



Innovations in Cardiovascular Interventions



December 7-9, 2008 | Tel-Aviv, Israel



Drug Eluting Balloon SeQuent[®] Please Results of the PEPCAD Clinical Program

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Potential conflicts of interest

Speaker's name: Dr. Bodo Cremers, MD

I have the following potential conflicts of interest to report:

Consulting & speaker honoraria:

B. Braun Vascular Systems (Berlin, Germany)

Local Drug Delivery: Paclitaxel-DEB vs. DES

Drug-Eluting Balloon

- Immediate release
- Short-lasting exposure
- ~ 300 - 600 μg dose
- No polymers
- Wiped off the balloon surface
- Premounted stent optional

Drug-Eluting Stent

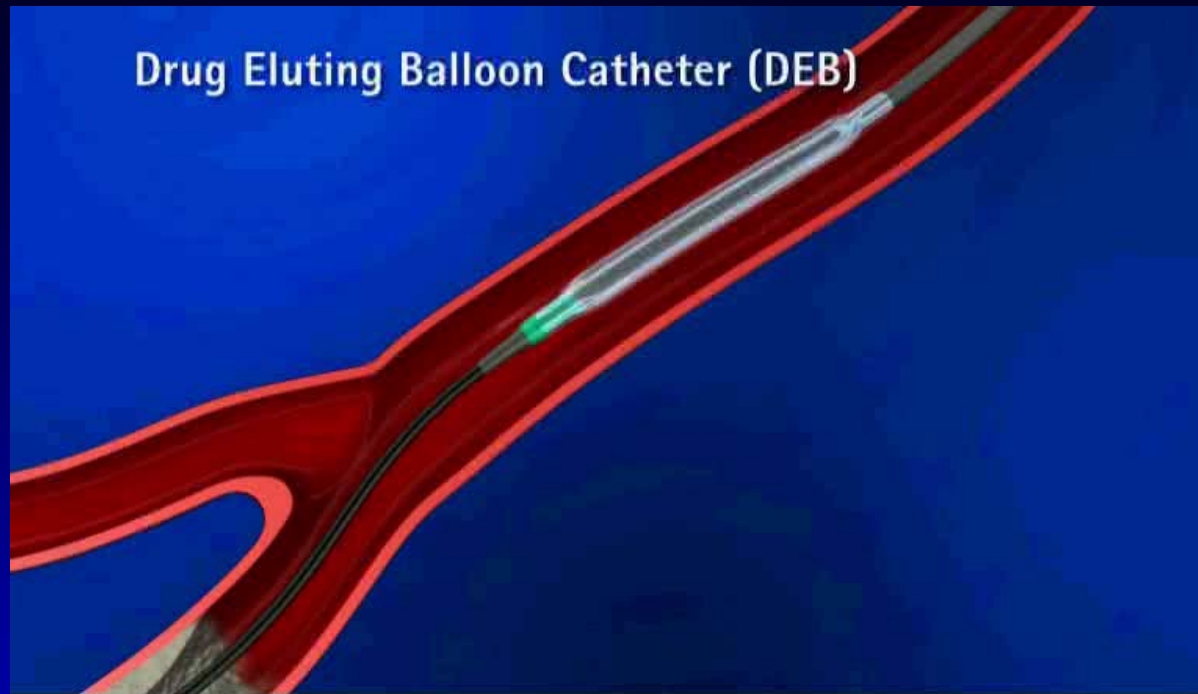
- Slow release
- Persistent drug exposure
- ~ 100 - 200 μg dose
- Polymer
- Diffusion from stent struts
- Stent mandatory



- Conventional angioplasty balloon catheters
- Coated with paclitaxel
(+ contrast medium as matrix builder and release supporting additive)
- Controlled dose, homogeneity of coating, non-toxic excipients



Local Drug Delivery: Possibilities of a Drug-Eluting Balloon (DEB)



