Intervention with Pharamacologic Magic (STOP-IC Study)

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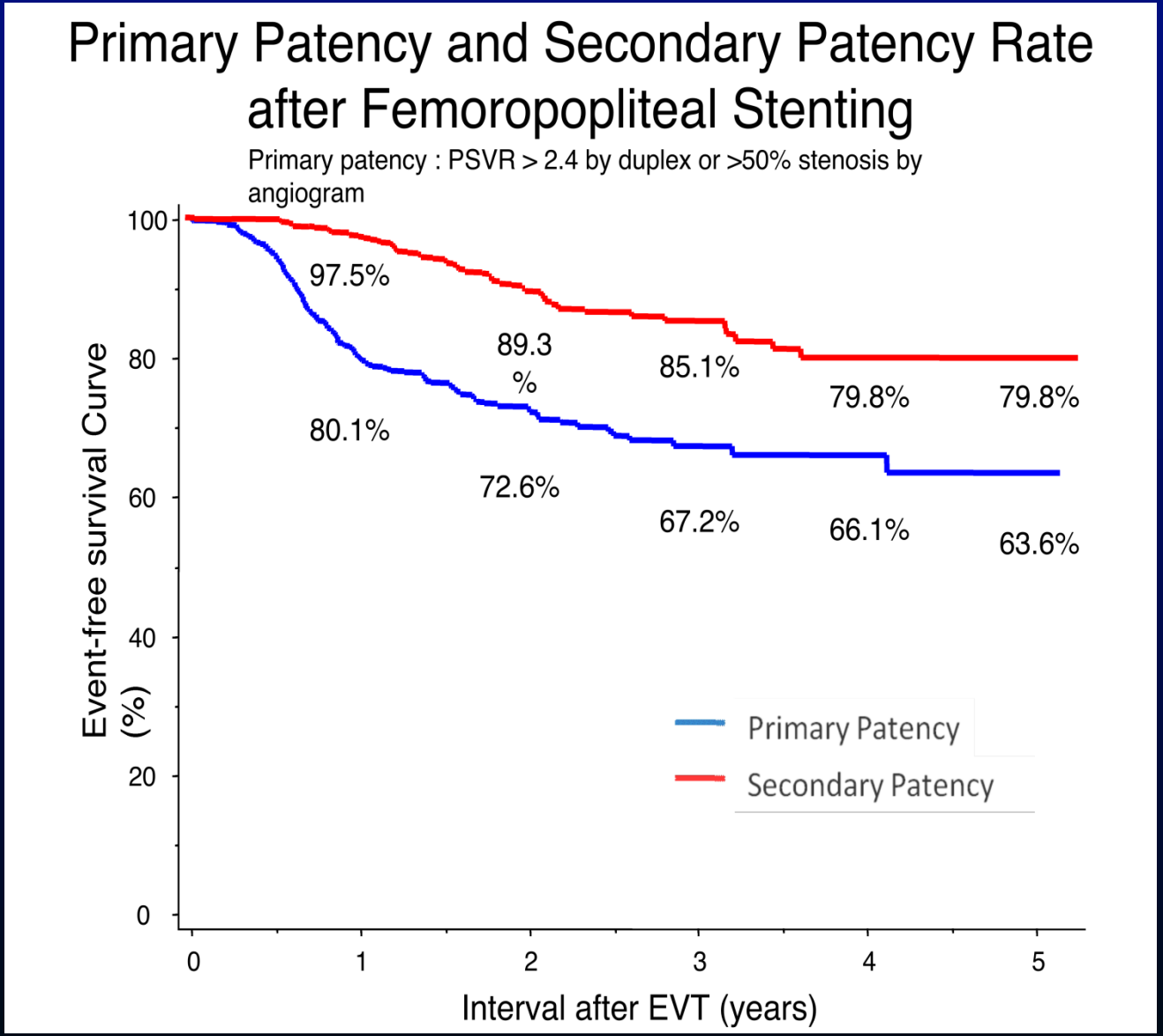
Disclosure Statement of Financial Interest

- 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

Mid-Term Clinical Outcome and Predictors of Vessel Patency after Femoropopliteal stenting with Self-Expanding Nitinol Stent (n=639)



