Drug Coated Balloon (DCB);

Current Status and Future Perspective

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Conflict of Interest Statement

I have nothing to disclose.

Restenosis
After Balloon Angioplasty

1. Recoil and remodeling
2. Neointimal hyperplasia

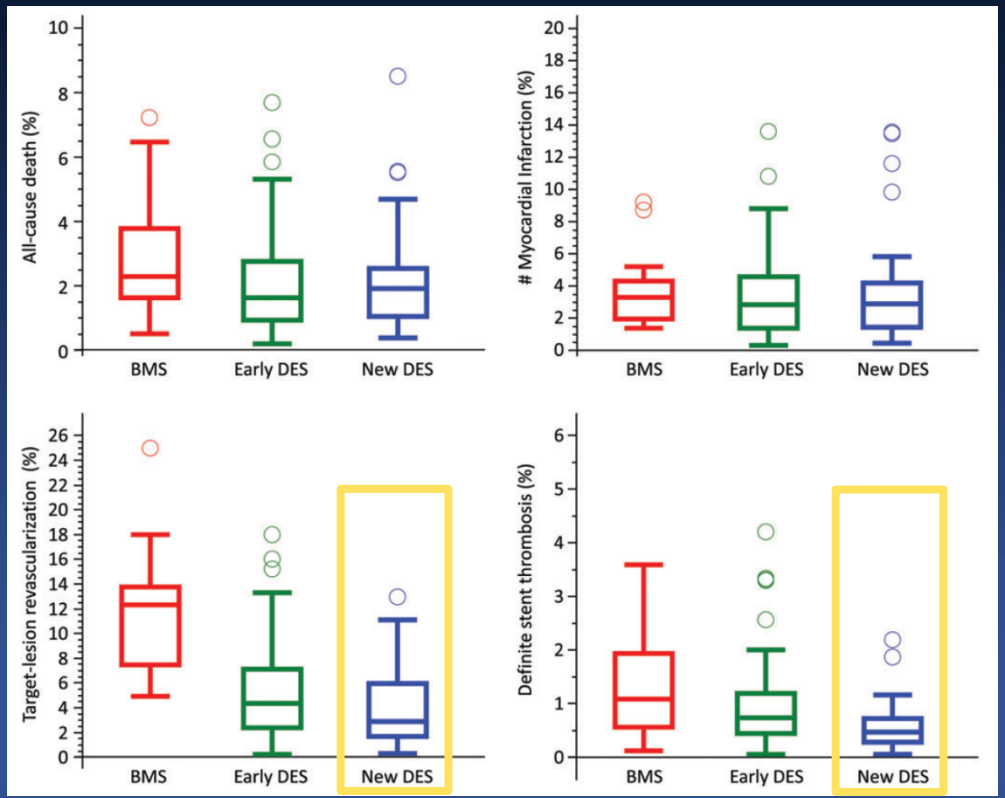
Solution of Restenosis
After Balloon Angioplasty

1. **Stents** to prevent vascular recoil and remodeling
2. **Active therapeutic agent** to prevent neointimal hyperplasia

Solution of Restenosis
After Balloon Angioplasty

DES Won !

Systematic Review of 158 RCTs



Byrne RA et al., Eur Heart J. 2015;36:2608-20

The Concept of DCB
"Leaving Nothing Behind"

Balloon-based local delivery of antiproliferative drugs to the arterial wall without a permanent metallic implant

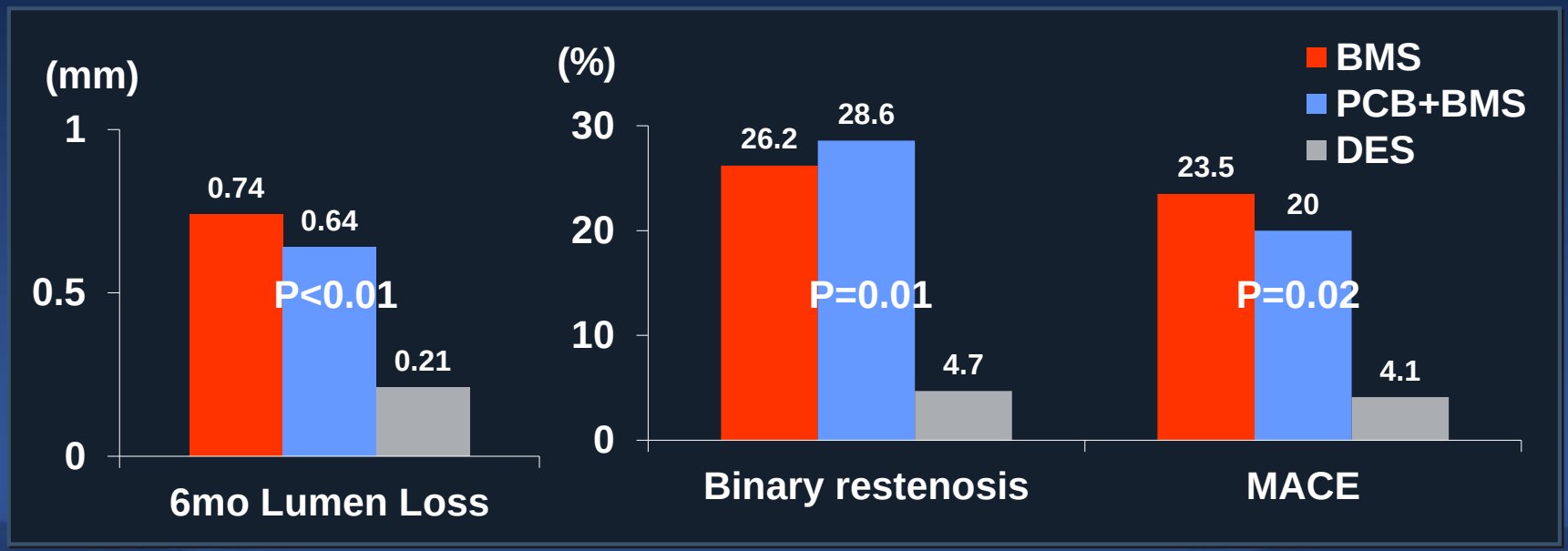
Limitation of the DCB,
Tissue retention time is limited

For stent-based local drug delivery, the drug must be released for a period of several weeks for effective inhibition of neointimal proliferation.

