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The EGO-COMBO Study

COMBO Dual Therapy Stent
Patent, Stable & Healed Coronary Artery
24 Months FU with OCT

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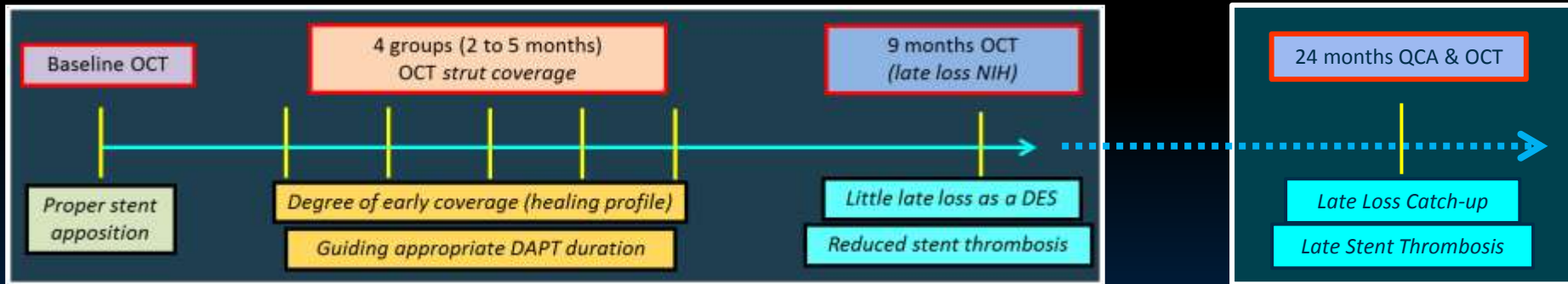
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Disclosure Statement of Financial Interest

I, (**Stephen Lee**) DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

- *Combo Stents provided as investigational device by OrbusNeich*
- *CRF Core Lab. expenses were supported by OrbusNeich*

The EGO-COMBO Study



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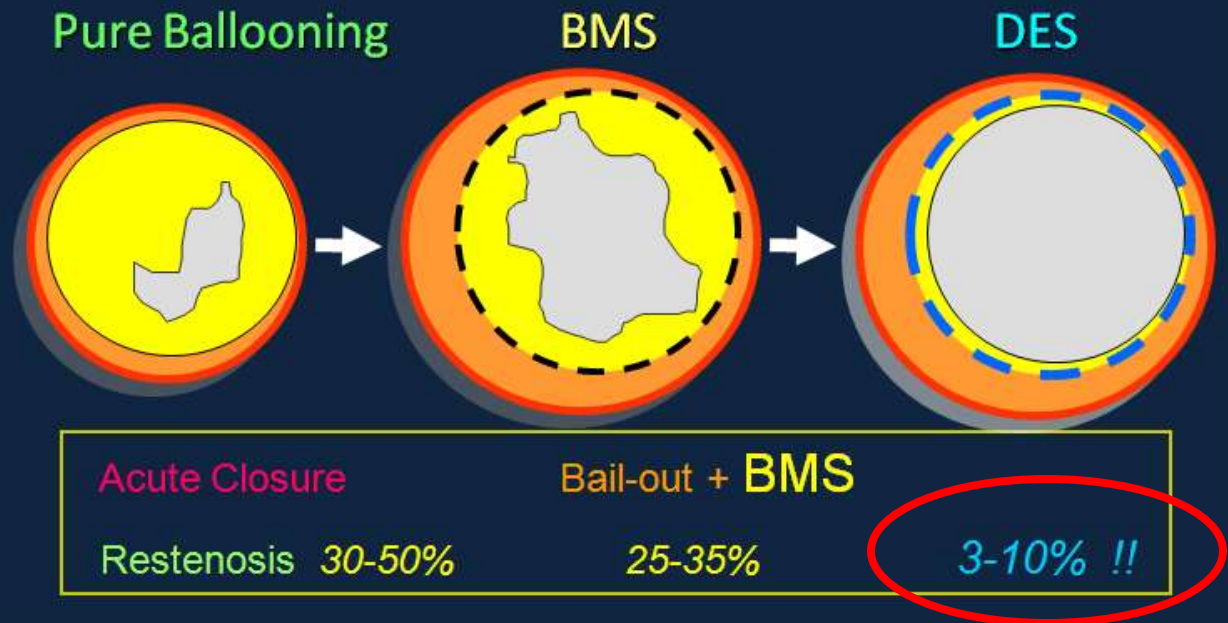
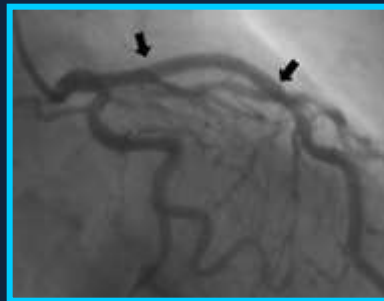
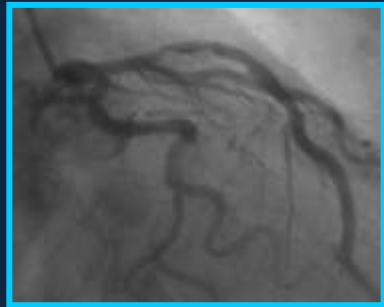
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CRF:- Clinical Event Adjudication, QCA and OCT Core Lab.

STUDY BACKGROUND: Can we do better with any DES ?



All current DES = can achieved neointimal suppression

PCI objective = purely for achieving revascularization
= without complicated issues of

- Acute failure
- Restenosis
- Stent thrombosis
- Prolonged DAPT

But many DES still show poor Stent Healing

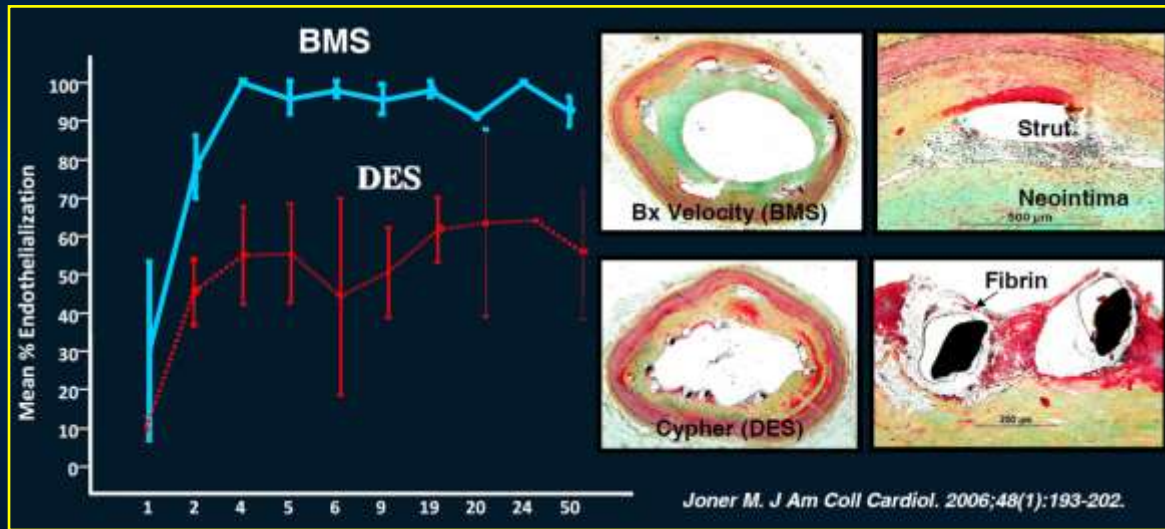
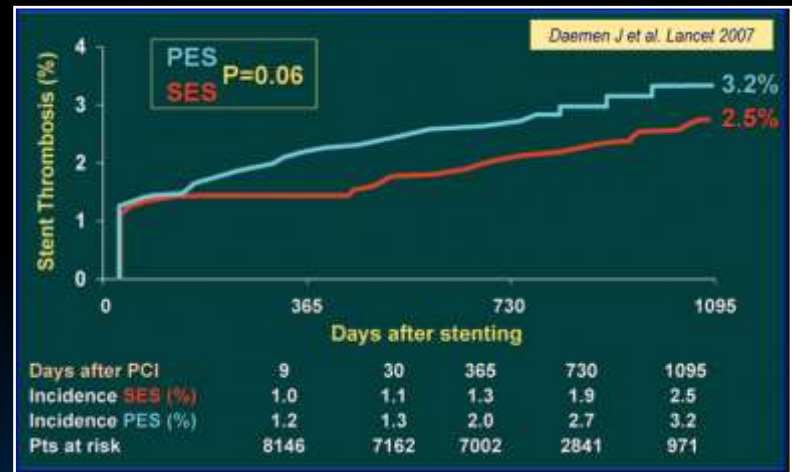
& Late Stent Failure - drug cytotoxicity, polymer hypersensitivity, local inflammatory reactions, loss endothelial and vasomotor functions

- Stent thrombosis
- MACE
- Late Stent Failure

STUDY BACKGROUND

Stent thrombosis &
Late stent failure is genuine...

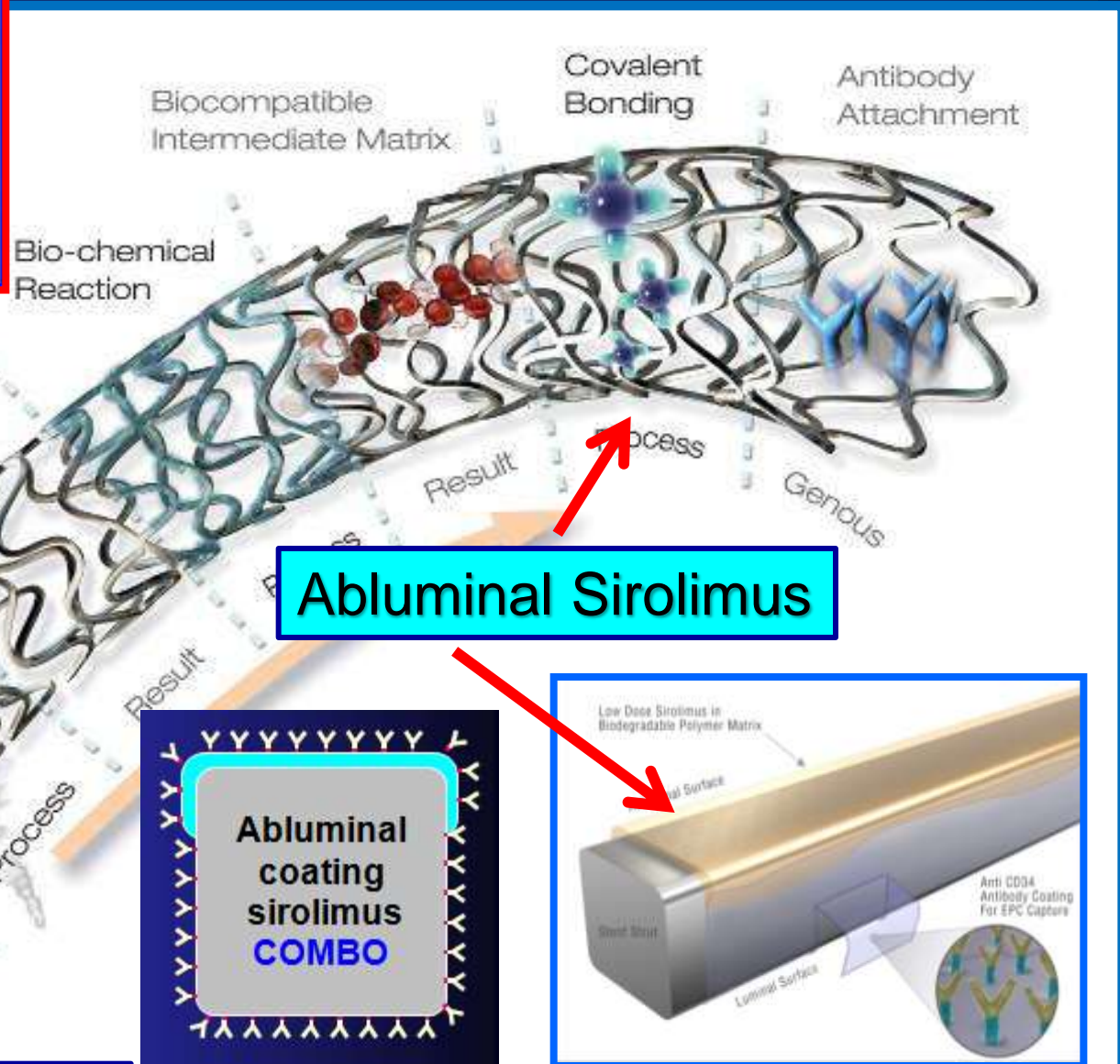
Can we predict & prevent it....
With a novel device ?!!



