Time to Move Beyond ISR

How and When Should I Consider Drug Coated Balloon (AGENT) to Treat De Novo Lesions?

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- Other: None

What Does the Guideline Say on Drug-coated Balloons (DCBs)?

2018 ESC/EACTS Guidelines on myocardial revascularization

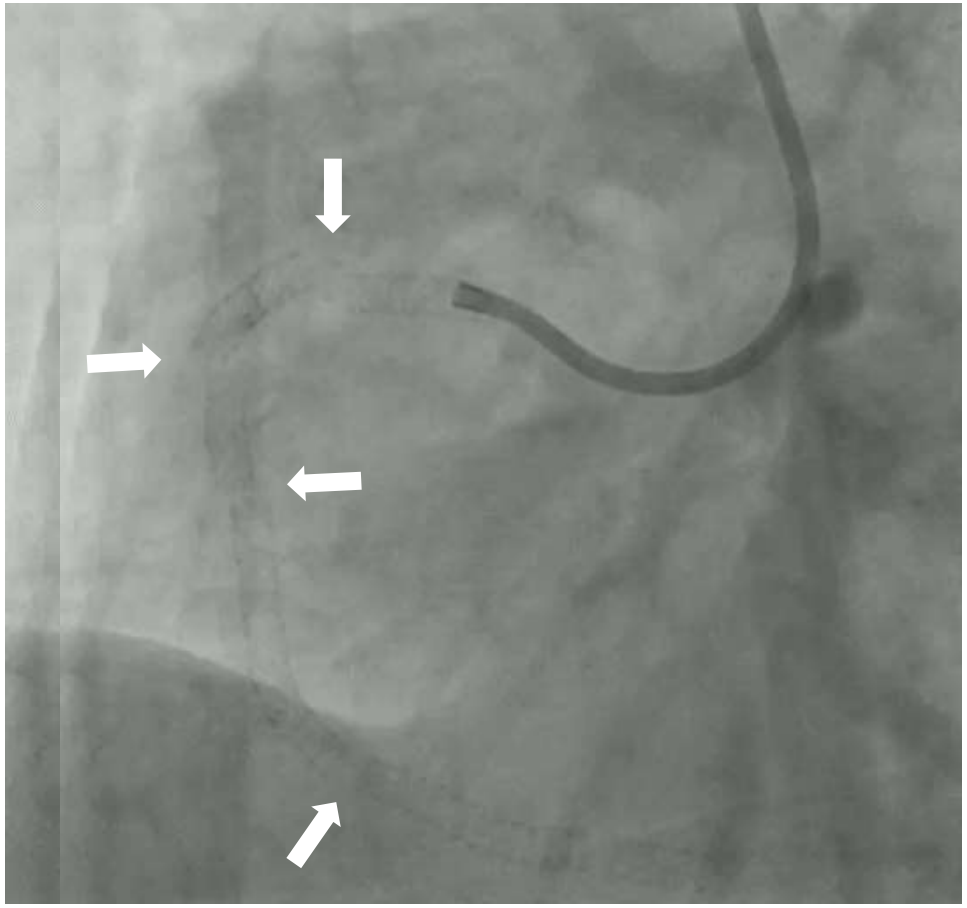
Restenosis		
DES are recommended for the treatment of in-stent restenosis of BMS or DES.[373,375,378,379]	I	A
Drug-coated balloons are recommended for the treatment of in-stent restenosis of BMS or DES.[373,375,378,379]	I	A
In patients with recurrent episodes of diffuse in-stent restenosis, CABG should be considered by the Heart Team over a new PCI attempt.	IIa	C
IVUS and/or OCT should be considered to detect stent-related mechanical problems leading to restenosis.	IIa	C

DCBs are recommended for treatment of ISR of BMS or DES (Class I, LOE A)
How about DCBs for de novo lesions?

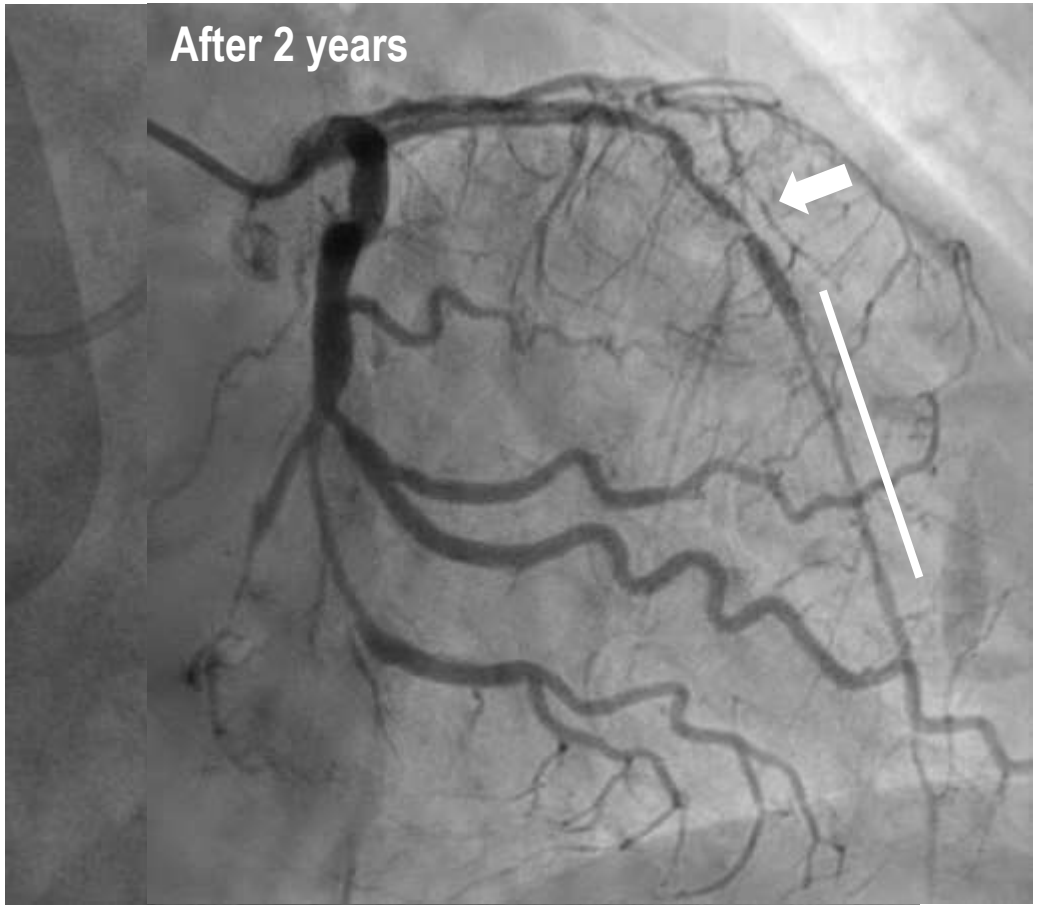
Neumann FJ et al. EHJ 2019;40:87–165

Problems Arising from Leaving Metals and Polymers

Full metal jacket at p-dRCA → Multiple stent fractures



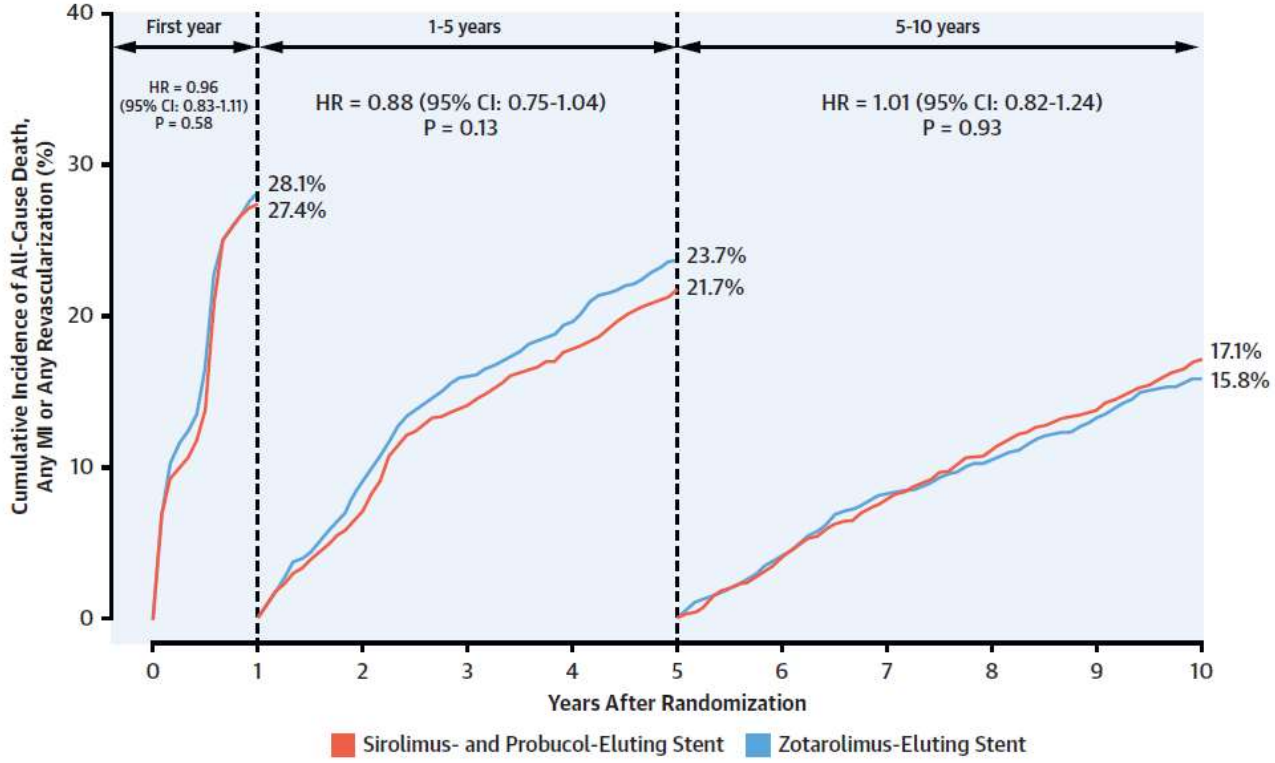
Multiple and long stenting → Recurrent ISR



