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Original article

The ‘all comer’ Coroflex Please drug-eluting stent registry in Europe and Asia – An overall and transcontinental assessment of the 10-month major adverse cardiac events

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ABSTRACT

Background: Randomized trials assess the potential of a medical device in well defined indications while “all comer studies” reveal the device performance in the real clinical environment.

Aims: This ‘all comers’ registry assessed the 10-month outcome of the Coroflex® Please drug-eluting stent in Europe and Asia by clinically driven major adverse cardiac events.

Methods: The Coroflex® Please Registry was an international, prospective, multicenter registry enrolling patients with symptomatic ischemic heart disease. The primary endpoint was clinically driven target lesion revascularization (TLR) at 9 months. Secondary endpoints were technical success, in-hospital outcomes, definite stent thrombosis and major adverse cardiac events (death, myocardial infarction, or TLR) for subgroup analyses. **Results:** Of the enrolled 1230 patients (63.6 ± 11.2 years, 33.9% diabetics), 339 (27.6%) had an acute coronary syndrome, 148 (12.1%) STEMI and 191 (15.6%) NSTEMI. After 10.5 ± 3.8 months (follow-up rate 92.8%), the target lesion revascularization rate (TLR) was 7.8% overall, 8.3% in STEMI, and 11.3% in NSTEMI patients. Total MACE was 11.1% and significantly higher in ACS with either diabetes mellitus (22.9%, $p = 0.017$) or age ≥ 75 years (25.4%, $p = 0.026$). In European and Asian patients MI rates (5.2% vs 3.1%, $p = 0.135$) and cardiac death rates (1.6% vs 0.9%, $p = 0.414$) were similar. The MACE rate was higher in Europe (13.6% vs 4.7%, $p < 0.001$) driven by a six times higher TLR rate.

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Conclusions: TLR and MACE occurred within the range of previously published data. The incidence of MI and cardiac death were not different between Europe and Asia. MACE were higher in Europe driven by target lesion revascularization.

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1. Introduction

Often randomized trials assess the potential of a medical device and are used to obtain approval of a device demonstrating its safety and efficacy. Thus, studies introducing new devices to treat coronary artery lesions are small in sample size. However, “all comer studies” reveal the real benefits during routine use and derive their conclusions by analyzing data from larger and less selected patient populations. This type of study also adds information on the type of patients and lesions that benefit the most (or the least) from such a device and shed additional light on the cost–benefit–risk ratio of the product tested. Often, the outcomes of a device in an ‘all comer’ registry are inferior to their ‘parent’ randomized controlled trials (RCT). One example are the randomized Cypher trials with MACE rates in the range of 5–8%¹ while in the German Cypher Registry, the overall 6-month MACE rate was 14.2% in an unselected patient population.²

The device analyzed in this study, the Coroflex® Please stent was associated with favorable acute and long-term outcomes in two small studies angiographically^{3–6} up to six months and clinically up to three years.⁵ The sample sizes were small. Thus, in order to allow a more firm assessment of the device performance beyond the currently available literature, a large patient number registry is warranted. Moreover, registries conducted in different countries or even continents may face challenges that must be considered when interpreting these findings. Therefore, an intercontinental subgroup comparison was performed.

2. Methods

2.1. Objectives

The primary intention of this ‘all comer’ registry was to further document the safety and efficacy of the Coroflex® Please paclitaxel-eluting stent which has been previously studied in the PECOPS I and II trials.^{3–6}

2.2. Endpoints

The primary endpoint was clinically driven target lesion revascularization at 9 months post procedure (TLR) as defined by re-PCI or coronary bypass grafting.

Secondary endpoints included the procedural success rate, definite acute/subacute stent thrombosis based on the ARC criteria, and major adverse cardiac events (MACE) as the composite of TLR, cardiac death, and myocardial infarction (MI). Cardiac death was defined as death from all causes except when the cause of death was proven non-cardiac.

2.3. Definitions

Major adverse cardiac events include target lesion revascularization (TLR), myocardial revascularization, and death of cardiac or unknown origin.

Stent thrombosis was defined according to the ARC criteria.⁷

Myocardial infarction was diagnosed with corresponding ECG changes and/or CK-elevation 3-times the upper normal limit.