- Most powerful histological predictor of stent thrombosis = **endothelial coverage**
- Most powerful surrogate indicator of endothelialization = **neointimal coverage**
- Best morphometric predictor of LST = **ratio of uncovered to total stent struts**

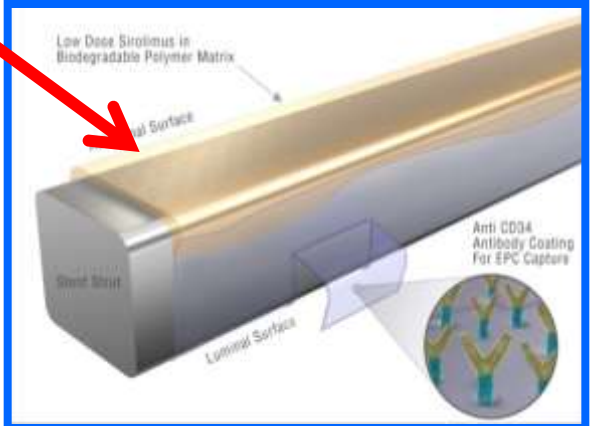
Finn et al. Circulation 2007;115;2435-2441

Dual Therapy Combo Stent



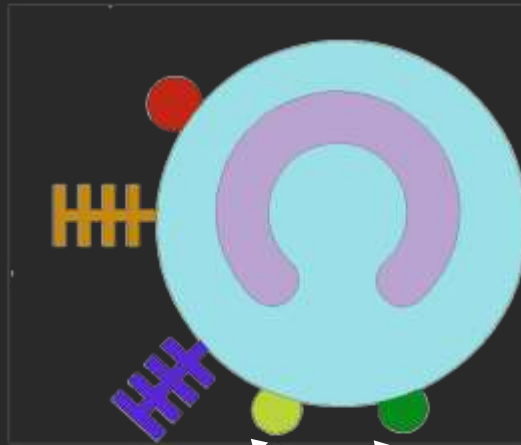
Abluminal Sirolimus

Abluminal coating sirolimus COMBO



Anti-CD34 EPC Capture Coating

Endothelial Progenitor Cell (EPC)



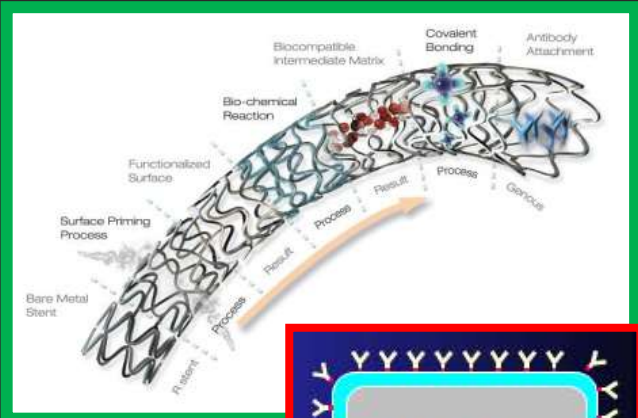
CD34 Cell Surface Antigen

Anti-CD34 Antibody

Endothelium Coverage "Healing"

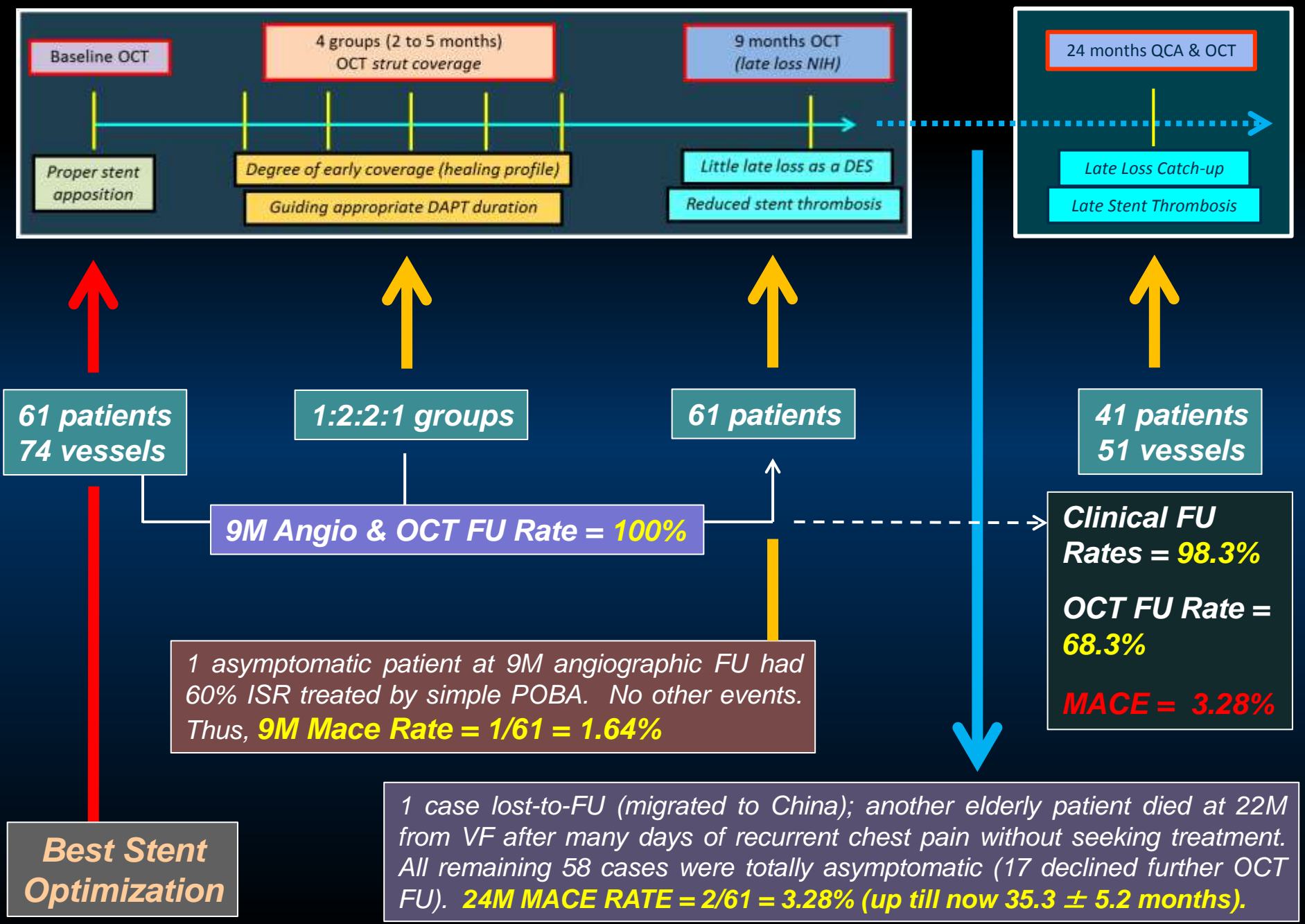


Stent Inner Surface (EPC Capture Coating)
Abluminal Surface (Polymer + Sirolimus)

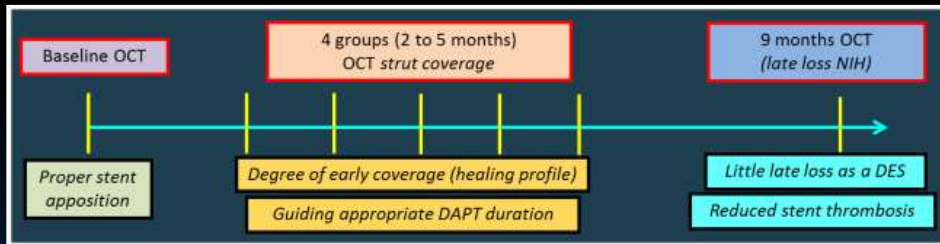


Anti-proliferative sirolimus elution

EGO-COMBO Study Design (2 Protocols 4 OCT Assessments at 0-24 Months)



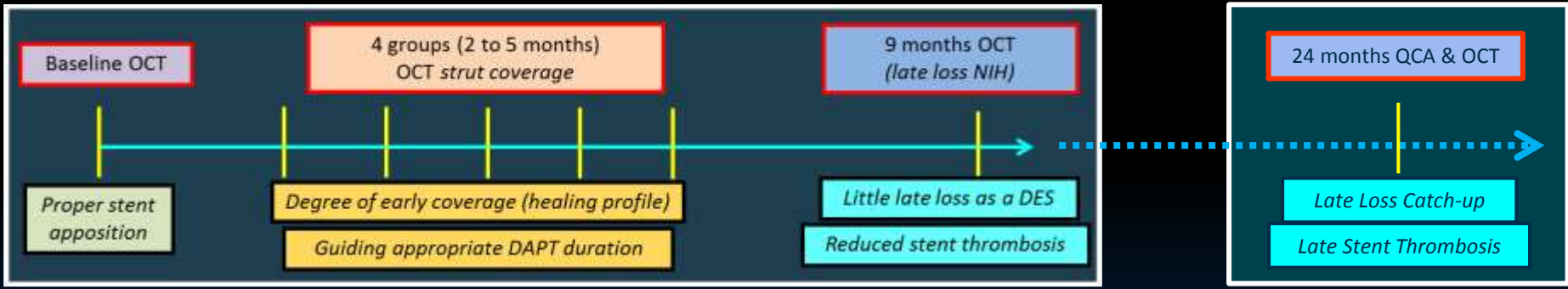
The EGO-COMBO Study (Demographics)



Patient Demographics	
Age (yr.)	62.2±11.25
Sex (M)	47 (77%)
Smoking	25 (41%)
DM	20 (33%)
HT	39 (64%)
Hyperlipidemia	41 (67%)
Previous MI	19 (31%)
Previous PCI	21 (34%)
CHF	3 (4.9%)

Procedural Characteristics	
Patients Treated	n = 61
Vessels treated	n = 74
COMBO Stents Used	n = 88
Lesion Location	
LAD	32 (43.2%)
CIR	16 (21.6%)
RCA	26 (35.1%)
ACC/AHA Lesion Class	
A	26 (35.1%)
B1	12 (16.2%)
B2	30 (40.5%)
C	6 (8.1%)
Mean Lesion Length (mm)	18.37±9.39
Mean Stent Length (mm)	23.9±7.62
Mean Stent Size (mm)	3.06±0.39
Pre-procedural RD (mm)	3.13±0.37
Pre-procedure MLD (mm)	1.17±0.35
Pre-procedure DS%	61.85±10.17%
Post-procedural MLD (mm)	2.89±0.38
Post-procedural DS%	7.56±6.89%

EGO-COMBO Study Design (2 Protocols 4 OCT Assessments at 0-24 Months)

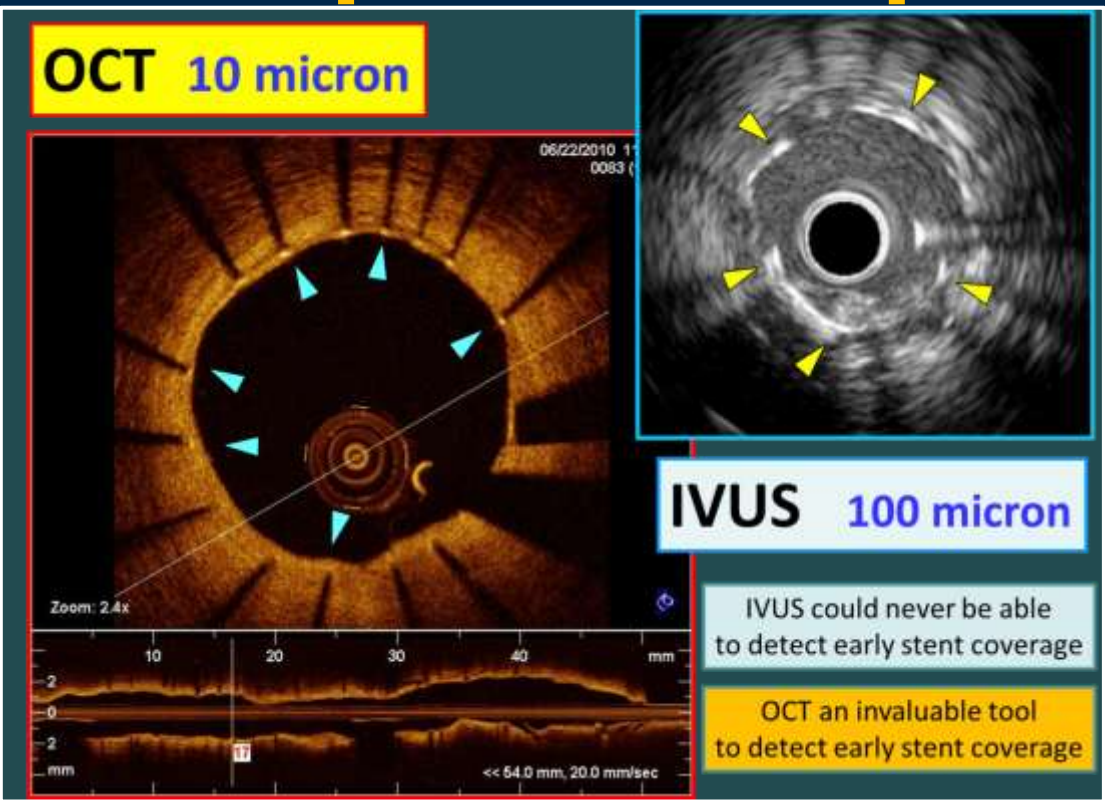


1:2:2:1 groups

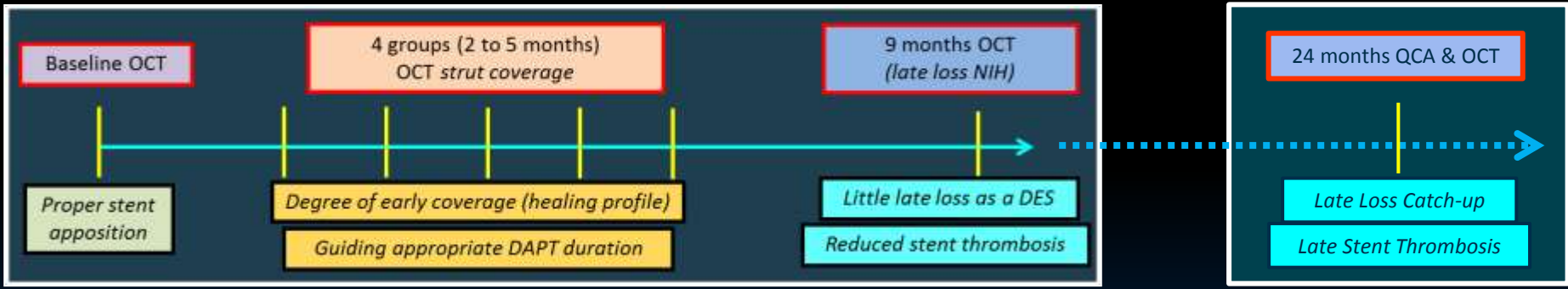
OCT Stent Healing Profile (Stent Coverage) Early FU (2nd to 5th month)

Guide DAPT duration

In this study, still using 9M DAPT



EGO-COMBO Study Design (2 Protocols 4 OCT Assessments at 0-24 Months)