- **Non-**
- -> ad
- -> del
- -> no
- -> no
- -> hor

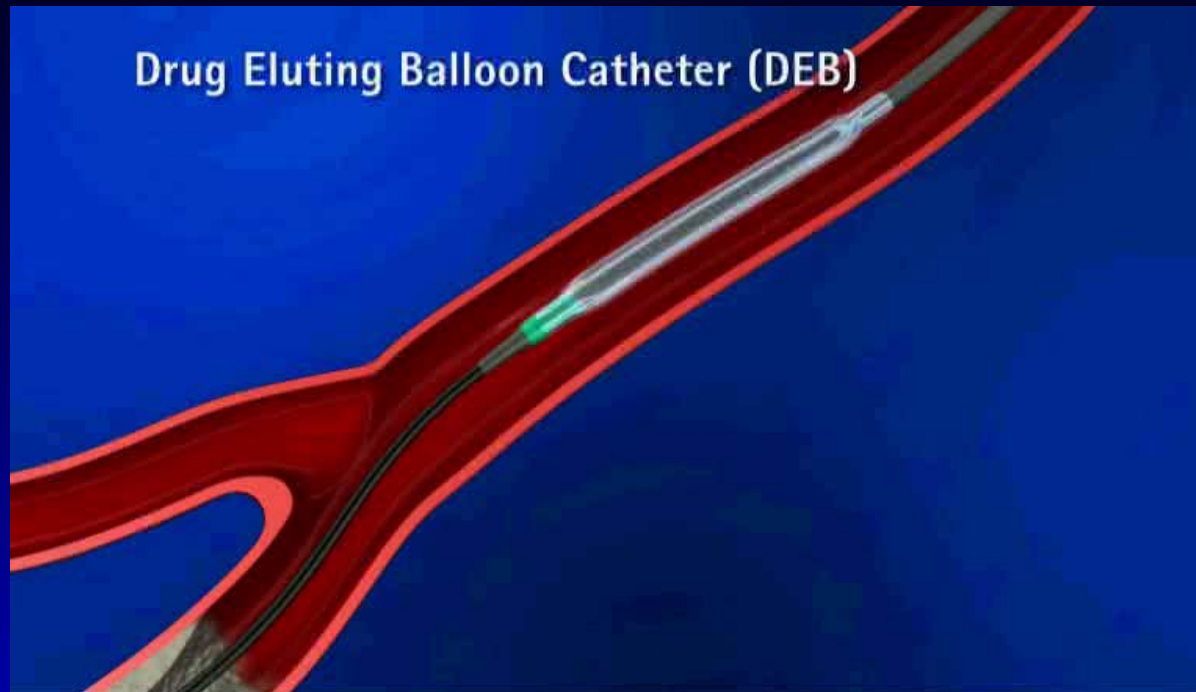


ous vessels)
ation

DEB Paccocath



Local Drug Delivery: Possibilities of a Drug-Eluting Balloon (DEB)



- **Non-Stent based delivery of antiproliferative drugs with DEB**
- -> additional flexibility and efficacy
- -> deliver drugs to vessel areas not directly covered by the stent (edges, small vessels, tortuous vessels)
- -> no sustained drug release from stent struts to allow for early healing and re-endothelialization
- -> no polymers or other sustained release technology inducing inflammation
- -> homogenous drug distribution to the arterial wall

FIM Treatment of Coronary In-Stent Restenosis with DEB

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Treatment of Coronary In-Stent Restenosis with a Paclitaxel-Coated Balloon Catheter

Bruno Scheller, M.D., Christoph Hehrlein, M.D., Wolfgang Bocksch, M.D., Wolfgang Rutsch, M.D., Dariush Haghi, M.D., Ulrich Dietz, M.D., Michael Böhm, M.D., and Ulrich Speck, Ph.D.

Primary endpoint (late lumen loss in-segment)

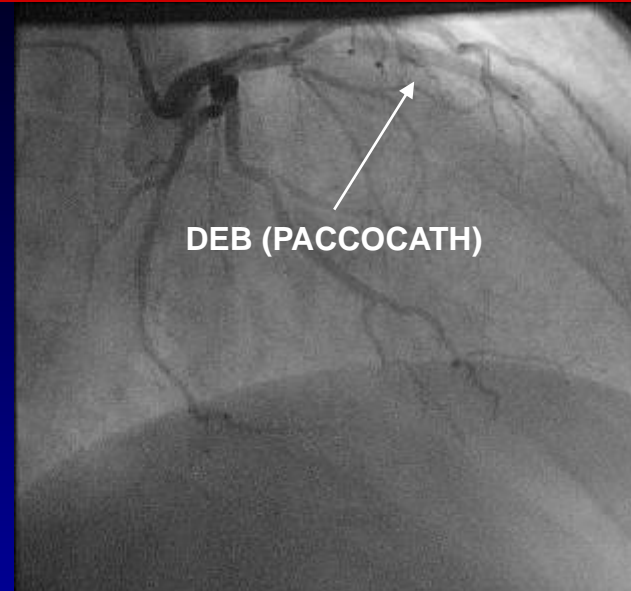
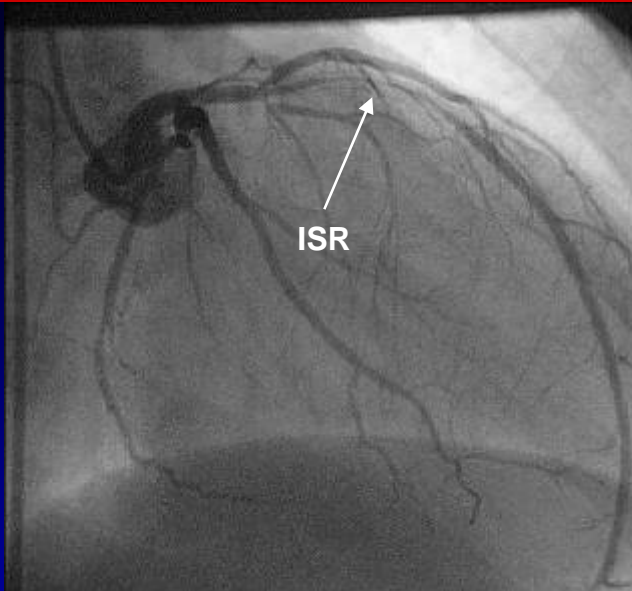
Uncoated balloon	PACCOCATH
0.74 ± 0.86 mm	0.03 ± 0.48 mm