Clever YP et al., Circ Cardiovasc Interv. 2016;9:e003543.

Limitation of the DCB,
Tissue retention time is limited

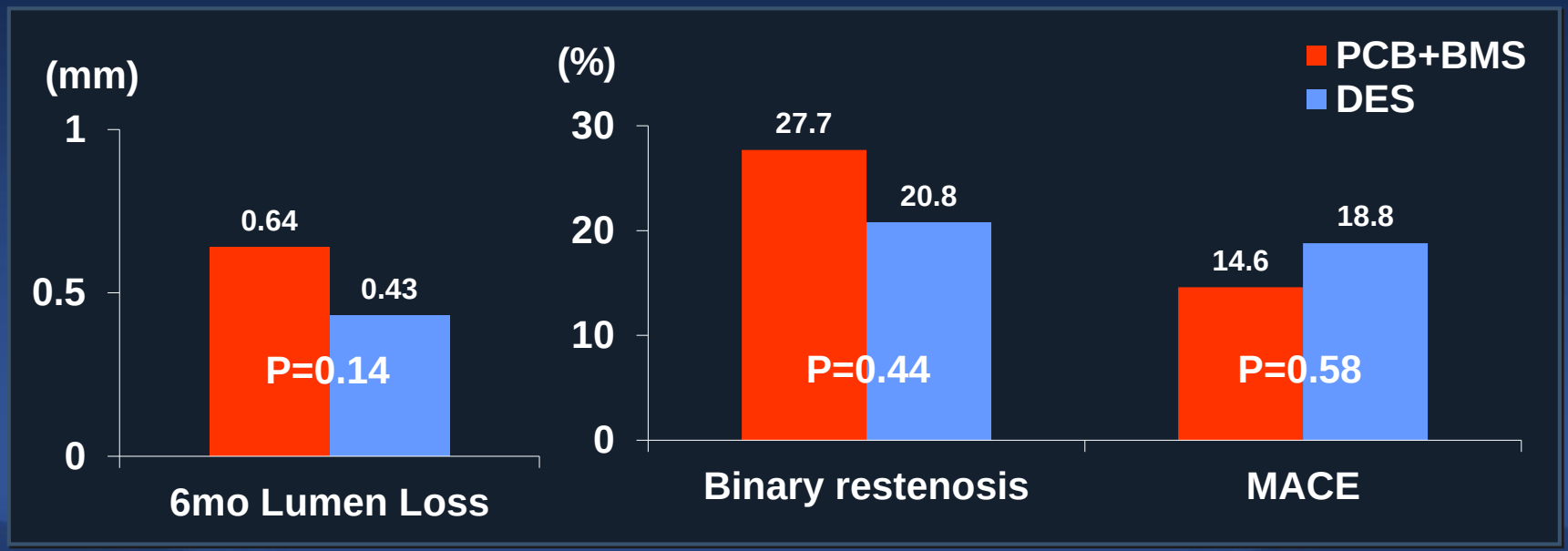
In de novo coronary artery disease, the combination of PCB and BMS was inferior to current generation of DES.



DEB-AMI Trial, Belkacemi A et al., J Am Coll Cardiol. 2012;59:2327-37

Limitation of the DCB,
Tissue retention time is limited

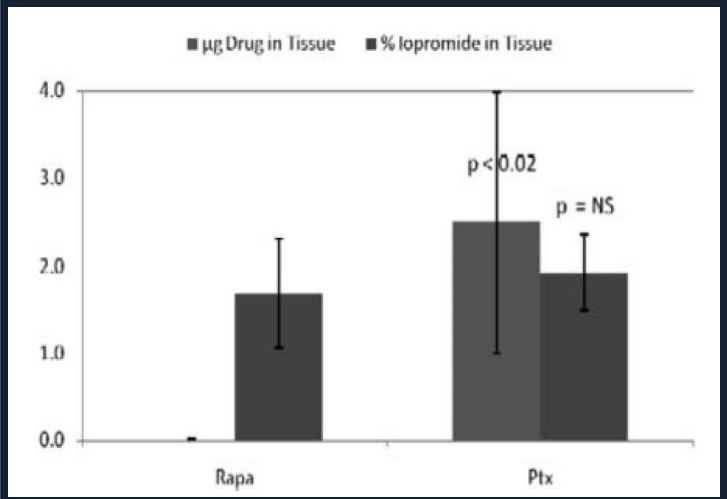
In de novo coronary artery disease, the combination of PCB and BMS was not superior to DES.

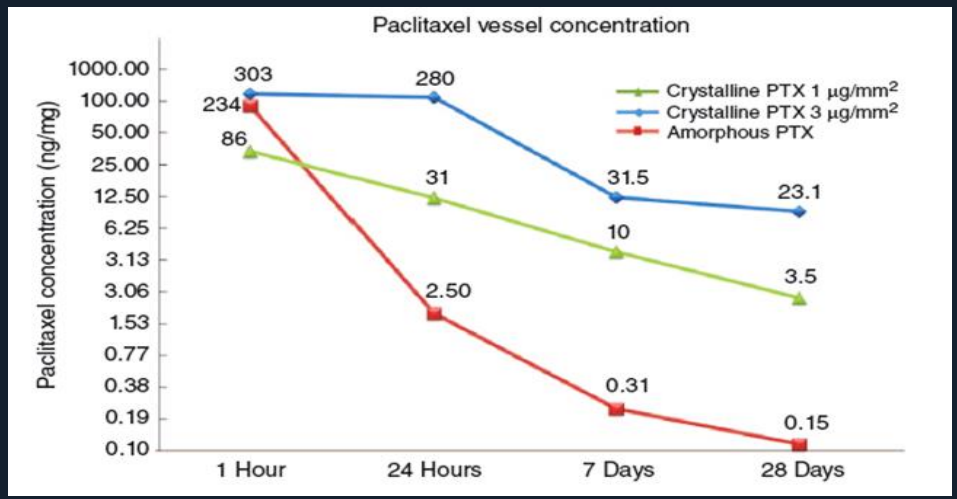


PEPCAD-CTO Trial, Wöhrle J et al., Catheter Cardiovasc Interv. 2013;81:793-9.

