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The efficacy of novel drug-coated balloon with citrate ester excipient in PCI of *de novo* lesions: an all-comers registry study

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Conflict of interest

Speaker's name : Tuomas T. Rissanen

☑ I have the following potential conflicts of interest to declare:

Receipt of grants / research supports: Boston Scientific

All comers registry studies on DCB including *de novo* lesions in large vessels (9-12 mo TLR rate 1-5%)

Study and ref.	Device	Number of patients (de novo) n=3253	≥ 2.75mm DCB used in de novo (%)	≥ 3.0 mm DCB used in de novo (%)	Bailout stenting (%)	MACE (%, de novo)	TLR (%, de novo)
Toelg et al.	Pantera Lux	105	N.R.	23	22	9.4 at 12 mo	3.1 at 12 mo (TVR)
Widder et al.	In.Pact Falcon	374	25	N.R.	4.8%	8.0 at 12 mo	4.9 at 12 mo
Venetsanos et al.	SeQuent Please, In.Pact Falcon, Pantera Lux	985	N.R.	6	8%	NR	3.0 at 12 mo
Rosenberg et al.	SeQuent Please	731	21	N.R.	6	5.6 at 9 mo	2.3 at 9 mo
Uskela et al.	SeQuent Please	463	79	60	12	6.1 in stable CAD at 12 mo	1.4 in stable CAD at 12 mo
Yu et al.	SeQuent Please	595	36	N.R.	0.5	0 at 10 mo	0 at 10 mo

Toelg R Coronary artery treatment with paclitaxel-coated balloon using a BTHC excipient: clinical results of the international real-world DELUX registry. EuroIntervention.2014;10:591-599.
Widder JD Coronary artery treatment with an urea-based paclitaxel-coated balloon: The European wide Falcon all comers DCB Registry (FALCON-Registry). EuroIntervention.2018.
Venetsanos D Long-term efficacy of drug coated balloons compared with new generation drug-eluting stents for the treatment of de novo coronary artery lesions. Catheter Cardiovasc Interv.2018.
Rosenberg M The DCB-only All-Comers Registry. Catheter Cardiovasc Interv.2018.
Uskela S Percutaneous coronary intervention with drug-coated balloon-only strategy in stable coronary artery disease and in acute coronary syndromes: An all-comers registry study. Catheter Cardiovasc Interv.2018.
Yu X Treatment of large de novo coronary lesions with paclitaxel-coated balloon only: results from a Chinese institute. Clin Res Cardiol.2018.

BASKET-SMALL 2: RCT on DCB in small vessels

Drug-coated balloons for small coronary artery disease (BASKET-SMALL 2): an open-label randomised non-inferiority trial

Raban V Jeger, Ahmed Farah, Marc-Alexander Ohlow, Norman Mangner, Sven Möbius-Winkler, Gregor Leibundgut, Daniel Weilenmann, Jochen Wöhrle, Stefan Richter, Matthias Schreiber, Felix Mahfoud, Axel Linke, Frank-Peter Stephan, Christian Mueller, Peter Rickenbacher, Michael Coslovsky, Nicole Gilgen, Stefan Osswald, Christoph Kaiser, Bruno Scheller, for the BASKET-SMALL 2 Investigators

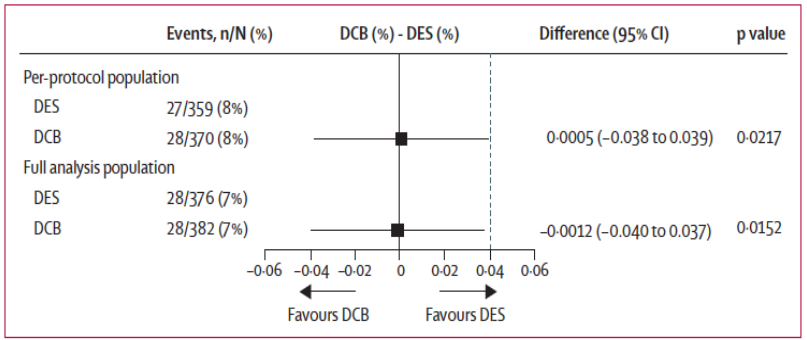


***Figure 2*: Major adverse cardiac events by study group**
Data are absolute difference in event rates between the DCB and DES groups. The p-value tests whether the absolute difference in rates is equal to the pre-defined non-inferiority margin (0·04). DCB=drug-coated balloons. DES=drug-eluting stents.

