Clinical Experience of 3-month Dual Antiplatelet Therapy in Coroflex-ISAR stent

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Healing factors after stent deployment

For Designed to Heal….

- Polymer Load, duration, or free from Polymer Exposure
- Polymer and Drug Location,
  - Abluminal or systemic exposure of drugs
- Stent platform, strut thickness, design

Polymer is associated with…..
- In general, delayed healing and increase inflammations

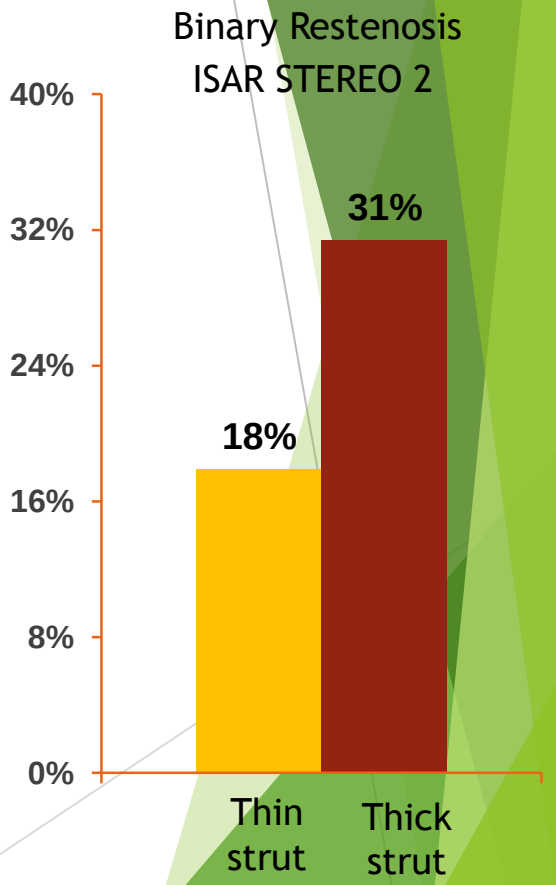
- Inflammation/hypersensitivity
- Delayed endothelization
- Stent thrombosis, prolonged duration,
- Aneurysm
- Late catch-up
- Polymer disruption
- Remodeling…….

Thin struts improve both acute performance and clinical outcomes

The greater the initial injury to the vessel wall, the more healing that needs to occur.

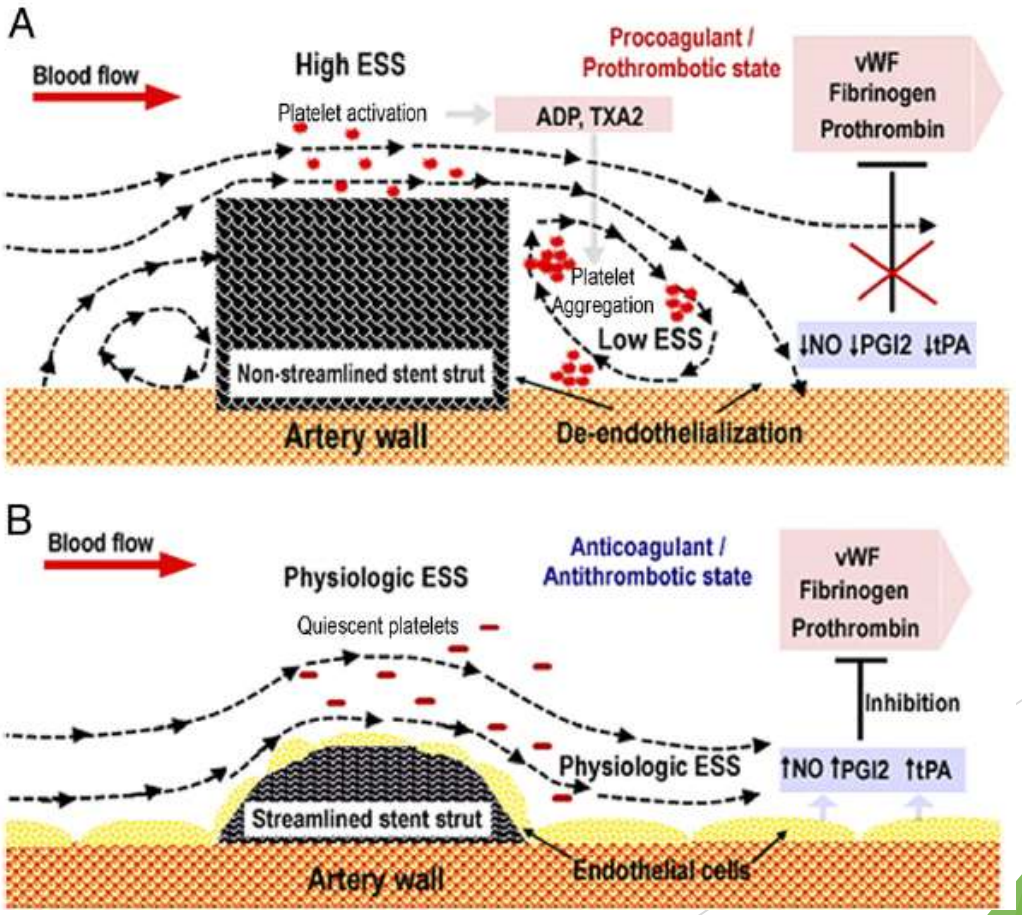
Thin strut

Thick strut



1 ISAR STEREO II JACC Vol. 41, No. 8, 2003 April 16, 2003:1283-8

Impact of Strut Thickness on Platelet Deposition and Thrombus Formation



Coroflex-ISAR, Stent Platform

Best Stent Performance through ultra-low strut thickness with **Cobalt Chromium**

CX-Blue Ultra

For 2.0 - 2.5 mm diameter

- 50 µm stent
- less metal, less foreign response
- less injury

CX-Blue Neo

For 2.75 - 4.0 mm diameter

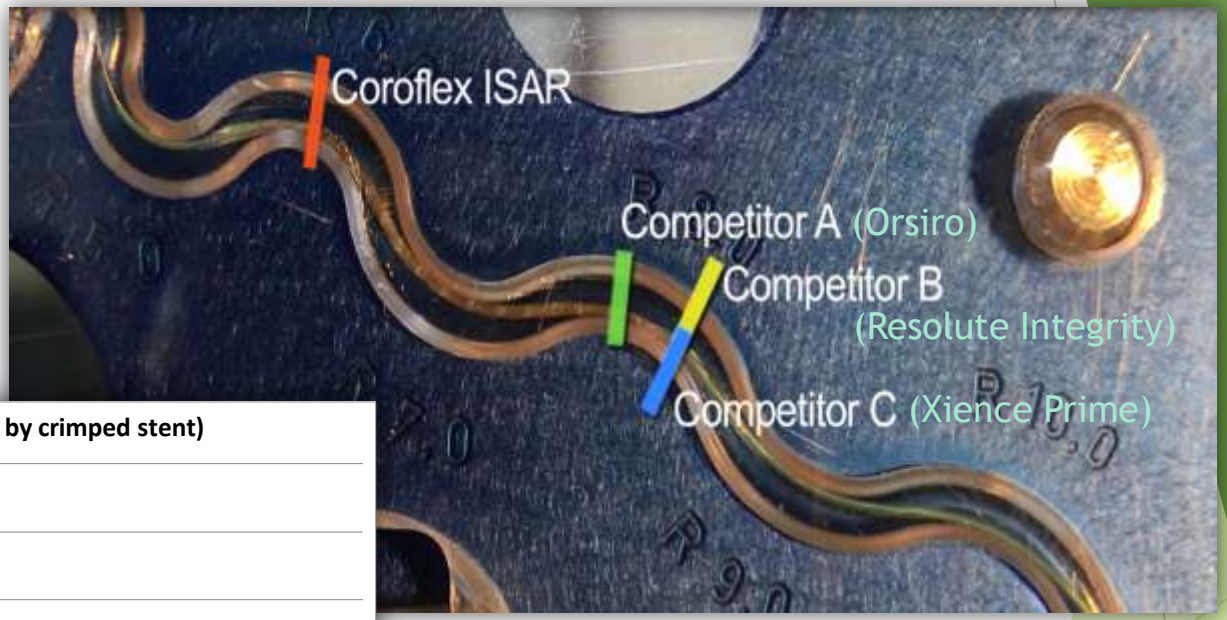
- 60 µm stent
- best crimp-profile
- high flexibility