Limitation of the DCB, DCB Technology Improved

1. Rapid absorption
2. Improving bioavailability at target site





Gray WA, Granada JF. Circulation. 2010;121:2672-2680. Granada JF. Interventional Cardiology. 2016

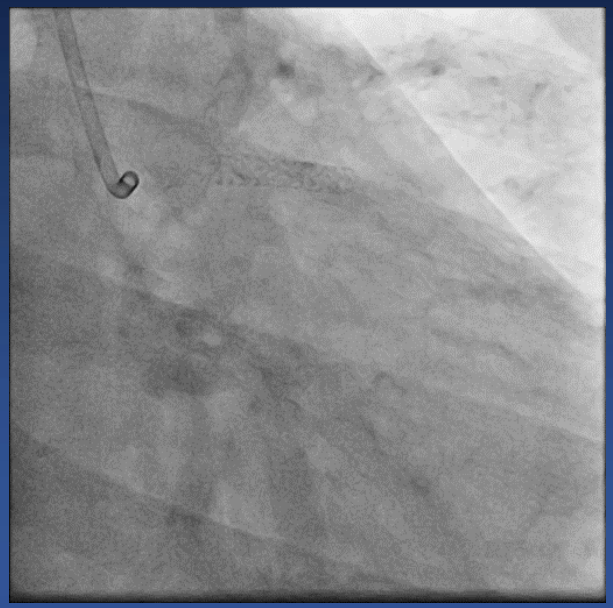
Limitation of the DCB, DCB Technology Improved

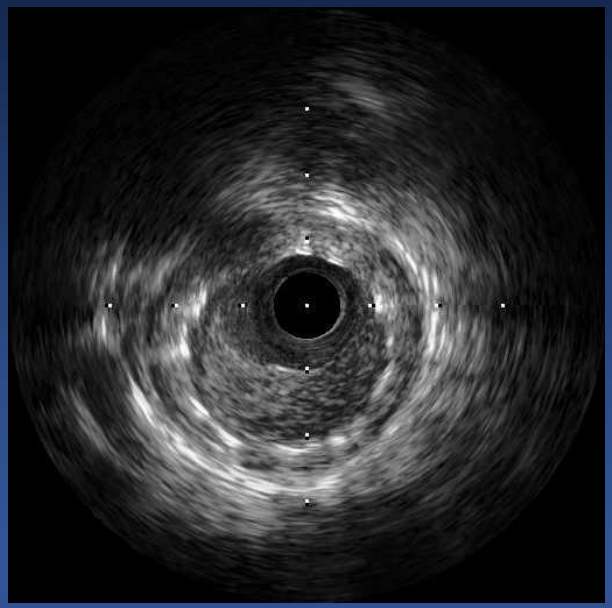
1. Rapid absorption
2. Improving bioavailability at target site

	DCB	DES
Drug load per device ($3\text{-}\mu g/mm^2$)	300-1,000 μg	100-200 μg
Drug transferred and absorbed by tissue after implantation (%)	16%	5-10%

Limitation of the DCB,
Acute Closure or Recoil occurs

Coronary in-stent restenosis became main target of DCB Treatment



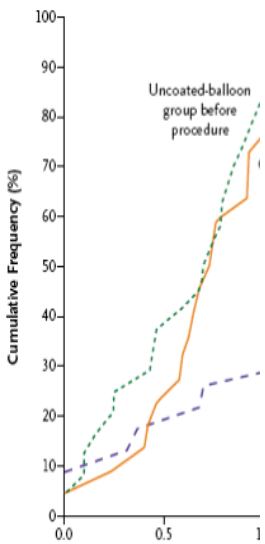


Lots of RCTs,
DCB for BMS or DES ISR

The NEW

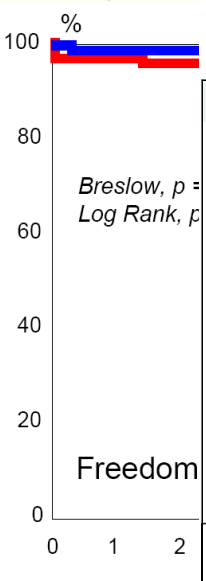
Treatment of
with a Paclita

Bruno Scheller, M.D.,
Wolfgang Rutsch,
Michael



A Randomized
Versus Everoli
Bare-Metal St
The RIBS V Clini
Stents: Paclitaxel-

Fernando Alfonso, MI
Bruno García del Blan
Manuel Gómez-Recio,
Arturo García-Toucha
Rafael Melgares, MD,

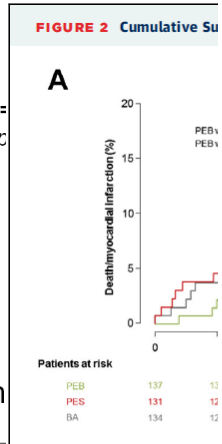


Long-Terr
Paclitaxel-
Treatment
Restenosis

3-Year Results

Sebastian Kufner, MD,* S
Stefanie Schulz-Schüpke,
Karl-Ludwig Laugwitz, M
and Angiographic Results
Investigators

FIGURE 2 Cumulative Su



Cumulative survival analysis
in Figure 1.

