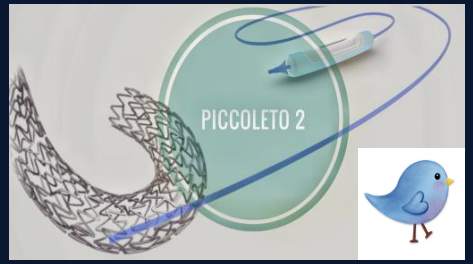


Drug-coated balloon vs. drug eluting stent for small coronary vessel disease: 6-mo. primary outcome of the PICCOLETO II randomized clinical trial.

A study from the Italian Society of Interventional Cardiology GISE.

(NCT 03899818)

Bernardo Cortese, MD, FESC
Director of Cardiology, San Carlo Clinic Milano
Fondazione G. Monasterio Toscana-CNR
bcortese@gmail.com
bernardocortese.com

disclosures

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, Stentys, Daiiki-Sankyo, Philips-Spectranetics, Reva, Bayer, Cardinal.

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

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

Small vessel PCI with DES-1 year outcome

Prospective-SPIRIT SV trial

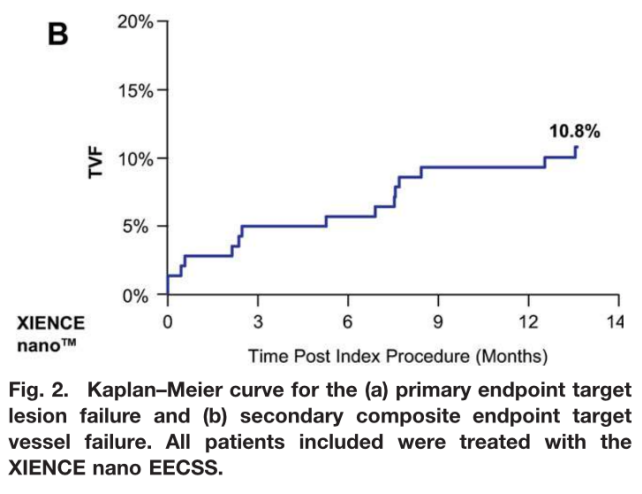
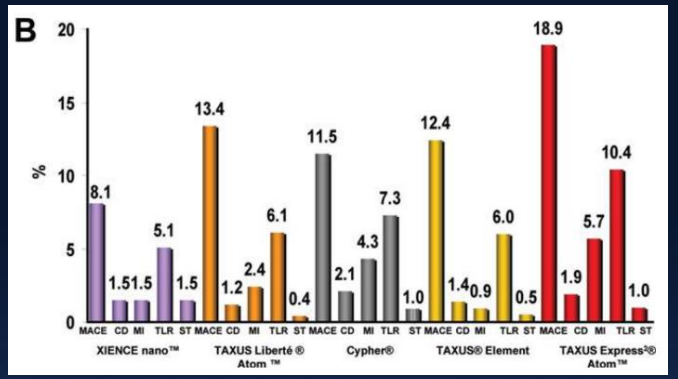
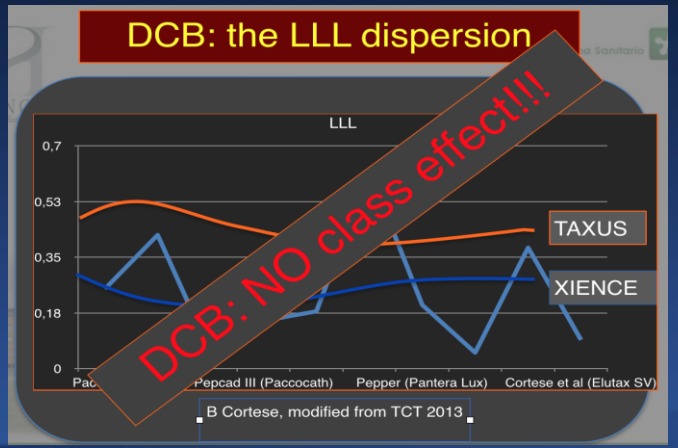


Fig. 2. Kaplan–Meier curve for the (a) primary endpoint target lesion failure and (b) secondary composite endpoint target vessel failure. All patients included were treated with the XIENCE nano EECSS.