Table 2. Procedural Data and Angiographic Findings during Intervention and at 6 Months (Intention-to-Treat Analysis).*

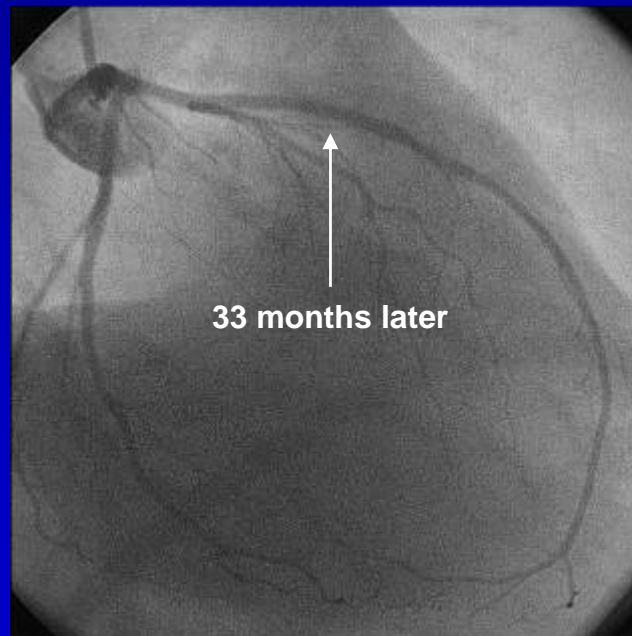
Variable	Uncoated Balloon (N=26)	Paclitaxel-Coated Balloon (N=26)	Absolute Difference (95% CI)	P Value
Angiographic findings at 6 mo				
No. of patients	23	22		
Minimal luminal diameter — mm				
In-stent	1.60±0.89	2.31±0.66	-0.71 (-1.18 to 0.24)	0.004
In-segment	1.57±0.86	2.22±0.57	-0.65 (-1.09 to 0.21)	0.005
Late luminal loss — mm				
In-stent	0.76±0.86	0.09±0.49	0.67 (0.24 to 1.09)	0.003
In-segment	0.74±0.86	0.03±0.48	0.70 (0.28 to 1.12)	0.002
Restenosis — no. (%)				
In-stent	10 (43)	1 (5)	0.39 (0.15 to 0.63)	0.002
In-segment	10 (43)	1 (5)	0.39 (0.15 to 0.63)	0.002