Comparison of d
drug-coated ball
of drug-eluting c
A randomized RE

Yiu Tung Anthony Wong, MD, [a,1] Do-Y
Eun-Seok Shin, MD, [f] Sung-Ho Her, M
Cheol Hyun Lee, MD, [b] Pil Hyung Le
Young-Hak Kim, MD, [b] Cheol Whan Le
Hong Kong: Seoul, Daegu, Gwangj

Background This study sought
Methods This is a prospective,
(DEB) versus second-generation everol
loss at 9-month routine angiographic
Results A total of 172 patients
primary end point was not different be
mm, *P* = .54). The secondary end poir
P = .03), in-stent MLD (1.90 ± 0.71 m
26% ± 15%, *P* = .05), and in-stent pe
the DES group. The composite of dea
between the 2 groups (DEB group 7.(
Conclusions Treatment of DES
angiographic follow-up, whereas DE
stenosis. Both treatment strategies wer

A Randomized Comparison of
Paclitaxel-Eluting Balloon Versus
Everolimus-Eluting Stent for the
Treatment of Any In-Stent Restenosis

The DARE Trial

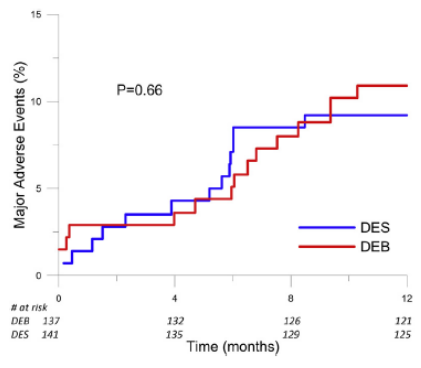
Jan Baan, Jr, MD, PhD,[a] Bimmer E. Claessen, MD, PhD,[a] Kirsten Boerlage-van Dijk, MD, PhD,[b] Jeroen Vendrik, MD,[a] René J. van der Schaaf, MD, PhD,[b] Martijn Meuwissen, MD, PhD,[c] Niels van Royen, MD, PhD,[d] A.T. Marcel Gosselink, MD, PhD,[e] Marleen H. van Wely, MD,[f] Atilla Dirkali, MD,[g] E. Karin Arkenbout, MD, PhD,[h] Robbert J. de Winter, MD, PhD,[a] Karel T. Koch, MD, PhD,[a] Krischan D. Sjauw, MD, PhD,[a] Marcel A. Beijk, MD, PhD,[a] M. Marije Vis, MD, PhD,[a] Joanna J. Wykrzykowska, MD, PhD,[a] Jan J. Piek, MD, PhD,[a] Jan G.P. Tijssen, PhD,[a] José P.S. Henriques, MD, PhD[a]

TABLE 4 Kaplan-Meier Estimates of Major Adverse Clinical Events at 12-Month Follow-Up

	Drug-Eluting Balloon (n = 137)	Drug-Eluting Stent (n = 141)	p Value
Death	0.7 (1)	1.4 (2)	0.58
Cardiac death	0	0.7 (1)	0.32
Myocardial infarction	2.2 (3)	2.8 (4)	0.74
Target vessel-related myocardial infarction	1.4 (2)	0.7 (1)	0.54
Stent thrombosis	0	0	n/a
Stroke	0.7 (1)	1.4 (2)	0.58
Target vessel revascularization	8.8 (12)	7.1 (10)	0.65
TVR percutaneous coronary intervention	8.8 (12)	5.7 (8)	0.36
TVR coronary artery bypass graft surgery	0	1.4 (2)	0.16
Coronary artery bypass graft surgery all	0.7 (1)	4.3 (6)	0.06
Percutaneous coronary intervention all	13.9 (19)	11.3 (16)	0.58
Composite major adverse events*	10.9 (15)	9.2 (13)	0.66

Values are % (n). *Defined as death, target vessel-related myocardial infarction, and target vessel revascularization.
TVR = target vessel revascularization.

FIGURE 3 Kaplan Meier Estimates of Major Adverse Events at 12-Month Follow-Up



Event rates at 12 months: DEB 10.9% versus DES 9.2%; p = 0.66. Abbreviations as in Figure 1.

Scheller B et al., NEJM 2006 Alfonso F et al., JACC 2014 Kufner S et al., JACC Interv 2015 Wong YTAKang DY et al., AHJ 2018 Baan J et al., JACC 2018

12 RCTs,
DCB for BMS or DES ISR

ISR	Intervention	N	End point	Study
BMS	PCB-POBA	108	In-segment LLL	PACCPCATH ISR
	PCB-PES	131	In-segment LLL	PEPCAD 2 ISR
	PCB-EES	189	In-segment MLD	RIBS V
	PCB-EES	136	LLL	ISR study
DES	PCB-POBA	110	LLL	PEPCAD-DES
	PCB-POBA	208	TVF	Habara et al
	PCB-POBA	50	In-segment LLL	Habara et al
	PCB-PES	402	In-segment DS	ISAR-DESIRE 3
	PCB-PES	220	In-segment LLL	PEPCAD-ISR-China
	PCB-EES	309	In-segment MLD	RIBS IV
	PCB-EES	172	In-segment LLL	RESTORE
	PCB-EES	278	In-segment MLD	DARE

Many Meta-analyses,
DCB for BMS or DES ISR

Percutaneous cor… treatment of in-s…

George C M Siontis, Giulio G Stefanini, Din…
Adnan Kastrati, Bernhard Meier, Georgia S…

	EES	DCB
EES	99·6 (0·98)	−9·0% (−15·8 to −2·2)
DCB	..	73·7 (0·00)
SES	..	..
PES	..	..
VBT	..	..
BMS	..	..
BA	..	..
ROTA	..	..

Estimates are expressed as differences in percent di…
appendix. Negative differences show that the inten…
efficacy ranking. Surface under the cumulative rank…
surface under the cumulative ranking curve value, t…
PES=paclitaxel-eluting stents. VBT=vascular brachy…

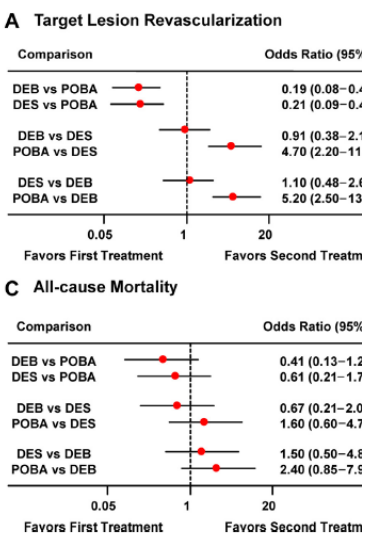
Table 2: Estimated differences of the effect of…