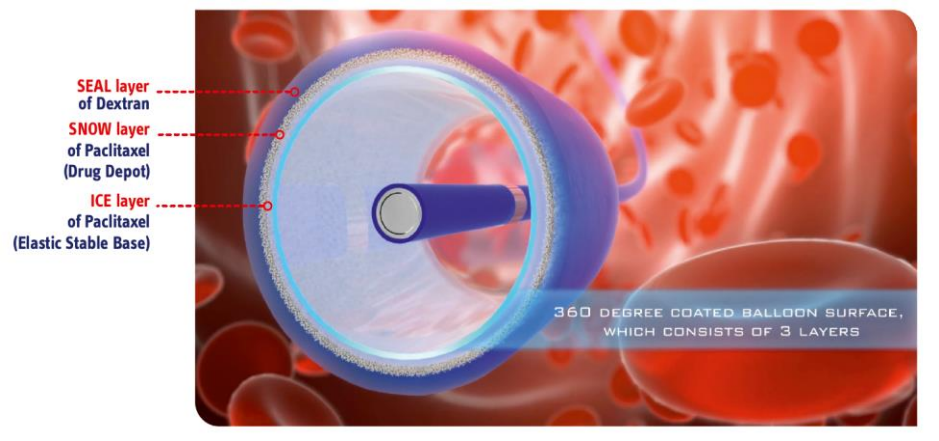


Cannon, CCI 2012

Background of PICCOLETO II

- Higher rates of adverse events with DES (if compared with other settings).
- New generation DCB were born in order to improve drug deliverability and tissue retention in the vessel wall, and to reduce drug dispersion/embolization.
- This goal was pursued working on:
  - Newer delivery systems
  - Newer carriers
  - Newer drugs
- This study sought to evaluate the angiographic efficacy and clinical performance of Elutax SV DCB as compared to EES in a SVD setting.

Elutax SV/Emperor DCB



- SEAL layer made of DEXTRAN, an hydrogel with hydrophilic features, to obtain a longer drug absorption in time
- drug deployed on inflated balloon
- lower dose PTX (2.2 micrg/mm2)
- higher PTX persistance at 30 days (5-8% of the drug)

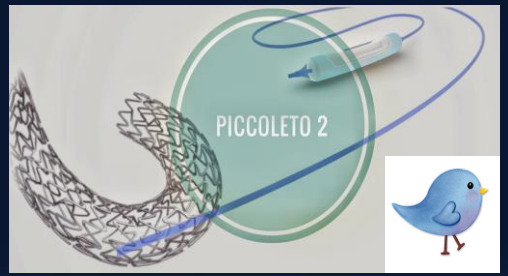
Elutax SV: DCB-RISE registry

Table 4 Clinical endpoints at the longest available follow-up

	n = 507		
	13.3 (7.4)		
Average duration of follow-up, months (SD)	ISR (n = 269)	*de novo* (n = 238)	*P*
TLR, n (%)	24 (9%)	6 (2.6%)	0.006
TLR managed with CABG, n (%)	3 (1%)	1 (0.4%)	0.64
TLR managed with PCI, n (%)	21 (7.8%)	5 (2.1%)	0.003
Target-vessel MI, n (%)	3 (1.1%)	0	0.14
Stroke, n (%)	1 (0.3%)	1 (0.4%)	1
All-cause death	6 (2.2%)	6 (2.5%)	0.36
Cardiac death	3 (1.1%)	0	0.27
DOCE	30 (11%)	6 (2.6%)	0.001

B. Cortese, J CV Med 2018

PICCOLETO II-PIs and participating Centers



GISE
Società Italiana di Cardiologia Interventistica

Steering Comm.: B. Cortese, G. Di Palma F. Alfonso

Clinical Ev. Comm.: D. Pellegrini, G. Zambelli

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

Datamanager: D. Gattuso

Clinicaltrials.gov: **NCT 03899818**

Bernardo Cortese MD, Chairman and PI
- San Carlo Clinic Milano, Italy

Fernando Alfonso MD,
- Hospital de la Princesa, Madrid, Spain

Gaetano Di Palma MD,
- San Carlo Clinic Milano, Italy

Marcos Garcia Guimaraes MD,
- Hospital de la Princesa, Madrid, Spain

Davide Piraino MD,
- Univ. of Palermo, Italy

Pedro Silva Orrego MD,
- Fatebenefratelli Hospital, Milano, Italy

Dario Pellegrini MD,
- Univ. of Milano Bicocca, Italy; Radboud UMC, Nijmgen, The Netherlands

