DOMENICA 10 OTTOBRE

Back to the future. L'impiego del pallone medicato (DEB) al posto dello stent

Bernardo Cortese, *Paderno Dugnano - MI*

Conoscere e Curare il Cuore 2021

38° Congresso di Cardiologia

del Centro per la Lotta contro l'Infarto - Fondazione Onlus

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Fondazione Ricerca e Innovazione Cardiovascolare

Back to the future. L'impiego del pallone medicato (DCB) al posto dello stent

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Disclosure Statement of Financial Interest

Speaker's name: Bernardo Cortese MD

I have the following potential conflicts of interest to report (last 2 years):

Consultant: Abbott Vascular, Astra Zeneca, Kardia, Innova HTS, Stentys, Daiiki-Sankyo, Philips-Spectranetics, Reva, Bayer, Cardinal-Cordis, BBraun, Cardionovum, Microport, Balton, Eukon, Chiesi.

Honorarium: Amgen, Stentys, Sanofi, B.Braun, Servier, Alvimedica, Intramedicals.

Institutional grant/research support: AB Medica, St Jude, Abbott Vascular.

Advisory Board: Cordis, Concept Medical, AR Baltic, Amgen, Microport, Boston Scientific.

Sistema Sanitario Regione Lombardia

DCB

- respects anatomy;
- no scaffold;
- fewer reinterventions??

DES

- straightens vessel;
- may occlude SB;
- metal=foreign body;
- requires maintenance.

2014 ESC/EACTS Guidelines on myocardial revascularization

Repeat revascularization

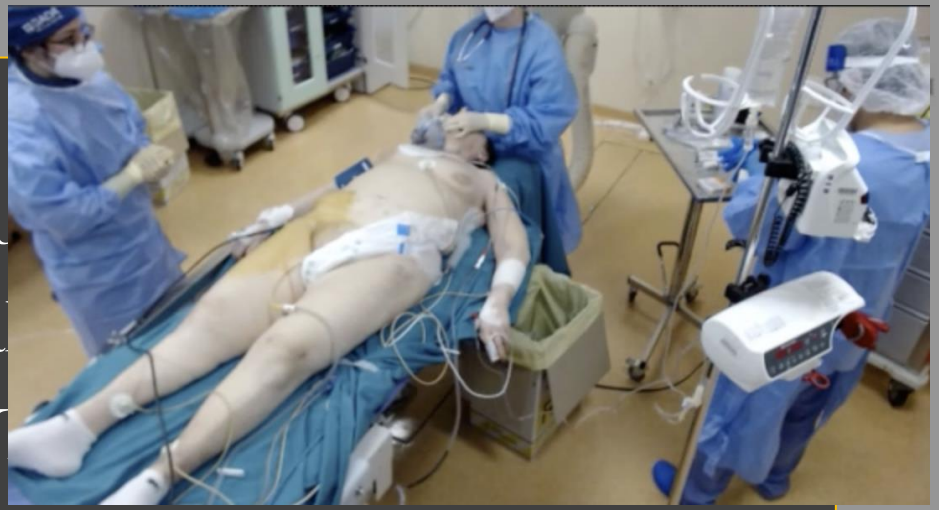
Recommendations	Class[a]	LoE[b]	Ref[c]
Early post-operative ischaemia and graft failure			
Coronary angiography is recommended for patients with: • symptoms of ischaemia and/or abnormal biomarkers suggestive of perioperative myocardial infarction • ischaemic ECG changes indicating large area of risk • new significant wall motion abnormalities • haemodynamic instability.	I	C	
It is recommended to make the decision on redo CABG or PCI by *ad hoc* consultation in the Heart Team and based on feasibility of revascularization, area at risk, comorbidities and clinical status.	I	C	
PCI should be considered over re-operation in patients with early ischaemia after CABG if technically feasible.	IIa	C	
If PCI is performed, revascularization of the native vessels or IMA grafts rather than occluded or heavily diseased SVGs should be considered.	IIa	C	
Disease progression and late graft failure			
Repeat revascularization is indicated in patients with severe symptoms or extensive ischaemia despite medical therapy if technically feasible.	I	B	54,143
PCI should be considered as a first choice if technically feasible, rather than re-do CABG.	IIa	C	
PCI of the bypassed native artery should be the preferred approach, if technically feasible.	IIa	C	
IMA, if available, is the conduit of choice for re-do CABG.	I	B	481
Re-do CABG should be considered for patients without a patent IMA graft to the LAD.	IIa	B	481
Re-do CABG may be considered in patients with lesions and anatomy not suitable for revascularization by PCI.	IIb	C	
PCI may be considered in patients with patent IMA graft if technically feasible.	IIb	C	
DES are recommended for PCI of SVGs.	I	A	489–495
Distal protection devices are recommended for PCI of SVG lesions if technically feasible.	I	B	484,485
Restenosis			
Repeat PCI is recommended, if technically feasible.	I	C	
DES are recommended for the treatment of in-stent re-stenosis (within BMS or DES).	I	A	501,502,508 511,524
Drug-coated balloons are recommended for the treatment of in-stent restenosis (within BMS or DES).	I	A	507– 511,524
IVUS and/or OCT should be considered to detect stent-related mechanical problems.	IIa	C	

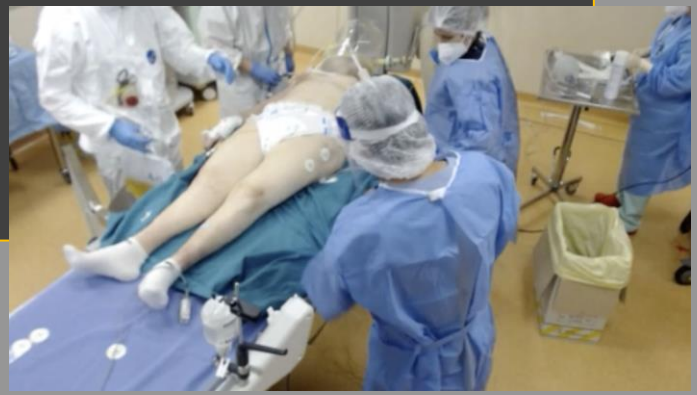
Restenosis			
Repeat PCI is recommended, if technically feasible.	I	C	
DES are recommended for the treatment of in-stent re-stenosis (within BMS or DES).	I	A	501,502,508 511,524
Drug-coated balloons are recommended for the treatment of in-stent restenosis (within BMS or DES).	I	A	507– 511,524
IVUS and/or OCT should be considered to detect stent-related mechanical problems.	IIa	C	

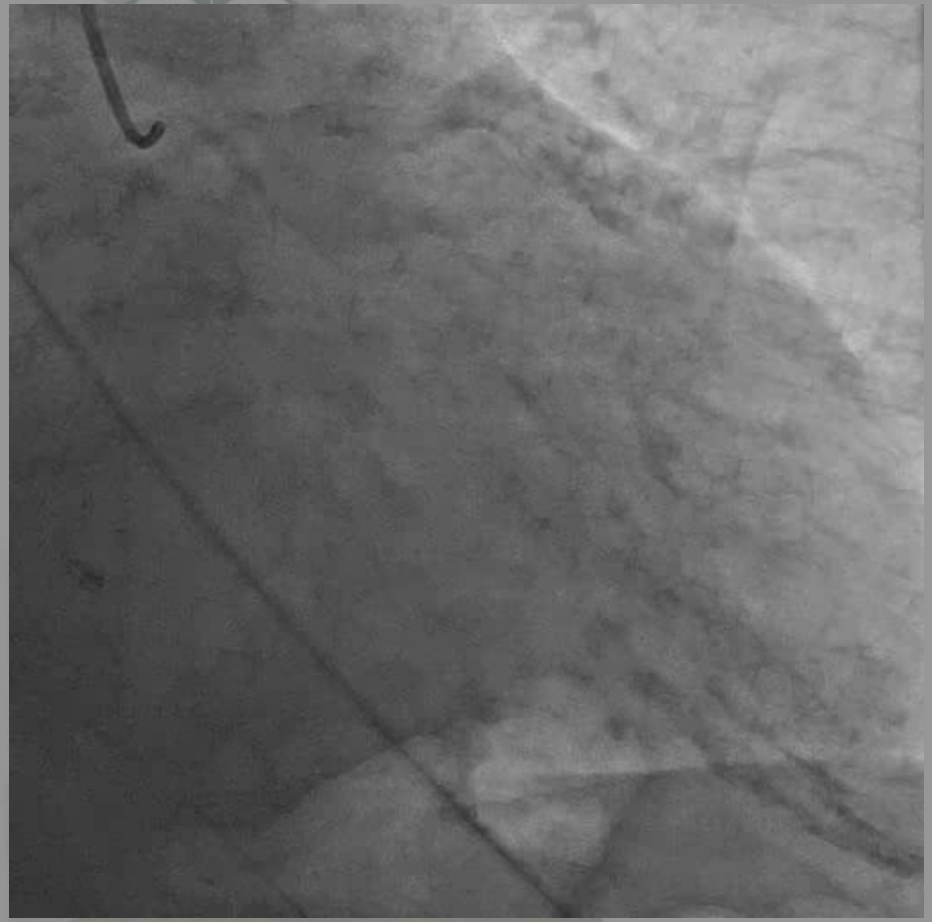
2018 ESC/EACTS Guidelines on myocardial revascularization

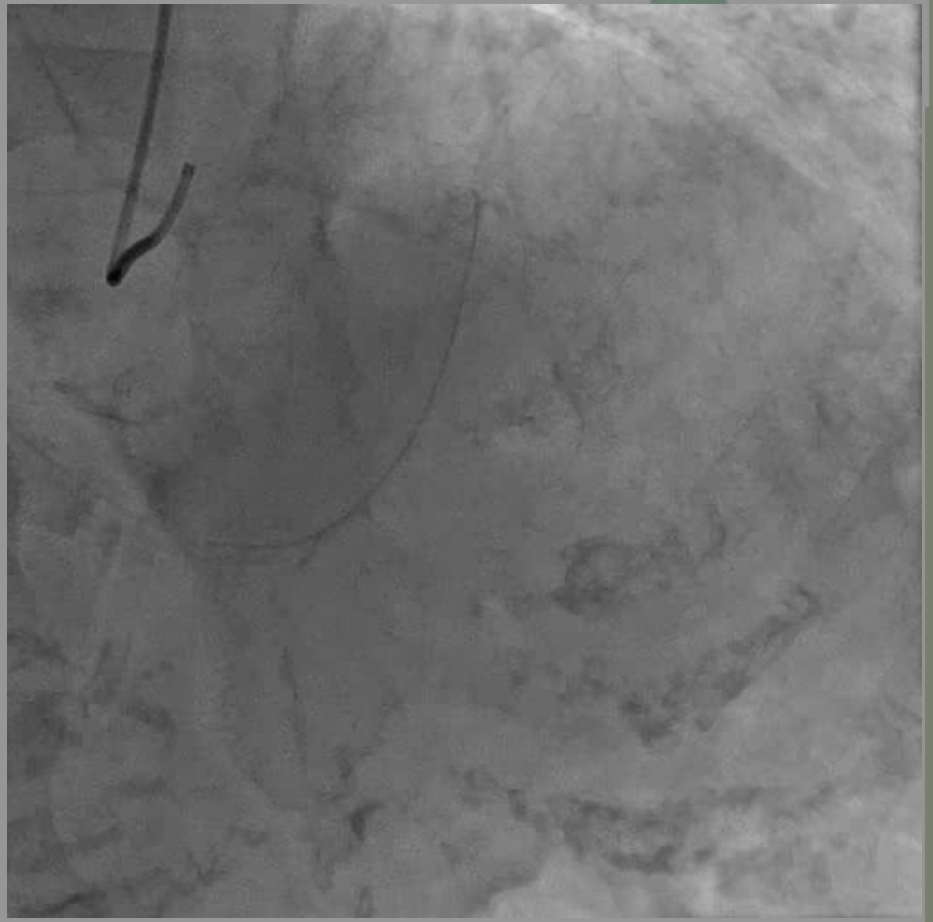
Restenosis		
DES are recommended for the treatment of in-stent restenosis of BMS or DES.[373,375,378,379]	I	A
Drug-coated balloons are recommended for the treatment of in-stent restenosis of BMS or DES.[373,375,378,379]	I	A

- 70 y.o. diabetic woman
- 04.20 anterior positive nu
- Covid -no action underta
- 12.12.20 ANTERIOR S
- Acute pulmonary edema-CPAP
- Hb 5 g/dl-4 Unites blood
- Cath lab









- No antiplt per os
- UFH 5000 IU
- Cangrelor bolus
- Scoring balloon 2.5, 3.0mm
- Dual-DCB PCI, no metal

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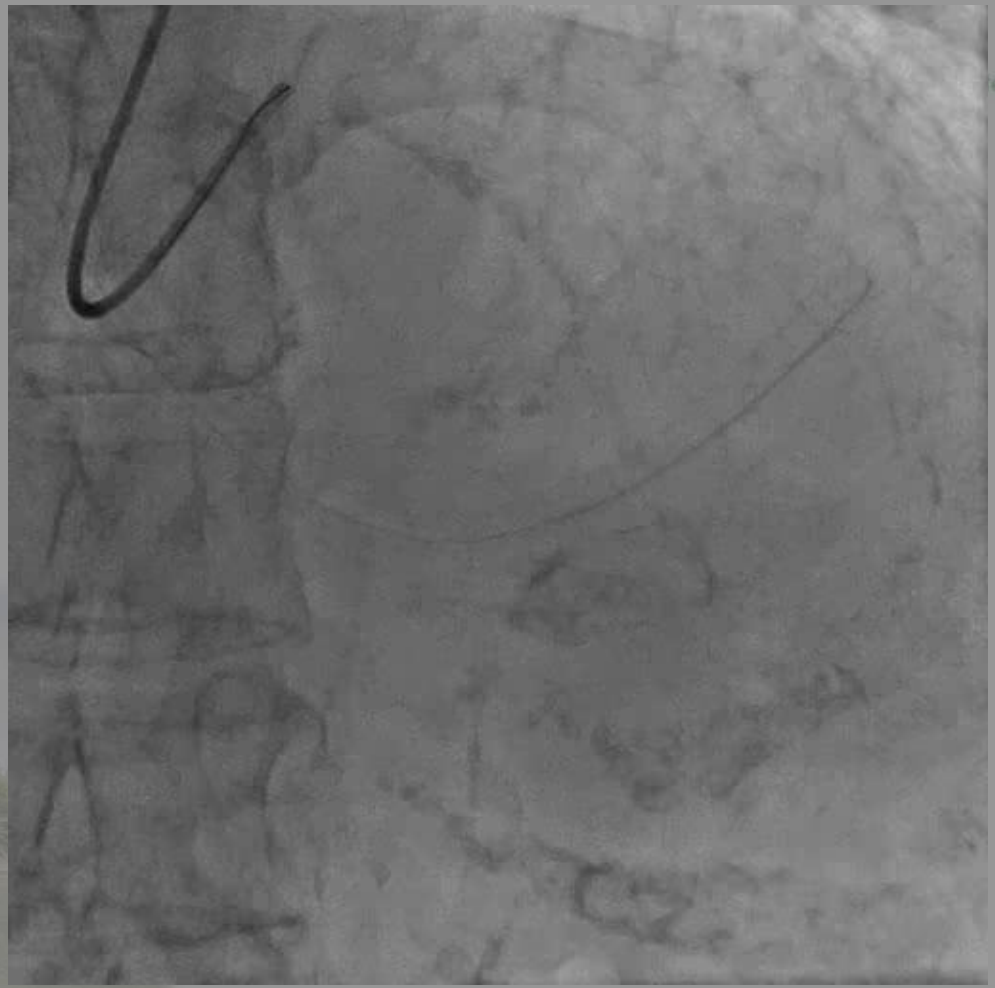

