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Two-Year Clinical Outcome After Abciximab-Coated Stent Implantation in Patients With Coronary Artery Disease

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Background: Despite abciximab-coated stents having an inhibitory effect on coronary artery restenosis, the medium-term clinical outcome is unknown.

Methods and Results: This prospective, randomized study compared the effects of the abciximab-coated stent, which was implanted in 95 patients, with those of control bare metal stents (BMS) implanted in 93 patients for de novo coronary lesions. Stent implantation was performed without any complications associated with the procedure. The 6-month intravascular ultrasound analysis showed that the area of neointimal hyperplasia was significantly smaller in the abciximab-coated stent group compared with the control stent group (+2.0±1.6 mm^2 vs +3.4±1.7 mm^2, P=0.001). However, at 2-year clinical follow up, there were no statistically significant differences in the incidences of total major adverse cardiac events (16% vs 24%, P=0.19) and cardiac death (0% vs 1.1%, P=0.3), target vessel revascularization (16% vs 21%, P=0.4) or non-fatal myocardial infarction (0% vs 2.3%, P=0.16) in the abciximab-coated stent group compared with the control stent group.

Conclusions: Although abciximab-coated stents are safe and inhibit neointimal hyperplasia, they have no superiority over BMS in 2-year clinical outcome. (*Circ J* 2010; **74:** 442–448)

Key Words: Abciximab; Restenosis; Stents; Thrombosis

Recently, the incidence of coronary artery disease (CAD) has greatly increased and it has become a major cause of death in adults. In the drug-eluting stent (DES) era, coronary artery stenting reduces the incidence of acute vascular events after percutaneous coronary intervention (PCI) to <1%.[1] However, in-stent restenosis (ISR) and stent thrombosis (ST) remain significant clinical problems to be solved.[2] The apparent rate of ISR is 30–40% in PTCA, 15–30% with bare metal stents (BMS), and <10% in DES, and the incidence of ST is 0.5–2.5% with BMS and 0.58–3.3% with DES.[3–5]

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Many DES are designed and manufactured to overcome restenosis and ST. The abciximab-coated stent was developed for this purposes. Abciximab, a potent antiplatelet agent that blocks the final pathways to platelet aggregation, improves the outcomes of high-risk PCI and decreases the incidence of major adverse cardiac events (MACE).[6–9] Different to other kinds of platelet glycoprotein IIb/IIIa receptor blockers, abciximab also binds to CD11b/18 (Mac-1) on vascular endothelial cells (ECs) and macrophages, thereby inhibiting the inflammatory response and smooth muscle cell (SMC) proliferation after vascular injury.[10–15] We recently demonstrated that the abciximab-coated stent has an inhibitory effect on coronary restenosis and revascularization,[16–18] so the purpose of the present study was to investigate the safety and clinical efficacy of implantation of the abciximab-coated stent compared with BMS.

Methods

Study Design and Population

We performed a prospective, randomized trial to compare the effects of the abciximab-coated stent, which was implanted in 95 patients, with those of conventional BMS implanted in 93 patients for de novo coronary lesions. The inclusion criteria were CAD patients who were scheduled to undergo elective PCI for single de novo lesions in native coronary

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Table 1. Baseline Clinical Characteristics

	Abciximab stent (n=95)	Control stent (n=93)	P value
Age (years, mean±SD)	56.71±9.90	57.34±10.17	0.663
Male gender (%)	77 (81)	66 (71%)	0.105
Risk factor (%)			
Hypertension (%)	48 (51)	46 (51%)	0.995
Hypercholesterolemia (%)	34 (35.8)	30 (32.3)	0.686
Diabetes mellitus (%)	19 (20.2)	16 (17.8)	0.674
Current smoking (%)	52 (55.3)	48 (53.3)	0.787
Familial history (%)	4 (4.2)	4 (4.3)	0.950
Previous MI (%)	7 (7.4)	6 (6.5)	0.814
Previous PCI (%)	7 (7.4)	9 (9.7)	0.554
Clinical diagnosis (%)			0.786
SAP (%)	14 (14.7)	12 (12.9)	0.716
UAP (%)	50 (52.6)	51 (54.8)	0.762
NSTEMI (%)	9 (9.5)	7 (7.5)	0.632
STEMI (%)	22 (23.2)	23 (24.7)	0.800
Ejection fraction (mean±SD)	63.05±10.10	63.37±11.56	0.841

