"Paclitaxel-Eluting PTCA-Balloon in Combination with the Coroflex Blue Stent vs the Sirolimus Coated Cypher Stent in the Treatment of Advanced Coronary Artery Disease"

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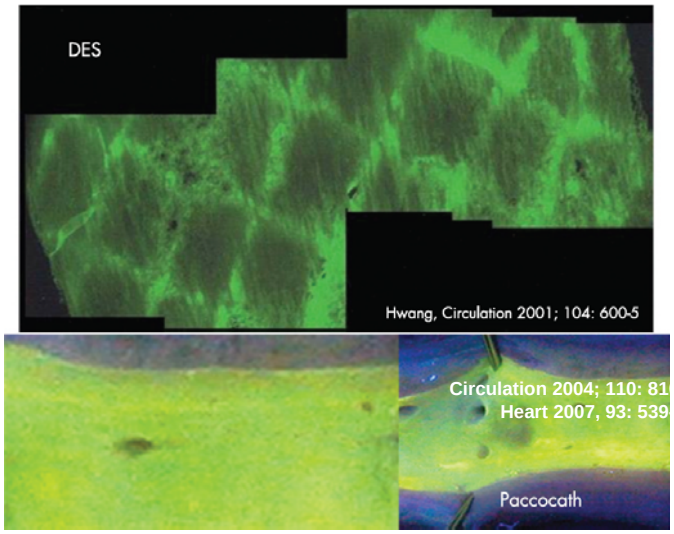
Presenter Disclosure Information: PEPCAD III

KERCKHOFF KLINIK

Consulting or speaker honorarium

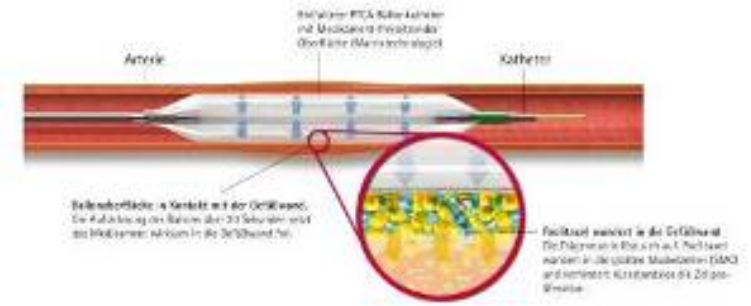
- Braun
- Cordis
- Medtronic
- Abbott

Drug-Eluting Balloon (DEB)



Drug Eluting Stent

- Slow release
- Persistent exposure
- ~ 100 - 200 µg dose
- Polymer



Drug Eluting Balloon

- Immediate release
- Short-lasting exposure
- ~ 300 - 600 µg dose
- No polymers

- **Treatment of coronary in-stent restenosis**
  - Superior to POBA and DES
    - [New Engl J Med 2006,355:2113-24. Clin Res Cardiol 2008;97:779-81. Circulation 2009;119:2986-94]
- **De-novo and restenotic lesions in SFA**
  - Superior to conventional PTA
    - [N Engl J Med 2008;358:689-99. Circulation 2008;118:1358-65]
- **Coronary de-novo lesions: DEB with BMS?**

Objective and Study Design

Comparison of the combination of a Paclitaxel-Coated Balloon + Bare-Metal Stent (DEB+BMS, 'Coroflex® DEBlue') with the Sirolimus-Eluting Cypher® (DES) stent in the treatment of de-novo stenoses in native coronary arteries.

Prospective, randomized, multi-center, two-armed phase-II pilot study conducted in Europe.

Design: non-inferiority versus Cypher®

Inclusion and Exclusion Criteria

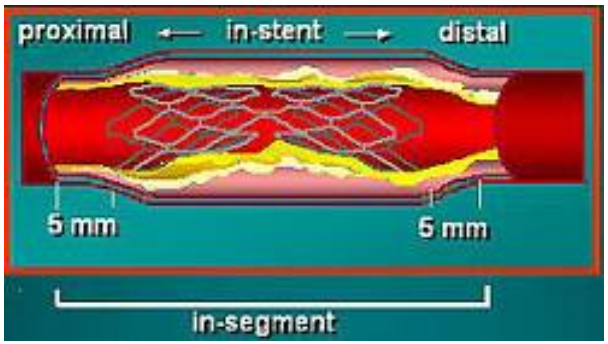
- **Inclusion Criteria**
  - Patients with stable or unstable angina or documented ischemia due to a significant lesion in a native coronary artery
  - Intention to treat one lesion with one stent
  - Significant stenoses in native coronary arteries with nominal stent diameters between ≥ 2.5 mm and ≤ 3.5 mm and < 24 mm in length