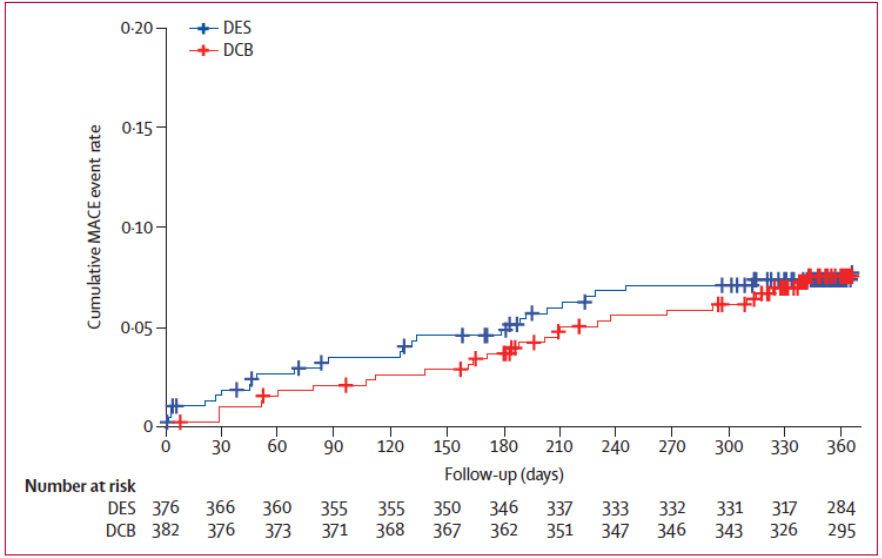
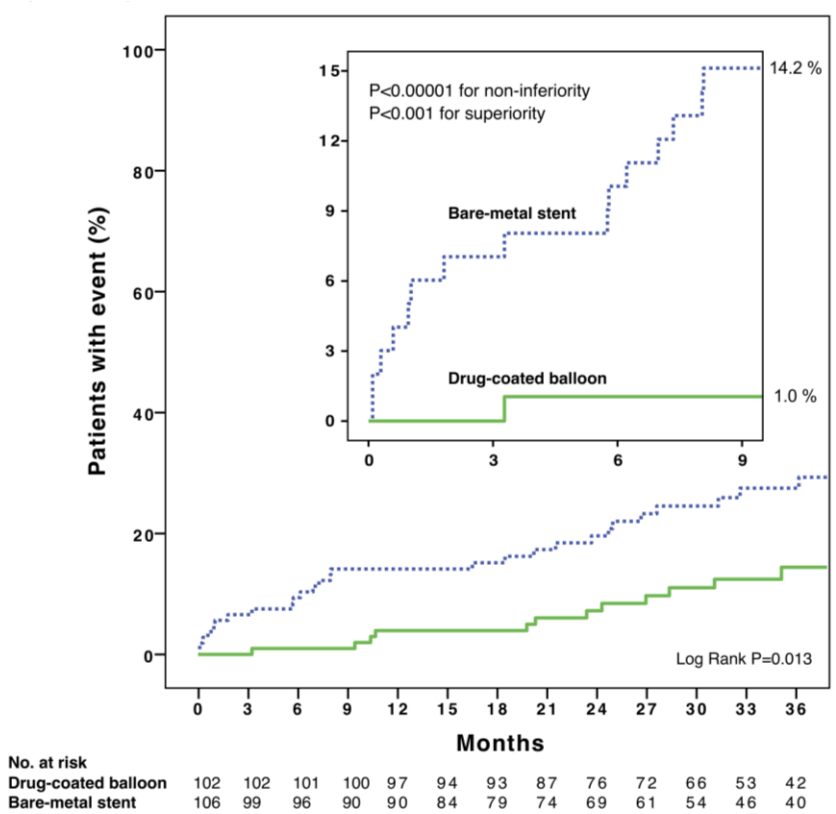


***Figure 3*: Cumulative incidence rates for MACE**
Full analysis population. MACE=major adverse cardiac events. DCB=drug-coated balloons. DES=drug-eluting stents.