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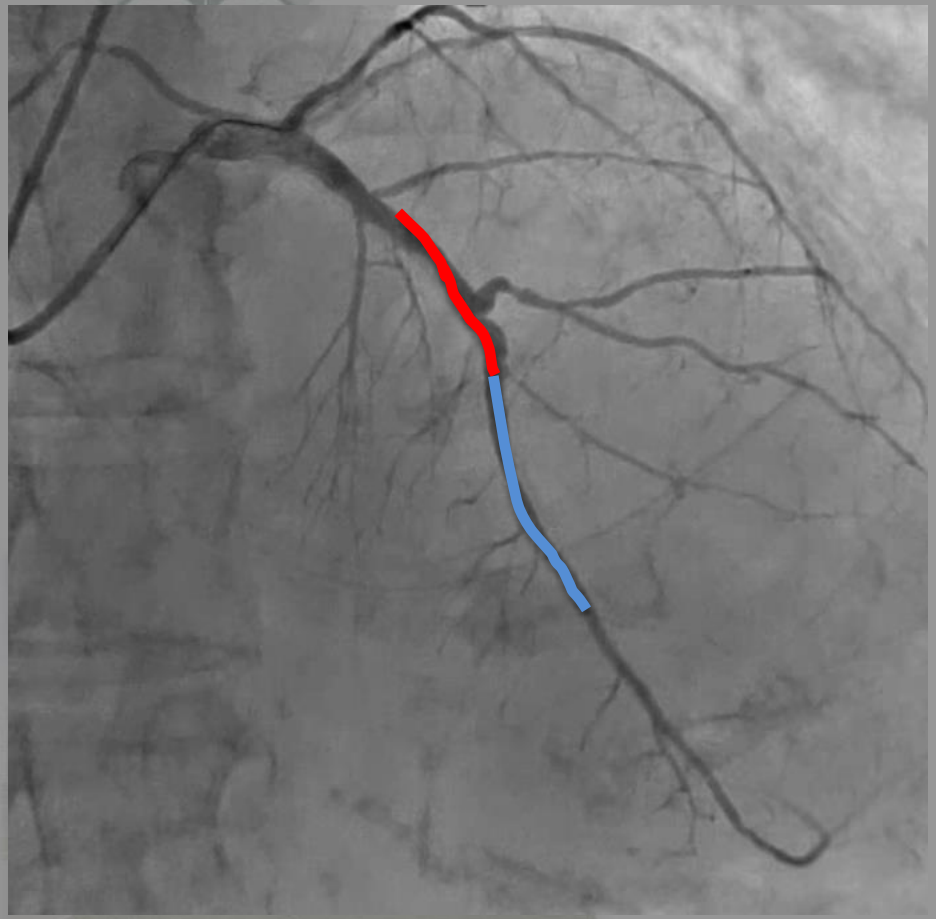
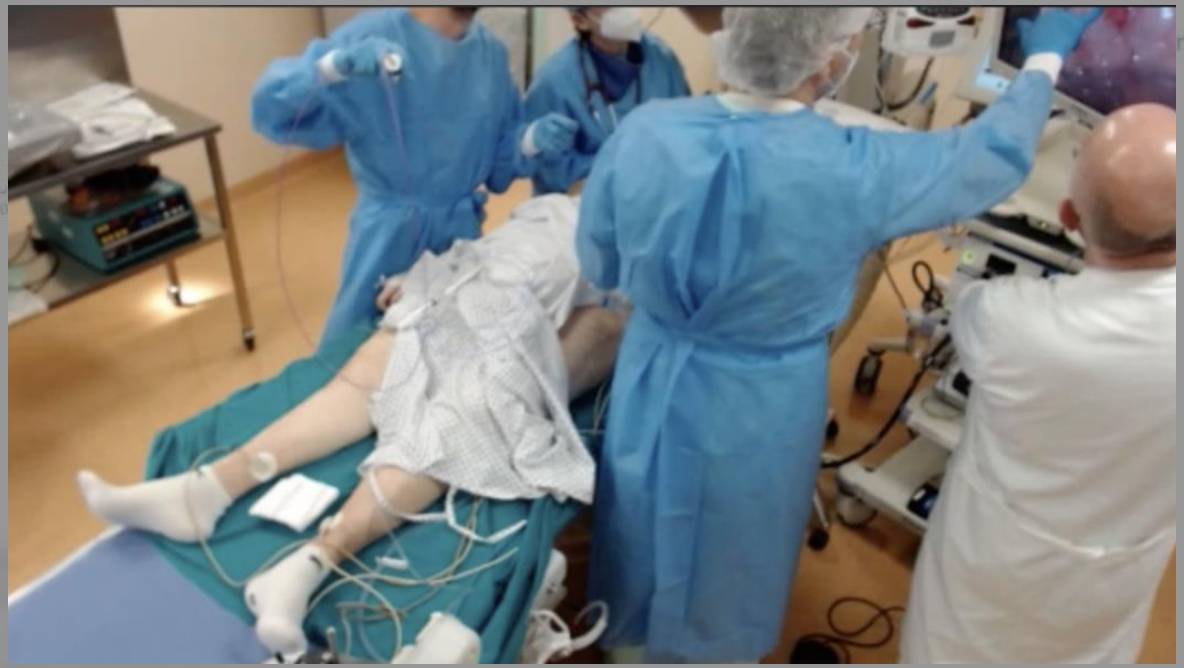
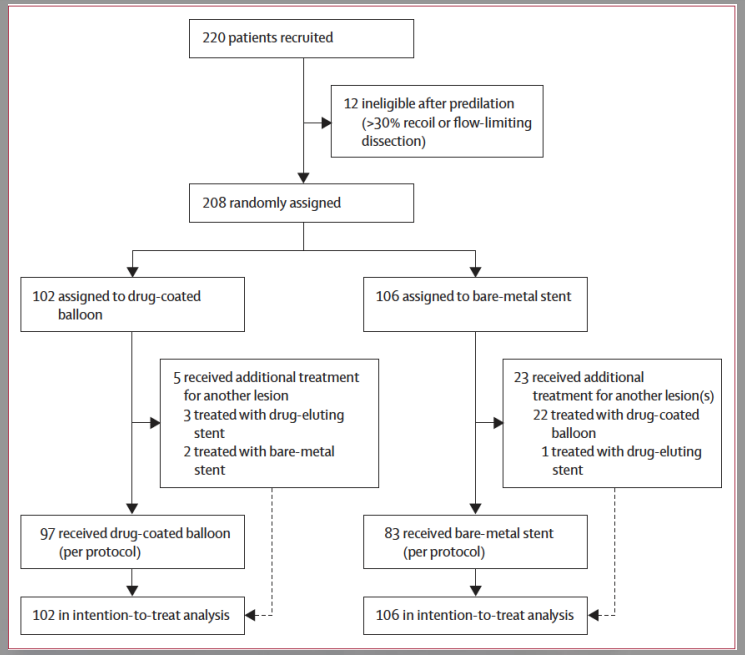


- PCB 3.0/30 prox
- SCB 2.5/40 dist



- In-cath lab gastroscopy with multiple cauterizations
- Cangrelor infusion 48 hours, then clopidogrel (SAP)



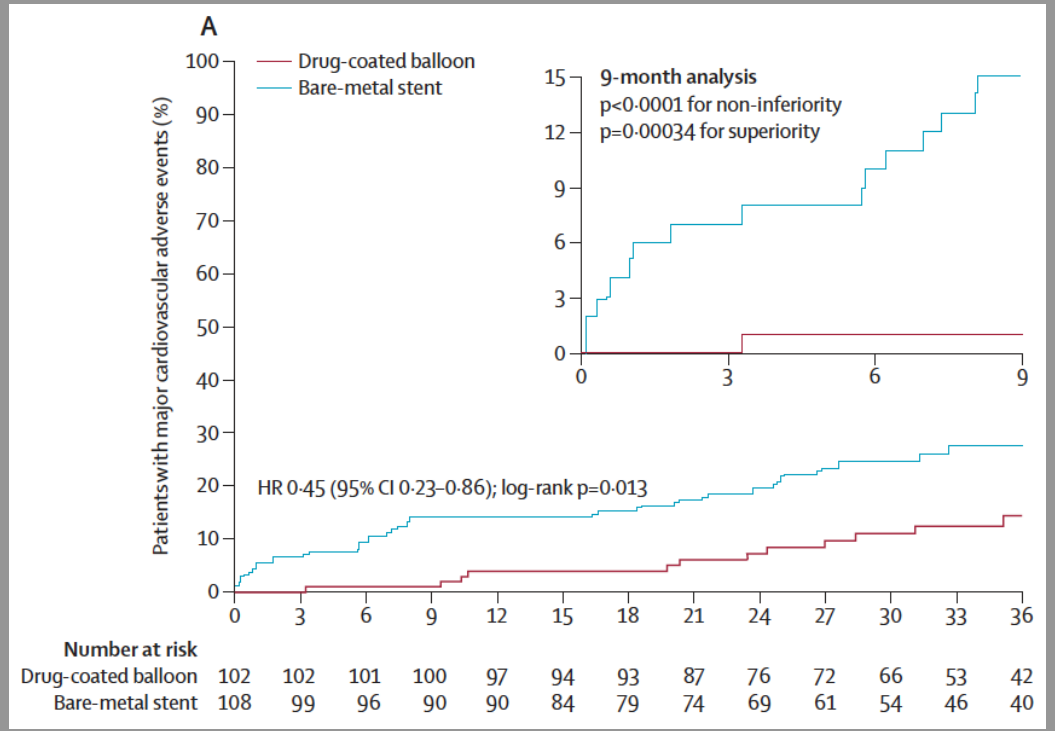
Drug-coated balloon for treatment of de-novo coronary artery lesions in patients with high bleeding risk (DEBUT): a single-blind, randomised, non-inferiority trial

Tuomas T Rissanen, Sanna Uskela, Jaakko Eränen, Pirjo Mäntylä, Annika Olli, Hannu Romppanen, Antti Siljander, Mikko Pietilä, Mikko J Minkkinen, Jerry Tervo, Jussi M Kärkkäinen, on behalf of the DEBUT trial investigators*

Lancet 2019; 394: 230–39
Published Online June 13, 2019

Summary

Background The optimal technique of percutaneous coronary intervention in patients at high bleeding risk is not known. The hypothesis of the DEBUT trial was that percutaneous coronary intervention with drug-coated balloons is non-inferior to percutaneous coronary intervention with bare-metal stents for this population.

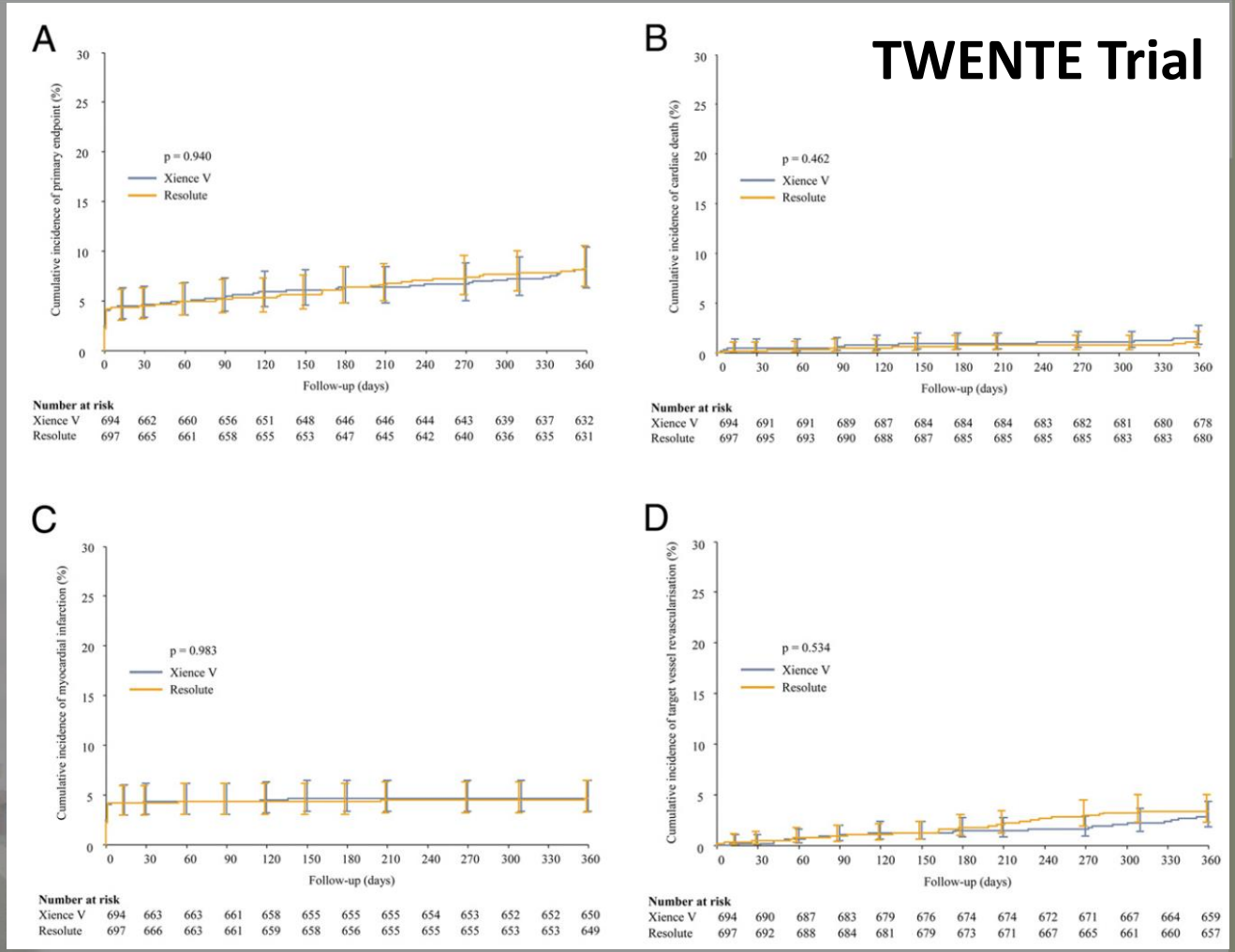


Frail, high bleeding risk patients

DCB

- ISR
- frail, high bleeding risk patient
- …what else?

DES are really good!



Von Birgelen C, et al. JACC. 2012

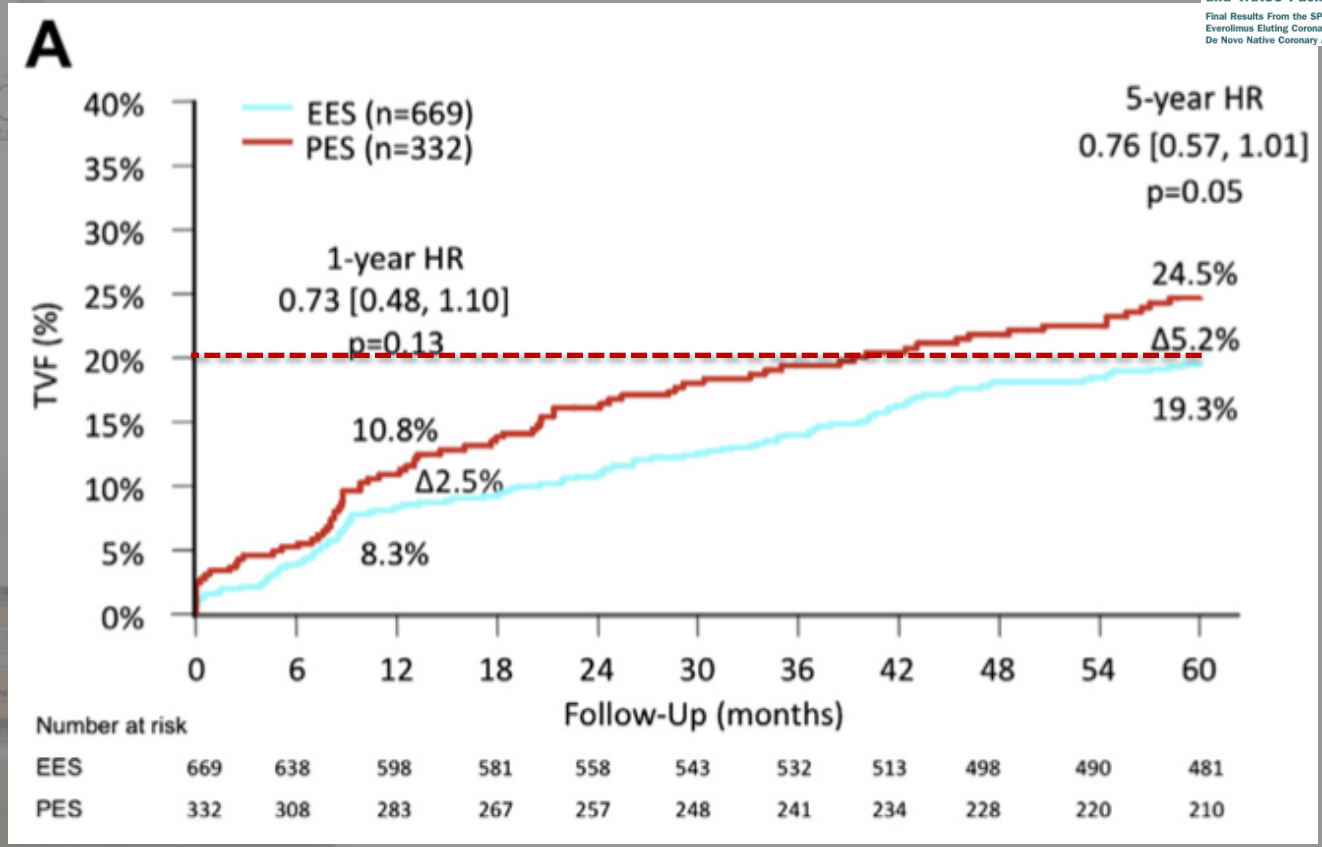
	Everolimus stent (n=223)	Paclitaxel stent (n=77)	All patients (n=300)
Age (years)	62±10	62±9	62±10
Male gender (%)	71	79	73
Current smoker (%)	32	30	31
Diabetes (%)	23	24	23
Hypertension requiring medication (%)	67	65	67
Hyperlipidaemia requiring medication (%)	69	75	70
Prior target vessel intervention (%)	4	4	4
Prior MI (%)	35	25	32
Stable angina (%)	62	62	62
Unstable angina (%)	27	32	28
Target vessel (%)	Number of lesions=260	Number of lesions=91	Number of lesions=351
Left anterior descending	41	47	42
Left circumflex	29	19	26
Right coronary artery	30	34	31
AHA/ACC lesion class (%)			
A	1	0	1
B1	21	20	21
B2	65	67	66
C	13	13	13
Reference vessel diameter (mm±SD)	2.70±0.52	2.82±0.58	2.73±0.54
Lesion length (mm±SD)	13.0±5.7	13.2±6.4	13.0±5.9

JACC: CARDIOVASCULAR INTERVENTIONS VOL. 6, NO. 12, 2013
© 2013 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER INC. http://dx.doi.org/10.1016/j.jcin.2013.07.009

CLINICAL RESEARCH

5-Year Results of a Randomized Comparison of XIENCE V Everolimus-Eluting and TAXUS Paclitaxel-Eluting Stents

Final Results From the SPIRIT III Trial (Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System in the Treatment of Patients With De Novo Native Coronary Artery Lesions)



Brugaletta, S. et al. J Am Coll Cardiol. 2021;77(9):1165-78.