Very Long Term Clinical Outcome after Drug-Eluting Stent Implantation

ISAR-TEST 5 Trials, Patient N=3,002
Coroflex ISAR vs. Resolute

CENTRAL ILLUSTRATION Landmark Analysis, Patient-Oriented Outcomes According to Treatment Groups

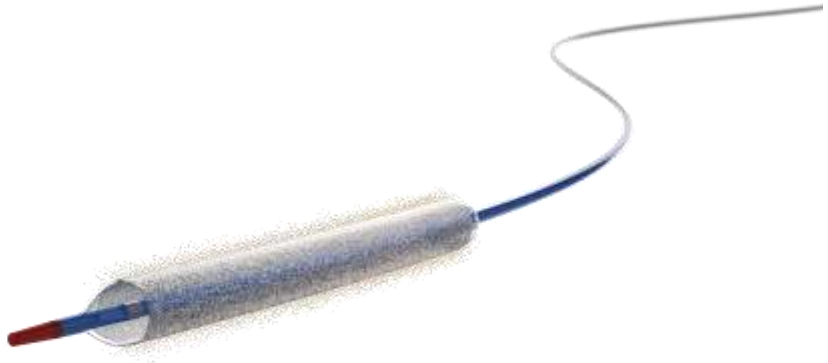


Regardless of stent type,
Death, MI, revascularization occur in linear fashion along with the time.

J Am Coll Cardiol. 2020;76(2):146–58.

Advantages of DCB Treatment – “Leave Nothing Behind”

AGENT™



TransPax™ Coating	EMERGE™ Catheter
Paclitaxel + Novel Excipient Acetyle Tributyl Citrate (ATBC)	Balloon and Tip Design Bi-Segment™ Inner Shaft
Low Ptx load at 2 µg/mm²	Broad Size Matrix
Coating integrity before and during deployment	Deliverability

- Up to 10% of positive remodelling of the treated vessel segment might occur after DCB treatment because no metallic material is left in the vessel to prevent later enlargement.
- The recommended duration of dual antiplatelet therapy is short (1 month for stable coronary artery disease) after PCI using DCB.

Kleber FX et al. Clin Res Cardiol 2015;104:217–25.
Rissanen TT et al. Lancet. 2019 Jul 20;394(10194):230-239

Evidence Supporting DCBs for De-novo Lesions

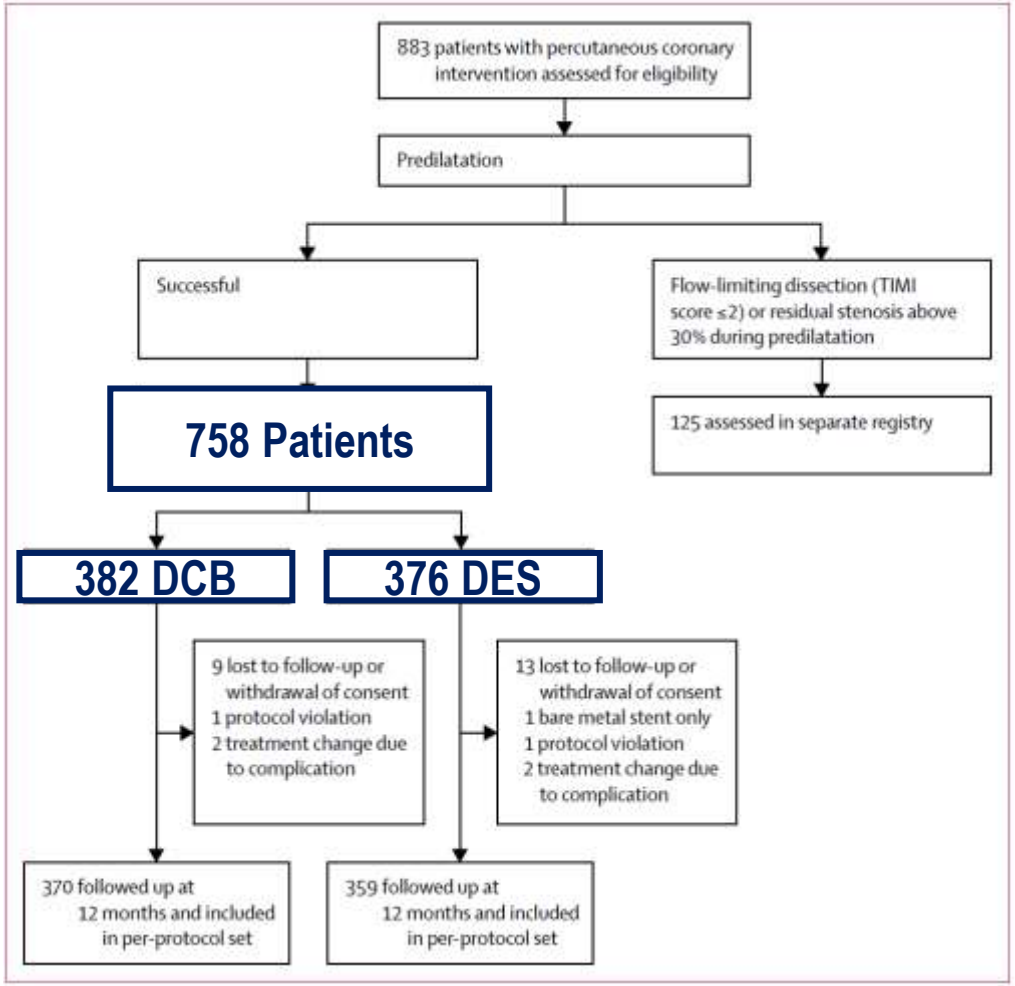
BASKET-SMALL2 (DCB vs. DES)

- Target Population
  - Patients who were indicated PCI in native coronary arteries with a diameter of 2~3 mm

- Primary hypothesis
  - DCB is non-inferior to DES with respect to the major adverse cardiac events (MACE), defined as cardiac death, non-fatal myocardial infarction, and target vessel revascularization after 12 months.

  - Non-inferiority design, assumed margin 4.0%
    - Standard treatment – DES, 10%
    - Testing treatment – DCB, 7%

Study Flow



Jeger RV et al. Lancet. 2018 Sep 8;392(10150):849-856.

Evidence Supporting DCBs for De-novo Lesions

BASKET-SMALL2 (DCB vs. DES)

Baseline Characteristics

	DCB (n=382)	DES (n=376)
Age, mean	67.2 (10.3)	68.4 (10.3)
Male	295 (77%)	262 (70%)
Hypercholesterolemia	262 (69%)	259 (70%)
HTN	324 (85%)	332 (89%)
DM	122 (32%)	130 (35%)
CKD	54 (14%)	59 (16%)
ACS	112 (30%)	102 (27%)
LVEF, median	60% (50-60)	60% (55-65)

Procedure Characteristics

	DCB (n=382)	DES (n=376)
Target vessel, LAD	128 (34%)	116 (31%)
Multivessel disease	313 (82%)	285 (76%)
Bifurcation lesion	22 (6%)	29 (8%)
Procedural success	96%	98%
Mean number	1.68	1.26
Mean length	23.93 mm	23.18 mm
Mean diameter	2.75 mm	2.57 mm
Inflation time	48.45 sec	23.36 sec

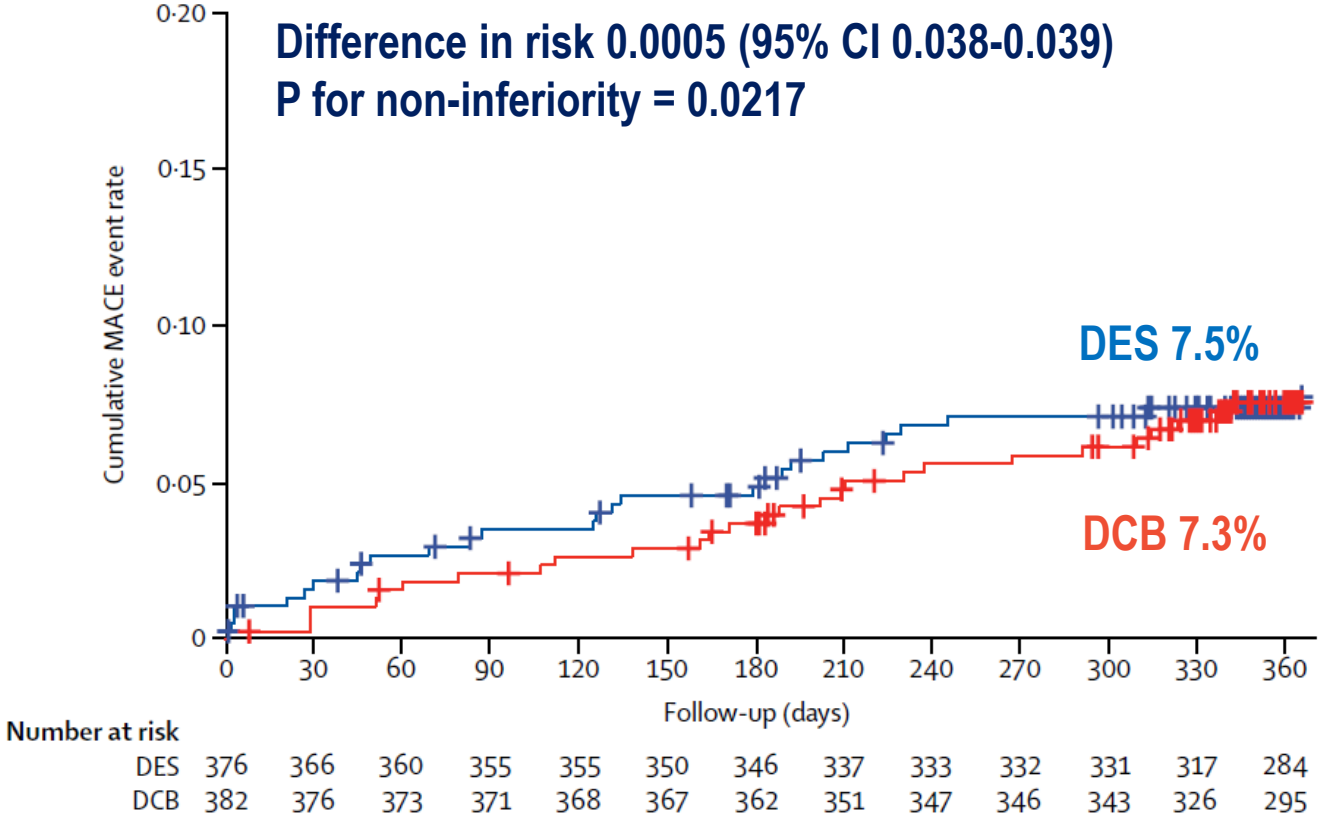
DCBs were performed for the de novo lesions in coronary artery with mean diameter of 2.75mm (± 2.14mm).