- **Exclusion Criteria**
  - Unprotected left main
  - In stent restenosis
  - PCI 6 months prior to enrolment
  - Indication for more than one lesion to treat
  - Intended bifurcational stenting
  - Chronic total occlusions
  - Art. / vein grafts
  - Chronic anticoagulation required
  - Acute MI (STEMI, NSTEMI)
  - Cardiogenic shock

Primary and Secondary Endpoints

Primary Endpoint

- Late lumen loss (in stent) at 9 months*



Secondary Endpoints

- Procedural success
- 30-day complication rate (by phone)
- Percent diameter stenosis at 9 months
- Binary restenosis rate at 9 months
- MACE rate at 9 months, 1 & 3 years
- Indication for premature follow-up

* Assessed by an independent, blinded Core-Lab (U. Dietz).

Medication

Medication before Intervention

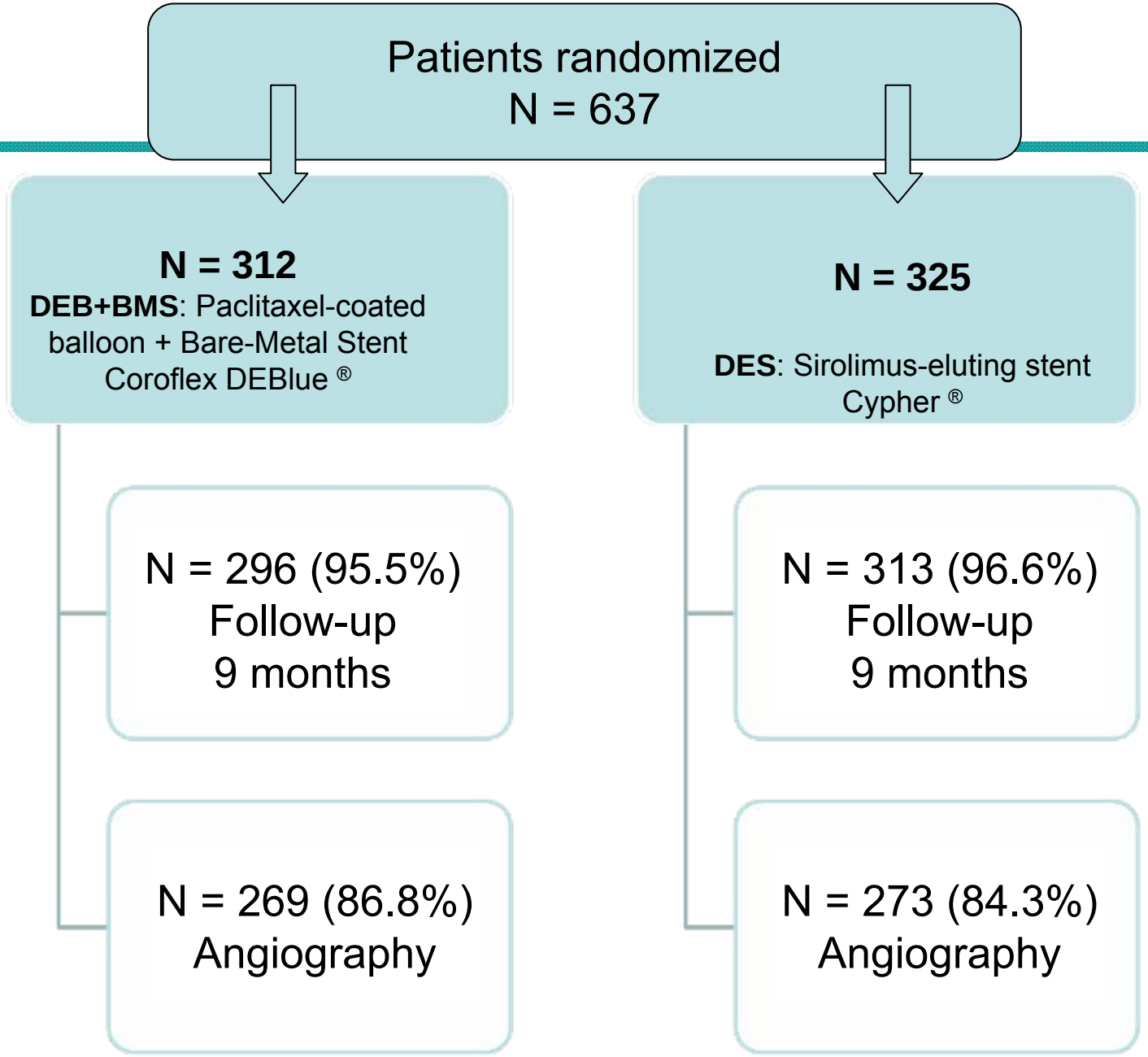
- ASA
- loading dose Clopidogrel of 300 mg > 6 hours before
  or 600 mg < 6 hours before the procedure