PACCOCATH ISR I/II: Case Report, Follow-up 3 years

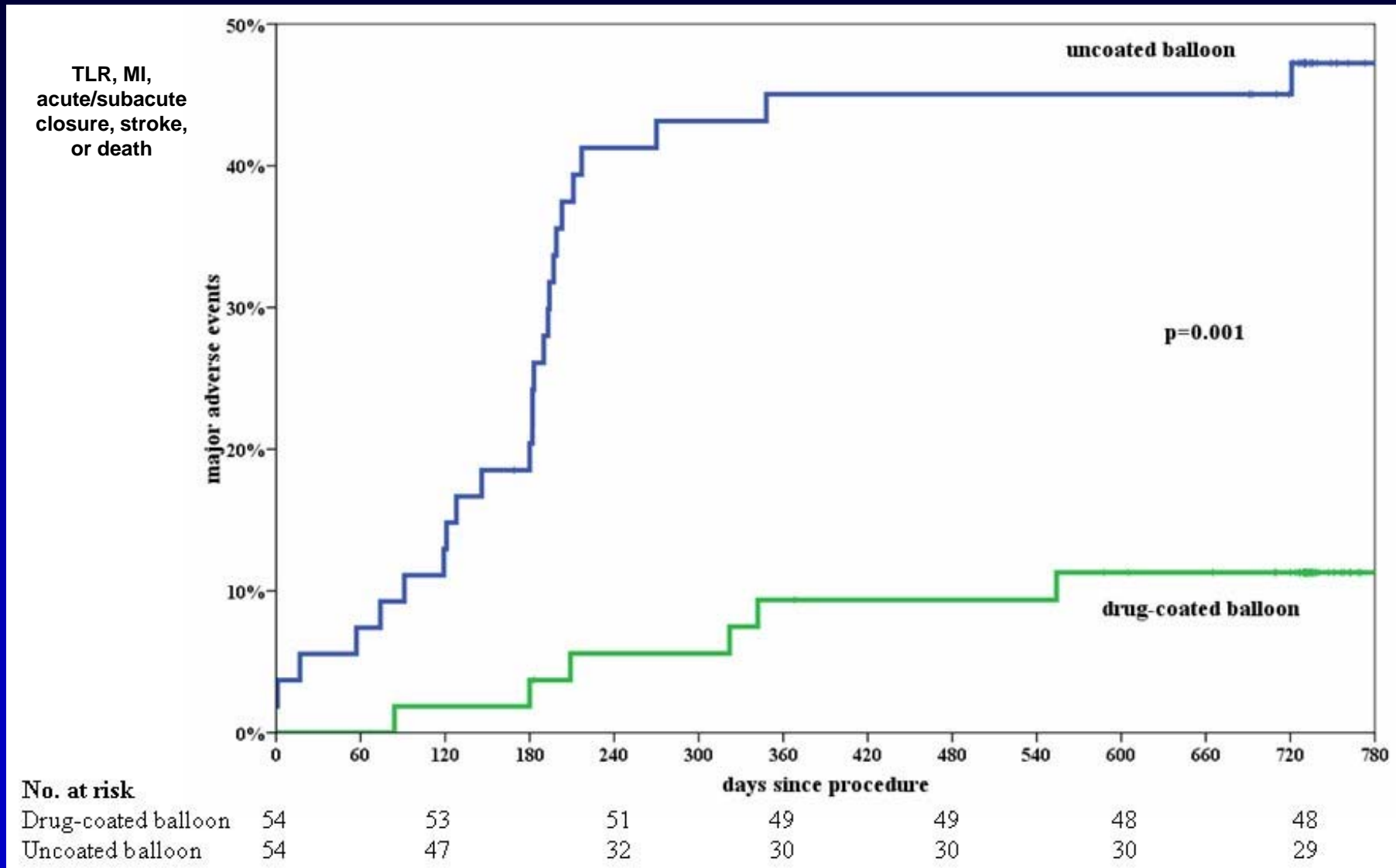


Treatment of coronary ISR with Paclitaxel-coated PACCOCATH Balloon Catheter

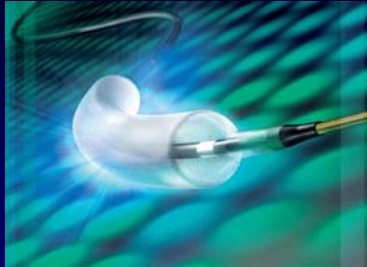


PACCOATH ISR I/II

MACE (Major Adverse Cardiac Events), 24 month follow-up



SeQuent[®] Please: Next Generation DEB



SeQuent[®] (uncoated balloon)



SeQuent[®] Please* (Paclitaxel coated balloon)

***SeQuent[®] Please (B.Braun Vascular Systems, Berlin, Germany) is manufactured based on the PACCOCATH technology with 3 μg paclitaxel / mm^2 ; CE mark expected in Q1 2009**

PACCOATH[®]-Technology: The Matrix Coating of SeQuent[®] Please

PACCOATH technology creates a unique matrix coating

pure paclitaxel



matrix coating:

paclitaxel + hydrophilic spacer

(iopromide = Ultravist[®])



the hydrophilic spacer leads to:

- porous coating with a high contact surface between the lipophilic drug molecules and the vessel wall
- uniform and complete release of the target drug dose after first balloon expansion

that guarantees:

- a high bioavailability of paclitaxel on the target side for rapid drug absorption by the vessel wall

PEPCAD I SVD

“The Paclitaxel-Eluting PTCA-Balloon Catheter to Treat Small Vessel Coronary Artery Disease. A Pilot Study”

prospective, non-randomized, multi-center, one-arm phase-II pilot study
De-novo lesions, reference diameter 2.25 - 2.8 mm; SeQuent Please

PI: M. Unverdorben, Clinical Research Institute, Rotenburg a.d.F. / Richmond, VA

CRO und Core Lab: R. Degenhardt, Clinical Research Institute, Rotenburg a.d.F.