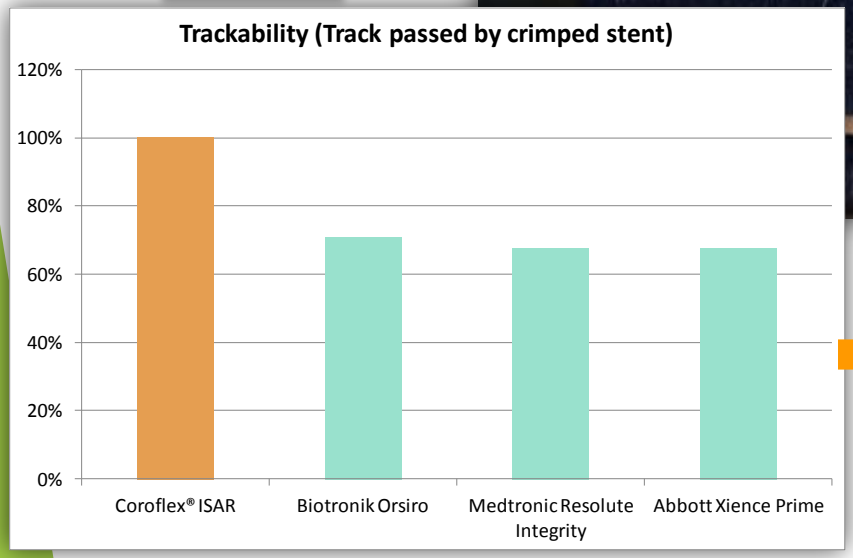
- **Polymer-Free** Sirolimus Drug Eluting Stent
- Outstanding **Deliverability** for Complex Anatomies

Coroflex-ISAR, Trackability

Trackability (track length passed by 3.0 x 18/19 mm)

30% better tracking



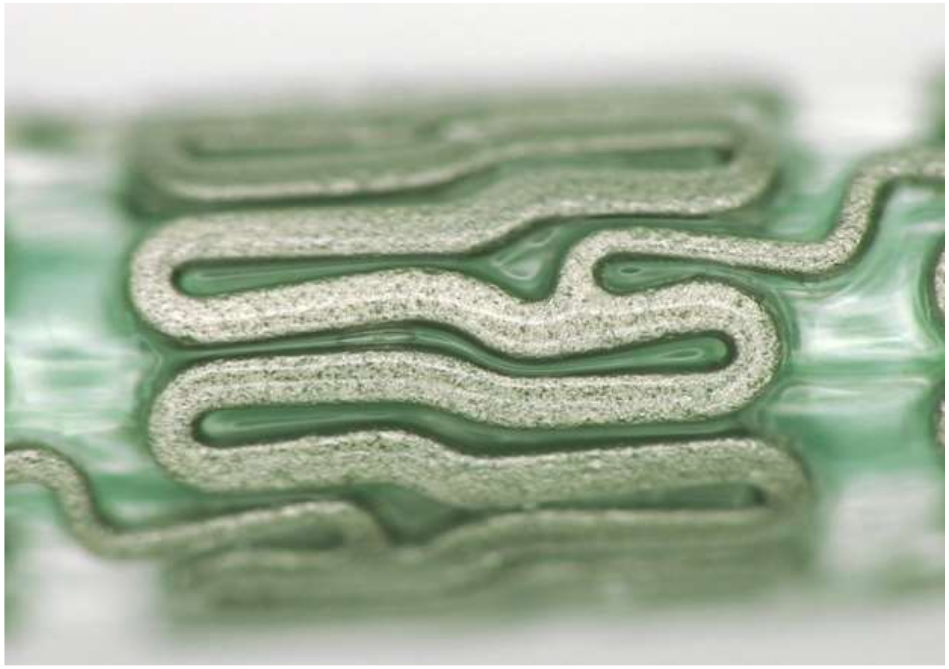


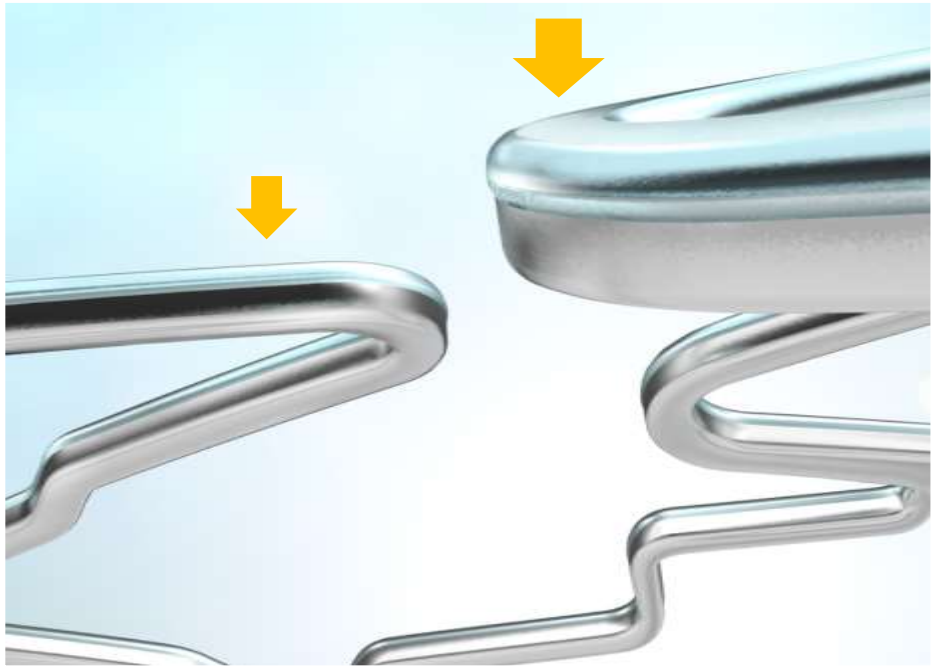
Coroflex ISAR shows the best trackability and continues the superior performance of all Coroflex stent delivery systems.

Coroflex-ISAR, Polymer-Free Matrix

Abluminal Microporous Stent Surface and Abluminal Coating on Surface

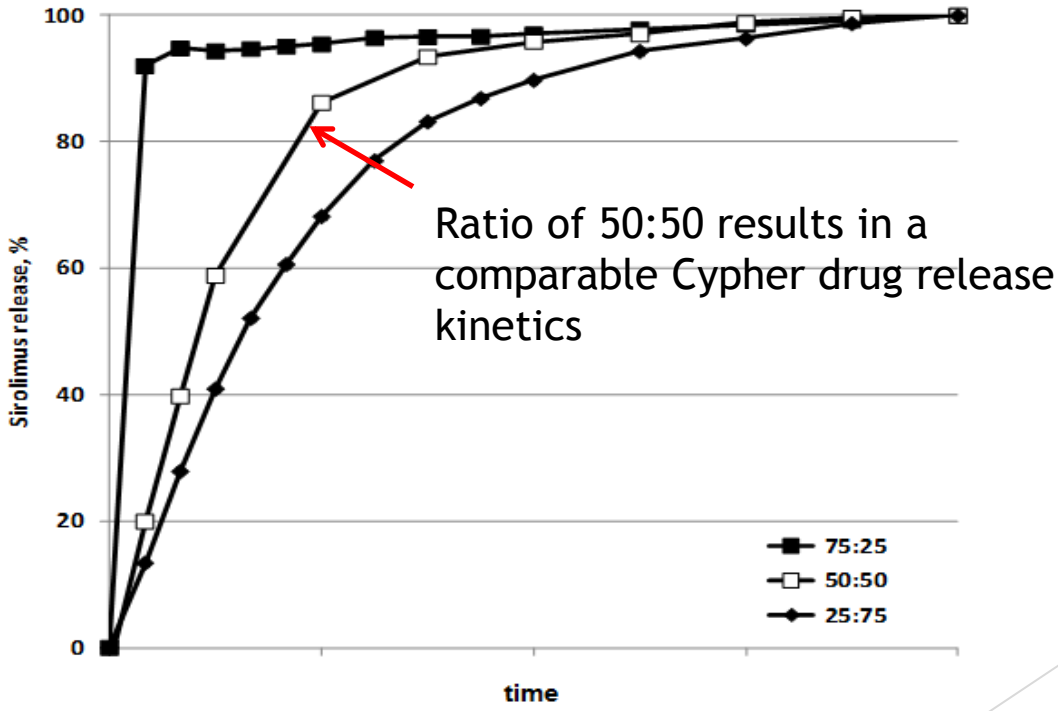
Improved healing, More targeted tissue release, Less systemic exposure