Medication during Intervention

- Heparin according to ESC guidelines
- GP IIb/IIIa and bivalirudin local clinical routine

Medication post intervention

- ASA 100mg to 325 mg 1x daily
- Clopidogrel 75 mg/d for 6 months


Patients randomized
N = 637
N = 312
DEB+BMS: Paclitaxel-coated balloon + Bare-Metal Stent Coroflex DEBlue ®
N = 325
DES: Sirolimus-eluting stent Cypher ®
N = 296 (95.5%)
Follow-up
9 months
N = 313 (96.6%)
Follow-up
9 months
N = 269 (86.8%)
Angiography
N = 273 (84.3%)
Angiography

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Baseline Clinical Characteristics

	DEB+BMS Coroflex DEBlue®	DES Cypher®	P-value
Age	63.9 ± 10.2	65.1 ± 9.2	0.16
Female	28.2 %	21.8 %	0.06
Diabetes mellitus	27.1 %	27.7 %	0.87
Hypertension	74.8 %	80.1 %	0.11
Hyperlipidemia	66.8 %	66.5 %	0.93
Smoker Current smoker	61.3 % 49.7 %	58.3 % 37.3 %	0.48 <0.05
Stable Angina	75.0 %	73.1 %	0.59
Prior MI	15.1 %	14.8 %	0.93
Prior PCI	21.5 %	22.2 %	0.82
Renal insuffiency	6.5 %	6.2 %	0.90

Intention-to-treat analysis

Angiographic Baseline Characteristics

	DEB+BMS Coroflex DEBlue®	DES Cypher®	P-value
1- Vessel	60.1 %	55.6 %	0.08
2-Vessel	23.8 %	21.3 %	
3-Vessel	16.1 %	23.1 %	
Prox. LAD	14.8%	15.1%	0.91
TIMI flow 3	84.2%	86.1%	0.51
% Diameter Stenosis	83.7 ± 10.2	83.0 ± 10.1	0.30

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Intention-to-treat analysis

Stent Implantation

	DEB+BMS Coroflex DEBlue®	DES Cypher®	P-value
Stent length [mm]	16.5 ± 4.0	16.5 ± 4.6	0.24
Stent diameter [mm]	3.1 ± 0.4	3.1 ± 0.4	0.78
Inflation pressure [bar]	14.1 ± 2.0	14.6 ± 2.5	< 0.01
Inflation duration [sec]	51.9 ± 20.7	25.0 ± 14.8	< 0.0001
Direct Stenting	46.6 %	44.4%	0.58

Intention-to-treat analysis

Quantitative Coronary Angiography

	DEB+BMS Coroflex DEBlue®	DES Cypher®	P-value
Reference diameter	2.87 ± 0.38	2.87 ± 0.37	0.68
MLD before	0.67 ± 0.37	0.67 ± 0.38	0.97
MLD final In-stent In-segment	 2.59 ± 0.40 2.16 ± 0.48	 2.62 ± 0.36 2.16 ± 0.43	 0.41 0.98
MLD 9 months In-stent In-segment	 2.17 ± 0.63 1.95 ± 0.62	 2.46 ± 0.49 2.05 ± 0.50	 < 0.0001 0.07
Late Lumen Loss In-stent In-segment	 **0.41 ± 0.51 mm** **0.20 ± 0.52 mm**	 **0.16 ± 0.39 mm** **0.11 ± 0.40 mm**	 **<0.001** **0.06**