**Presented at TCT October 24, 2007, Washington DC
Late Breaking Trials: PEPCAD I SVD and PEPCAD II ISR**

PEPCAD I SVD

Primary Variable

- 6-month late lumen loss

Secondary Variables

- Procedural success ($\leq 30\%$ stenosis)
- 6-month binary restenosis rate
- 6-month MACE
- MACE at 1 and 3 years

Inclusion Criteria

- Stable or unstable angina (no MI)
- De-novo lesion in native coronary arteries

Medication

- ASS ≥ 100 mg daily
- Clopidogrel 75 mg daily
 - 1 month DEB only
 - 3 months DEB with additional non-DES stent

PEPCAD I SVD – QCA, 6 months FU

ITT, n=120

Diabetic patients	41 / 120 (34.2 %)
Reference diameter	2.36 ± 0.19 mm
Lesion length	11.46 ± 4.72 mm
MLD pre PCI MLD post PCI	0.71 ± 0.25 mm 1.89 ± 0.30 mm
Follow-up	6.4 ± 1.3 months
Control angiography	104 / 120 (86.7 %)
Late lumen loss	0.32 ± 0.56 mm
Binary restenosis in-segment	18 / 104 (17.3 %)
Binary restenosis in-lesion	17 / 104 (16.3 %)
TLR	14 / 120 (11.7 %)
Total MACE	18 / 120 (15.0 %)

PEPCAD I SVD – Outcome, 6 months FU

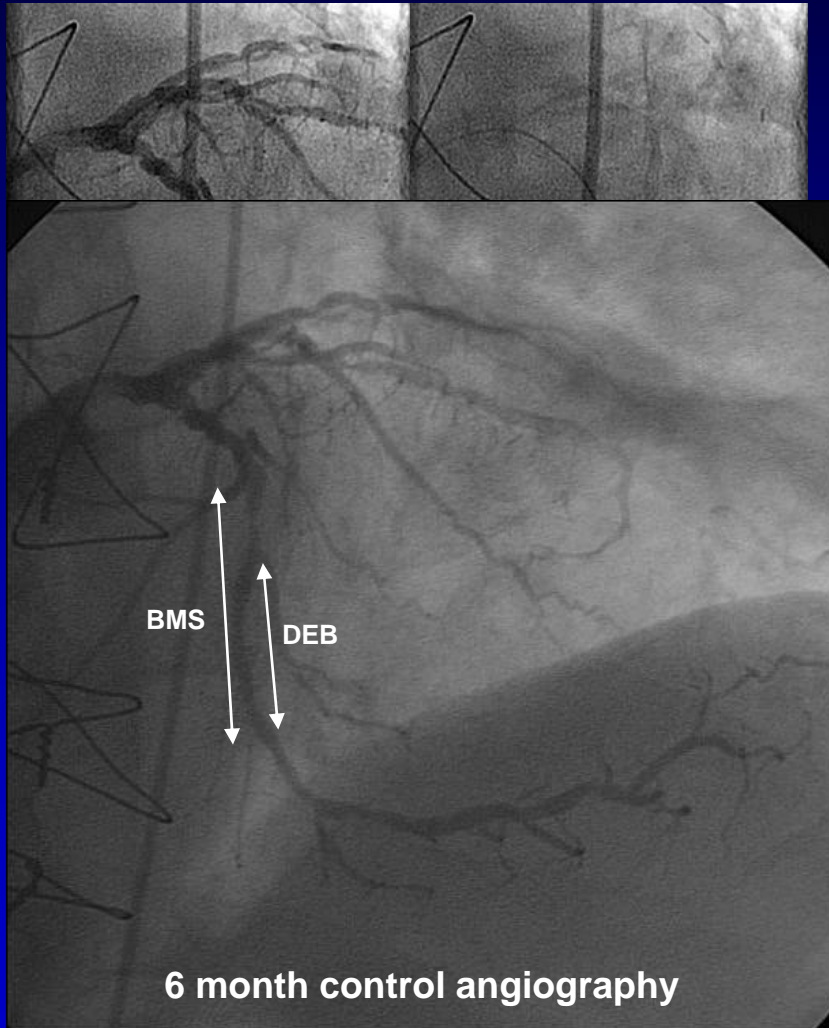
	DEB only	DEB & BMS	p
n	82	32	
Follow-up	6.4 ± 1.2 months	6.5 ± 1.5 months	0.9
Control angiography	73 (89 %)	29 (91 %)	1
Late lumen loss	0.18 ± 0.38 mm	0.73 ± 0.74 mm	0.0006
Binary restenosis in-segment	4 / 73 (5.5 %)	13 / 29 (44.8 %)	<0.0001
Binary restenosis in-lesion	4 / 73 (5.5 %)	12 / 29 (41.3 %)	<0.0001
TLR	4 (4.9 %)	9 (28.1 %)	0.001
Stent thromboses and TLR	N/A	2 (6.3%)	
Myocardial infarction	1 (1.2 %)	1 (3.3 %)	1
Death	0 (0 %)	0 (0 %)	1
Total MACE	5 (6.1 %)	12 (37.5 %)	<0.0001