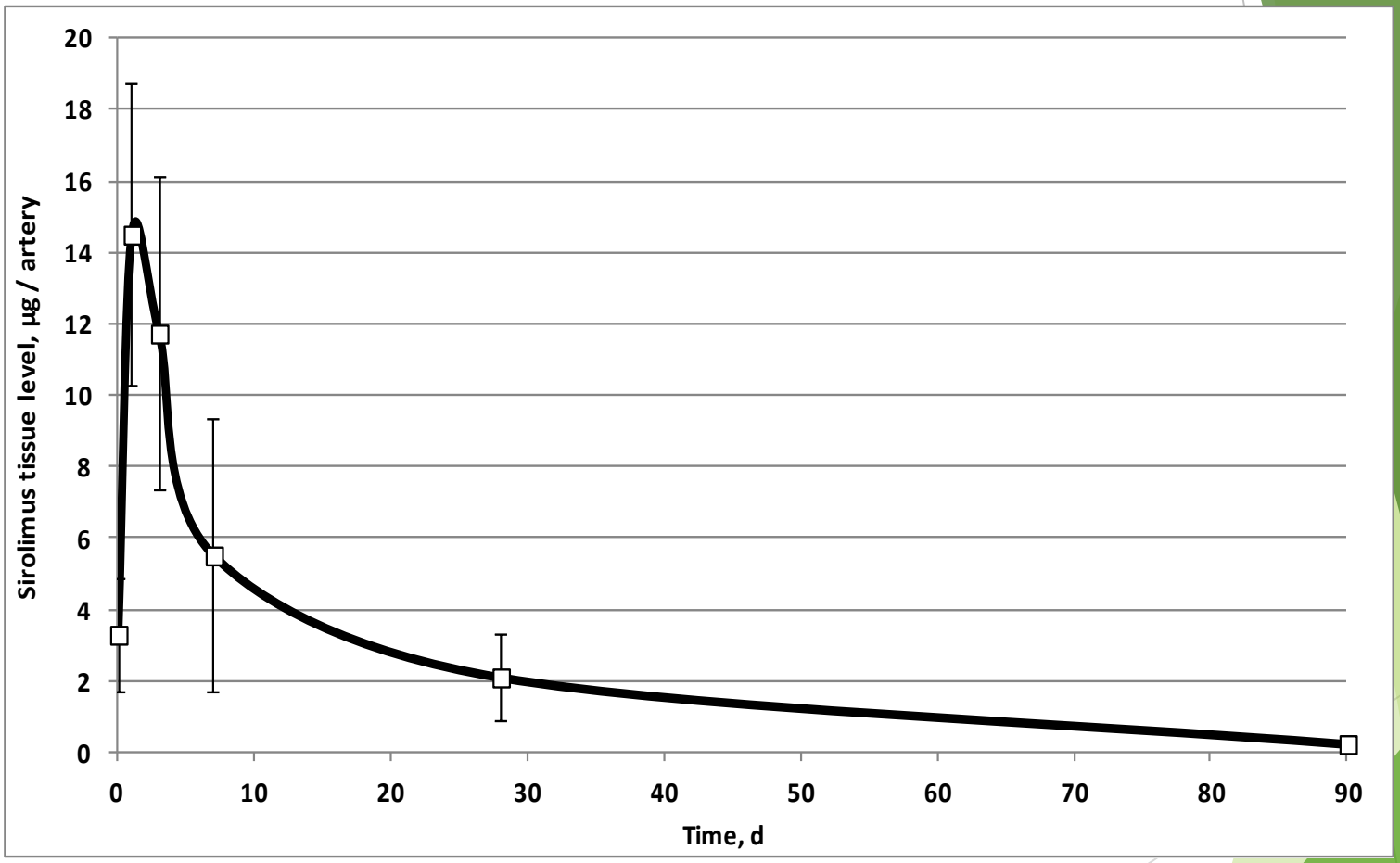
Matrix Coating Technology

Sirolimus release as function of the sirolimus:probucol ratio in the coating of CX ISAR



The 50:50 ratio corresponds to the drug release of the Cypher stent without using a non-degradable polymer!

Matrix Coating Technology



CX-ISAR Drug Matrix is >80% released after 30 days

The release has been completed at 90 days.

Klugherz BD, Llanos G, Lieuallen W, et al; Twenty-eight-day efficacy and phamacokinetics of the sirolimus-eluting stent. Coron Artery Dis. 2002 May;13(3):183-8

Pre-Clinical Evaluation with Sirolimus

Porcine Coronary Overstretch Studies[1] - Results

28 Days (overlap)	Stenosis (%)	Neointimal thickness (mm)	Inflammation score (0-3)	Endotheliali-zation (%)
CX-ISAR	26.89	0.17	0.33	98.75
Cypher	26.87	0.14	1.50	86.92
CX-ISAR (without drug)	45.16	0.33	0.33	99.17

Porcine Model - Results

1. **Equally effective as Cypher (stenosis/neointimal thickness)**
2. **Decreased inflammation score compare to Cypher**
3. **Safe as the uncoated control**

[1] Data on file at B. Braun Vascular Systems

Test reports from CVPath Institute Inc., Gaithersburg, U.S.A.