Jeger et al., Lancet 2018; 392:849-856

DEBUT: RCT on DCB in *de novo* lesions in bleeding risk patients incl. large vessels



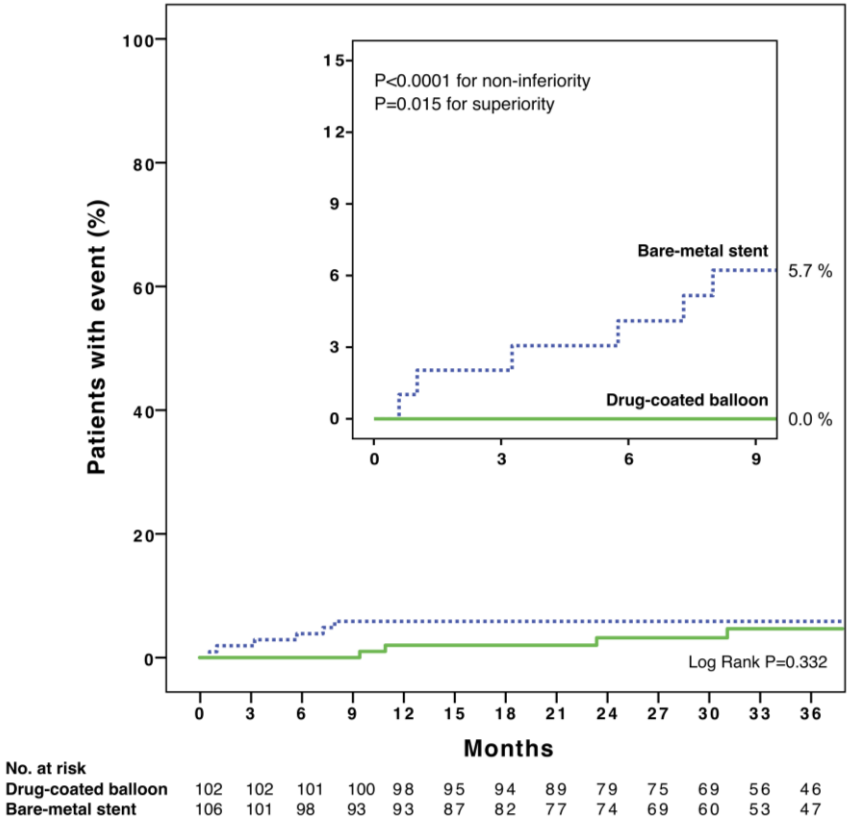
Primary endpoint (MACE) at 9 mo
- 1 patient (1.0%) in the DCB group
- 15 patients (14.2%) in the BMS group

Risk difference −13.2 % points
(95% CI: −6.2% to −21.1%)
Risk ratio 0.07
(95% CI: 0.01 to 0.52)

P<0.00001 for noninferiority
P<0.001 for superiority

Rissanen TT et al., Lancet, in press

DEBUT: RCT on DCB in *de novo* lesions in bleeding risk patients incl. large vessels



Secondary end point (TLR) at 9 mo

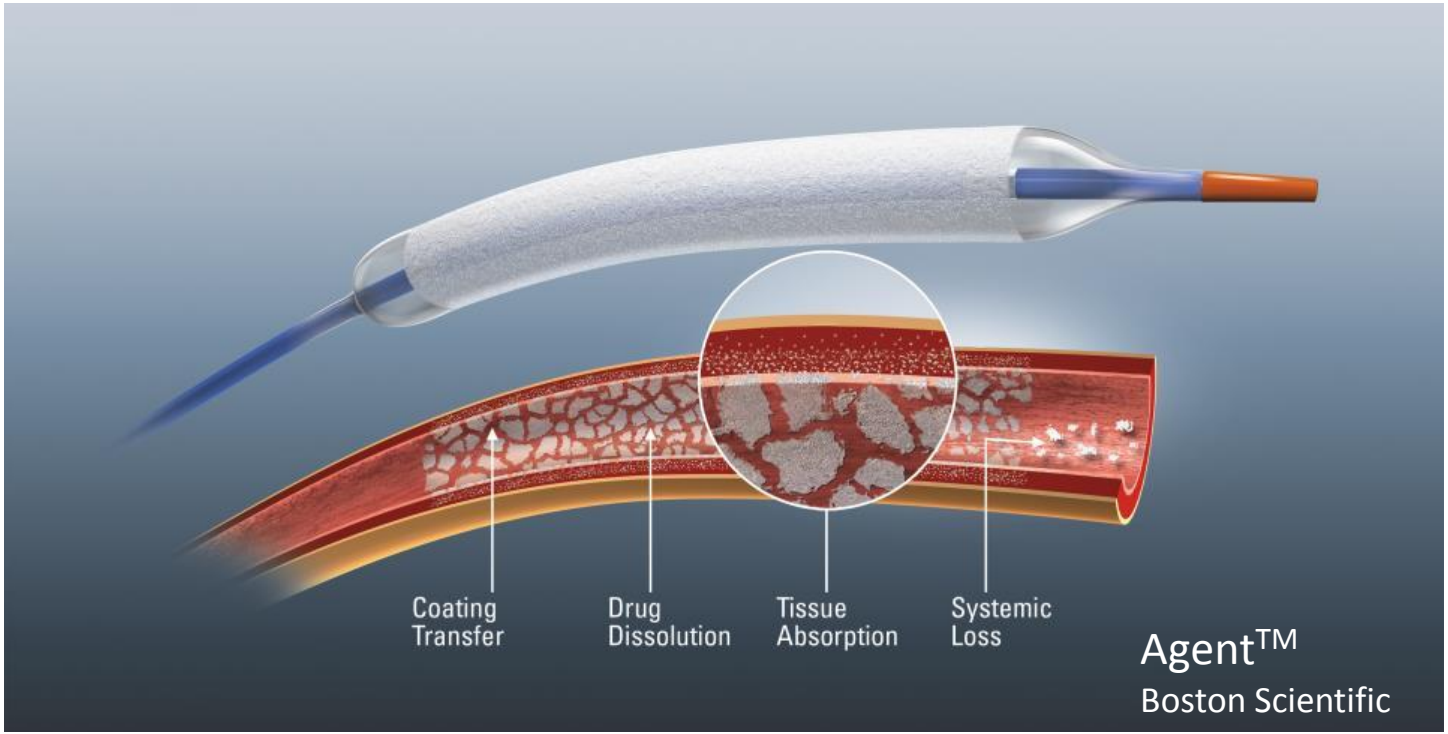
- 0 in the DCB group
- in 6 patients (5.7%) in the BMS group