Jeger RV et al. Lancet. 2018 Sep 8;392(10150):849-856.

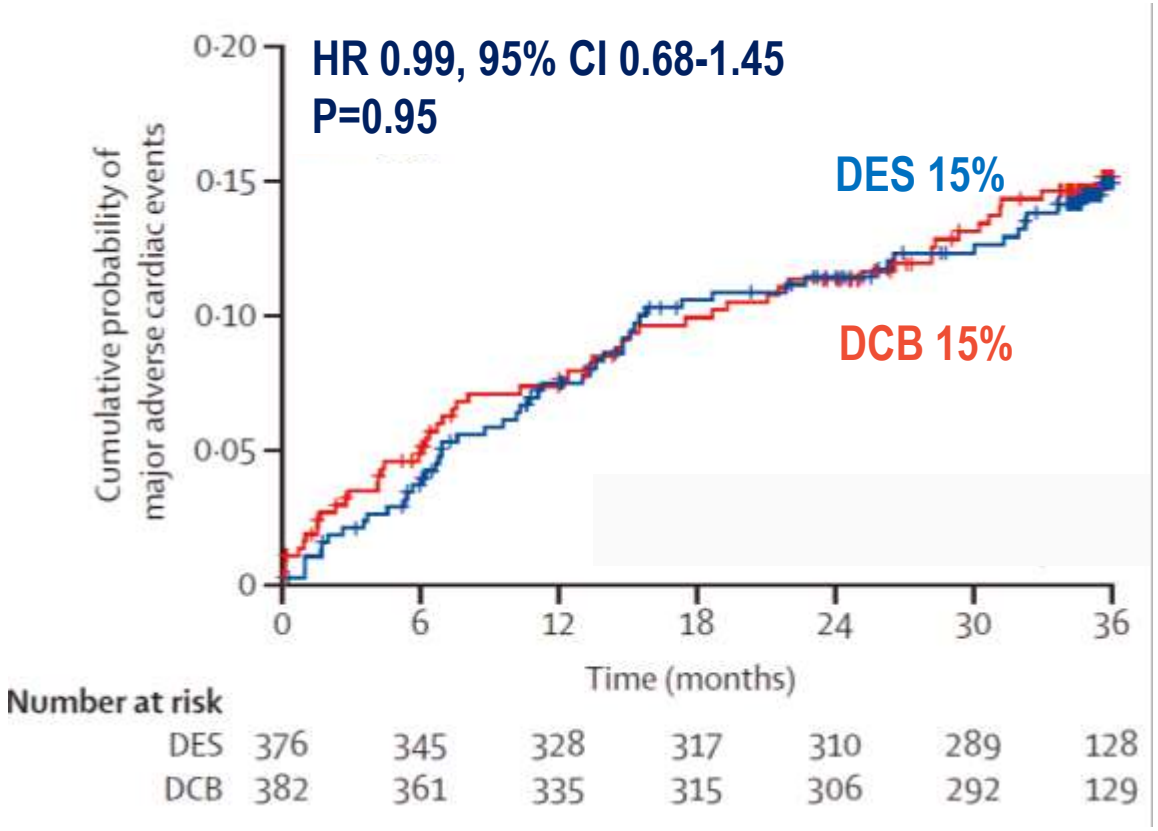
Evidence Supporting DCBs for De-novo Lesions

BASKET-SMALL2 (DCB vs. DES)

Main Results – 12M MACE (Cardiac death, non-fatal MI, TVR)



Main Results – 3Y MACE (Cardiac death, non-fatal MI, TVR)



Jeger RV et al. Lancet. 2018 Sep 8;392(10150):849-856; Lancet 2020;396:1504-1510

Evidence Supporting DCBs for De-novo Lesions

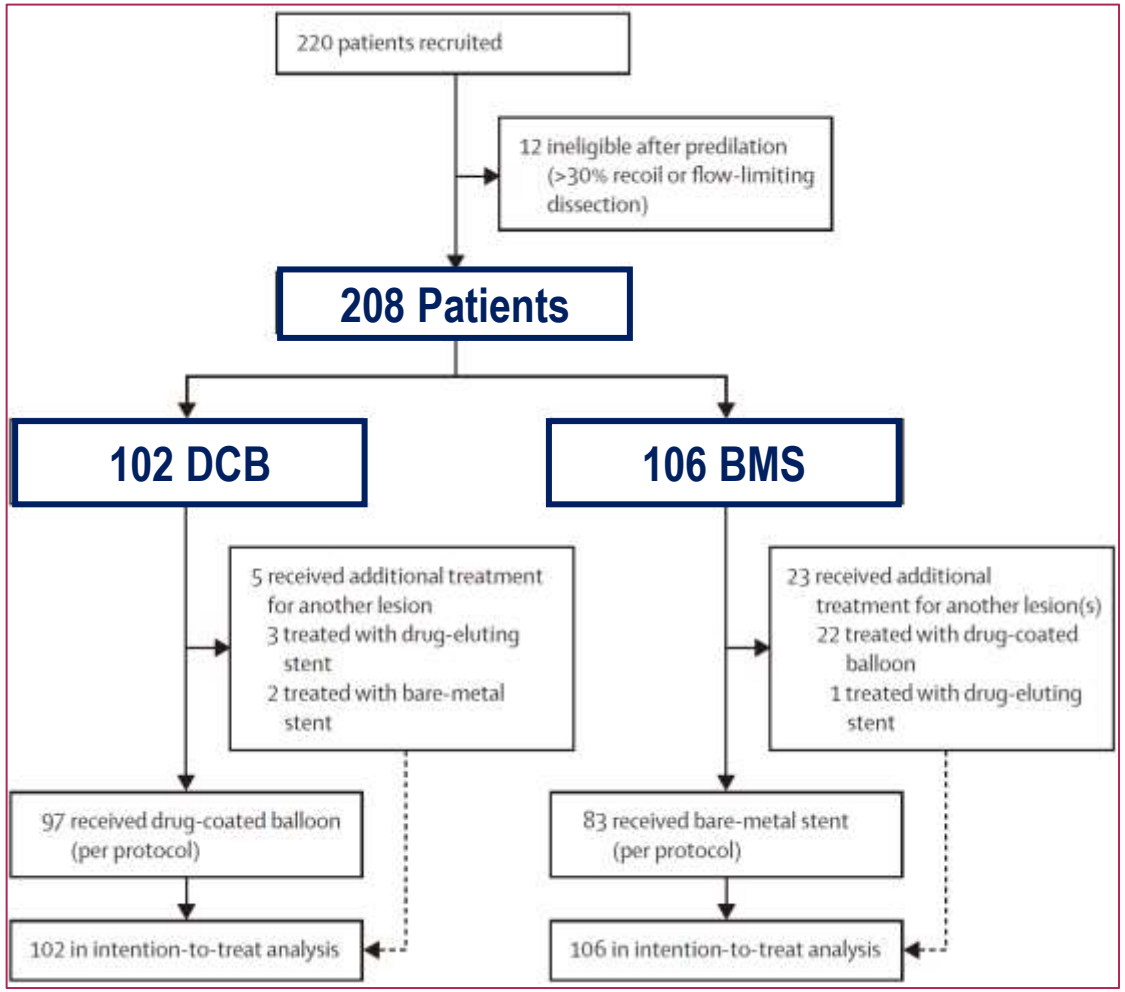
DEBUT (DCB vs. BMS in High-bleeding Risk)

- Target Population
  - Patients with high-bleeding risk (≥80 years, anemia, thrombocytopenia, active malignancy, previous CVA, severe renal dysfunction or hepatic failure, planned non-cardiac surgery, frailty, poor drug compliance, previous bleeding)

- Primary hypothesis
  - DCB is non-inferior to BMS for the patients with HBR, in aspect of MACE at 9 months.