MI, myocardial infarction; PCI, percutaneous coronary intervention; SAP, stable angina pectoris; UAP, unstable angina pectoris; NSTEMI, non-ST-elevation MI; STEMI, ST-elevation MI.

arteries having a diameter between 2.5 and 4.0 mm and critical stenosis (>70%) on angiography. Patients with graft-vessel stenosis, cardiogenic shock, left ventricular ejection fraction <35% or contraindications for antiplatelet agents were excluded from the study.

All procedures were performed by standard techniques: randomly selected stents were deployed at 10–20 atm after predilation with a balloon catheter. In cases of residual stenosis after stenting, adjunct balloon angioplasty was performed. None of the patients received glycoprotein IIb/IIIa receptor blockers. All patients received aspirin (300 mg ≥12 h before stent implantation and 100–200 mg/day indefinitely) and ticlopidine (500 mg ≥6 h before stent implantation and 250 mg/day for 2 months) or clopidogrel (300 mg ≥6 h before stent implantation and 75 mg/day for 2 months). Heparin was administered as a 5,000-unit bolus followed by 1,000 units/h and an additional 5,000 units immediately before PCI to keep the activated clotting time at 250–300 s. Clinical evaluation was done for 2 years to assess patient symptom frequency and cardiac event rates. The clinical primary endpoint was the composite of cardiac death, any myocardial infarction (MI), and need for percutaneous or surgical revascularization of the target lesion or vessel during the evaluation period, and the secondary endpoint was neointimal hyperplasia, which was measured by intravascular ultrasound (IVUS) at 6-month follow-up coronary angiography (CAG) after the procedure.

The study protocol was reviewed and approved in sequence by the Ministry of Health and Welfare and the Ethics Committee of Chonnam National University Hospital, and informed consent was given by all patients.

Manufacture of Abciximab-Coated Stent

Abciximab-coated stents were used according to the protocol previously described.[17,18] Briefly, a plasma polymerization reaction was performed to attach amine radicals to the stent surface. Stents were fixed in a tubular reactor, which was made of a Pyrex glass tube, and the pressure was decreased to <5 mTorr. For the attachment of amine radicals to the stent surface, diaminocyclohexane monomer was drifted into the tubular reactor at a constant dose, and plasma was generated using a radiofrequency power generator. The abciximab used was a human-murine chimeric antibody Fab fragment (c7E3 Fab) that blocks the glycoprotein IIb/IIIa receptor directly. The carboxy radical of abciximab was introduced to the amine radicals attached to the stent to achieve covalent bonding and improved attachment between the stent and abciximab. The abciximab coating on the surface of the stent was confirmed by scanning electron microscopy. To evaluate the release kinetics of abciximab from the stent, the stent was placed in a glass vial and immersed in 100 ml of phosphate-buffered saline. The amount of abciximab released to the buffer solution was measured using an absorbance test for ultraviolet at 278 nm.