After 1 year, metal is metal.

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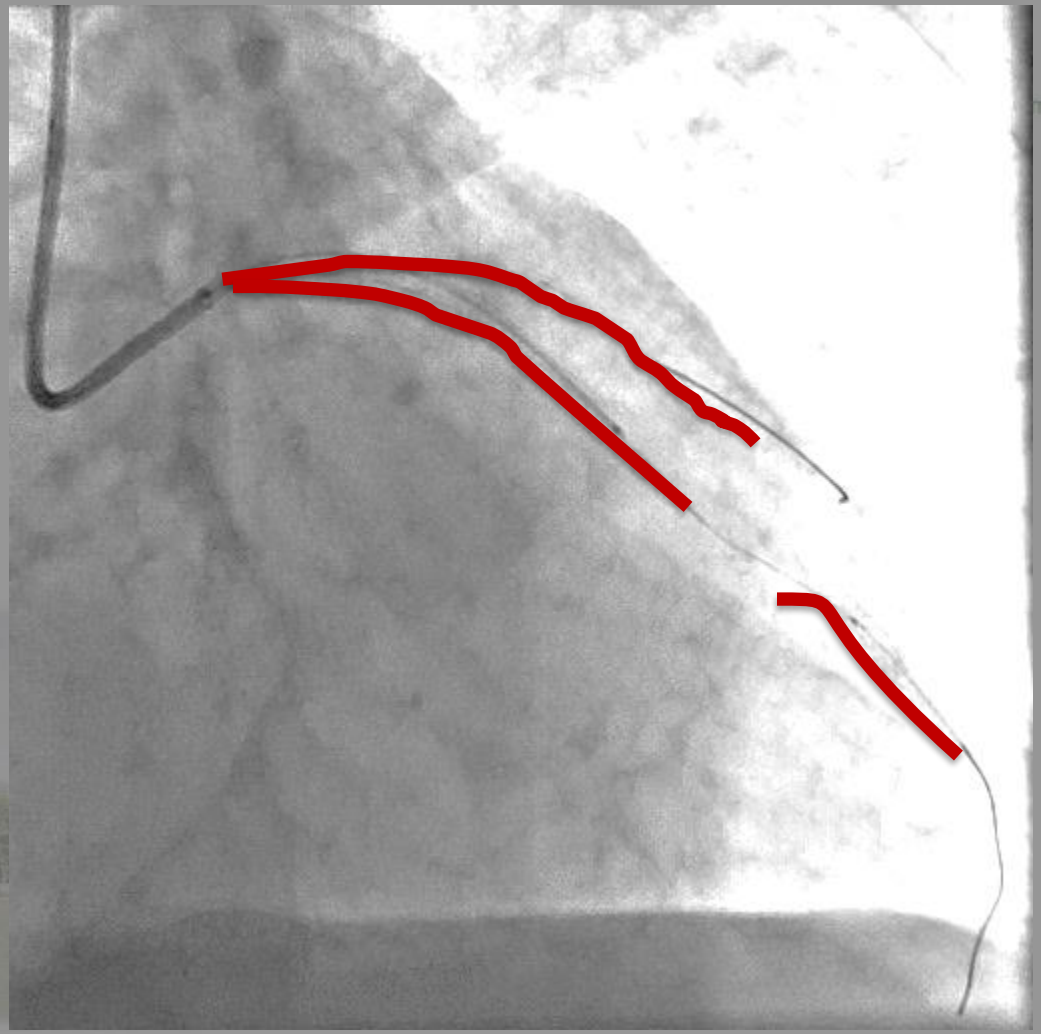
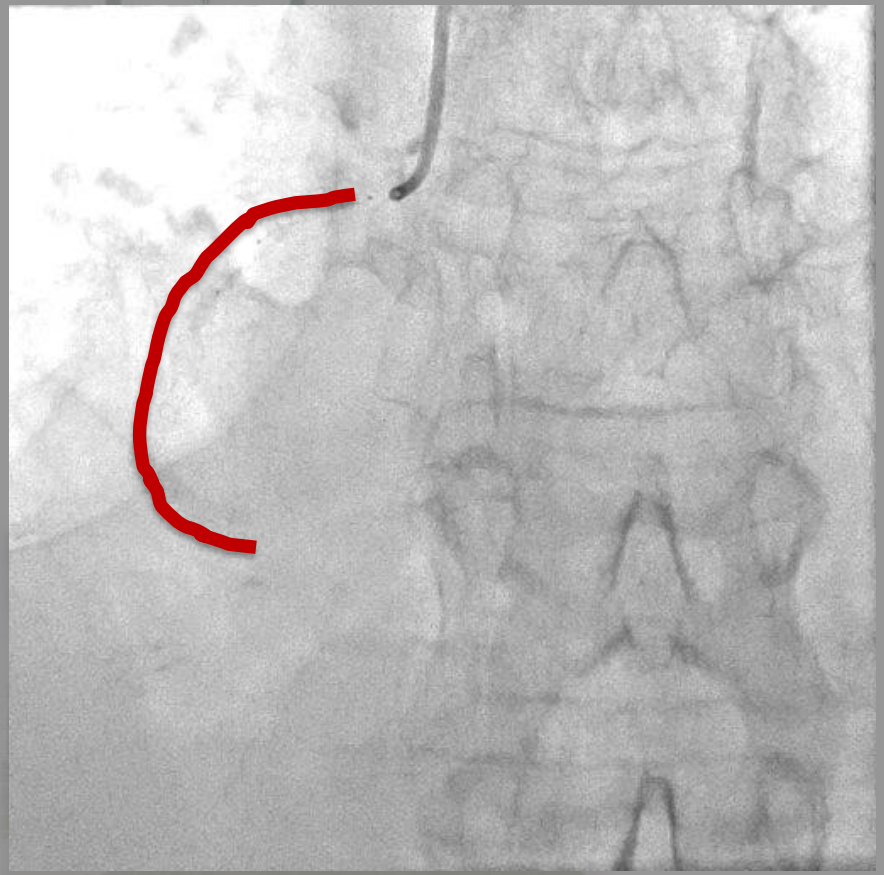
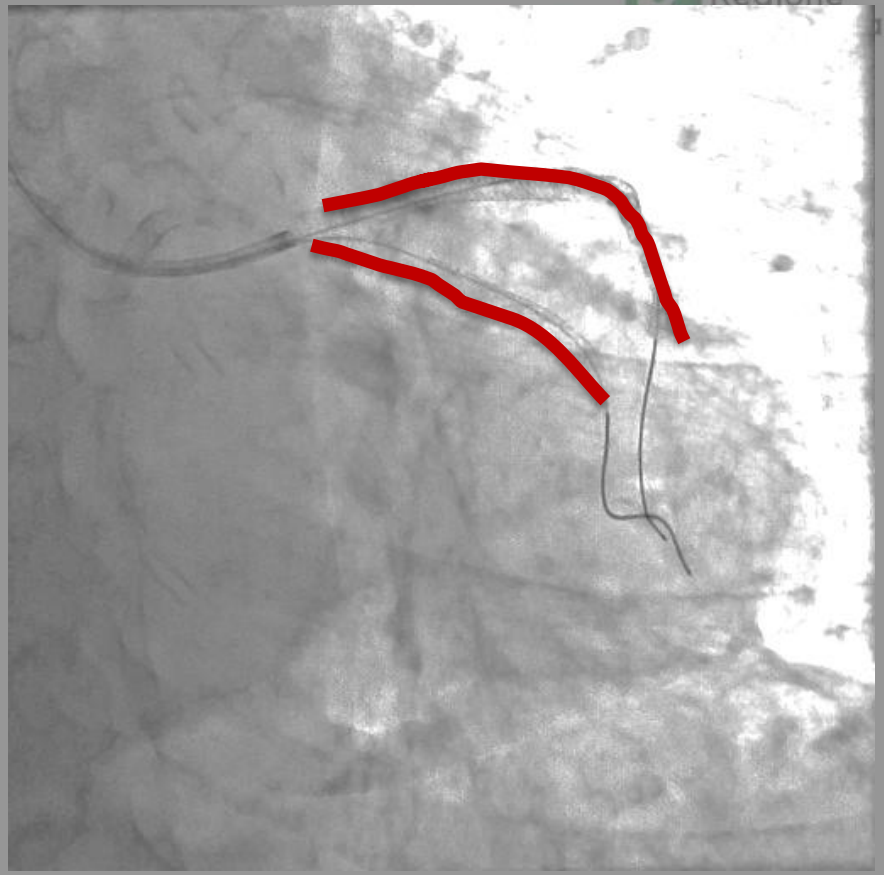


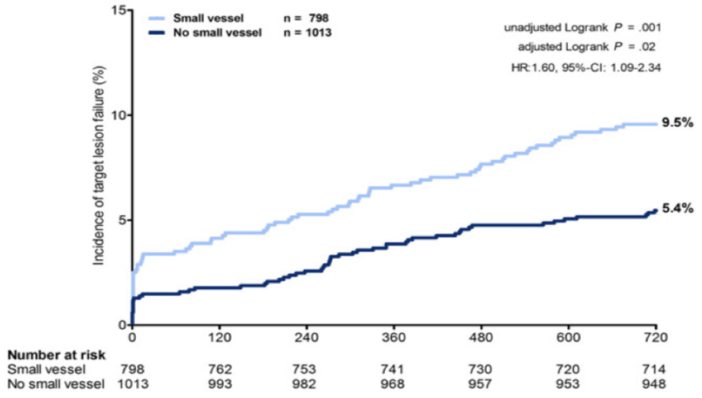




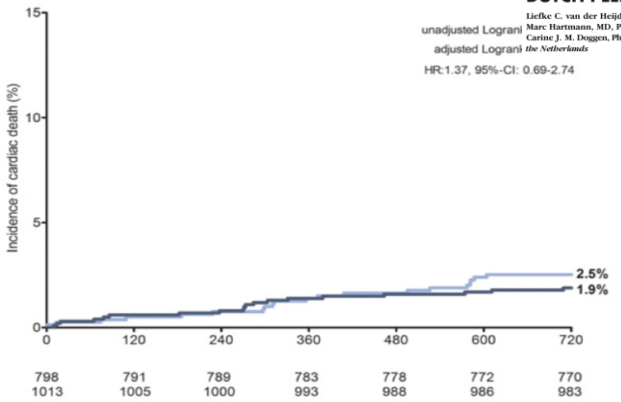
Small-vessel treatment with contemporary newer-generation drug-eluting coronary stents in all-comers: Insights from 2-year DUTCH PEERS (TWENTE II) randomized trial

Liefke C. van der Heijden, MD,[a] Marlies M. Kok, MD,[a] Peter W. Danse, MD, PhD,[b] Alexander R. Schramm, MD,[c] Marc Hartmann, MD, PhD,[a] Marije M. Löwik, PhD,[a] Gerard C. M. Linssen, MD, PhD,[d] Martin G. Stoel, MD, PhD,[a] Carine J. M. Doggen, PhD,[a] and Clemens von Birgelen, MD, PhD[a,e] *Enschede, Arnhem, Emmen, and Almelo and Hengelo, the Netherlands*

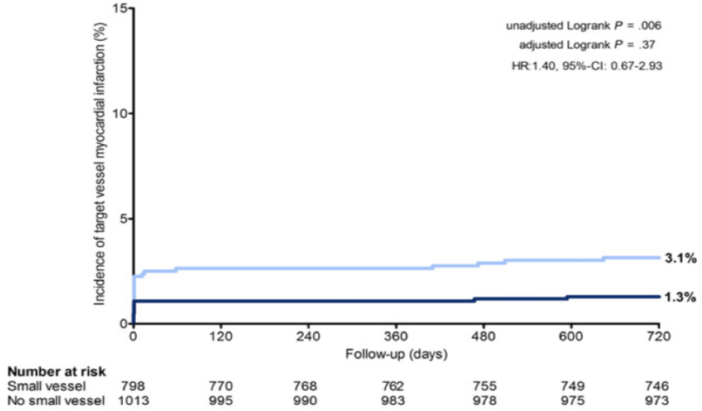
A) Target lesion failure



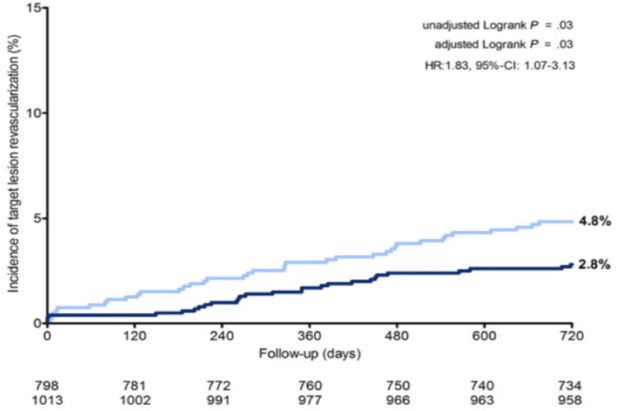
B) Cardiac death



C) Target vessel myocardial infarction



D) Clinically indicated target lesion revascularization

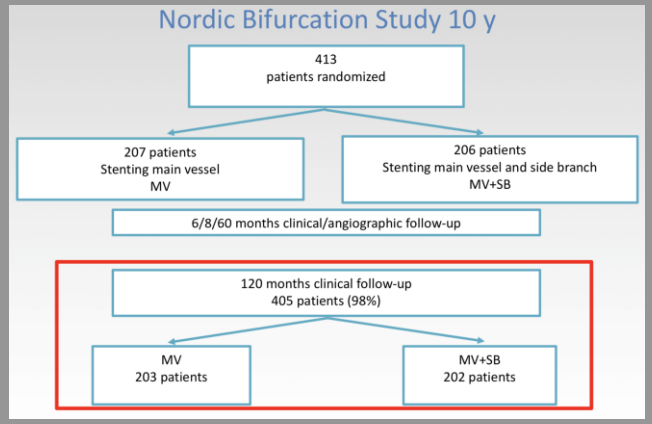


Stent Length

Clinical outcomes of long stenting: patient-level pooled analysis from the GRAND-DES registry

- Analysis of 9,217 stented patients with new generation DES for a single lesion during follow-up 730 days.
- From GRAND-DES registry, Republic of Korea.
- Short stenting group (<40mm) 8,035 vs Long stenting (>40mm) 1,182.
- **TLF: HR 1.88, p<0.001.**
- **ST: HR 2.2, p<0.001.**

