CRT 17 CARDIOVASCULAR RESEARCH TECHNOLOGIES

Long-term Clinical Outcomes of a Unique Sirolimus-eluting Stent with Fully Absorbable Polymer Coating

5-Year Results from DESSOLVE I and II Trials

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Relations of Interest Disclosure

Institutional Research Grants:

Micell Technologies, MicroPort, St Jude-Abbott, Terumo

Advisory Board & honoraria:

MicroPort

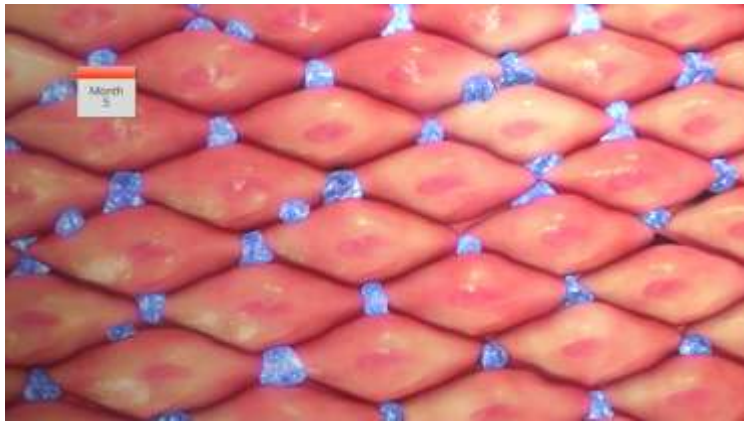
Shareholder & non-executive Board member:

Argonauts, Genae

Crystalline Sirolimus with a Rapidly Absorbed Polymer Coating

MiStent Crystalline Sirolimus

- *Unique to MiStent SES, micro-crystalline morphology*
- *Controlled and prolonged elution, as opposed to use of an amorphous, rapid-release form of the drug*



MiStent Rapidly Absorbable Polymer

- *Flows off the stent struts in 45 - 60 days*
- *Rapidly absorbed from tissue within 90 days*
- *Quickly eliminates source of inflammatory response*

MiStent Thin-Strut Stent

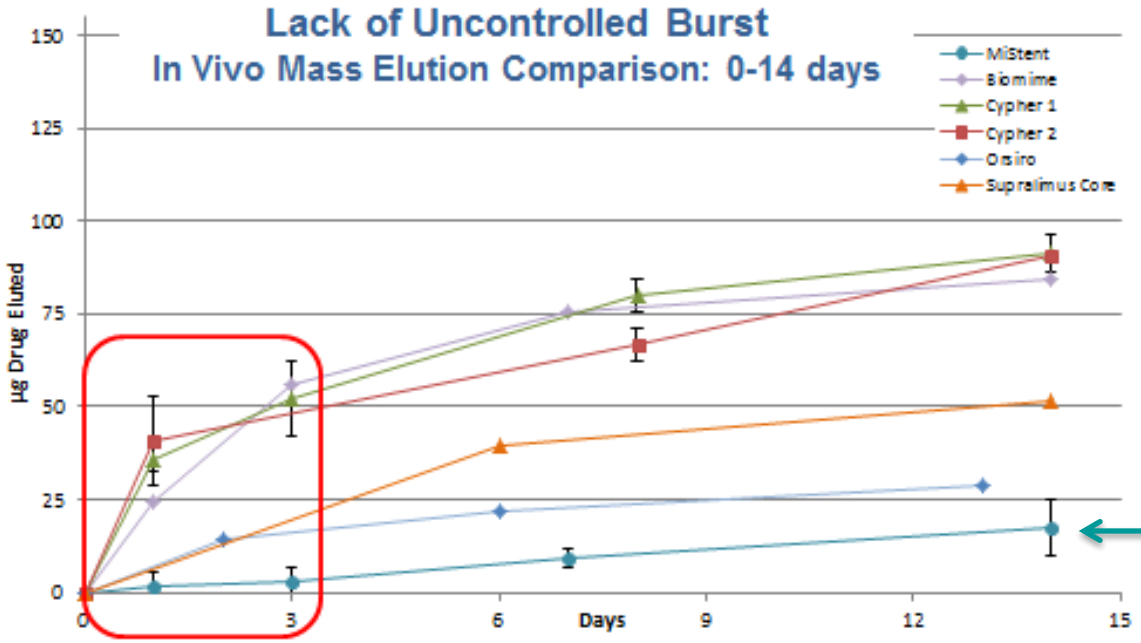
- *Cobalt-chromium*
- *Strut thickness 64 microns*