Comparison Among Drug-Eluting Stent, … Angioplasty for the Restenosis

A Network Meta-analysis of 11…

Joo Myung Lee, MD, MPH,* Jonghanne Park, MD,*
Sang Eun Lee, MD, PhD,* Jung-Kyu Han, MD, PhD,
Kyung Woo Park, MD, PhD,* Hyun-Jae Kang, MD,…

FIGURE 3 Results of Bayesian Network Meta-analysis for 1-Year Rate…

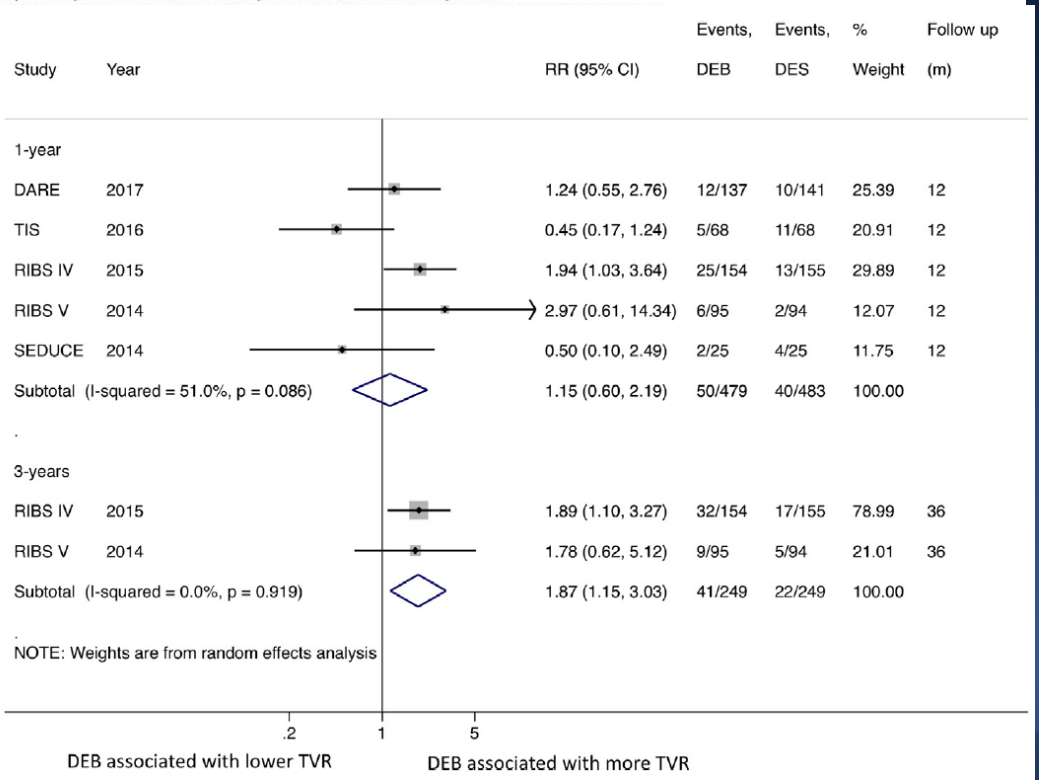


Results of a Bayesian network meta-analysis with a random-effects model f…
(C), major adverse cardiovascular events within 1-year follow-up period (D…

Drug-eluting balloons versus everolimus-eluting stents for in-stent restenosis: A meta-analysis of randomized trials☆

Islam Y. Elgendy [a,*], Ahmed N. Mahmoud [a], Akram Y. Elgendy [a], Mohammad K. Mojadidi [a], Ayman Elbadawi [b], Parham Eshtehardi [c], María José Pérez-Vizcayno [d], Siddharth A. Wayangankar [a], Hani Jneid [e], R. David Anderson [a], Fernando Alfonso [f]

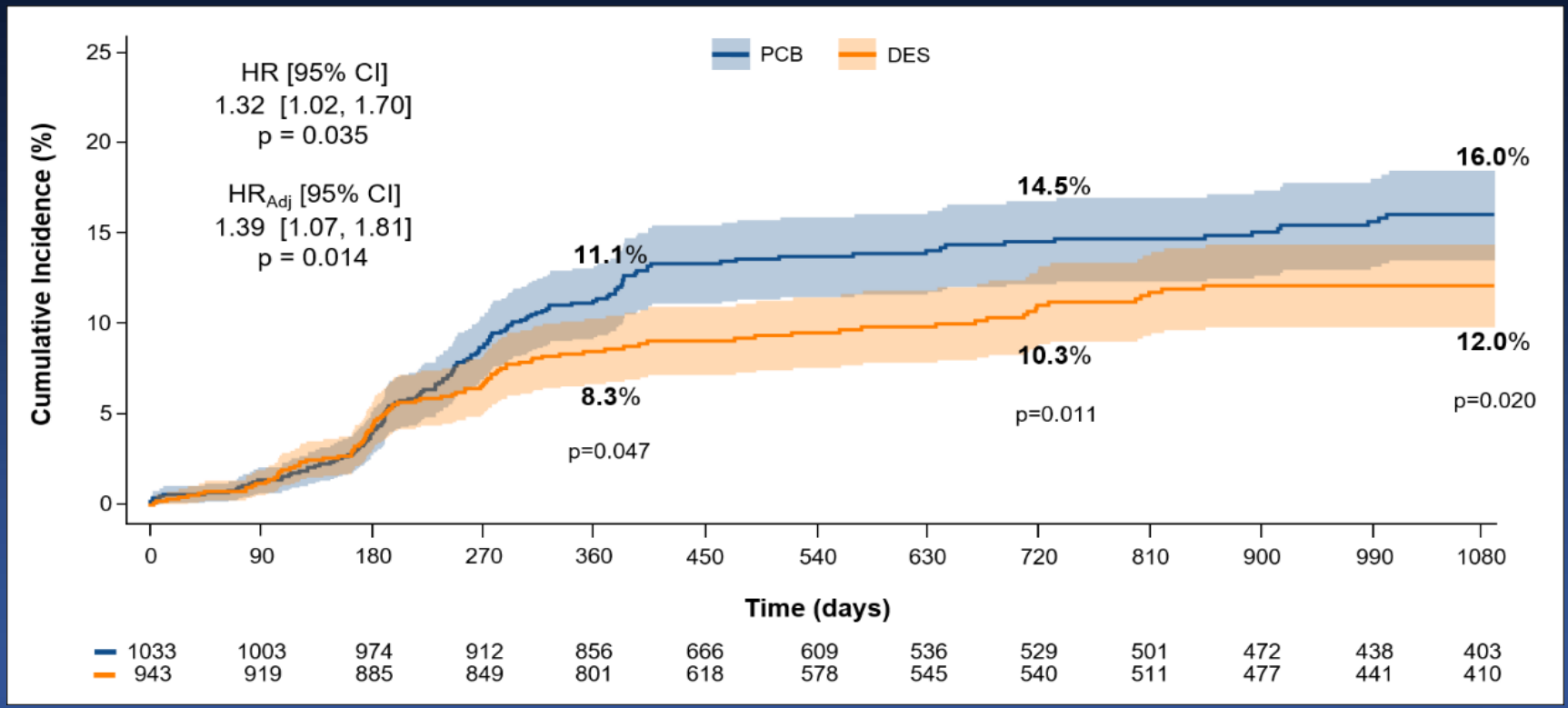
[a] Division of Cardiovascular Medicine, Department of Medicine, University of Florida, Gainesville, FL, United States of America
[b] Department of Medicine, Rochester General Hospital, Rochester, NY, United States of America