Kong MG, et al. EuroIntervention. 2021



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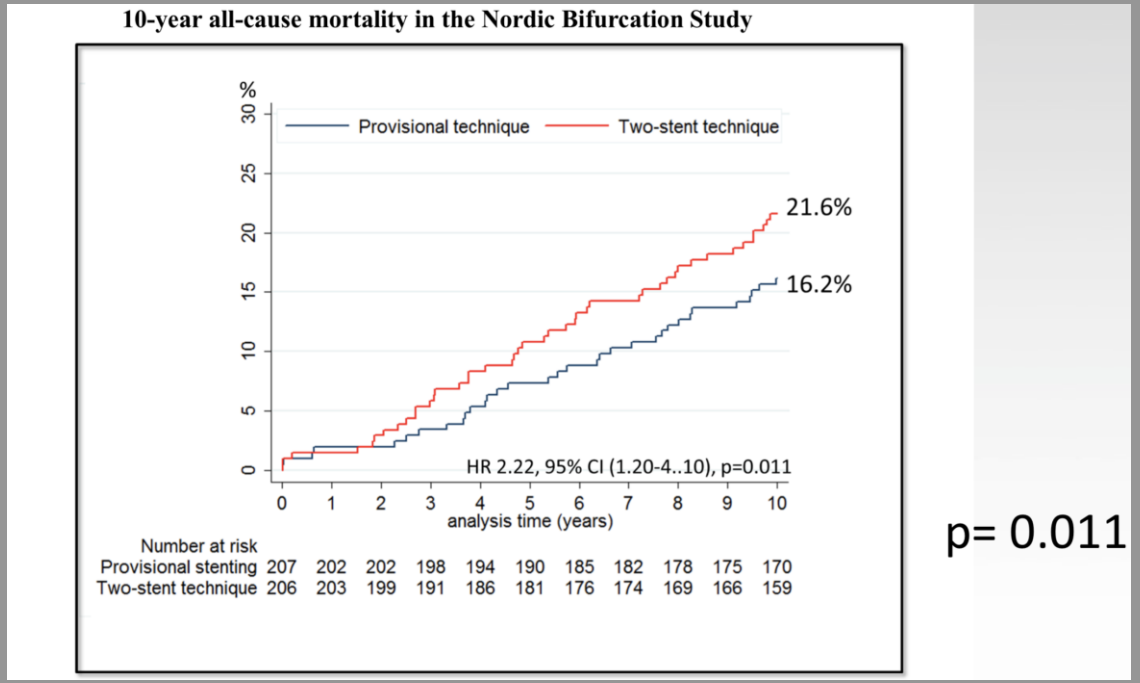
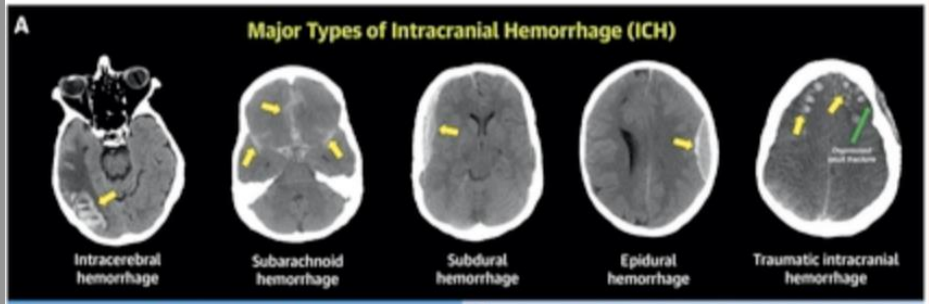
DES and mortality= complex vs. easy lesions



p= 0.011

CENTRAL ILLUSTRATION: Epidemiology, Clinical Sequelae, and Potential Therapies of Antiplatelet-Associated Intracranial Hemorrhage

A



B

Global burden of ICH:

Total estimated cases of intracerebral and subarachnoid hemorrhage in 2019: ≈ 4.6 million

Age-standardized risk of intracerebral or subarachnoid hemorrhage: ≈ 55 cases per 100,000 person years

≈ 30% of patients with ICH in North America and Western Europe were treated with antiplatelet agents upon presentation

Among patients with intracerebral hemorrhage, baseline antiplatelet use is associated with:

Larger baseline hemorrhagic volume

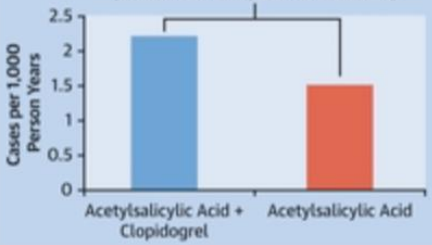
Greater risk of hemorrhagic growth

Higher risk of hematoma expansion

C

Risk of Intracranial Hemorrhage Between Patients Treated with Dual Antiplatelet Therapy and Single Antiplatelet Therapy

2.2 vs. 1.5 cases per 1,000 person years
(hazard ratio: 1.42, 95% CI: 1.05-1.92)



D

Existing/proposed medical therapies for patients with antiplatelet-associated ICH:

- Hemostatic agents *(recombinant activated factor VII, fibrinogen concentrate, factor XIII concentrate)*
- Antifibrinolytic agents *(e.g. tranexamic acid)*
- Pooled platelet transfusion
- Desmopressin
- Serum albumin
- Platelet-rich plasma
- Sorbent hemadsorption *(for ticagrelor)*
- Monoclonal antibody fragment *(bentracimab for ticagrelor)*

} Requires prospective evaluation in human studies

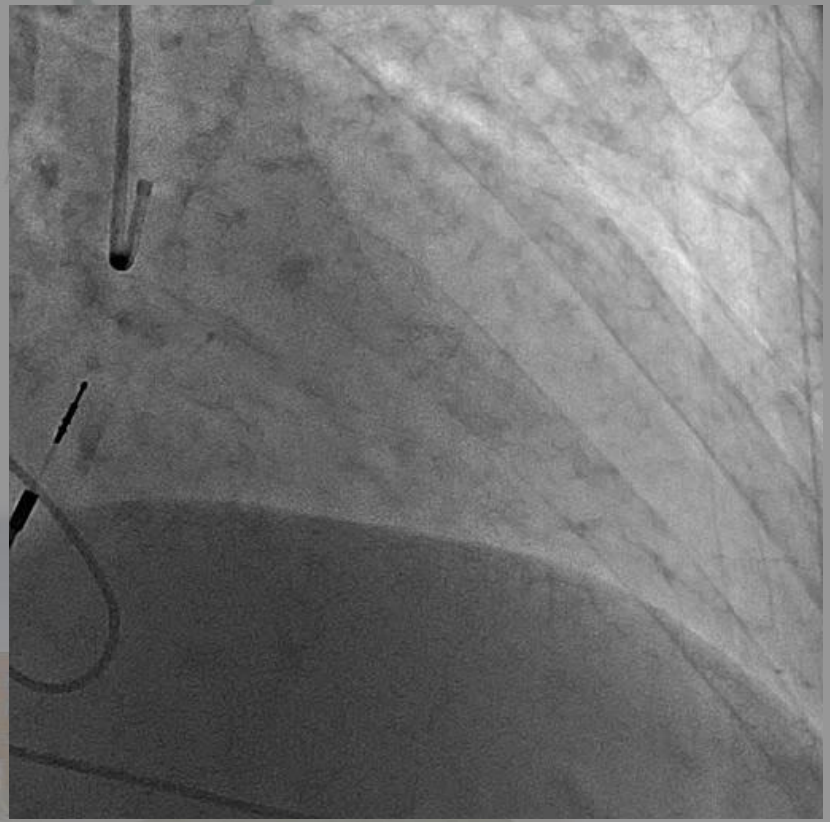
Ha, A.C.T. et al. J Am Coll Cardiol. 2021;78(13):1372-1384.

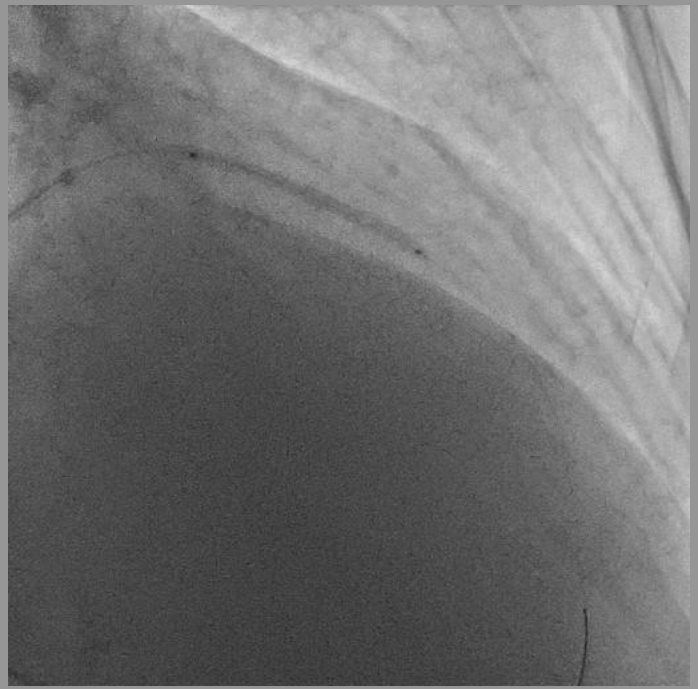
DCB

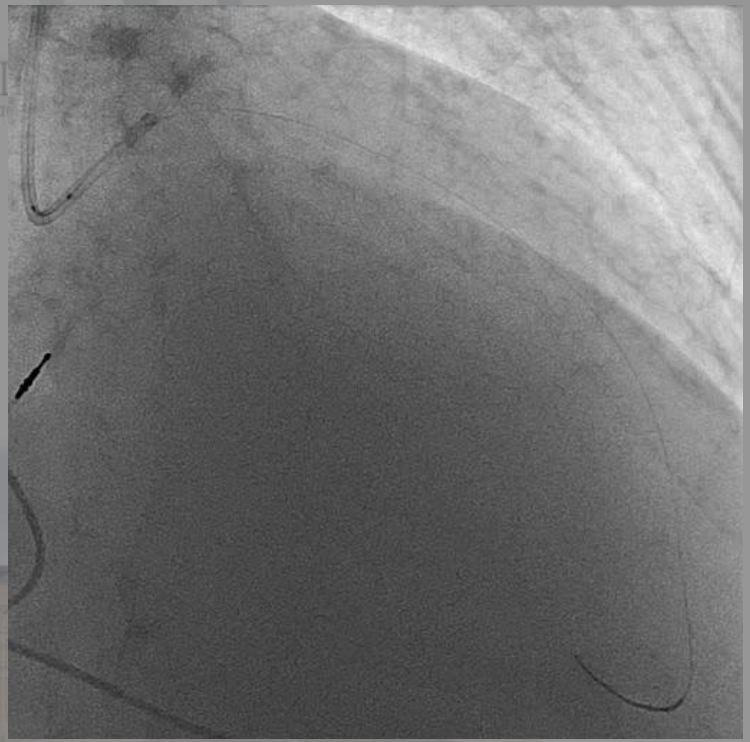
Fondazione
Ricerca e Innovazione
Cardiovascolare

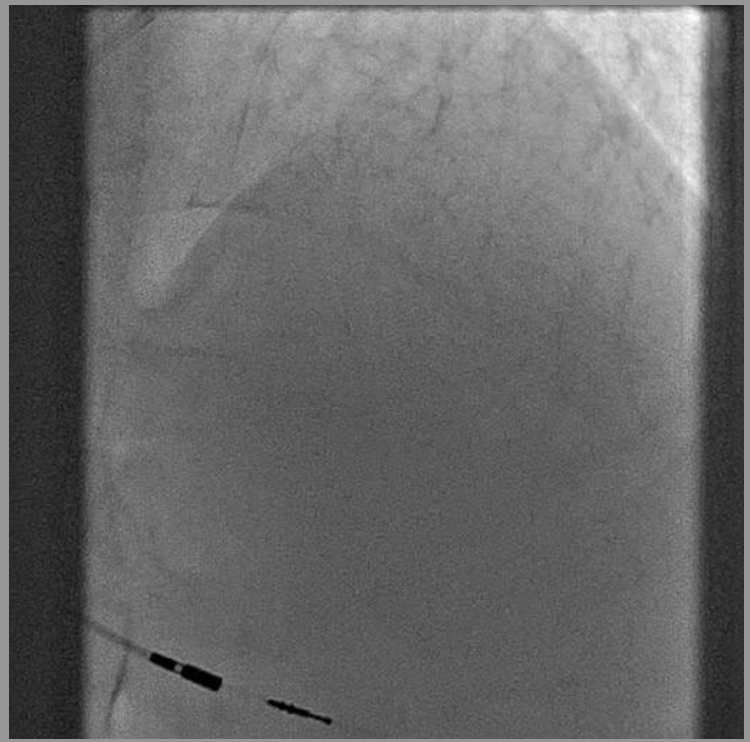
Think different.

Lesion prep., then long 2.5/40 PCB

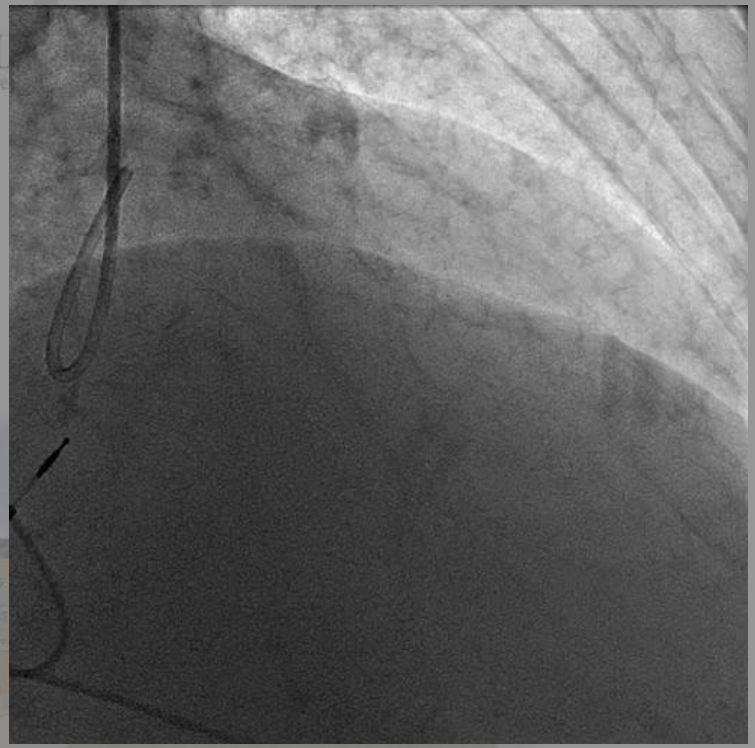


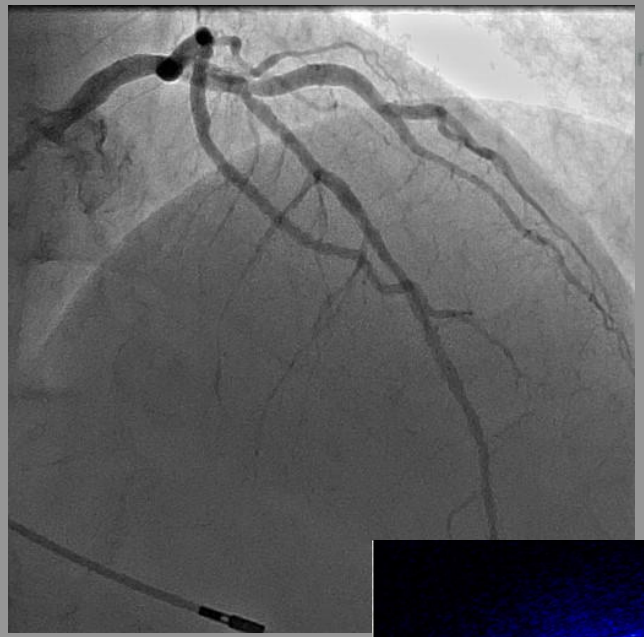


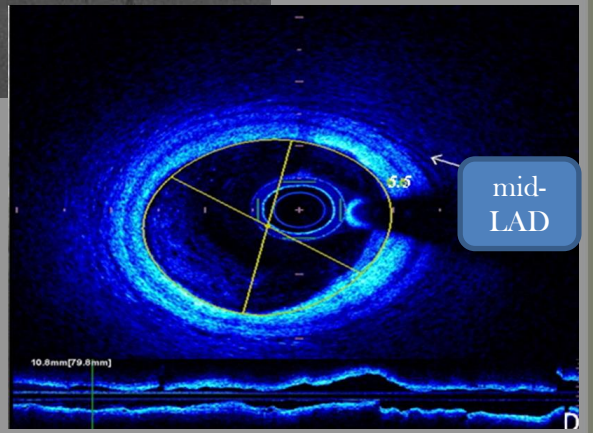


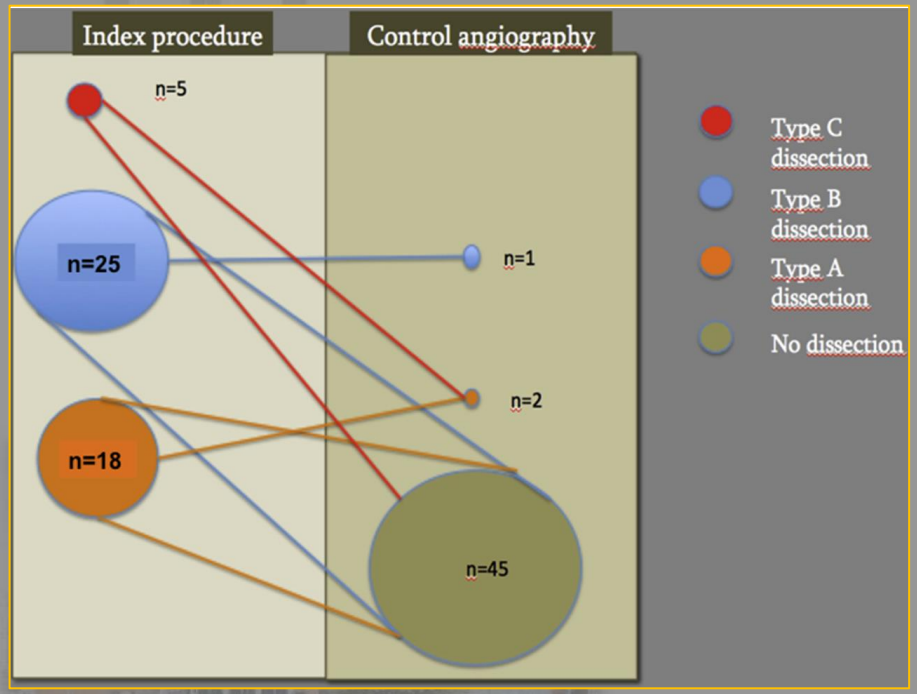


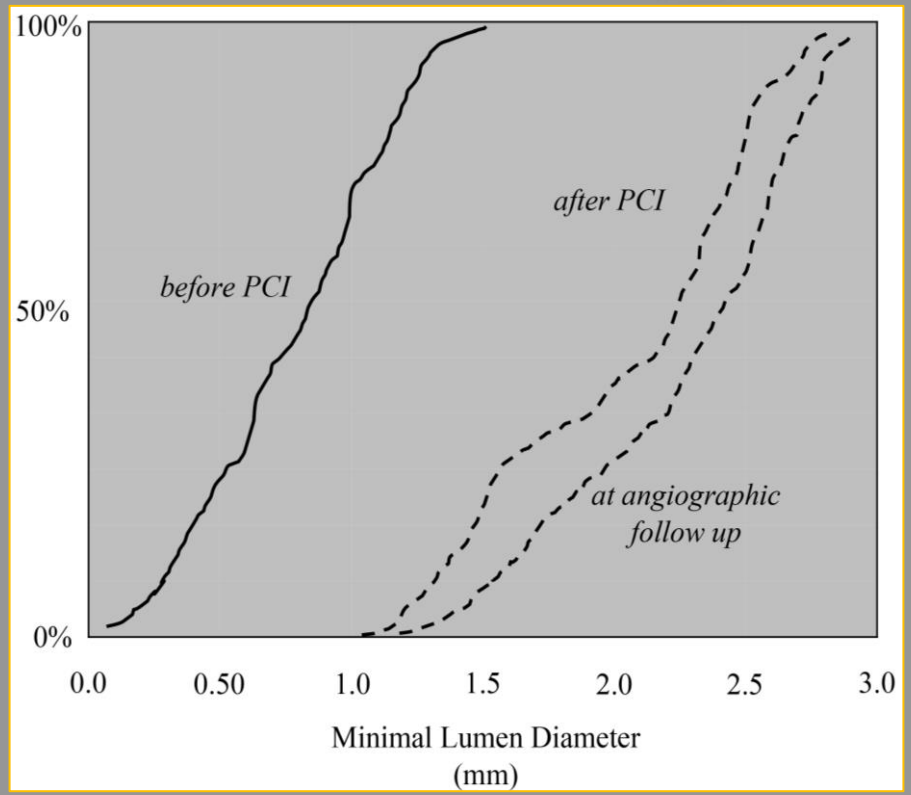
6-mo. angio follow up











B Cortese, JACC Int 2015

BASKET-SMALL 2

Patient Flow

883 patients with percutaneous coronary intervention assessed for eligibility / informed consent obtained