CAG and IVUS

Quantitative diameter measurements of the coronary arteries were obtained by a blinded reviewer using a workstation with dedicated software (Phillips H5000 or Allura DCI program). From 2 orthogonal views, minimal lumen diameter (MLD) and interpolated reference diameter were calculated as a mean. IVUS studies were performed at baseline and repeated at 6 months after the procedure with follow-up angiography. The images were acquired with motorized pullback at a constant speed of 1 mm/s (Galaxy, Boston Scientific, Natick, MA, USA or Endosonics, EndoSonics Corporation, Rancho Cordova, CA, USA). Trained catheterization laboratory personnel performed the IVUS measurements, according to previously described methods.[19] Pre-interventional lesion and proximal and distal reference segment external elastic membrane (EEM), lumen, and plaque and media (P&M=EEM−lumen) cross-sectional areas (CSA) were measured. The lesion was the site with the smallest lumen CSA; if there were multiple image slices with the same minimum lumen CSA, then the slice with the largest EEM and P&M was measured. The proximal and distal reference segments were the least-diseased image slices (largest lumen with least plaque) proximal and distal to the lesion, but within the same segment and before any major side branch. Post-interventional and follow-up stent, lumen, and NIH (stent minus lumen CSA) areas were measured.

Table 2. Procedural and Lesion Characteristics

	Abciximab stent (n=95)	Control stent (n=93)	P value
Target artery (%)			
LAD (%)	53 (55.8)	59 (63.4)	0.285
LCX (%)	16 (16.8)	13 (14.0)	0.587
RCA (%)	26 (27.4)	20 (21.5)	0.350
LM (%)	0 (0)	1 (1.1)	0.311
No. of diseased vessels (%)			
1 (%)	81 (85.3)	73 (78.5)	0.228
2 (%)	11 (11.6)	17 (18.3)	0.197
3 (%)	3 (3.2)	3 (3.2)	0.979
Lesion length (mm)			
<10 (%)	4 (4.2)	8 (8.6)	0.218
10–20 (%)	89 (93.7)	76 (81.7)	0.012
>20 (%)	2 (2.1)	9 (9.7)	0.027
ACC/AHA classification (%)			
Type A (%)	0 (0)	1 (1.1)	0.311
Type B1 (%)	85 (89.5)	73 (78.5)	0.04
Type B2 (%)	9 (9.5)	17 (18.3)	0.08
Type C (%)	1 (1.1)	2 (2.2)	0.548
Pre-PCI TIMI flow (%)			
0 (%)	2 (2.1)	4 (4.3)	0.392
1 (%)	1 (1.1)	1 (1.1)	0.998
2 (%)	25 (26.3)	16 (17.2)	0.130
3 (%)	67 (70.5)	72 (77.4)	0.282
Pre-dilation balloon (mm)			
Length (mm)	20.0±0	20.22±1.47	0.158
Size (mm)	3.31±0.34	3.28±0.42	0.578
Stent size (mm)	3.32±0.34	3.30±0.42	0.65
Stent length (mm)	17.08±0.96	17.45± 4.04	0.396

LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery; LM, left main; ACC/AHA, American College of Cardiology/American Heart Association; PCI, percutaneous coronary intervention.

Table 3. Clinical Outcome at 2-Year Follow-up After Stent Implantation

	Abciximab stent (n=95)	Control stent (n=93)	P value
Follow-up, n (%)	82 (86)	82 (88)	
2-year MACE (%)	14 (16)	19 (24.0)	0.190
Cardiac death (%)	0 (0)	1 (1.1)	0.319
MI (%)	0 (0)	2 (2.3)	0.160
TLR (%)	14 (16)	17 (20)	0.575
TVR (%)	14 (16)	18 (21.0)	0.433
CABG (%)	0 (0)	0 (0)	1.00
In-stent restenosis (%)	17 (21)	22 (26.8)	0.420
Focal	9 (10.9)	10 (12.1)	0.782
Diffuse	5 (6.0)	8 (9.75)	0.370
Stent thrombosis (%)	0 (0)	0 (0)	1.00

MACE, major adverse cardiac events; MI, myocardial infarction; TLR, target lesion revascularization; TVR, target vessel revascularization; CABG, coronary artery bypass graft.