Sionitis GC et al., Lancet, 2015 Lee et al., JACC CV Interv. 2015 Elgendy IY, Alfonso F et al., Cardiovasc Revasc Med. 2018

Patient-level Pooled analysis of 10 RCTs: DAEDALUS study

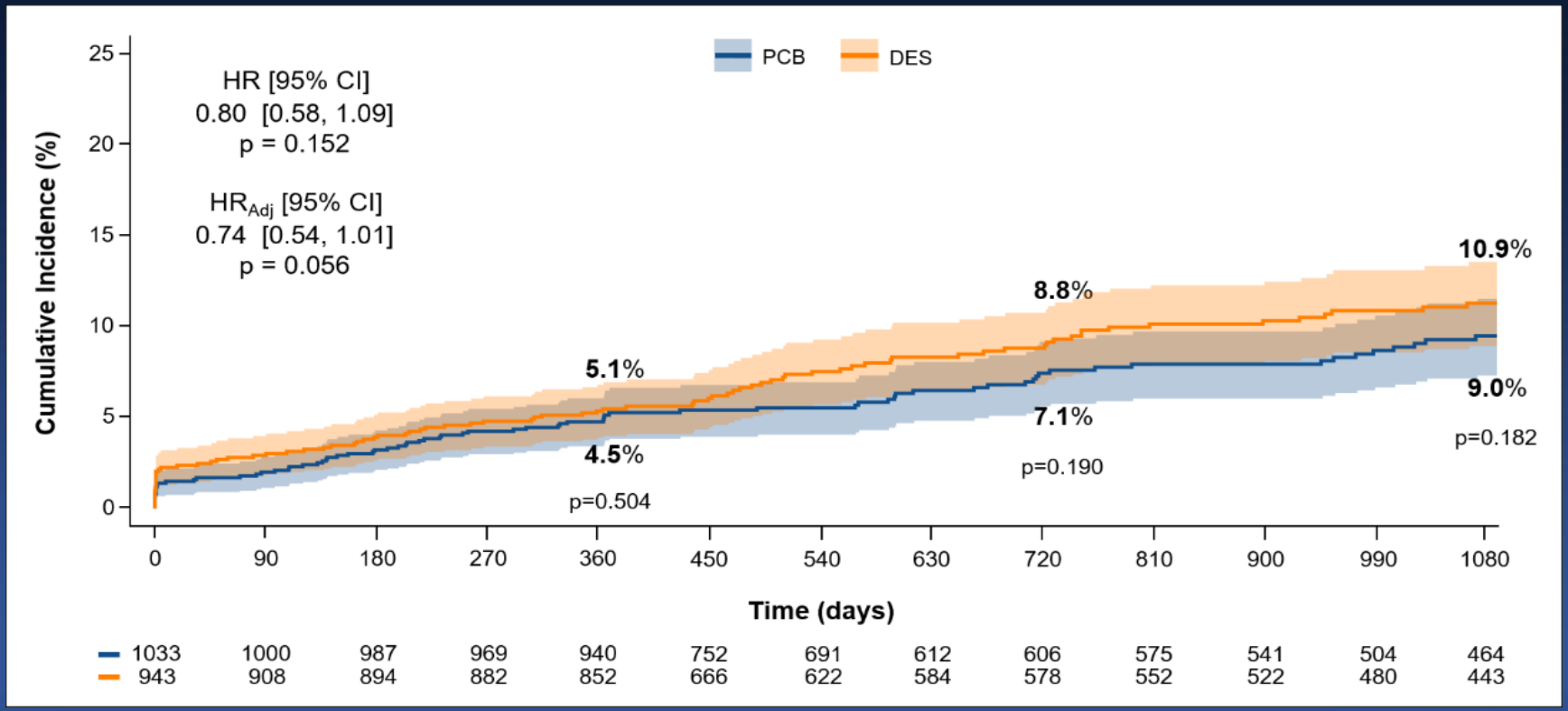
Target Lesion Revascularization of ISR



Giacoppo D et al., presented at EuroPCR 2018

Patient-level Pooled analysis of 10 RCTs: DAEDALUS study

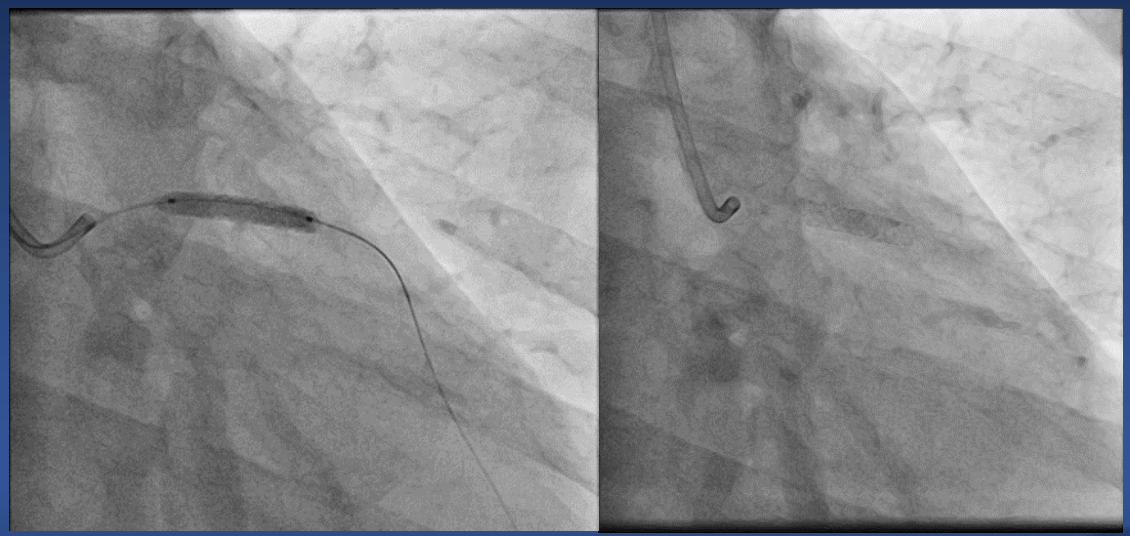
Composite of all-cause death, MI, or target lesion thrombosis