predilatation

successful

flow-limiting dissection (TIMI≤2) a/o residual stenosis >30% during predilatation

125 assessed in Registry

758 randomized in Trial and included in full analysis set

382 assigned to DCB

376 assigned to DES

9 lost to follow up / withdrawal of consent

1 protocol violation

2 treatment change due to complication

13 lost to follow up / withdrawal of consent

1 bare metal stent only

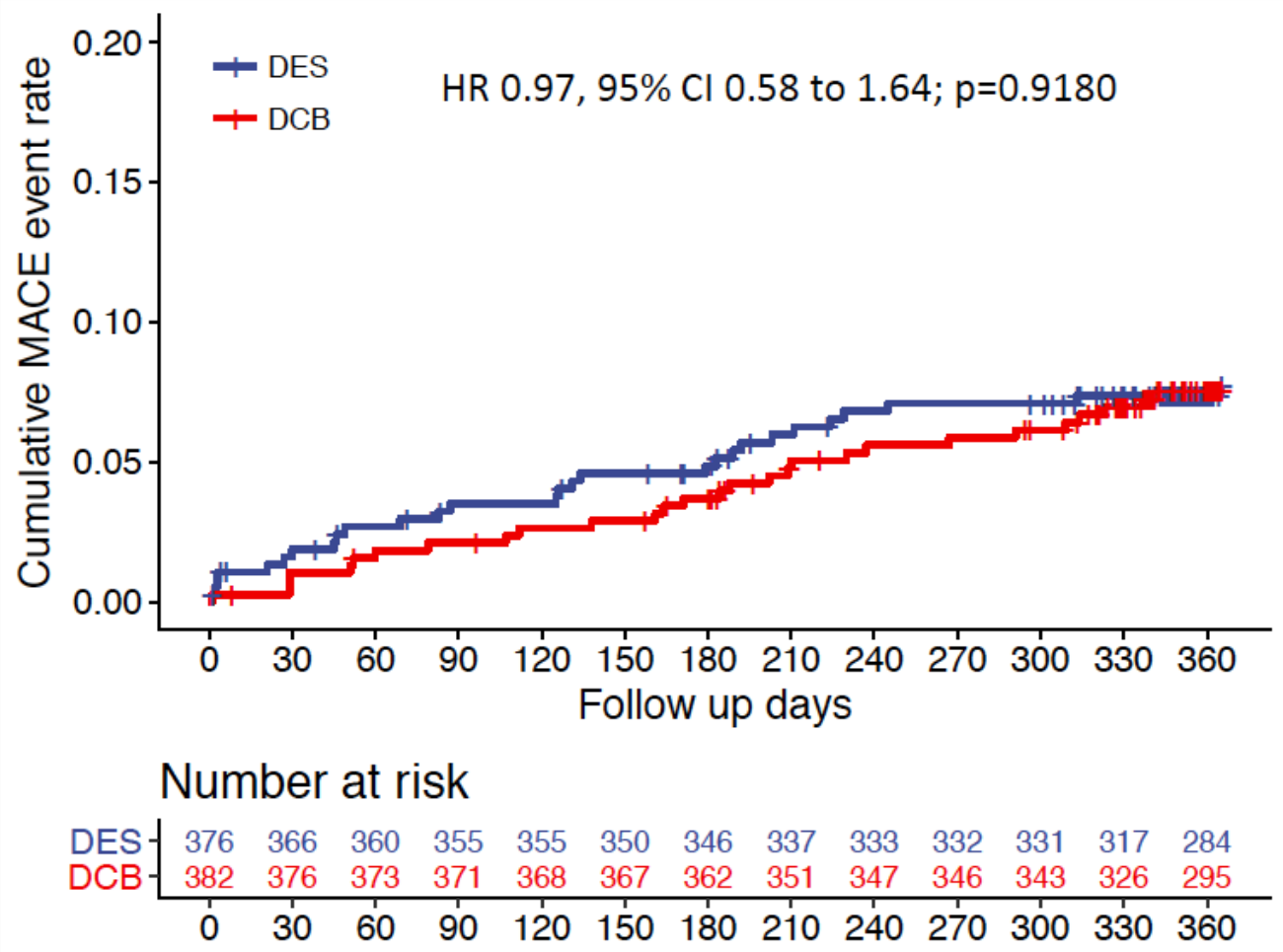
1 protocol violation

2 treatment change due to complication

370 followed up at 12 months and included in per protocol set

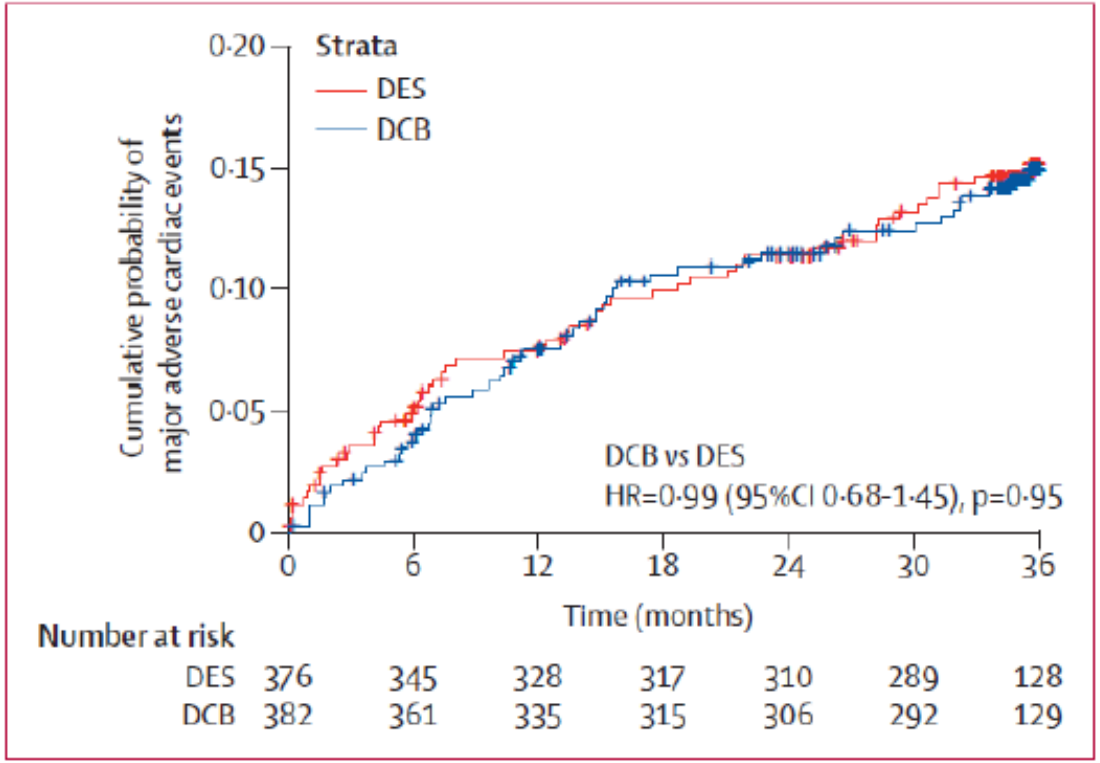
359 followed up at 12 months and included in per protocol set

MACE (12 Months)



The Lancet 2018

36-month Follow-Up:



36 months: The Lancet 2020

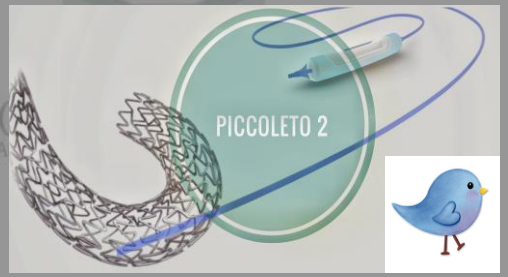
BASKET-SMALL 2 (3-year data available – October 2020)

- **Secondary outcome:**
  - **@ 12 months** DCB vs. DES
    cardiac death: 3.1 vs. 1.3 %, MI 1.6 vs. 3.5 % or TVR 3.4 vs. 4.5%
  - **@ 36 months** DCB vs. DES
    cardiac death: 5 vs. 4 %, MI 6 vs. 6 % or TVR 9 vs. 9%
- **Other Endpoints:**

@ 12 months: Probable or definite thrombosis were low and comparable between DCB and DES patients (0.79 vs. 1.60 %). **Rates of major bleeding** were low and similar in DCB and DES patients (1.1 vs. 2.4 %).

@ 36 months: Probable or definite thrombosis (1% in DCB and 2% in DES, p=0.18). **Rates of major bleeding** (2% in DCB vs. 4% in DES, p=0.088) were numerically lower in the DCB group without statistical significance.

PICCOLETO II-PIs and participating Centers



GISE
Società Italiana di Cardiologia Interventistica

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Clinical Ev. Comm.: G. Zambelli

Independent Core lab.: Cardiovasc. Inst., University of Ferrara

Datamanagement: Advicepharma

Clinicaltrials.gov: **NCT 03899818**

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B. Cortese et Al., JACC Int, 11.20

Multicenter, investigator-driven, open-label, prospective RCT

170 screened and not enrolled

patients with *de novo* lesions in SVD

(diameter ≤2.75 mm)

January 2015-May 2018

232 enrolled
centralized blocks RANDOMIZATION 1:1 (prior to GW)

