

PLACE



PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

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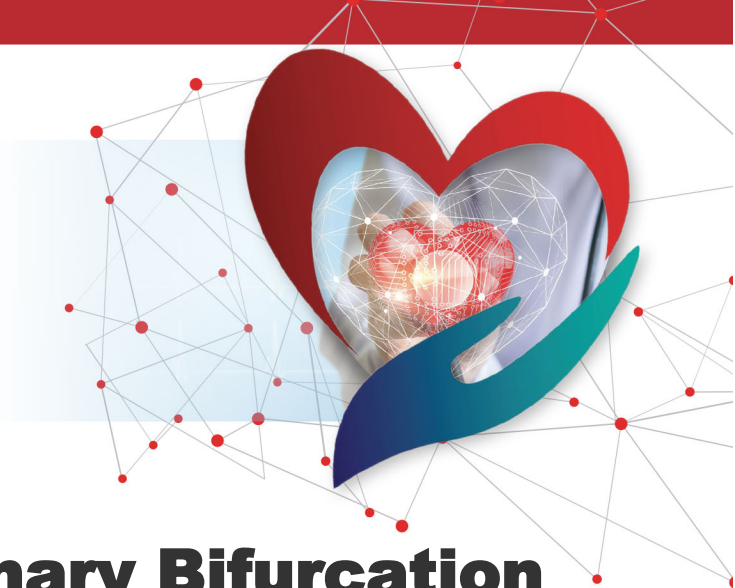
**Auditorium
della Tecnica**

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Drug Coated Balloon in Coronary Bifurcation

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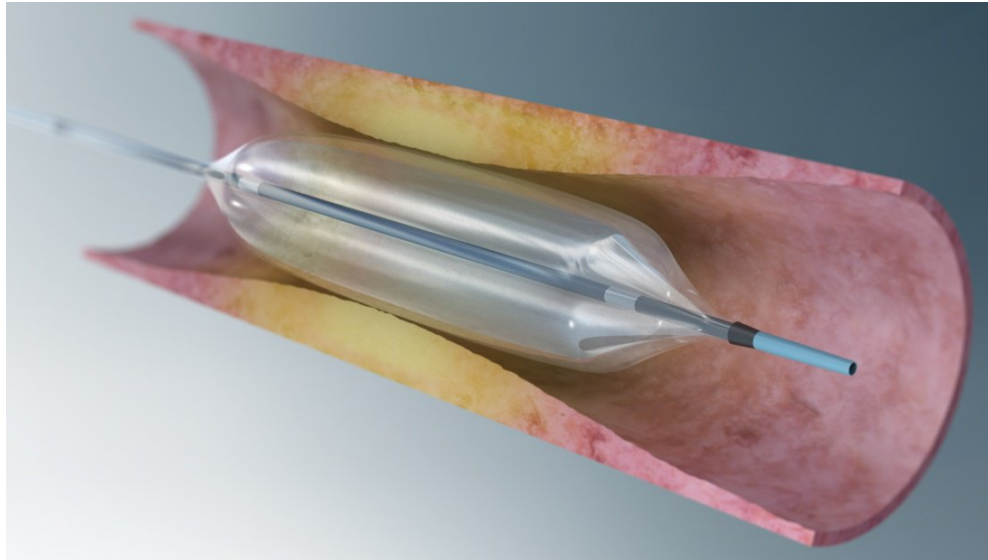
**I.R.C.C.S. Ospedale
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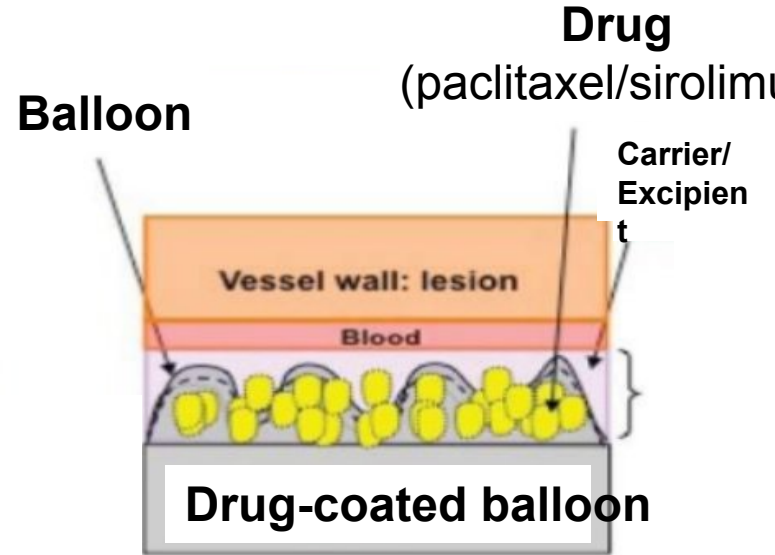
DCB: a Metal Free Approach



DCB were designed to allow stent-independent drug-delivery at the target lesion site reducing the amount of metal within the vessel wall ☺ *"leaving nothing behind philosophy"*



Balloon platform
(usually semi-compliant)



