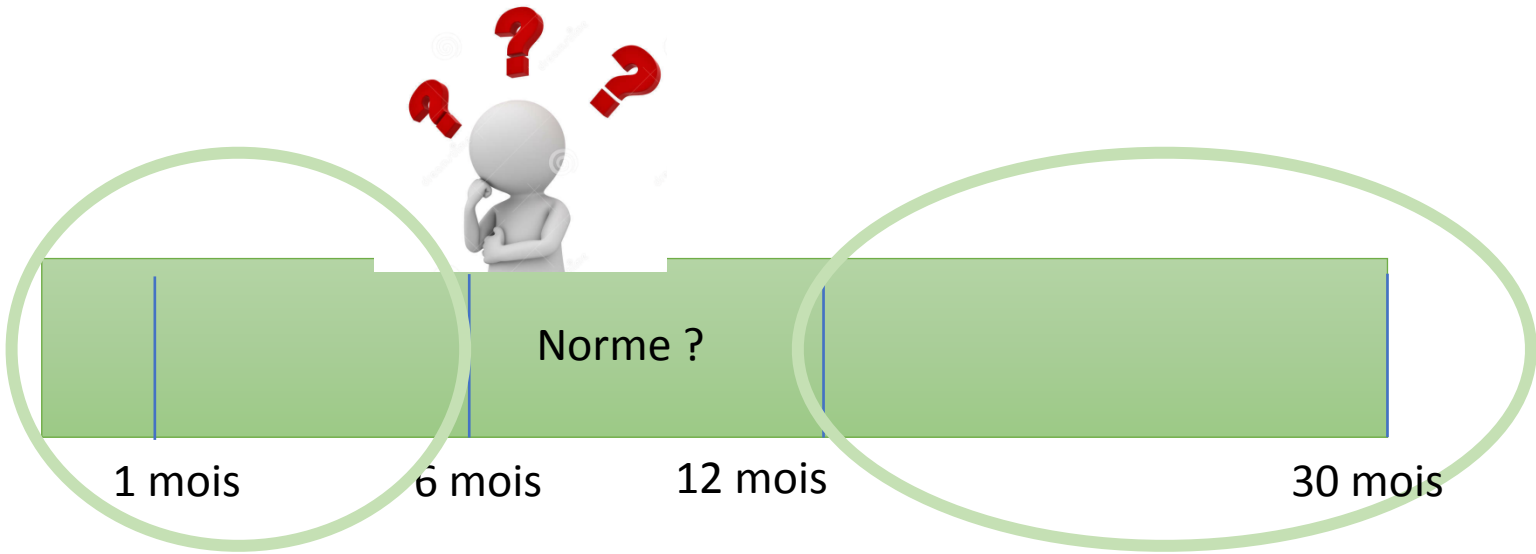
La DAPT au centre des débats de la cardiologie interventionnelle

Peut on se permettre d'être flexible avec la nécessité de la DAPT ?

Durée de la Bithérapie post SCA/DES



Durée courte IMPOSEE

Risque Ischémique IATROGENE

Risque de TS

Durée longue FLEXIBLE

Risque hémorragique

Complications hémorragiques

Coût

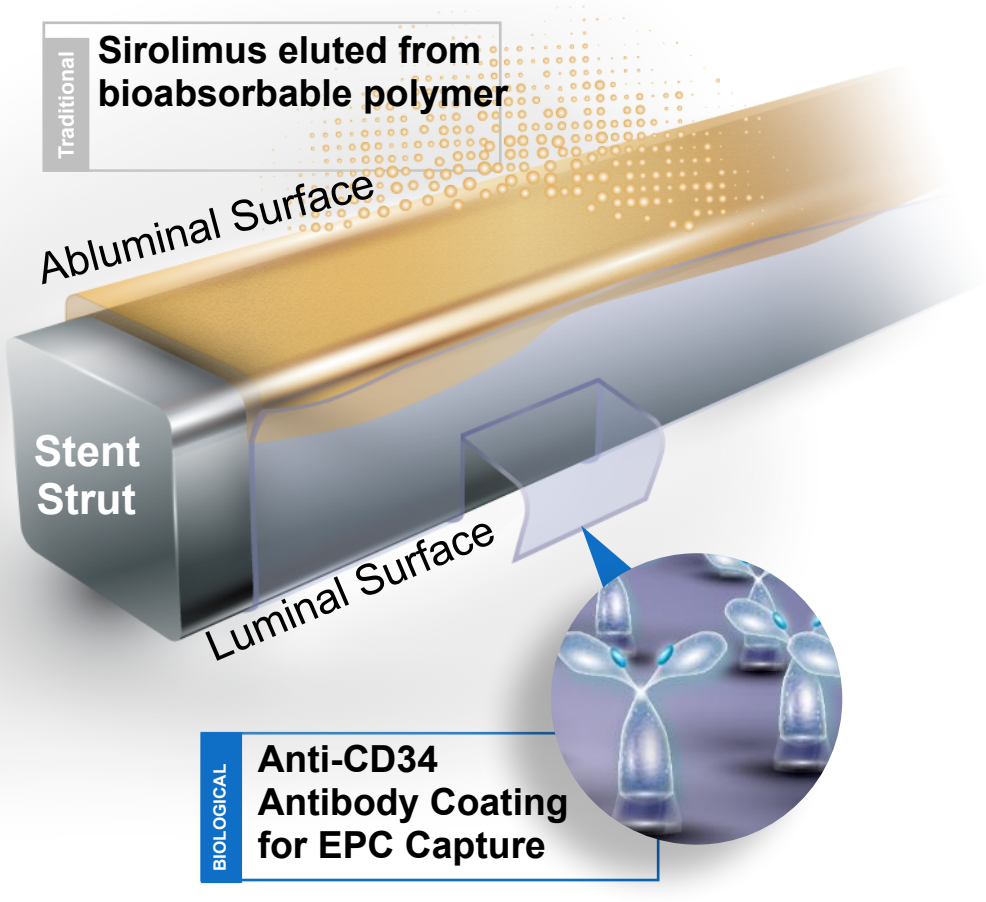
The Dual Therapy Stent:
Traditional DES with biological therapy

COMBO+ PLUS DUAL THERAPY STENT

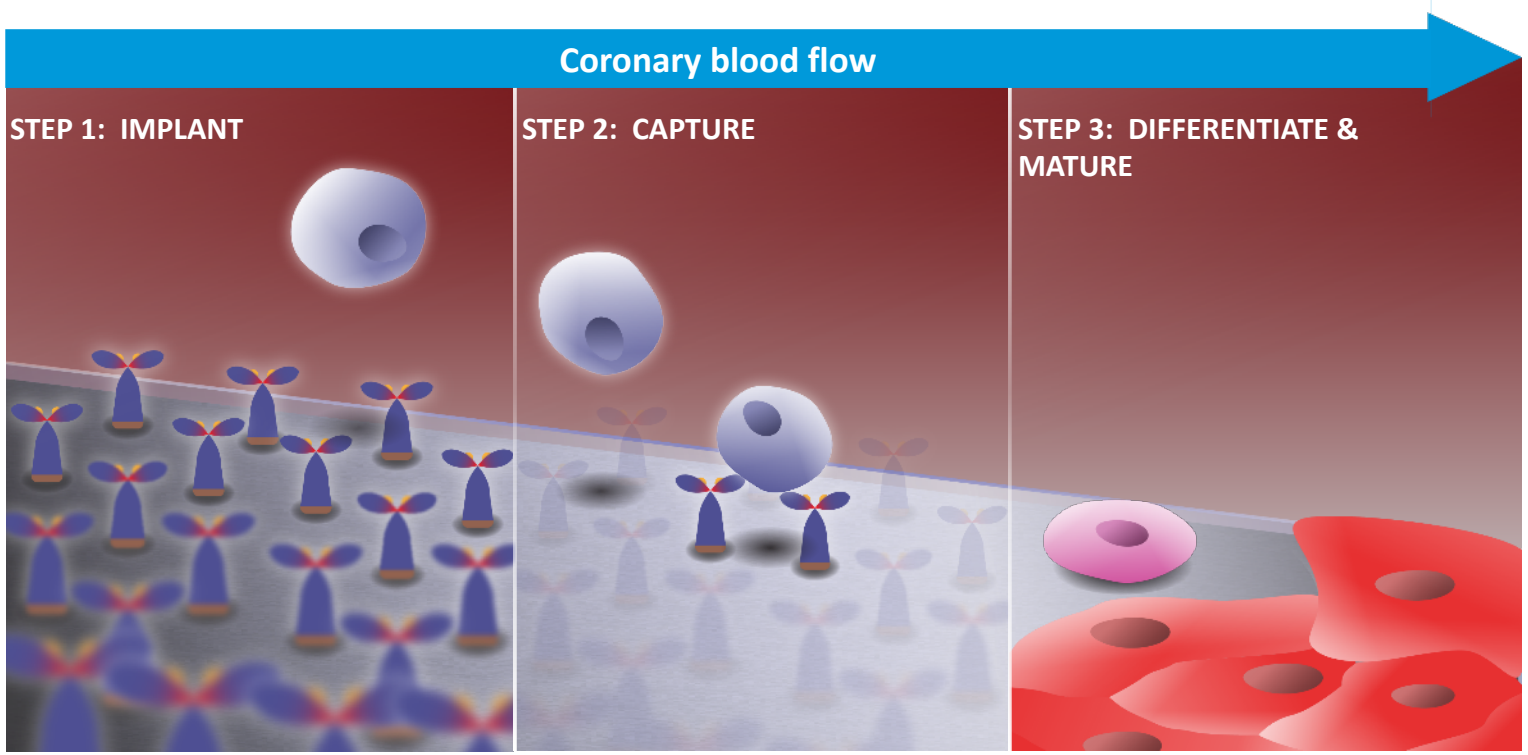
Luminal (Biological therapy)
Immobilized CD34 antibodies enable active capture of EPCs for fast endothelial coverage