118 Elutax SV DCB
Predilatation, DCB dilatation for at least 30" (better 60")

5 lost
8 refused

114 Xience EES
Predilatation, stent dilatation and postdilatation at operator's discretion

3 lost
7 refused

105 with angio *(89%)*

104 with angio *(90%)*

Primary endpoint
(6 months)
Core lab

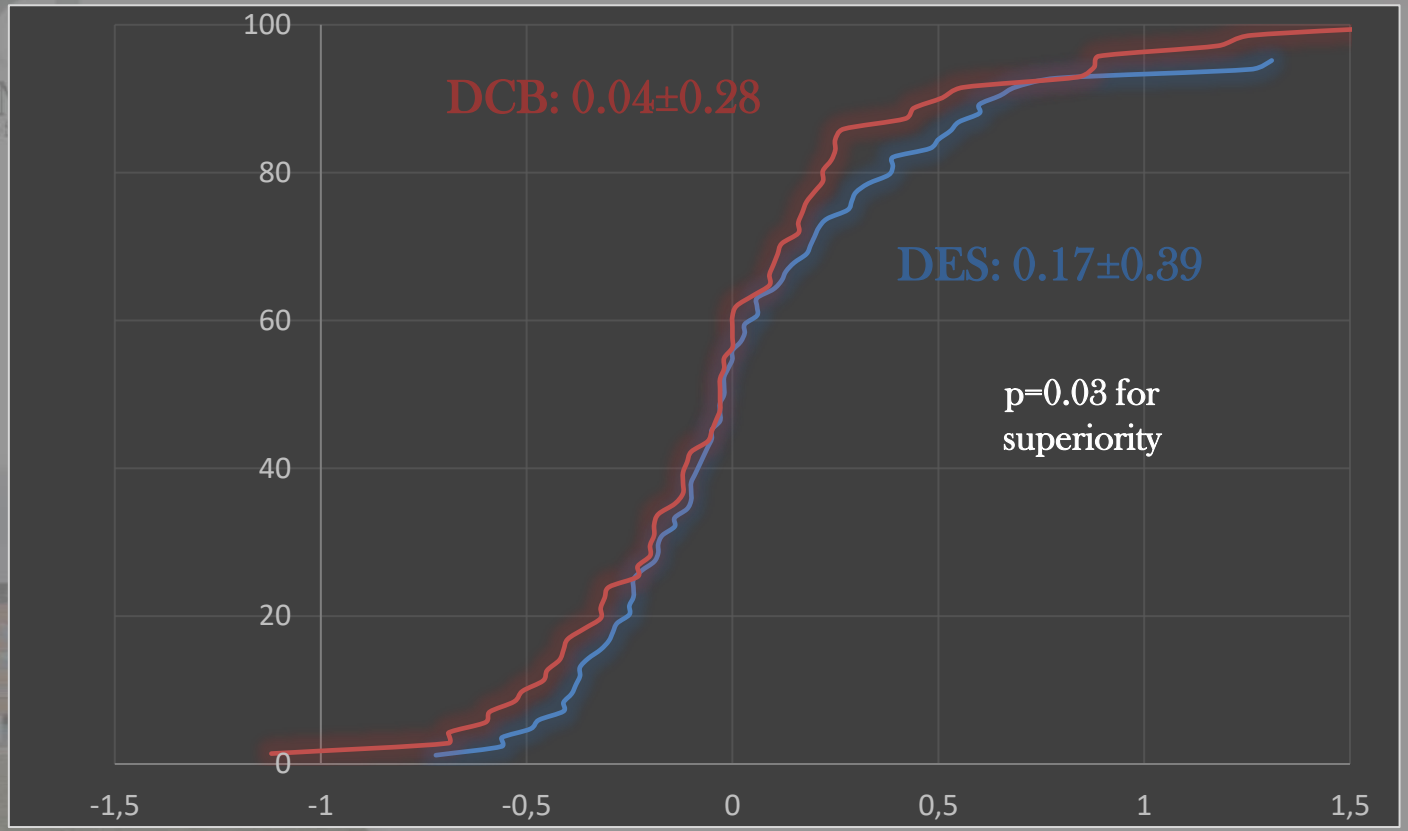
112 6-mo. clinical fup

108 6-mo. clinical fup

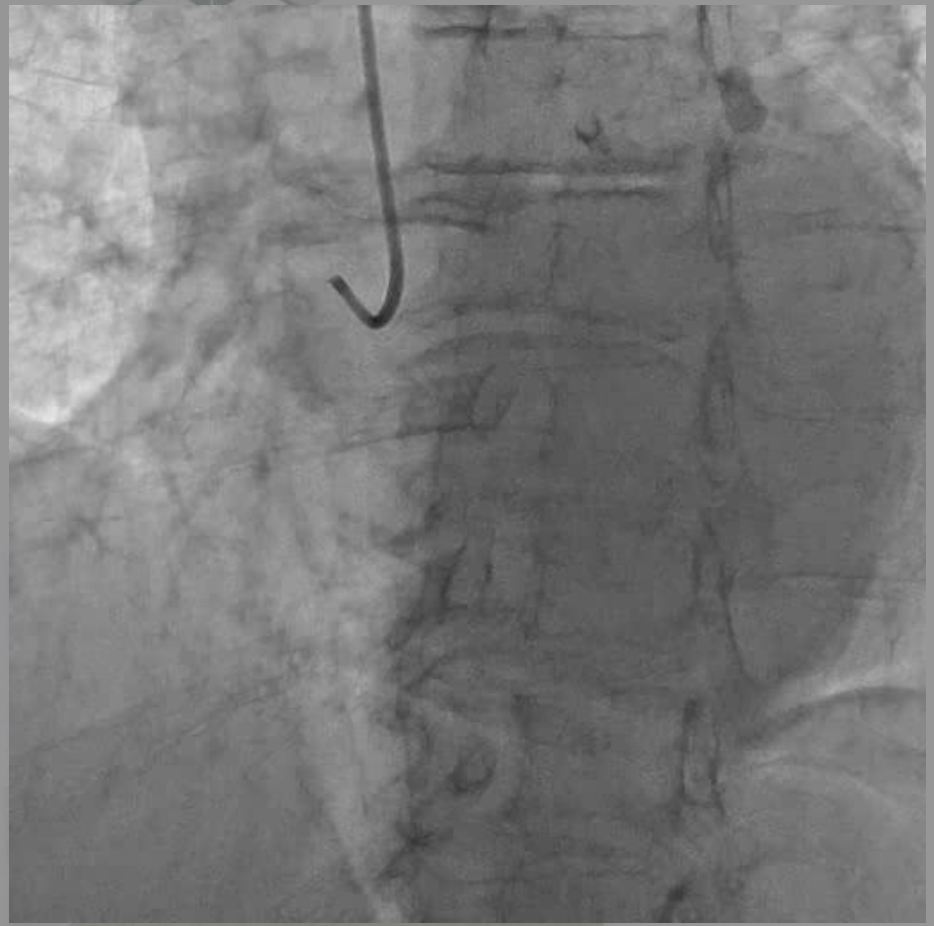
108 12-mo. clinical fup

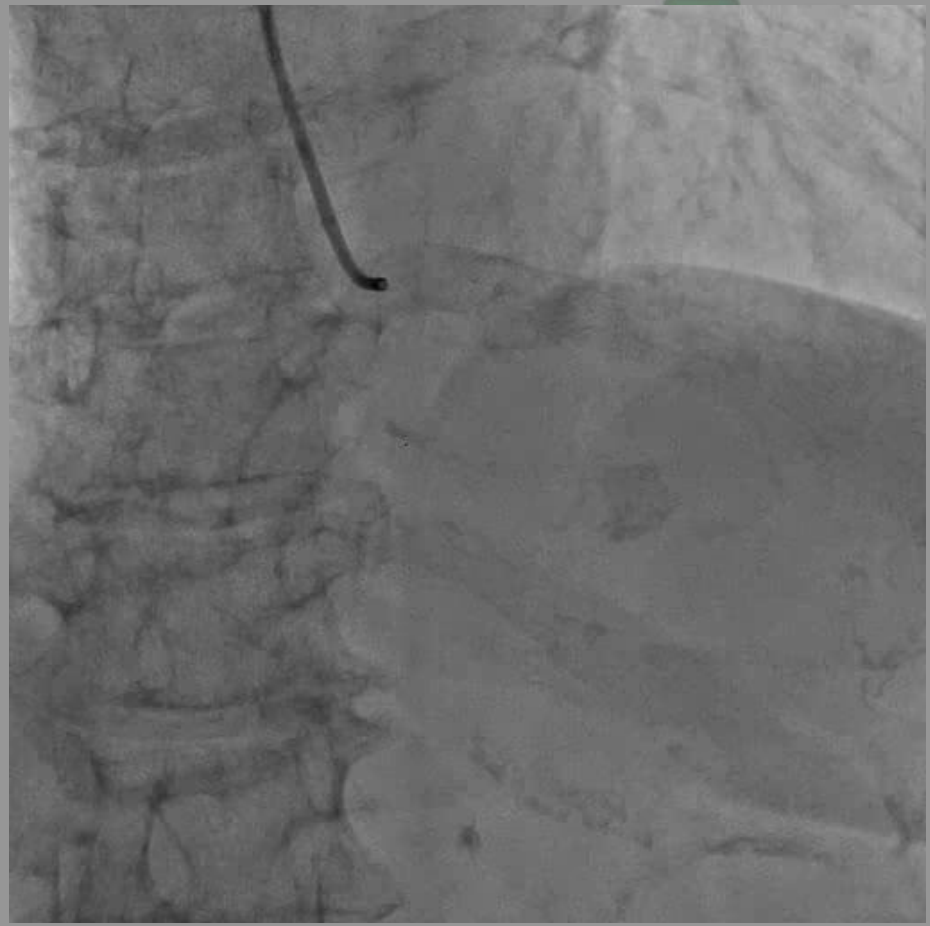
106 12-mo. clinical fup

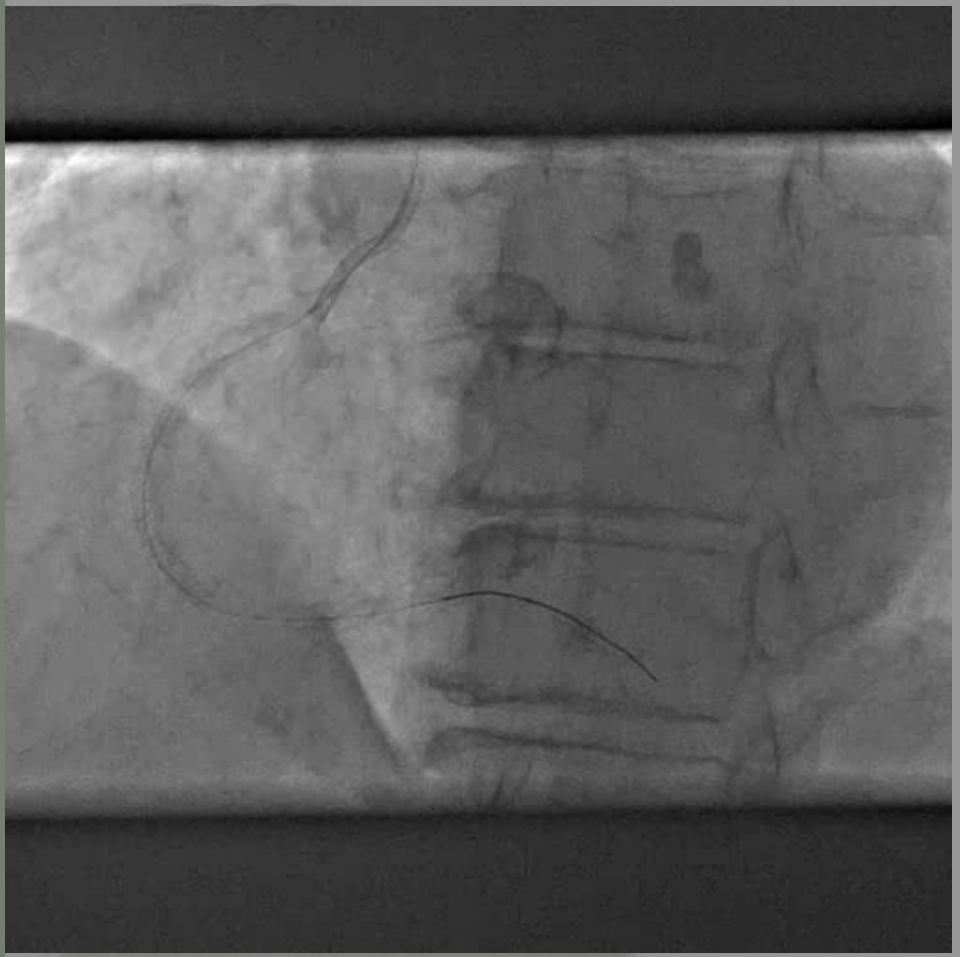
In-lesion LLL (primary study endpoint)

