TCT-569

Biodegradable-polymer-based, argatroban-eluting, cobalt chromium stent (JF-04) for treatment of native coronary lesions: Final results of the first-in-man study in Japan

Yoshihiro Morino,[1] Tetsuya Tobaru,[2] Satoshi Yasuda,[3] Kazuaki Kataoka,[4] Kengo Tanabe,[5] Atsushi Hirohata,[6] Ken Kozuma,[7] Takeshi Kimura[8]
[1]Iwate Medical University, Morioka, Iwate, Japan; [2]Sakakibara Heart Institute, Fuchu, Tokyo, Japan; [3]National Cerebral and Cardiovascular Center, Osaka, Japan; [4]Houai Hospital, Osaka, Japan; [5]Mitsui Memorial Hospital, Tokyo, Japan; [6]The Sakakibara Heart Institute of Okayama, Okayama, Japan; [7]Teikyo University Hospital, Tokyo, Japan; [8]Kyoto University Graduate School of Medicine, Kyoto, Japan

BACKGROUND Activation of coagulation and thrombus formation were considered as the initial steps in the mechanism of arterial restenotic reaction, which could be potential targets for action of drug eluting stent. Initial animal studies suggested that local delivery of direct thrombin inhibitor, argatroban, suppressed platelet aggregation and smooth muscle cell proliferation after balloon angioplasty. Furthermore, several human trials of local delivery of this drug demonstrated significant reduction of angiographic restenosis rates. Accordingly, argatoroban-eluting stent (JF-04) was developed, which composed of cobalt-chromium thin strut (70μm) stent platform, carrier biodegradable polymer (50:50 poly DL-lactide-co-glycolide), and argatroban. Drug elution was designed to complete within 40 days, whereas polymer remained up to 9 months. The objective of this first-in-man study was to test the safety and feasibility of the JF-04 stent to treat coronary lesions.

METHODS A total of 31 patients with either stable angina or unstable angina, or silent myocardial ischemia, who had de novo coronary lesions (legion length: 6 - 26 mm, reference diameter: 2.5 - 3.5 mm by visual estimation) were enrolled in the 7 Japanese sites. The lesions were treated with the JF-04 stent after pre-dilatation. The primary endpoint was set as angiographic in-stent late loss at 6-month after implantation. The secondary endpoints consisted of angiographic, intravascular ultrasound (IVUS), and optical coherence tomography (OCT) representative parameters at 6-month and clinical outcomes at 9-month. Major adverse cardiac events (MACE) were defined as composites of cardiac death, any myocardial infarction, and target vessel revascularization (TVR). Dual antiplatelet therapy was mandated at least for 6-month after implantation.

RESULTS Procedural success was achieved in 100%. Angiographic in-stent late loss was 1.01 ± 0.48 mm and binary restenosis rate (in-segment) was 29.0%. Other representative angiographic, IVUS, and OCT parameters are summarized in Table. No stent thrombosis occurred during 9-month follow-up period. Composite MACE rate was 12.9%, which was exclusively attributed to TVR.

Pre	
Lesion length, mm	16.2 ± 6.9
Reference vessel diameter, mm	2.98 ± 0.58
AHA Type (A/ B1/ B2/ C), %	9.7/ 19.4/ 45.2/ 25.8
Post	
In-stent MLD, mm	2.73 ± 0.48
6 month follow-up	
In-stent MLD, mm	1.72 ± 0.75
In-stent late loss, mm	1.01 ± 0.48
In-segment late loss, mm	0.74 ± 0.51
Angiographic binary restenosis, %	29.0
Focal/Diffuse/Occlusive/Proliferative, %	3.2/ 19.4/ 3.2/ 3.2
In-stent volume obstruction by IVUS, %	31.9 ± 13.7
Uncovered strut rate by OCT, %	1.63 ± 5.21
Malapposed strut rate by OCT, %	0.26 ± 1.26

CONCLUSIONS The first-in-man study of biodegradable polymer-based argatroban-eluting stent failed to show sufficient inhibition of neointimal hyperplasia in de novo native coronary lesions, which resulted in relatively high restenosis rate as well as advanced angiographic restenotic patterns. Estimated potential mechanisms of these unfavorable outcomes included 1) limited capability inherent to argatroban for inhibition of cellular proliferation and 2) an unignorable gap in duration of elution/ absorption between drug and polymer.