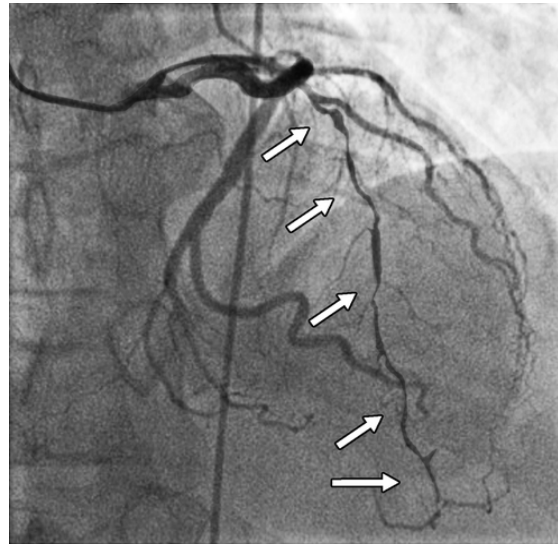
Scenarios Favouring DCB PCI



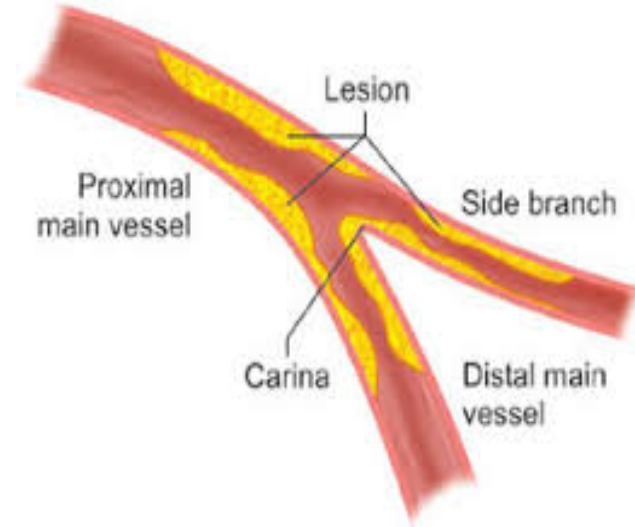
Situations favouring avoidance of implantation of metal stent layers



In-stent restenosis



Diffuse CAD

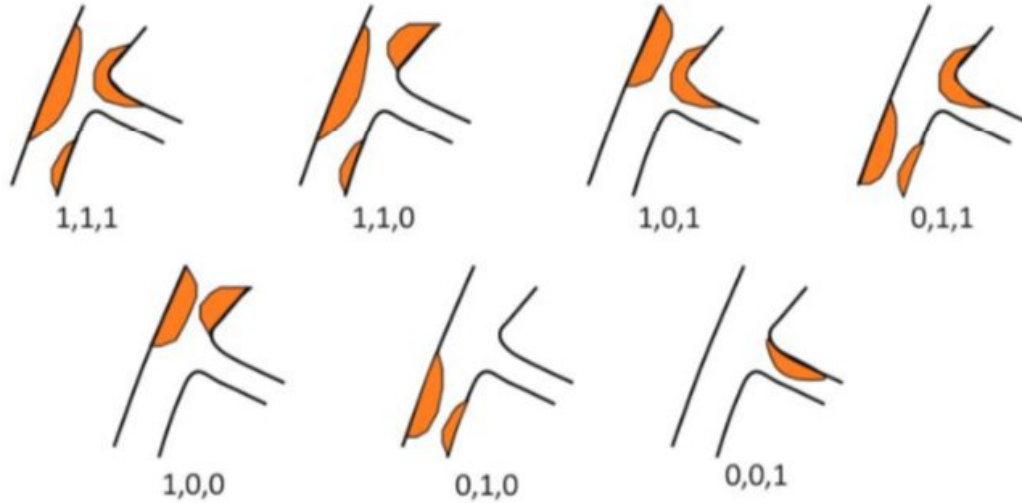


Bifurcations



PCI in Bifurcation Lesions

- Coronary bifurcation lesions (CBL) encountered in up to 20% of percutaneous PCI
- CBL still remains a challenging scenario because of its potential technical complexity

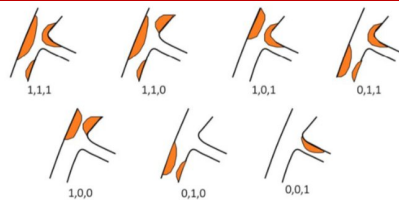


DCB in De Novo Bifurcation Lesions

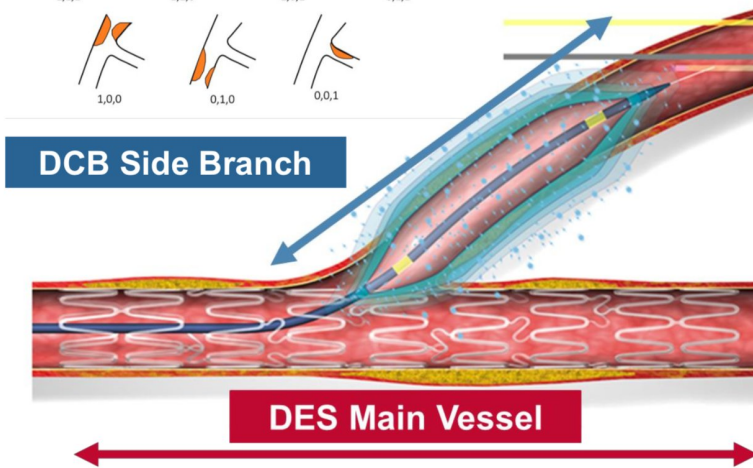
Why?