  - Non-inferiority design, assumed margin 3.0%
    - Standard treatment – BMS, 10%
    - Testing treatment – DCB, 7%

Study Flow



Rissanen TT et al. Lancet. 2019 Jul 20;394(10194):230-239

Evidence Supporting DCBs for De-novo Lesions

DEBUT (DCB vs. BMS in High-bleeding Risk)

Baseline Characteristics

	DCB (n=102)	BMS (n=106)
Age, mean	77.6 (8.4)	76.2 (8.5)
Male	63 (62%)	68 (64%)
Hypercholesterolemia	80 (78%)	89 (84%)
HTN	89 (87%)	96 (91%)
DM	27 (26%)	52 (49%)
ACS	112 (30%)	102 (27%)
Age ≥80 years	54 (53%)	53 (50%)
Severe renal dysfunction	3 (3%)	8 (8%)
Anticoagulation	58 (57%)	66 (62%)

Procedure Characteristics

	DCB (n=102)	BMS (n=106)
Target vessel, LAD	50 (40%)	45 (38%)
Bifurcation lesion	21 (17%)	15 (13%)
Calcified lesion	13 (10%)	13 (11%)
Mean number	1.68	1.26
Mean device diameter	3.0 mm	3.1 mm
Dilatation time	35.8 sec	
Mean length of device	19.6 mm	16.2 mm

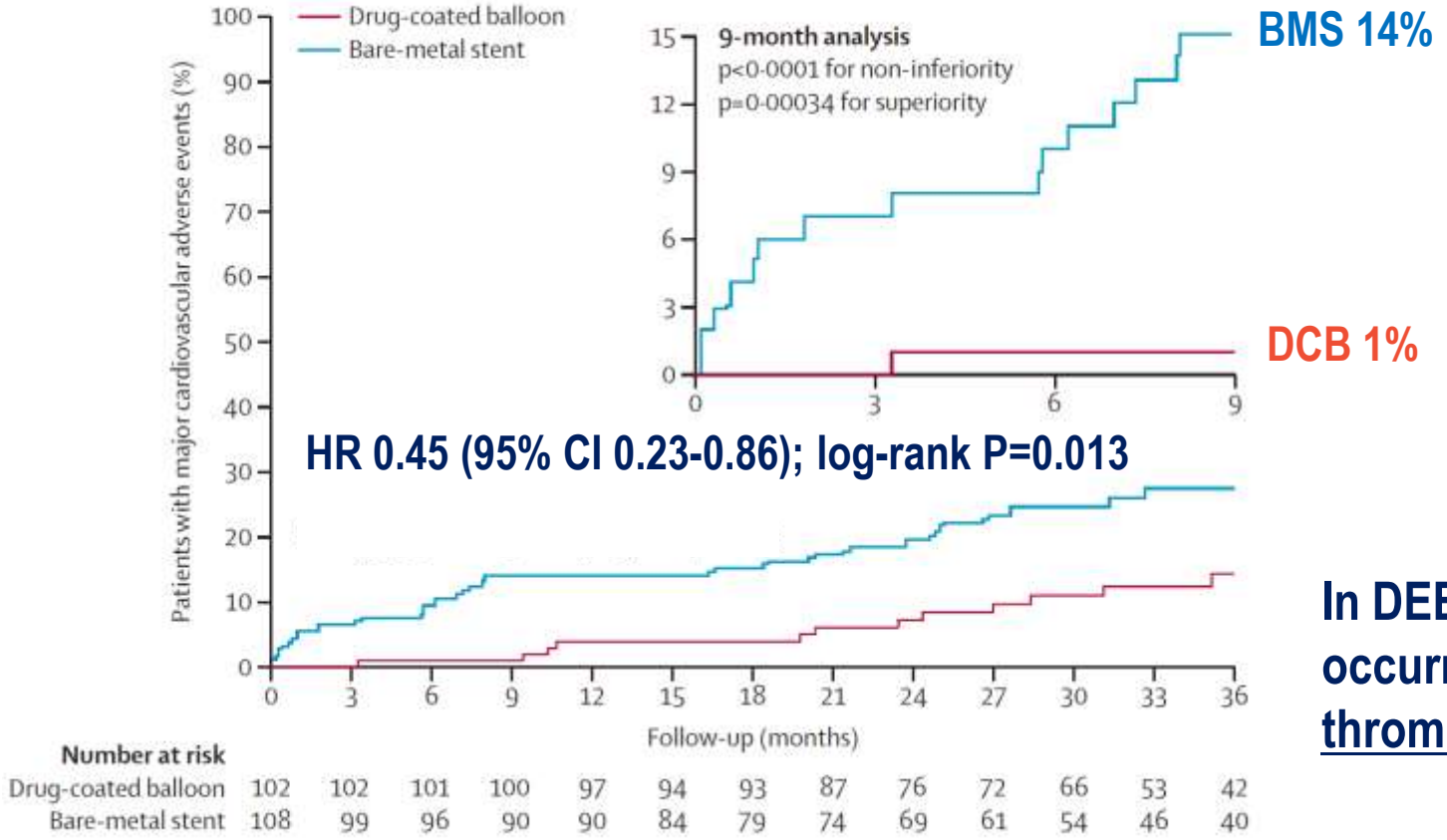
DCBs were performed for the de novo lesions in HBR patients with mean diameter of 3.0mm (± 0.4mm).

Rissanen TT et al. Lancet. 2019 Jul 20;394(10194):230-239

Evidence Supporting DCBs for De-novo Lesions

DEBUT (DCB vs. BMS in High-bleeding Risk)

Main Results – 9M MACE
(CV death, non-fatal MI, or ischemia-driven TLR)



BMS 14%

DCB 1%

In DEBUT trial, no vessel closures of the target lesions occurred after treatment with DCB, but 2 definitive stent thrombosis events occurred in the BMS group.

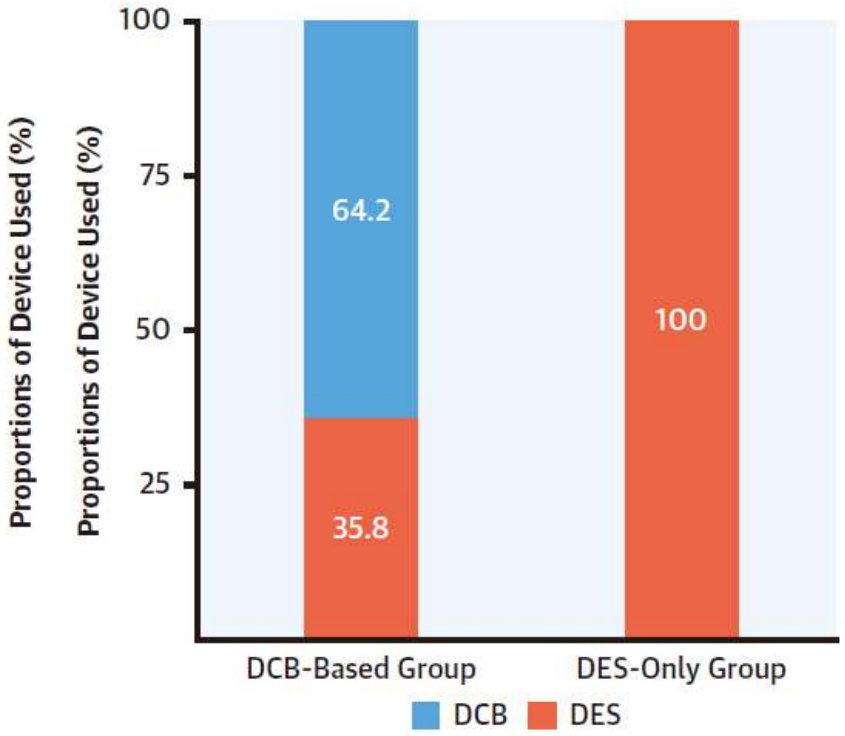
Rissanen TT et al. Lancet. 2019 Jul 20;394(10194):230-239

Evidence Supporting DCBs for De-novo Lesions

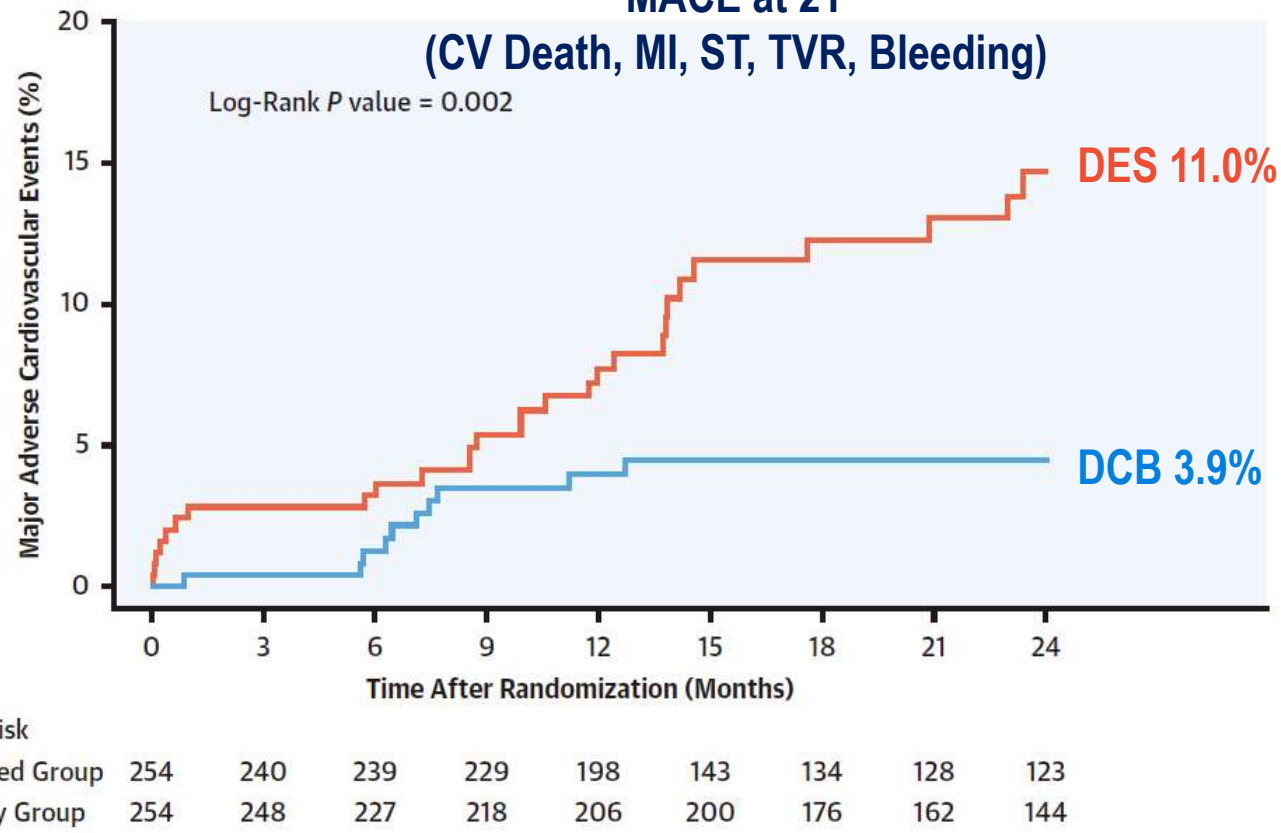
DCB-Based vs. DES for Multivessel Disease (NCT04619277)

254 Patients Matched with PTRG-DES Registry

Proportions of Device Used



MACE at 2Y
(CV Death, MI, ST, TVR, Bleeding)



DCB-based treatment approach showed a significantly reduced stent burden for MVD, which related to lower rate of MACE than DES-only treatment.