Gianluca Campo MD,
- Cardiovascular Institute, Univ. of Ferrara, Italy

Dario Buccheri MD,
- San Giovanni di Dio Hosp., Agrigento, Italy

Andrea Erriquez MD,
- Cardiovascular Institute, Univ. of Ferrara, Italy

Fernando Rivero MD,
- Hospital de la Princesa, Madrid, Spain

Giulia Zambelli MD,
- Az. Osp. Policlinico Giaccone, Palermo, Italy

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)

5 lost
8 refused

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

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

3 lost
7 refused

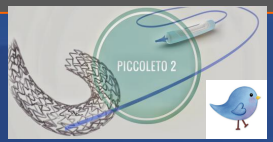
105 with angio
(89%)

104 with angio
(90%)

Primary endpoint
(6 months)
Core lab

112 6-mo. clinical fup

108 6-mo. clinical fup



Inclusion/exclusion criteria

- **Clinical inclusion criteria**
  - Age above 18 years
  - Stable/unstable CAD
  - Recent MI (>72 hours)
  - Informed written consent
- **Angiographic inclusion criteria**
  - Native, de novo coronary artery
  - RVD ≤2.75 (visual estimation)
  - Target lesion with a visually estimated stenosis >70%.
  - Target lesion length <25 mm

Clinical exclusion criteria

- Recent MI (<72 hours)
- Left ventricular ejection fraction <30%
- Creatinine cl. <30 ml/min

Angiographic exclusion criteria

- Left main lesions
- Aorto-ostial lesion
- Presence of a stent at target vessel
- Chronic total occlusion
- Heavily calcific or tortuous vessel
- Visible target vessel thrombus
- Bifurcation lesion requiring 2 stents

Study endpoints

Primary endpoint

In-lesion late lumen loss at 6-months (core lab)

Secondary endpoints

- minimal lumen diameter (MLD)
- % diameter stenosis
- binary restenosis
- MACE (cardiac death, non-fatal MI, TLR) thru 2 years
- the single components

Sample size and statistical assumptions

Study hypothesis

PCI with PTX-eluting Elutax SV is non-inferior to PCI with best-in-class DES for the native small coronary vessels, in terms of in-lesion LLL.

Assumptions

- Mean LLL in the EES arm hypothesized 0.20 mm, delta 0.35, alpha 5%, power 90%, inferiority margin of 0.25 mm
- population of 99 patients per group needed
- attrition rate (angio follow up): 10%
- total population needed 230 patients

Baseline clinical characteristics

	DES	DCB	p
Number of patients	114	118	
Male, n (%)	87 (76.9)	83 (70.3)	0.25
Age, years, median (IQR)	66 (15.75)	64 (16)	0.32
Hypertension, n (%)	76 (67.2)	77 (65.2)	0.74
Diabetes, n (%)	40 (35.4)	45 (38)	0.65
Insulin depend. diabetes, n (%)	15 (13.3)	21 (17.8)	0.66
Smoke, n (%)	19 (16.7)	23 (19.5)	0.84
Dyslipidemia, n (%)	63 (55)	72 (61)	0.66
Renal failure, n (%)	12 (10.6)	4 (3.3)	*0.03*
Previous MI, n (%)	34 (30)	45 (38)	0.19
Previous CABG, n (%)	4 (3.5)	4 (3.3)	0.95
Previous PCI, n (%)	60 (53)	59 (50)	0.33
LVEF, Median (IQR)	58 (7)	58 (10)	0.89

Clinical indication to PCI

	DES	DCB	p
Clinical presentation			
Stable Angina, n (%)	63 (55.7)	64 (54.2)	0.81
Unstable Angina, n (%)	18 (16)	17 (14.4)	0.74
NSTEMI (recent), n (%)	23 (20.3)	25 (21.1)	0.87
STEMI (recent), n (%)	9 (8)	12 (10.3)	0.34