Definitions

Successful PCI was defined as a patent vessel at the treatment site with anterograde TIMI 3 flow and angiographic residual stenosis <20% without occurrence of any MACE (MI, acute or subacute stent occlusion, need for coronary bypass or target lesion revascularization). ISR was defined as an in-stent luminal diameter stenosis ≥50%. Late lumen loss was defined as the difference between the MLD immediately after stenting and the MLD at follow-up. Acute MI was defined as the elevated cardiac biomarkers with ischemic symptoms or ischemic changes on the ECG or imaging evidence of new loss of viable myocardium or new regional wall motion abnormality. ST was defined as an acute coronary syndrome with angiographic documentation of either vessel occlusion (TIMI 0 or 1) or thrombus within or adjacent to a previously successfully stented vessel (TIMI 1 or 2).

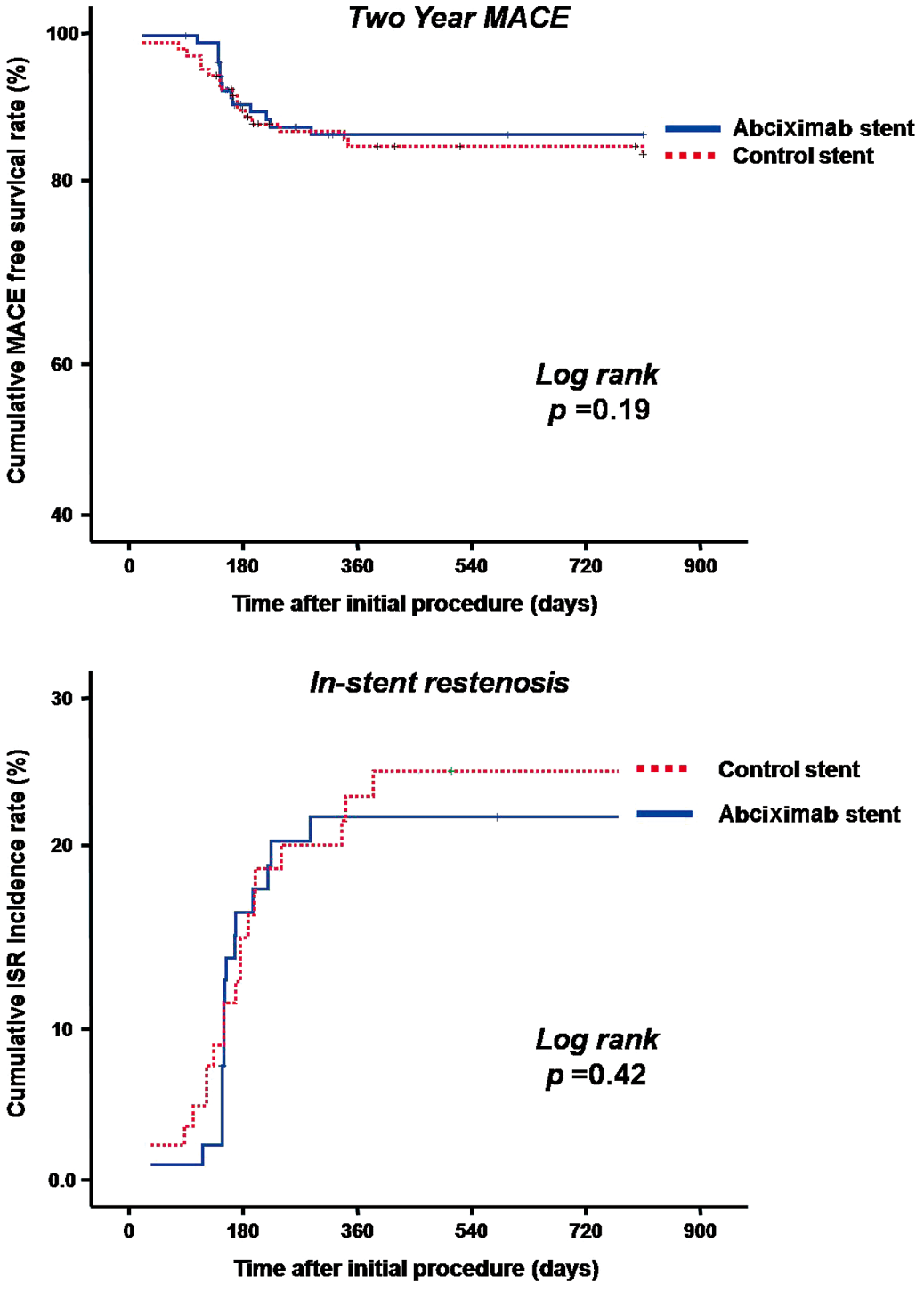

Figure. Kaplan-Meier plots of cumulative major adverse cardiac event (MACE)-free survival rate and cumulative in-stent restenosis (ISR) incidence rate for abciximab-coated stent and control bare metal stent. There was a trend of lower incidences of total MACE and ISR in the abciximab-coated stent group compared with the control stent group for 2-year clinical follow-up.

Statistical Analysis

The Statistical Package for Social Sciences (SPSS) for Windows, version 15.0 (Chicago, IL, USA) was used for all analyses. Continuous variables are presented as the mean value±1SD; comparisons were conducted by Student's t-test or nonparametric Wilcoxon test if the normality assumption was violated. Discrete variables are presented as percentages and relative frequencies; comparisons were conducted by chi-square or Fisher's exact test as appropriate. Revascularization of the target lesion or vessel and the composite of MACE

Table 4. Intravascular Ultrasound Results