Risk difference −5.7 % points;
(95% CI: −0.9% to −11.8%)
Risk ratio 0.08
(95% CI 0.01 to 1.40)

P<0.0001 for noninferiority
P=0.015 for superiority

Rissanen TT et al., Lancet, in press

DCB coated with paclitaxel + citrate ester excipient (CEE)

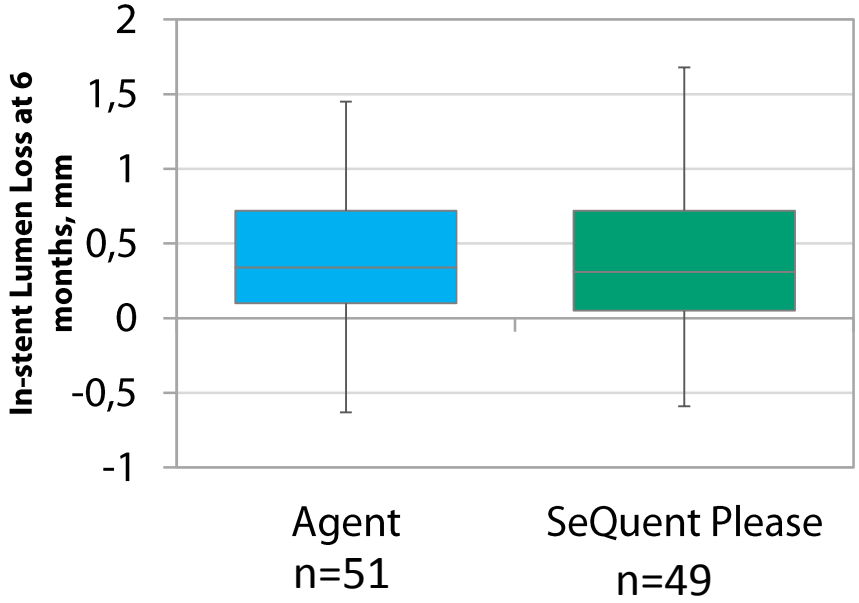


Embedded Paclitaxel crystalline particles serve as sustained release reservoirs

Paclitaxel 2 µg/mm^2 + acetyl tributyl citrate i.e. citrate ester (TransPax)

DCB coated with paclitaxel+CEE in ISR

Primary Endpoint: Late Loss at 6 months



Noninferiority criteria met for primary endpoint

Agent (N=51)	SeQuent Please (N=49)	Difference [95% CI]	Noninferiority Margin	$P_{noninferior}$
0.397 ± 0.43	0.393 ± 0.536	0.004 [-0.189, 0.196]	0.2	0.046

Measured by core laboratory. Noninferiority test from a 2-sided Student t-test comparing the difference between Agent and SeQuent Please to the noninferiority margin