2.4. Centers

Registry patients were prospectively enrolled in 16 European and 13 Asian centers. All sites in Asia (Malaysia, Vietnam, Thailand) and Europe (Germany, Spain, Russia, Hungary, Cyprus) fulfilled national reimbursement requirements for the study device.

2.5. Materials

Coroflex® Please is a paclitaxel-eluting DES based on the Coroflex® stainless steel platform. Its coating (P-Matrix®) is polysulfone with a long track record of biocompatibility especially in hemodialysis membranes.^{8–10} The stent features a multicellular stent architecture with a crossing profile of less than 1.1 mm and is characterized by a high coating integrity after stent expansion. Its temporal drug release pattern is between the Taxus® slow and medium release kinetics.⁴

2.6. Inclusion and exclusion criteria

Patients 18 years of age or older with stable angina, objective proof of ischemia (e.g., positive exercise stress test) or acute coronary syndrome had to meet the commonly accepted requirements for percutaneous coronary stenting. In single or multivessel coronary artery disease, presenting one or several de novo or restenotic lesions (maximum length: 20 mm) with vessel reference diameters from 2.5 mm to 4.0 mm (inclusive) could be treated. A maximum of four stents was allowed per patient.

2.7. Procedural approach

Femoral and radial access was permitted with recommended introducer sheaths of at least 5 Charrière French in diameter. Direct stenting was allowed according to the discretion of the operator. Intravenous heparin (70 IU/kg) was given in all patients and supplemented as needed in long lasting procedures. With the exception of patients on glycoprotein IIb/IIIa antagonists, activated clotting time was maintained at a minimum of 180 s. Dual anti-platelet therapy was initiated

with a bolus of at least 300 mg of clopidogrel along with 500 mg of acetylsalicylic acid (ASA).

2.8. Postprocedural medication

Clopidogrel 75 mg/d was administered for at least 6 months post procedure and acetylsalicylic acid 100–325 mg/d for life.

2.9. Data collection

Baseline and clinical follow-up data were collected through a web based data acquisition system with the exception of centers that had limited internet access. These centers provided paper hard copies that were subsequently entered into the database by the data management team. The National principal investigators were responsible for the accuracy of their datasets and performed source data verification when the routinely performed web based plausibility checks indicated discrepancies.

2.10. Statistical analysis

The Kolmogorov–Smirnov-test was used to prove Gaussian distribution allowing for calculation of the mean and standard deviation unless otherwise indicated. Discriminant variables were evaluated using the Chi²-test. Continuous variables were compared with the unpaired two-tailed Student's *t*-test. In non-normal distributed parameters, samples were described using the means and standard deviations for inferential statistics. Non-parametric test such as the Wilcoxon–Mann–Whitney rank test were used whenever applicable. For all tests the significance level α was 0.05. Statistical analyses were done with SPSS version 18.0 (IBM, Munich, Germany).

2.11. Patients

2.11.1. Patient and lesion related baseline data

Between September 01, 2006 and February 29, 2008, a total of 1230 patients underwent percutaneous coronary intervention (PCI) using the Coroflex® Please stent (Table 1).

3. Results

3.1. Procedural data

Technical success for the stent to cross the lesion was achieved in 1230 patients in 98.5% (1550/1574) of all stent implantations (Table 2).

3.2. Follow-up data

All patients were available for in-hospital follow-up while at 10.5 ± 3.8 months post procedure a total of 1142/1230 (92.8%) patients either reached the clinical endpoint prematurely or were available for the clinical follow-up (Tables 3–5).

Major adverse cardiac events (MACE) during hospitalization are given in Table 3.

Stent thrombosis rates were statistically not different ($p = 0.66$) in diabetics (1.67%) and in non-diabetics (1.35%).

There were two clopidogrel non-responders and one clopidogrel low-responder.

3.3. MACE rates at 10 months relative to cardiovascular risk factors

In all patients with ACS only the presence of diabetes mellitus and age of >75 years was associated with significantly higher MACE rates (see Fig. 1, $p = 0.017$ and $p = 0.026$).

In non-ACS patients diabetes mellitus was not associated with a significantly higher MACE rate as compared to non-diabetic subjects ($p = 0.234$) while neither the presence of hypertension ($p = 0.200$) nor age ≥ 75 years ($p = 0.162$) did affect patient outcome (Fig. 2).

3.4. MACE rates at 10 months relative to lesion characteristics

MACE rates for different lesion characteristics are given in Table 5.