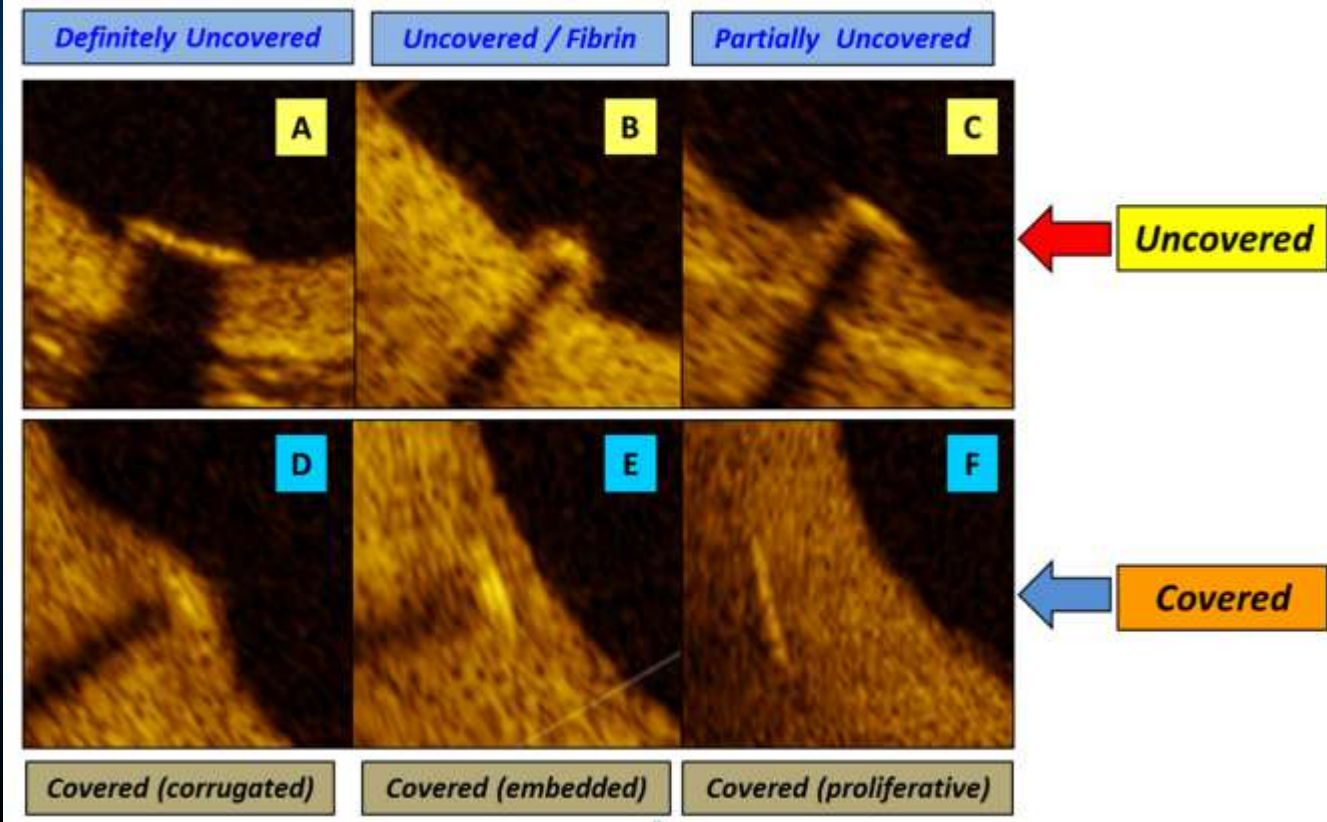
9 Month DAPT

**2nd – 5th Months
1:2:2:1 Ratio**

**CRF Core Lab.
Dr. Akiko Maehara**

**A stringent 6 category
coverage classification**

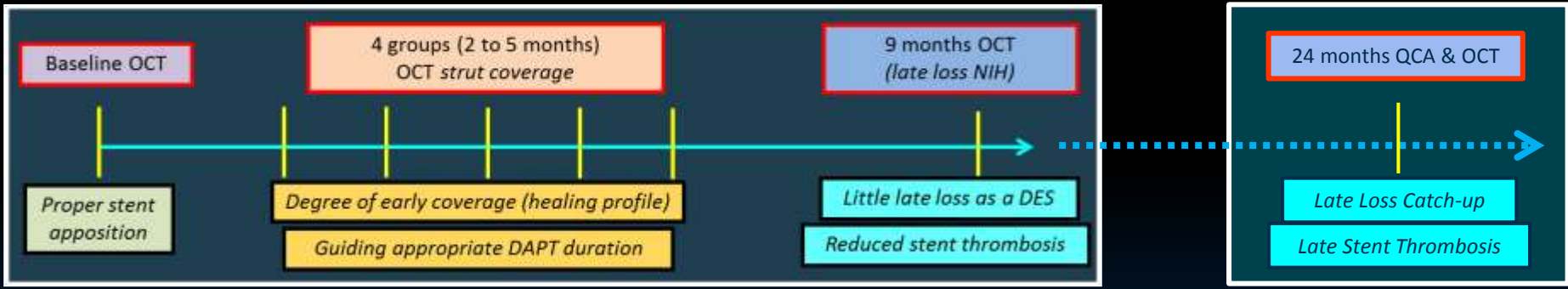
Frame by frame basis



Uncovered

Covered

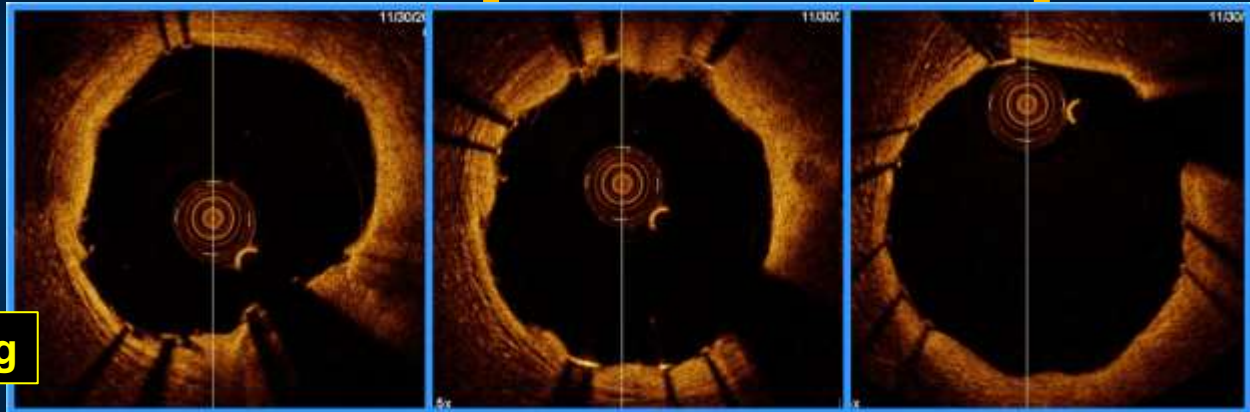
EGO-COMBO Study Design (2 Protocols 4 OCT Assessments at 0-24 Months)



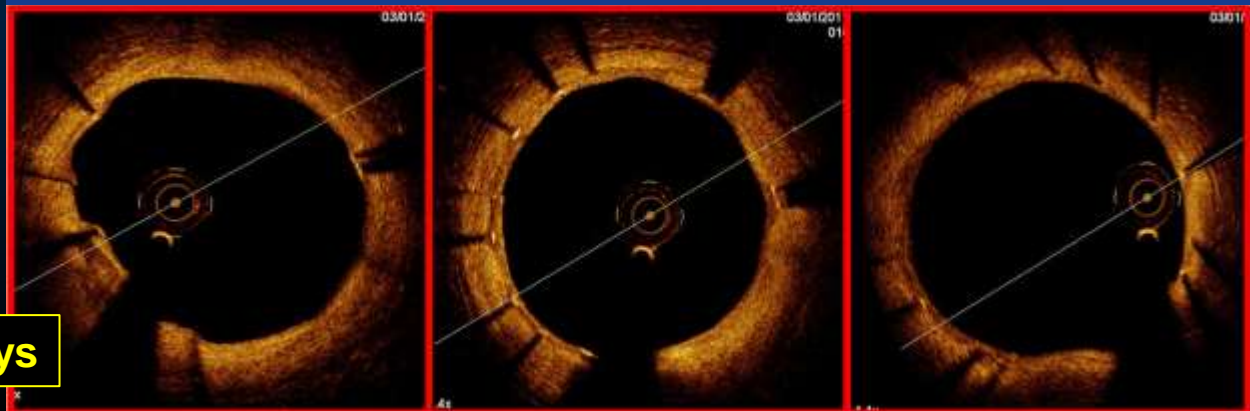
2nd – 5th Months
1:2:2:1 Ratio

9 Month DAPT

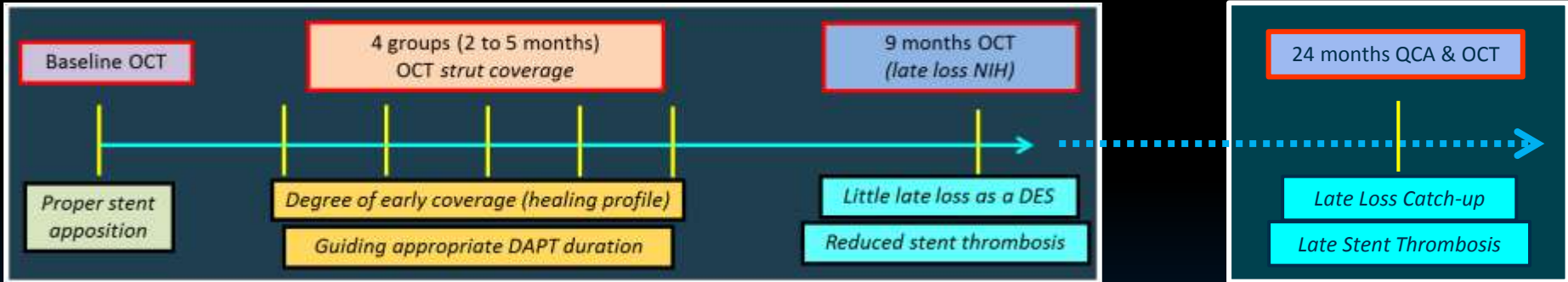
Baseline post stenting



Matching frames 90 days

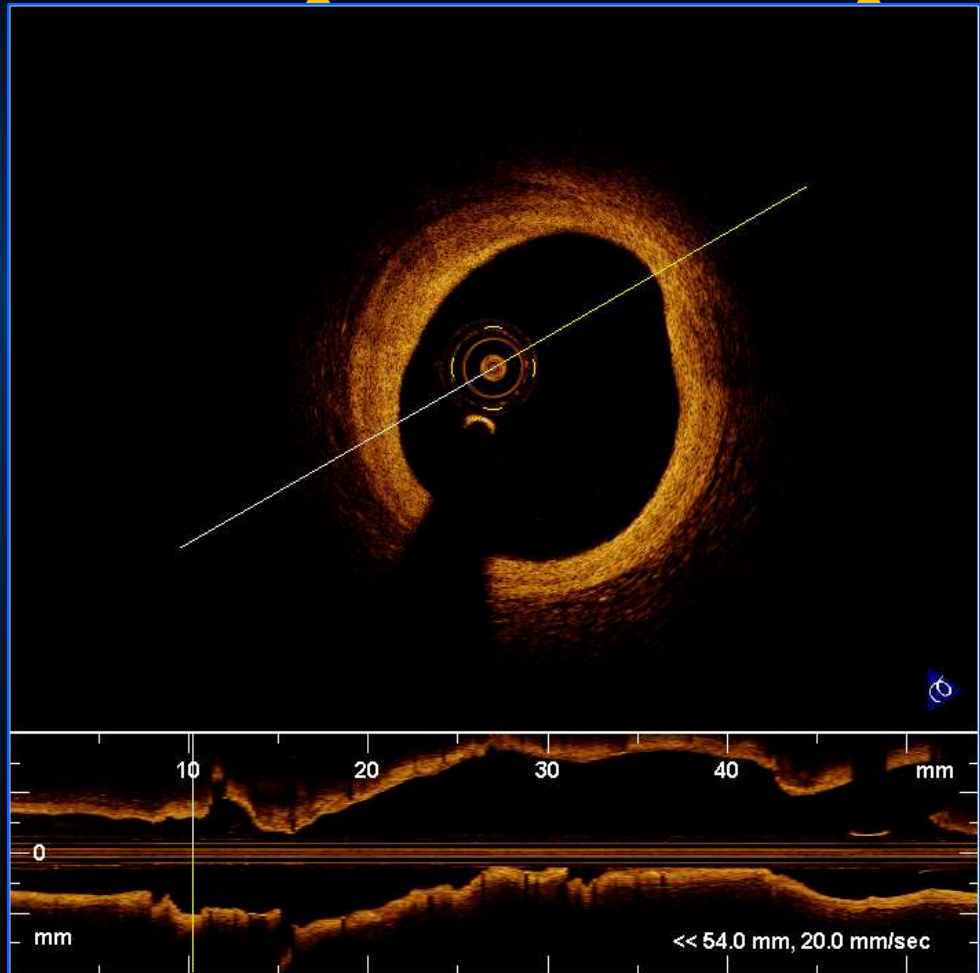


EGO-COMBO Study Design (2 Protocols 4 OCT Assessments at 0-24 Months)