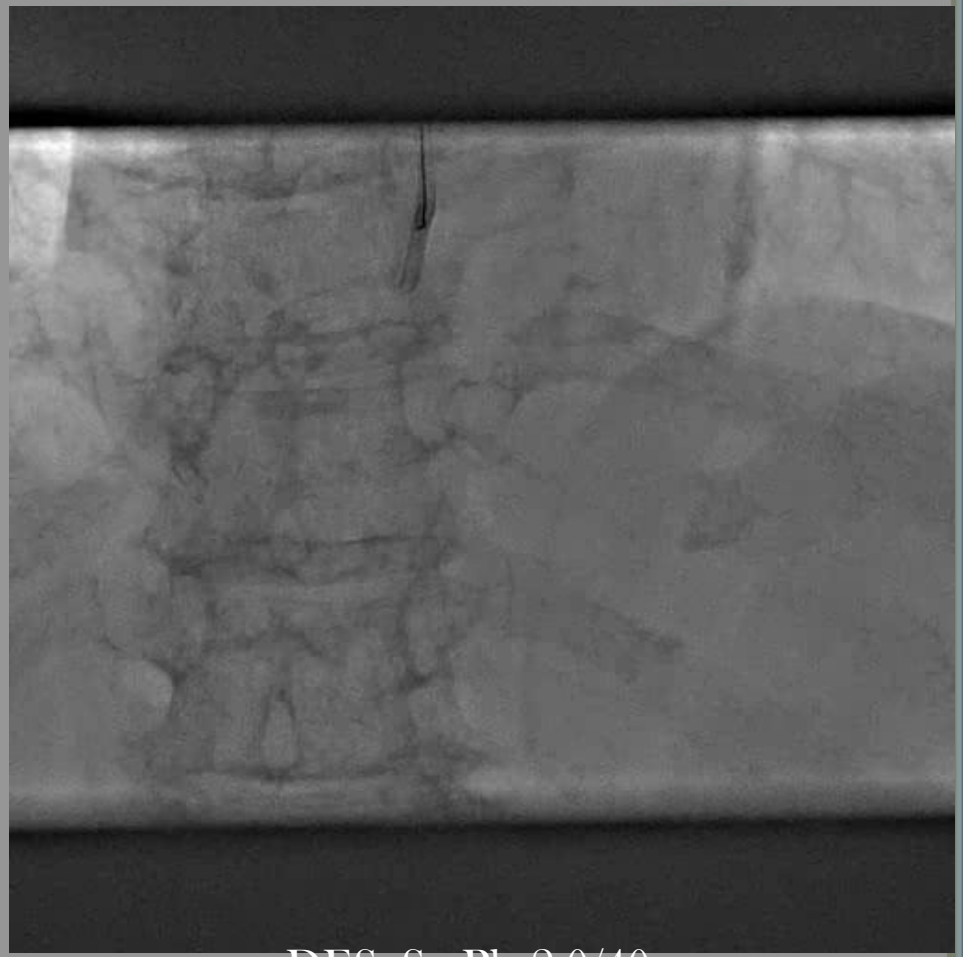


B. Cortese et Al., JACC Int, 11.20

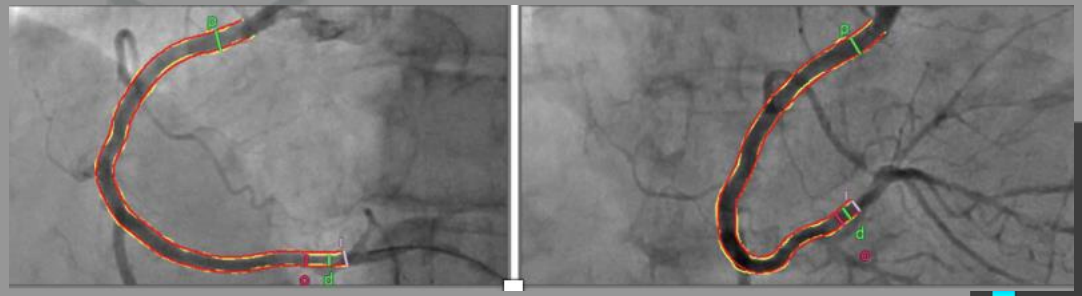


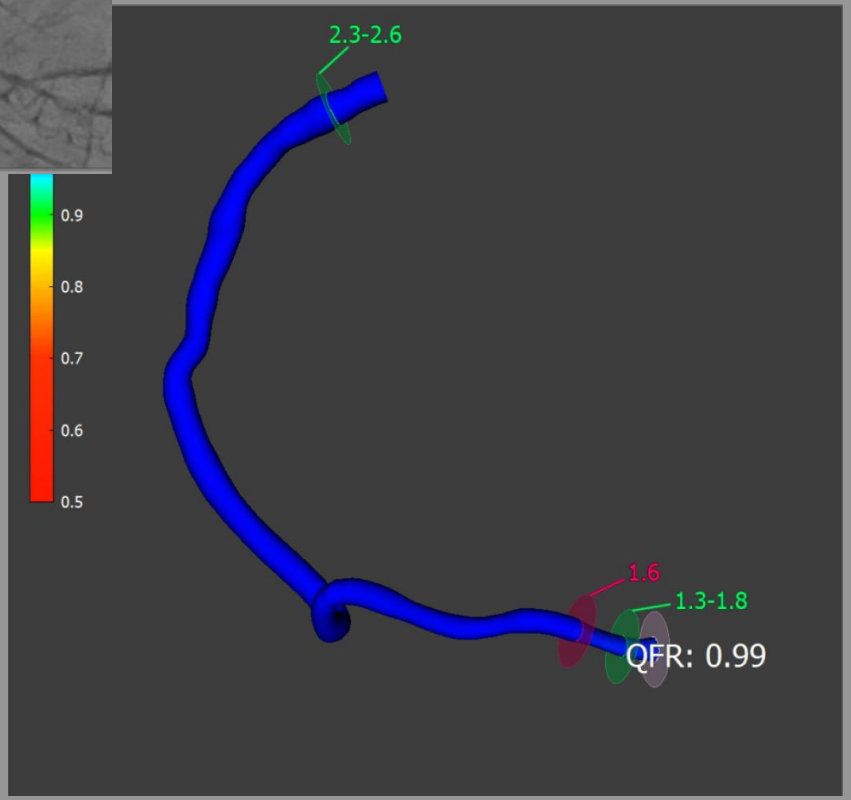


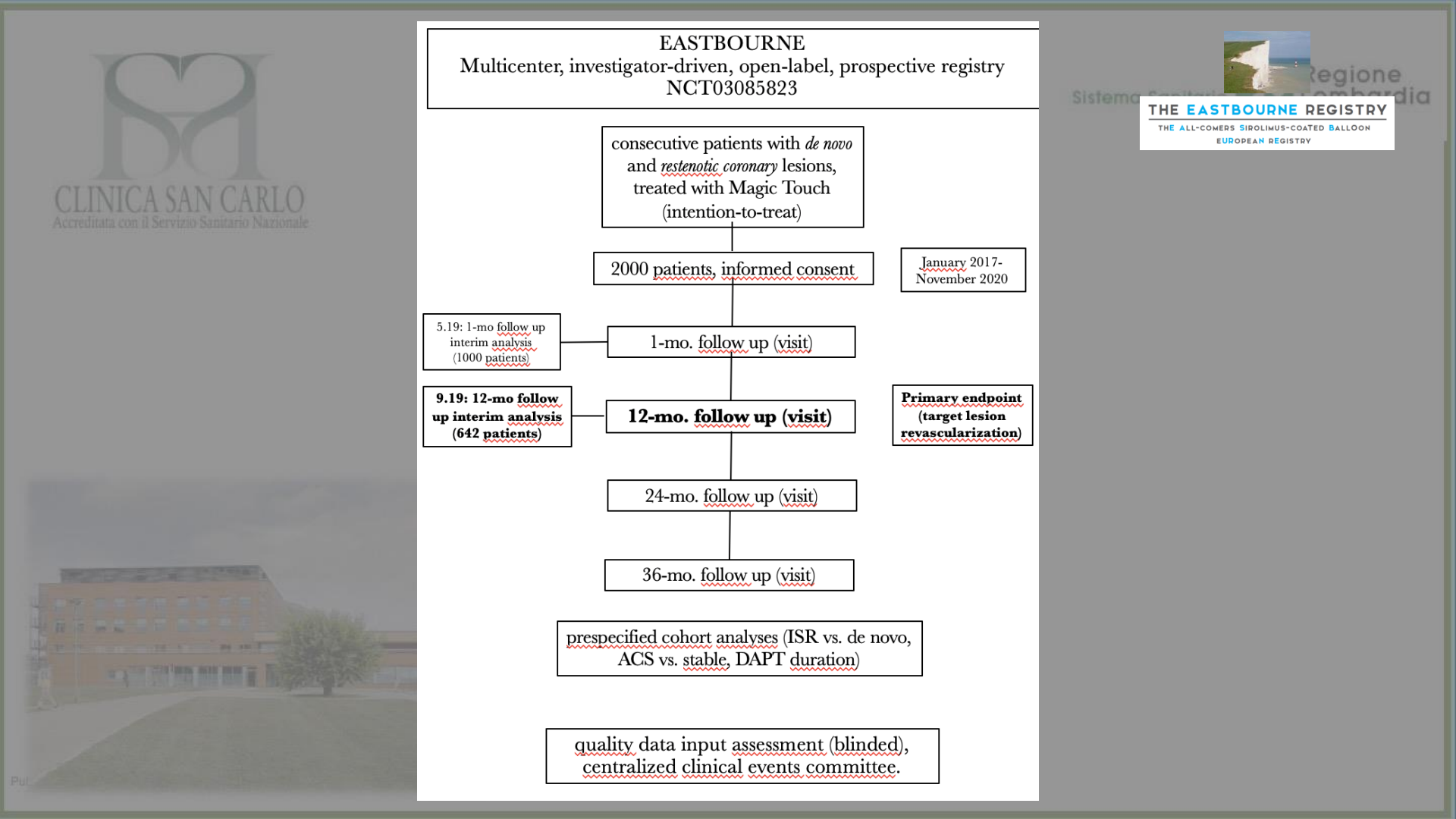


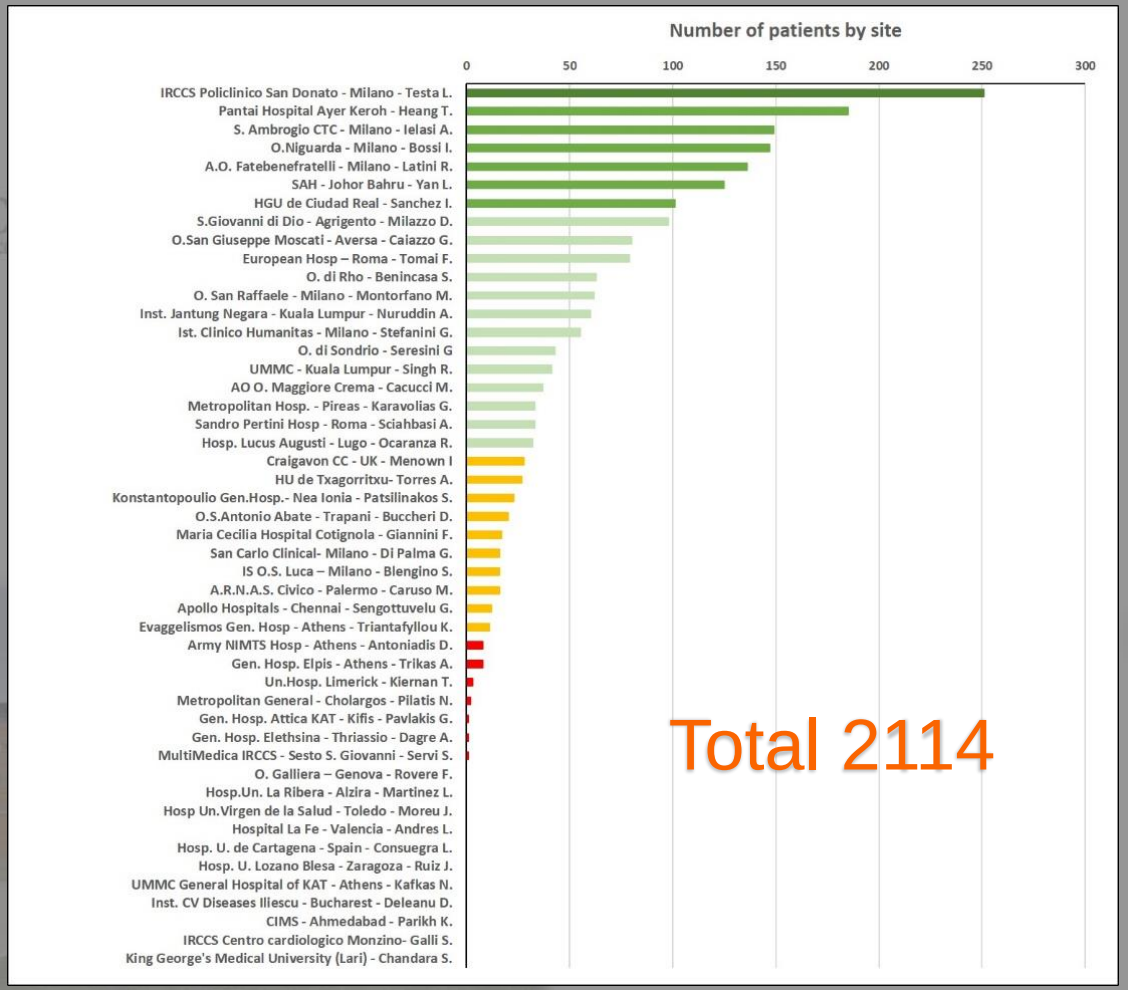


DES, Sq Pls 2.0/40




2.3-2.6
0.9
0.8
0.7
0.6
0.5
1.6
1.3-1.8
QFR: 0.99


EASTBOURNE
Multicenter, investigator-driven, open-label, prospective registry
NCT03085823
consecutive patients with *de novo* and *restenotic coronary* lesions, treated with Magic Touch (intention-to-treat)
2000 patients, informed consent
January 2017-November 2020
5.19: 1-mo follow up interim analysis (1000 patients)
1-mo. follow up (visit)
9.19: 12-mo follow up interim analysis (642 patients)
12-mo. follow up (visit)
Primary endpoint (target lesion revascularization)
24-mo. follow up (visit)
36-mo. follow up (visit)
prespecified cohort analyses (ISR vs. de novo, ACS vs. stable, DAPT duration)
quality data input assessment (blinded), centralized clinical events committee.



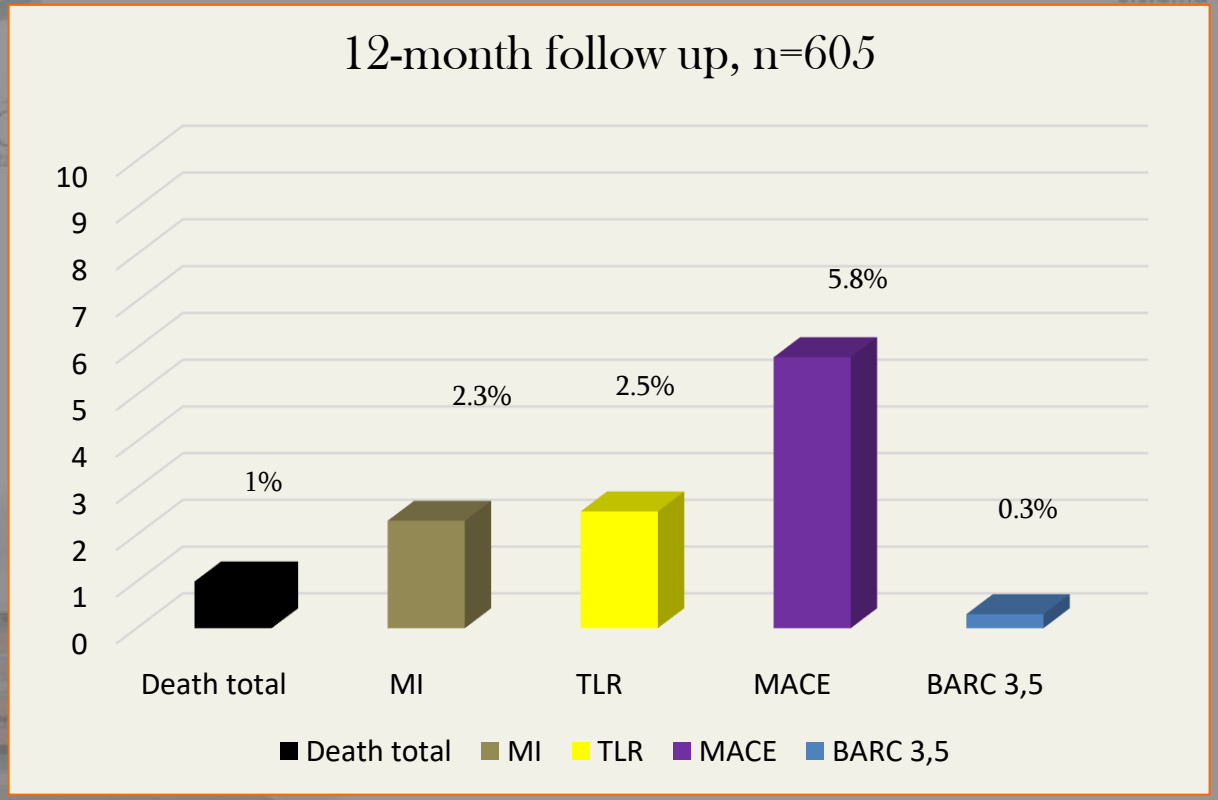
Total 2114

THE EASTBOURNE REGISTRY

THE ALL-COMERS SIROLIMUS-COATED BALLOON EUROPEAN REGISTRY

November 2020 Enrollment completed

EASTBOURNE 1y. interim analysis



THE EASTBOURNE REGISTRY
THE ALL-COMERS SIROLIMUS-COATED BALLOON EUROPEAN REGISTRY

B. Cortese, TCT 2019

J. CV Med, 2020

events not yet adjudicated

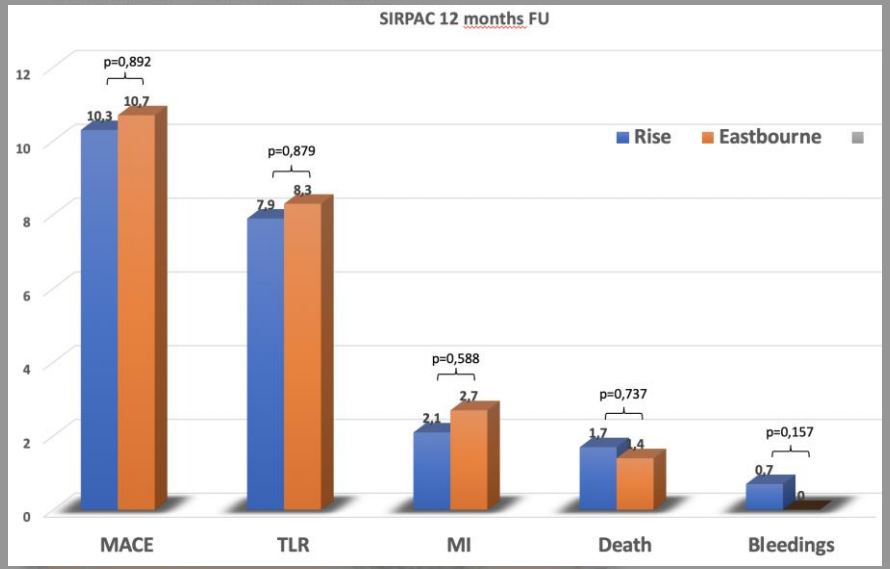
SIRPAC study-first comparison between PTX and SIR DCB

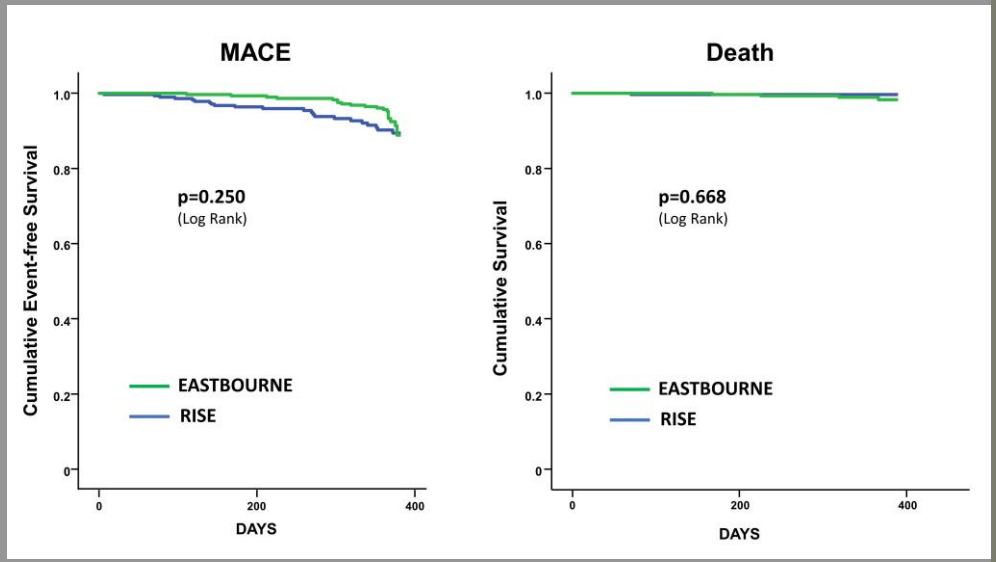
- Investigator-initiated studies
- Comparison between DCB RISE study (all-comer Italian registry, Elutax SV, 544 pts, J CV Med '18) and EASTBOURNE interim analysis (all come international registry, MT, 596 pts (TCT LBCT '19)
- 12 months clinical follow up
- PE: 12-month MACE rate

- 1140 pts enrolled
- After propensity score matching, 290 pts per group

B. Cortese, EuroPCR 2020, LBCT; Cardiovasc Revasc Med '21

SIRPAC study-first comparison between PTX and SIR DCB

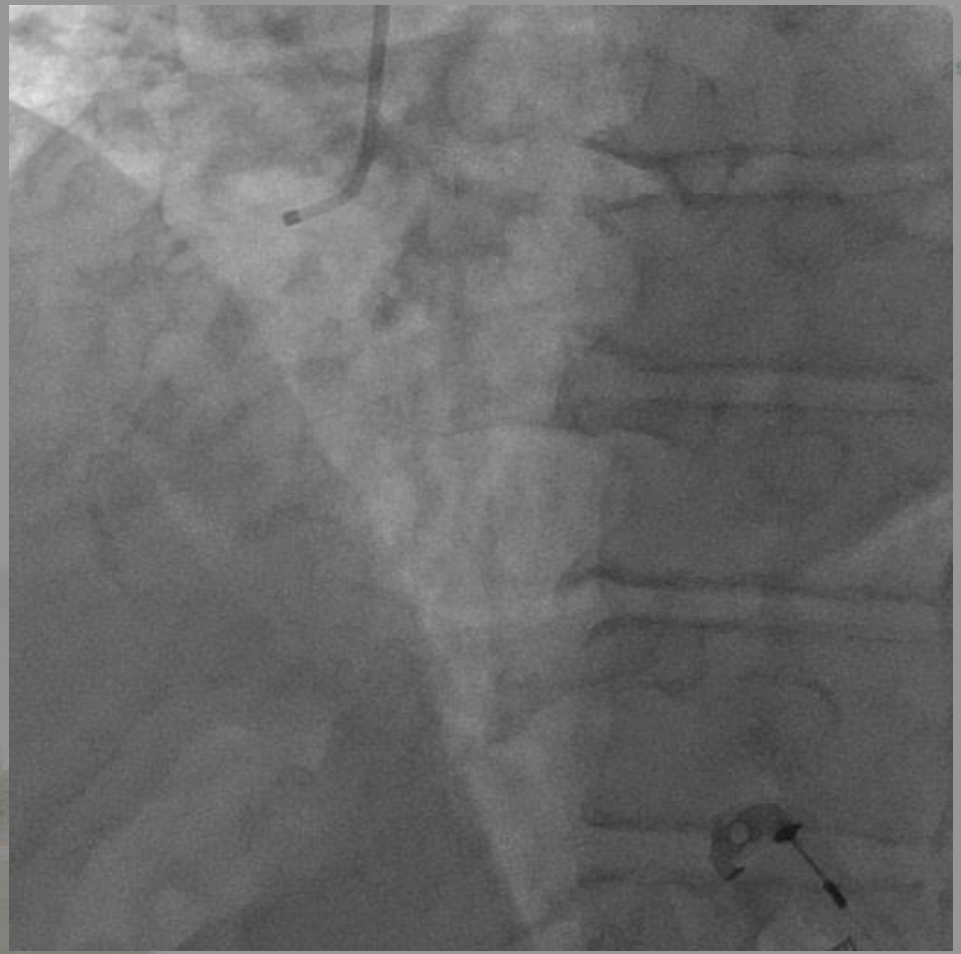


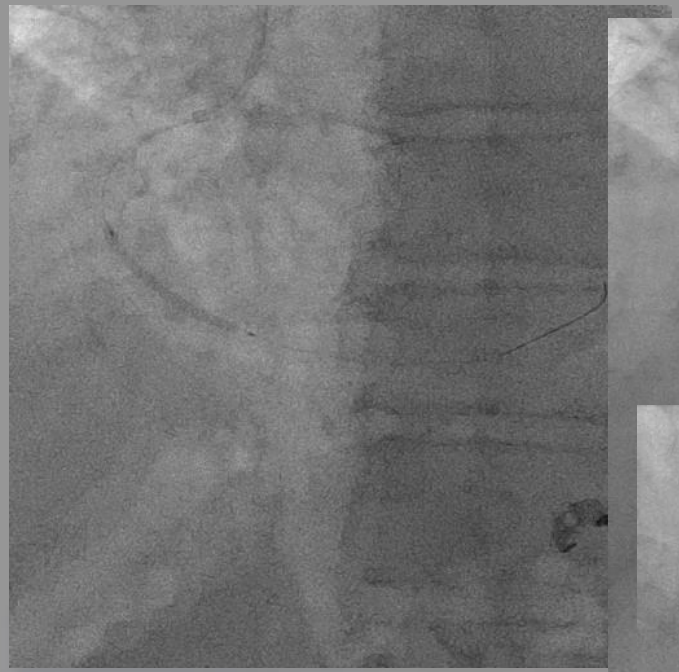


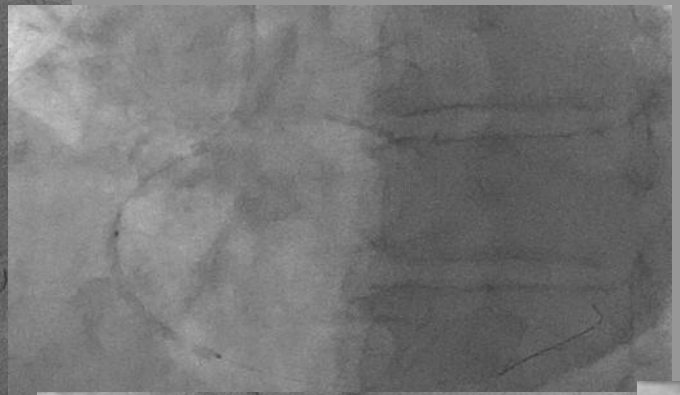
B. Cortese, EuroPCR 2020, LBCT; Cardiovasc Revasc Med '21