Advantagess of Coroflex-ISAR for short duration of DAPT

Polymer Free
Complete Absorption

Strut Thickness of only
50/60 µm

Lowest Crossing Profile
0,031“ - 0,035“

Abluminal
drug coating

Low Rate of Stent Thrombosis

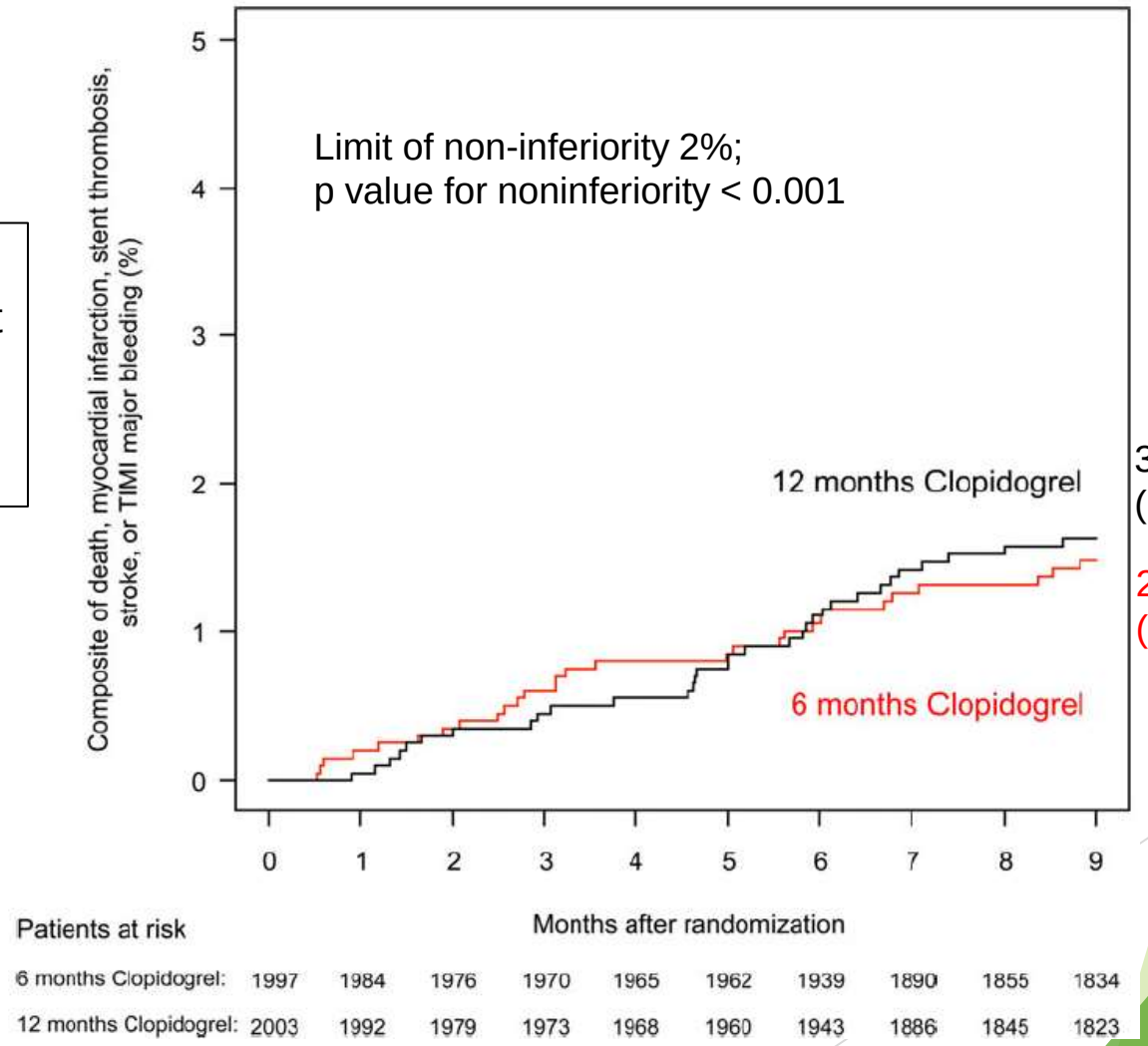
Less Trauma
Fast Endothelialization

Excellent Crossability

Improve
Fast Endothelialization

ISAR-SAFE : Primary composite endpoint
New generation DES followed by 6- vs 12-month DAPT

MACE:
Death, MI, stent thrombosis, stroke or TIMI major bleeding



32/2,003 patients (1.6%)

29/1,997 patients (1.5%)

Schulz-Schüpke S, et al. Eur Heart J. 2015 Jan 23.

Study Design and Aims

- Comparison the Efficacy and Safety between 3-Month DAPT vs. 6-Month DAPT regimen treated with Coroflex- ISAR Stent;
- A Prospective, Multicenter, Randomized, Open-Label Clinical Trial

Study Population

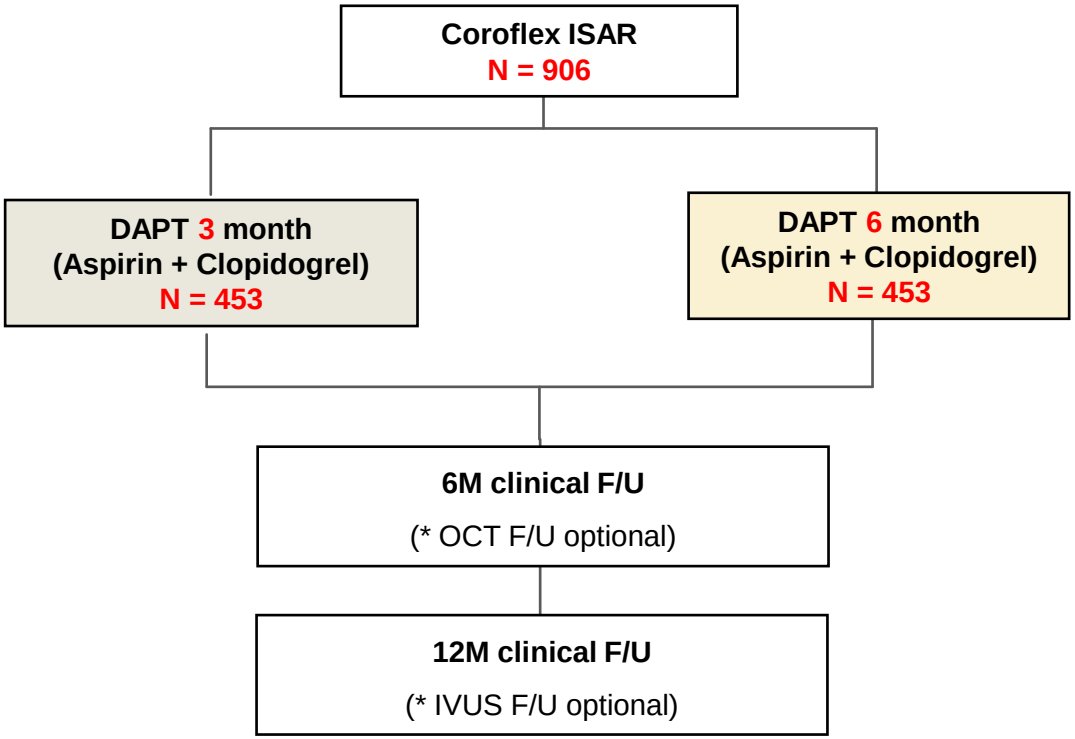
- We will enrolled 906 patients
  - 3-Month DAPT group: 453 patients
  - 6-Month DAPT group: 453 patients
- We assumed about 5% of the patients with early drop out during 1-year clinical follow-up.

• Non-inferiority margin (D)	Difference of primary outcome, 3%
• Type 1 Error	p = 0.025
• Randomization	r = 1:1
• Power of Test	f = 80%

Patient Selection

- **Inclusion Criteria**
  - “De novo” lesions in native coronary arteries
  - Written informed consent
- **Exclusion Criteria**
  - Acute myocardial infarction (STEMI or NSTEMI)
  - Cardiogenic shock
  - Contraindication, intolerance, or hypersensitivity to aspirin, clopidogrel
  - CTO, ISR
  - PCI with BMS or DES in non-target lesions less than 6 months
  - Scheduled elective surgery within 12 months after the index procedure requiring to stop antiplatelet medication more than 2 weeks
  - Comorbidities with a life expectancy < 12 months