H. Nef et al EuroPCR 2018

Aim of the study

- Aim was to study the efficacy and safety of the novel DCB coated with paclitaxel + CEE (Agent, Boston Scientific) in PCI of *de novo* lesions including large arterial segments
- Single-center all-comers retrospective registry study of consecutive PCIs (n=338) between 27th Aug 2014 – 14th Nov 2018
  - Inclusion criterion: at least one *de novo* lesion treated with DCB coated with paclitaxel + CEE
  - Exclusion criterion: ISR
- Stable CAD and ACS (unstable angina, NSTEMI and STEMI)
- Median follow-up time was 23.4 months

Treatment of *de novo* lesions with DCB

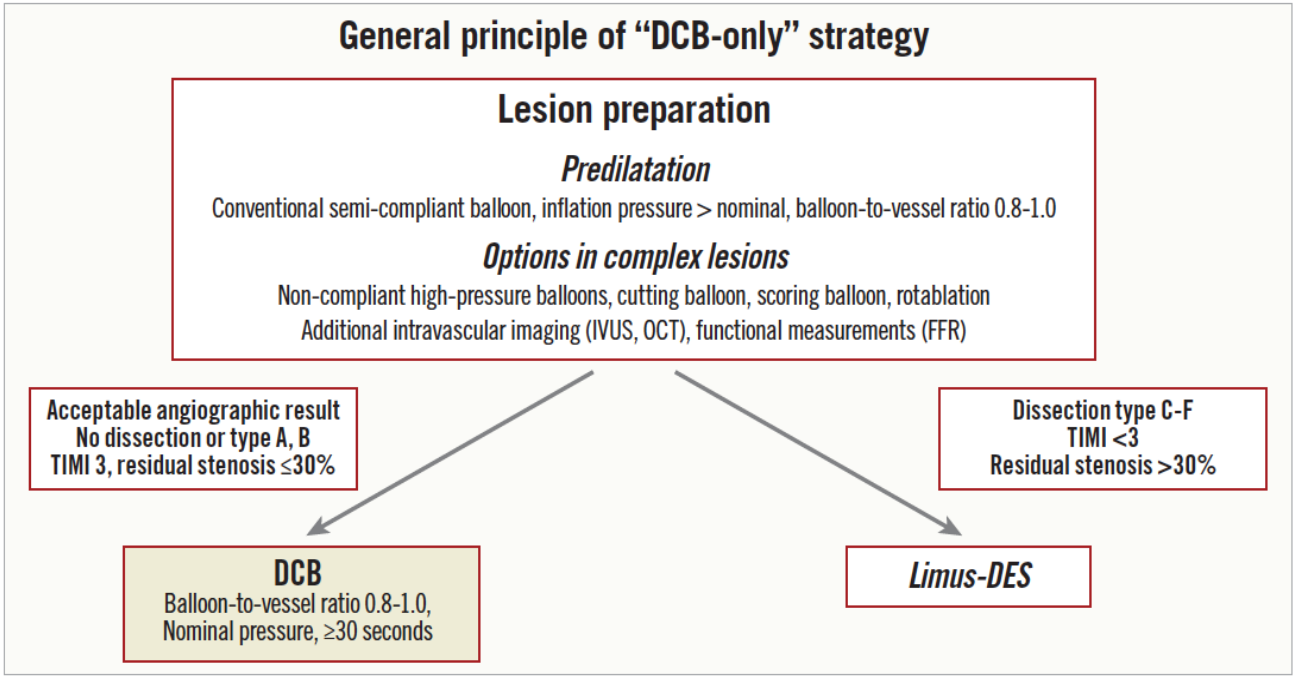


Figure 5. *General principle of DCB-only strategy. Adapted from[53,104]. Original figure was published in EuroIntervention, 2011[53].*

Alfonso F., Scheller B. EuroIntervention 2017;13:680-695

Baseline characteristics of patients

	n = 338	%
Age, years	**71 ± 11**	
Sex, male	**230**	**68**
Risk factors		
Smoker or ex-smoker	119	35
Diabetes	126	37
Hypertension	238	70
Hypercholesterolemia	260	77
Prior myocardial infarction	73	22
ACS	**161**	**48**
Unstable angina or NSTEMI	121	36
STEMI	40	12
CCS-class		
CCS1	17	5
CCS2	120	36
CCS3	118	35
CCS4	75	22

Bleeding risk factors (DEBUT criteria)

	n	%
Anticoagulation	72	21
Anemia	115	34
Age ≥ 80 years	82	24
Active malignant disease	5	1
Prior stroke	30	9
Severe renal dysfunction (eGFR <30 mL/kg/min)	5	1
Severe liver dysfunction (Bil > 2x or ALAT > 3x)	0	0
Planned elective surgery <12 months after PCI	15	4
General frailty or cachexy (BMI < 20 kg/m^2)	5	1
Patient not compliant to use DAPT	12	4
Prior bleeding requiring intervention	21	6