EBC Recommendation:
PCI on bifurcation should adhere to a KISS
(*keep it simple and safe*) principle



Burzotta F et al, Eurointervention 2021



DCB in De Novo Bifurcation Lesions



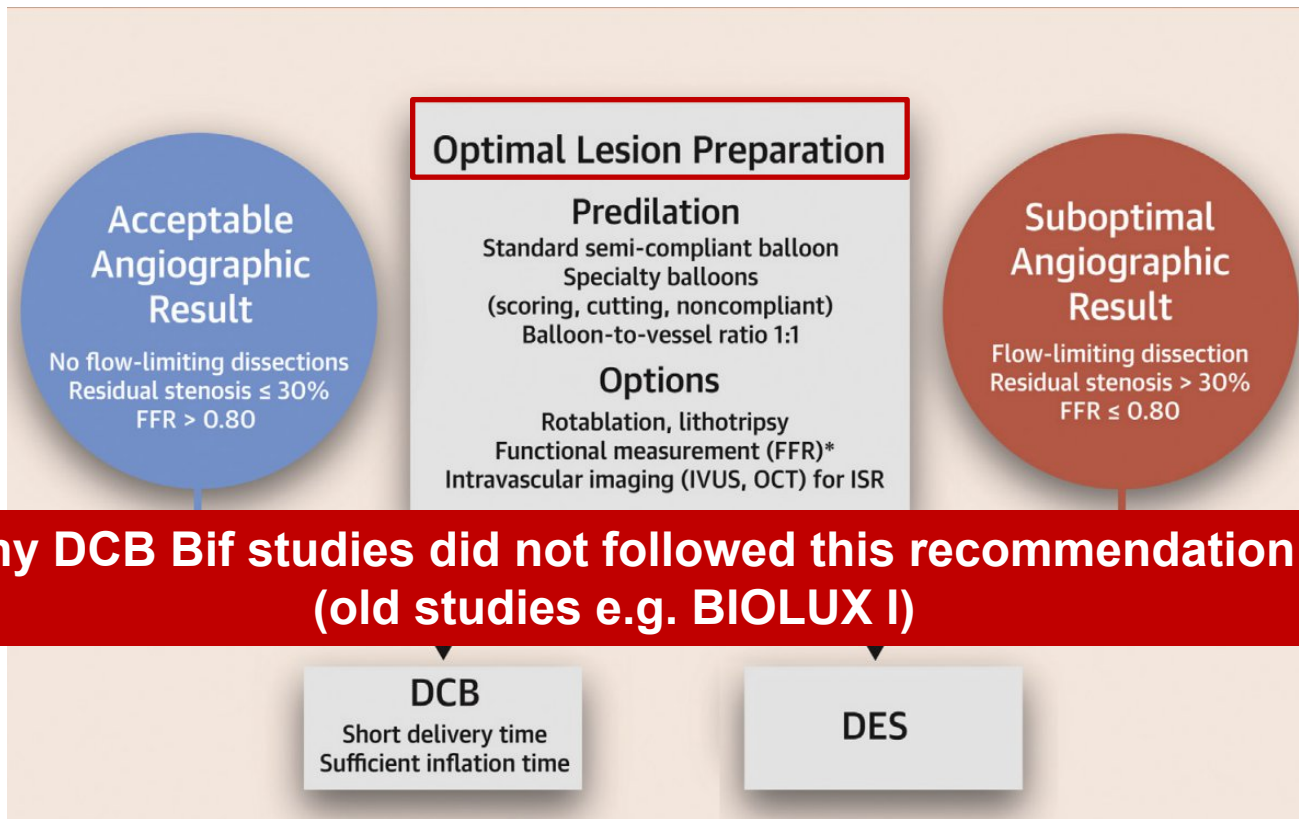
Data

First author/Study	Year	Study type	DCB	DCB	Study strategy	Patient enrolled (n)	Follow-up	Main findings	Comments
Worthley S <i>et al.</i> [37]	2015	Observational Registry	Pantera (Biotronik)	Lux	Sequential DCB inflation in SB and MV stenting with DES, followed by final KBI	35	9 months (angiographic and IVUS); 12 months (clinical assessment)	60% of post-procedural device success rate	LM, severely calcified and bifurcation near to ostial LAD, LCx and RCA origin excluded
<p>BIOLUX-1</p> <p>SB LLL: 0.10 ± 0.43 mm (per OCA) and -0.03</p>									
<p>Heterogeneous designs, especially considering the type of bifurcation studied (according to Medina classification), the applied strategy (usually old) and the step in which DCB was delivered</p>									
<p>SARFEDON</p>									
Kleber FX <i>et al.</i> [39]	2015	RCT	Sequent Please (B Braun)	Sequent Please (B Braun)	DCB-only strategy vs POBA	64 (32 vs 32)	9 months (angiographic follow-up)	1-year MACE (any death, non-fatal MI, TVR): 19%	LM bifurcations and bifurcations with proximal MV involvement were excluded (Medina 1.0.0)
<p>PEPCAD-BIF</p>									
Bruch <i>et al.</i> [40]	2016	Observational Registry	Sequent Please (B Braun)	Sequent Please (B Braun)	DCB-only strategy vs DCB + stenting	127 (70 vs 57)	9 months	No difference between the two groups in terms of MACE (6.1% DCB-only vs 7.3%) and TLR (4.5% DCB-only vs 3.6%)	
Vaquero B <i>et al.</i> [41]	2016	Observational Registry	DIOR (Eurocor GmbH)	DIOR (Eurocor GmbH)	DCB-only strategy for SB	49	7-months (angiographic follow-up); 1 year (clinical follow-up)	86% of angiographic success 22.5% of binary restenosis 14.3% of MACE	Only Medina 0.0.1 included; LM CBL excluded
Kitani S <i>et al.</i> [42]	2021	Observational Registry	Sequent Please (B Braun)	Sequent Please (B Braun)	DCB-only strategy with lesion preparation with directional coronary atherectomy followed by DCB inflation	129	6-15 months (angiographic follow-up); 12 months (clinical follow-up)	3.1% of TLR 10.9% of TVF (with 1 clinically-driven TVR)	Only major bifurcation included
<p>DCA/DCB Registry</p>									



DCB Bifurcation Lesions

First Mandatory Step





DCB in SBs of True Bifurcation Lesions

When?

