

Pre-clinical Performance of the polymer-free Yukon DES

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Original Title:

Inhibition of Neointima Formation by a Novel Drug-Eluting Stent System that allows for Dose-Adjustable, Multiple, and On-Site Stent Coating

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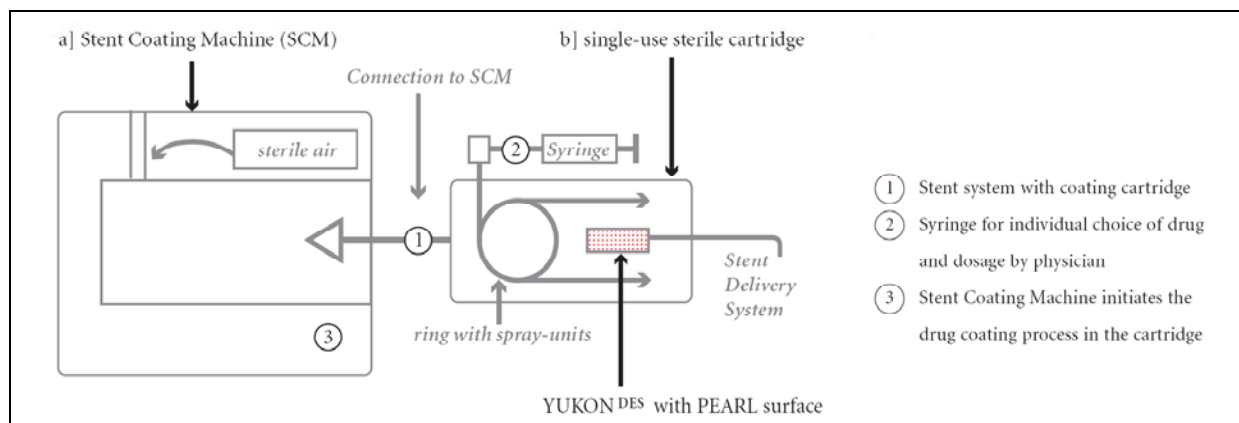
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STUDY DESIGN:

A preclinical study designed to evaluate a stent-coating system permitting individual, on-site coating of stents with a unique microporous surface allowing for individualizable, dose-adjustable and multiple coatings with identical or various compounds, designated ISAR (Individualizable drug-eluting Stent system to Abrogate Restenosis).

16 juvenile German landrace pigs underwent implantation of: bare metal stent (n = 8), Cypher sirolimus-eluting stent (SES, n = 8), and single-coated (REMP, n = 8) or double-coated rapamycin-eluting microporous stent YUKON^{DES} (REMP, n = 8). Stents in each group were equally distributed in the RCA and LAD of those 16 pigs. For determination of rapamycin blood level of stented animals, blood samples were taken at the end of PCI, as well as 4 hours and 24 hours after stenting. 30 days after stenting pigs were euthanized and their hearts underwent histomorphometric analysis. An additional 2 pigs for each time point were stented in the RCA and LAD and euthanized on days 1, 3 and 6 after stenting to determine rapamycin tissue levels.

The picture of ISAR DES platform with basic description of its components:



The ISAR DES platform consists of 2 components, the mobile coating device (Translumina Stent Coating Machine, T-SCM2003) and the disposable stent cartridge holding the premounted, microporous Translumina YUKON^{DES} stent. The microporous surface of the stent platform allows for drug deposition and retarded drug release without obligate application of a polymer.

STUDY ENDPOINTS:

Study endpoints included: pharmacokinetics of rapamycin-coated microporous stent and histomorphometrical assessment of stented vessels and assessment of endothelial coverage score and inflammation score 30 days after stenting.

RESULTS:

In each group all animals survived PCI and there was no evidence of acute or subacute stent thrombosis or occurrence of death.

Time dependent HPLC-based analysis of rapamycin elution from single-coated and dual-coated REMP stents (YUKON^{DES}, n = 3 each group) showed sustained rapamycin release for >21 days with more than two-thirds stent-based rapamycin released within the first 6 days.

Blood samples drawn immediately after the intervention and subsequently at 4 and 24 hours after stenting showed perceptible rapamycin blood levels only immediately after 4 hours and undetectable rapamycin levels after 24 hours. Peak rapamycin concentrations within the vascular wall reached 3 days after stent implantation, but there were substantial rapamycin levels detectable at 6 days after stenting.

Histomorphometrical assessment

	Bare-Metal	SES	Single REMP	Dual REMP
Area within internal elastic membrane, mm	5,05 ± 0,68	4,49 ± 1,74	4,39 ± 1,31*	4,67 ± 1,46
Neointimal area, mm	2,32 ± 0,95	1,62 ± 0,94*	1,73 ± 0,87*	1,61 ± 0,65*
Diameter stenosis, %	45,9 ± 17,1	36,2 ± 13,9*	38,4 ± 14,1*	33,5 ± 10,3*
Mean injury score	1,71 ± 0,62	1,82 ± 0,75	1,98 ± 0,518	1,96 ± 0,51

*P<0,05 compared to corresponding bare metal stent values

P=NS between all values of the various drug-eluting stent platforms

Other parameters 30 days after stenting

	Bare-Metal	SES	Single REMP	Dual REMP
Endothelial coverage score	2,67 ± 0,49	2,52 ± 0,73	2,76 ± 0,44	2,88 ± 0,33
Inflammation score	0,78 ± 1,09	1,95 ± 1,0*	0,6 ± 0,89	0,55 ± 0,79

* P<0,05 vs. bare-metal and single and dual REMP stents

CONCLUSION:

In this animal model of vascular injury in the absence of atherosclerotic lesions, there was no statistically significant difference of REMP (YUKON^{DES}) on the magnitude of the inhibition of in-stent neointimal formation and diameter stenosis compared with SES (Cypher). Assessment of strut-associated inflammation showed a significantly increased score for SES (Cypher), whereas there was no detectable difference between bare-metal and REMP (YUKON^{DES}) stents. These data show that the Translumina drug-eluting stent platform as a novel concept for stent coating allows for a safe, effective, on-site stent coating process, thus justifying further clinical evaluation to decrease in-stent restenosis in humans.