Mean DAPT duration after DCB coated with paclitaxel + CEE

- 3.8 ± 3.6 months in stable CAD (13% SAPT)
- 7.2 ± 6.7 months after ACS (15% SAPT)

Number of lesions

	n	%
PCIs	338	100
Lesions	686	100
Number of lesions treated with		
DCB	497	72
DCB paclitaxel + CEE	**406**	**59**
DES	182	27
BMS	2	0
POBA	5	1
Number of lesions treated per patient		
1	121	36
2	124	37
3	60	18
4	28	8
5	5	1
Rotational atherectomy followed by DCB paclitaxel + CEE	**44**	**11**

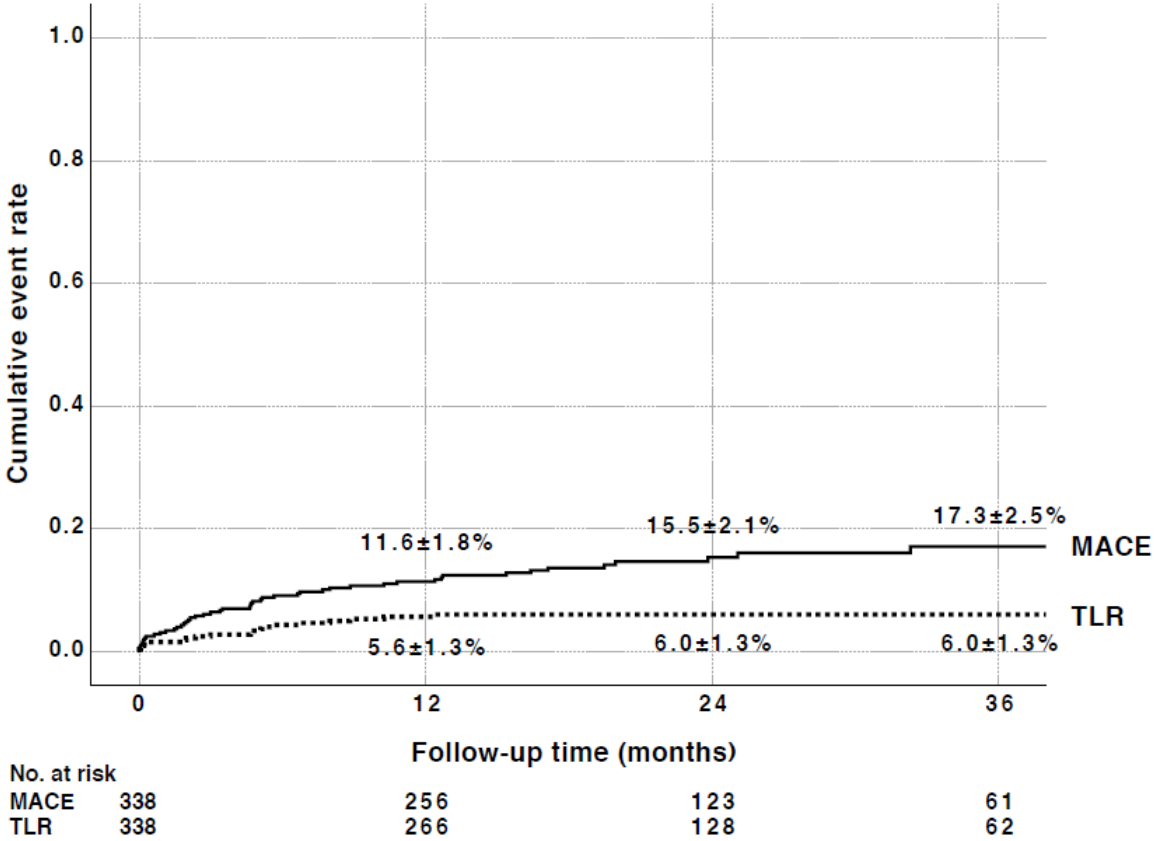
Target vessels treated using DCB coated with paclitaxel + CEE

	n	%
LM	9	2
LAD	134	33
RCA	90	22
LCX	52	13
Marginal or diagonal branch	101	25
RPD or RPL	13	3
Vein graft	7	2