Soga.Y . et al : **J Vasc Surg.,52:608-15,2010**

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

Soga.Y . et al : **J Vasc Surg.,52:608-15,2010**

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

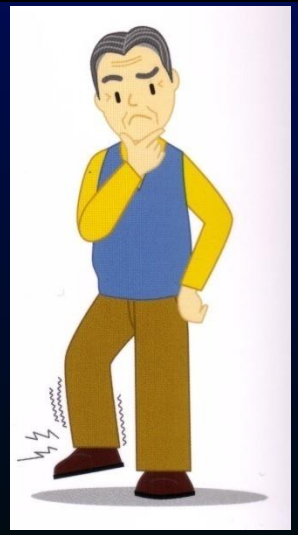
Mildly increases heart rate

Increases HDL-C

Produces vasodilation

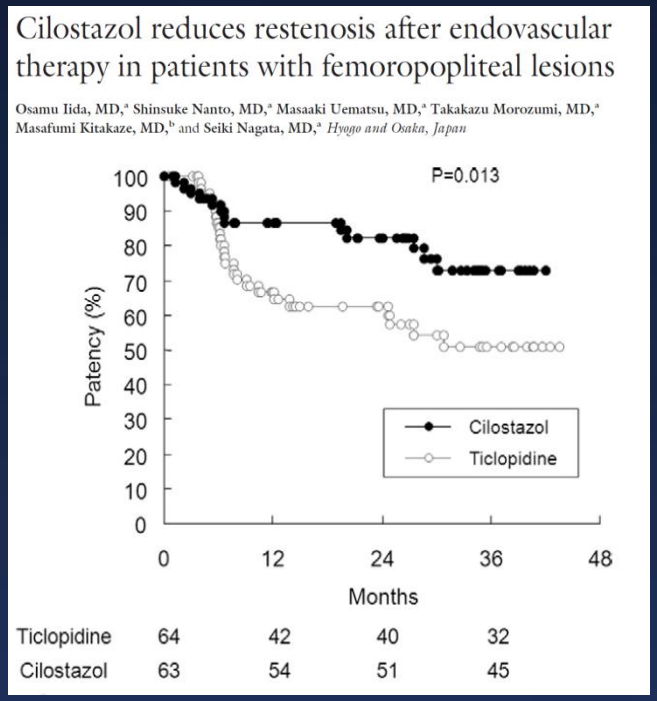
Increases blood flow

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

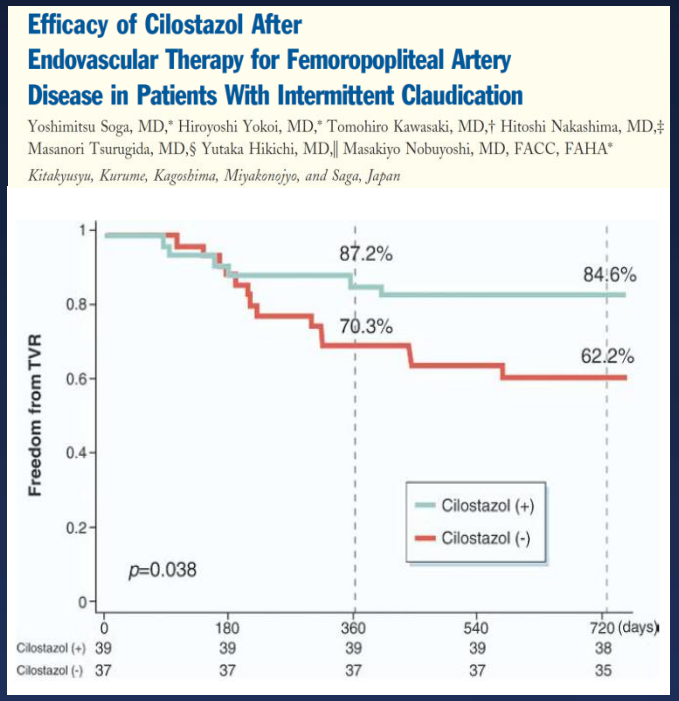


Background

- 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.