ESC Guideline recommends
DCB for in-stent restenosis treatment

Drug-coated balloons are recommended for the treatment of in-stent restenosis of BMS or DES

I	A



Neumann FJ et al. Eur Heart J. 2019;40:87165

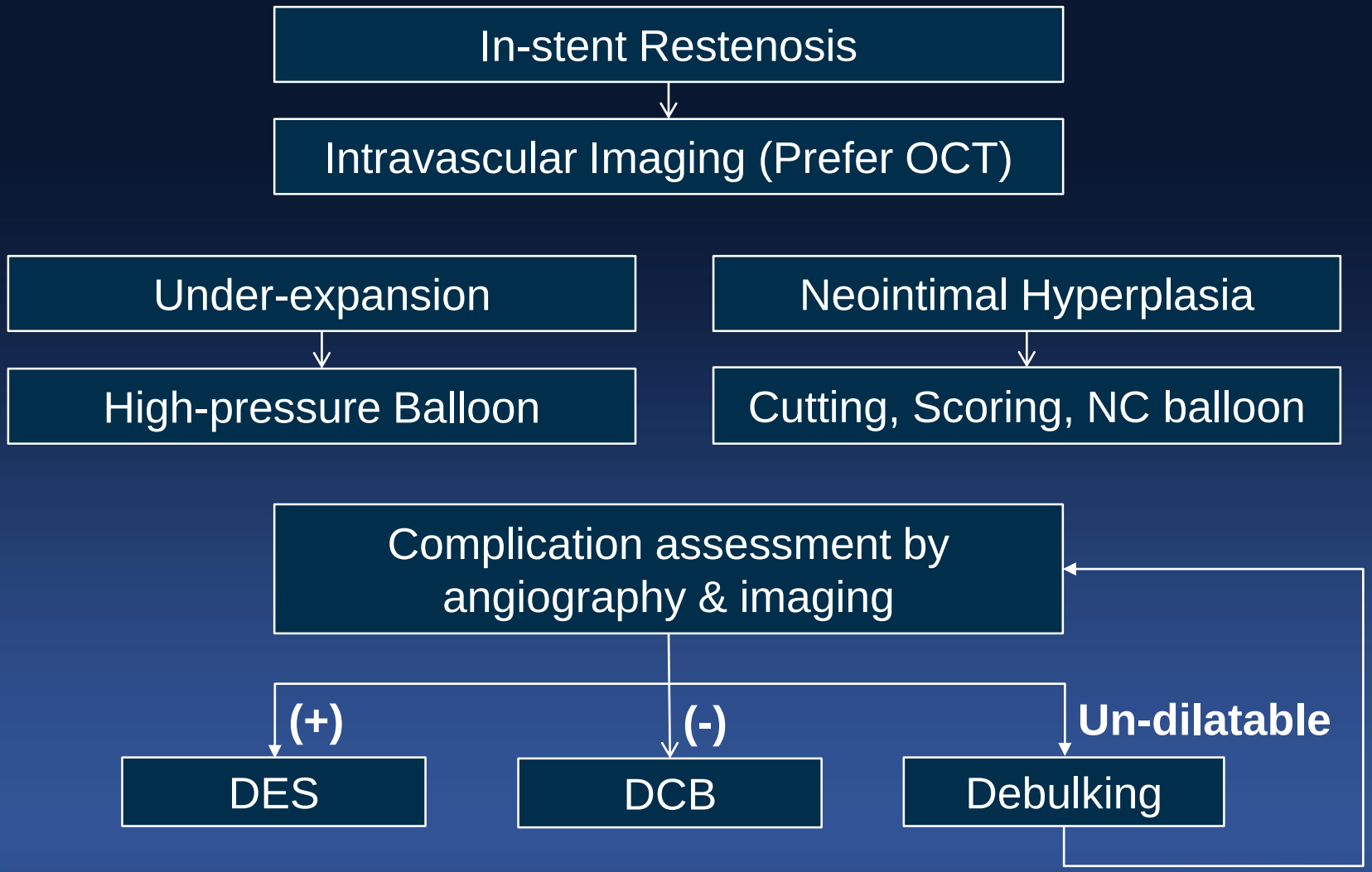
Data on DCB vs. DES for ISR consistently shows that…

- Angiographic outcomes are slightly better with DES.
- TLR is more frequent with DEB.
- Hard outcomes (death, MI, thrombosis) are comparable between DEB vs. DEB.

DCB as First-line Tx for ISR?