Study Flow



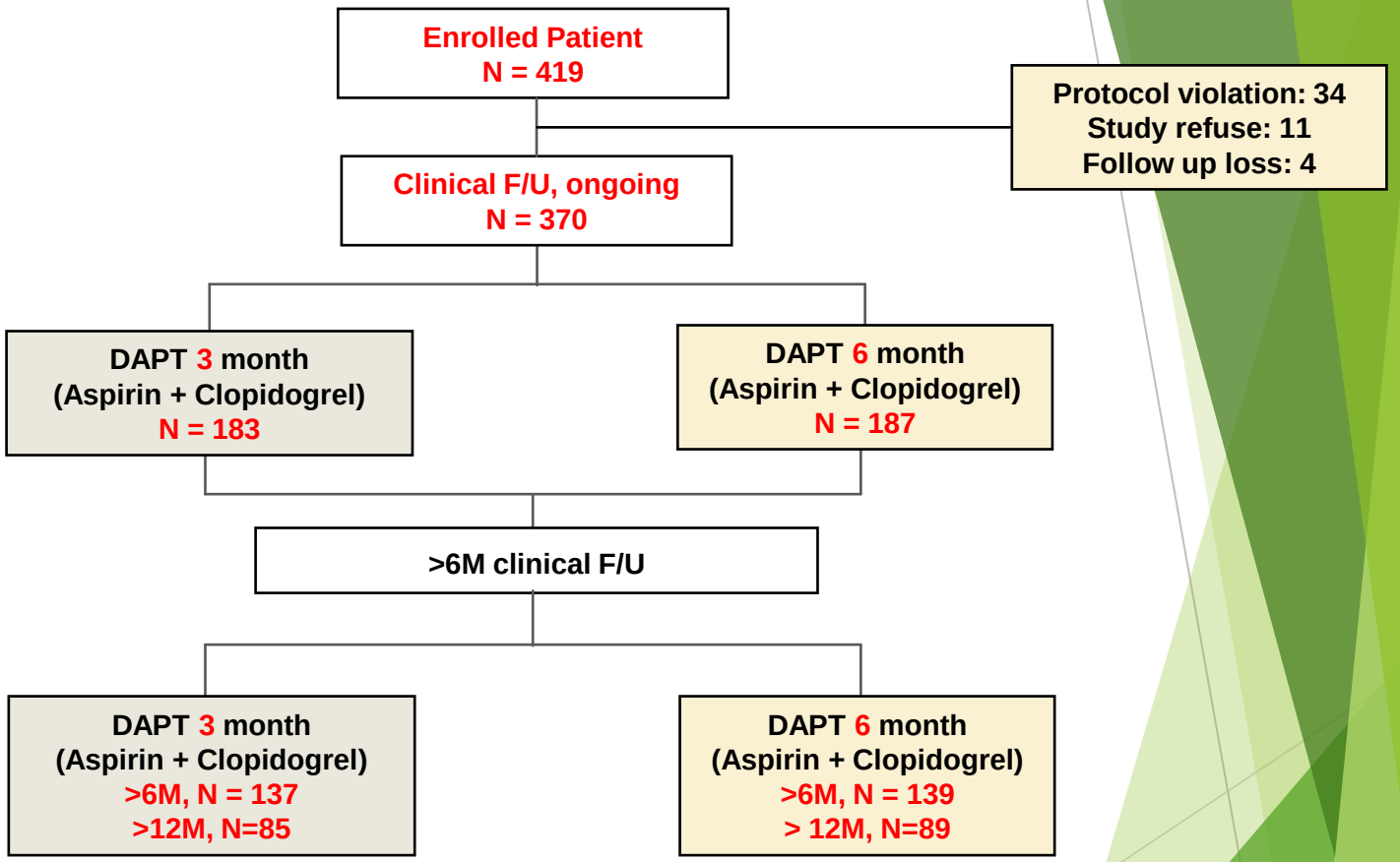
Primary Endpoint : MACE at 12M

Secondary Endpoint :

1) MACE at 6M
2) Any death, cardiac death, MI, ST, TLR, TVR, Bleeding any revascularization at 6M
3) Any death, cardiac death, MI, ST, TLR, TVR, Bleeding any revascularization at 12M

- **MACE: cardiac death, myocardial infarction, stent thrombosis, TLR, TVR**

Study Flow

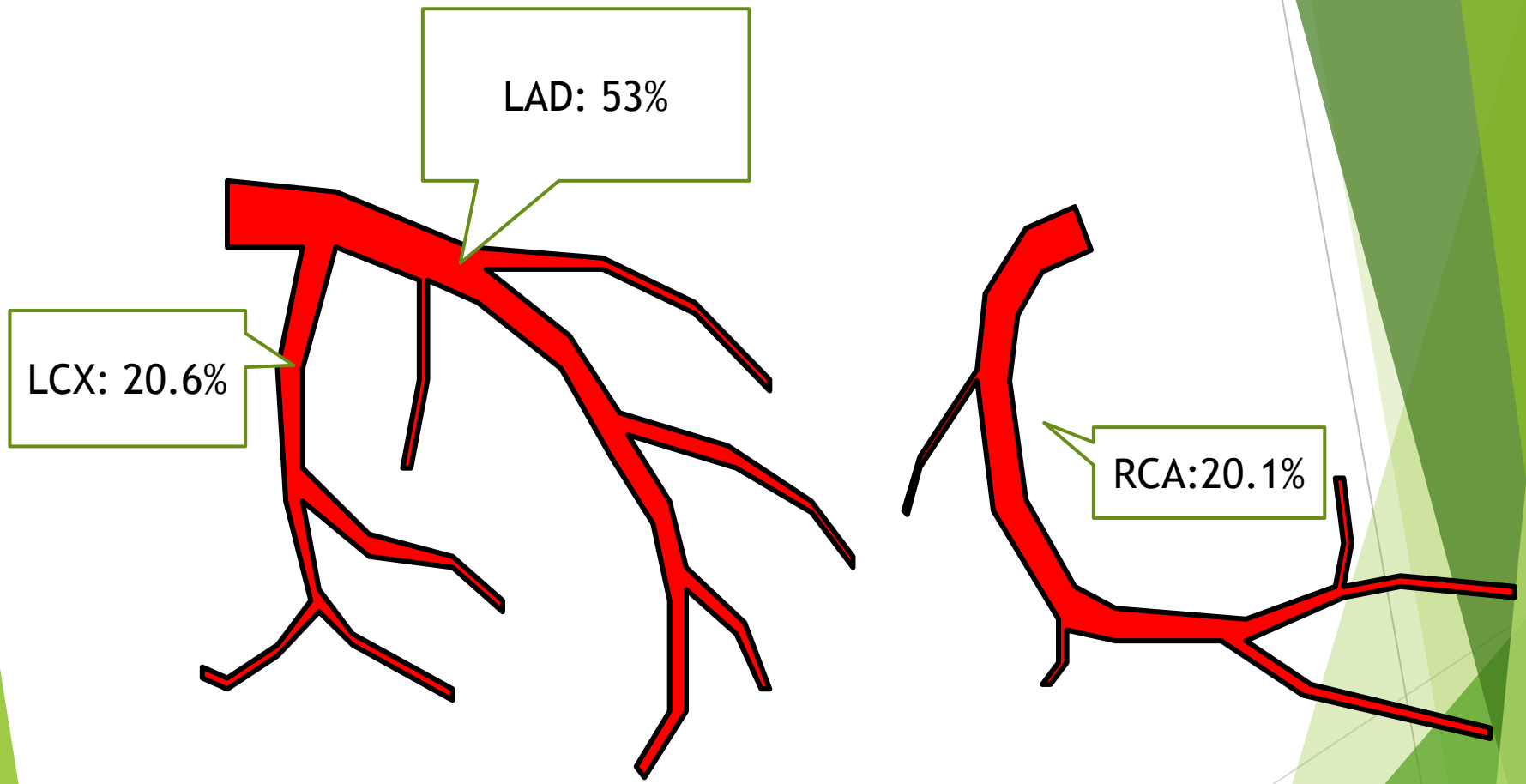


- MACE: cardiac death, myocardial infarction, stent thrombosis, TLR

Patients Characteristics

		3 Month N=183	6 Month N=187	p Value
Age, years	64.8 ± 9.8	64.6 ±10	64.9 ±9.5	0.607
Gender, male	267 (72.2%)	132 (72.1%)	135 (72.2%)	1.000
Diagnosis				
SA	178 (48.1%)	87 (47.6%)	91 (48.5%)	
UA	169 (45.7%)	83 (45.4%)	86 (46.1%)	
Others	23 (6.2%)	13 (7.0%)	10 (5.4%)	
Hypertension	191 (51.6%)	98 (53.6%)	93 (49.7%)	0.469
Dyslipidemia	88 (23.8%)	47(25.7%)	41 (21.9%)	0.464
Diabetes Mellitus	94 (25.4%)	42 (44.7%)	52 (55.3%)	0.339
Pre-PCI Hx	63 (17.0%)	29 (15.8%)	34 (18.2%)	0.582
Cholesterol (mg/dl)	184 ± 43	182 ± 43	169 ± 40	0.153
Cr (mg/dl)	0.91 ± 0.23	0.89 ± 0.19	0.93 ± 0.24	0.278
EF (%)	65.5 ± 8.7	66.7 ± 7.9	64.3 ± 8.9	0.187