Baseline angiographic characteristics

	DES	DCB	p
Number of patients and lesions	114	118	
Bifurcation lesion, n (%)	14 (12.3)	15 (12.7)	0.94
Multivessel disease, n (%)	86 (76)	86 (72.8)	0.5
Target vessel LAD, n (%)	44 (39)	47 (40)	
Target vessel LCX, n (%)	35 (31)	44 (37.2)	0.6
Target vessel RCA, n (%)	34 (30.2)	27 (22.8)	
Total Procedural Time, min, median (IQR)	55 (28-96)	58 (34-98)	0.4

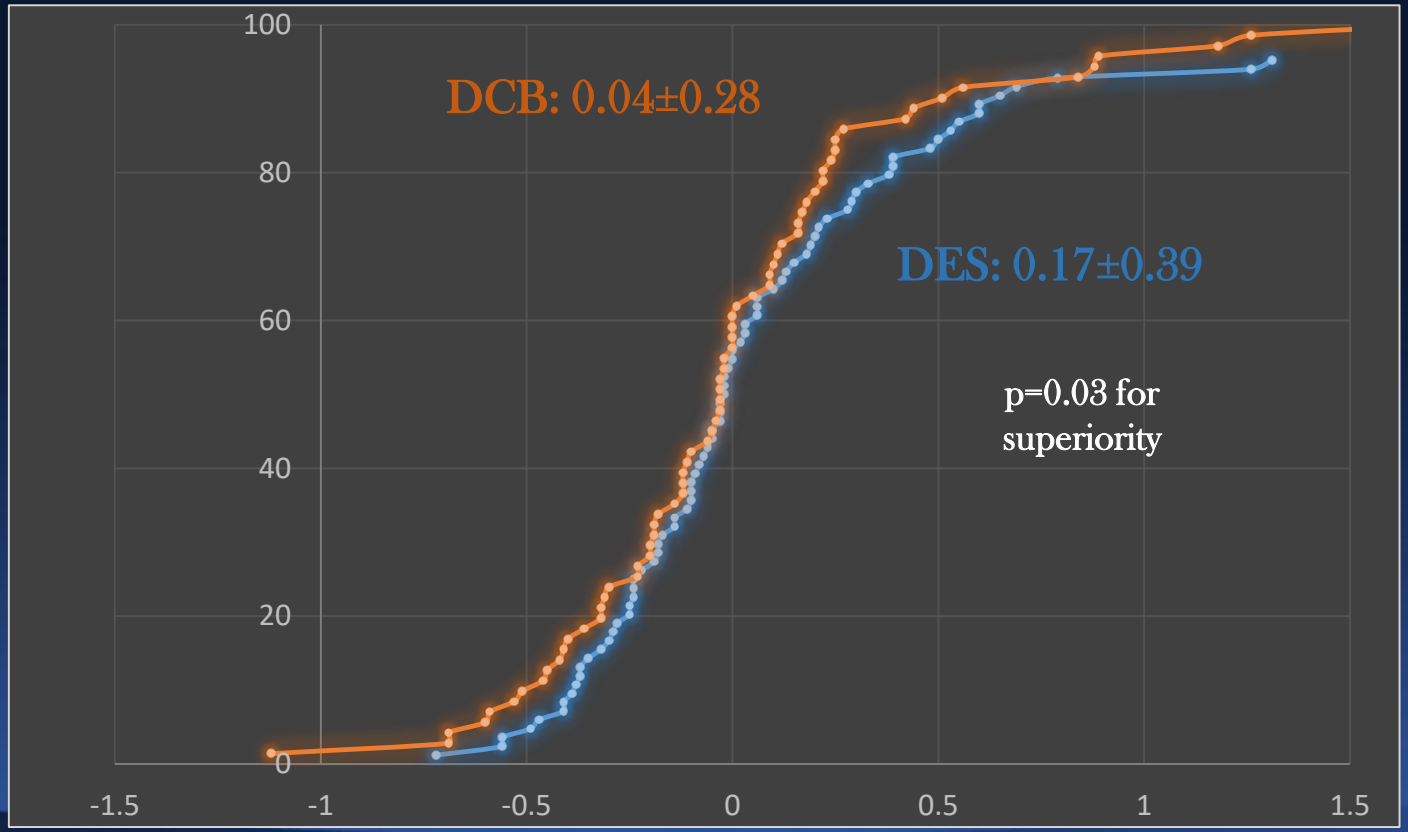
Baseline procedural characteristics

	DES	DCB	p
Number of patients and lesions	114	118	