	Abciximab stent (n=43)	Control stent (n=42)	P value
Pre-intervention			
Proximal reference EEM CSA (mm^2)	14.2±3.1	13.7±2.8	0.232
Lesion site EEM CSA (mm^2)	13.8±3.6	12.7±3.9	0.204
Lesion site lumen area (mm^2)	4.1±1.0	4.0±0.8	0.777
Lesion site plaque+media CSA (mm^2)	9.7±3.2	8.7±3.6	0.280
Lesion site plaque burden (%)	70.3±6.3	66.5±8.5	0.119
Distal reference EEM CSA (mm^2)	12.7±3.2	12.4±2.8	0.604
Post-intervention stent CSA			
Stent CSA (mm^2)	7.8±2.2	7.7±1.4	0.898
Lumen CSA (mm^2)	7.8±2.2	7.7±1.4	0.898
NIH area (mm^2)	0.0±0.0	0.0±0.0	1.000
Follow-up			
Proximal reference EEM CSA (mm^2)	14.1±3.5	13.5±3.0	0.211
Stent CSA (mm^2)	7.7±2.0	7.6±1.5	0.178
Intrastent lumen area (mm^2)	5.7±1.6	4.2±0.8	0.001
Intrastent NIH area (mm^2)	2.0±1.6	3.4±1.7	0.001
Distal reference EEM CSA (mm^2)	12.4±2.8	12.1±2.4	0.587
Serial (after intervention to follow up) comparison			
ΔProximal reference EEM CSA (mm^2)	−0.1±0.7	−0.2±1.0	0.821
ΔStent CSA (mm^2)	−0.1±1.1	−0.1±1.2	0.978
ΔIntrastent lumen area (mm^2)	−2.1±1.6	−3.5±1.8	0.001
ΔIntrastent NIH area (mm^2)	+2.0±1.6	+3.4±1.7	0.001
ΔDistal reference EEM CSA (mm^2)	−0.3±1.2	−0.3±1.4	0.967

EEM, external elastic membrane; CSA, cross-sectional area; NIH, neointimal hyperplasia.

during follow-up were analyzed using the Kaplan-Meier method. A value of $P<0.05$ was considered significant.

Results

Baseline and Procedural Characteristics

The baseline clinical characteristics are summarized in Table 1. There were no significant differences between the 2 groups in age, gender, risk factors for CAD, clinical presentation or left ventricular ejection fraction. Procedural characteristics are summarized in Table 2. PCI was performed with a success rate of 100% in both groups without any complications associated with the procedure. There were no significant differences between the 2 groups in target vessels or the number of diseased vessels, except for lesion length and lesion type.