Overall only the B2/C lesions ($p = 0.002$) and the presence of calcification ($p = 0.016$) had a significant impact on MACE (see Table 5).

Patients with one vessel disease had significantly fewer MACEs (5.5%) as compared to those with two or three vessel disease (9.5%; $p < 0.001$). Patients with two vessel disease had lower MACE rates than those with three vessel disease (11.3%; $p = 0.02$). The MACE rates were also higher when the patients received more than one stent compared to single stent deployment (13.4%, vs 7.2%; $p = 0.001$).

4. Discussion

In this all comer registry the technical success rate was 98.5% in a patient population angiographically characterized by more than 50% complex lesions such as B2/C (56.4%), total occlusions (12.8%), bifurcations (17.8%), and acute coronary syndrome (27.5%). Additionally, moderate to severe calcifications (40.4%) and angiographically visible intracoronary thrombus (11.4%) contributed to the lesion complexity.

4.1. MACE and TLR in-hospital

The in-hospital rates for MACE (2.7%), TLR (1%) and myocardial infarction (1.8%) of this registry are similar to those of another large observational registry¹¹ with rates for MACE of 3.1%, for TLR of 1% and for myocardial infarction of 2.6%.

4.2. MACE and TLR at 10 months

The 10-month follow-up in the 1142/1230 (92.8%) patients revealed a total MACE rate of 11.1% (127/1142) mainly driven by target lesion revascularization (7.8%; 89/1142). With the limitations of historic comparisons, the data are similar to those reported in a RCT conducted with the same stent in Germany^{4,5} reporting 6- and 12-month MACE rates of 10.4% and 15.3%. The corresponding TLR rates were 8% and 8.8%, respectively. The current study was less controlled than the aforementioned RCT and, hence, enrolling more complex (B2/

Table 1 – Patient demographics and lesion characteristics at baseline.

	All	Asian patients	European patients	p-values**
Patients	1230	363	867	–
Age	63.6 ± 11.2 y*	60.3 ± 10.9 y	64.9 ± 11.0 y	< 0.001
Diabetics	33.9% (417/1230)	32.8% (119/363)	34.4% (298/867)	0.591
Hypertension	75.0% (922/1230)	67.5% (245/363)	78.1% (677/867)	< 0.001
Lesions	1379	399	980	–
Lesion length	15.6 ± 7.5 mm*	17.1 ± 8.2 mm	15.0 ± 7.1 mm	< 0.001
Vessel diameter	2.97 ± 0.42 mm	2.93 ± 0.45 mm	2.99 ± 0.41 mm	0.009
Percent stenosis	83.9 ± 13.4%	82.0 ± 13.3%	84.7 ± 13.4%	< 0.001
Stents deployed	1574	439	1135	–
Stents per patient	1.26 ± 0.53	1.21 ± 0.49	1.28 ± 0.55	0.012
STEMI	12.0% (148/1230)	15.2% (55/363)	10.7% (93/867)	< 0.001
NSTEMI	15.5% (191/1230)	7.2% (26/363)	19.0% (165/867)	
No MI	72.4% (891/1230)	77.7% (282/363)	70.2% (609/867)	
Multivessel stenting	6.4% (78/1230)	7.4% (27/363)	5.9% (51/867)	0.312
Intracoronary thrombus visible	11.4% (157/1379)	8.5% (34/399)	12.6% (123/980)	0.033
A/B1 lesions	43.6% (601/1379)	44.6% (178/399)	43.2% (423/980)	0.623
B2/C lesions	56.4% (778/1379)	55.4% (221/399)	56.8% (557/980)	
Restenosis	15.1% (208/1379)	2.0% (8/399)	20.4% (200/980)	< 0.001
Total occlusions	12.8% (176/1379)	9.0% (36/399)	14.3% (140/980)	0.028
Bifurcations	17.8% (245/1379)	12.5% (50/399)	19.9% (195/980)	0.001
Diffuse lesions	54.2% (744/1379)	28.3% (113/399)	64.4% (631/980)	< 0.001
Severe tortuosity (>45°)	10.7% (147/1379)	4.8% (19/399)	13.1% (128/980)	< 0.001
Moderate to severe calcification	40.4% (557/1379)	19.3% (77/399)	49.0% (480/980)	0.001
Ostial lesions	7.8% (108/1379)	4.8% (19/399)	9.1% (89/980)	0.007

*Mean ± SD; ** p-values for comparison between Asian and European patients. Significant differences are marked bold.