Predilatation, n (%)	78 (69)	99 (84)	0.007
Postdilatation, n (%)	66 (59.4)	4 (3.3)	0.001
Number of devices used (mean), n	1.12	1.03	0.04
Length of device used (mean), mm (SD)	18.3 (6.9)	21.8 (8.2)	0.04
Mean inflation pressure, atm (SD)	13.7 (2.5)	11.4 (3.3)	0.07
Mean duration of inflation, sec (SD)	21.4 (11.8)	49.2 (14.5)	0.003
Bailout stenting, n (%)	-	8 (6.8)	-
Angiographic success, n (%)	113 (99.1)	116 (98.3)	0.88
Procedural success, n (%)	112 (98.2)	116 (98.3)	0.92

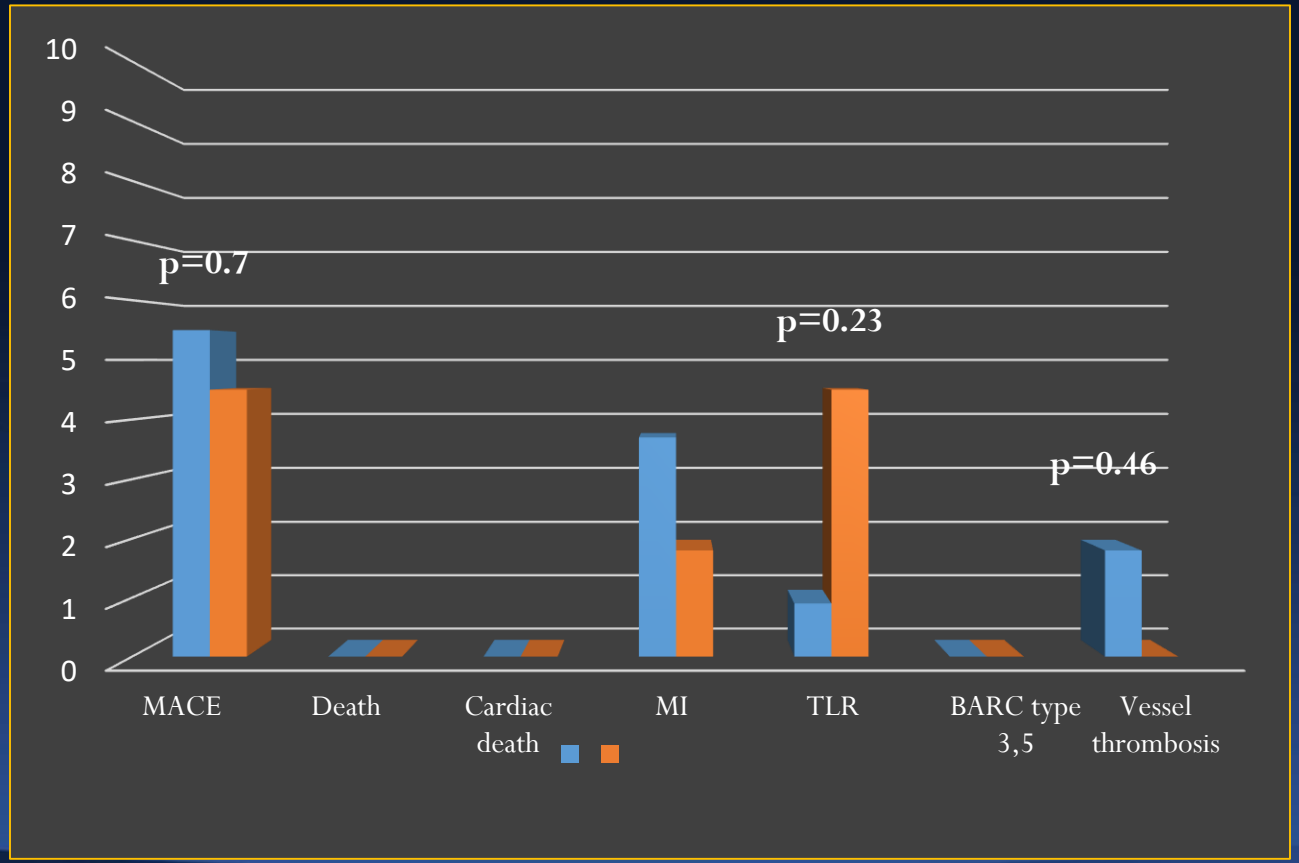
Basal QCA data (Medis QAngio, NL)

