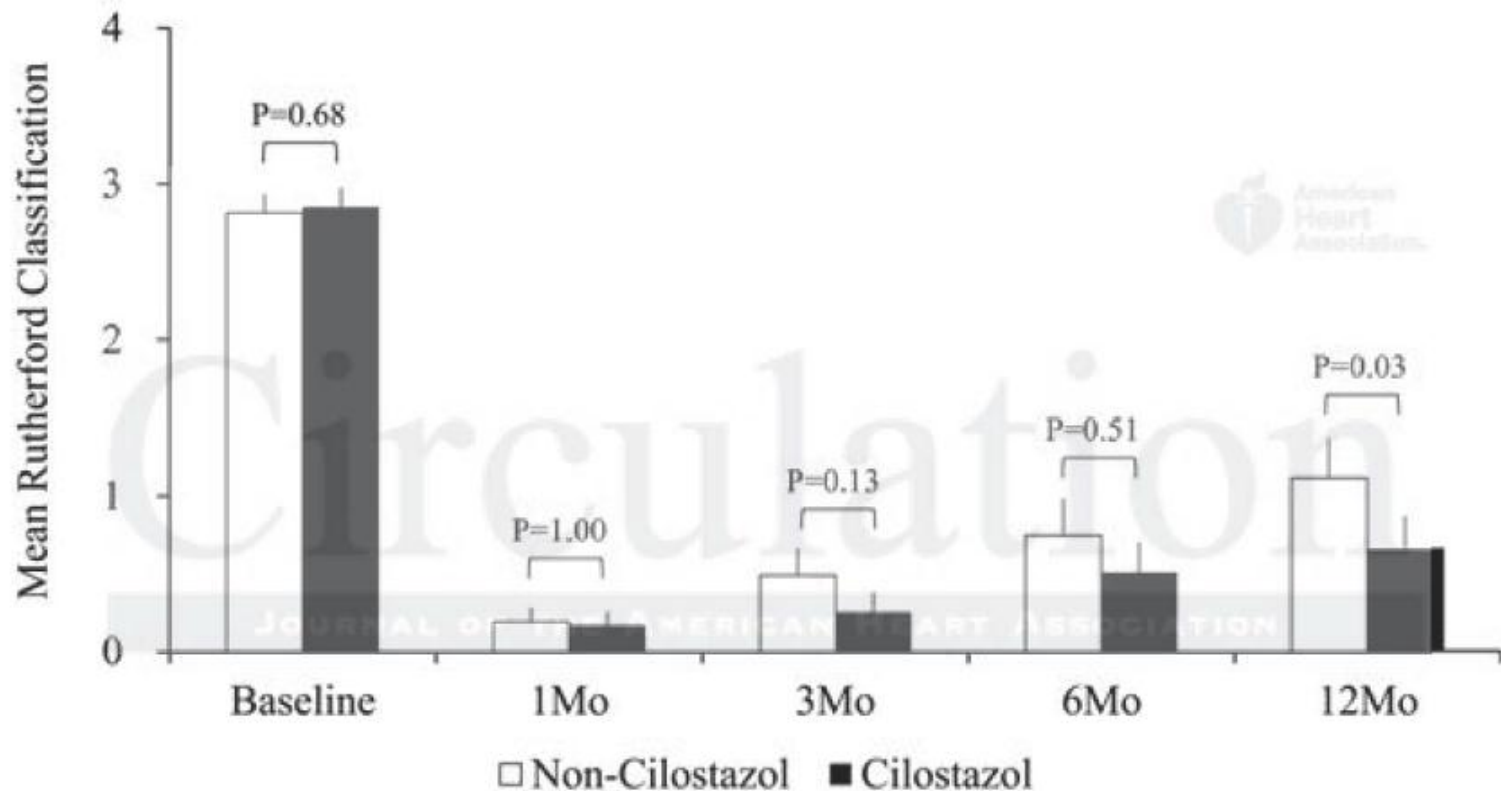
Event-free survival (ITT analysis)



Changes in ABI (ITT analysis)



Changes in Rutherford Classification (ITT analysis)





Summary

- ❑ There were no differences between the 2 groups in patient, lower limb and lesion characteristics, except for ABI before EVT.
- ❑ The number of stents implanted was similar between the two groups. The occurrence of stent fracture, as observed at follow-up, was also similar.
- ❑ 12-month angiographic restenosis rates were significantly lower in the cilostazol group.
- ❑ Target lesion revascularization was also significantly lower in the cilostazol group.

Cilostazol Reduces Angiographic Restenosis after Endovascular Therapy for Femoropopliteal Lesions in the Sufficient Treatment of Peripheral Intervention by Cilostazol (STOP-IC) Study

Osamu Iida, Hiroyoshi Yokoi, Yoshimitsu Soga, Naoto Inoue, Kenji Suzuki, Yoshiaki Yokoi, Daizo Kawasaki, Kan Zen, Kazushi Urasawa, Yoshiaki Shintani, Akira Miyamoto, Keisuke Hirano, Yusuke Miyashita, Taketsugu Tsuchiya, Norihiko Shinozaki, Masato Nakamura, Takaaki Isshiki, Toshimitsu Hamasaki and Shinsuke Nanto
on behalf of the STOP-IC investigators

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Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION



Cilostazol: The "Poor Man's" Replacement of Drug Eluting Stents and Balloons?

Thomas Zeller and Dietmar Trenk

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Conclusion

Cilostazol reduced angiographic restenosis rates after EVT for FP lesions.