Studied Lesion Location



Angiographic Results

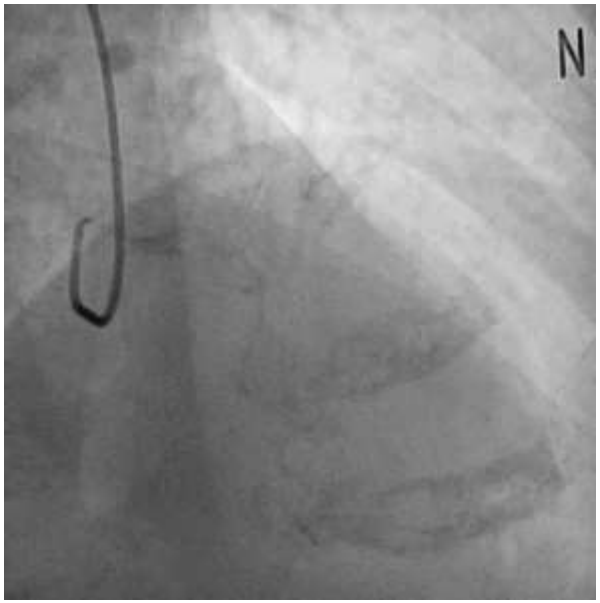
		3 Month	6 Month	p Value
Pre-PCI				
Ref. vessel size (mm)	3.18 ± 0.35	3.14 ± 0.34	3.21 ± 0.35	0.137
Lesion length (mm)	22.2 ± 9.0	21.2 ± 7.3	23.4 ± 10.5	0.086
MLD (mm)	0.59 ± 0.30	0.60 ± 0.30	0.58 ± 0.31	0.575
DS (%)	80.9 ± 9.0	80.4 ± 8.7	81.7 ± 9.3	0.315
Post-stent				
MLD (mm)	2.90 ± 0.34	2.90 ± 0.32	2.93 ± 0.37	0.609
DS (%)	7.6 ± 2.0	7.6 ± 2.0	7.6 ± 2.1	0.985
Stent Number per person	1.40 ± 0.66	1.44 ± 0.74	1.34 ± 0.53	0.310
Stent length per person (mm)	29.0 ± 15.9	29.6 ± 18.3	28.3 ± 12.8	0.597

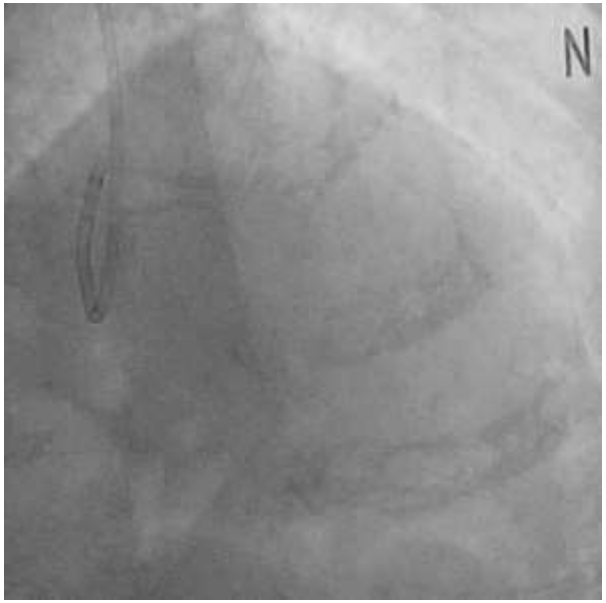
Clinical Outcomes

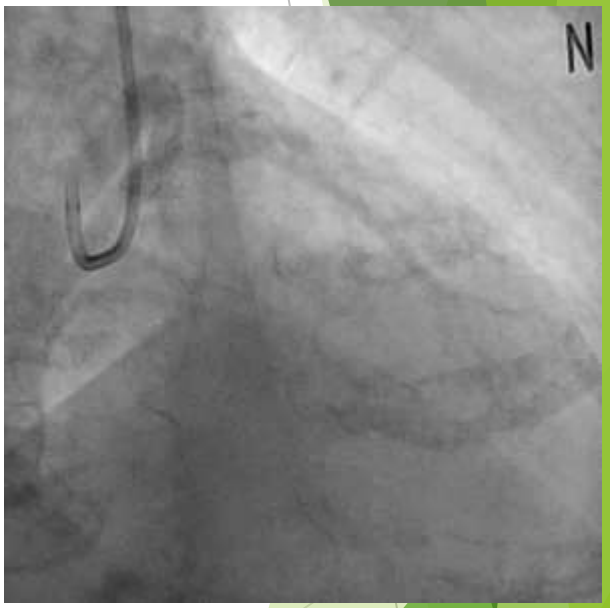
≥6 months Follow-up	Total Patients N=276	3 Month N=137 (16±8 months)	6 Month N=139 (16±8 months)
MACE	**5 (1.8%)**	**3 (2.2%)**	**2 (1.4%)**
TLR	**4 (1.4%)**	**2 (1.5%)**	**2 (1.4%)**
TVR	**0**	**0**	**0**
Non-Fatal MI	**1 (0.4%)**	**1 (0.7%)**	**0**
Stent thrombosis	**0**	**0**	**0**
Cardiac death	**0**	**0**	**0**
Non-Cardiac Death	2	1	1
Non-Target vessel Revascularization	3	2	1
Minor Bleeding	2	1	1

Case 1, 6-Month F/U

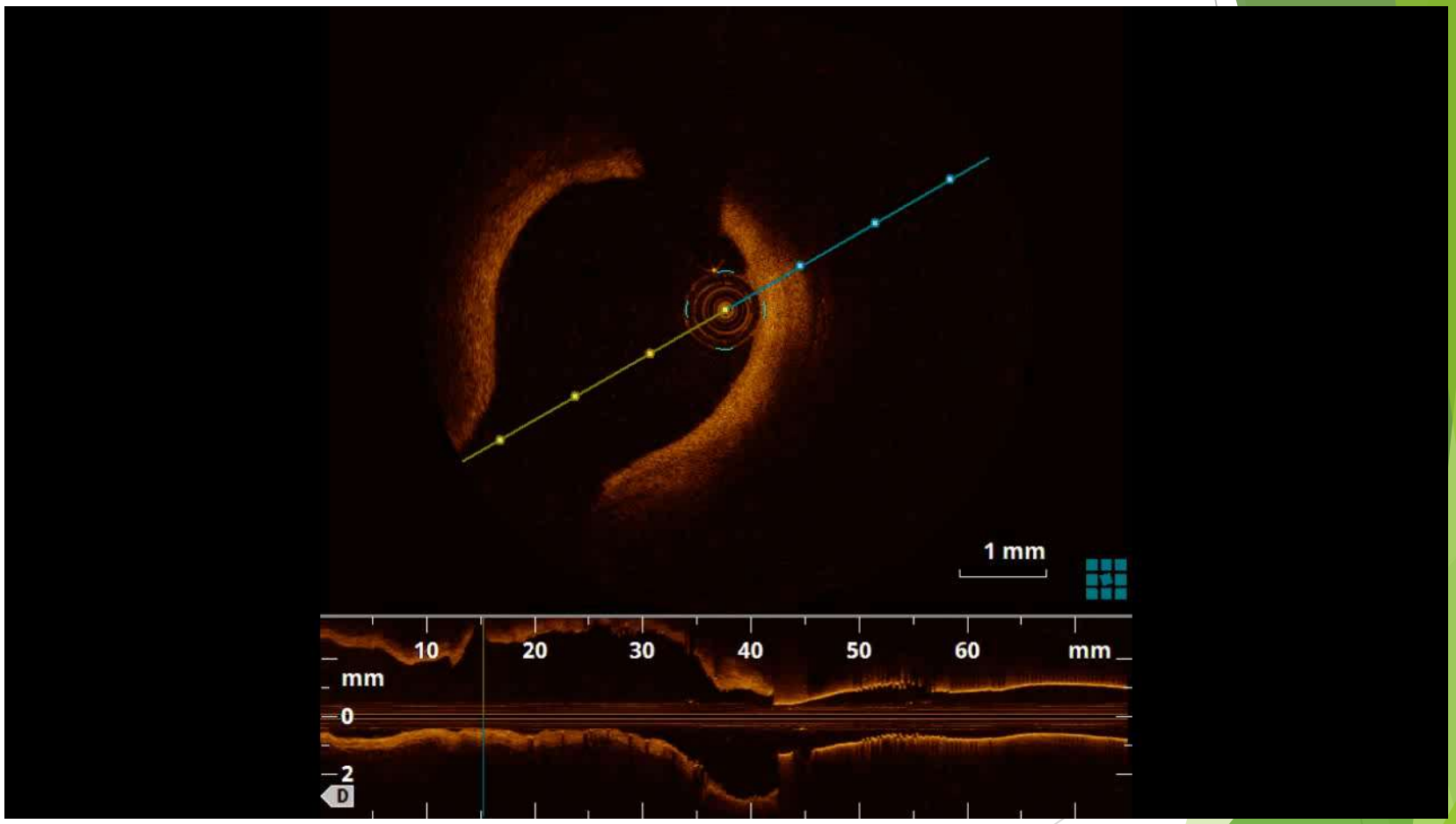
- KKB, 75/F, SA,
- 1VD, pLAD, stent: 3.5/16 mm





