Rapamycin Dose-Finding Study of the polymer-free YUKON^{DES}

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Prevention of restenosis by a novel drug-eluting stent system with a dose-adjustable, polymer-free, on-site stent coating
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STUDY DESIGN:

A prospective, open-label dose finding study for the evaluation of four sequentially increasing rapamycin doses in a polymer-free stent coating for the prevention of restenosis. A total of 602 patients were sequentially assigned to receive a microporous BMS (155 patients) and a rapamycin-eluting stent with a dose of 0,5% rapamycin (139 patients), 1,0% rapamycin (161 patients), 2,0% rapamycin (147 patients). Excluded were patients suffering form AMI, lesions located in the left main stem and lesions with in-stent restenosis.

Baseline demographic and clinical characteristics of the study patients

Characteristic	BMS (155 patients)	Rapamycin-eluting stent			P
		0,5% conc. (139 patients)	1,0% conc. (161 patients)	2,0% conc. (147 patients)	
Age, years	66,7 ± 10,9	65,8 ± 10,7	67,6 ± 10,3	67,4 ± 10,2	0,44
Women, %	26,5	20,9	22,4	26,5	0,57
Diabetes, %	26,5	26,6	30,4	32,7	0,58
Current smokers, %	19,4	13,7	15,5	14,3	0,53
Hypercholesterolaemia, %	67,7	73,4	77,6	75,5	0,22
Arterial hypertension, %	63,9	57,6	64,0	56,5	0,38
Previous MI, %	30,3	34,5	43,5	30,6	0,05
Previous bypass surgery, %	6,5	12,2	10,6	12,9	0,25
Unstable angina, %	47,7	33,1	42,2	43,5	0,08
Left ventricular ejection fraction, %	54,1 ± 14,3	57,2 ± 11,2	54,3 ± 13,4	54,3 ± 13,7	0,16

Stenosis characteristics

Characteristic	BMS (186 lesions)	Rapamycin-eluting stent			P
		0,5% conc. (171 lesions)	1,0% conc. (182 lesions)	2,0% conc. (171 lesions)	
Lesion length, mm	12,5 ± 6,7	12,5 ± 6,7	11,6 ± 5,6	13,0 ± 5,9	0,20
Vessel size, mm	2,96 ± 0,50	2,80 ± 0,53	2,81 ± 0,51	2,80 ± 0,49	0,01
Stenosis grade, %	60,3 ± 16,8	57,2 ± 13,6	54,4 ± 12,2	59,6 ± 13,6	0,01
Complex stenosis morphology, %*	71,5	64,3	76,4	77,2	0,03
Chronic occlusions, %	5,4	1,1	0,5	4,1	0,01
*Defined as type B2 or C lesions according to the modified American College of Cardiology grading system					

STUDY ENDPOINTS:

The primary endpoint of the study was in-segment restenosis at 6-month follow-up angiography. Secondary endpoints were the target lesion revascularization (TLR, PCI or bypass surgery) and the combined incidence of death and myocardial infarction during 1-year follow-up.

RESULTS:

Angiographic outcomes:

Follow-up angiography was performed in 484 of 598 (80,9%) eligible patients.
When compared with the BMS group, the in-segment restenosis rate demonstrated a significant dose-dependent reduction with increasing rapamycin doses (P=0,024). Consequently, the in-segment late lumen loss was lowest with 0,36 ± 0,55 mm in 2% rapamycin-eluting stent patients.

Angiographic results at follow-up

Results	BMS (147 lesions)	Rapamycin-eluting stent			P
		0,5% conc. (143 lesions)	1,0% conc. (145 lesions)	2,0% conc. (136 lesions)	
In-stent analysis					
Minimum lumen diameter, mm	1,94 ± 0,88	2,08 ± 0,81	2,23 ± 0,77	2,17 ± 0,74	0,011
Late lumen loss, mm	0,95 ± 0,76	0,68 ± 0,67	0,46 ± 0,55	0,46 ± 0,58	<0,001
Stenosis grade, %	34,3 ± 25,4	28,1 ± 22,9	24,6 ± 20,3	25,3 ± 21,0	0,001
Incidence of restenosis, % (confidence intervals)	23,8 (16,9-30,7)	15,4 (9,5-21,3)	14,5 (8,8-20,2)	11,8 (6,3-17,2)	0,012
In-segment analysis					
Minimum lumen diameter, mm	1,89 ± 0,86	1,92 ± 0,75	2,04 ± 0,72	2,00 ± 0,71	0,147
Late lumen loss, mm	0,72 ± 0,80	0,52 ± 0,62	0,37 ± 0,55	0,36 ± 0,55	<0,001
Stenosis grade, %	35,9 ± 24,6	33,7 ± 20,9	31,1 ± 18,7	31,6 ± 19,6	0,073
Incidence of restenosis, % (confidence intervals)	25,9 (18,8-32,9)	18,9 (12,5-29,3)	17,2 (11,1-23,4)	14,7 (8,8-20,7)	0,024

Clinical outcomes:

During the first 30 days after randomisation:
Two patients of the overall study population suffered from a thrombotic stent occlusion: one lesion in the 0,5% and one in the 2,0% rapamycin dose groups. None of the patients died.

During one year after randomisation:

Result:	BMS (155 patients)	Rapamycin-eluting stent			P
		0,5% conc. (139 patients)	1,0% conc. (161 patients)	2,0% conc. (147 patients)	
Death or myocardial infarction,%	3,9	1,4	3,7	2,7	0,59
TLR, %	21,5	16,4	12,6	8,8	0,006

CONCLUSION:

In comparison with BMS, rapamycin-eluting stents markedly reduced the risk of restenosis in patients with a wide range of coronary lesions. All indices of restenosis improved with increasing rapamycin doses on the stent. When compared with the BMS group, the biologic potency of the polymer-free rapamycin-eluting stent was evidenced by a maximal 43% relative reduction in the risk of angiographic in-segment restenosis, with a corresponding 59% reduction in the need for TLR. The study demonstrates that the placement of a polymer-free rapamycin-eluting stent with a microporous strut surface was feasible and safe.