PEPCAD I SVD – DEB + BMS

Geographic Mismatch

DEB 2.5 17 mm

BMS 2.5 25 mm



	Restenosis (N=13)	No restenosis (N=16)	p
Geographic mismatch	10 / 13 (77 %)	3 / 16 (19 %)	0.029
Total stent length	19.4 ± 8.4 mm	14.4 ± 10.2 mm	0.035
Balloon length – stent length	-2.31 ± 10.72 mm	2.75 ± 7.71 mm	0.096

PEPCAD I SVD - Outcome

Clinical follow-up 12 months, as treated

	SeQuent Please	SeQuent Please + BMS	p
Number of patients	82	32	
Target lesion revascularization	4 (4.9 %)	9 (28.1 %)	0.0005
Myocardial infarction	1 (1.3 %)	1 (3.1 %)	0.49
Death	0	0	
Stent thrombosis	0	2(6.3 %)	0.14
Target lesion revascularization, myocardial infarction, stent thrombosis, or death	5 (6.1 %)	12 (37.5 %)	<0.0001

PEPCAD I SVD: Conclusion

“The Paclitaxel-Eluting PTCA-Balloon Catheter to Treat Small Vessel Coronary Artery Disease”

SeQuent[®] Please for the treatment of small coronary vessels

- Safe, high procedural success rate
- DEB only
 - 5.5 % restenosis rate
- DEB + BMS
 - additional stenting in 28 % of patients
 - no geographical mismatch: 19 % restenosis
 - geographical mismatch
 - high recurrence rates
 - DEB must overlap the stented area!



PEPCAD II ISR: FIM Comparison to DES

“The Paclitaxel-Eluting PTCA-Balloon Catheter in Coronary Artery Disease to Treat In-Stent Restenoses: A Comparison to the Paclitaxel-Eluting Taxus™ Stent”

prospective, randomized, multi-center, two-armed phase-II study
Taxus vs. SeQuent Please in coronary ISR

PI: M. Unverdorben, Clinical Research Institute, Rotenburg a.d.F. / Richmond, VA
CRO und Core Lab: R. Degenhardt, Clinical Research Institute, Rotenburg a.d.F.

Presented at TCT October 24, 2007, Washington DC
Late Breaking Trials: PEPCAD I SVD and PEPCAD II ISR



PEPCAD II ISR

Primary Variable

- 6-month late lumen loss

Secondary Variables

- Procedural success ($\leq 30\%$)
- 6-month binary restenosis rate
- 6-month MACE
- MACE at 1 and 3 years

Inclusion Criteria

- Stable or unstable angina (no MI)
- ISR in native coronary arteries

Medication

- ASS ≥ 100 mg daily
- Clopidogrel 75 mg daily
 - 3 months DEB
 - 6 months DES

PEPCAD II ISR

ITT, n=131

	SeQuent Please	Taxus	p
n	66	65	
1-vessel disease	28.8 %	35.4 %	0.7
2-vessel disease	40.9 %	35.4 %	
3-vessel disease	30.3 %	29.2 %	
Lesion length	15.7 ± 6.6 mm	15.4 ± 6.6 mm	0.8
Mehran I	31 (47.0 %)	25 (38.5 %)	0.7
Mehran II	20 (30.3 %)	26 (40.0 %)	
Mehran III	14 (21.2 %)	12 (18.5 %)	
Mehran IV	1 (1.5 %)	2 (3.1 %)	
MLD pre PCI	0.74 ± 0.27 mm	0.77 ± 0.30 mm	0.6
Stenosis pre PCI	74 ± 9 %	73 ± 9 %	0.5
MLD post PCI	2.30 ± 0.40 mm	2.56 ± 0.41 mm	<0.0001
Stenosis post PCI	20 ± 10 %	11 ± 8 %	<0.001

PEPCAD II ISR - Outcome, 6 months FU

Real Treatment, n=126

	SeQuent Please	Taxus	p
n	66	60	
Follow-up	6.2 ± 0.8	6.2 ± 0.8	0.7
Control angiography	58 (87.9 %)	54 (90.0 %)	0.8
Late lumen loss	0.19 ± 0.38	0.47 ± 0.71	0.03
Binary restenosis in segment	2 / 58 (3.4 %)	11 / 54 (20.4 %)	0.007
TLR	2 / 64 (3.1 %)	10 / 60 (16.7 %)	0.02
Myocardial infarction	0 / 64 (0.0 %)	1 / 60 (1.7 %) <small>NSTEMI due to side branch occlusion</small>	1
Death	2 / 64 (3.1 %) <small>1 non-cardiac, 1 cardiac but not lesion related</small>	1 / 60 (1.7 %) <small>non-cardiac death</small>	1
MACE (w / o noncardiac death)	3 / 64 (4.7 %)	11 / 60 (18.3 %)	0.02