Sufficient Treatment Of Peripheral Intervention by Cilostazol

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and

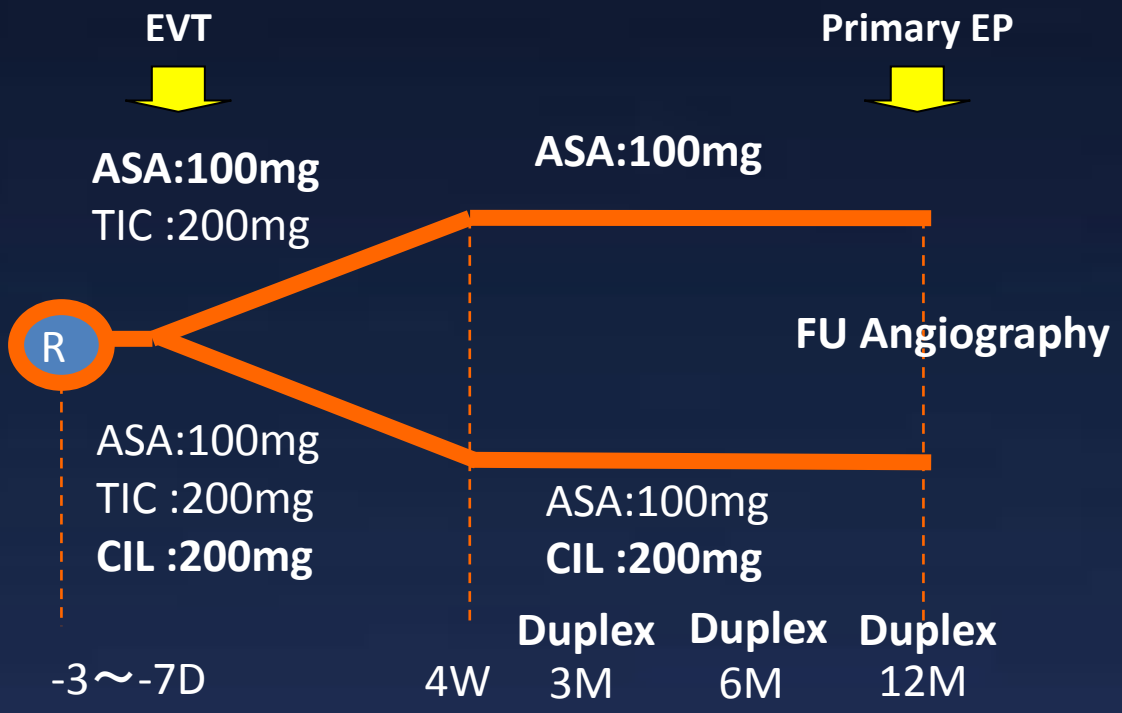
STOP-IC Invetigators

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 Labolatory
- 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

Randomization according to inclusion/exclusion criteria
n = 200

Cilostazol group
Baseline n = 100

Non-Cilostazol group
Baseline n = 100

7 patients → No indication for endovascular therapy after angiography assessment (n=10) ← 3 patients

Cilostazol group
Baseline n = 93

Non-Cilostazol group
Baseline n = 97

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% (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)	36% (66)	
B	21% (19)	22% (21)	21% (40)	
C	25% (23)	27% (25)	26% (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

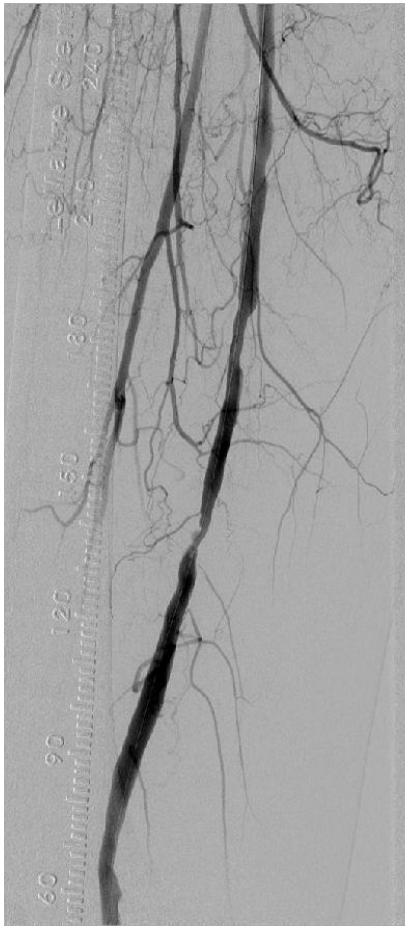
Cilostazol group	Non-cilostazol group
Baseline n = 93	Baseline n = 97
7 patients	4 patients
- Pneumonia 2 - Sepsis 1 - Lung cancer 1 - Myocardial infarction 2 - Unknown 1	- Pneumonia 2 - Myocardial infarction 1 - Multiple organ failure 1
86 patients	93 patients
11 patients	17 patients
12-month FU Angiography n=75 /86 (87%)	12-month FU Angiography n=76/93 (82%)