Shin ES et al. JACC Intervention. 2023 Feb, 16 (3) 292–299

When I Consider DCB for De-novo Lesions

Candidates for DCB

Lesions with Small vessel (2.5±0.25 mm)
Patients with HBR
Patients with MVD

Safety

Abrupt vessel closure after DCB: about 0~1%

Bail-out stenting

DEBUT	2/102 (2%)
BASKET-SMALL 2	19/349 (5%)

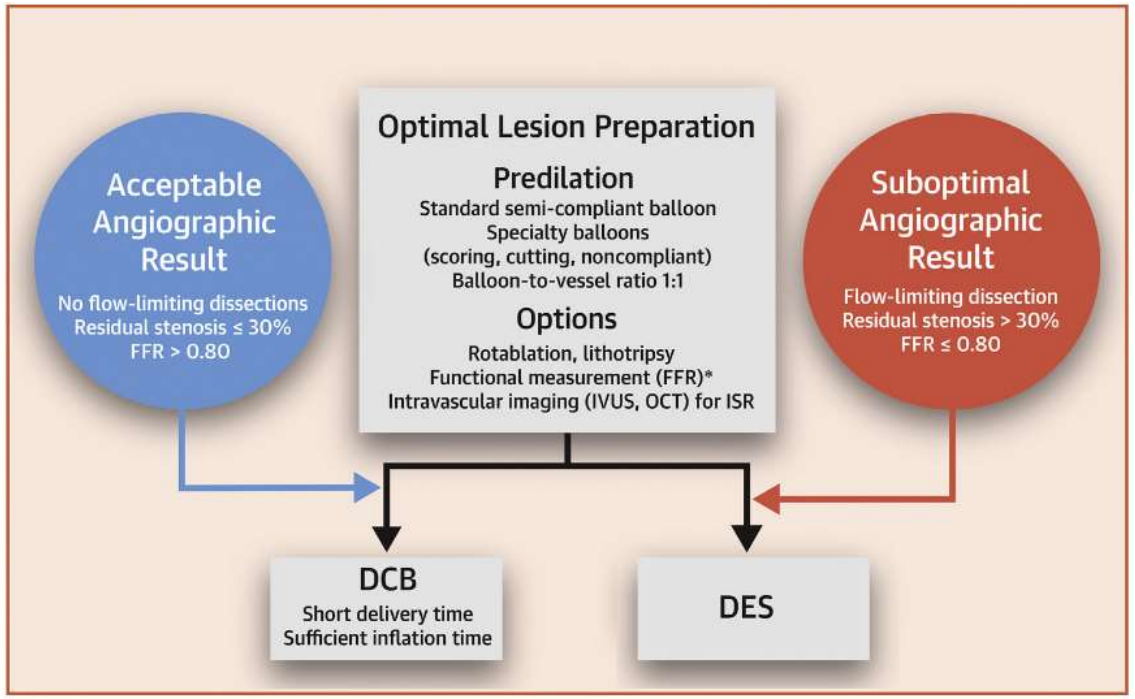
Myocardial Infarction

DEBUT(9M)	DCB 0% vs. BMS 6%
BASKET-SMALL 2(1Y)	DCB 2% vs. DES 4%
BASKET-SMALL 2(3Y)	DCB 6% vs. DES 6%

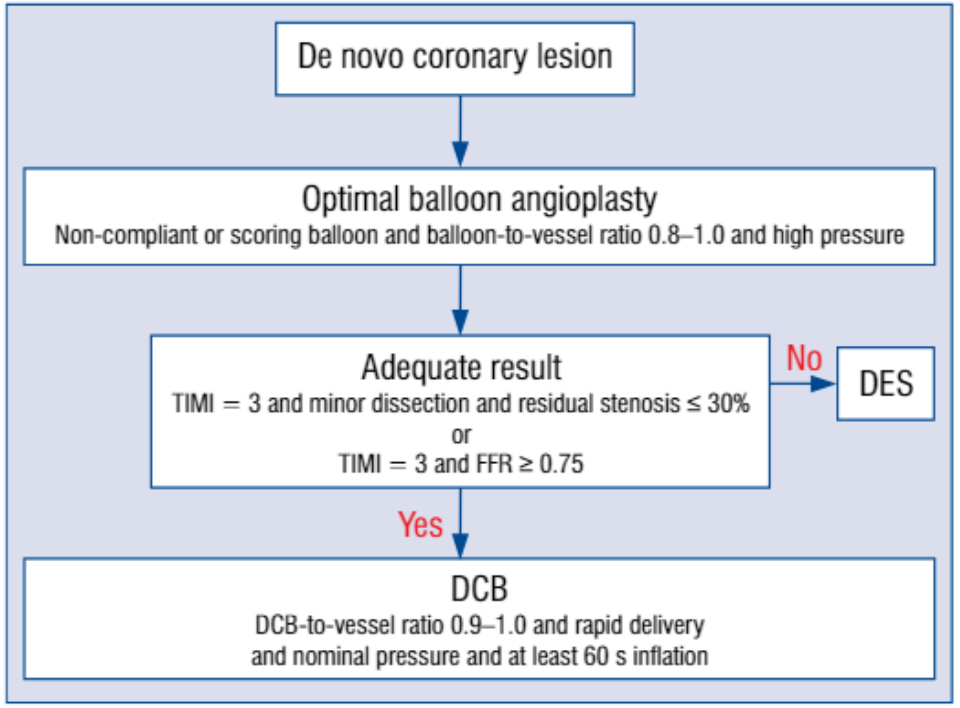
Jeger RV et al. Lancet. 2018 Sep 8;392(10150):849-856; Lancet 2020;396:1504-1510
Rissanen TT et al. Lancet. 2019 Jul 20;394(10194):230-239; Shin ES et al. JACC Intervention. 2023 Feb, 16 (3) 292–299

How to Perform DCB Treatment?

2020 International DCB Consensus Group



2021 Asia-Pacific DCB Consensus Group



Lesion preparation (mechanical expansion) is a crucial step for DCB treatment.

Jeger RV et al. JACC Intervention 2020;13(12):1391-1402
Her AY et al. Cardiol J 2021;28(1):136-149

How to Perform DCB Treatment?

Strong back-up catheter (e.g., XB, EBU, SPB for LCA; Amplatz for RCA)
Extra support guidewire (e.g., Sion blue ES)
Consider guide extension catheter