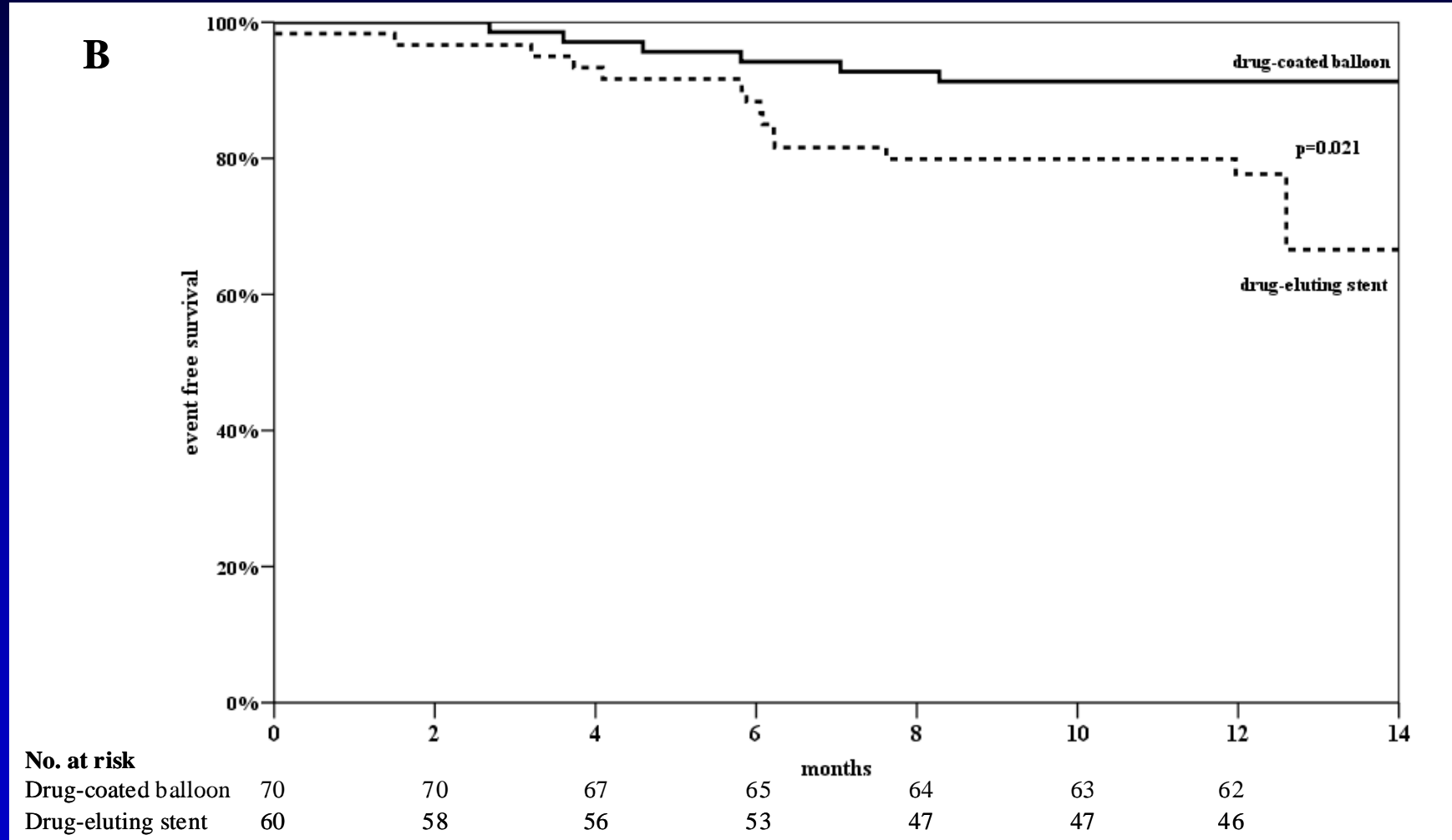
PEPCAD II ISR - Outcome

Clinical follow-up 12 months

	SeQuent Please	Taxus	p
n	66	65	
Target lesion revascularization	4 (6.3%)	10 (15.4%)	0.08
Myocardial infarction	0	1 (1.5%)	0.31
Death cardiac / non-cardiac	2 (3.0%) 1 (1.5%) / 1 (1.5%)	3 (4.6%) 0 / 3 (4.6%)	0.64 0.32 / 0.30
Stent thrombosis	0	0	
Target lesion revascularization, myocardial infarction, stent thrombosis, or cardiac death	5 (7.6%)	11 (16.9%)	0.10
Target lesion revascularization, myocardial infarction, stent thrombosis, or all-cause death	6 (9.1%)	14 (21.5%)	0.05