C: 56.4% vs 20.8%) and longer lesions (15.7 ± 7.5 mm vs 11.6 ± 0.4 mm). The data of the current study are superior to the PECOPS II RCT, which showed at six months a MACE rate of 15.5% mainly driven by a TLR rate of 14.5% in shorter lesions of 12.5 ± 4.6 mm, which were less complex (B2/C 31.8%).⁶ Stent thrombosis rates were 1.6% in this registry (10 months), 1.6% (PECOPS I) and 0.8% (PECOPS II) at 6 months. The data, however, are inferior to the EVENT registry in which primarily a sirolimus-eluting stent was deployed. This registry revealed a 12-month TLR rate of 4.2% in even longer (37 ± 23 mm) and more complex lesions (B2/C 67%).¹²

4.3. MACE and TLR and their predicting factors

At 10 months, the differences in TLR rates trended ($p = 0.25$) higher in NSTEMI (11.3%) than in STEMI (8.3%). In contrast, in stable coronary artery disease the TLR rate was 7.0%. The

incidence of myocardial infarction was not significantly ($p = 0.5$) different between ACS patients and patients without MI at baseline. However, cardiac mortality was significantly ($p = 0.001$) higher in patients with NSTEMI/STEMI as compared to those with stable coronary artery disease. NSTEMI was the predictor for higher MACE rates ($p = 0.003$).

None of the cardiovascular risk factors such as diabetes mellitus, hypertension, and age ≥ 75 years did influence the outcome in stable patients while in STEMI or NSTEMI, diabetes mellitus ($p = 0.017$), and age ≥ 75 years ($p = 0.026$) higher MACE rates were calculated. Among the baseline lesion characteristics, B2/C vs A/B1 ($p = 0.002$) and ostial lesions ($p = 0.04$) were associated with higher MACE rates. The comparison between restenoses and de novo lesions showed a borderline difference ($p = 0.08$). MACEs trended ($p = 0.23$) higher in diffuse (9.7%) vs non-diffuse lesions (7.6%).

Table 2 – Procedural data.

	All	Asian patients	European patients	p-values**
Technical success	98.5% (1550/1574)	99.8% (438/439)	98.0% (1112/1135)	0.009
Lesions	1379	399	980	–
Lesion length	15.6 ± 7.5 mm	17.1 ± 8.2 mm	15.0 ± 7.1 mm	< 0.001
Stent length	18.1 ± 5.1 mm	18.9 ± 4.8 mm	17.8 ± 5.2 mm	< 0.001
Stent diameter	3.02 ± 0.44 mm	2.96 ± 0.44 mm	3.05 ± 0.44 mm	< 0.001
Stents deployed	1574	439	1135	–
Direct stenting	7.1% (111/1574)	23.9% (105/439)	0.5% (6/1135)	< 0.001
Deployment pressure	14.9 ± 4.3 atm	13.9 ± 6.0 atm	15.3 ± 3.4 atm	< 0.001

*Mean ± SD; ** p-values for comparison between Asian and European patients. Significant differences are marked bold.

Table 3 – MACE during hospitalization.

Parameter	Myocardial infarction			Target lesion revascularization			Cardiac death			All MACE ^a		
	Total	Asia	Europe	Total	Asia	Europe	Total	Asia	Europe	Total	Asia	Europe
STEMI	4.1% (6/148)	1.8% (1/55)	5.4% (5/93)	1.4% (2/148)	0.0% (0/55)	2.2% (2/93)	1.4% (2/148)	0.0% (0/55)	2.2% (2/93)	5.4% (8/148)	1.8% (1/55)	7.5% (7/93)
NSTEMI	1.6% (3/191)	3.8% (1/26)	1.2% (2/165)	1.6% (3/191)	0.0% (0/26)	1.8% (3/165)	1.0% (2/191)	0.0% (0/26)	1.2% (2/165)	3.7% (7/191)	3.8% (1/26)	3.6% (6/165)
No MI	1.5% (13/891)	2.8% (8/282)	0.8% (5/609)	0.8% (7/891)	0.0% (0/282)	1.1% (7/609)	0.1% (1/891)	0.4% (1/282)	0.0% (0/609)	2.0% (18/891)	2.8% (8/282)	1.6% (10/609)
Total population	1.8% (22/1230)	2.8% (10/363)	1.4% (12/867)	1.0% (12/1230)	0.0% (0/363)	1.4% (12/867)	0.4% (5/1230)	0.3% (1/363)	0.5% (4/867)	2.7% (33/1230)	2.8% (10/363)	2.7% (23/867)

^a MACE = major adverse cardiac event, N = 1230 (all recruited patients).