- No additional metallic stent layers
- Repeatable option of the procedure
- Reduced need for prolonged DAPT
- Disadvantage in angiographic outcomes and TLR
- But, similar hard outcomes
- Optimal lesion preparation is crucial
- Intravascular imaging guidance can be helpful

My Treatment Strategy for ISR



Another indication of DCB, Patients unsuitable for DES

Small vessel disease

Side branch disease in bifurcation lesion

Patients with high bleeding risk

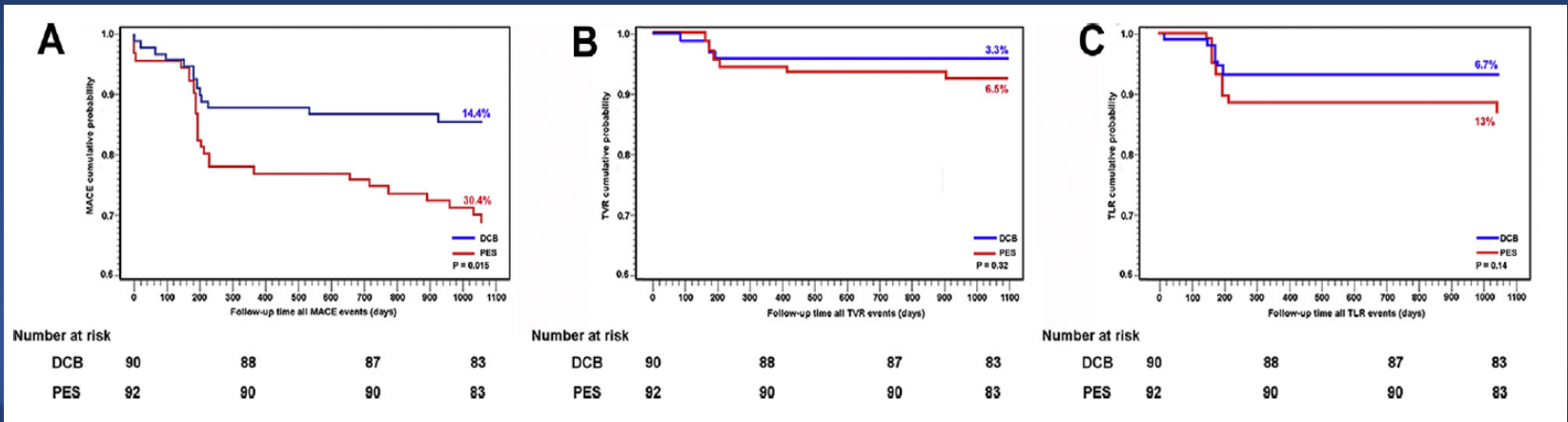
Small vessel disease, "Leave Nothing Behind"

RCT showed similar outcomes compared with DES

BELLO Trial

(<2.8mm, DCB vs. PES, Bail-out BMS 20.2% in DEB)

MACE TVR TLR



Latib A et al. JACC CV Interv. 2015;8:1132-1134.

Small vessel disease, "Leave Nothing Behind"

RCT showed similar outcomes compared with DES

BASKET SMALL-2 Trial (<3mm, DCB vs. PES/EES, Bail-out stent 5.1%)

MACE (cardiac death, non-fatal MI, TVR) at 12 mo

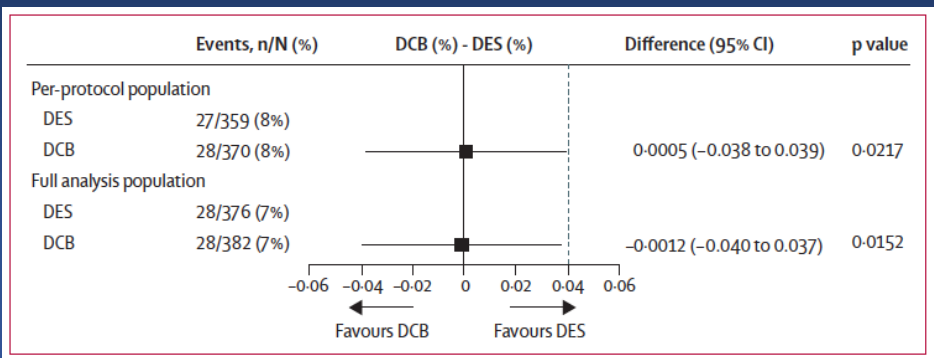


Figure 2: **Major adverse cardiac events by study group**
Data are absolute difference in event rates between the DCB and DES groups. The p-value tests whether the absolute difference in rates is equal to the pre-defined non-inferiority margin (0·04). DCB=drug-coated balloons. DES=drug-eluting stents.

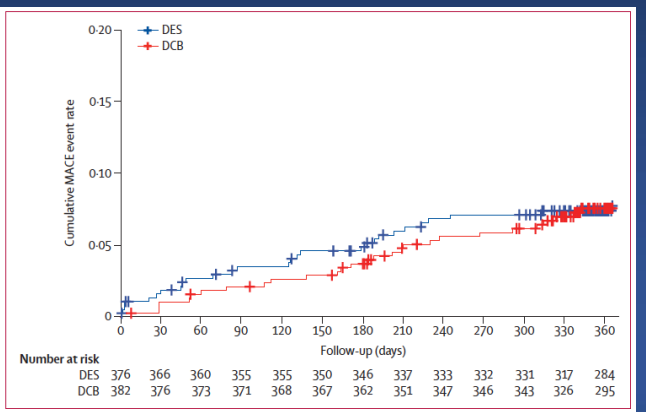


Figure 3: **Cumulative incidence rates for MACE**
Full analysis population. MACE=major adverse cardiac events. DCB=drug-coated balloons. DES=drug-eluting stents.

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

In conclusion,
DCB is…

- A reasonable alternative to repeated stenting with DES in ISR
- Not yet widely tested in de novo coronary disease

In conclusion,
DCB in the future…

- It will play an important role in the treatment of ISR with intravascular imaging guidance
- DCB-only strategy will be a reasonable alternative in selected patients.
- I am awaiting for newer-generation DCBs with better drug & technology.

Thank You !!

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