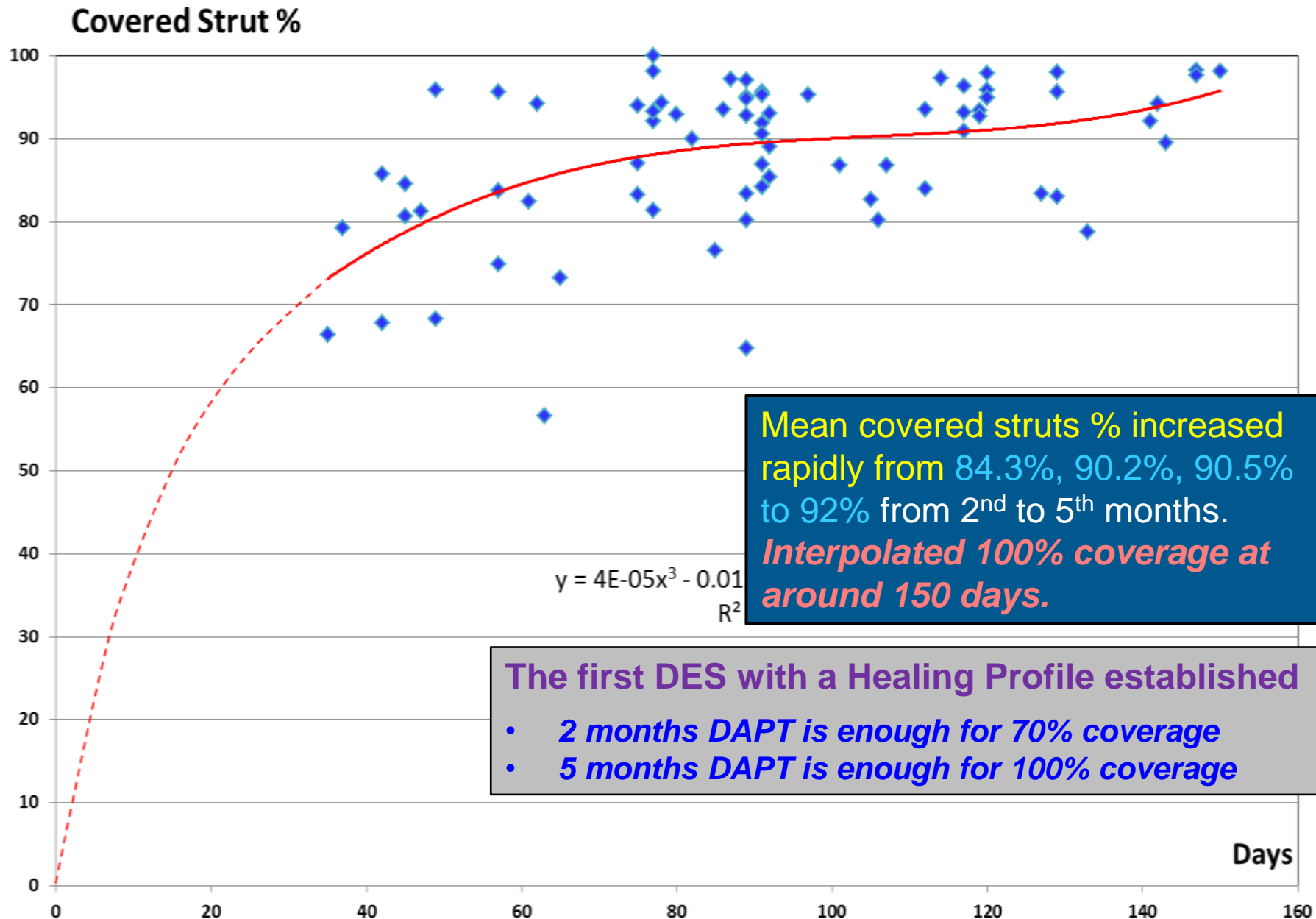


2nd – 5th Months
1:2:2:1 Ratio

COMBO Dual Therapy
Stent at 90 days

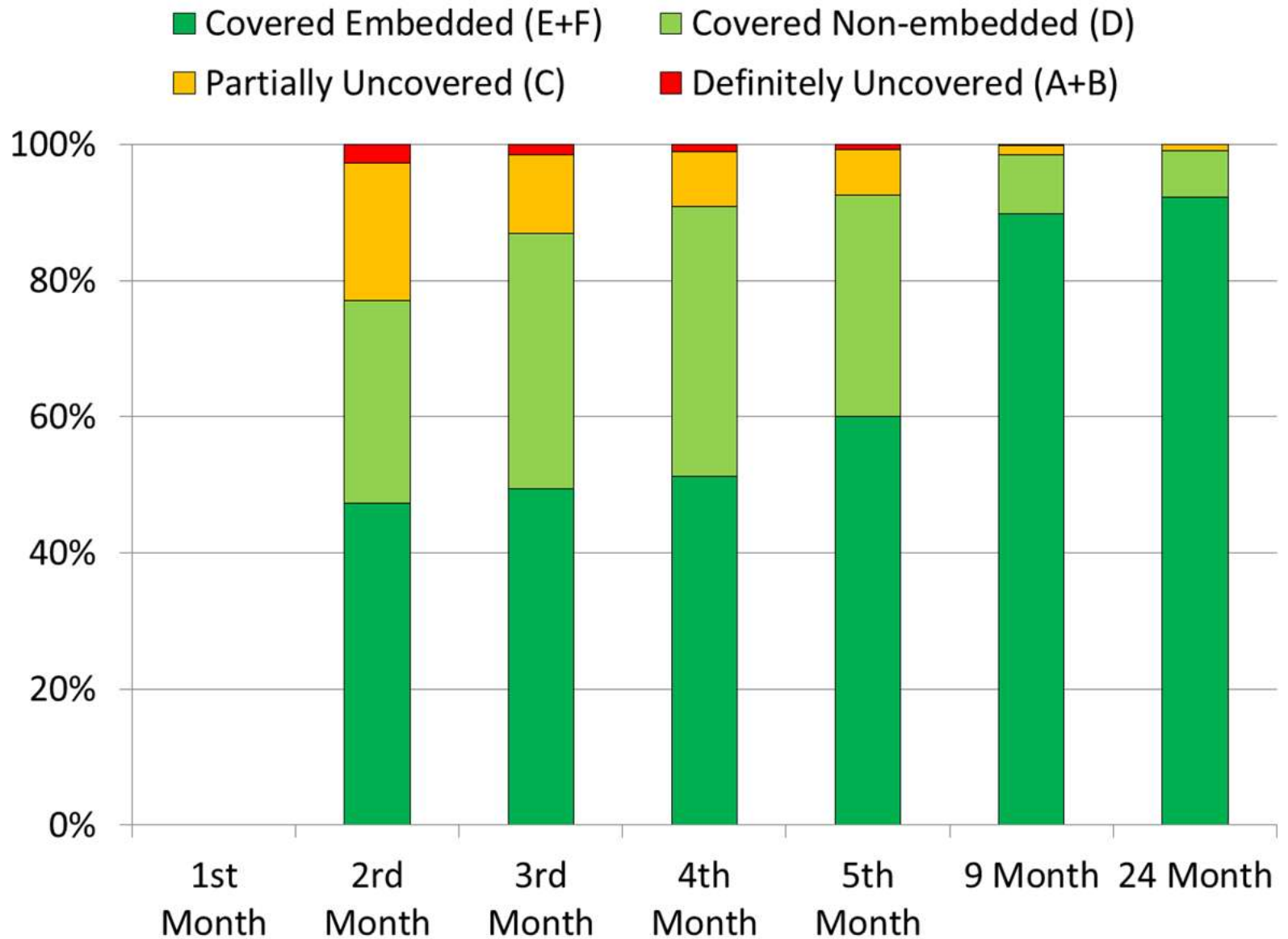


EGO-COMBO Study Design (Healing Profile of a DES)

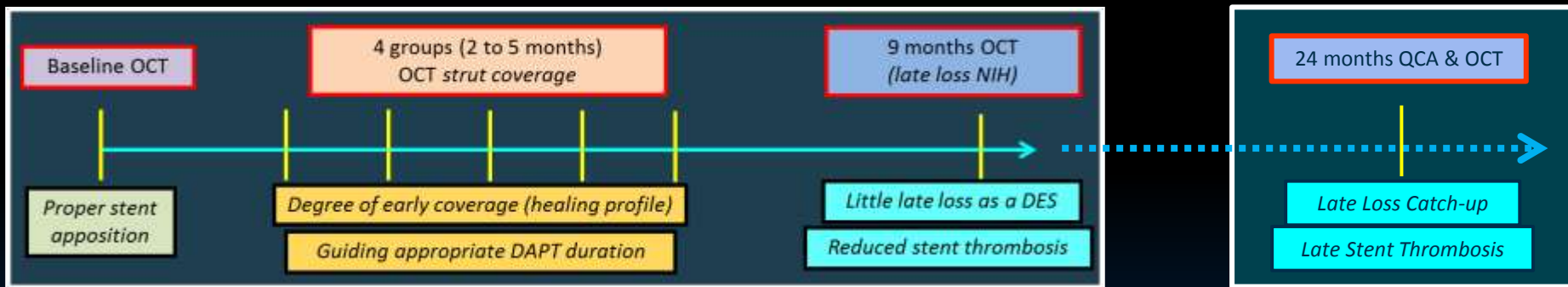


EGO-COMBO Study Design (Healing Profile of a DES)

Percentage of Strut Coverage (%)



EGO-COMBO Study Design (2 Protocols 4 OCT Assessments at 0-24 Months)



EGO-COMBO Angiographic QCA Results (CRF Core Laboratory)

	Early Follow-Ups				Late FU
	2 nd Month (N=12)	3 rd Month (N=25)	4 th Month (N=23)	5 th Month (N=14)	9 th Month (N=74)
MLD (mm)					
In-stent (mean ± SD)					2.66 ± 0.43
In-segment (mean ± SD)					2.47 ± 0.43
Percent diameter stenosis					
In-stent (mean ± SD)	6.15 ± 4.76	6.25 ± 5.51	6.8 ± 6.04	5.47 ± 6.5	12.53 ± 9.79
In-segment (mean ± SD)	13.26 ± 5.43	15.94 ± 8.75	18.67 ± 9.32	18.95 ± 6.66	18.71 ± 9.39
Late lumen loss (mm)					
In-stent (mean ± SD)	-0.05 ± 0.17	0.04 ± 0.22	0.02 ± 0.31	0.06 ± 0.18	0.23 ± 0.36
In-segment (mean ± SD)	-0.16 ± 0.23	0.02 ± 0.24	-0.02 ± 0.28	0.07 ± 0.17	0.09 ± 0.35

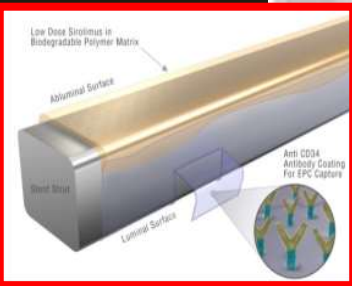
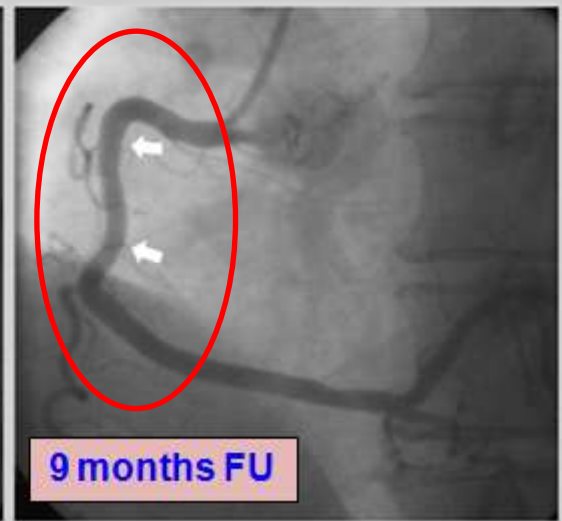
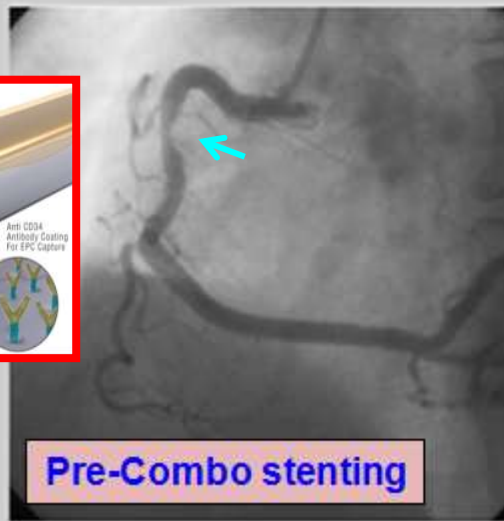
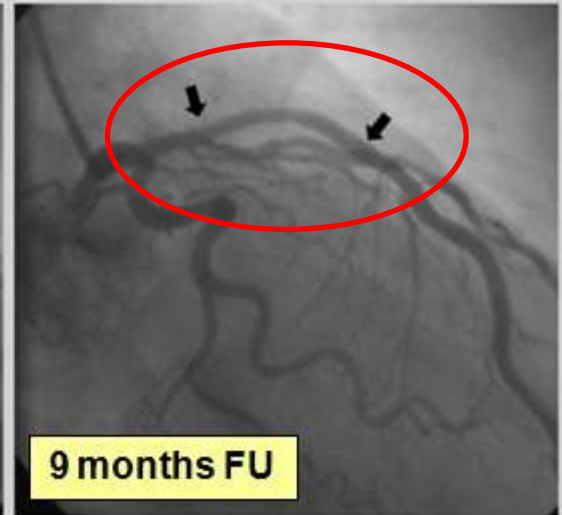
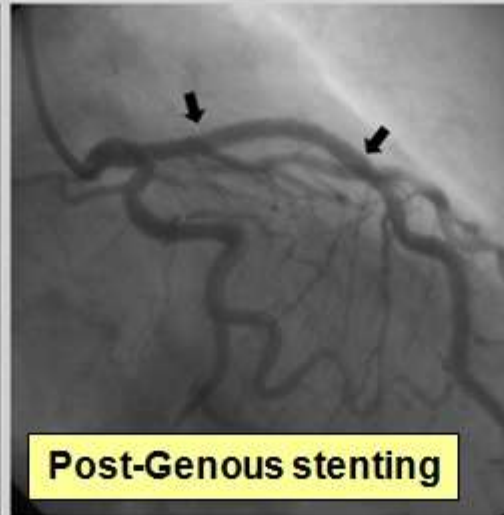
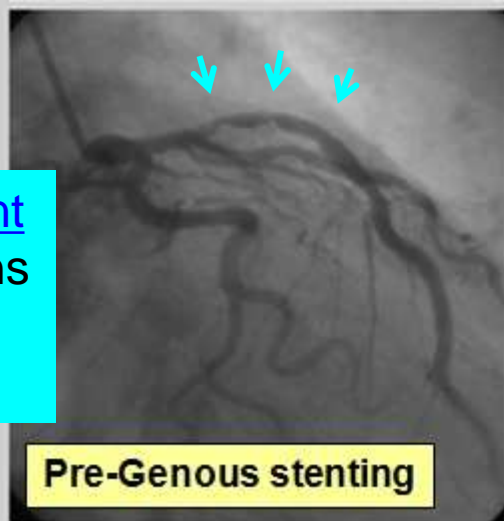
9M QCA Late Loss = 0.23 mm
9M TLR / TVF = 1.64%
Very durable results to 38 months

* N = number of vessels treated in each monthly group.

Genous Stent:- a pro-healing EPC capturing stent

But similar to a bare metal stent still with some late loss !!