4.4. Asia vs Europe

Comparison of demographic and lesion data of the Asia and European patients showed a significantly higher risk situation for recurrence in the European population in all but two analyzed attributes (i.e., STEMI and lesion length) (Table 1). The procedural success rate was significantly ($p = 0.009$) higher in the Asian patients (99.8% vs 98%).

The in-hospital MACE rates between the Asian and European patients were similar ($p = 0.9$) (Table 3). At 10 months, however, MACEs occurred more often ($p < 0.001$) in the European population mainly driven by a nearly six times higher TLR rate while the combined rate of cardiac death and myocardial infarction, which is less prone to subjective decision making than TLR, was not different ($p = 0.11$) between Asia (3.8%) and Europe (6.2%). This is noteworthy in given the fact that the angiographic baseline data exhibited a negative bias with respect to these events in the European population (total occlusions 14.3% vs 9.0%, $p = 0.03$; bifurcations 19.9% vs 12.5%, $p = 0.001$; diffuse lesions 64.4% vs 28.3%, $p < 0.001$; NSTEMI 19% vs 7.2%, $p < 0.001$; ostial lesions 9.1% vs 4.8%, $p = 0.007$; lesion length 15 mm vs 17.1 mm, $p < 0.001$). The difference in target lesion revascularization and thus, MACE may at least in part be explained by the different health care systems: In many Asian countries that participated in this registry patients are required to financially contribute to the procedures. The local infrastructure with a more difficult access to the study sites may have played a role as well.

Subgroup comparison demonstrated significantly superior 10-month MACE rates in non-diabetic vs diabetic Europeans with ($p = 0.017$) or without ($p = 0.006$) acute coronary syndrome while the presence or absence of the disease had no impact on the Asian population ($p = 0.872$, diabetic Asians 5.0% vs non-diabetic Asians 4.6%). These data are in agreement with a recent publication that reported higher rates of myocardial infarction, overall deaths, and target vessel revascularization in diabetics.¹³ For another paclitaxel-eluting stent the 9-month recurrence rate trended ($p = 0.12$) higher in diabetics (13.0%) than non-diabetics (9.6%).¹⁴ Though that study enrolled only de novo lesions, the recurrence rate was higher than in the current registry, which included higher risk lesions in all comers. Higher recurrence rates in diabetics than in non-diabetics are especially common in limus-coated stents as suggested by meta-analyses.^{1,15}

Age of 75 years and above was associated with an overall inferior outcome in the acute coronary syndrome (25.4% vs 13.8%, $p = 0.03$) whereas in stable patients the difference of 12.4% vs 8.6% did not reach the level of significance ($p = 0.16$). Asian patients of at least 75 years compared to the younger ones had more MACEs overall (<75 y: 3.5% vs ≥ 75 y: 16.1%, $p = 0.002$) and in stable coronary artery disease (11.4% vs 2.7%, $p = 0.003$). In the acute coronary syndrome the difference was borderline (33.5% vs 16.5%, $p = 0.08$). In the older (25.0%) vs younger (16.5%) European patients MACE trended ($p = 0.14$) higher only in the acute coronary syndrome while in stable patients the numbers were close (11.4% vs 11.9%, $p = 0.9$). In a recent study, MACE in STEMI patients was 11.0% in patients <75 and 6.0% in those ≥ 75 years of age¹⁶ ($p < 0.005$) confirming the well known less favorable outcome in the elderly.¹⁷ It

Table 4 – 10-Month clinical outcomes.