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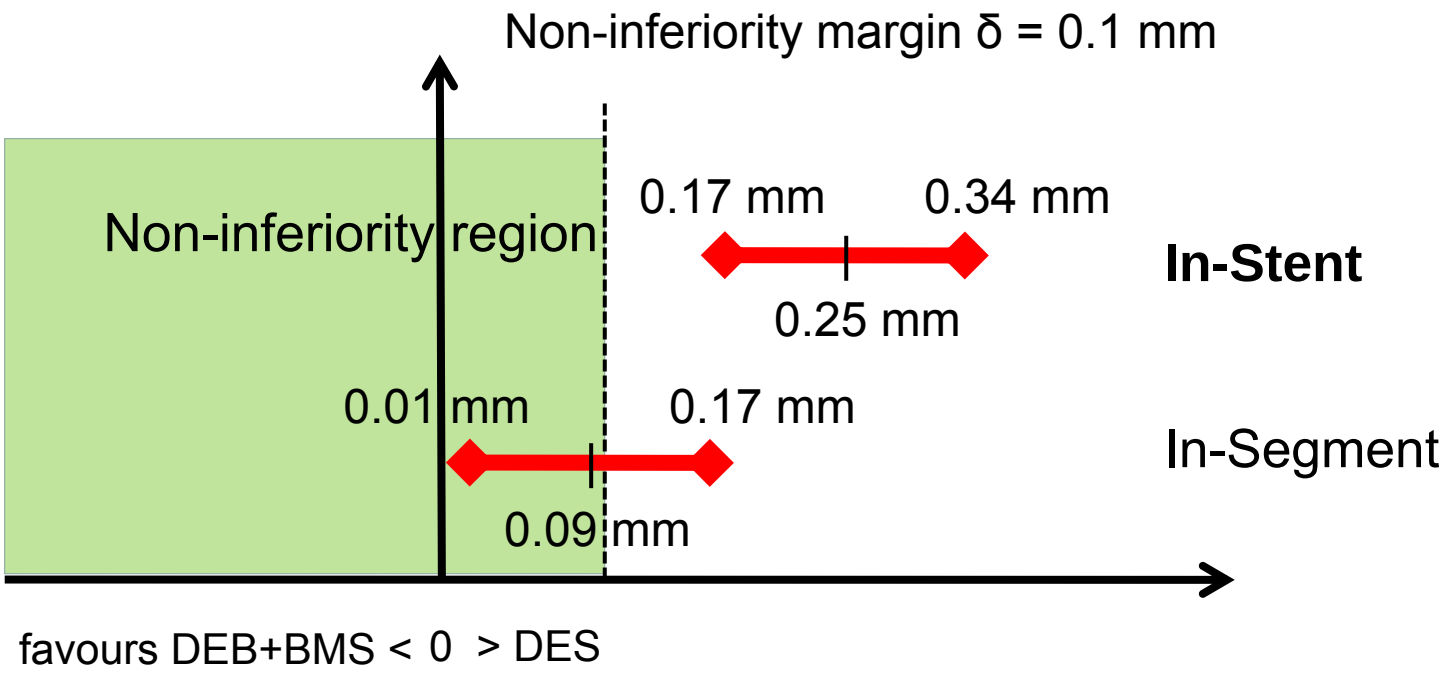
Per protocol analysis