Death before 12-month follow-up (n=11)

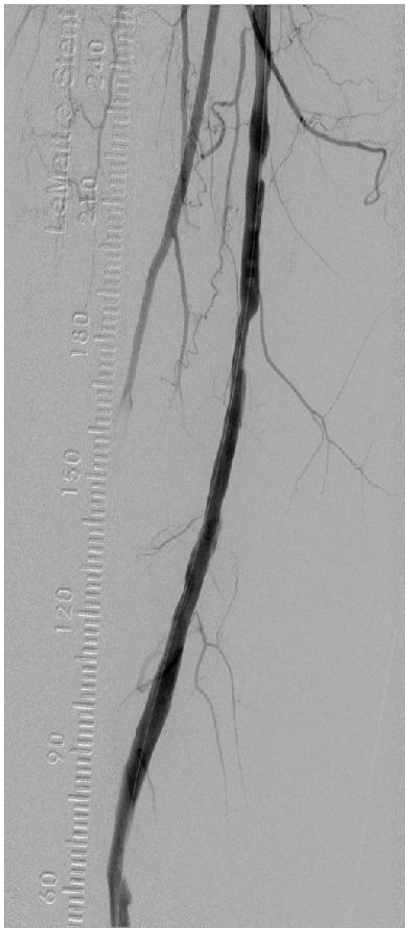
Eligible 12-montf FU

Lost to 12-month follow-up angiography (n=28)

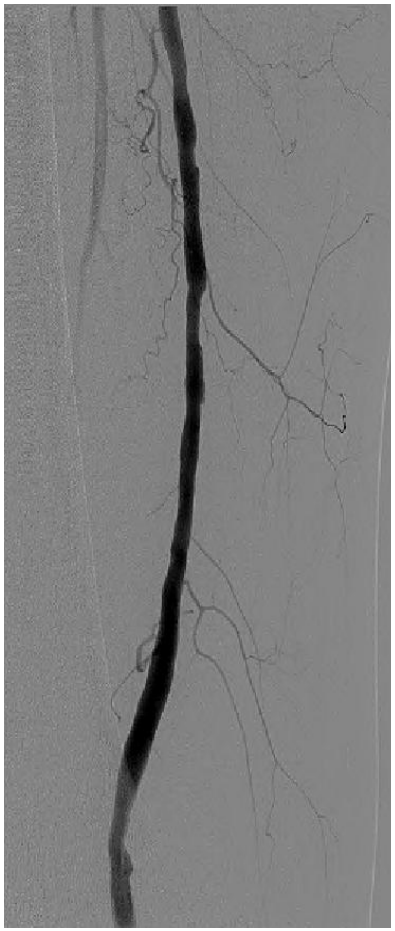
12-month FU Angiography 151/179 (84%)