	All patients	Asian patients	European patients	p-values**
Patients clinical follow-up [N]	92.8% (1.142/1230)	87.6% (318/363)	95.0% (824/867)	< 0.001
Re-PCI	6.8% (78/1142)	1.6% (5/318)	8.9% (73/824)	< 0.001
CABG	1.3% (15/1142)	0.0% (0/318)	1.8% (15/824)	0.015
TLR	7.8% (89/1142)	1.6% (5/318)	10.2% (84/824)	< 0.001
TLR in STEMI patients	8.3% (11/132)	2.2% (1/46)	11.6% (10/86)	0.061
TLR in NSTEMI patients	11.3% (20/177)	0.0% (0/21)	12.8% (20/156)	0.081
TLR in patients without ACS	7.0% (58/833)	1.6% (4/251)	9.3% (54/582)	< 0.001
Myocardial infarction	4.6% (53/1142)	3.1% (10/318)	5.2% (43/824)	0.135
MI in STEMI patients	8.3% (11/132)	4.3% (2/46)	10.5% (9/86)	0.226
MI in NSTEMI patients	6.2% (11/177)	4.8% (1/21)	6.4% (10/156)	0.769
MI in patients without ACS	3.7% (31/833)	2.8% (7/251)	4.1% (24/582)	0.350
Death cardiac	1.4% (16/1142)	0.9% (3/318)	1.6% (13/824)	0.414
Cardiac death in STEMI patients	4.5% (6/132)	4.3% (2/46)	4.7% (4/86)	0.936
Cardiac death in NSTEMI patients	2.8% (5/177)	4.8% (1/21)	2.6% (4/156)	0.568
Cardiac death in patients without ACS	0.7% (6/833)	0.3% (1/251)	0.9% (5/582)	0.141
MACE	11.1% (127/1142)	4.7% (15/318)	13.6% (112/824)	< 0.001
MACE in STEMI patients	14.4% (19/132)	6.5% (3/46)	18.6% (16/86)	0.060
MACE in NSTEMI patients	17.5% (31/177)	9.5% (2/21)	18.6% (29/156)	0.305
MACE in patients without ACS	9.2% (77/833)	4.0% (10/251)	11.5% (67/582)	0.001
Stent thrombosis	1.6% (18/1142)	0.6% (2/318)	1.9% (16/824)	0.110
ST in STEMI patients	0.0% (0/148)	0.0% (0/318)	0.0% (0/824)	–
ST in NSTEMI patients	2.6% (5/191)	0.0% (0/318)	0.6% (5/824)	0.402
ST in patients without ACS	1.5% (13/891)	0.6% (2/318)	1.3% (11/824)	0.241

*Mean $\pm$ SD; ** p-values for comparison between Asian and European patients. Significant differences are marked bold.

needs emphasizing that the higher MACE rates in the elderly apparently are neither lesion nor procedure related since the target lesion revascularization rates do not exhibit an age dependency.^{17,18} Typical factors that affect cardiac events encompass the co-morbidity in the elderly and the advanced stage of cardiac disease.

Among the angiographic characteristics, B2/C (13.7% vs 7.9%, $p = 0.002$) and ostial lesions (15.5% vs 10.5%, $p = 0.04$) were identified as predictors of major adverse cardiac events mainly driven by the European population while restenotic lesions showed borderline significance ($p = 0.08$). The less favorable outcome of B2/C lesions is commonly accepted¹⁹ as is the higher adverse event rate in calcified lesions. For a sirolimus-eluting stent calcification was associated with

a significantly higher (13.8% vs 6.1%) vs non-calcified lesions²⁰ and identified as an independent predictor of MACE in another trial.²¹

In patients with NSTEMI and STEMI the MACE rates were not different (17.5% vs 14.4%, $p = 0.5$). These data are somewhat lower than those from the CADILLAC trial, in which the one-year MACE rates for NSTEMI and STEMI patients were 24.0% and 16.6% ($p = 0.007$), respectively.²² In stable coronary artery disease the MACE rate was even lower (9.2%) in the current study.

It is within the nature of ‘all comers’ registry that ‘off label’ use occurs with the investigational device. According to the instructions for use, bifurcation and ostial lesions along with severely calcified lesions were described as contra-

Table 5 – 10-Month MACE relative to lesion related risk factors.