DCB can be theoretically inflated:

- Before MB stenting (then avoiding SB rewiring and final kissing-balloon inflation –KBI-)
- Sequentially after MB stenting without KBI (POT-side DCB-POT)
- After MB stenting and before KBI
- During the KBI
- After KBI (KBI-POT-side DCB-POT)

No data addressing the best moment to inflate DCB in a SB!

DCB in De Novo Bifurcation Lesions Strategies



- 1) DCB in SB and DES in main branch (MB) ☾ (**Hybrid strategy**)
- 2) DCBs in both MB and SB or on SB only -Medina 001- ☾ (**DCB only strategy**)

DCB Only in Bifurcation Lesions



PEPCAD Bif Trial Medina 1,X,X excluded

DCB in Bifs Medina 001

	POBA	DCB (SQP)	p
Binary restenosis	25.7 %	5.9 %	0.045
Late lumen loss	0.47 ± 0.61 mm	0.08 ± 0.31 mm	0.006



n=64 patients with SB RVD 2.0-3.5 mm and
 No proximal MB disease randomized after predilation to DCB only vs.
 POBA only

n=49 pts (84% angiographic follow-up)
 MACE rate 14.3% @12-month
 Binary restenosis 22.5%
 LLL 0.32 ± 0.73 mm



A Hybrid Approach Evaluating Drug-Coated Balloon in Combination with New Generation Drug-Eluting Stent in the Treatment of De Novo Diffuse Coronary Artery Disease: **The HYPER Pilot Study** (NCT03939468)



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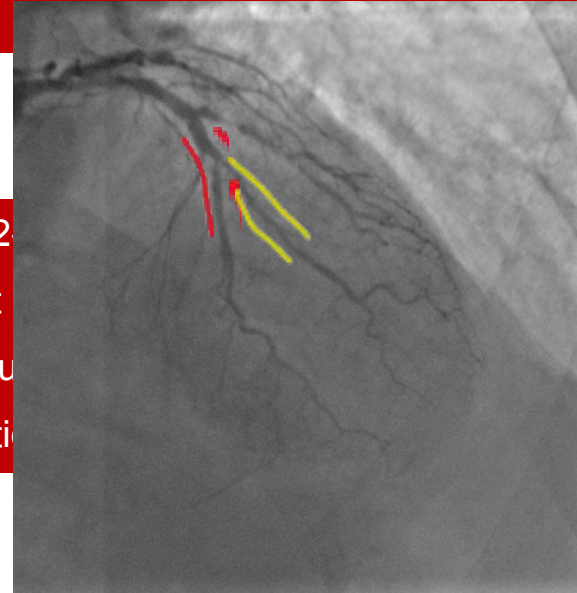
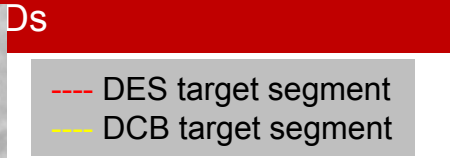
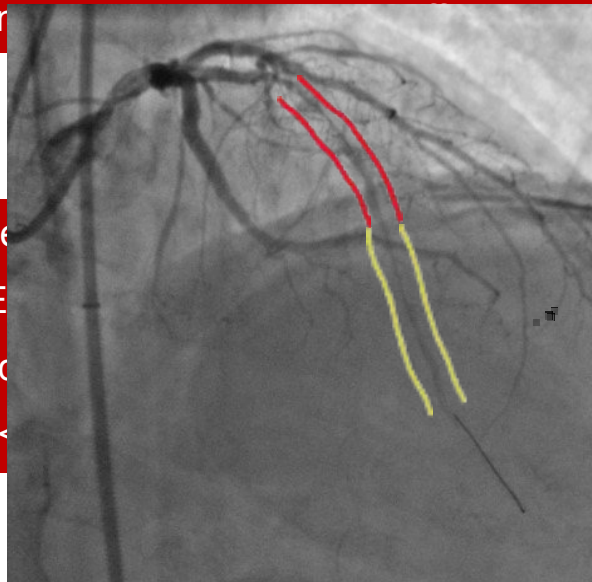


HYPER Pilot Study

Aim and Methods

Prospective, single-arm, multi-center, pilot, study.

To assess the feasibility and the 1-year clinical results following the use of a hybrid approach for the treatment of *de novo* diffuse (>28 mm in length) CAD (e.g. long lesions and/or true bifurcations) involving coronary arteries.