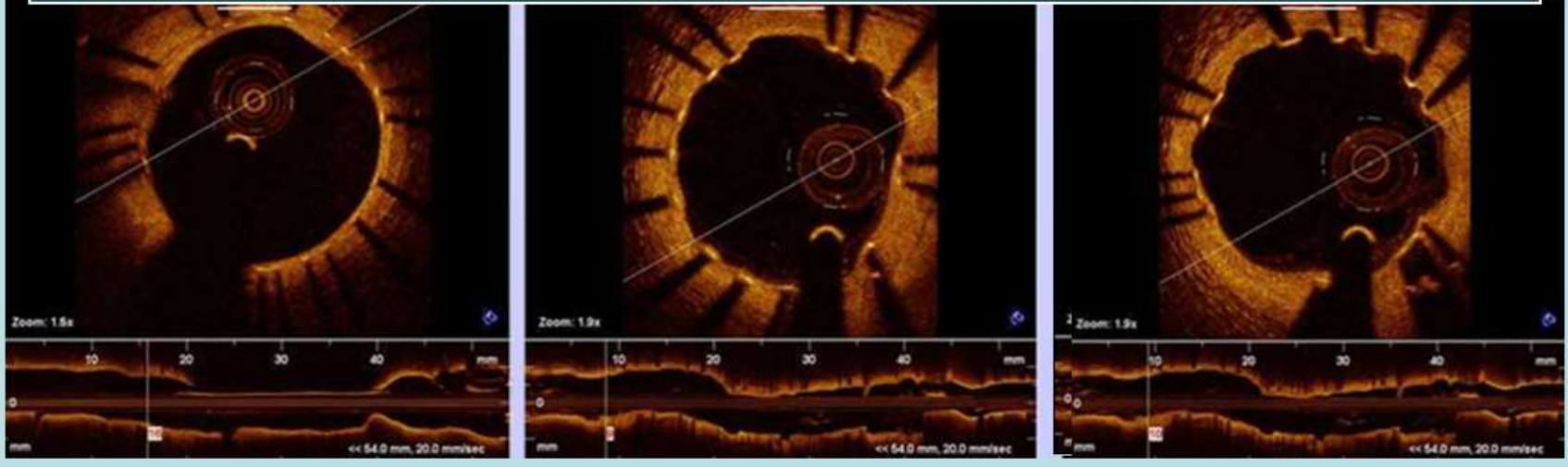
Same patient
with 2 lesions
treated the
same time



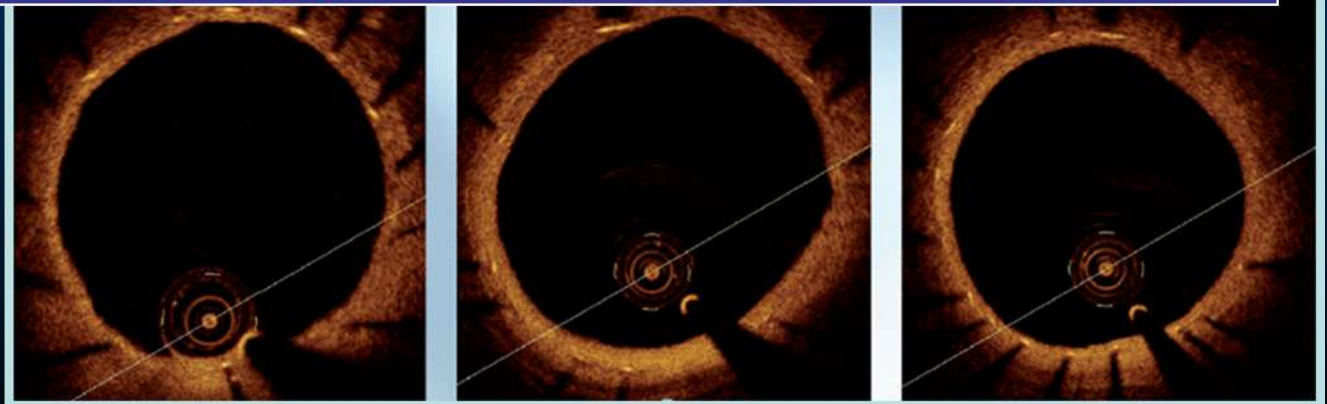
Dual Therapy COMBO Stent:- a DES with EPC capturing + sirolimus coating
Benefits of pro-healing + neointimal suppression & less late loss like DES.

EGO-COMBO Study (2 Protocols 4 OCT Assessments at 0-24 Months)

By 9 months, most DESs still exhibit variable neointimal healing, coverage & sun-flowering (scalloping, positive remodelling)



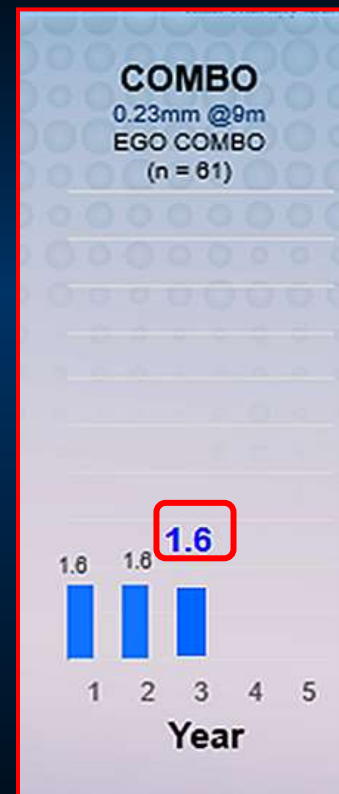
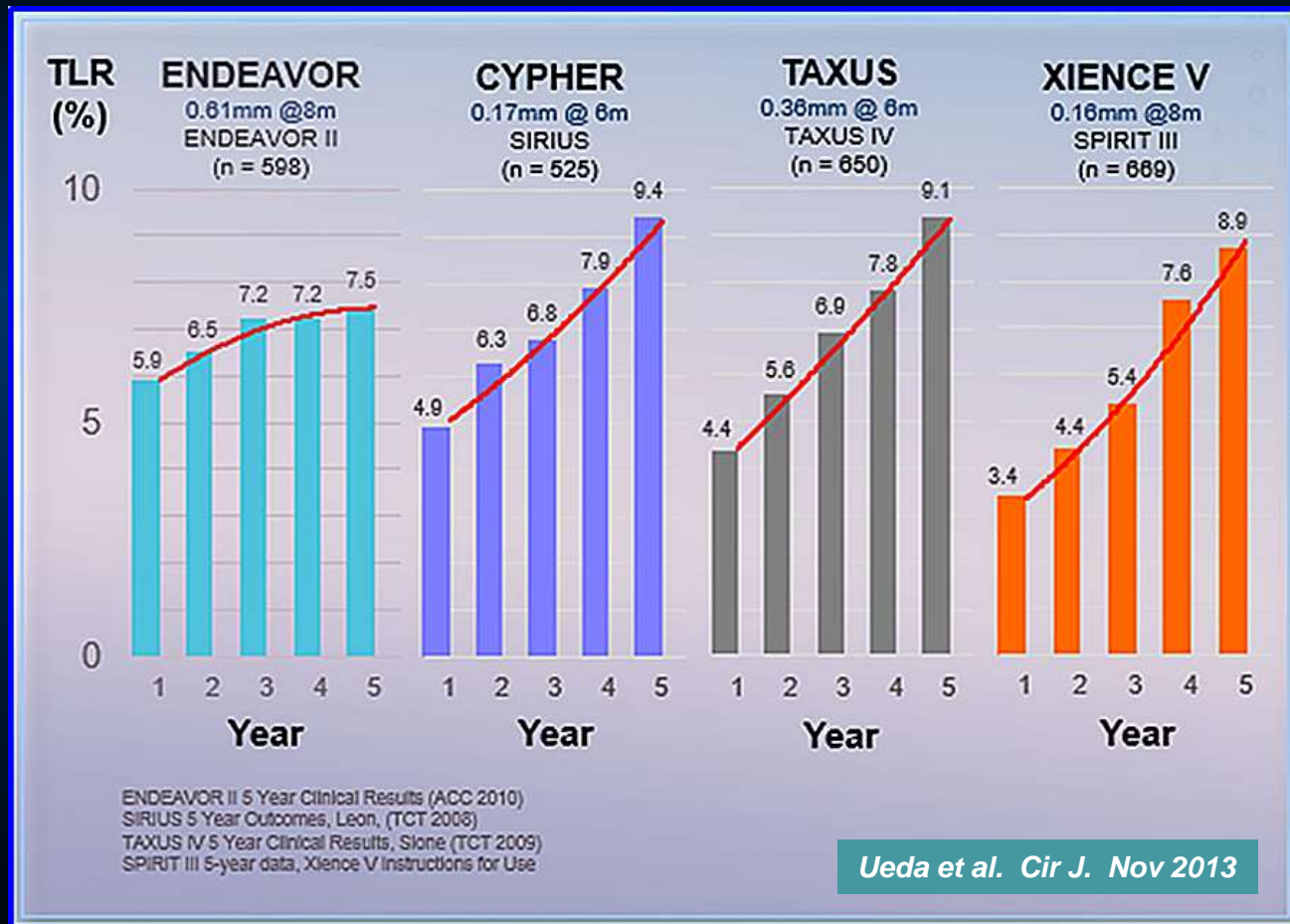
COMBO Stent: homogenous, stable neointimal with no sun-flowering



An evidence of EPC-capturing pro-healing benefit !!

Durability of Long Term Anti-restenotic Efficacy in *DES without Healing*

Continuous restenosis (increasing TLR%) + late-loss catch-up.... !!
Despite initial claims of minimal late loss before 1 year....!!

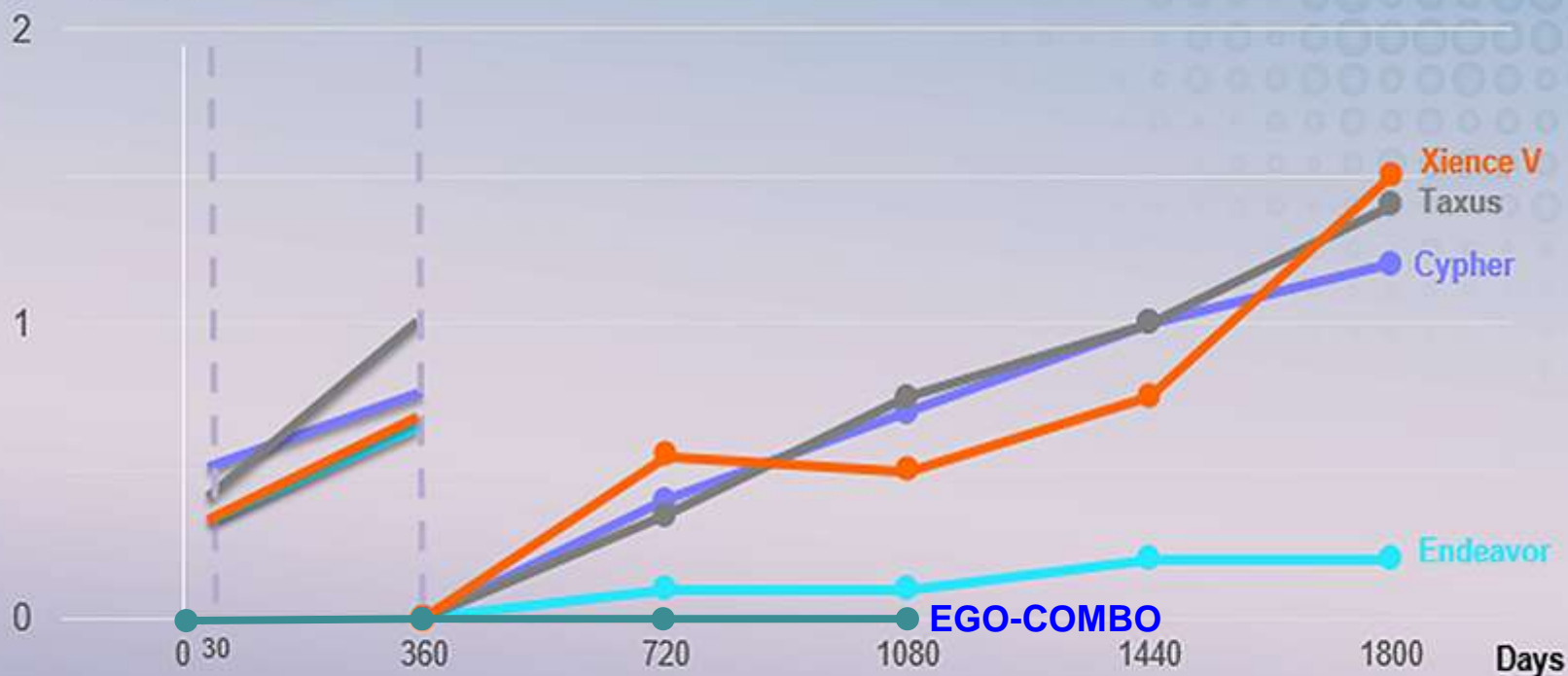


REMEDEE Results
EuroPCR 2014

Durability of Long Term Safety & Efficacy in *DES without Healing*

Worst of all - Continuous occurrence of late stent thrombosis.... !!
And prolonged DAPT.... !!

ARC (Def/Prob) ST (%)