1. Optimal Lesion Preparation

Balloon-to-vessel ratio 1.0
NC balloon, cutting/scoring balloon

Options:
Rotablation

2. Assessment of Mechanical Expansion

Residual stenosis ≤30%
No flow-limiting dissection
TIMI 3 flow

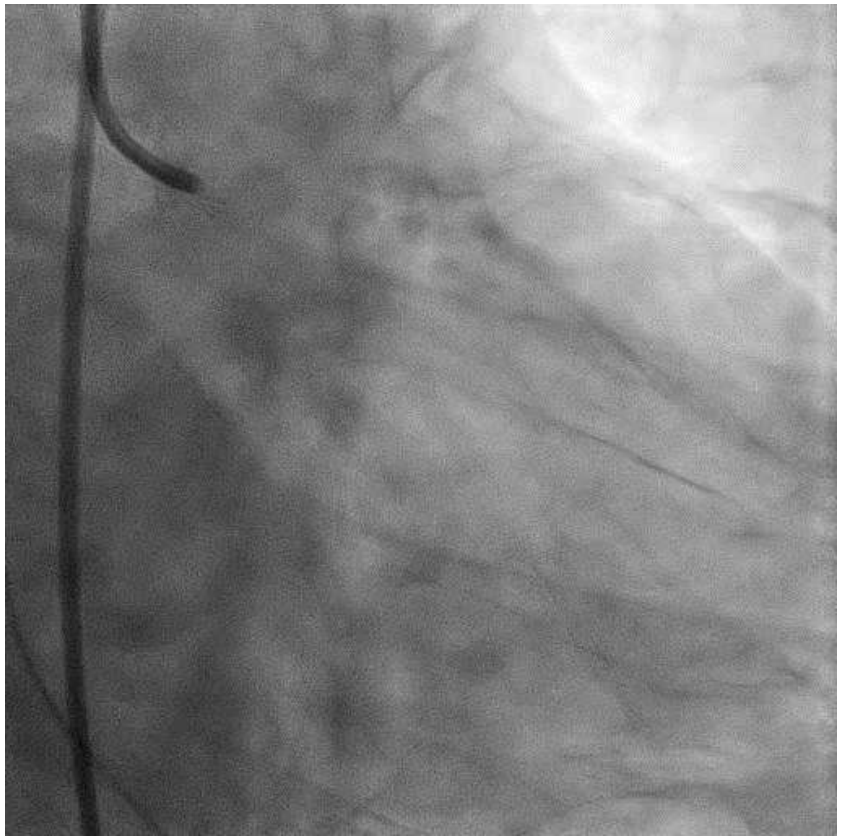
Options:
Intravascular imaging
FFR

3. Drug Delivery

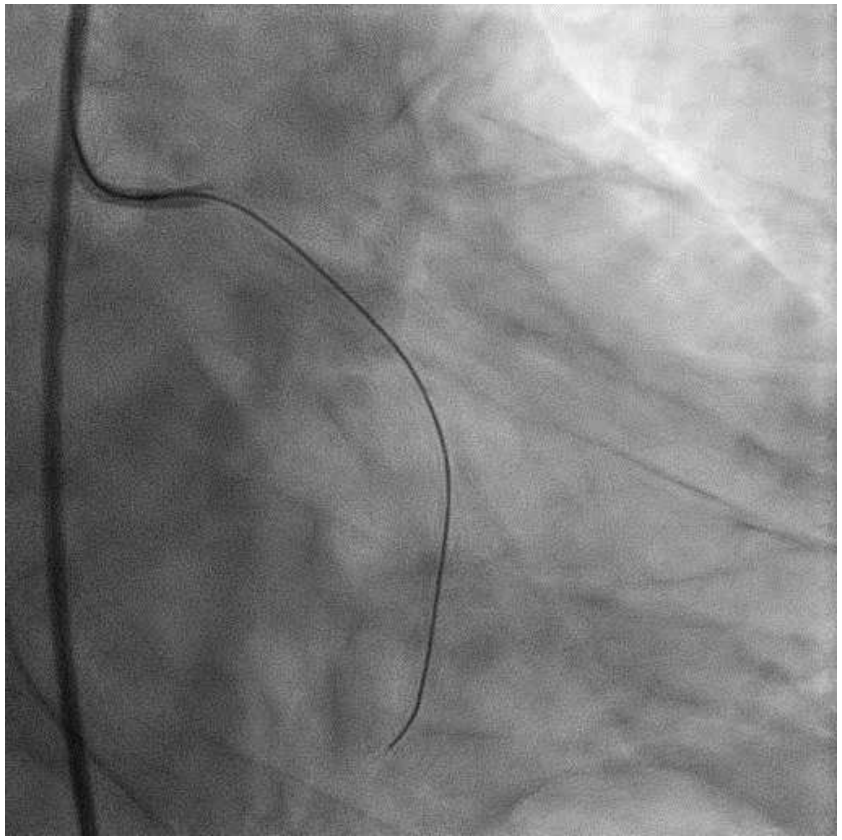
DCB-to-vessel ratio : at least 0.9
Longer DCB (2mm) than prepared lesion
Delivery time <30 sec
Inflation time >60 sec

Case #1 - 67 YO Male

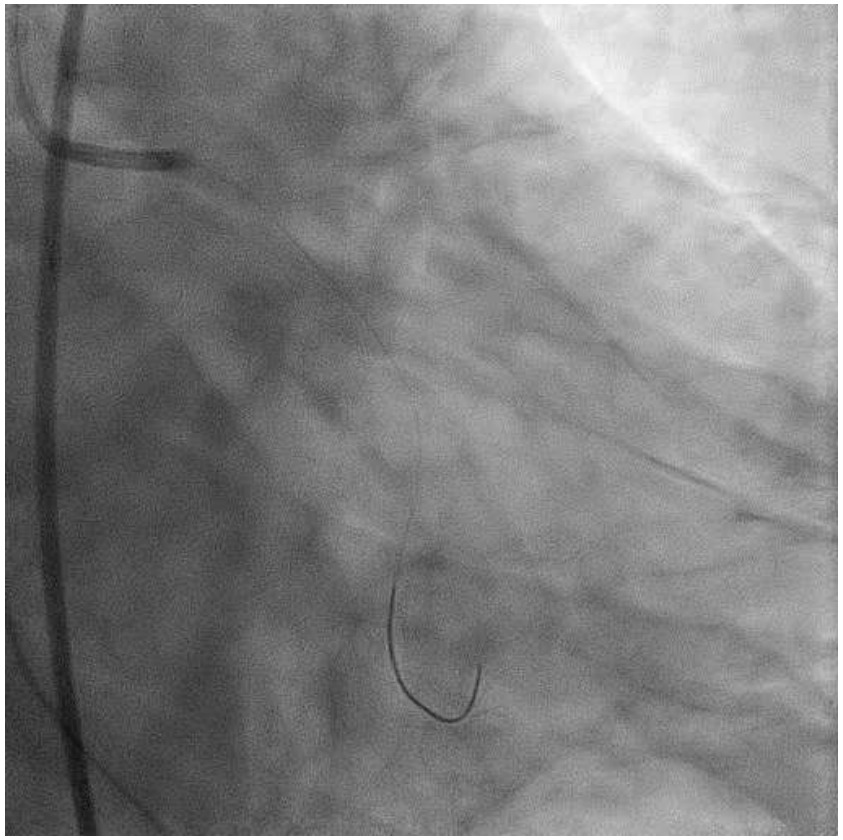
CTO at dLCX with collateral flow from interarterial branch (Gr. II)



6F EBU3.75 guiding catheter



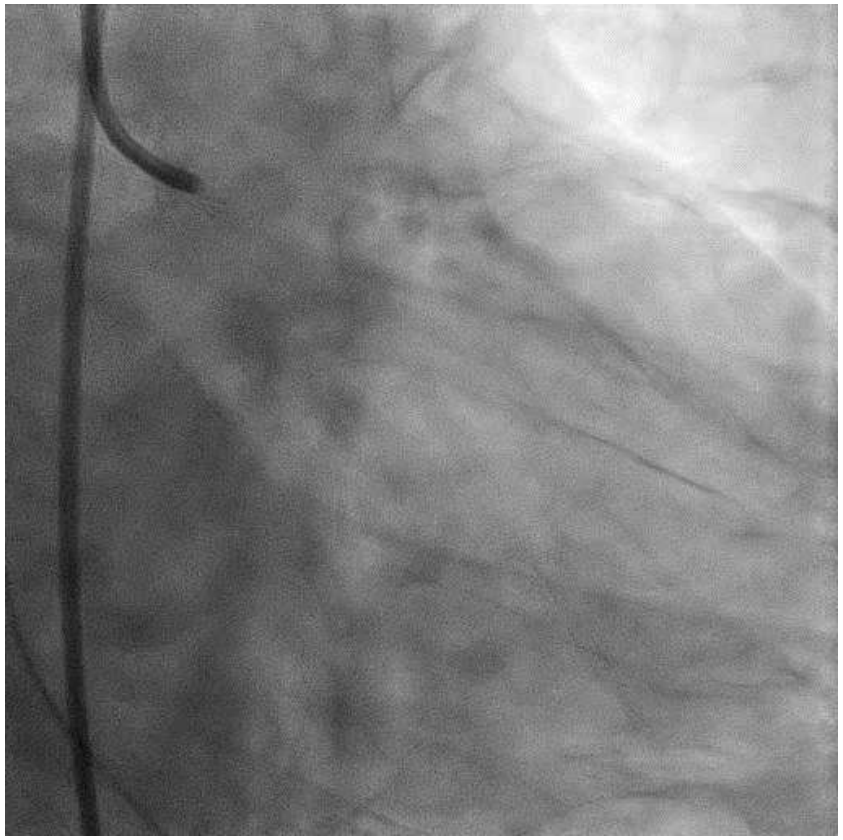
UB3 guidewire + Corsair Pro XS



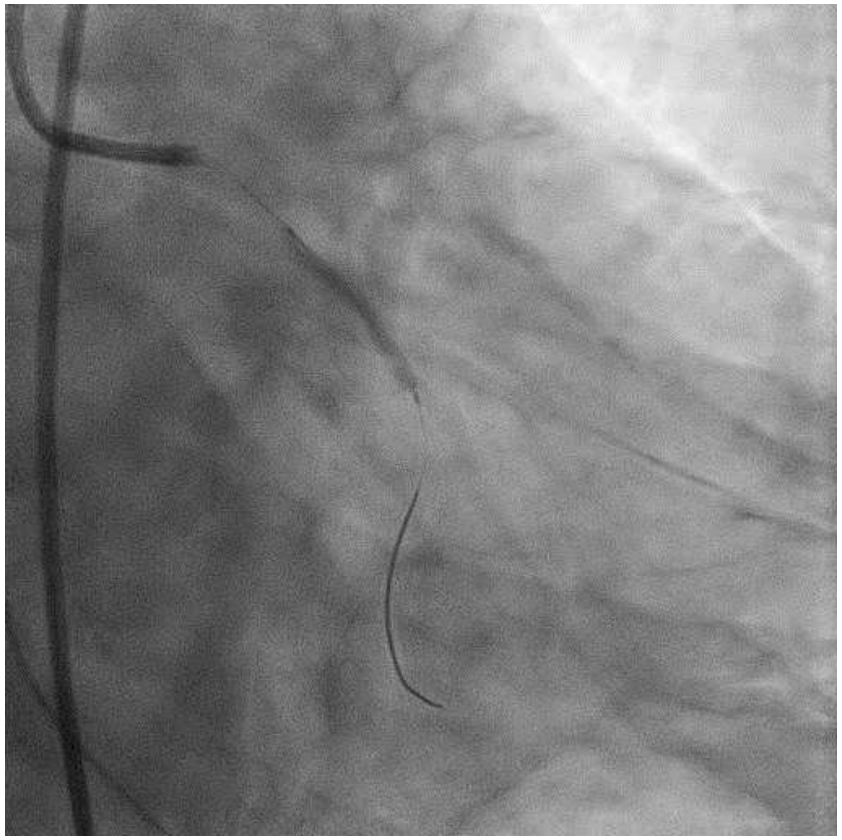
Lesion preparation with 1.5mm
→ 2.0mm balloon