Reference: Carlyle, W., et al. J. Control Release. 2012

No Drug Burst with Therapeutic Tissue Levels Up To 9 Months

Elimination of Polymer Within 90 Days

No Detectable Sirolimus Blood Levels

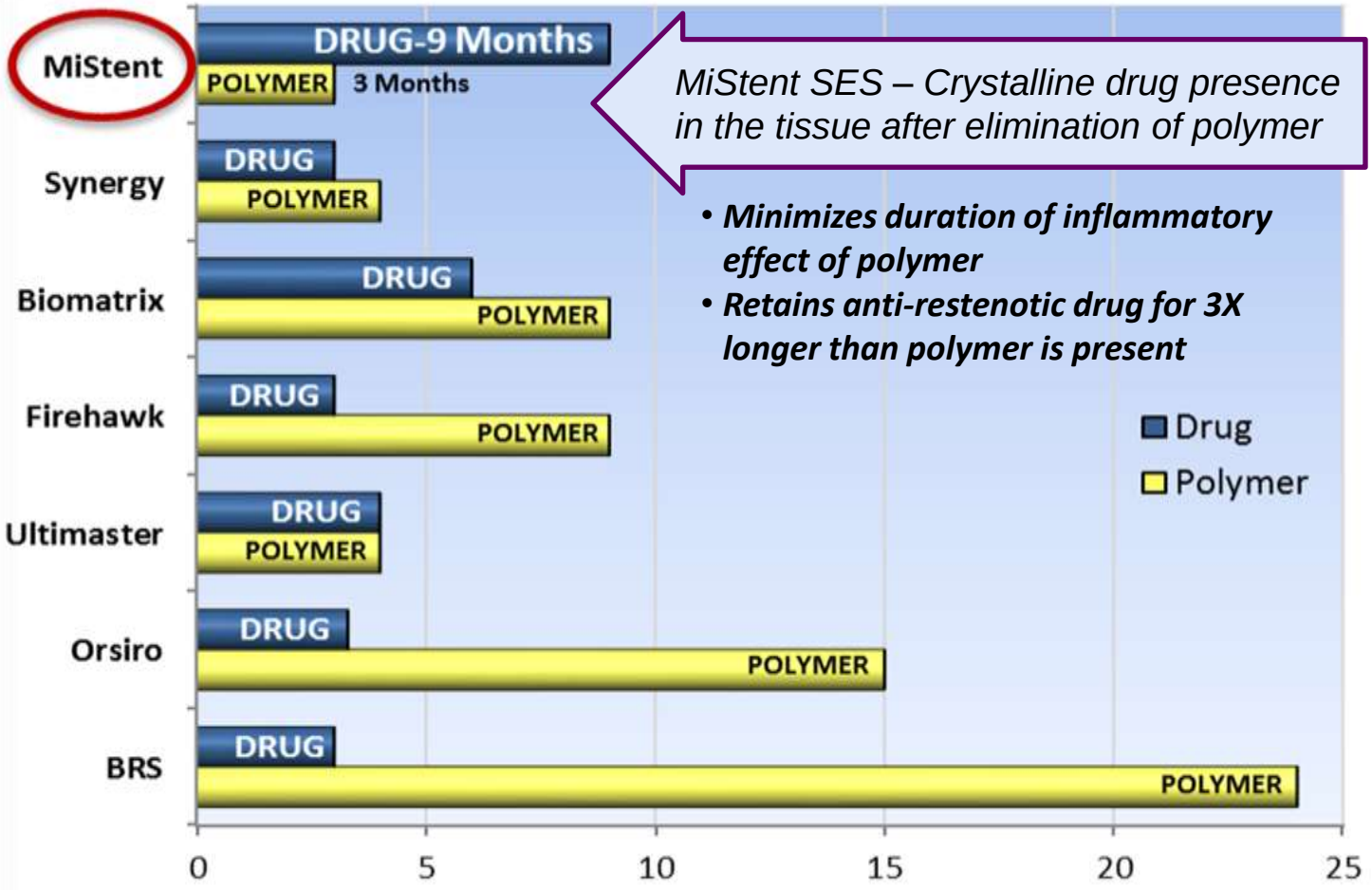


MiStent SES

An initial uncontrolled burst of drug may delay re-endothelialization and coverage of the stent struts[1]

[1] Deconinck, E., et al. J. Pharm. Sci. 2008

MiStent SES®
Highly Differentiated Drug-Eluting Stent



MiStent SES – Crystalline drug presence in the tissue after elimination of polymer

- ***Minimizes duration of inflammatory effect of polymer***
- ***Retains anti-restenotic drug for 3X longer than polymer is present***

Carlyle, W., et al. J. Control Release. 2012
Adapted from K. Dawkins, TCT 2014 & product websites

DESSOLVE I and II Investigational Sites

STUDY PRINCIPAL INVESTIGATORS

William Wijns, MD PhD & **John Ormiston,** MB ChB

Belgium
Genk - Mathias Vrolix*
Antwerp - Stefan Verheye
Brussels - Danny Schoors
Aalst - William Wijns*
Leuven - Walter Desmet
Hasselt - Edouard Benit

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London - Carlo Di Mario
Southampton - Iain Simpson
Norwich - Alisdair Ryding
Cambridge - Cameron Densem
Brighton - David Hildick-Smith

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Zwolle - Marcel Gosselink
Nieuwegein - Maarten Jan Suttorp
Utrecht - Pieter Stella
Tilburg - Wilbert Aarnoudse

France
Massy - Marie-Claude Morice
Toulouse - Jean Fajadet
Quincy - Philippe Garot

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Orebro - Leszek Zagozdzon
Gothenberg - Per Albertsson

New Zealand
Christchurch - Dougal McClean
Mercy - John Ormiston*
Auckland - Jim Stewart*
Wellington - Scott Harding