Clinical Follow-up

The 2-year clinical follow-up was completed in 82 patients (86%) in the abciximab-coated stent group and in 82 patients (88%) in the control stent group. During follow up, there were no cardiac deaths or MI in the abciximab-coated stent group. There were 17 cases of ISR (21.0%) in the abciximab-coated stent group compared with 22 (26.8%) in the control BMS group. There were no statistically significant differences in the incidences of MACE and ISR in the abciximab-coated stent group compared with the control stent group (Table 3, Figure).

ST did not occur at 2-year follow-up, despite of the use of short-duration dual antiplatelet therapy.

IVUS Analysis

Serial IVUS measurements are shown in Table 4. Baseline stent and reference measurements were similar between the 2 groups. At follow-up IVUS, the intra-stent lumen area was larger in the abciximab-coated stent group compared with the control stent group (5.7±1.6 mm^2 vs 4.2±0.8 mm^2, P=0.001), and the intra-stent neointimal hyperplasia (NIH) area was smaller (+2.0±1.6 mm^2 vs +3.4±1.7 mm^2, respectively; P=0.001).

Discussion

This study is the first randomized, prospective clinical trial evaluating the medium-term outcome of abciximab-coated stent implantation in patients with CAD. The abciximab-coated stent was safe to use and inhibited neointimal hyperplasia but failed to prove superior clinical efficacy compared with BMS at 2-year clinical follow up.

The DES is a device releasing into the bloodstream single or multiple bioactive agents that affect tissues adjacent to the stent. Avoiding systemic toxicity, stent-based local drug release at the site of vascular injury via a polymer-coated stent is an attractive method of achieving an effective local concentration of a drug.[20] Abciximab is a platelet glycoprotein IIb/IIIa inhibitor, which are the most potent antiplatelet agents currently available, exerting their effect by blocking the final common pathway of platelet aggregation. The use of abciximab in patients with acute coronary syndrome is associated with reductions in the magnitude of the rise in the levels of circulating inflammatory markers such as C-reactive protein, interleukin-6, and tumor necrosis factor-α, which increase over the 24–48 h after PCI. Abciximab administration also decreases the levels of these inflammatory markers after stent implantation.[21] The effect may be caused by the interaction between CD11b/CD18 (macrophage-1 receptor), which is a receptor located on the surface of neutrophils and monocytes, and abciximab. The interac-

tion between CD11b/18 and abciximab results in the inhibition of cell-to-cell adhesion and interaction between cells and the extracellular matrix.[13–15,22] Also, abciximab has an affinity for the vitronectin receptor on SMCs, ECs, and platelets and the blockade of this receptor by abciximab inhibits the migration and proliferation of SMC after stenting and may prevent ISR.[10–12]

Follow-p IVUS at 6 months showed a larger intra-stent lumen area and smaller neointimal area in the abciximab stent group, which suggested an anti-restenotic effect of the coated stent. According to our previous reports, patients who received the abciximab stent were free of procedure-related complications, and the incidence of in-hospital, 30 day MACE was low, especially ST, which did not occur in any of the abciximab-coated stent group.[18] Unfortunately, the beneficial effects of the abciximab-coated stent were not maintained out to 2 years in a real-world population.

These results are less favorable than those of sirolimus-eluting stents (SES). In several trials, ISR with SES was 8.2–9.4% during long-term clinical follow-up.[20,23] However, there have been safety concerns with DES, because of ST.[24] ST is an uncommon but serious complication of coronary artery stenting that often presents as death or MI. In several trials, the incidence of ST was 0.58–1.3% with DES.[3,4] In the present study ST did not occur in the abciximab stent group at 2 year follow-up. Although the patient number was relatively small, the absence of episodes of acute MI by acute or subacute thrombotic occlusion during the 2 year follow-up in patients who received an abciximab-coated stent may suggest that platelet aggregation was effectively inhibited by abciximab and that this effect could be maintained. Also, the optimal duration of dual antiplatelet therapy has not been determined for DES. In the abciximab-coated stent group, postprocedural clopidogrel or ticlopidine was given for 2 months, according to the protocol, whereas it was prescribed for a more prolonged period of time in the trials using other DES. In spite of the use of short duration dual antiplatelet therapy, ST did not occur after clopidogrel or ticlopidine was stopped in the abciximab-coated stent group.