	All	p	Asian patients	p	European patients	p
Ostium	15.5% (15/97)	0.155	0.0% (0/14)	0.395	18.1% (15/83)	0.209
No ostium	10.7% (112/1044)		4.9% (15/304)		13.1% (97/741)	
B2/C	13.7% (87/637)	0.002	5.8% (10/171)	0.305	16.5% (77/466)	0.005
A/B1	7.9% (40/505)		3.4% (5/147)		9.8% (35/358)	
Restenosis	14.6% (29/198)	0.083	0.0% (0/8)	0.524	15.3% (29/190)	0.444
De novo	10.4% (98/944)		4.8% (15/310)		13.1% (83/634)	
Diffuse lesion	12.2% (75/617)	0.228	7.2% (6/83)	0.209	12.9% (69/534)	0.446
No diffuse lesion	9.9% (52/525)		3.8% (9/235)		14.8% (43/290)	
Total occlusion	14.8% (22/149)	0.129	6.9% (2/29)	0.561	16.7% (20/120)	0.288
No total occlusion	10.6% (105/993)		4.5% (13/289)		13.1% (92/704)	
Tortuosity	12.6% (15/119)	0.589	13.3% (2/15)	0.108	12.5% (13/104)	0.728
No tortuosity	11.0% (112/1023)		4.3% (13/303)		13.8% (99/720)	
Calcification	13.8% (64/463)	0.016	9.7% (6/62)	0.040	14.5% (58/401)	0.477
No calcification	9.3% (63/679)		3.5% (9/256)		12.8% (54/423)	

Significant differences are marked bold.

Fig. 1 – ACS patients in Europe and Asia and their MACE rates in subgroups of risk factors for MACE.

Fig. 2 – Non-ACS patients in Europe and Asia and their MACE rates in subgroups of patient related risk factors.

indications. Nevertheless, it is at the discretion of the treating physician to decide on a deviating clinical strategy in the best interest of the patient. The documented 'off label' use within this clinical assessment amounted to 22.2% (273/1230) when considering bifurcations and ostial lesions. When considering the presence of severe calcifications, the overall 'off label' use is approximated at 30–35%.

4.5. Limitations

Study limitations pertain mainly to the fact that with registries a less stringent control of data collection and study monitoring may introduce some inaccuracies into the study. The high follow-up rate of 92.4% and the large number of patients enrolled in this registry compensate for some of these deficits. Though further subgroup analyses would have been desirable these were not performed owing to lack of statistical power in such cases.

Moreover, it would have been beneficial to apply the Syntax score classification to our data set for lesion complexity assessment. However, this registry was designed prior to the introduction of the Syntax score. Retrospective score calculation was impossible for logistical reasons.

Electronic reminder emails to enter the 9-month clinical follow-up were not always responded too promptly. This led to the one-month delay compared to the targeted follow-up interval.

5. Summary

The current registry data confirm the results of two small RCT with the same device with respect to the occurrence of major cardiac events that are within the range of other paclitaxel-eluting devices. The incidence of myocardial infarction and cardiac death is statistically not different between European and Asian patients while target lesion revascularization differed by a factor of six, which may only in part be explained by the difference in baseline data. Thus, when comparing the data of registries between these two continents major adverse cardiac events need to be interpreted with caution.

Conflicts of interest

Prof. M. Leschke received a research grant from B. Braun for data acquisition and analysis purposes limited to this clinical assessment. Prof. M. Unverdorben and Dr. M. Waliszewski are full-time employees of B. Braun.