Australia
Melbourne - Robert Whitbourn*

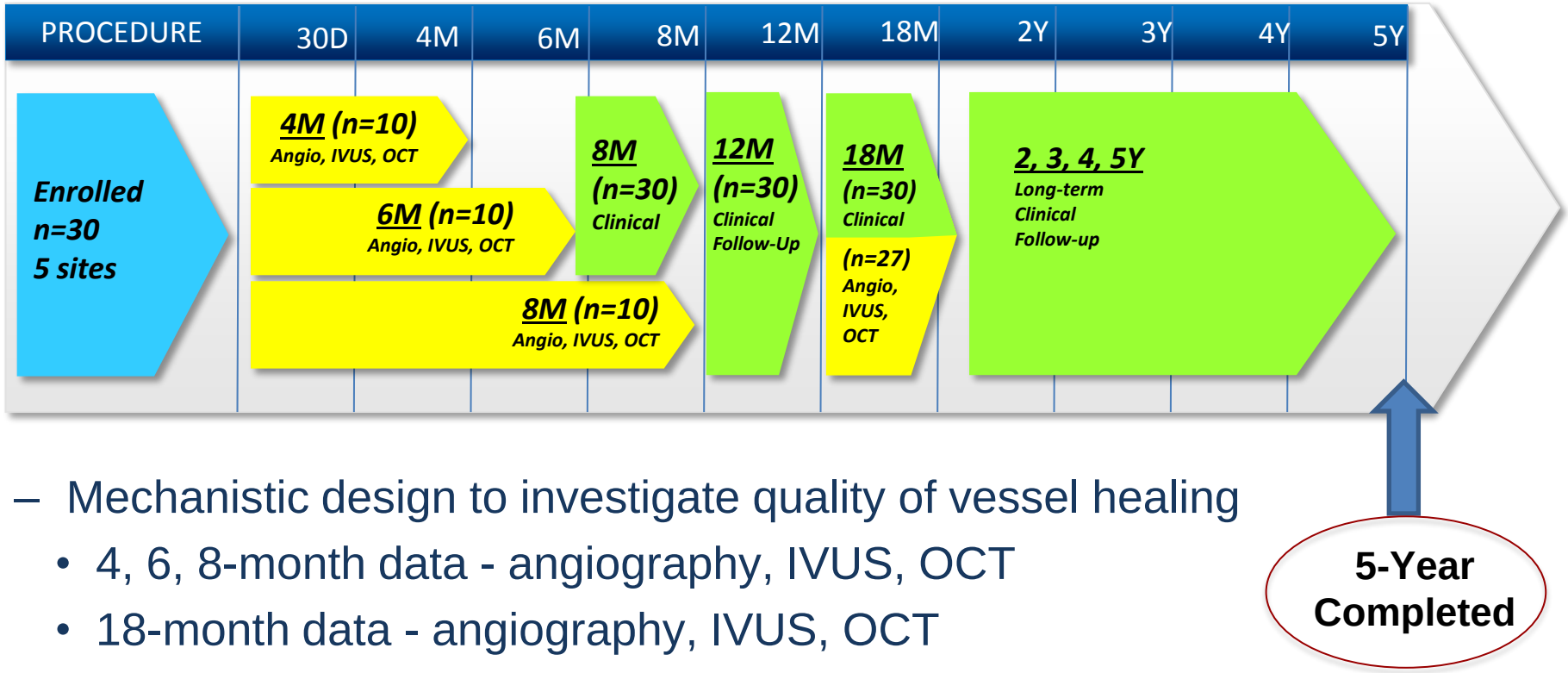
DESSOLVE I sites

Data Management and Monitoring
Harvard Clinical Research Institute (HCRI)
Genae Associates
Pacific Clinical Research Group (PCRG)

Core Labs
Angiography - Yale - Alexandra Lansky
IVUS - Stanford - Peter Fitzgerald
OCT - Case Western - Hiram Bezerra, Marco Costa

DESSOLVE I: Study Design

First-in-Human, 30 patients, 5 sites



– Mechanistic design to investigate quality of vessel healing
  - 4, 6, 8-month data - angiography, IVUS, OCT
  - 18-month data - angiography, IVUS, OCT

Ormiston et al. *JACC CI* 2013;*6*:1026-33

DESSOLVE I
Imaging Results

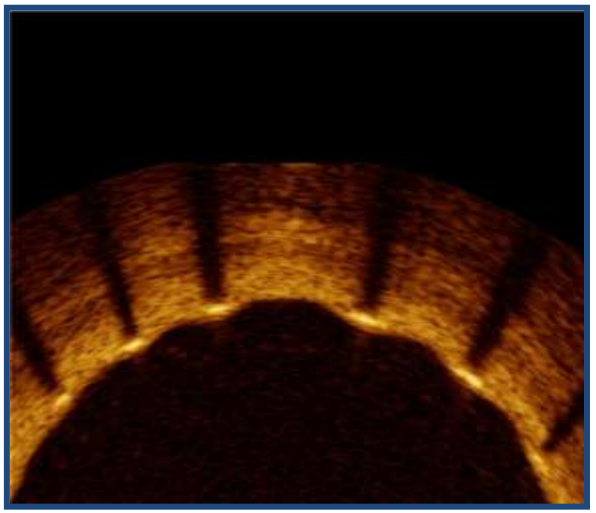
Healing demonstrated by OCT through 18 months

OCT Results

- Imaging with OCT demonstrated thin, homogeneous coverage with high rates of stent strut coverage at 6 - 8 months
- No evidence of definite neoatherosclerosis at 18 months

Median	4-Month Group	6-Month Group	8-Month Group	18-Month Group
% Strut Coverage	93%	97%	96%	100%