Abluminal (Traditional DES)
Bioabsorbable polymer matrix combined with Sirolimus for control of neo-intimal proliferation

Stent (Traditional DES)
Highly conformable stent with excellent radial strength



So what about COMBO? Why do we think we heal better?

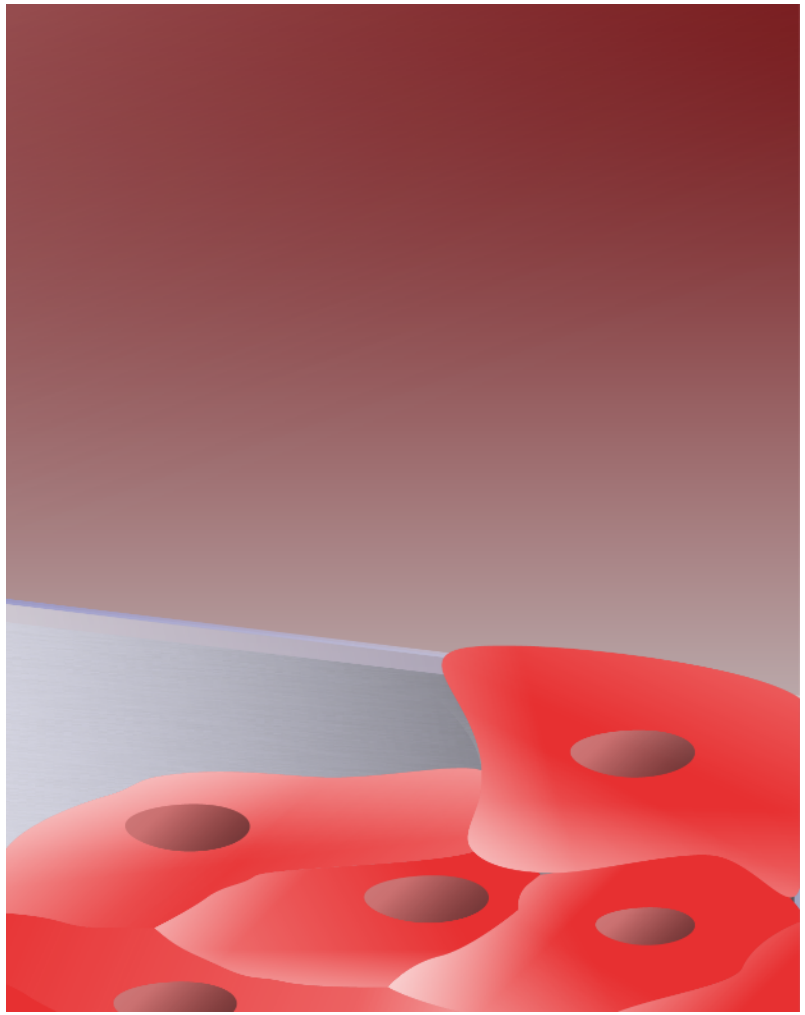


Immobilized anti-CD34 antibodies on the stent surface

Circulating endothelial progenitor cells (EPC) are captures by antibody

EPCs attached to the surface of the stent differentiate and mature into functional endothelial cells

Step 3: EPC differentiation and maturation



…and **mature** into functional endothelial cells

Data shows confluence within weeks
and maturation within 6 to 9 months

Not to scale

COMBO Technology

1 Proven healing concept

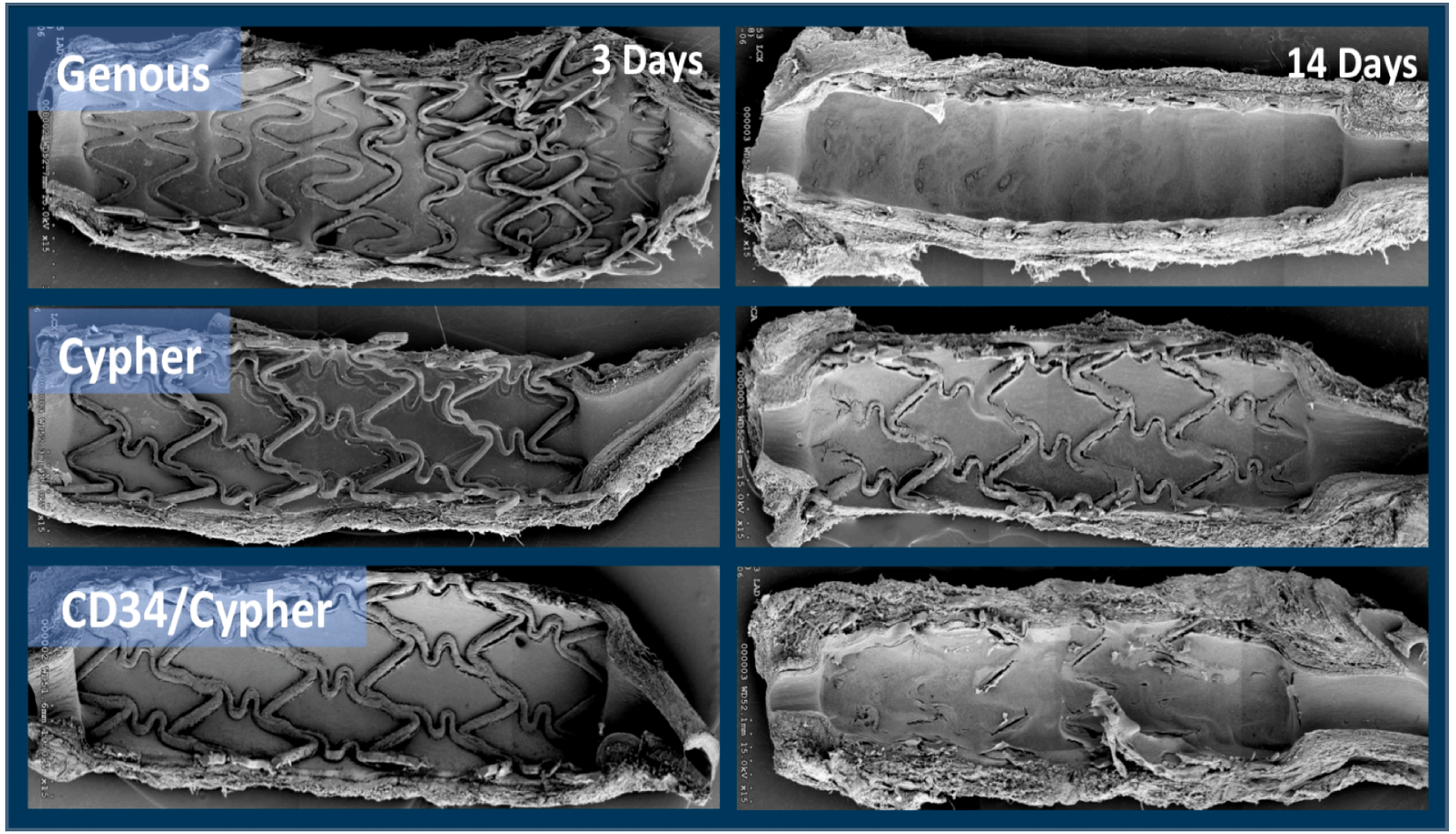
Evidence:

- Porcine study
  - Better coverage at 14 days
- Rabbit model study
  - Better endothelialization vs EES at 28 days
- EGO COMBO
  - Progression of coverage
  - regression of neointima 9 => 24 mo
- HARMONEE OCT sub-study

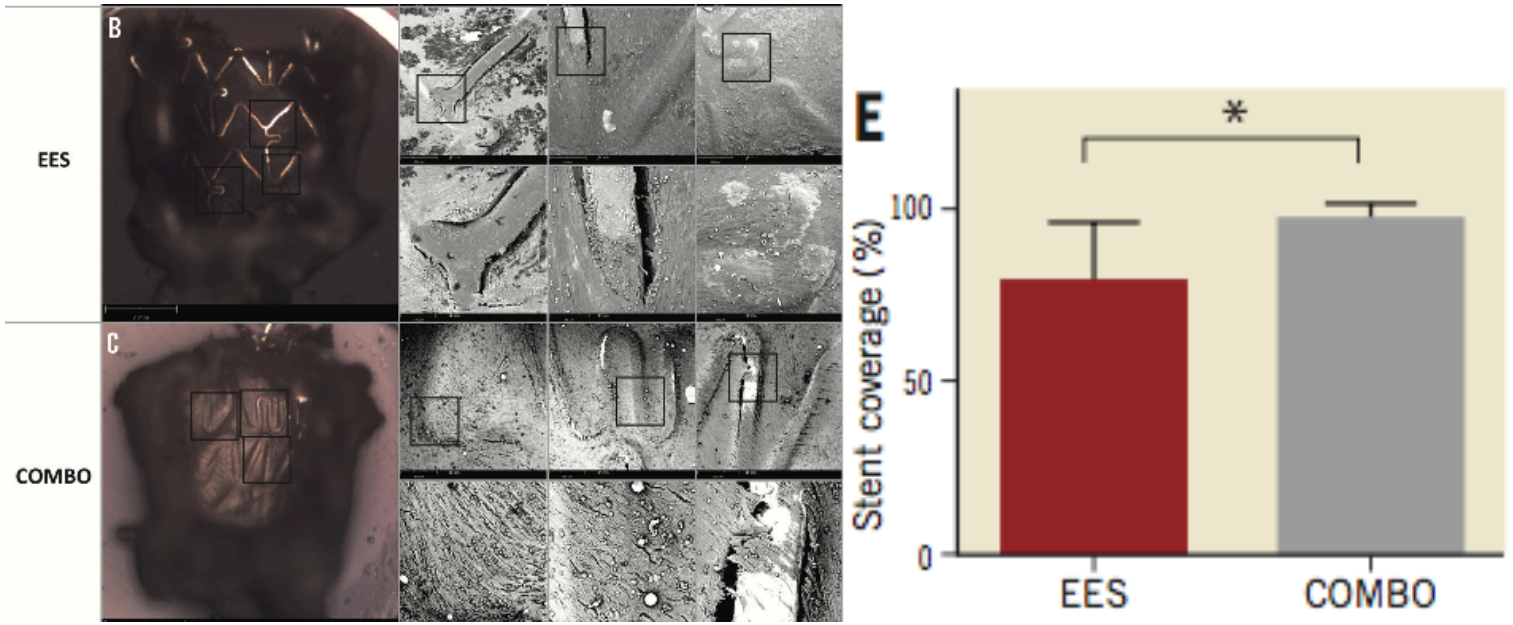
TCT2017

  - Superior coverage with healthy neointima at 12 months
  - More homogeneous neointima vs EES

Porcine Model at 14 days

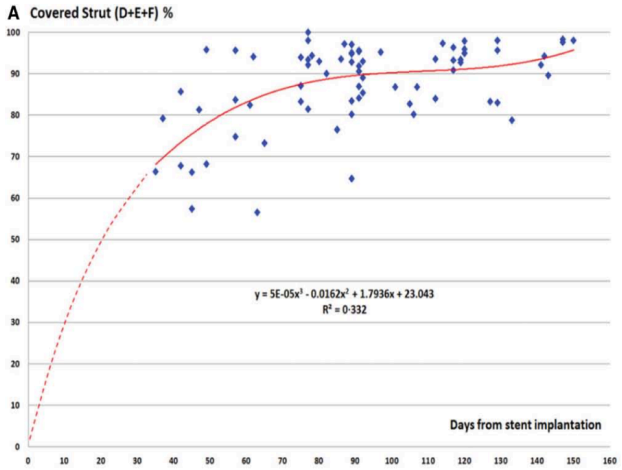


Rabbit Model at 28 days

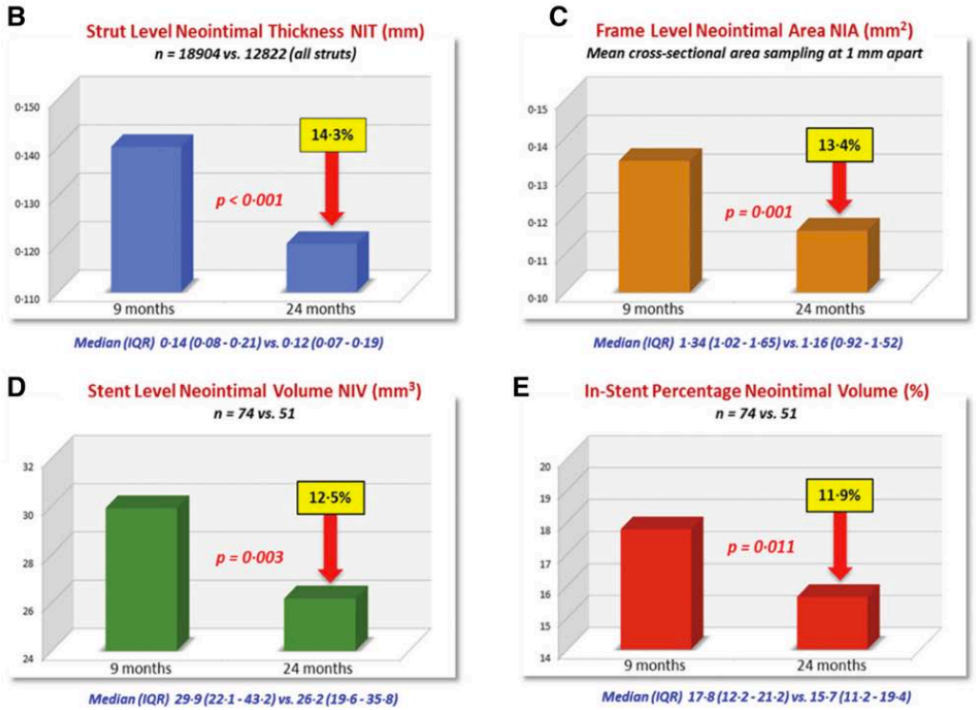


*Quantification of stent strut coverage showed a significantly improved endothelialisation of the COMBO stent compared to the EES (E). *: $p<0.05$*