Study Limitations

One of the main limitations is that this clinical study included only 188 patients undergoing de novo, single vessel stenting in a single center and therefore the present trial is underpowered to reveal potential small differences in the primary endpoints. These findings should be confirmed by the results of the large-scale, prospective randomized trials.

Conclusion

Two-year clinical follow up showed no statistical superiority of the abciximab-coated stent over BMS. The abciximab-coated stent was safe and inhibited neointimal hyperplasia, but did not improve clinical outcomes at 2 years after stent implantation.

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References

1. Serruys PW, Jaegere PD, Kiemeneij F, Macaya C, Rutsch W, Heyndrickx G, et al. A Comparison of balloon-expandable stent implantation with balloon angioplasty in patients with coronary heart disease. *N Eng J Med* 1994; **331:** 489–495.
2. Honda Y. Drug-eluting stents: Insights from invasive imaging technologies. *Circ J* 2009; **73:** 1371–1380.
3. Schuhlen H, Kastrati A, Pache J, Dirschinger K, Schomiq A. Incidence of thrombotic occlusion and major adverse cardiac events between two and four weeks after coronary stent placement: Analysis of 5,678 patients with a four-week ticlopidine regimen. *J Am Coll Cardiol* 2001; **37:** 2066–2073.
4. De la Torre-Hernandez JM, Alfonso F, Hernandez F, Elizaga J, Sanmartin M, Pinar E, et al. Drug-eluting stent thrombosis: Results from the multicenter Spanish registry ESTROFA (Estudio ESpanol sobre TROmbosis de stents FArmacoactivos). *J Am Coll Cardiol* 2008; **51:** 986–990.
5. Wenaweser P, Daemen J, Zwahlen M, van Domburg R, Juni P, Vaina S, et al. Incidence and correlates of drug-eluting stent thrombosis in routine clinical practice: 4-year results from a large 2-institutional cohort study. *J Am Coll Cardiol* 2008; **52:** 1134–1140.
6. EPIC (Evaluation of 7E3 in Preventing Ischemic Complications) Investigators. Use of a monoclonal antibody directed against the platelet glycoprotein IIb/IIIa receptor in high-risk coronary angioplasty. *N Engl J Med* 1994; **330:** 956–961.
7. EPILOG (Evaluation in PTCA to improve Long-Term outcome GP IIb/IIIa Blockade Study Group) Investigators. Platelet glycoprotein IIb/IIIa receptor blockade and low-dose heparin during percutaneous coronary revascularization. *N Engl J Med* 1997; **336:** 1689–1696.
8. CAPTURE (C7E3 Fab AntiPlatelet Therapy in Unstable Refractory angina) Investigators. Randomized placebo-controlled trial of abciximab before and during coronary intervention in refractory unstable angina. *Lancet* 1997; **349:** 1429–1435.
9. Platelet Receptor Inhibition in ischemic Syndrome Management in Patients Limited by Unstable Sings and Symptoms (PRISM-PLUS) Study Investigators. Inhibition of the platelet glycoprotein IIb/IIIa receptor with tirofiban in unstable angina and non-Q-wave myocardial infarction. *N Engl J Med* 1998; **338:** 1488–1497.
10. Tam SH, Sassoi PM, Jordan RE, Nakada MT. Abciximab (ReoPro, chimeric 7E3 Fab) demonstrates equivalent affinity and functional blockade of glycoprotein IIb/IIIa and alpha(v) beta3 integrins. *Circulation* 1998; **98:** 1085–1091.