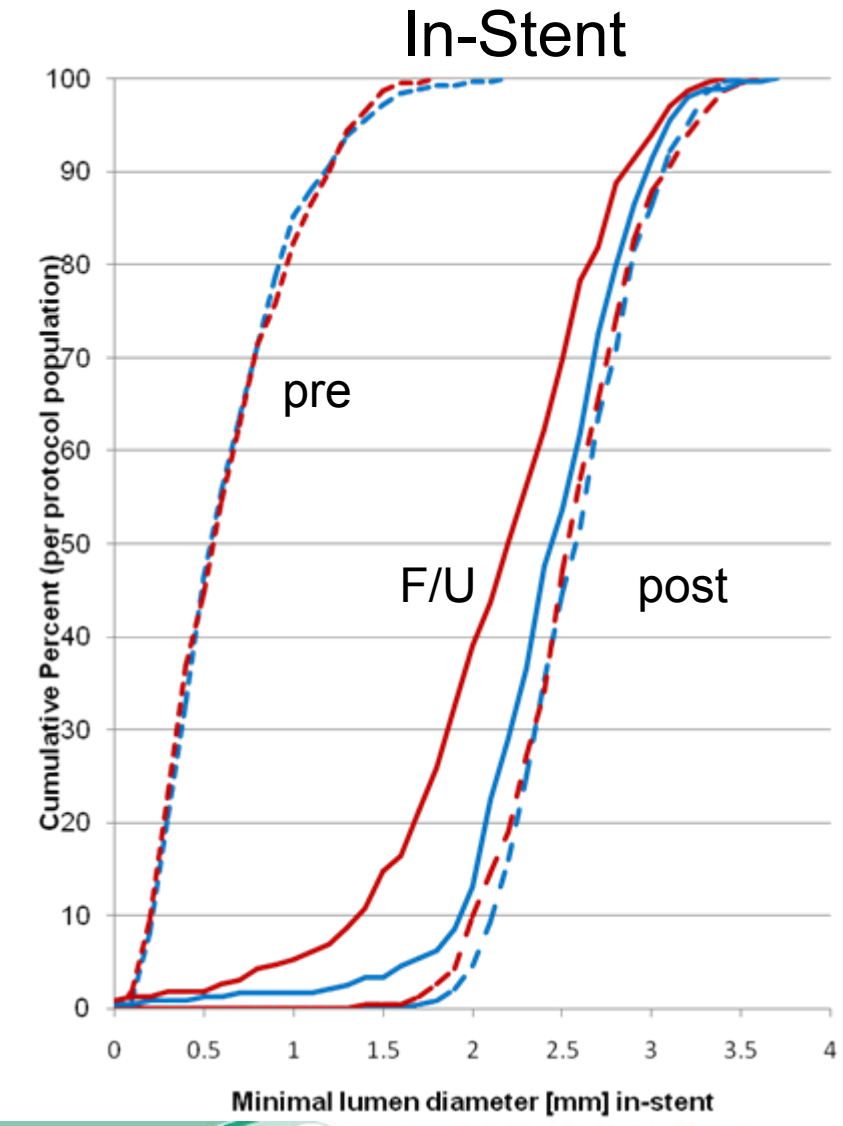
Late Lumen Loss

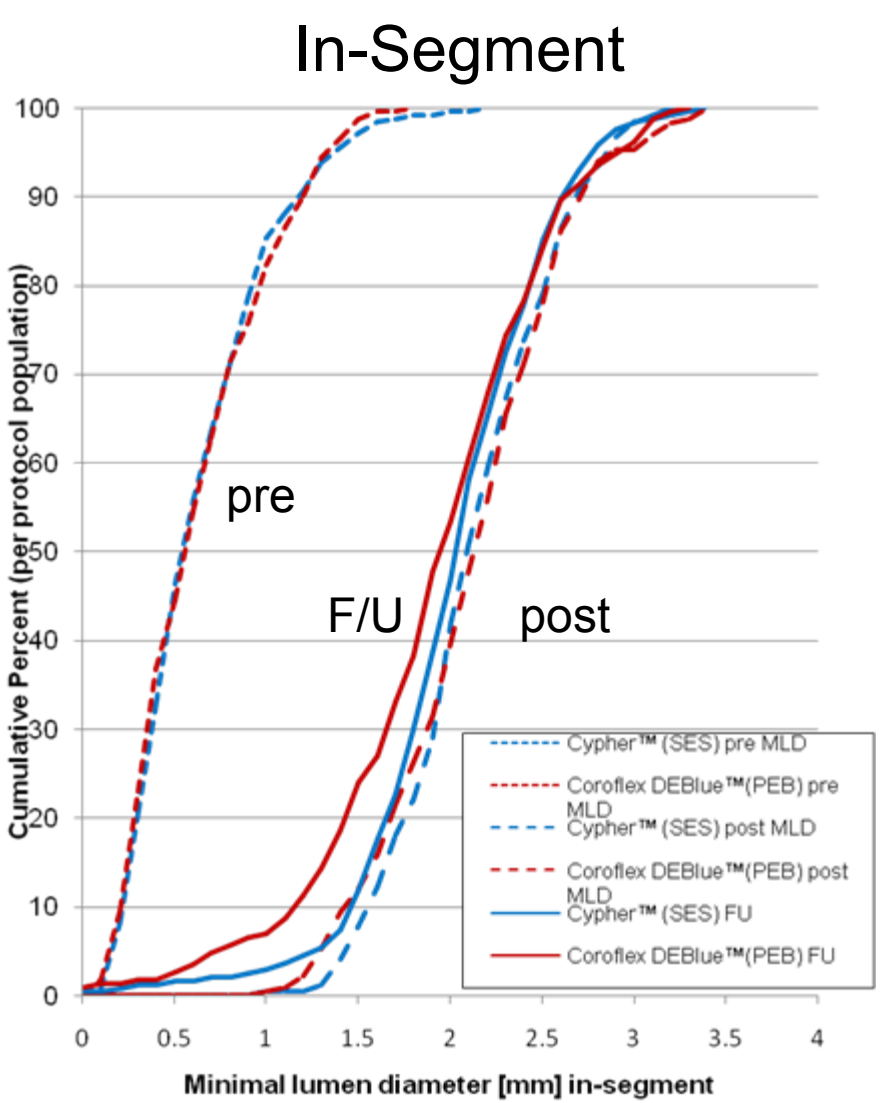


Difference LLL Coroflex DEBlue® and Cypher ®

Per protocol analysis

MLD Distribution





PEPCAD III

Per protocol analysis

Angiographic 2nd Endpoints

	DEB+BMS Coroflex DEBlue®	DES Cypher®	P - value
Binary Restenosis			
In-stent*	10.0 %	2.9 %	<0.01
In-segment*	13.8 %	4.9 %	<0.001
TVR**	13.8 %	6.9 %	<0.01
TLR**	10.5 %	4.7 %	<0.01

PEPCAD III

*Per protocol analysis
**Intention-to-treat analysis

Safety Endpoints

	DEB+BMS **Coroflex DEBlue®** **N = 310**	**DES** **Cypher®** **N = 324**	**P - value**
Procedural Success Stent placed + expanded QCA: TIMI3 + In-stent stenosis < 30%	91.6%	94.1 %	0.22
Death (9 months) Cardiac death	1.0 % 0.7 %	0.3 % 0.0 %	0.29
MI (9 months) STEMI NSTEMI	4.6 % 3.0 % 2.0 %	0.3 % 0.3 % 0.3 %	<0.001
Stent Thrombosis (ARC) Definite Probable	2.0 % 1.3 % 0.6 %	0.3 % 0.3 % 0.0 %	< 0.05

Intention-to-treat analysis

Summary / Conclusions

- **This first Drug-Eluting Balloon / Stent system did not meet the non-inferiority criteria versus Cypher®**
- **Safety aspects need to be investigated**

- **However,**