EGO COMBO Study

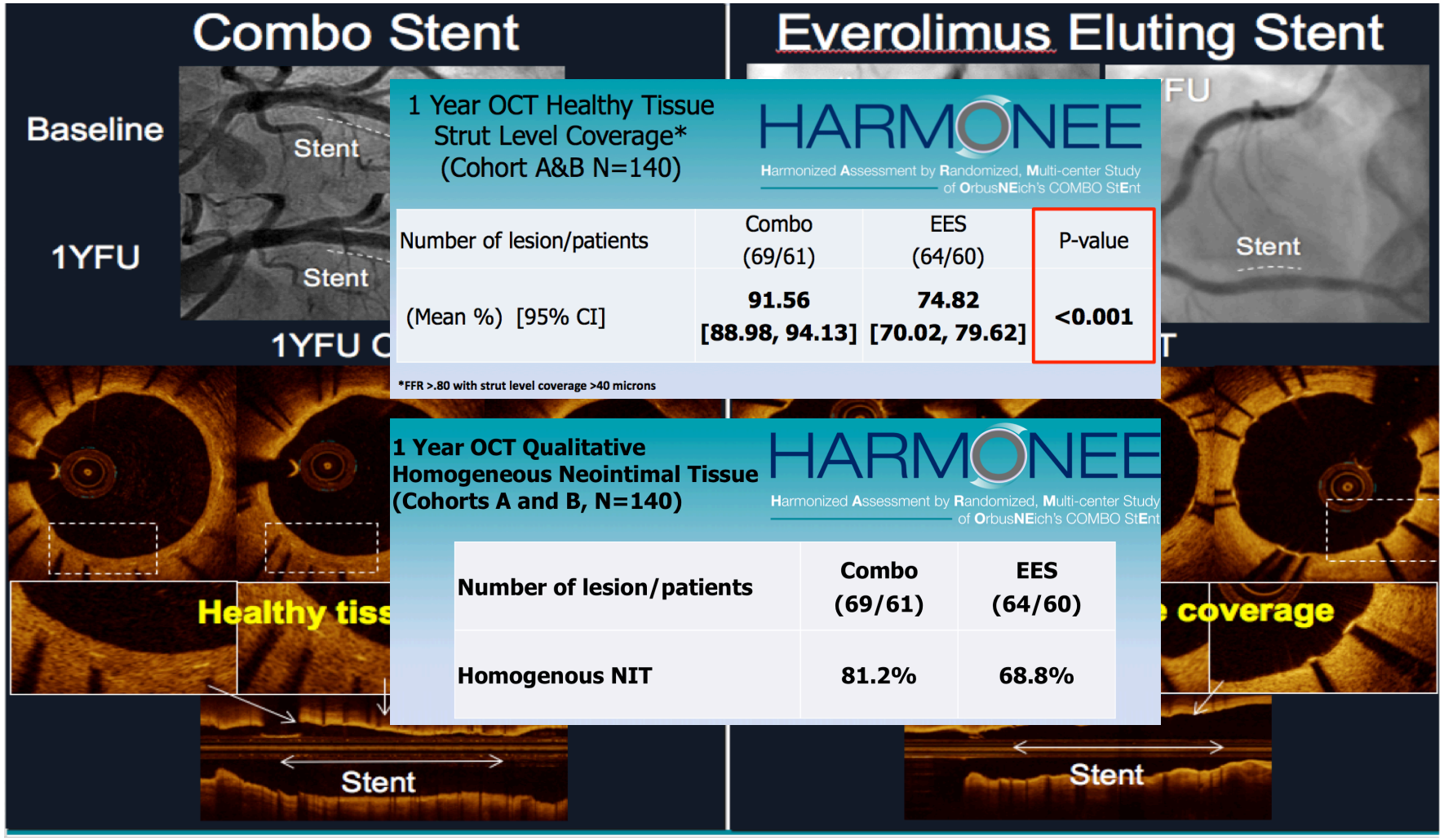


- Approaching 70% coverage at 50 days;
  near 100% by 150 days
- Neointimal regression 9 => 24 months



HARMONEE OCT Substudy

TCT2017



1 Year OCT Healthy Tissue Strut Level Coverage* (Cohort A&B N=140)

HARMONEE
Harmonized Assessment by Randomized, Multi-center Study of OrbusNEich's COMBO StEnt

	Combo (69/61)	EES (64/60)	P-value
Number of lesion/patients			
(Mean %) [95% CI]	**91.56 [88.98, 94.13]**	**74.82 [70.02, 79.62]**	**<0.001**

*FFR >.80 with strut level coverage >40 microns

1 Year OCT Qualitative Homogeneous Neointimal Tissue (Cohorts A and B, N=140)

HARMONEE
Harmonized Assessment by Randomized, Multi-center Study of OrbusNEich's COMBO StEnt

	Combo (69/61)	EES (64/60)
Number of lesion/patients		
Homogenous NIT	**81.2%**	**68.8%**

Courtesy Dr. Akiko Maehara, CRF OCT Core Laboratory

COMBO in perspective

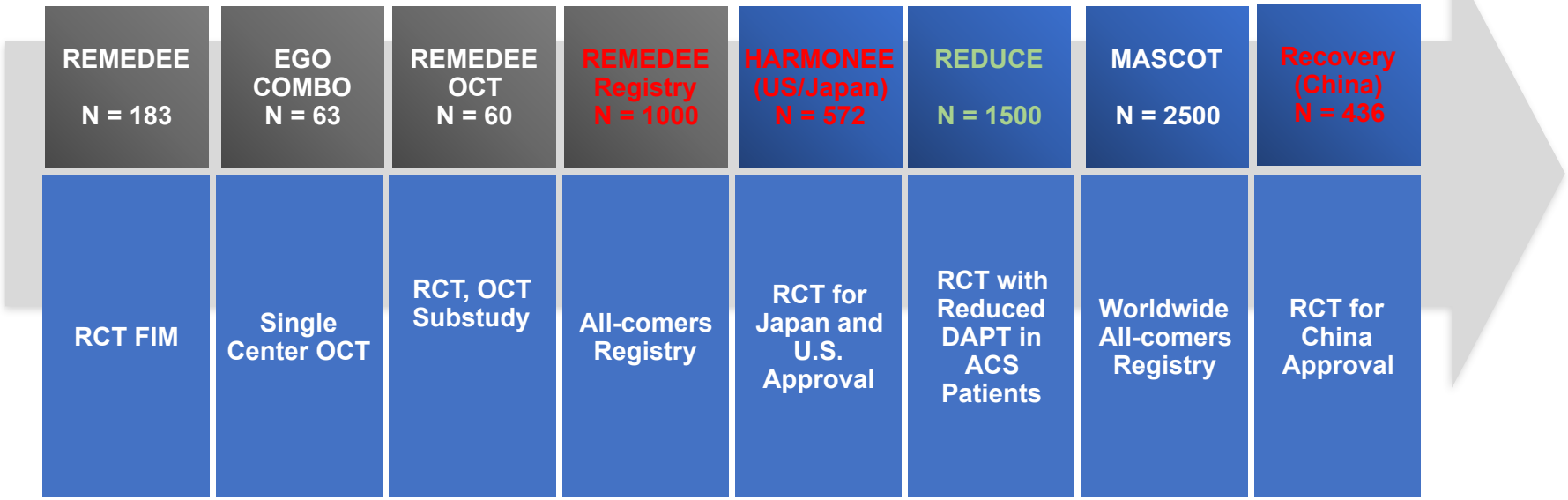
2 COMBO non-inferior to modern DES

Evidence:

- REMEDEE Registry
  - COMBO at 3 years
- MASCOT Registry TCT2017
- HARMONEE RCT TCT2017
- RECOVERY RCT TCT2017

COMBO Dual Therapy Stent Clinical Trial Program

6,000+ Patients planned for clinical trials



REMEDEE Registry

3 year Clinical Outcomes

TCT2017

Three Year Clinical Performance of the Dual-Therapy COMBO stent:

Long-term results from the REMEDEE Registry

Deborah N Kalkman, MD, Pier Woudstra, MD, Laura Kerkmeijer, MD, Marcel A Beijk, MD, PhD, Ian BA Menown, MD, Peter den Heijer, MD, PhD, Harry Suryapranata, MD, PhD, Arnoud WJ van 't Hof, MD, PhD, Andrejs Erglis, MD, Karin E Arkenbout, MD, PhD, Andrés Iñiguez, MD, PhD, Philippe Muller, MD, Jan G Tijssen, PhD Robbert J de Winter, MD, PhD

Academic Medical Center - University of Amsterdam, The Netherlands, Craigavon Cardiac Centre, United Kingdom, Radboud University Medical Center, the Netherlands, Amphia Hospital Breda, The Netherlands, Hospital Álvaro Cunqueiro - Complejo Hospitalario Universitario, Spain, Isala Klinieken, the Netherlands, Pauls Stradins Clinical University Hospital, Latvia, Tergooi Ziekenhuis, the Netherlands, Institut National de Cardiochirurgie et de Cardiologie Interventionnelle, Luxembourg

Background

The bio-engineered COMBO stent (OrbusNeich, The Netherlands) is a dual-therapy stent. This device comb… layer with a novel circumferential … antibody coating captures circulating … 1, step 1), that can differentiate int… surface (Figure 1, step 3). This techno… of dual antiplatelet therapy after p… There is, however, no 3 years clinica… present the first results of all-comers … with a follow-up duration of 3 years.

cardiac death, target vessel myocardial infarction and target lesion revascularization) at 3 year follow-up is the primary focus of this

Results

Endpoints are presented in Table 2. Kaplan-Meier estimate of target

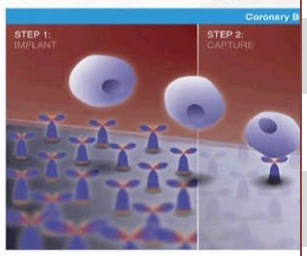
Events at 1, 2 and 3 years (matched analysis)	1 year	2 years	3 years
N	1000	1000	1000
TLF	**5.70%**	**8.50%**	**10.70%**
Cardiac death	1.70%	3.00%	4.10%
Target vessel MI	0.70%	1.20%	2.00%
Target Lesion Revasc	4.30%	5.90%	7.10%
Def/prob ST	0.60%	0.70%	0.80%

…l 3 year follow-up

…r follow-up		Three year follow-up	
…=	(%)	N=	(%)
…4	(8.5)	105	(10.7)
…0	(3.0)	40	(4.1)
…2	(1.2)	19	(2.0)
…8	(5.9)	69	(7.1)
6	(0.6)	7	(0.7)
1	(0.1)	1	(0.1)

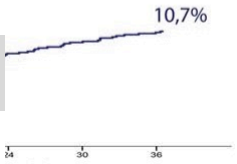
…et vessel revascularization. TVF: target vessel

Figure 1. The dual-therapy stent …



The endothelial progenit cell (EPC) capturing … differntiate into mature endothelium, re-estab…

…ear follow-up



Methods

The prospective, multicentre, investigator-initiated, REMEDEE Registry evaluates clinical outcomes after COMBO stent treatment in a 1000 all-comers patient population. Patients were enrolled between June 2013 and March 2014. Patients had a mean of 65yrs ±11, 26% are females and 18% of patients have diabetes mellitus (DM). In 30% of patients there was an urgent indication for PCI, 60% of lesions were AHA/ACC lesion type B2 or C. Target lesion failure (a composite of

AHA/ACC lesion type B2/C	58.9	
Lesion length, mm	15.0	12-20
Reference vessel diameter, mm	3.0	3.0-3.5
Percentage stenosis by visual estimate	90	80-99
Total stent length, mm	21.4	±10.5
Total stent diameter, mm	3.2	±0.5

Values are valid %, mean ± SD, or median (interquartile range). CAD: coronary artery disease. CABG: coronary artery bypass graft. PCI: percutaneous coronary intervention. TIMI grade flow. AHA/ACC: American Heart Association/American College of Cardiology classification.

Conclusion

Three year clinical outcomes after COMBO stent placement are presented in this analysis. Low event rates are observed in all-comers patients treated with the dual-therapy stent.

Moderated poster session TCT 2017
Date: October 31, 2017
Session N°: COMBO Stent Studies
Abstract N°: 427

Contact information:
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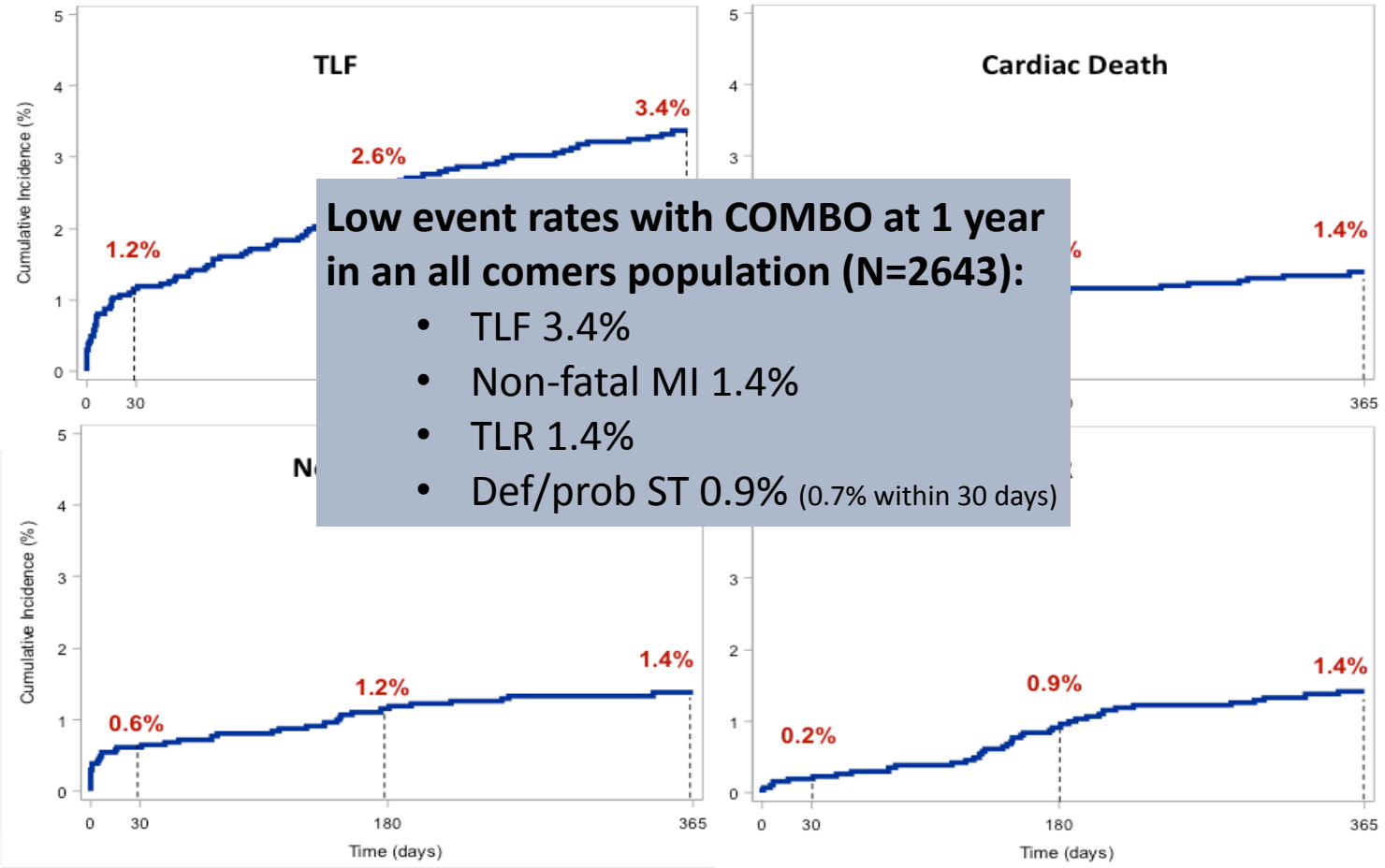
The Academic Medical Center received an unrestricted research grant from OrbusNeich Medical BV.