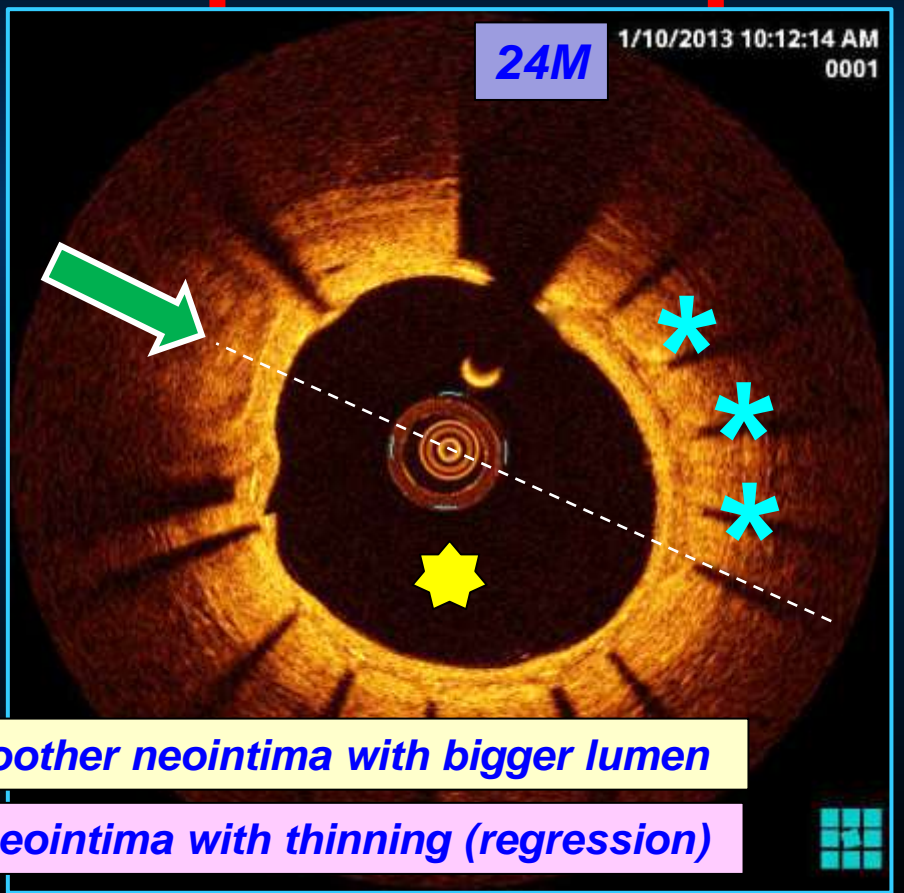
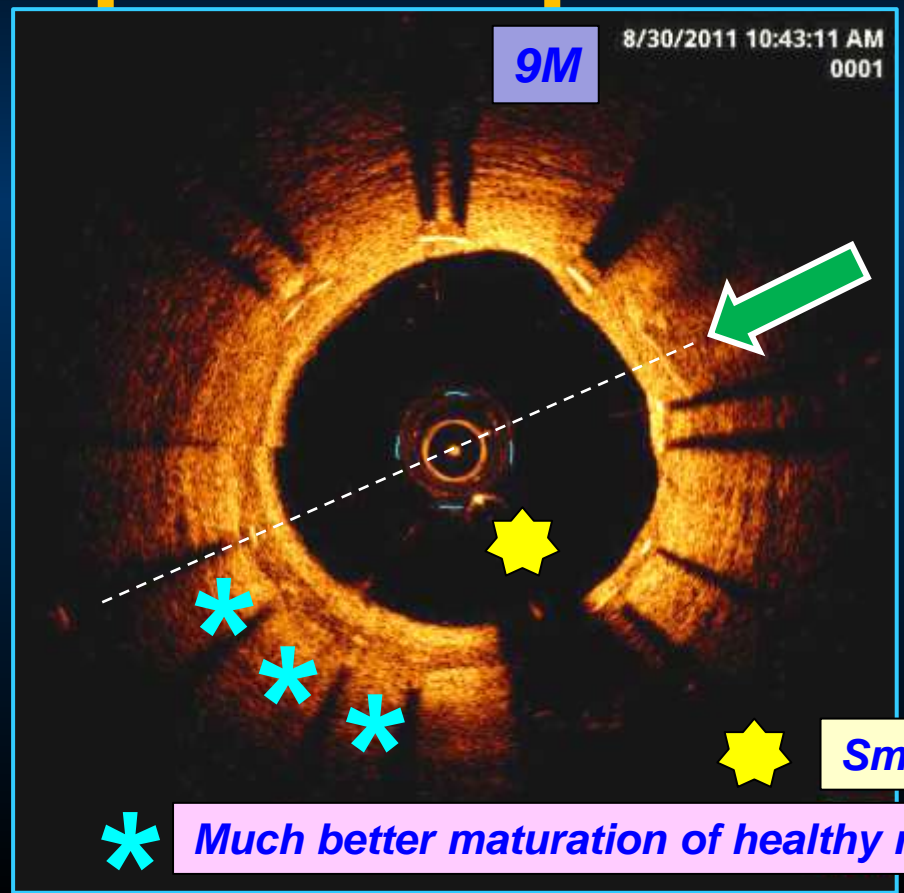
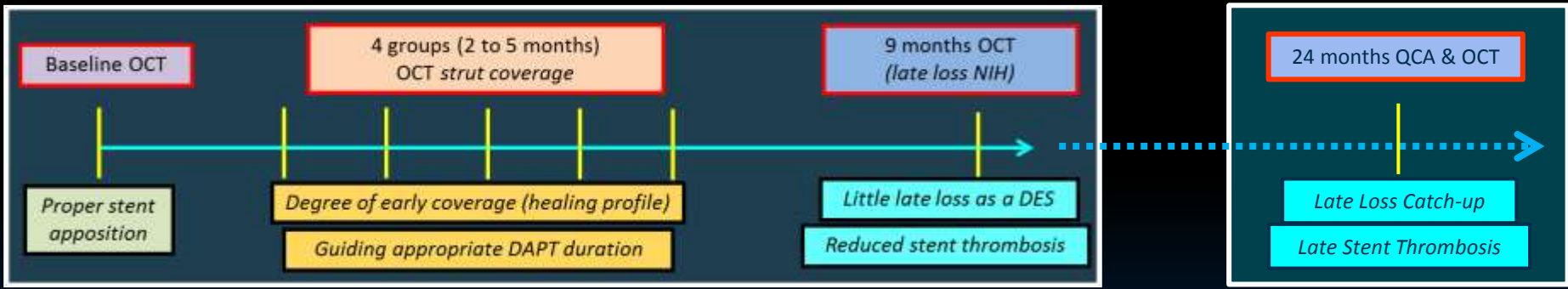
Results come from separate clinical trials and may differ in a head-to-head comparison. Stent thrombosis is a low-frequency event that current DES clinical trials are not adequately powered to fully characterize. The true rate of VLST is unknown, however pooled data exist from the various DES programs that are shown here.

ENDEAVOR II % Presented by Popma et al (PCR 2009)
SIRIUS 5 Year Outcomes, Welsh et al (JACC Vol. 53, No. 17, 2009)
TAXUS Mauri L et al (New England J Med., 2007; 356:1020-1029)
XIENCE SPIRIT III 5-year data, Xience V Instructions for Use

REMEDEE 2 Year Clinical Results, EuroPCR 2013
EGO COMBO 2 Year Clinical Results, AsiaPCR 2014

REMEDEE Results
EuroPCR 2014

EGO-COMBO Study Design (2 Protocols 4 OCT Assessments at 0-24 Months)

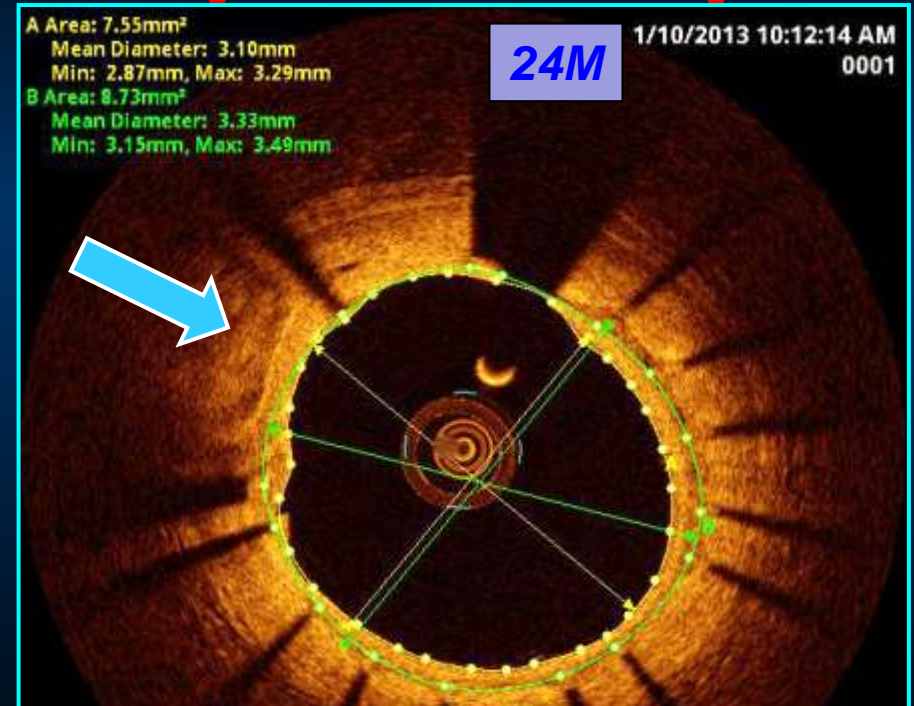
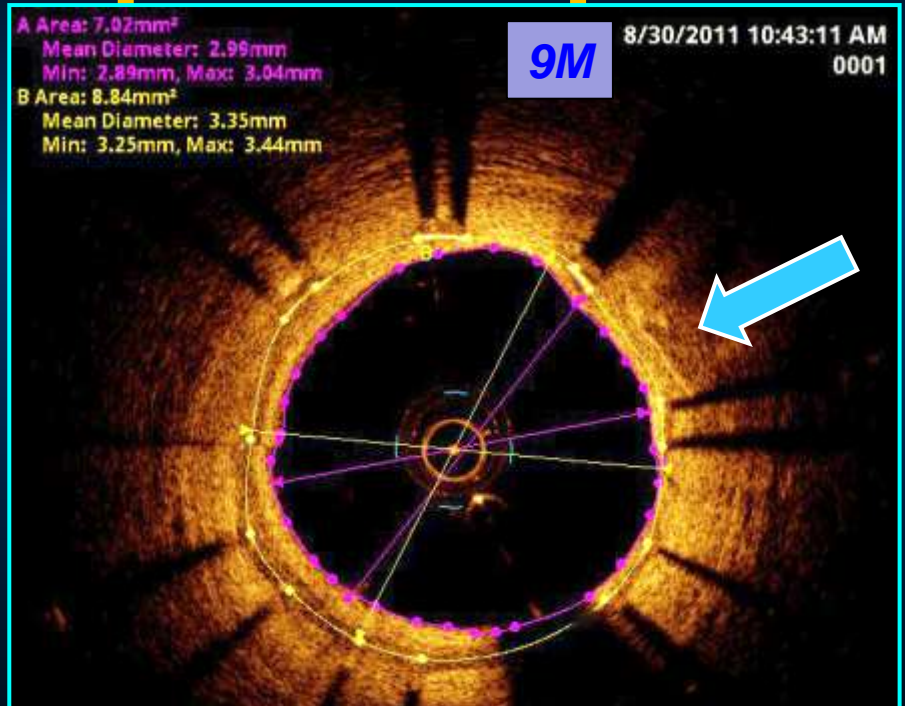
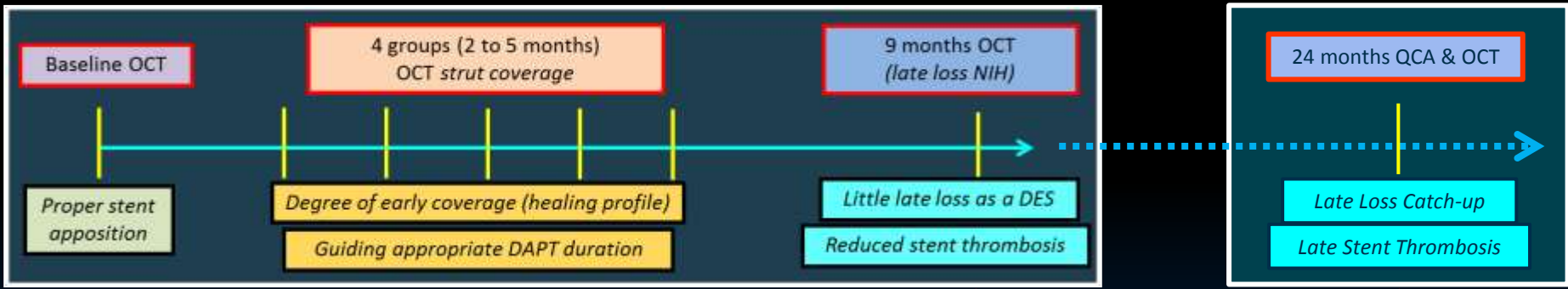


Smoother neointima with bigger lumen

Much better maturation of healthy neointima with thinning (regression)



EGO-COMBO Study Design (2 Protocols 4 OCT Assessments at 0-24 Months)