The DES and DCB target segments are overlapping or slightly (2-5 mm-, more proximal part of the DCB target segment) inflation for a contiguous segment or at a SB of a bifurcation.

generation of a bifurcation, 2.0 mm



Participating Centers



IRCC Ospedale Galeazzi Sant'Ambrogio, Milan
Dr IELASI, Dr Pellicano, Dr Buono, Dr Tespili

Istituto Clinico Sant'Anna, Brescia
Dr Tedeschi

April 2019

n=106
Patients/Lesions enrolled
n=50 bifurcation lesions

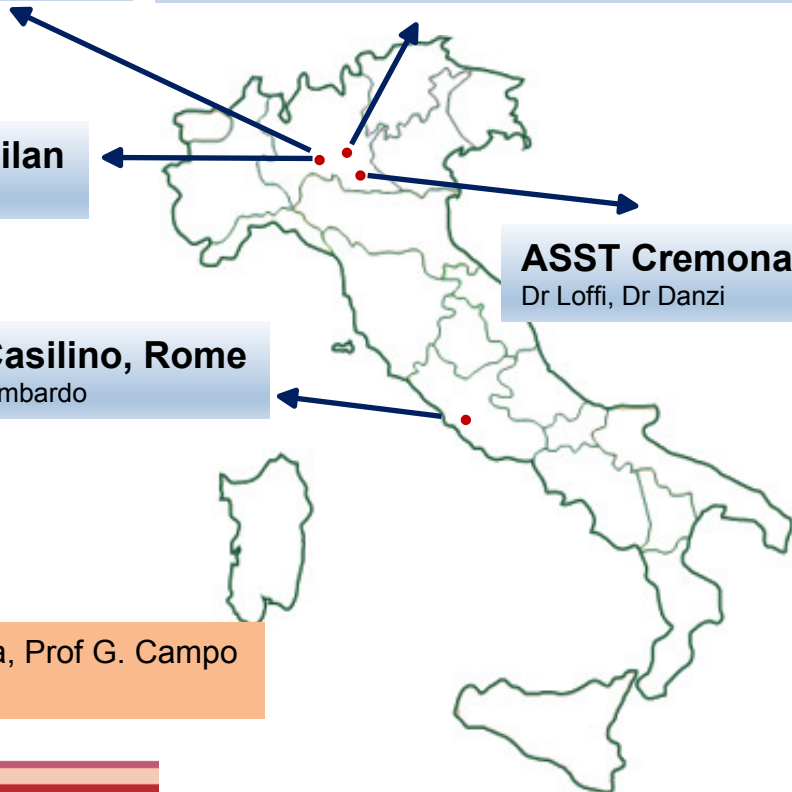
Istituto Clinico Humanitas, Milan
Dr Regazzoli, Dr Reimers

Policlinico Casilino, Rome
Dr Donahue, Dr Zimbardo

ASST Cremona
Dr Loffi, Dr Danzi

December 2020

QCA Core Lab: Cardiology Unit, Azienda Ospedaliero-Universitaria S.Anna, Prof G. Campo
Independent adverse events adjudication committee



Primary End-Point

Overall Population



Patients	n=106
In-hospital Outcome	
Procedural success, n (%)	102 (96.2)
Peri-procedural MI, n (%)	3 (2.9)
Flow-limiting dissection requiring stenting, n (%)	3 (2.9)
DCB did not reached the target lesion, n (%)	1 (0.9)
Major bleeding (according BARC classification)	3 (2.8)
1-Year Outcome	
Device-oriented composite end-point, n (%)	4 (3.7)
Cardiac death, n (%)	0 (0)
Target vessel MI (excluding periprocedural MI), n (%)	0 (0)
Overall ID-TLR, n (%)	4 (3.7)
ID-TLR DES target segment, n (%)	1 (0.9)
ID-TLR DCB target segment, n (%)	3 (2.8)
Thrombosis at the DCB or DES target segment	0 (0)
MI: myocardial infarction; ID: ischemia driven, TLR: target lesion revascularization; DCB: drug-coated balloon; DES: drug-eluting stent. BARC: bleeding academic research consortium	

Baseline Clinical Characteristics

HYPER Bifurcation Subgroup



	Patients (n=50)
Age, (years), mean±SD	67.9±10.3
Male, n (%)	40 (80.0)
Diabetes mellitus, n (%)	18 (36.0)
Insulin-dependent diabetes mellitus, n (%)	10/18 (55.5)
LV ejection fraction, % ± SD	51.8±7.2
Acute coronary syndrome at admission, n (%)	4 (8)
Multivessel coronary artery disease, n (%)	24 (48)
Previous myocardial infarction, n (%)	13 (26)
Previous PCI, n (%)	18 (36)
Previous CABG, n (%)	4 (8)
Chronic kidney disease (eGFR <60 ml/min), n (%)	0
Peripheral artery disease, n (%)	2 (4)
Prior stroke, n (%)	1 (2)

HYPER Study

Medina Class Bifurcation Subgroup



1,1,1

n=38 (76%)



1,0,1

n=6 (12%)



0,1,1

n=6 (12%)

Major criteria:

- For left main bifurcation (Major 1)
 - SB lesion length ≥ 10 mm, and
 - SB diameter stenosis $\geq 70\%$
- For non-left main bifurcation (Major 2)
 - SB lesion length ≥ 10 mm, and
 - SB diameter stenosis $\geq 90\%$

Major 1 or 2

+ any 2 Minors

Minor criteria:

- > mild calcification
- Multiple lesions
- Bifurcation angle $< 45^\circ$ or $> 70^\circ$
- MV-RVD < 2.5 mm
- MV lesion length ≥ 25 mm
- Thrombus-containing lesions