  - Late lumen loss comparable to published data on Paclitaxel® eluting stents
  - In-segment analysis demonstrates efficacy at the stent margins
  - Further design evolution is warranted to improve this new approach

Study Centers

- Scheller B., Homburg / Saar, Germany (93)
- Hamm Ch., Bad Nauheim, Germany (64)
- Möbius-Winkler S., Leipzig, Germany (58)
- Zeymer U., Ludwigshafen, Germany (56)
- Vrolix M., Genk, Belgium (46)
- Heuer H., Dortmund, Germany (43)
- Huret B., Caen, France (31)
- Vallbracht Ch., Rotenburg a.d. Fulda, Germany (27)
- Schieffer B., Hannover, Germany (24)
- Janek B., Prague, Czech Republic (23)
- Wijns W., Aalst, Belgium (23)
- Kuck K.H., Hamburg, Germany (23)
- Brachmann J., Coburg, Germany (20)
- Bocksch W., Berlin, Germany (19)
- Appelman Y., Amsterdam, Netherlands (16)
- Hehrlein Ch., Freiburg, Germany (15)
- Nienaber Ch., Rostock, Germany (11)
- Haase K. K., Reutlingen, Germany (11)
- Angevaeren W., Arnhem, Netherlands (10)
- Kähler J., Hamburg-Eppendorf, Germany (9)
- Barragan P., Ollioules, France (7)
- Eeckhout E., Lausanne, Switzerland (6)
- Hoffmann R., Aachen, Germany (3)
- Coste P., Pessac, France (3)

Thank you!