MASCOT Registry

TCT2017

1 Year Clinical Outcome, 2643 patients

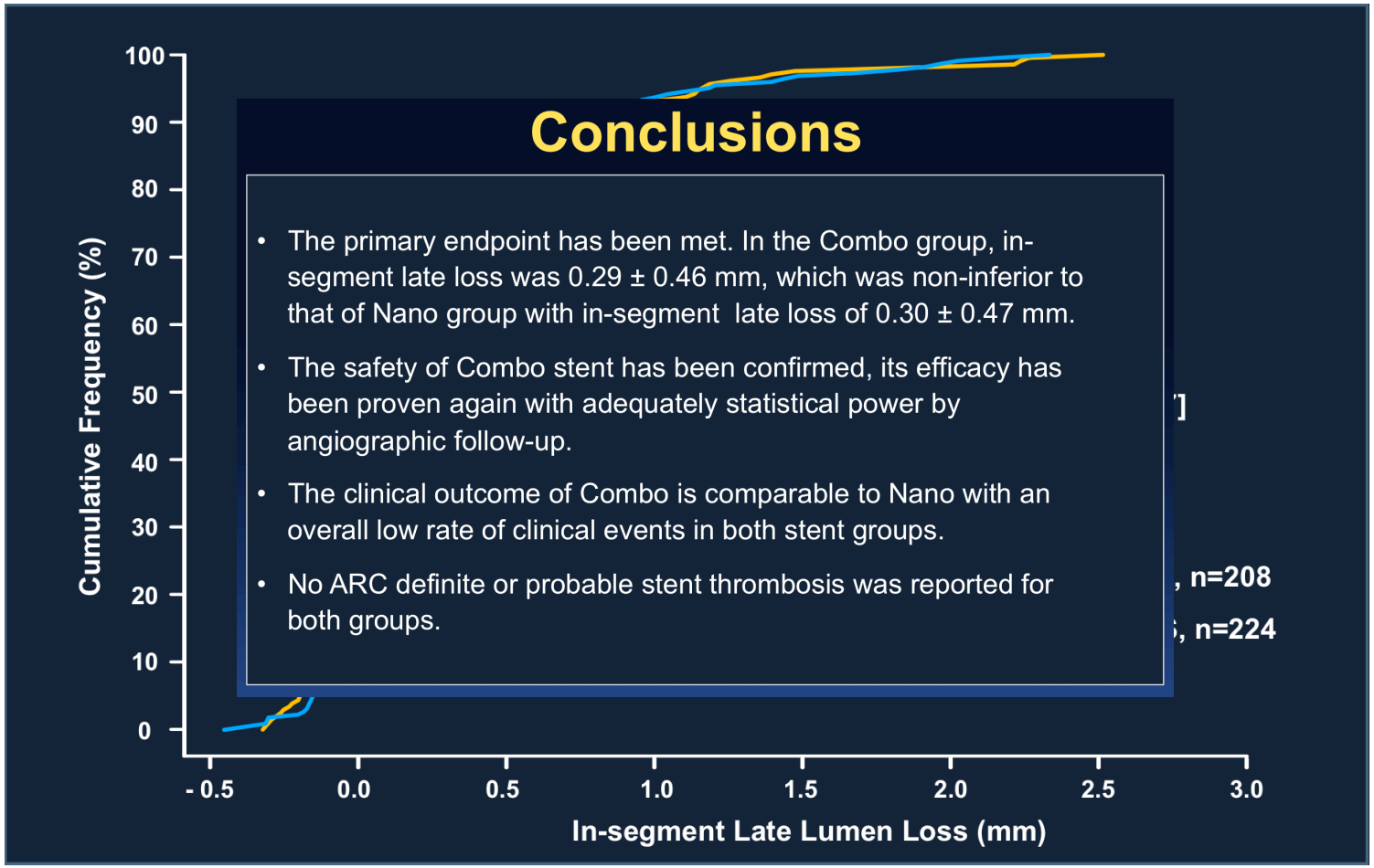


Low event rates with COMBO at 1 year in an all comers population (N=2643):

- TLF 3.4%
- Non-fatal MI 1.4%
- TLR 1.4%
- Def/prob ST 0.9% (0.7% within 30 days)

RECOVERY (N=440)

Cumulative Frequency Distribution of In-Segment LL



3 Proven clinical performance in ACS

Evidence:

- Singapore STEMI Registry (117 STEMI patients)
- REDUCE (1500 ACS patients)

TCT2017

SINGAPORE STEMI Registry

(N=117)

Table 3. Clinical outcomes at 30 days, 6 months, and 12 months.

	1 month (n=117)	6 months (n=117)	12 months (n=117)
Death	4 (3.4%)	4 (3.4%)	6 (5.1%)
Cardiac death	4 (3.4%)	4 (3.4%)	5 (4.3%)
MI	2 (1.7%)	3 (2.6%)	4 (3.4%)
TVMI	2 (1.7%)	3 (2.6%)	3 (2.6%)
Definite ST	2 (1.7%)	3 (2.6%)	3 (2.6%)
Definite/probable ST	4 (3.4%)	5 (4.3%)	5 (4.3%)
TLR	2 (1.7%)	4 (3.4%)	4 (3.4%)
TVR	2 (1.7%)	4 (3.4%)	4 (3.4%)
TLF	6 (5.1%)	8 (6.8%)	9 (7.7%)
MACE	6 (5.1%)	8 (6.8%)	11 (9.4%)

Values are n (%). MACE: major adverse cardiac events; MI: myocardial infarction; TLF: target lesion failure; TLR: target lesion revascularisation; TVMI: target vessel myocardial infarction; TVR: target vessel revascularisation; ST: stent thrombosis

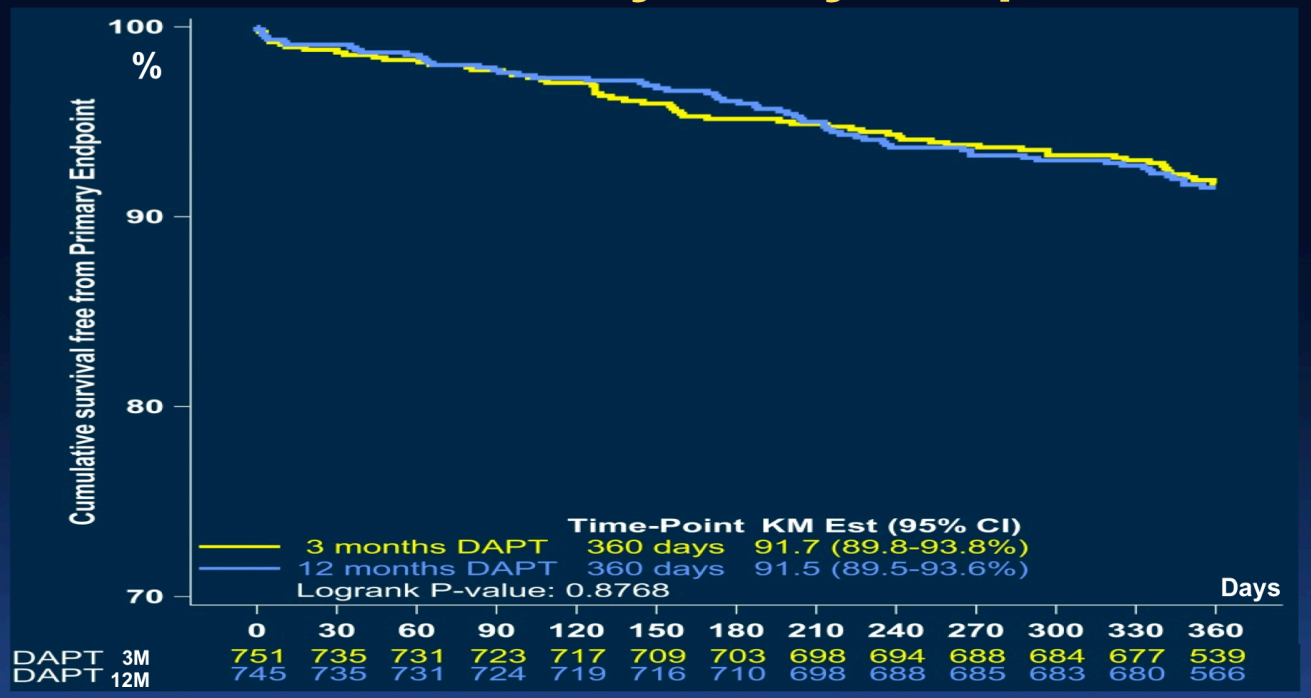
The COMBO dual therapy stent in patients presenting with acute ST-elevation myocardial infarction: a one-year follow-up study