	DES	DCB	p
Pre-procedure			
RVD, mm	2.18 ± 0.4	2.23 ± 0.4	0.46
MLD, mm	0.83 ± 0.4	0.82 ± 0.5	0.98
Stenosis, % of lumen diameter	76 ± 15	75 ± 17	0.83
Post-procedure in-lesion			
MLD, mm	2.29 ± 0.4	1.89	0.02
Stenosis, % of lumen diameter	13.1 ± 18	21.4 ± 22	0.20
Acute gain, mm	1.47 ± 0.3	0.99 ± 0.4	0.03
Post-procedure in-segment			
MLD, mm	1.93 ± 0.3	1.73 ± 0.3	0.04
Stenosis, % of lumen diameter	26.8 ± 12	29.6 ± 16	0.55
Acute gain, mm	**1.10** ± 0.2	**0.85** ± 0.2	**0.05**

In-lesion LLL (primary study endpoint)



Clinical outcome (6 months)



Angiographic follow up QCA data (6 months)

	DES	DCB	p
At follow up in-lesion			
MLD, mm	2.12 ± 0.53	1.85 ± 0.49	0.14
Stenosis, % of lumen diameter	21.6	25.1	0.37
Binary restenosis, n (%)	7 (6.5)	7 (6.3)	0.98
Late loss, mm	0.17 ± 0.39	0.04 ± 0.28	0.03 for superiority
At follow up in-segment			
MLD, mm	1.79	1.74	0.69
Stenosis, % of lumen diameter	32.2	36.6	0.78
Binary restenosis, n	10	11	0.94
Late loss, mm	0.14 ± 0.38	0.01 ± 0.25	0.03 for superiority

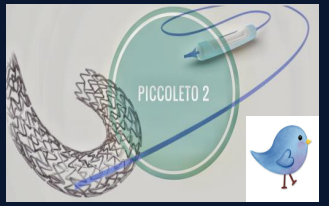
Comparison of various LLL in DCB studies (SVD setting)

STUDY	DCB	TYPE	DRUG	LLL DCB	LLL DES
PICCOLETO	Dior I	RCT	PTX	0.78	0.48
PEPCAD SVD	Paccocath tech.	Reg.	PTX	0.28 ± 0.53	-
BELLO	In.Pact Falcon	RCT	PTX	0.08 ± 0.38	0.29 ± 0.44
Dissections after DCB	Elutax SV 70%, Restore 30%	Reg.	PTX	0.14	-
RESTORE SVD	Restore	RCT	PTX	0.26 ± 0.42	0.30 ± 0.35
FASICO NATIVES	Magic Touch	Reg.	SIR	0.09 ± 0.34	-
PICCOLETO II	Elutax SV	RCT	PTX	0.04 ± 0.28	0.17 ± 0.39

PICCOLETO II-current limitations

- PII is a relatively small study, not powered for hard clinical endpoints
- these results have been obtained in DCB-expert centers, and it is possible that the outcome can be slightly different with less-experienced operators
- currently, we only have a short-term follow up (6 months)-a longer one is required to confirm these data.

conclusions



- PICCOLETO II study ougth to compare Elutax SV DCB vs EES in the small vessel disease setting, and non-inferiority was hypothesized.
- This new-gen PTX DCB outperformed EES in terms of LLL and was comparable in terms of % diameter stenosis and binary restenosis.
- Short term clinical outcome was comparable as well.
- The final 2-year follow up will be available in 2020.
- Pls remember that PICCOLETO II has only 1 T (NOT Piccoletto).