Statistical Hypothesis

Non-inferiority test problem: margin δ = 0.1 mm

Hypothesis: LLL Coroflex – LLL Cypher => δ

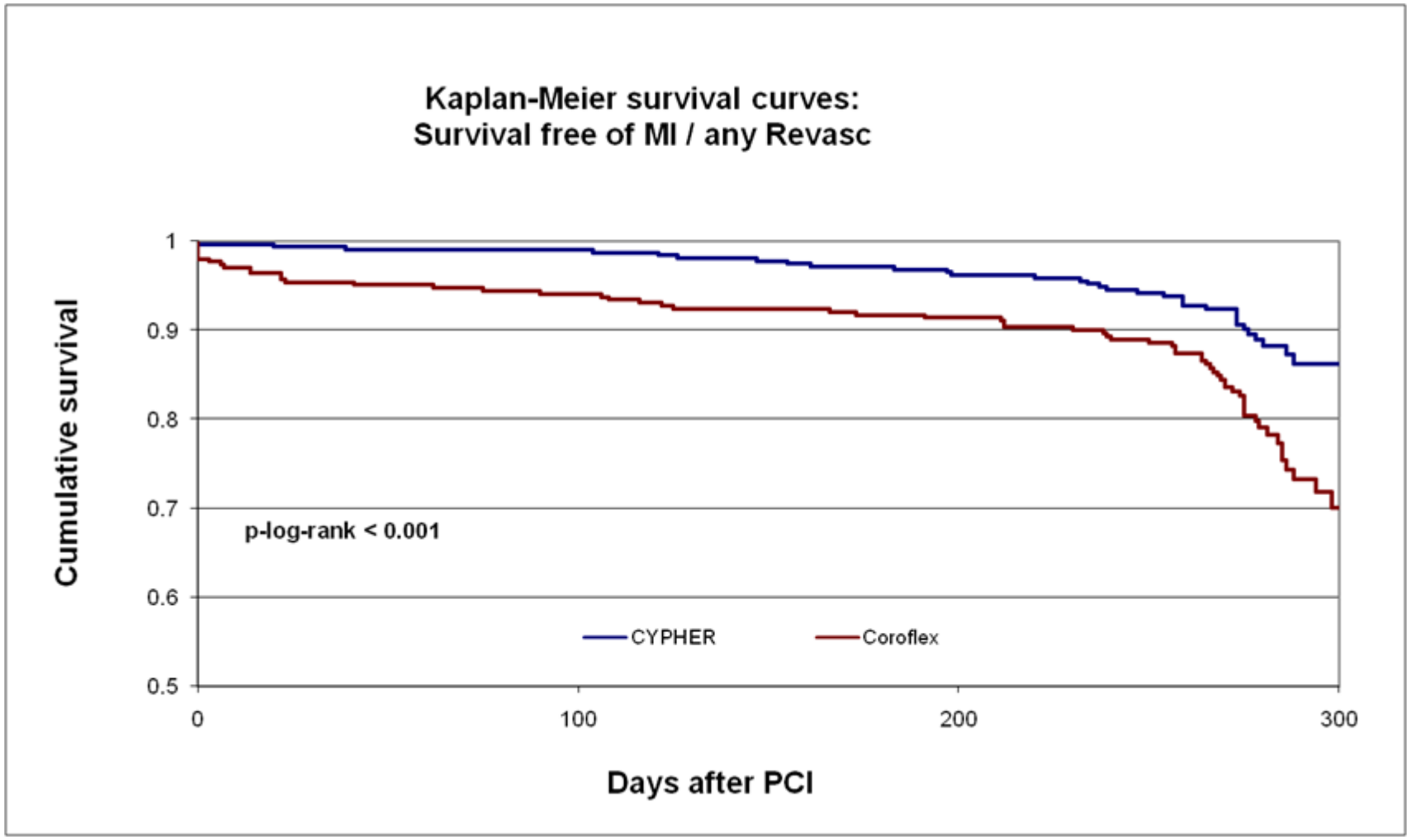
Alternative: LLL Coroflex – LLL Cypher < δ