Pre EVT



Post EVT



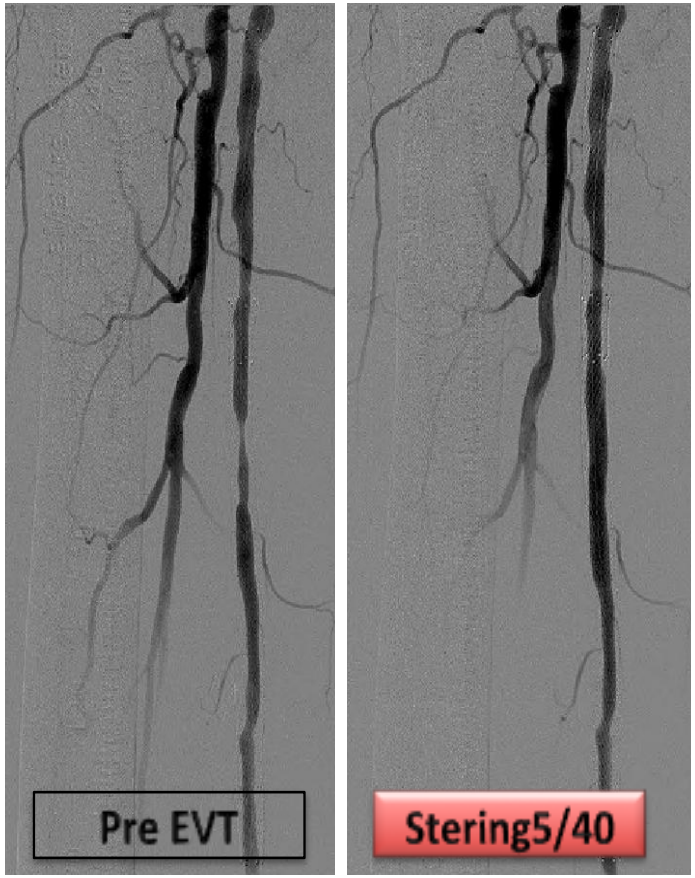
1yrs FU

2010/7/21

2011/8/2

Pre EVT | Post EVT

2010/8/19



1yrs FU | Post EVT

2011/7/14

Representative case

-Follow up angiogram@12 months-

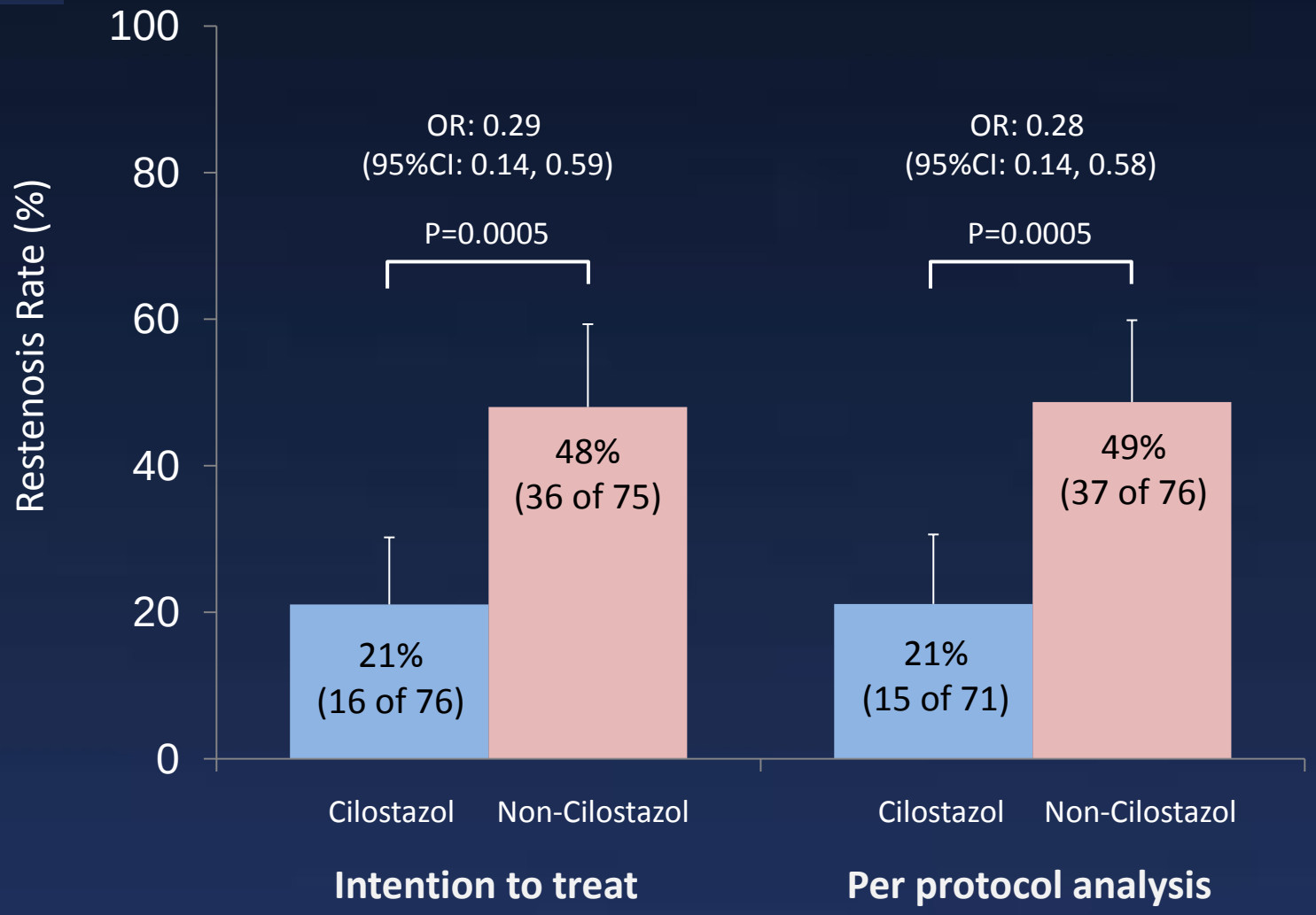
Lesion background: lesion length > 15cm, CTO, DM (+)
EVT procedure: S.M.A.R.T. stent 7.0*100mm*2