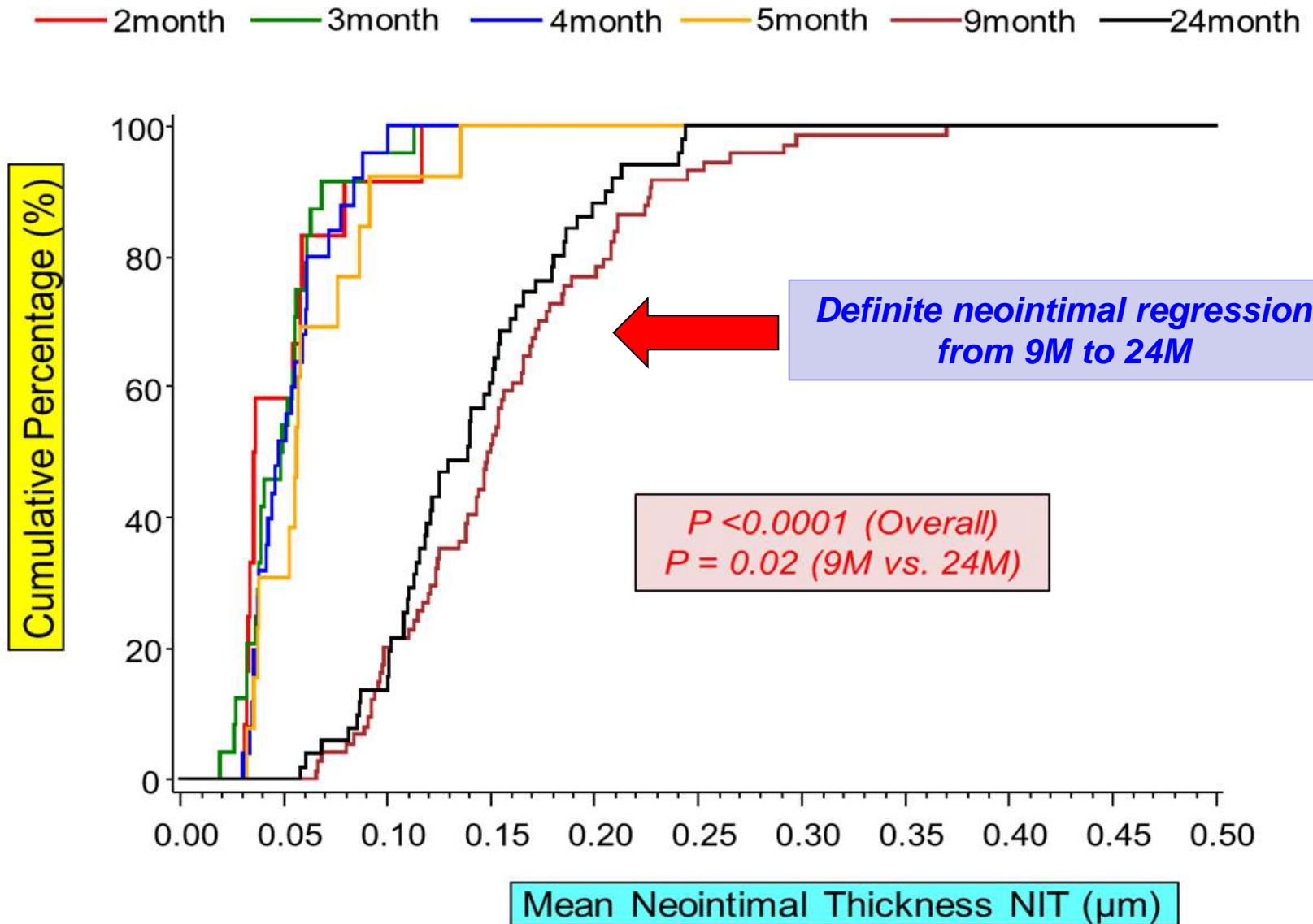


Actual measurement shows Plaque Regression

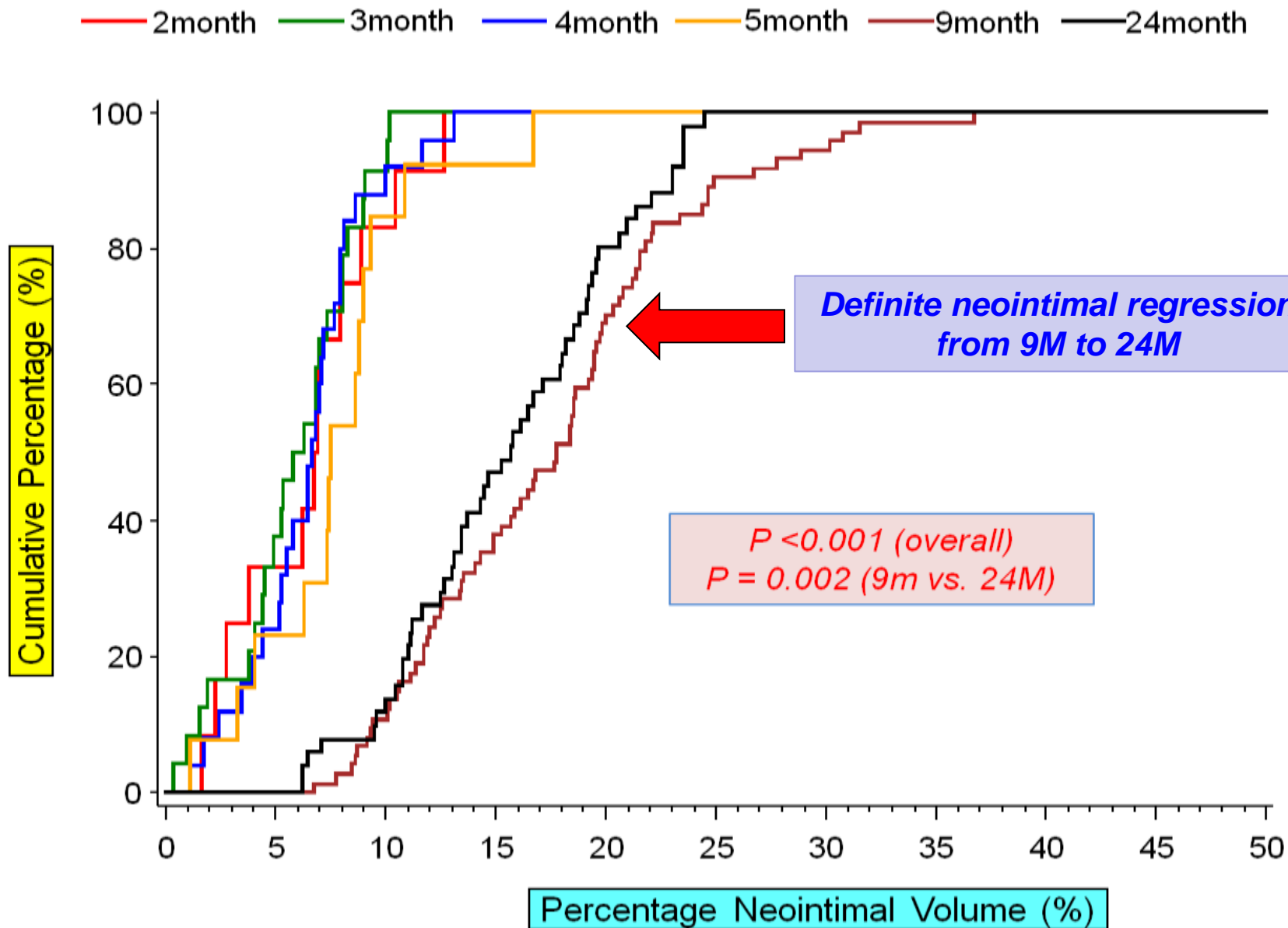
9M Lumen Area = 7.02mm² 24M = 7.55mm² (gained by 0.53mm²)
 9M NIA = 1.82mm² 24M = 1.18mm² (regressed by 0.64mm²)



COMBO Dual Therapy Stent (OCT Neointimal Regression of a DES)



COMBO Dual Therapy Stent (OCT Neointimal Regression of a DES)



OCT Plaque Regression (9M to 24M) Dual Therapy COMBO Stent

Strut Level Neointimal Thickness (mm)

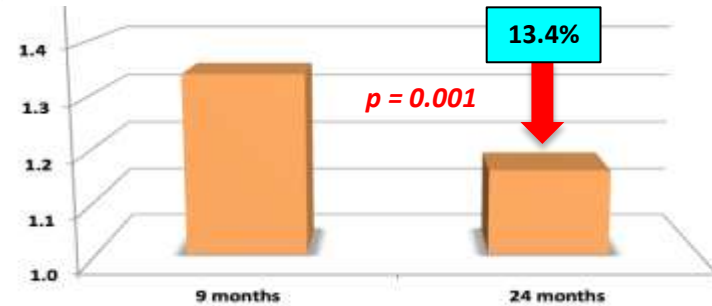
* n = 18904 vs. 12822 (all struts)



Median [IQR] 0.14 [0.08, 0.21] vs. 0.12 [0.07, 0.19]

Mean Neointimal Cross Sectional Area at 1 mm Sampling (mm²)

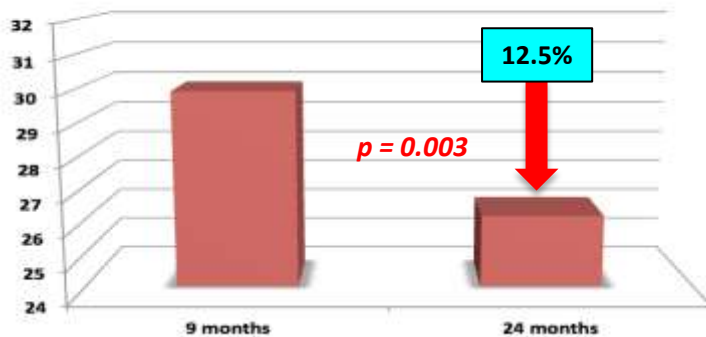
* n = 41 patients, 54 vessels



Median [IQR] 1.34 [1.02, 1.65] vs. 1.16 [0.92, 1.52]

Neointimal Volume (mm³)

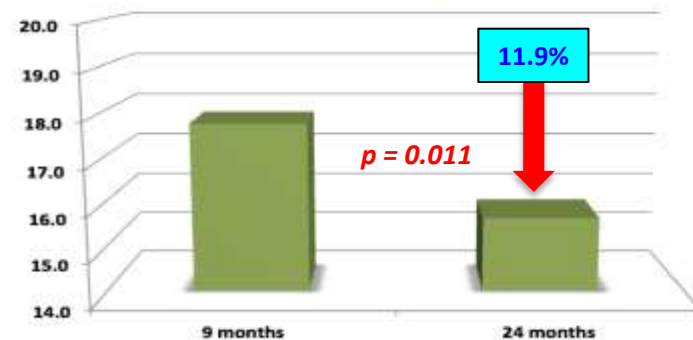
* n = 41 patients, 54 vessels



Median [IQR] 29.91 [22.13, 43.22] vs. 26.17 [19.64, 35.81]

In-Stent Percentage Neointimal Volume

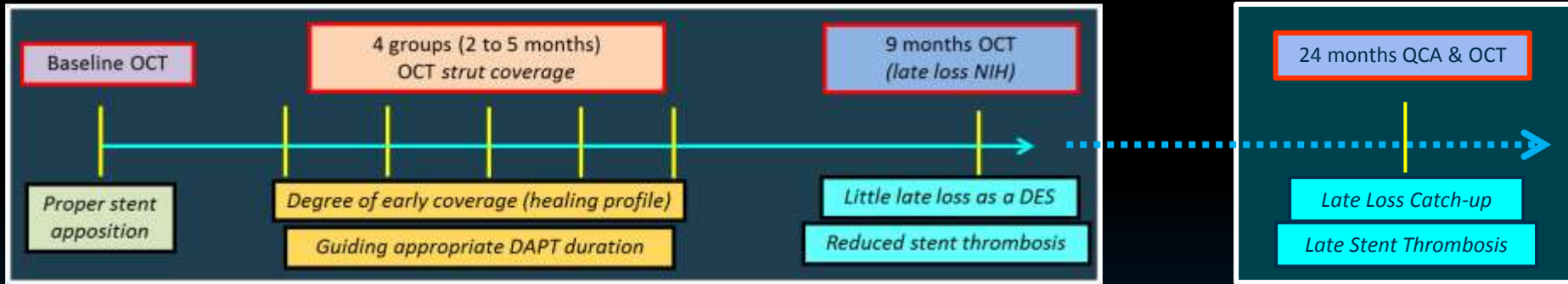
* n = 41 patients, 54 vessels



Median [IQR] 17.76 [12.21, 21.22] vs. 15.65 [11.17, 19.35]

- True plaque regression by OCT at 24 months..... First time for a DES !
- Very Durable 24M (38M) results: TLR / TVF (1/61) 1.64%; MACE Rate (2/61) 3.28%...
- No neoatherosclerosis or sun-flowering (late positive remodeling) recorded.
- No ARC Definite & Probable LST (not even micro-thrombus by OCT) recorded.

EGO-COMBO Study Design (Longitudinal Sequential OCT FUs 0-24M)



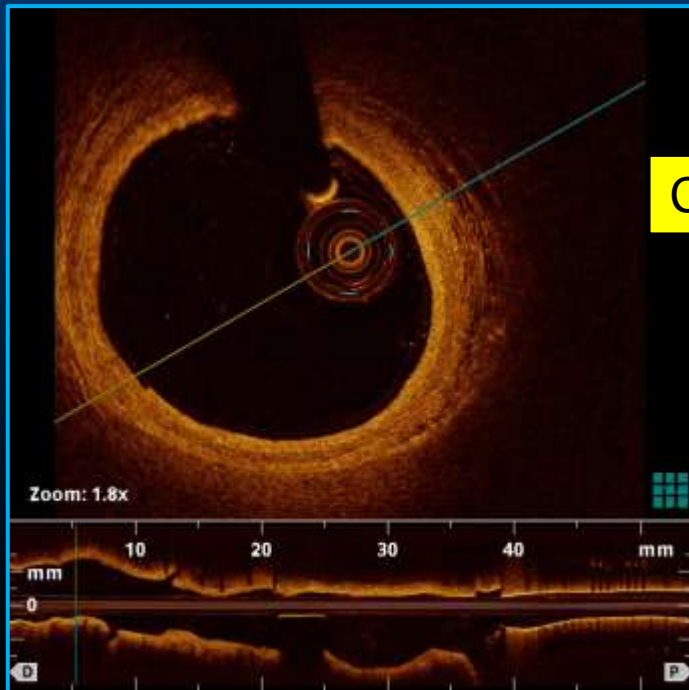
With core lab. adjudication, the dual therapy COMBO Stent is the first DES ever with a healing profile established, and appears to be a novel DES with durable outcomes.

Abluminal sirolimus drug coating

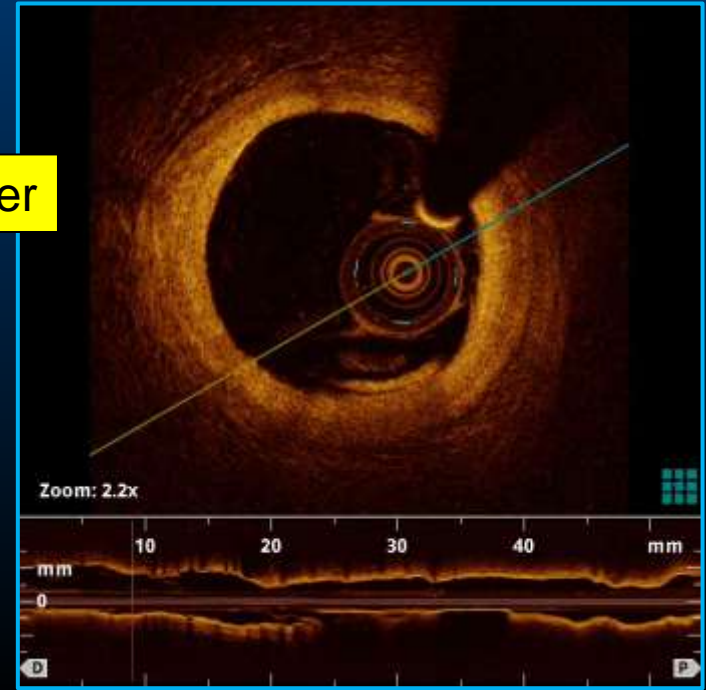
- Optimal neointimal suppression
- Low neointimal thickness
- Low neointimal volume
- Low in-stent % plaque volume
- **Durable patent artery without ISR**

Luminal antibody coating

- Excellent healing without neo-atherosclerosis
- Plaque regression rather than progression
- No sun-flowering or late positive remodeling
- No even a single micro-thrombus detected
- **Stable pro-healing benefits**