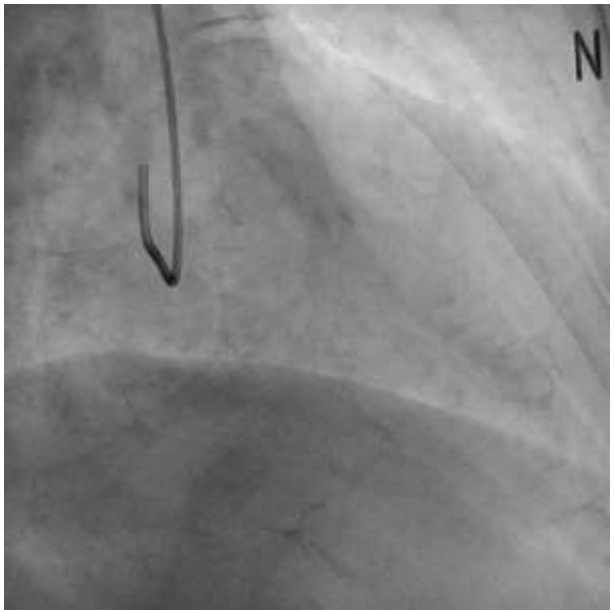


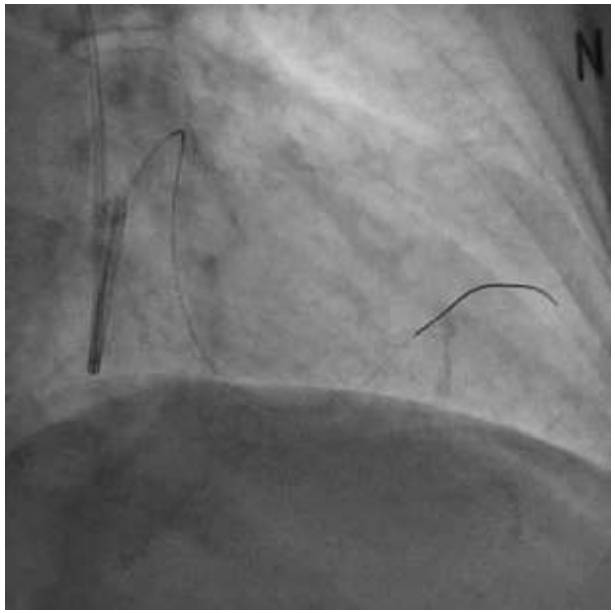
6-Month F/U OCT

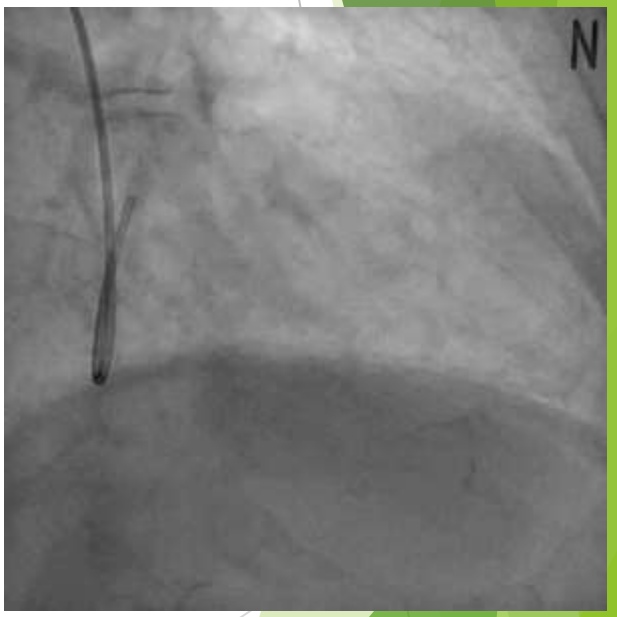


Case 2, 3-Month F/U

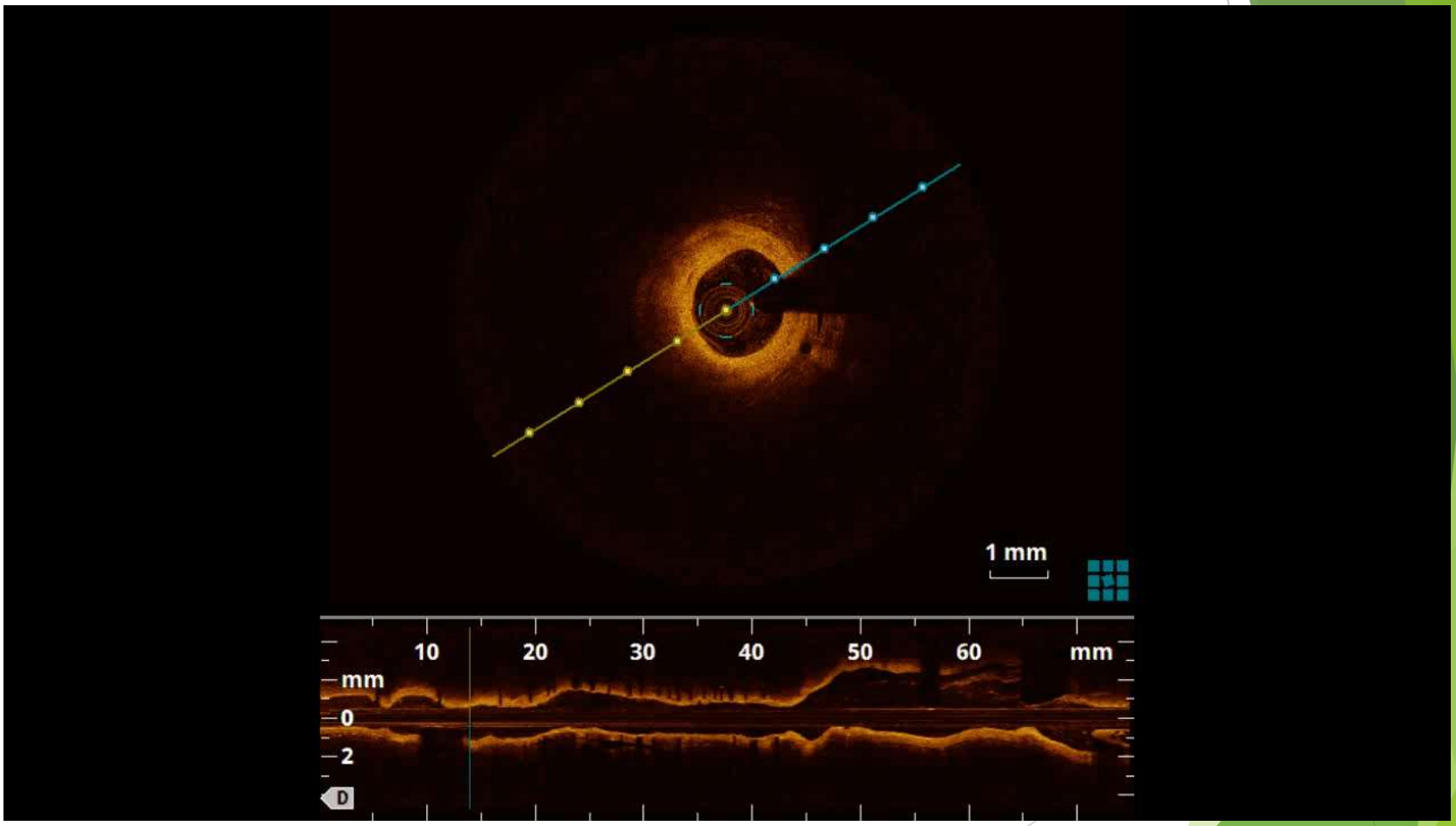
- 77/F, UA, HTN,
- 2VD, dLCx to OM, stent: 2.5/27 mm