PEPCAD II ISR - Outcome

Freedom from stent thrombosis, target lesion revascularization, myocardial infarction, and death



PEPCAD II ISR: Conclusion

“The Paclitaxel-Eluting PTCA-Balloon Catheter in Coronary Artery Disease to Treat In-Stent Restenoses: A Comparison to the Paclitaxel-Eluting Taxus™ Stent”

SeQuent® Please for the treatment of coronary in-stent restenosis

- Safe, high procedural success rate
- DEB (SeQuent® Please) avoids the stent-in-stent approach with a second layer of metal in a native coronary artery
- Confirms the findings of PACCOATH ISR I and II trials
- Sequent® Please superior to Taxus® in the treatment of ISR
- DEB reduces anti-platelet therapy compared to DES



SeQuent[®] Please: Conclusion

Proven clinical safety + efficacy

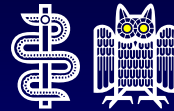
- Treatment of coronary ISR
- De-novo and restenotic lesions in PAVD
- De-novo lesions in small coronary vessels
 - DEB only: 5.5 % restenosis rate
 - DEB + BMS: overlap the stented area (geographic miss)
- No coating-related adverse events observed
- Handling identical to uncoated catheter

Further indications

- Diabetics (PEPCAD IV)
- Bifurcations (PEPCAD V)
- CTO (CTO Pilot)
- STEMI (PEPCAD AMI Pilot)
- Pediatric cardiology
- DEB with pre-mounted stent – alternative to DES ? (PEPCAD III)

Thank you for your attention !

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Bianca Werner

B.Braun Vascular Systems (Berlin)
Dr. Michael Boxberger, Dr. Michael Kühler

Institut für Medizintechnologie GmbH
(Magdeburg), **Dr. Dirk Mahnkopf**

Anakat GmbH (Berlin)
InnoRa GmbH (Berlin)

Clinical trials

CRO: Parexel (Berlin), Gimbel (Saarlouis), IKKF (München), CRI (Rotenburg)

Core Lab: Dietz (Wiesbaden), Degenhardt (Rotenburg), Beregi (Lille, FR)

Peripheral: Tepe (Tübingen), Zeller (Bad Krozingen), Ricke (Berlin), Albrecht (Berlin), Hosten (Greifswald)

Coronary: Antoni (München), Bocksch (Berlin), Buerke (Halle), Figulla (Jena), Haghi (Mannheim), Hamm (Bad Nauheim), Hehrlein (Freiburg), Hengstenberg (Regensburg), Heuer (Dortmund), Kleber (Berlin), Kücherer (Heidelberg), Leschke (Esslingen), Mathey (Hamburg), Nienaber (Rostock), Rutsch (Berlin), Schieffer (Hannover), Vallbracht (Rotenburg), Werner (Darmstadt), Zeymer (Ludwigshafen)

Barragan (Marseille, FR), Bronzvaer (Amsterdam, NL), Coste (Pessac, FR), Diaz (Huelva, ES), Eeckhout (Lausanne, SUI), Garcia (Madrid, ES), Huret (Caen, FR), Janek (Prag, CZ), Olivecrona (Lund, S), Rosli (Kuala Lumpur, MA), Safari (Pulau Pinang, MA), Sim (Kuching, MA), Unverdorben (USA), Vrolix (Gent, BE), Wan (Kuala Lumpur, MA), Wheeldon (Sheffield, UK), Wijns (Aalst, BE)



PACLITAXEL - RELEASING CORONARY BALLOON CATHETER



Balloon diameter	Balloon length	Order number
2.5 mm	10 mm	5022200
3.0 mm	10 mm	5022201
3.5 mm	10 mm	5022202
4.0 mm	10 mm	5022204*
2.0 mm	15 mm	5022205
2.5 mm	15 mm	5022206
2.75 mm	15 mm	5022207*
3.0 mm	15 mm	5022208
3.5 mm	15 mm	5022210
4.0 mm	15 mm	5022211*
2.0 mm	17 mm	5022212
2.5 mm	17 mm	5022213
2.75 mm	17 mm	5022214*
3.0 mm	17 mm	5022215
3.5 mm	17 mm	5022218
4.0 mm	17 mm	5022219*
2.0 mm	20 mm	5022220
2.5 mm	20 mm	5022221
2.75 mm	20 mm	5022222*
3.0 mm	20 mm	5022223
3.5 mm	20 mm	5022225
4.0 mm	20 mm	5022227*
2.5 mm	26 mm	5022230
2.75 mm	26 mm	5022231*
3.0 mm	26 mm	5022232
3.5 mm	26 mm	5022234
2.5 mm	30 mm	5022240
3.0 mm	30 mm	5022242
3.5 mm	30 mm	5022243

Order information

*Please contact your product specialist for ordering information.