75% Complex bifurcation according to DEFINITION Criteria Chen SL JACC Int 2014

Procedural Characteristics

Bifurcation Subgroup



	Lesions (n=50)
Radial access, n (%)	42 (84)
Contrast media (ml), mean± SD	158±60
Fluoroscopy time (mins). mean± SD	23±11
LAD-D1 lesion, n (%)	26 (52)
RCA-PDA-PL lesion, n (%)	16 (32)
I Cx-OM1, n (%)	8 (16)
Pre dilatation (MB and SB), n (%)	50 (100)
Pre-dilatation semi-compliant balloon (DCB target segment), n (%)	20 (40)
Pre-dilatation non-compliant balloon (DCB target segment), n (%)	30 (60)
MB DES diameter (mm), mean ± SD	2.98±0.49
MB DES length (mm), mean ± SD	29.0±9.5
SB DCB diameter (mm), mean ± SD	2.35±0.36
SB DCB length (mm), mean ± SD	22.8±6.9
SB DCB inflation pressures (atm), mean ± SD	10.4±2.1
SB DCB inflation time (seconds), mean ± SD	60.1±18.4

HYPER Pilot Study

DCB Inflation at the Bifurcation's SB



DCB at the SB of the bifurcation	Lesions (n=50)
SB DCB after MB stenting, n (%)	42 (84)
Kissing balloon inflation, n (%)	40 (95)
POT-SB DCB-POT, n (%)	2 (5)
SB DCB only before MB stenting, n (%)	8 (16)

HYPER Pilot Study

QCA Bifurcation Subgroup



	Baseline	Final	p value
DES-treated segment (MB)			
RVD (mm), mean ± SD	2.91±5.2		
MLD (mm), mean ± SD	0.44±0.47	1.9±0.6	0.0001
Diameter stenosis (%), mean ± SD	82.9±9.0	7.3±3.2	0.0001
Lesion length (mm), mean ± SD	25.8±7.3		
Acute gain (mm), mean ± SD		1.55±1.2	
DCB-treated segment (SB)			
RVD (mm), mean ± SD	2.3±0.5		
MLD (mm), mean ± SD	0.44±0.32	1.55±0.9	0.0001
Diameter stenosis (%), mean ± SD	81.9±11.7	22.9±5.9	0.0001
Lesion length (mm), mean ± SD	17.7±7.2		
Acute gain (mm), mean ± SD		1.10±0.56	
Target Vessel Quantitative Flow Ratio		0.92±0.1	

DES: drug-eluting stent; RVD: reference vessel diameter; MLD: minimal lumen diameter; SD: standard deviation; DCB: drug-coated balloon.

HYPER Pilot Study

Bifurcation Subgroup 1-Year Outcome



Patients	n=50
In-hospital Outcome	
Procedural success, n (%)	48 (96)
Peri-procedural MI, n (%)	1 (2)
Raise in cardiac biomarkers (>5-times the normal upper limit)	4 (8)
Flow-limiting dissection requiring stenting, n (%)	0 (0)
DCB did not reached the target lesion, n (%)	1 (2)
Major bleeding (according BARC classification), n (%)	1 (2)
1 Year Outcome	
Device oriented composite end point, n (%)	1 (2)
Cardiac death, n (%)	0 (0)
Target vessel MI (excluding periprocedural MI), n (%)	0 (0)
Overall ID-TLR, n (%)	1 (2)
ID-TLR DES target segment, n (%)	1 (2)
ID-TLR DCB target segment, n (%)	0
Thrombosis at the SB DCB or MB DES	0 (0)
MI: myocardial infarction; ID: ischemia driven, TLR: target lesion revascularization; DCB: drug-coated balloon; DES: drug-eluting stent. BARC: bleeding academic research consortium	

Conclusions



- The “*leaving nothing behind*” philosophy associated with the use of DCB is an attractive therapeutic option for CBLs.
- Studies exploring DCB efficacy in de novo CBL had major limitations
- Data from the bifurcation subgroup of the HYPER study showed a high procedural success rate and low 1-year DOCE following a hybrid approach (DCB at the SB, DES in the MB)
- RCTs with homogeneous populations and procedural steps, comparing a Provisional approach with DCB (on SB) vs. a full DES approach are needed