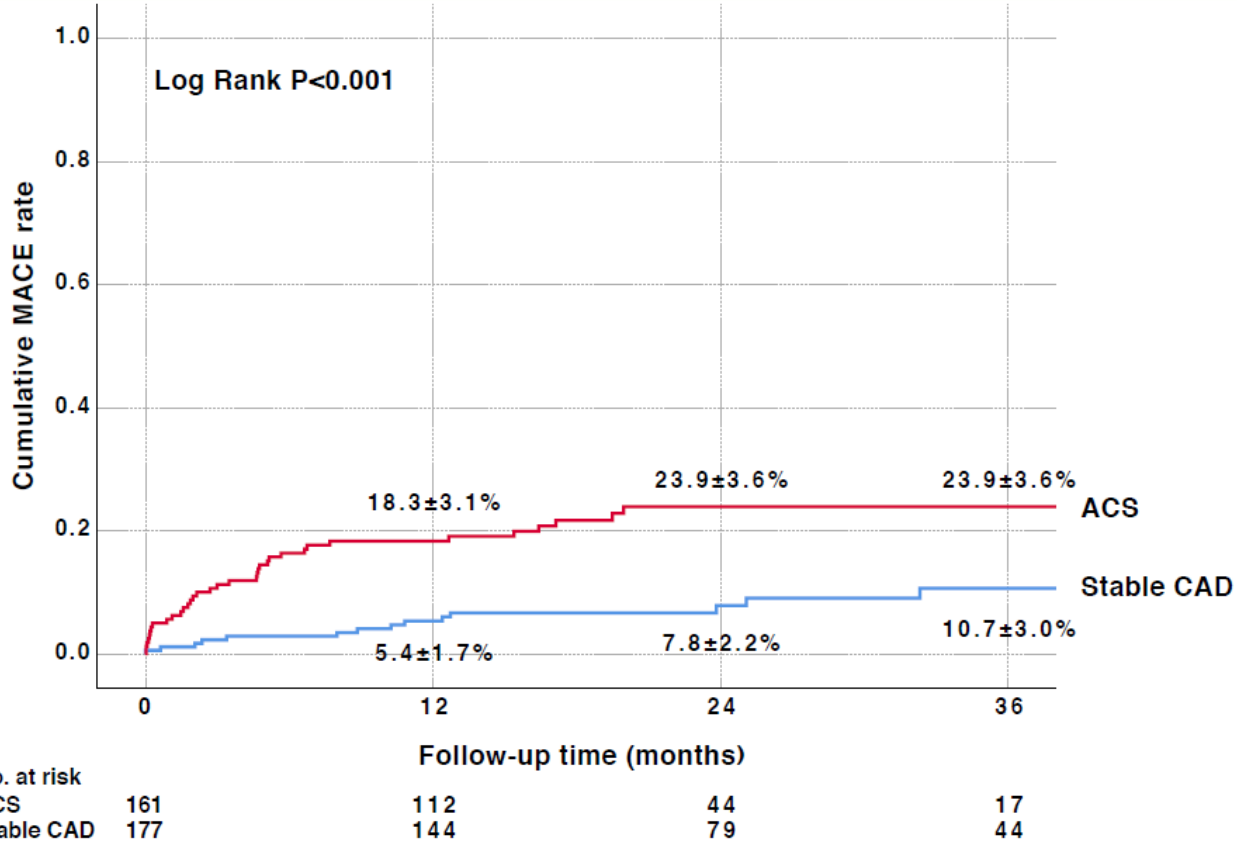
Diameter and length of DCB coated with paclitaxel + CEE:

DCB diameter (mm)	n	%	
2.0	54	13	56% small vessels
2.25	34	8	
2.5	**138**	**34**	
2.75	28	7	44% large vessels
3.0	**105**	**26**	
3.5	35	9	
4.0	11	3	
DCB length (mm)			
12	49	12	
15	**136**	**34**	
20	**146**	**36**	
30	69	17	
n.d.	5	1	