CATEGORIES CORONARY: Stents: Drug-Eluting

KEYWORDS First-in-Man Trial, Stent, drug-eluting, Stenting, coronary

TCT-570

3-Year Clinical Outcome of the DUTCH PEERS (TWENTE II) Randomized Trial: Cobalt-Chromium Zotarolimus-Eluting Resolute Integrity Versus Platinum-Chromium Everolimus-Eluting Promus Element Stents in All-Comer Patients

Clemens von Birgelen,[1] Liefke C. van der Heijden,[2] Marlies M. Kok,[2] Peter W. Danse,[3] Gillian A. Jessurun,[4] Raymond Hautvast,[5] Marc Hartmann,[2] Melvyn Tjon Joe Gin,[3] Alexander Schramm,[4] Hans W. Louwerenburg,[2] Marije M. Löwik,[2] Gerard C. Linssen,[6] Carine J. Doggen,[7] Martin G. Stoel[2]
[1]Thoraxcentrum Twente & University of Twente, Enschede, Netherlands; [2]Thoraxcentrum Twente, Enschede, Netherlands; [3]Rijnstate Hospital, Arnhem, Netherlands; [4]Scheper Hospital, Emmen, Netherlands; [5]Medical Center Alkmaar, Alkmaar, Netherlands; [6]Ziekenhuisgroep Twente, Almelo, Netherlands; [7]MIRA - Institute for Biomedical Technology and Technical Medicine, Enschede, Netherlands

BACKGROUND We compared the 3-year safety and efficacy of the newer generation zotarolimus-eluting Resolute Integrity stent (Medtronic) versus the everolimus-eluting Promus Element stent (Boston Scientific) in all-comer patients, who were enrolled in the DUTCH PEERS (TWENTE II) randomized trial (clinicaltrials.gov NCT01331707). Newer generation permanent polymer-based drug-eluting stents (DES) with flexible designs show a high conformability to challenging anatomies. Limited long-term data are available on the use of these newer generation DES following percutaneous interventions for complex and multiple coronary lesions.

METHODS In the randomized, multicenter, single-blinded, investigator-initiated DUTCH PEERS trial, a total of 1,811 all-comer patients were 1:1 randomly assigned to treatment with Resolute Integrity or Promus Element stents. Patients diagnosed with stable angina as well as acute coronary syndrome, any lesion type, and any number of lesions or vessels to be treated were enrolled at 4 study centers in the Netherlands. The primary endpoint of target vessel failure (TVF) is a composite of cardiac death, target vessel revascularization (TVR), or myocardial infarction (MI). Study monitoring and clinical event adjudication were performed by independent contract research organizations (Diagram, Zwolle, and Cardialysis, Rotterdam, the Netherlands).

RESULTS A total of 1,293 (71.7%) patients were treated for complex coronary lesions, while 455 (25.1%) patients were treated for multiple target lesions. The 3-year incidence of TVF (primary endpoint) and various secondary endpoints will be reported for both DES groups, including the individual components of the primary endpoint. In addition, the incidence of stent thrombosis, the composite endpoint target lesion failure, and the more patient-oriented composite clinical endpoints major adverse cardiac events and patient-oriented composite endpoint will be presented.

CONCLUSIONS Three-year clinical outcome data of the randomized, multicenter DUTCH PEERS trial will be reported at TCT 2015.

CATEGORIES CORONARY: Stents: Drug-Eluting

KEYWORDS Everolimus-eluting stents, Randomized clinical trial, Zotarolimus-eluting stent