Cilostazol (+)

Cilostazol (-)

Results

Primary Endpoint (12 months angiographic restenosis)



12-month Angiography Follow-up

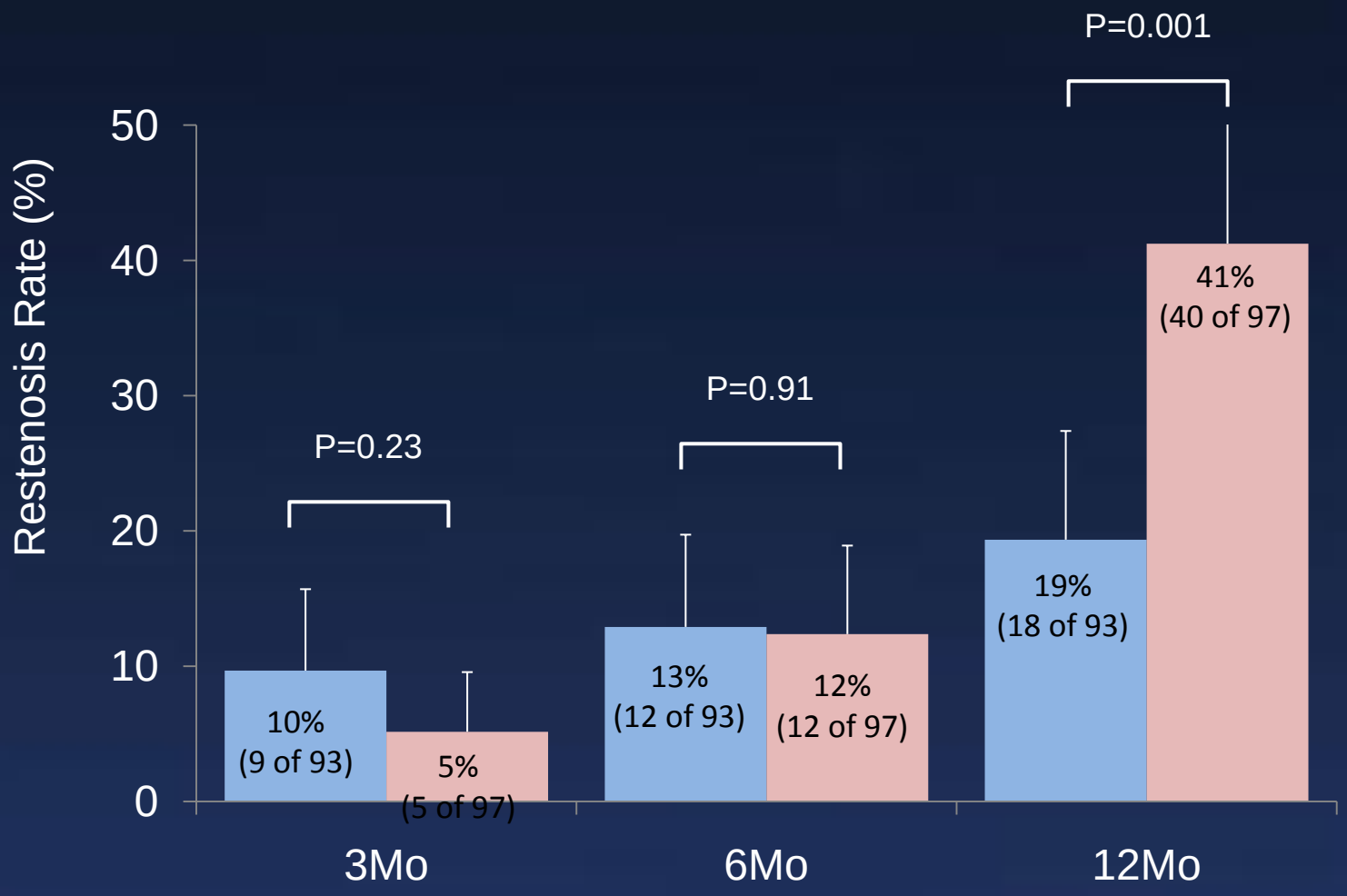
Randomization according to inclusion/exclusion criteria
n = 200