Rajiv Ananthakrishna, MD, DM; William Kristanto, MBBS; Li Liu, MD; Poay Huan Loh, MB, BCh; Edgar L. Tay, MBBS; Koo Hui Chan, BM, MD; Mark Y. Chan, MBBS, MHS; Chi-Hang Lee, MBBS, MD; Adrian F. Low, MBBS; Huay Cheem Tan, MBBS; Joshua P. Loh*, MBBS

Department of Cardiology, National University Heart Centre, Singapore, Singapore

REDUCE (1500 ACS patients)

Results: Primary Study Endpoint



Analysis set	3 month DAPT n = 729	12 month DAPT n = 734	Risk difference	Upper bound of 1 sided 97.5% CI	OR (95% CI)	P non-inferiority
Intention to treat	8.2	8.4	-0.002	0.027	0.97 (0.67-1.41)	<0.001

4 DAPT flexibility where needed

Evidence:

- REMEDEE Registry
- REDUCE
- MASCOT

REMEDEE Registry

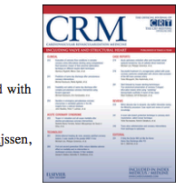
DAPT cessation

Table 2 Reason for DAPT cessation

DAPT: dual antiplatelet therapy, VKA: vitamin K antagonist, NOACs: novel oral anticoagulants, AF: atrial fibrillation.

Reason for DAPT cessation	30 days follow-up N =	180 days follow-up N =	Events at 1 year follow-up N=
patient taking VKA, warfarine			
or NOACs	27	40	0
for AF	17	23	0
for LV thrombus in apex	3	3	0
allergy	2	3	0
bleeding	3	4	0
planned surgery	0	2	0
non-adherence	2	8	0
physician advice	1	5	0
unknown	10	16	0
Total	48	78	0

Accepted Manuscript



Early Discontinuation of Dual Antiplatelet Therapy in Patients Treated with the Bio-Engineered Pro-healing Sirolimus-eluting (COMBO) Stent

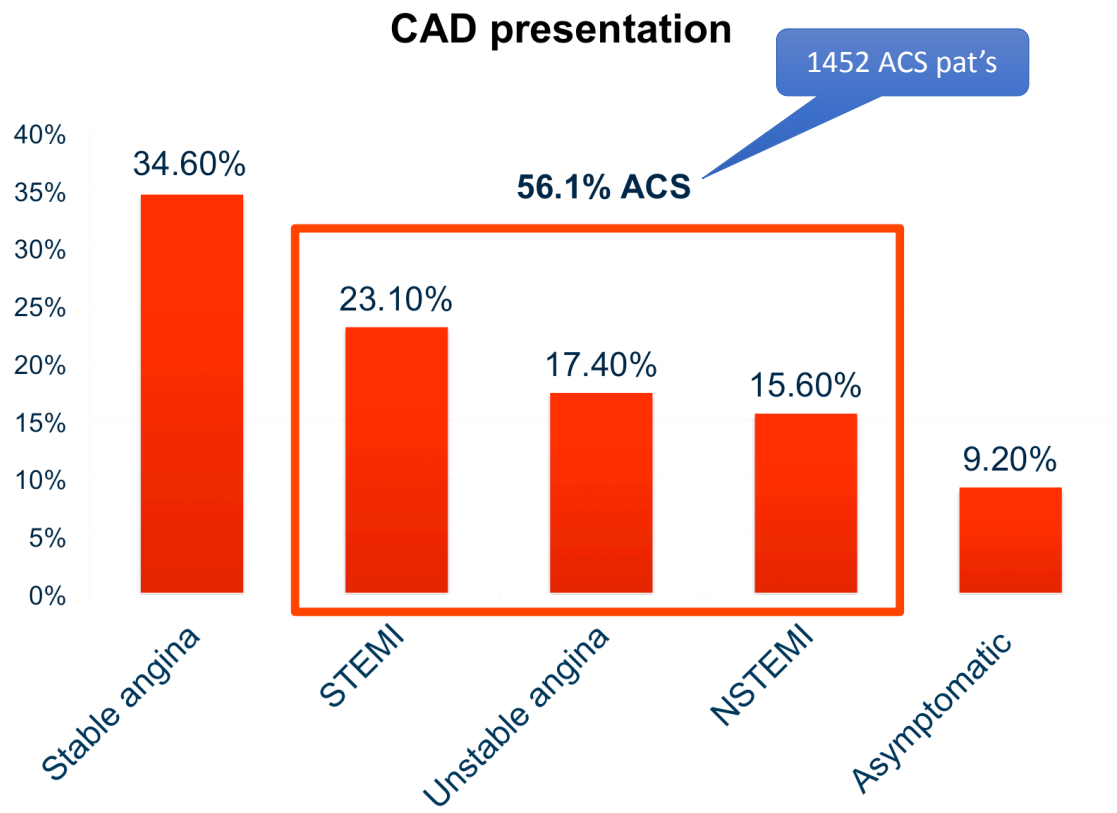
Deborah N. Kalkman, Pier Woudstra, Ian B.A. Menown, Jan G. Tijssen, Marcel A.M. Beijk, Robbert J. de Winter

PII: S1553-8389(17)30392-5
DOI: doi: 10.1016/j.carrev.2017.10.005
Reference: CARREV 1152

To appear in: *Cardiovascular Revascularization Medicine*

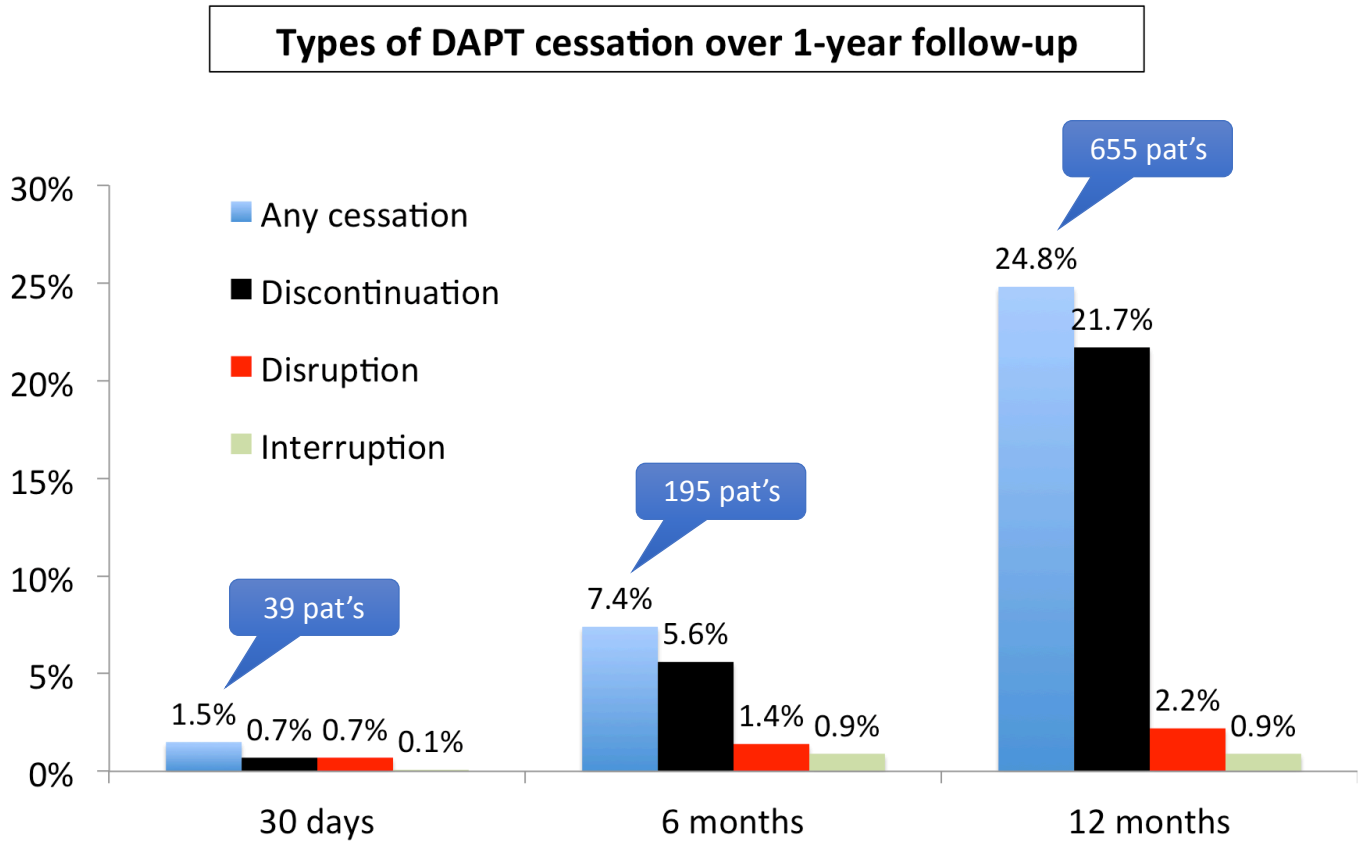
Received date: 7 March 2017
Revised date: 12 October 2017
Accepted date: 12 October 2017