Test niveau α = 5% Power 1 - β = 90%

Sample Size: 198 per group

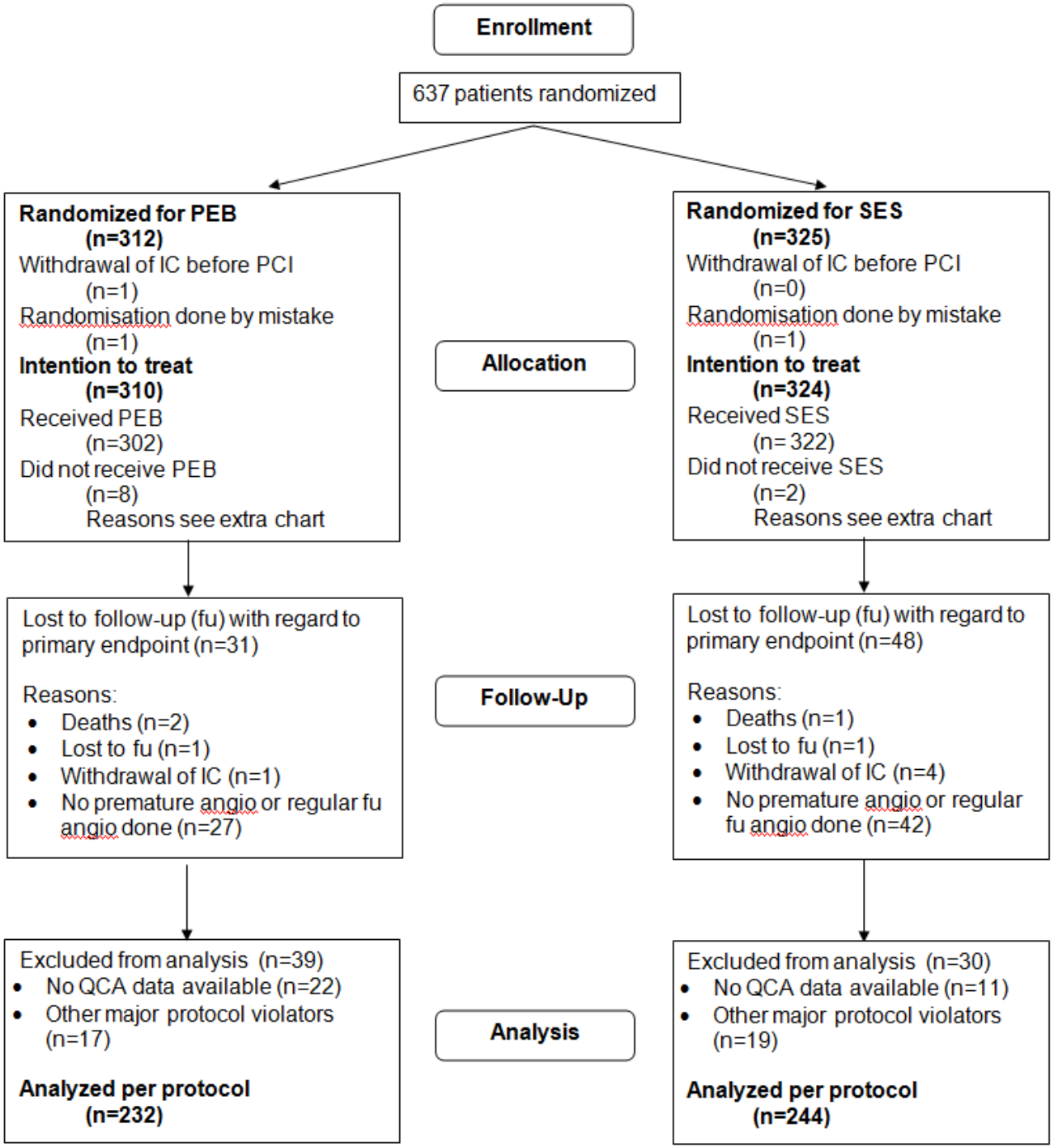
300 per group regarding drop-outs

Survival free of MACE (MI, Revasc)



PEPCAD III

Intention-to-treat analysis


Enrollment
637 patients randomized
Randomized for PEB
(n=312)
Withdrawal of IC before PCI
(n=1)
Randomisation done by mistake
(n=1)
Intention to treat
(n=310)
Received PEB
(n=302)
Did not receive PEB
(n=8)
Reasons see extra chart
Randomized for SES
(n=325)
Withdrawal of IC before PCI
(n=0)
Randomisation done by mistake
(n=1)
Intention to treat
(n=324)
Received SES
(n= 322)
Did not receive SES
(n=2)
Reasons see extra chart
Allocation
Lost to follow-up (fu) with regard to primary endpoint (n=31)
Reasons:
Deaths (n=2)
Lost to fu (n=1)
Withdrawal of IC (n=1)
No premature angio or regular fu angio done (n=27)
Lost to follow-up (fu) with regard to primary endpoint (n=48)
Reasons:
Deaths (n=1)
Lost to fu (n=1)
Withdrawal of IC (n=4)
No premature angio or regular fu angio done (n=42)
Follow-Up
Excluded from analysis (n=39)
No QCA data available (n=22)
Other major protocol violators (n=17)
Analyzed per protocol
(n=232)
Excluded from analysis (n=30)
No QCA data available (n=11)
Other major protocol violators (n=19)
Analyzed per protocol
(n=244)
Analysis