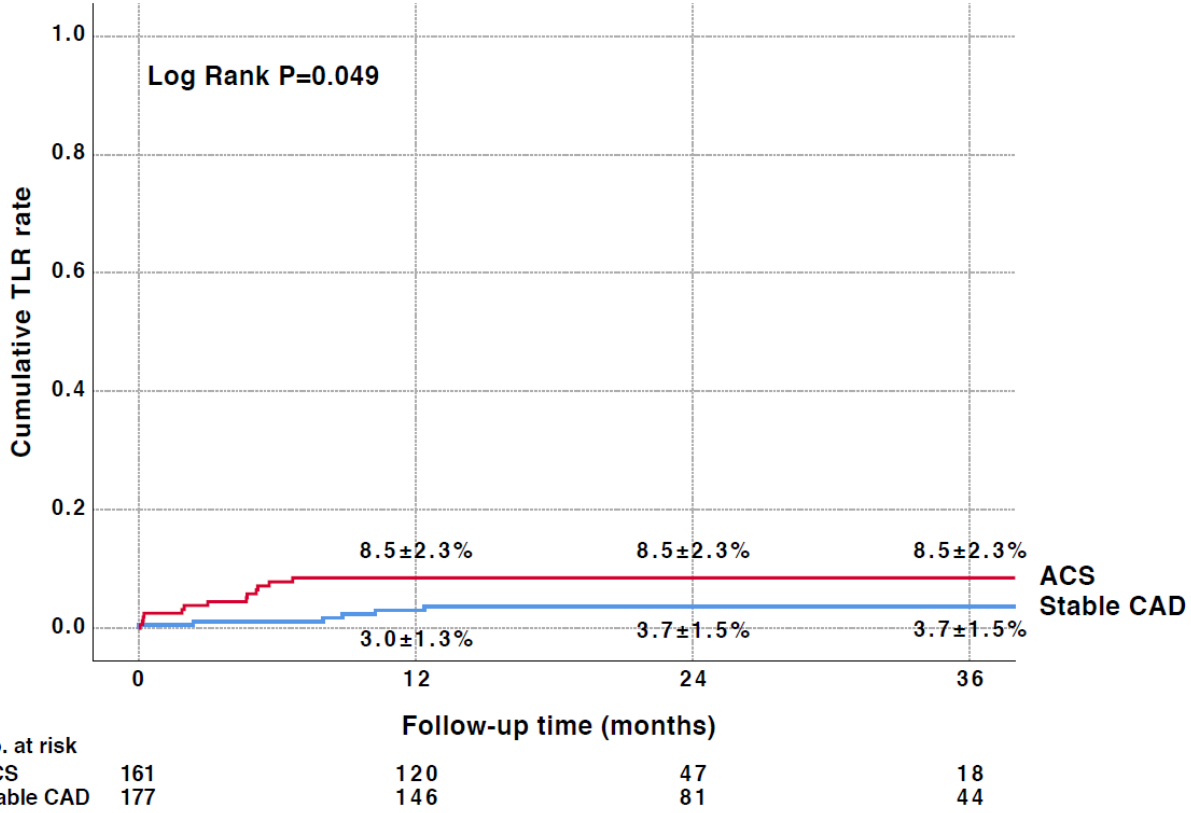
MACE and TLR (11.6% and 5.6% at 12 mo)



MACE: ACS and stable CAD



TLR: ACS and stable CAD



DCB coated with paclitaxel + CEE
Technical failure

	n	%
Delivery failure of DCB	**9**	**2**
Bailout stenting	**31**	**8**
Reason for bailout stenting after DCB		
Dissection	19	61
Recoil > 30%	16	39
Bailout stents used		
DES	39	93
BMS	3	7
Delivery failure of bailout stent	3	7
Dissection or recoil accepted without bailout stenting	**5**	**1**

Total number of PCI attempt 415; delivery failure of DCB in 9 resulting in 406 PCI DCB coated with paclitaxel + CEE

Reason for TLR after DCB coated with paclitaxel + CEE

	n (406 lesions)	%
TLR in total follow-up (per lesion)	**19**	**4.7**
Total number of TLR (per lesion)	**19**	**100**
Recoil >30% after DCB	14	74
Less than TIMI3 flow after DCB	0	0
TLR in bailout stent	2	11
No indentifiable reason	3	16
TLR (per lesion) during FU if DCB-only PCI was done according to the international consensus document recommendation	**5**	**1.2%**

Conclusions

- This is the first report of PCI using DCB coated with paclitaxel + citrate ester excipient in *de novo* coronary artery lesions
  - 44% of vessels large (≥ 2.75 mm)
- The DCB-only strategy using this novel DCB (Agent, Boston Scientific) was safe and effective in an all comers real-life population (11% rotablation, 21% with OAC, 24% ≥ 80yrs)
  - No acute vessel closures (406 lesions treated in 338 PCI procedures)
  - **12 month MACE rate was 11.6%** (5.4% in stable CAD)
  - **12 month TLR rate was 5.6%** (3.0% in stable CAD)
- Recoil >30% after predilatation was found to be a significant risk factor for restenosis after DCB-only PCI
  - 74% of TLR cases involved >30% recoil

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