Thank you



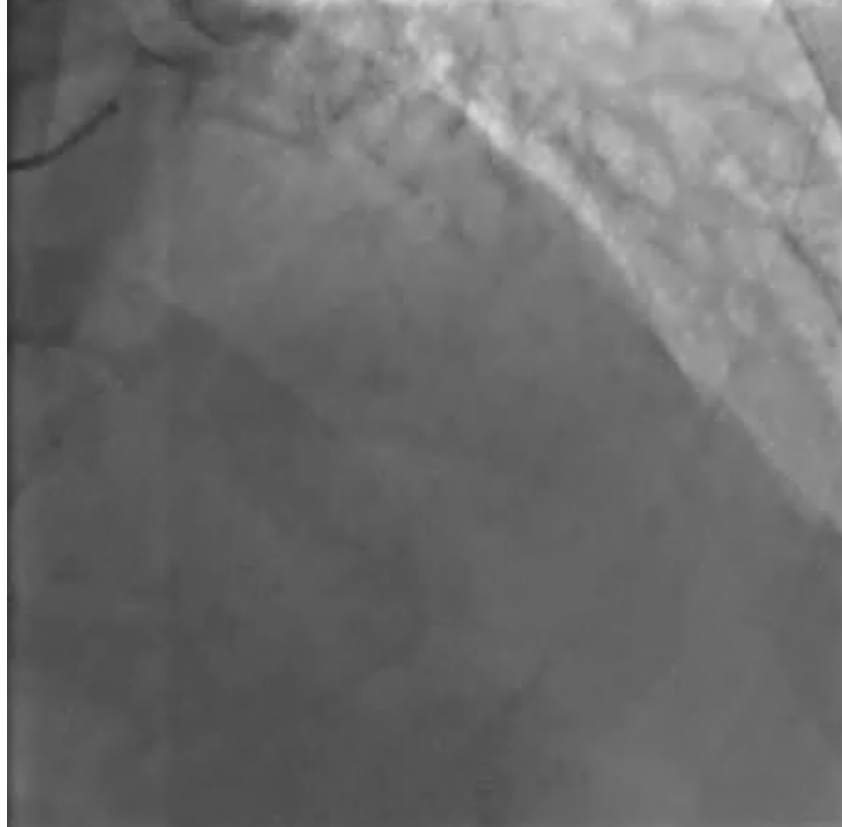
alielasi@hotmail.com

Case Example

Baseline Angio



68 yrs old male, IDDM
Unstable angina
MV CAD

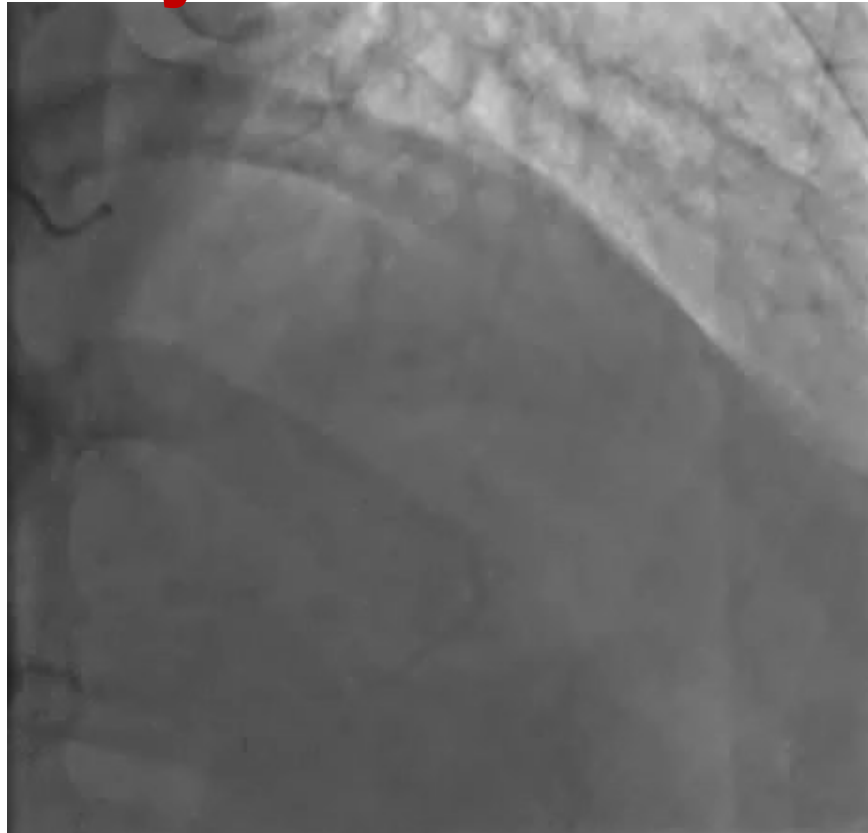


Case Example

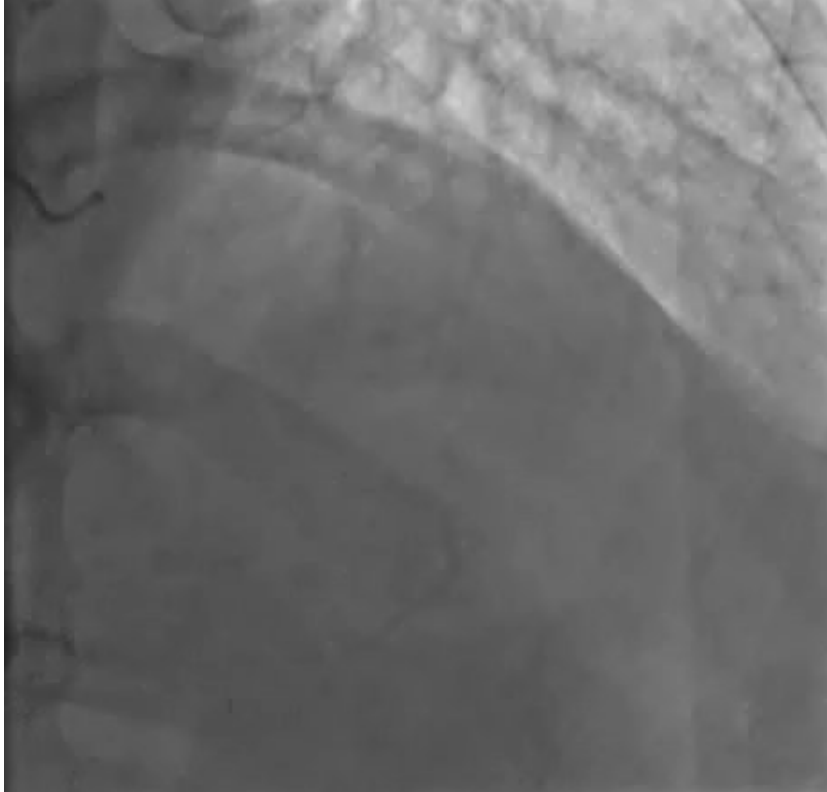
Hybrid DES DCB Bif



Hybrid DES/DCB LAD mid
DES (3.0x18 mm) and
Restore DCB (2.25x30 mm) ost-prox
2nd diagonal