No indication for endovascular therapy after angiography assessment

Cilostazol group	Non-cilostazol group
Baseline n = 93	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-montf 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%)

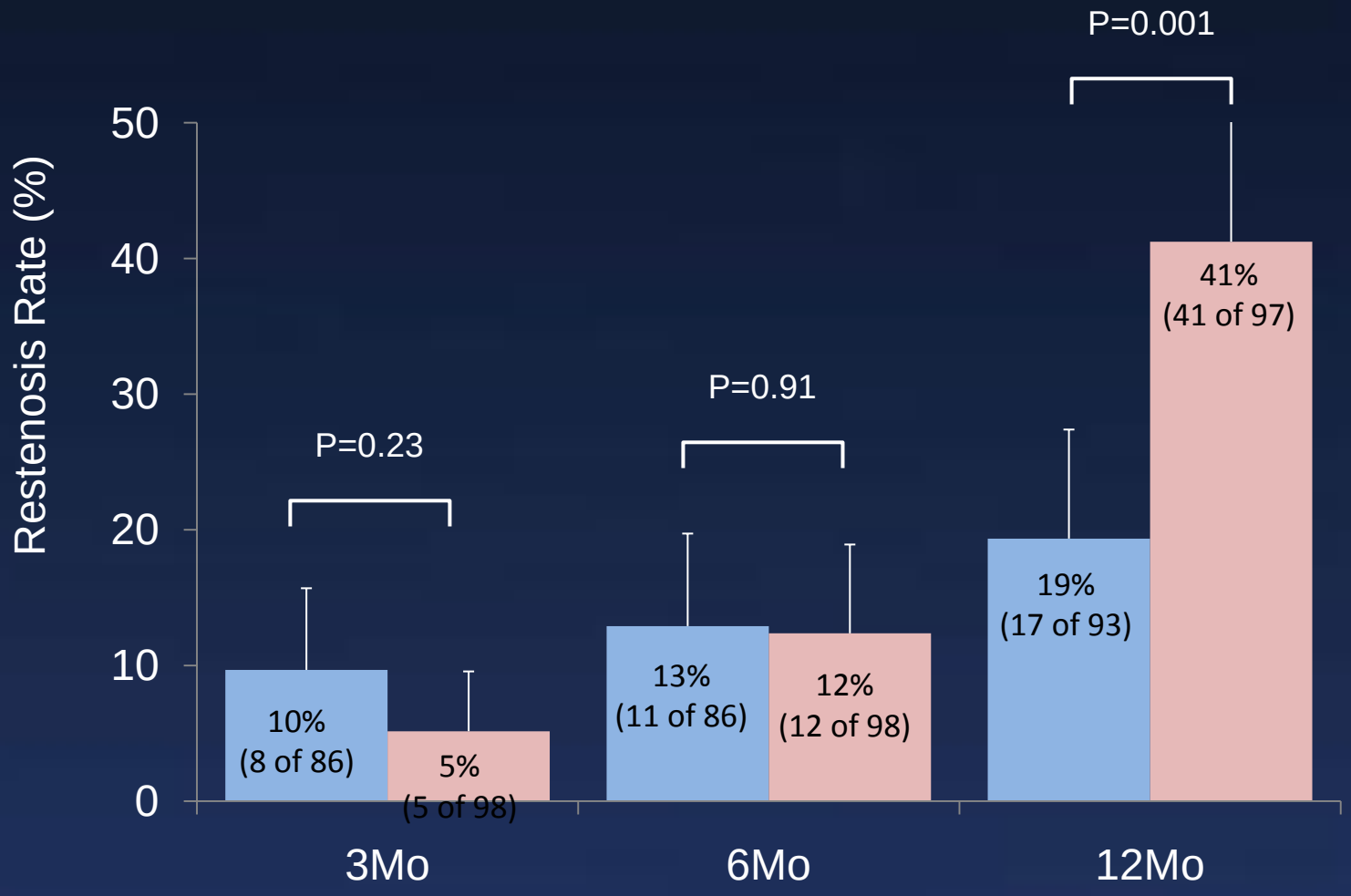
Results

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***)