MASCOT (N=2643)



MASCOT (N=2643)

DAPT cessation

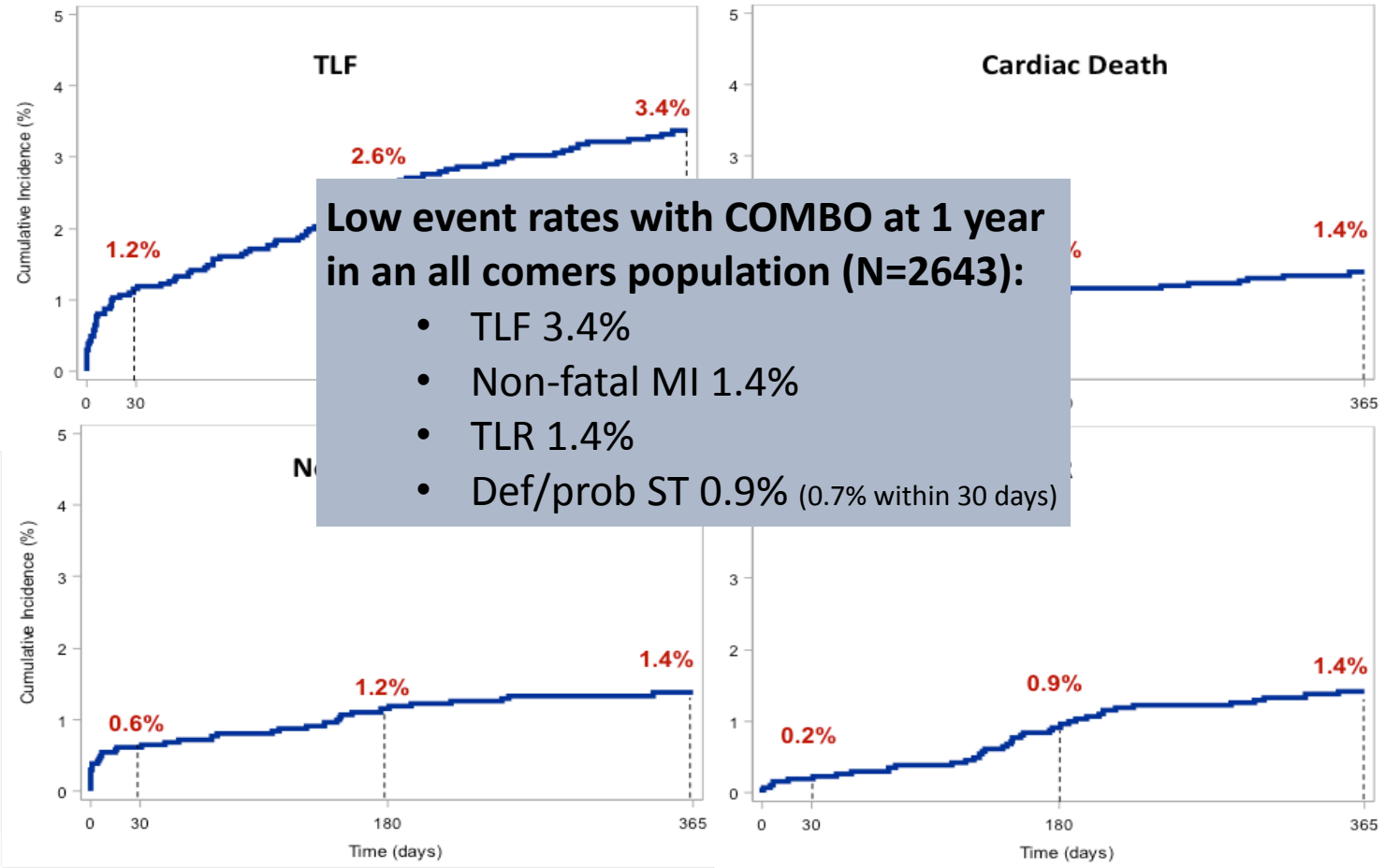


Awaiting subgroup analysis

MASCOT Registry

TCT2017

1 Year Clinical Outcome, 2643 patients



Low event rates with COMBO at 1 year in an all comers population (N=2643):

- TLF 3.4%
- Non-fatal MI 1.4%
- TLR 1.4%
- Def/prob ST 0.9% (0.7% within 30 days)

What the others do?

Study	Area	NCT #	Status	Primary Completi	Study Device	Manufacturer	Comparator	Population	DAPT duration	N
STOPDAPT	Japan	NCT01659034	completed	Oct-14	Xience	Abbott	none	All comer	3 months	1525
LEADERS FREE	EU, Asia	NCT01623180	completed	May-15	BioFreedom	BioSensors	BMS	HBR	1 mo	2456
SENIOR	EU	NCT02099617	ongoing	May-17	Synergy II	Boston Scientific	BMS	Elderly (>75)	1 mo (SCAD) 6 mo (ACS)	1200
DAPT STEMI	EU	NCT014							6 vs 12 mo	1100
REDUCE	**EU, Asia**	**NCT021**							**3 vs 12 mo**	**1500**
POEM	EU	NCT031							1 mo	1023
LEADERS FREE II	USA	NCT028							1 mo	1200
EVOLVE	EU, US, Jap, Bra	NCT02605447	ongoing	Apr-19	Synergy	Boston Scientific	none	HBR (SCAD)	3 mo	2250
e-Ultimaster	O-US	NCT02188355	ongoing	Sep-19	Ultimaster	Terumo	none	All comer	study non-compliance at > 1 month	37000
MASTER DAPT	EU, Asia, ME	NCT03023020	ongoing	Oct-19	Ultimaster 1 mo DAPT	Terumo	Ultimaster 12 mo DAPT	HBR	1 mo vs 12 mo	4300
XIENCE Short DAPT	US	NCT03218787	ongoing	Jun-20	Xience	Abbott	none	HBR	3 mo	2000
LEADERS FREE III	EU	NCT03118895	planned	tbd	BioFreedom	BioSensors	none	HBR	1 mo	370

- COMBO has randomized data 3 vs 12 mo DAPT
- Others have:
  - No data available yet …, or
  - no comparator,
  - BMS comparator,

Summary

- Proven healing concept
- non-inferior to modern DES (all comers)
- Proven clinical performance in ACS (N=3597)
- COMBO's safety profile allows individualized DAPT duration in high risk patients: REDUCE study