Case Example



Final



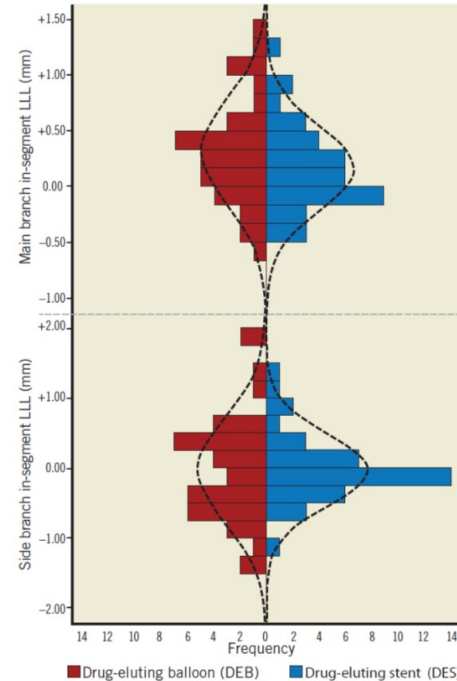
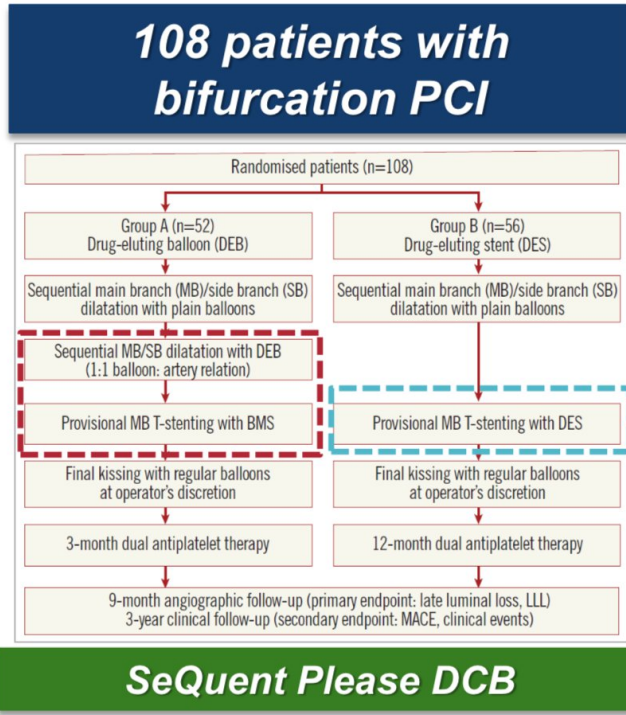
6-Month follow-up

DCB in SBs of Bifurcation Lesions

Provisional Strategy



BABILON Trial



In-segment MB LLL: 0.31 ± 0.48 mm in the pDEB group vs. 0.16 ± 0.38 mm in the DES group ($p=0.15$);

LLL in SB -0.04 ± 0.76 mm in the pDEB group vs. -0.03 ± 0.51 mm in the DES group ($p=0.983$)

MACE and TLR were higher in the pDEB group (17.3% vs. 7.1%; $p=0.105$, and 15.4% vs. 3.6%; $p=0.045$), due to higher MB restenosis (13.5% vs. 1.8%; $p=0.027$)

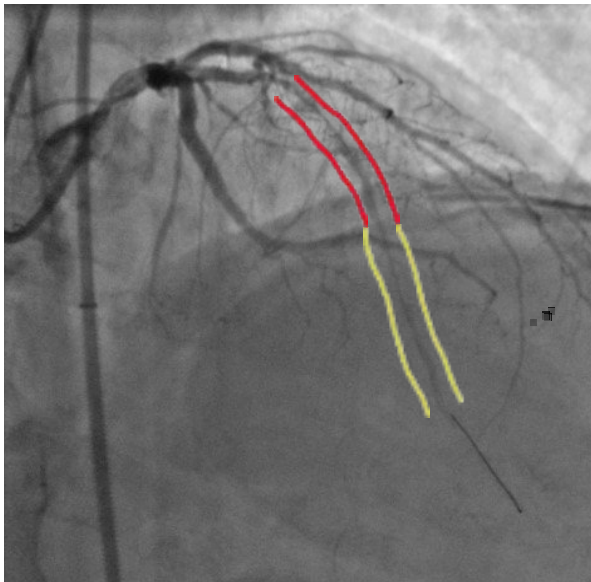
HYPER Pilot Study

Aim and Methods



Prospective, single-arm, multi-center, pilot, study.

To assess the feasibility and the 1-year clinical results following the use of a hybrid approach for the treatment of *de novo* diffuse (>28 mm in length) CAD (e.g. long lesions and/or true bifurcations) involving contiguous segments with different RVDs (>2.75 mm DES target segment and ≥ 2.0 mm and ≤ 2.75 mm DCB target segment)



--- DES target segment
--- DCB target segment