Case #1 - 67 YO Male

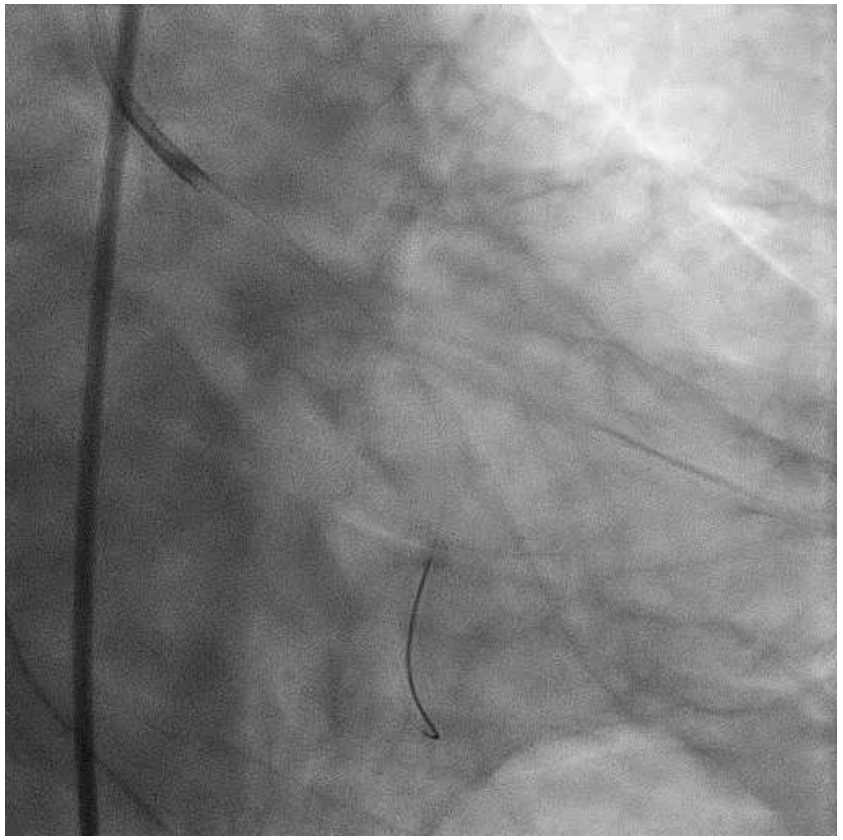
CTO at dLCX with collateral flow from interarterial branch (Gr. II)



Initial CAG



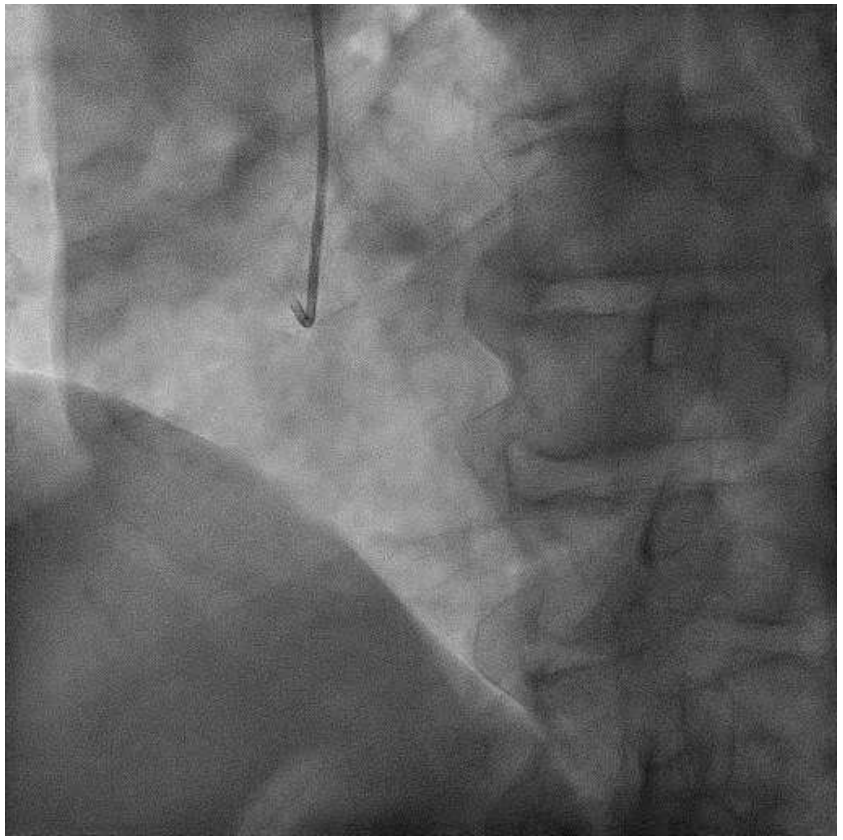
2.25x25mm DCB
delivery time=15sec, total inflation time=60sec



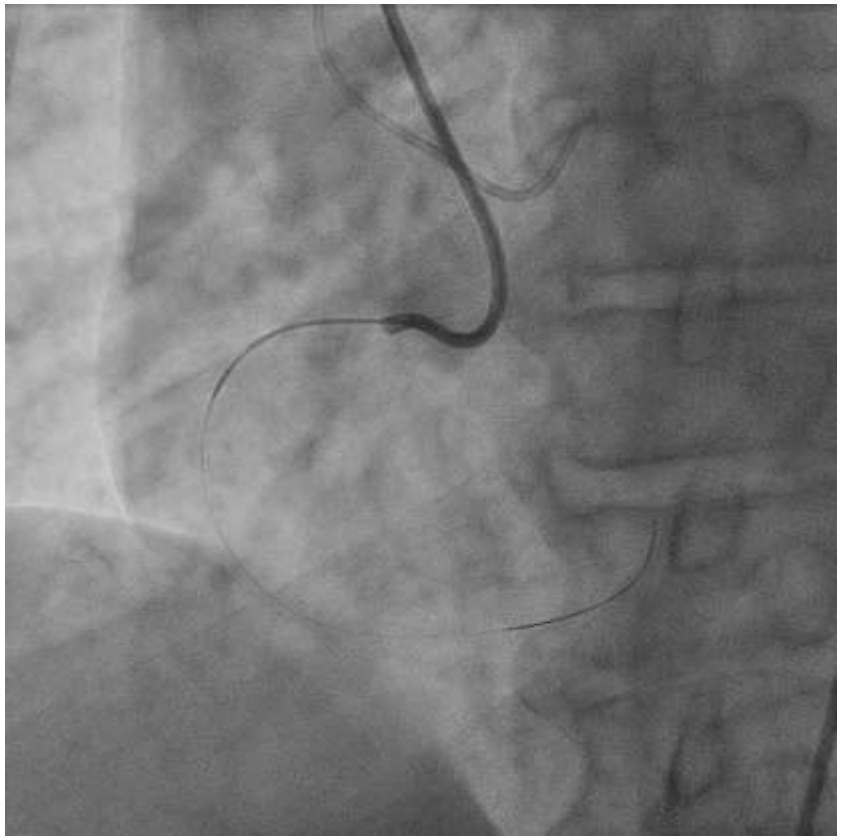
Final CAG

Case #2 - 67 YO Male

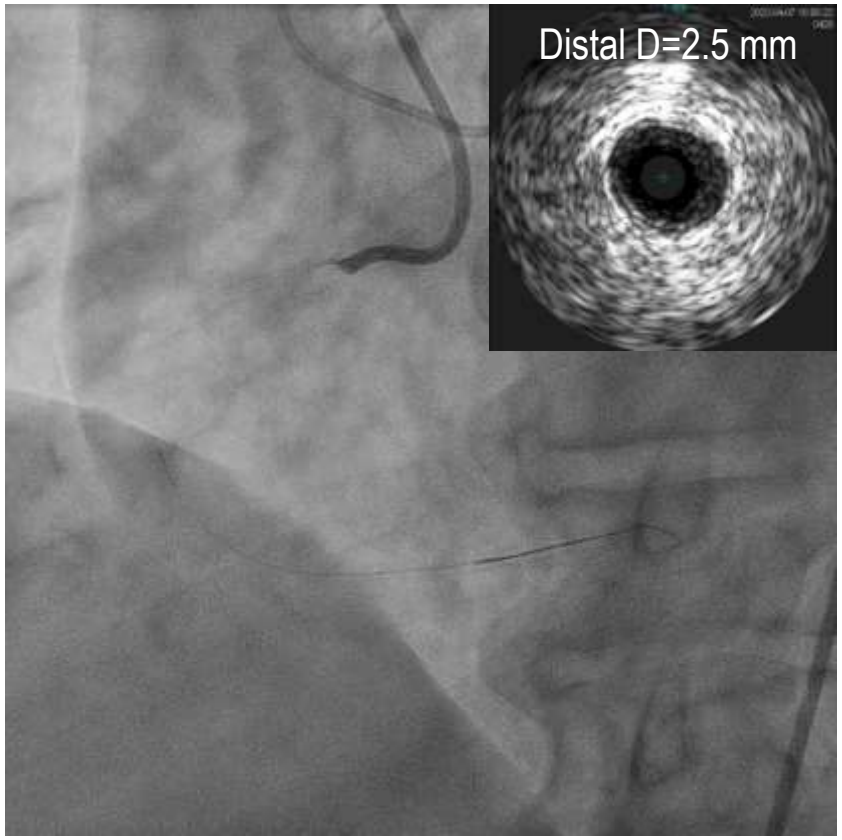
CTO at mRCA with collateral flow from bridging a. and LAD (Gr. II)