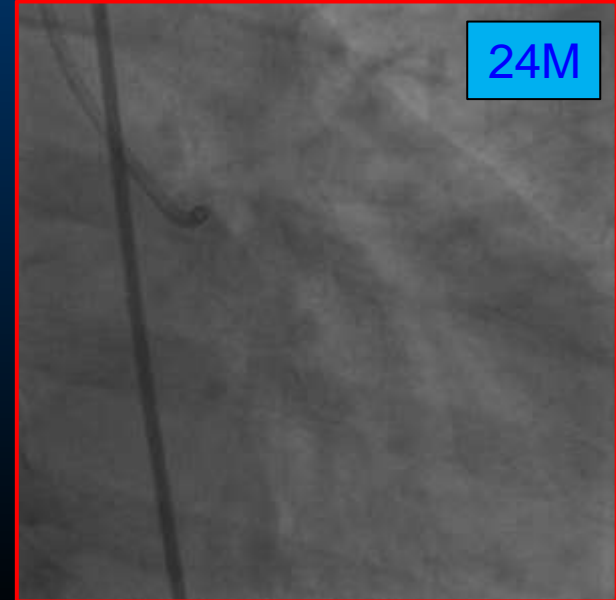
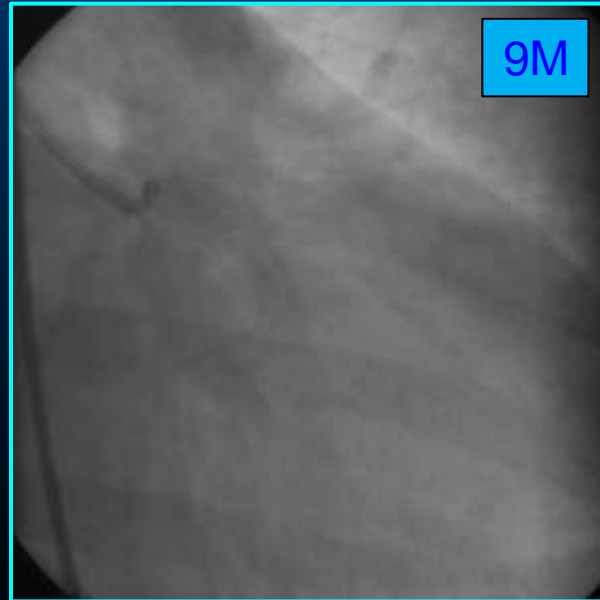
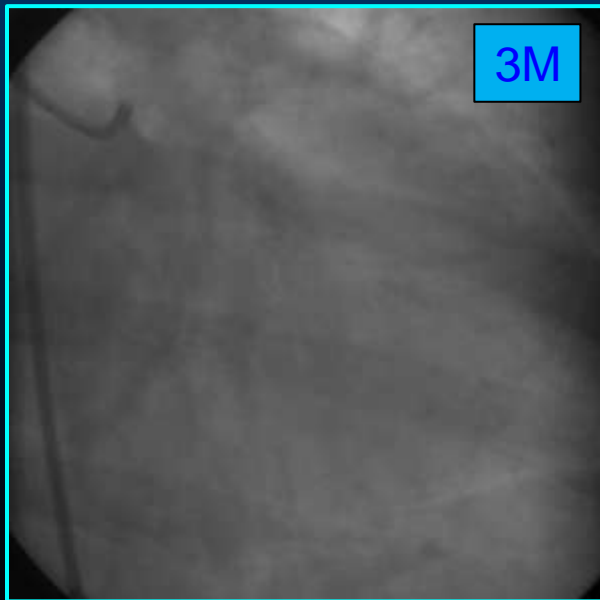
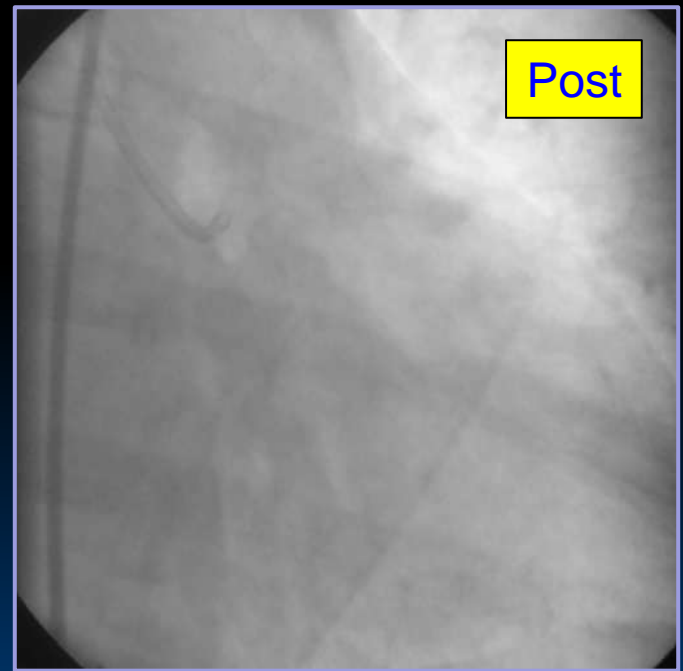
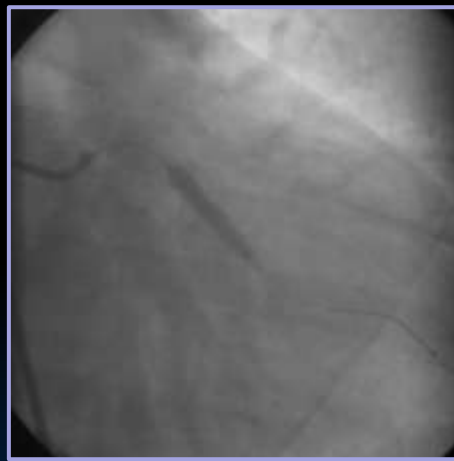
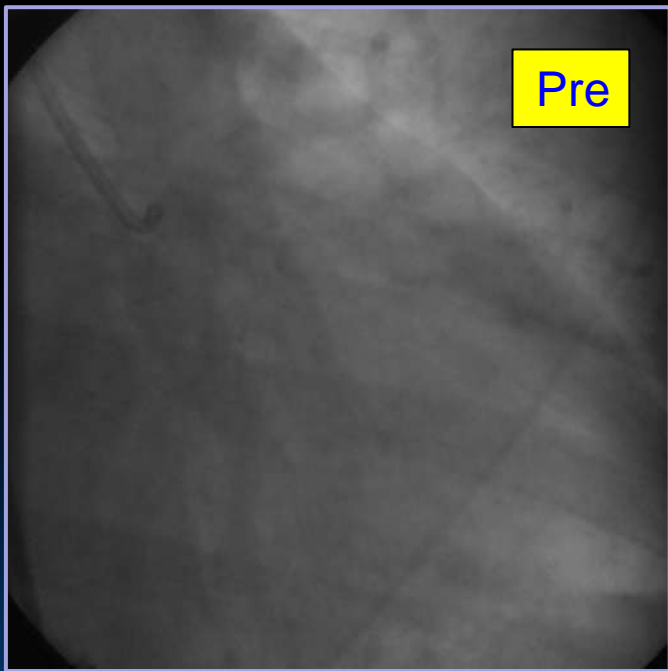


Combo



Cypher

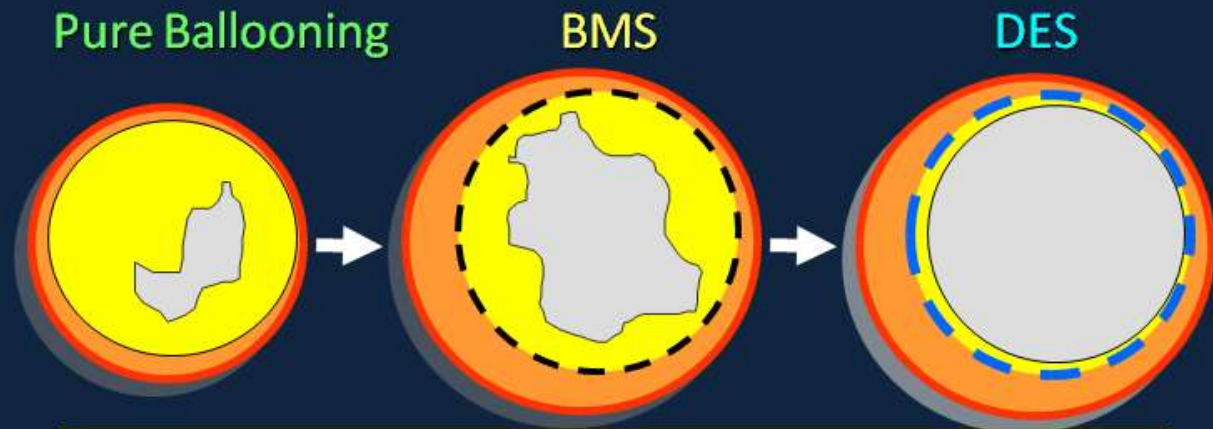
Same patient
2 lesions on LAD
24M Combo Proximal
22M Cypher Distal



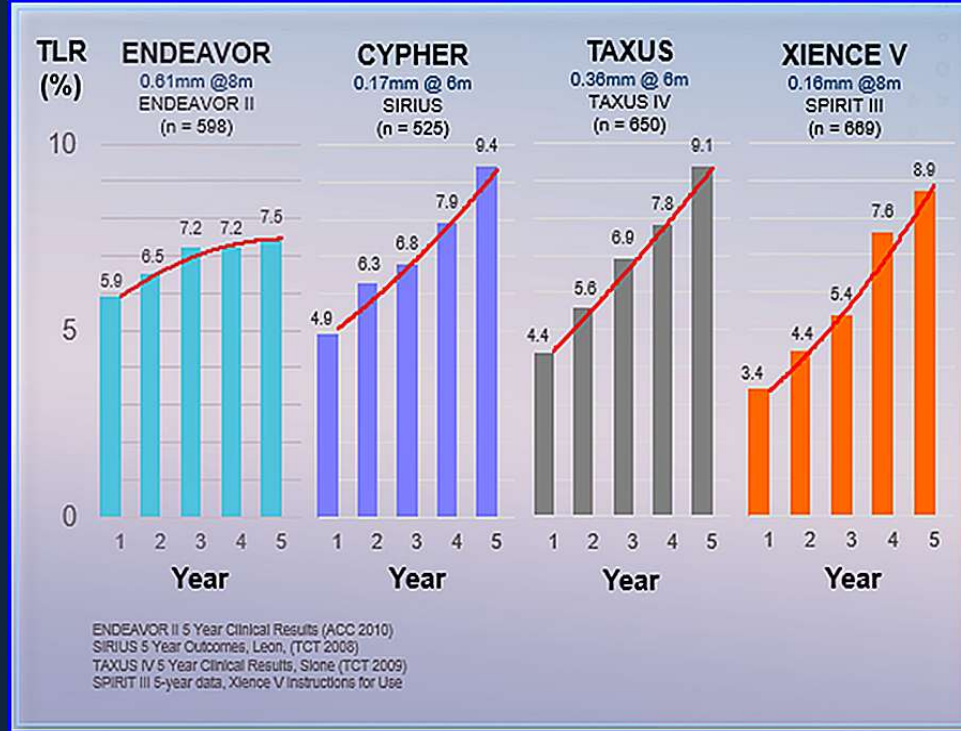
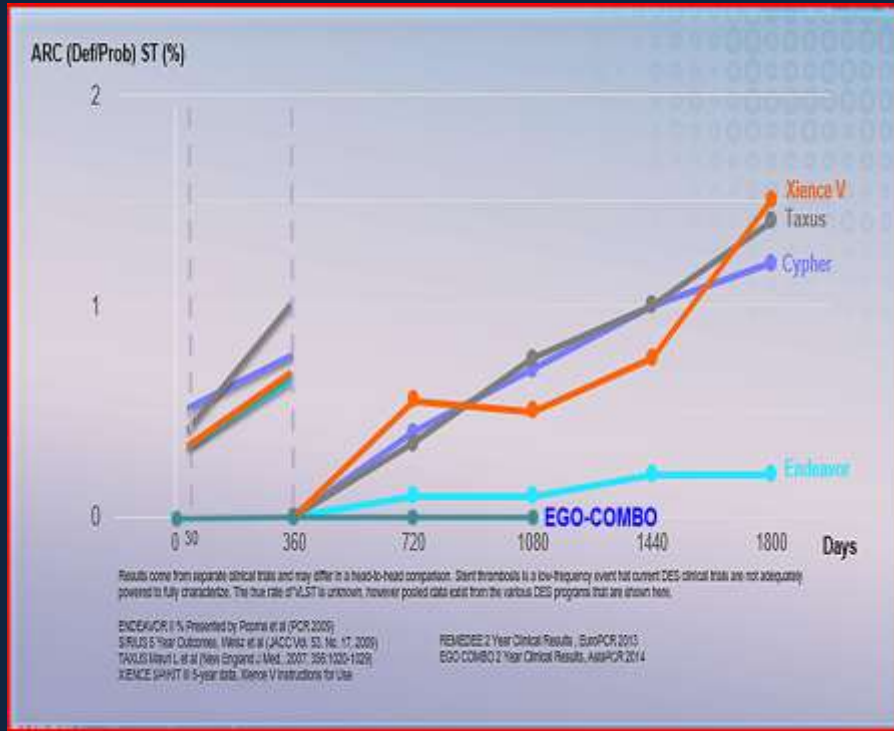
In Summary

All current DES = can achieved neointimal suppression with <10% restenosis in the 1st year

But many DES still show poor Stent Healing = Late Stent Failure (Thrombosis or Late-loss Catch-up)



Acute Closure	Bail-out + BMS	
Restenosis 30-50%	25-35%	3-10% !!



Durable Benefits of Dual Therapy COMBO DES vs. other Monotherapy DES

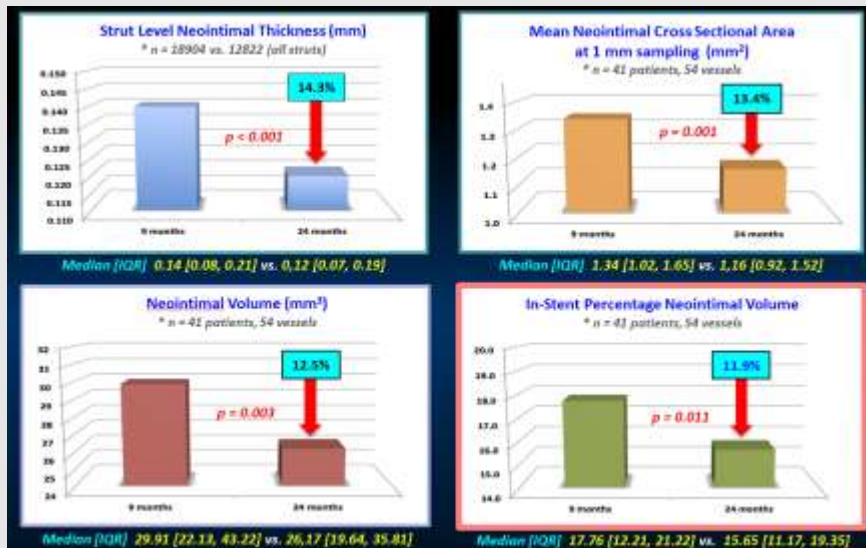
- Longitudinal sequential OCT DES assessment: could be a novel approach.
- First DES with healing profile established. 100% coverage (DAPT) by 5M.
- **Durable 24M (38M) results: TLR / TVF 1.64%; MACE Rate 3.28%.**
- **True plaque regression** by OCT at 24 months... first for a DES....!!
- No neoatherosclerosis or sun-flowering (late positive remodeling).
- No ARC Definite & Probable LST (not even micro-thrombus by OCT).

Abluminal sirolimus drug coating

- Optimal neointimal suppression
- Low neointimal thickness
- Low neointimal volume
- Low in-stent % plaque volume
- **Durable patent artery without ISR**

Luminal antibody coating

- Excellent healing without neo-atherosclerosis
- Plaque regression rather than progression
- No sun-flowering or late positive remodeling
- No even a single micro-thrombus detected
- **Stable pro-healing benefits**





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