11. Reverter JC, Beguin S, Kessels H, Kuman R, Hemker HC, Coller BS. Inhibition of platelet-mediated, tissue factor-induced thrombin generation by the mouse/human chimeric 7E3 Fab treatment of an acute thrombosis and "clinical restenosis". *J Clin Invest* 1996; **98:** 863–874.
12. Shappel SB, Toman C, Anderson DC, Taylor AA, Entman ML, Smith CW. Mac-1 (CD11b/CD8) mediates adherence-dependent hydrogen peroxide production by human and canine neutrophils. *J Immunol* 1990; **144:** 2702–2711.
13. Simon DI, Xu H, Ortelpp S, Rogers C, Rao NK. 7E3 monoclonal antibody directed against the platelet glycoprotein IIb/IIIa cross-reacts with the leukocyte integrin Mac-1 and blocks adhesion to fibrinogen and ICAM-1. *Thromb Vasc Biol* 1997; **17:** 528–535.
14. Mickelson JK, Ali MN, Kleiman NS, Lakkis NM, Chow TW, Hughes BJ. Chimeric 7E3 Fab (ReoPro) decreases detectable CD IIb on neutrophils from patients undergoing coronary angioplasty. *J Am Coll Cardiol* 1999; **33:** 97–106.
15. Lefkovits J, Topol EJ. Platelet glycoprotein IIb/IIIa receptor antagonists in coronary artery disease. *Eur Heart J* 1996; **17:** 9–18.
16. Hong YJ, Jeong MH, Kim W, Lim SY, Lee SH, Hong SN, et al. Effect of abciximab-coated stent on in-stent intimal hyperplasia in human coronary arteries. *Am J Cardiol* 2004; **94:** 1050–1054.
17. Kang KT, Jeong MH, Kim NH, Lee SH, Rhew JY, Park JC, et al. The inhibitory effect of platelet glycoprotein IIb/IIIa receptor blocker-coated stent on porcine coronary stent restenosis. *Korean J Med* 2001; **60:** 314–323.
18. Kim W, Jeong MH, Kim KH, Sohn IS, Hong YJ, Park HW, et al. The clinical results of a platelet glycoprotein IIb/IIIa receptor blocker (abciximab: ReoPro)-coated stent in acute myocardial infarction. *J Am Coll Cardiol* 2006; **47:** 933–938.
19. Nissen SE, Yock P. Intravascular ultrasound: Novel pathophysiological insights and current clinical applications. *Circulation* 2001; **103:** 604–616.
20. Schwartz RS, Edelman ER, Carter A, Chronos N, Rogers C, Robinson KA, et al. Drug-eluting stents in preclinical studies: Recommended evaluation from a consensus group. *Circulation* 2002; **106:** 1867–1873.
21. Ong AT, van Domburg RT, Aoki J, Sonnenschein K, Lemos PA, Serruys PW. Sirolimus-eluting stents remain superior to bare-metal stents at two years: Medium-term results from the Rapamycin-

Eluting Stent Evaluated at Rotterdam Cardiology Hospital (RESEARCH) registry. *J Am Coll Cardiol*. 2006; **47:** 1356–1360.
22. Lincoff AM, Kereiakes DJ, Mascelli MA. Abciximab suppresses the rise in levels of circulating inflammatory markers after percutaneous coronary revascularization. *Circulation* 2000; **104:** 163–167.
23. Schwarz M, Nordt T, Bode C, Peter K. The GP IIb/IIIa inhibitor abciximab (c7E3) inhibits the binding of various ligands to the leukocyte integrin Mac-1 (CD11b/CD18, alpha(M)beta(2)). *Thromb Res* 2002; **107:** 121–128.
24. Moses JW, Leon MB, Popma JJ, Fitzgerald PJ, Holmes DR, O'Shaughnessy C, et al. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. *N Engl J Med* 2003; **349:** 1315–1323.
25. Inoue T, Node K. Molecular basis of restenosis and novel issues of drug-eluting stents. *Circ J* 2009; **73:** 615–621.