7F AL1 guiding catheter



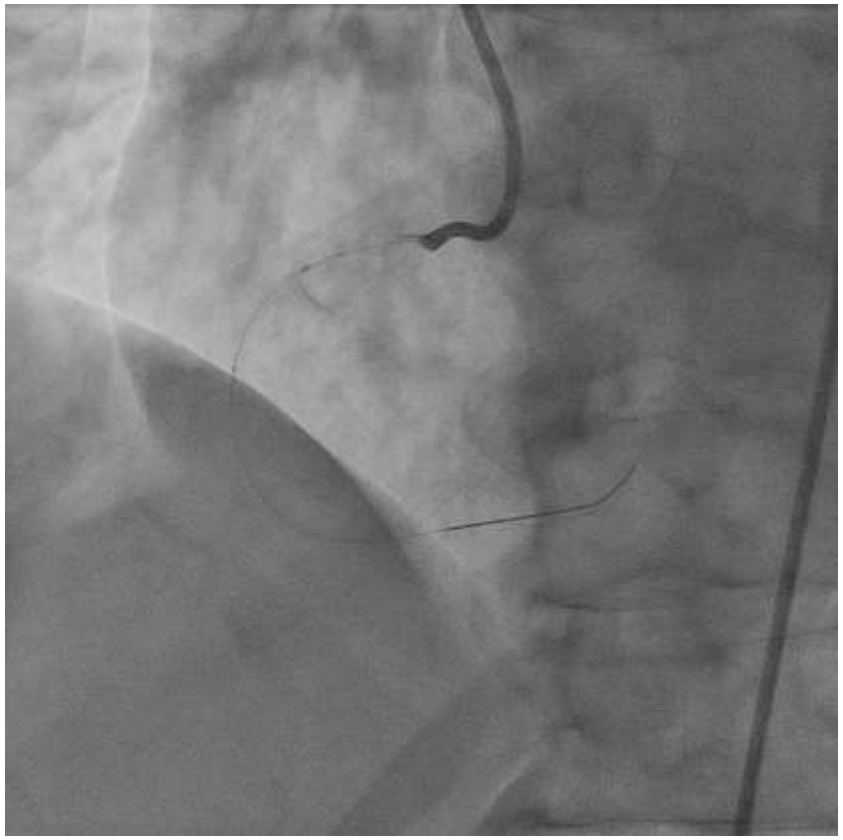
UB3 + Corsair Pro



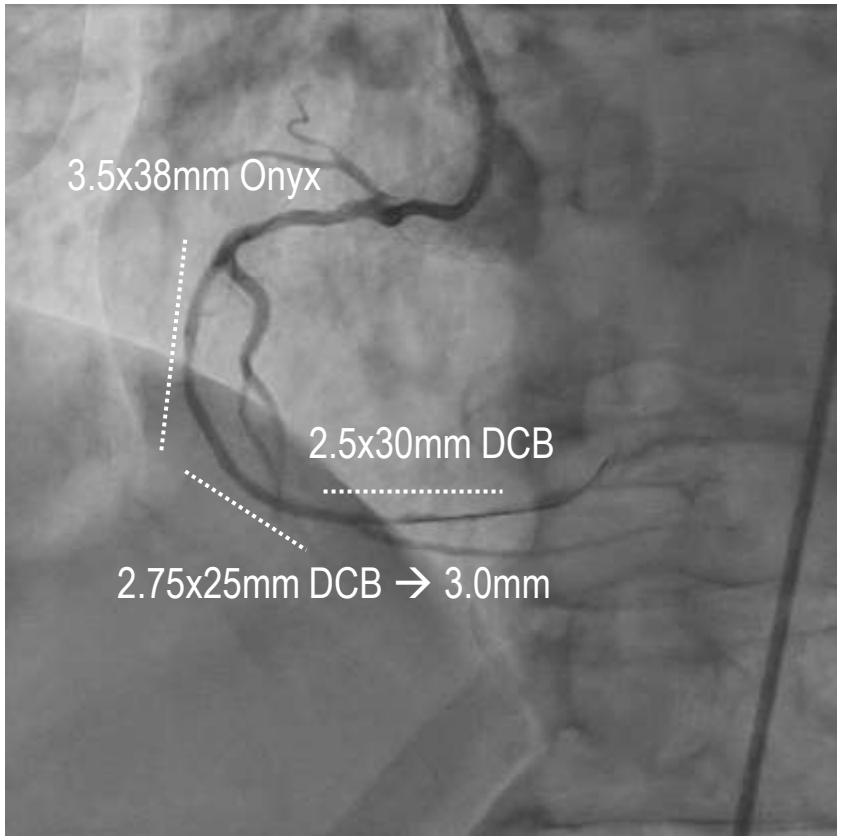
2.0x20mm balloon at CTO site → IVUS(+)

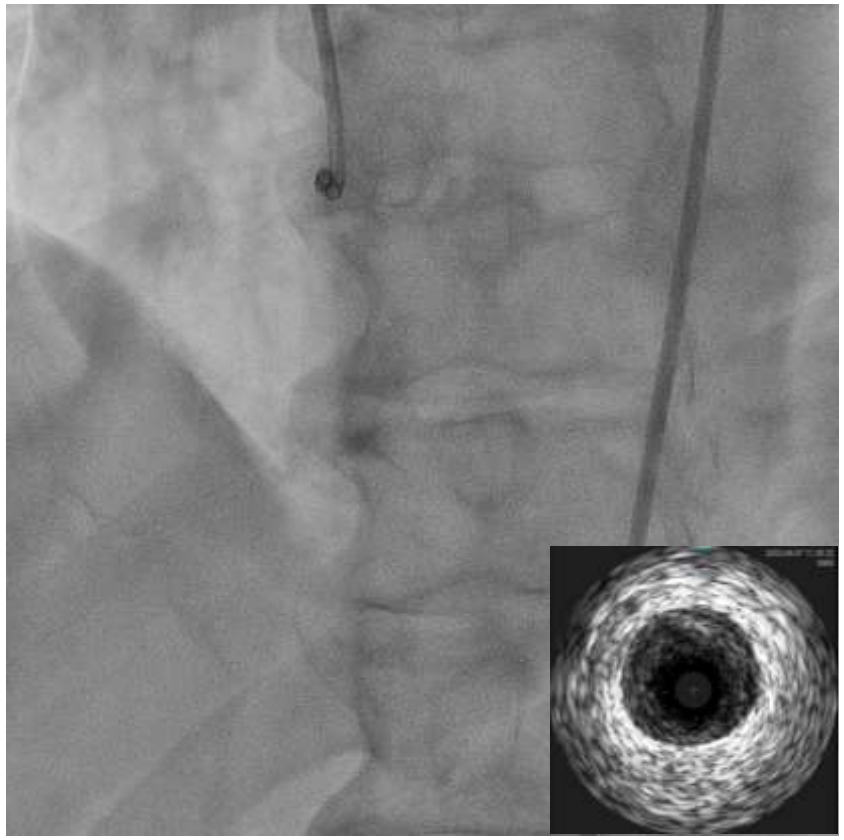
Case #2 - 67 YO Male

CTO at mRCA with collateral flow from bridging a. and LAD (Gr. II)



Lesion preparation with
2.5x20mm scoring balloon for mRCA-PL





Final CAG
MLA(DCB site)=5.5 mm^2

Boston Scientific Drug Coated Balloon

Design Objectives

MINIMIZE	Particulates and systemic PTx levels to ensure patient safety
IMPROVE	Coating durability and drug transfer efficiency for dose consistency
OPTIMIZE	Arterial tissue PTx levels for assured efficacy
MAINTAIN	BSC balloon/catheter performance

DCB-HBR

Ongoing Studies for De-novo Lesions

DCB-HBR Trial (NCT05221931)

Study Flow

1350 Patients with High Bleeding Risk
Undergoing Percutaneous Coronary Intervention and
1-3 months Dual Antiplatelet Agents

↓

Randomization (1:1) into DCB versus DES
(Stratified by Participating Centers and Clinical Presentation)

↓

Optimal Lesion Preparation
(Balloon with vessel ratio >0.90, residual stenosis≤35%, TIMI flow grade 3)

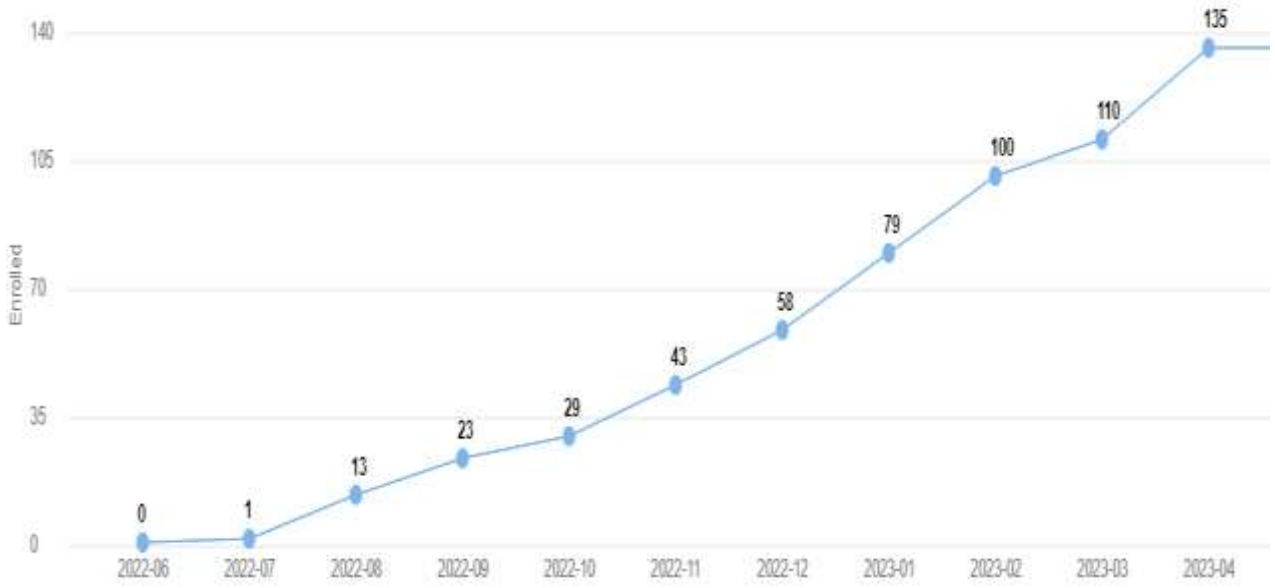
↓

DCB	DES
N = 675	N = 675

Primary Endpoint

TVF (a composite of CV death, target-vessel MI, TVR)

10 Centers in Korea (10% Enrolled)



We will test that DCB would be noninferior to DES for target-vessel failure (TVF) in de-novo coronary lesions in patients with HBR.