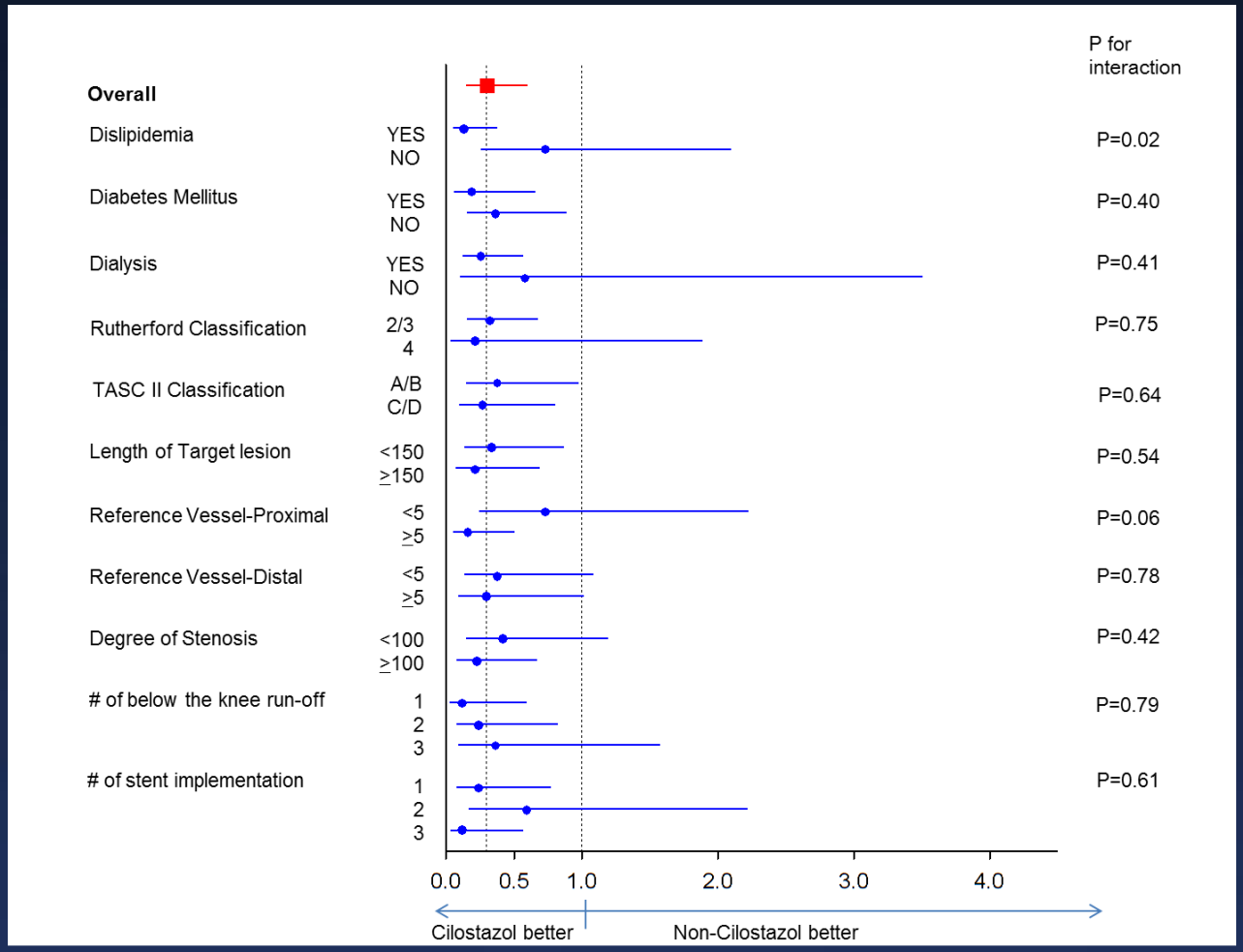
Results

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

Results

Subgroup analysis for efficacy of cilostazol on 12 months angiographic restenosis



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.

Conclusion

Cilostazol reduced angiographic restenosis rates after EVT for FP lesions.