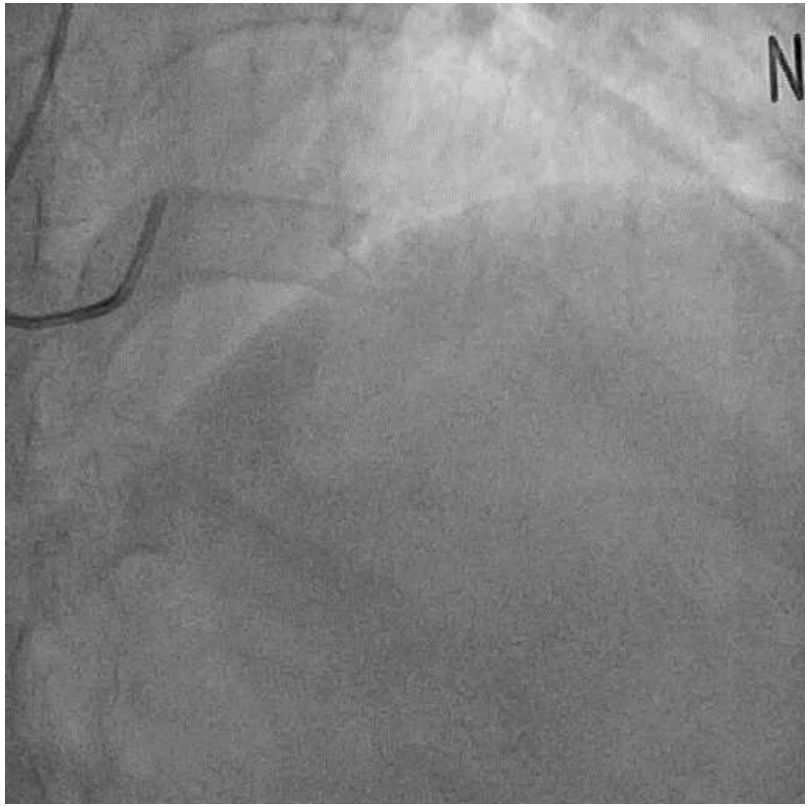


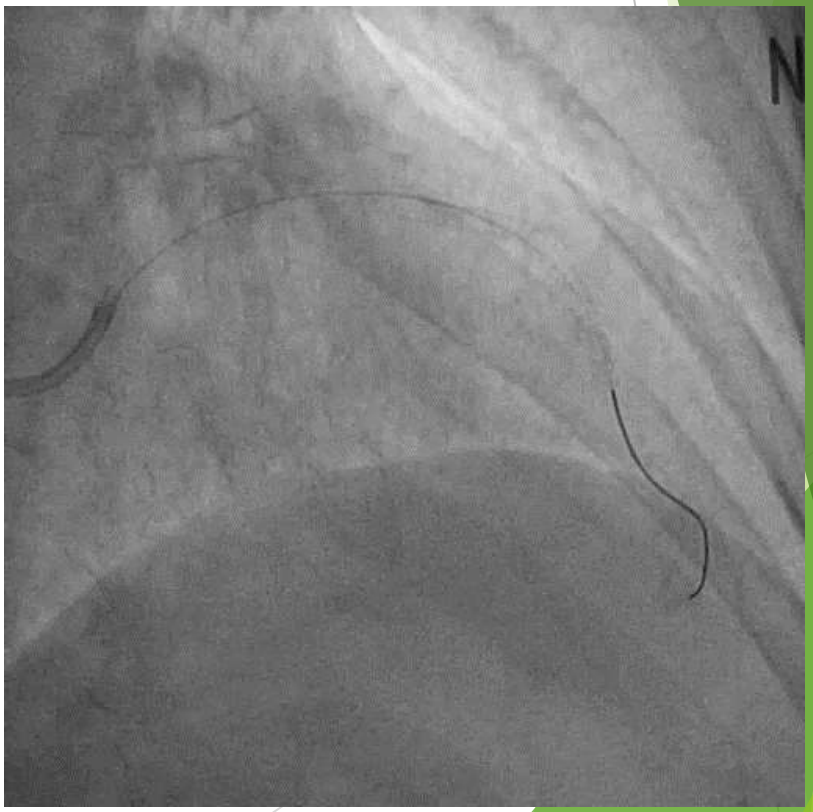
3-Month F/U OCT



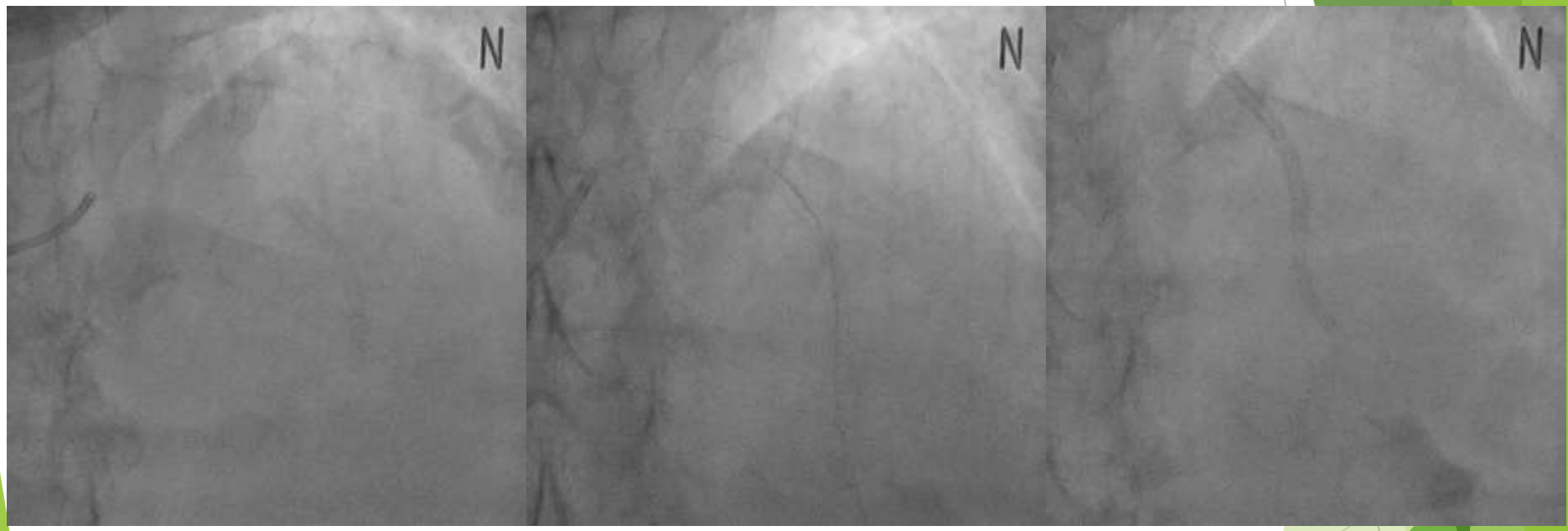
Case 3, ISR with non-fatal MI at 9 months

- F/69, UA, DM, HTN, EF 69%, No RWMAs,
- Stent deployment at mLAD, 2.75/19, 2.75/16 at index PCI





At 9 months after index PCI



Conclusions

- Both 3-month and 6-month DAPT after Coroflex-ISAR stent are comparable to previous 12-month DAPT (ISAR-SAFE).
- 3-Month DAPT in Coroflex-ISAR stent is safe and effective in clinical outcomes.

Thank you for your attention