REFERENCES

- Stettler C, Wandel S, Allemann S, et al. Outcomes associated with drug-eluting and bare-metal stents: a collaborative network meta-analysis. *Lancet*. 2007;370:937–948.
- Möllmann H, Elsässer A, Nef H, et al. Treatment of in-stent restenosis with sirolimus-eluting-stents: results from the prospective German Cypher stent registry. *Clin Res Cardiol*. 2008;97:432–440.
- Unverdorben M, Degenhardt R, Vallbracht C, et al. PECOPS I Investigators. The paclitaxel-eluting Coroflex Please stent pilot study (PECOPS I): acute and 6-month clinical and angiographic follow-up. *Catheter Cardiovasc Interv*. 2006;67:703–710.
- Unverdorben M, Degenhardt R, Wiemer M, et al. PECOPS I Investigators. The paclitaxel-eluting Coroflex Please stent pilot study (PECOPS I): the one-year clinical follow-up. *Clin Res Cardiol*. 2007;96:803–811.
- Unverdorben M, Degenhardt R, Wiemer M, et al. PECOPS I Investigators. The paclitaxel-eluting Coroflex Please stent study (PECOPS I): the 3-year clinical follow-up. *Catheter Cardiovasc Interv*. 2009;74:674–682.
- Wiemer M, Degenhardt R, Vallbracht C, et al. PECOPS II Investigators. The paclitaxel-eluting Coroflex stent study II (PECOPS II) acute and 6-month clinical and angiographic follow-up, 1-year clinical follow-up. *J Interv Cardiol*. 2010;23(2):160–166.
- Cutlip D, Windecker S, Mehran R. Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation*. 2007;115:2344–2351.
- Arad-Yellin R, Firer M, Kahana N, Green BS. Functionalized polysulfone as a novel and useful carrier for immunization and antibody detection. *React Funct Polym*. 2003;54:5–16.
- Hancock LF, Fagan SM, Ziolo MS. Hydrophilic, semipermeable membranes fabricated with poly(ethylene oxide)-polysulfone block copolymer. *Biomaterials*. 2000;21:725–733.
- Vanholder R, Van Loo A, Ringoir S. Clinical experience with polysulfone: 10 years. *Clin Nephrol*. 1994;42:S13–S20.
- Appleby CE, Mackie K, Dzavik V, Ivanov J. Late outcomes following percutaneous coronary interventions: results from a large, observational registry. *Can J Cardiol*. 2010;26(7):e218–e224.
- Stolker JM, Kennedy KF, Lindsey JB, et al. Predicting restenosis of drug-eluting stents placed in real-world clinical practice: derivation and validation of a risk model from the EVENT registry. *Circ Cardiovasc Interv*. 2010;3(4):327–334.
- Akin I, Bufe A, Schneider S, et al. Clinical outcomes in diabetic and non-diabetic patients with drug-eluting stents: results from the first phase of the prospective multicenter German DES.DE registry. *Clin Res Cardiol*. 2010;99(6):393–400.
- Mahmud E, Ormiston JA, Turco MA, et al. TAXUS Liberté attenuates the risk of restenosis in patients with medically treated diabetes mellitus: results from the TAXUS ATLAS program. *JACC Cardiovasc Interv*. 2009;2(3):240–252.
- Fröbert O, Lagerqvist B, Carlsson J, Lindbäck J, Stenestrand U, James SK. Differences in restenosis rate with different drug-eluting stents in patients with and without diabetes mellitus: a report from the SCAAR (Swedish Angiography and Angioplasty Registry). *J Am Coll Cardiol*. 2009;53:1660–1667.
- Ciszewski A, Karcz M, Kepka C, et al. Primary angioplasty in patients > or = 75 years old with ST-elevation myocardial infarction – one-year follow-up results. *Kardiologia Pol*. 2008;66:828–833.
- Vlaar P, Lennon RJ, Rihal CS, et al. Drug-eluting stents in octogenarians: early and intermediate outcome. *Am Heart J*. 2008;155:680–686.
- Costa JR, Sousa A, Moreira AC, et al. Drug-eluting stents in the elderly: long-term (> one year) clinical outcomes of octogenarians in the DESIRE (Drug-Eluting Stents In the REal world) registry. *J Invasive Cardiol*. 2008;20:404–410.
- Ryan TJ, Faxon DP, Gunnar RM, et al. Guidelines for percutaneous transluminal coronary angioplasty. A report of the American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Subcommittee on

- Percutaneous Transluminal Coronary Angioplasty). *Circulation*. 1988;78(2):486–502.
20. Kawaguchi R, Tsurugaya H, Hoshizaki H, Toyama T, Oshima S, Taniguchi K. Impact of lesion calcification on clinical and angiographic outcome after sirolimus-eluting stent implantation in real-world patients. *Cardiovasc Revasc Med*. 2008;9(1):2–8.
21. Mori S, Yasuda S, Kataoka Y, Morii I, Kawamura A, Miyazaki S. Significant association of coronary artery calcification in stent delivery route with restenosis after sirolimus-eluting stent implantation. *Circ J*. 2009;73(10):1856–1863.
22. Cox DA, Stone GW, Grines CL, et al. Comparative early and late outcomes after primary percutaneous coronary intervention in ST-segment elevation and non-ST-segment elevation acute myocardial infarction (from the CADILLAC trial). *Am J Cardiol*. 2006;98(3):331–337.