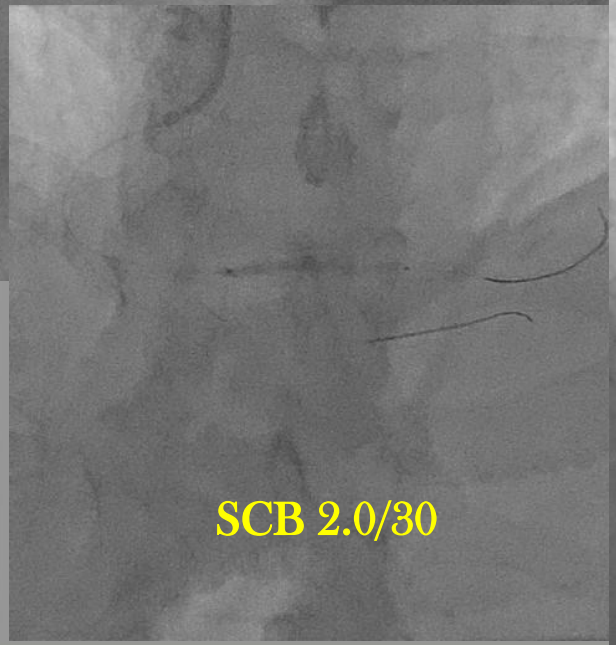
CLINICA SAN CARLO
Accreditata con il Servizio Sanitario Nazionale

stema Sanitario Regione Lombardia

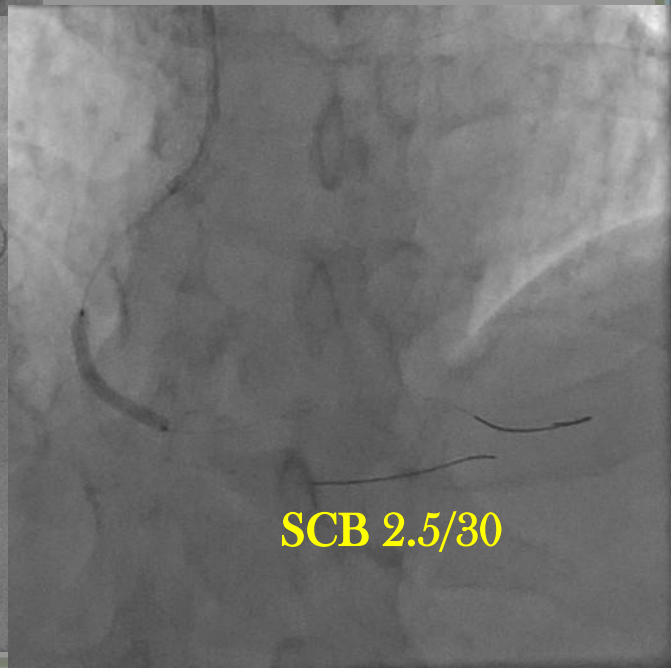




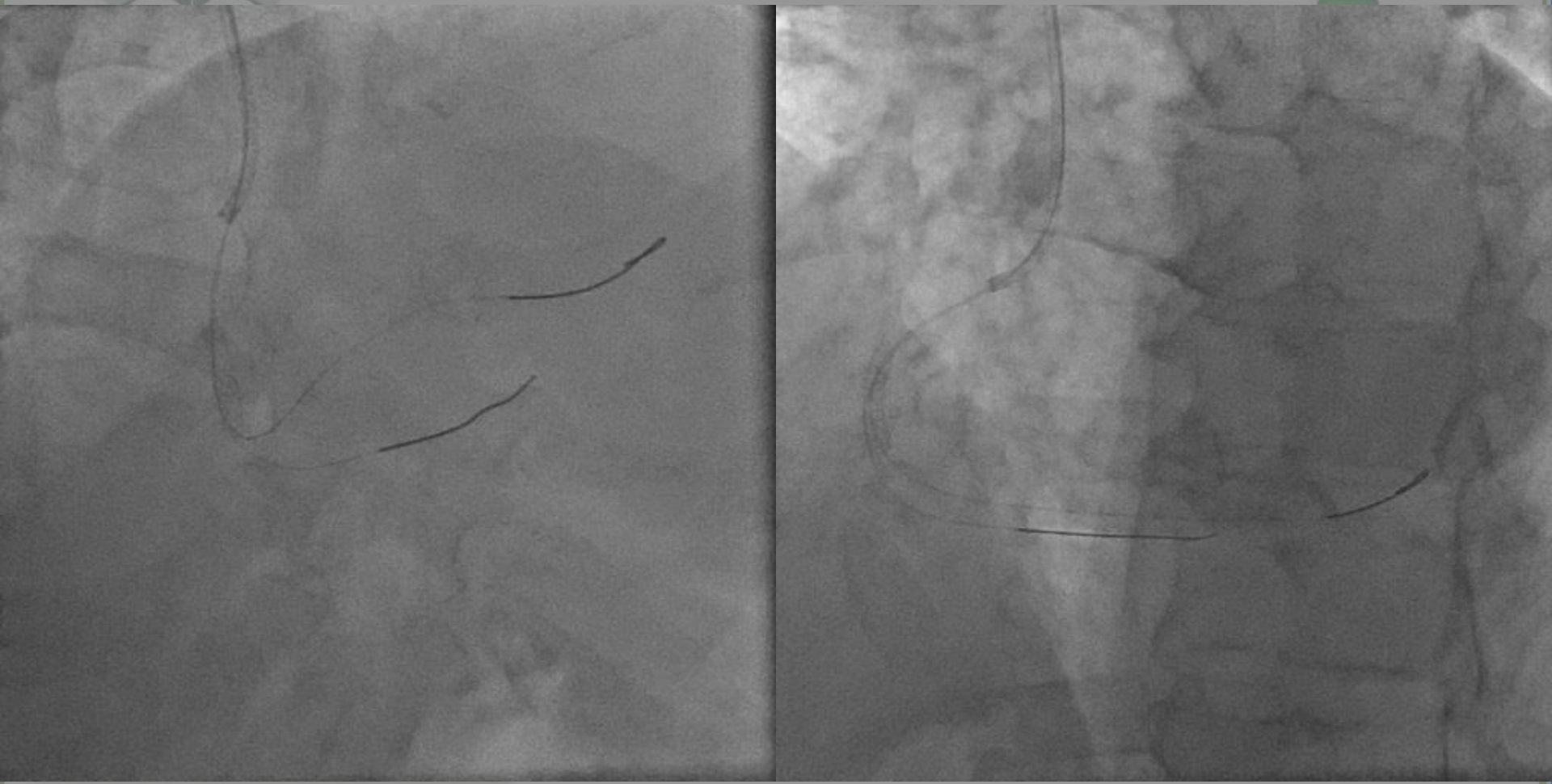


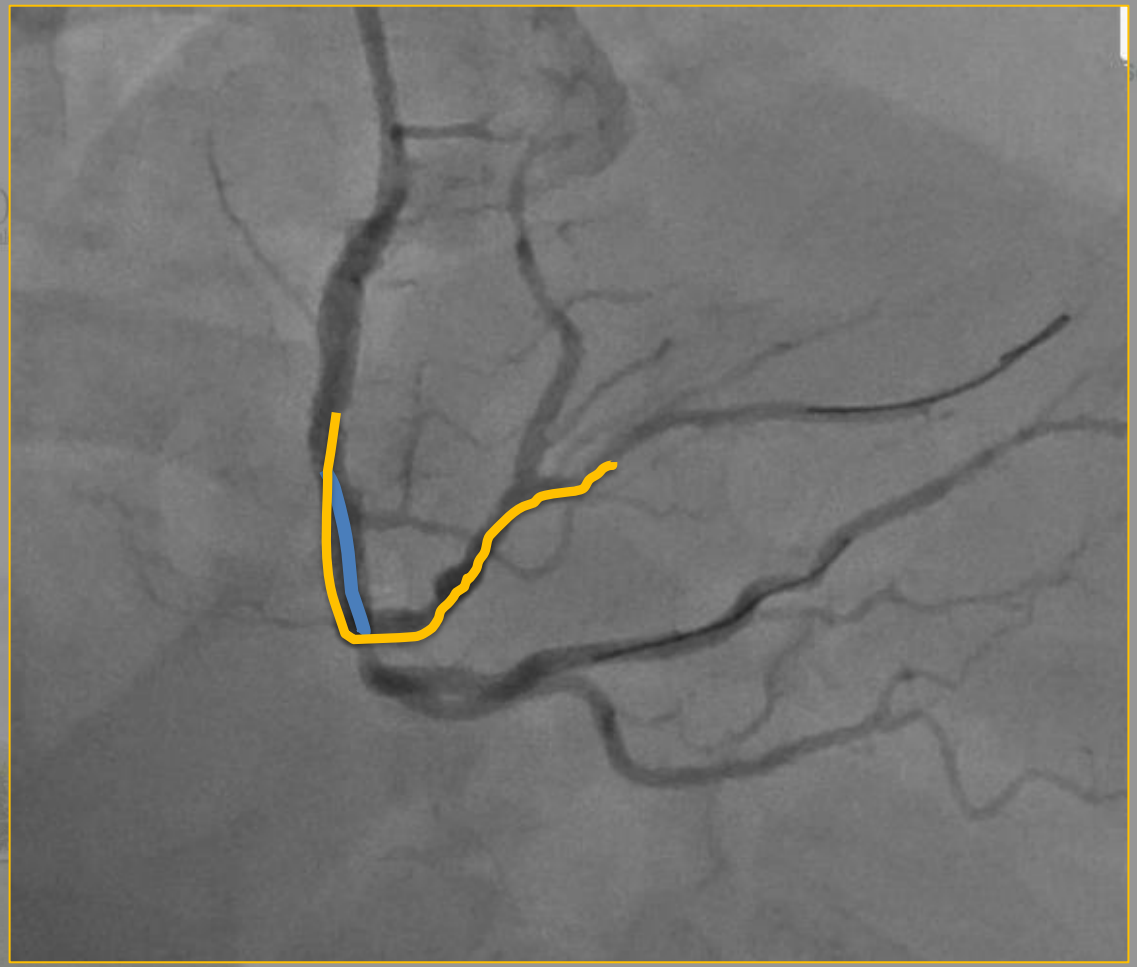


SCB 2.0/30



SCB 2.5/30





TRANSFORM II

Fondazione Ricerca e Innovazione Cardiovascolare

STEERING COMMITTEE

- Bernardo Cortese, Milano, study Chairman
- Roxana Mehran, NYC
- Alex Abizaid, Sao Paulo
- Stefano Rigattieri, Rome
- Fernando Alfonso, Madrid
- Jose Maria de la Torre Hernandez, Santander

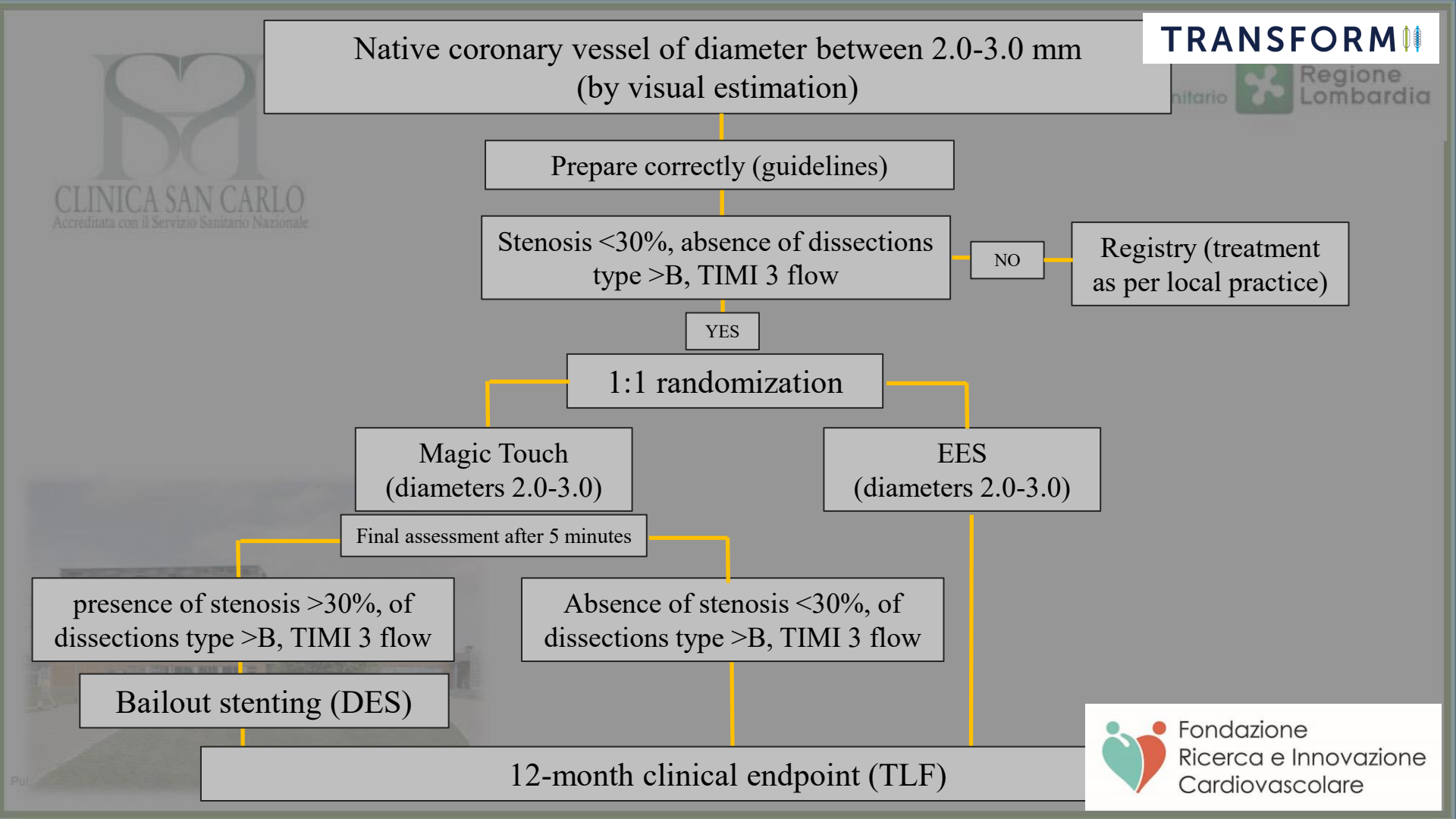
TRANSFORM II

FOLLOW UP AND STUDY DURATION

Clinical follow up, after 30 days and yearly through 5 years. Enrollment estimation time: 18-24 months.

INCLUSION CRITERIA

- age >18 years;
- patients with any clinical indication to PCI (stable coronary artery disease or acute coronary syndromes);
- de novo coronary lesions in vessels with diameter between 2.0-3.0 mm (visual estimation);
- lesion length ≤40 mm;
- informed consent to participate in the study.


TRANSFORM
Regione Lombardia
CLINICA SAN CARLO
Accreditata con il Servizio Sanitario Nazionale
Native coronary vessel of diameter between 2.0-3.0 mm (by visual estimation)
Prepare correctly (guidelines)
Stenosis <30%, absence of dissections type >B, TIMI 3 flow
NO
Registry (treatment as per local practice)
YES
1:1 randomization
Magic Touch (diameters 2.0-3.0)
EES (diameters 2.0-3.0)
Final assessment after 5 minutes
presence of stenosis >30%, of dissections type >B, TIMI 3 flow
Absence of stenosis <30%, of dissections type >B, TIMI 3 flow
Bailout stenting (DES)
12-month clinical endpoint (TLF)
Fondazione Ricerca e Innovazione Cardiovascolare

PICCOLETO III

- Native vessel disease (all)
- Complex lesions setting: (>40mm; CTOs)
- International, multicenter, RCT
- SCB vs PCB vs DES

Fondazione
Ricerca e Innovazione
Cardiovascolare

conclusions

- DCBs are a valid alternative to DES in some native vessel disease anatomical setting: vessels <3mm, BIF, as hybrid treatment with DES.
- DCBs are not created equal.
- Rely on newer-generation platforms/technologies and DCB with robust clinical program
- The new frontier will need to be patient-focalized, and not device-focalized: go for hybrid in complex patients!