Thin homogeneous tissue coverage



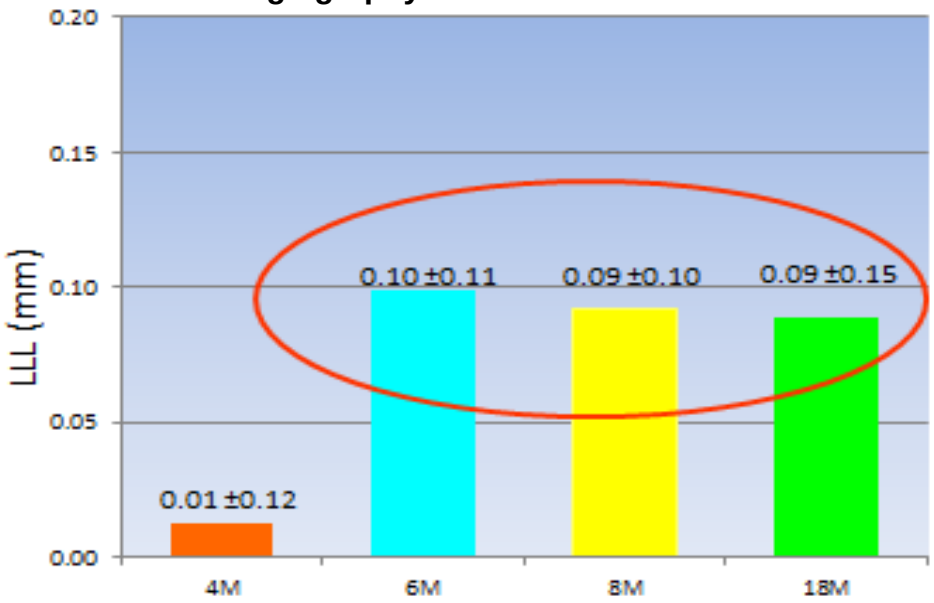
Ormiston, J., et al. JACC CI. 2013
Attizzani, G., et al. Am J Cardiol. 2013

DESSOLVE I Results

No Progression of In-stent Late Lumen Loss From 6/8 to 18 Months Follow Up

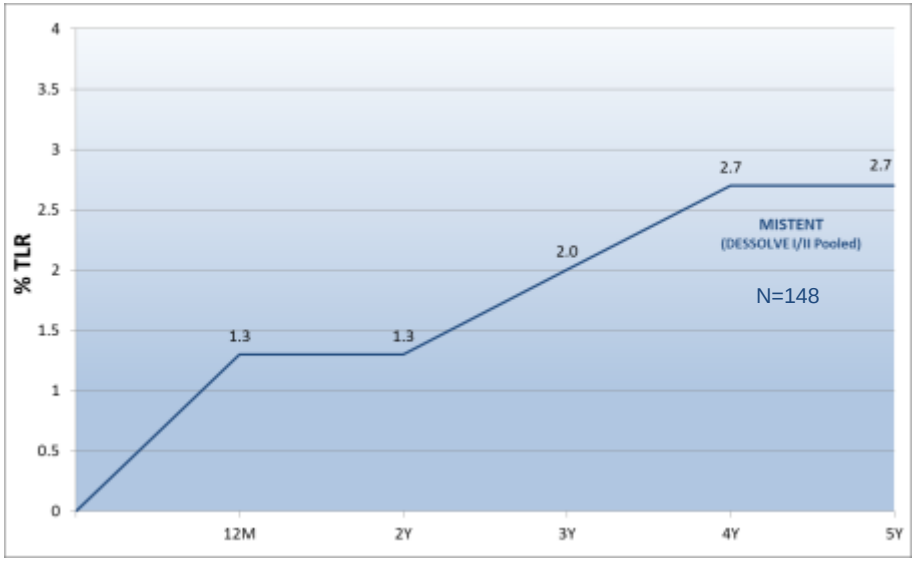
Results in low progression of target lesion revascularization (TLR) at 5 Years

Angiography In-Stent Late Lumen Loss



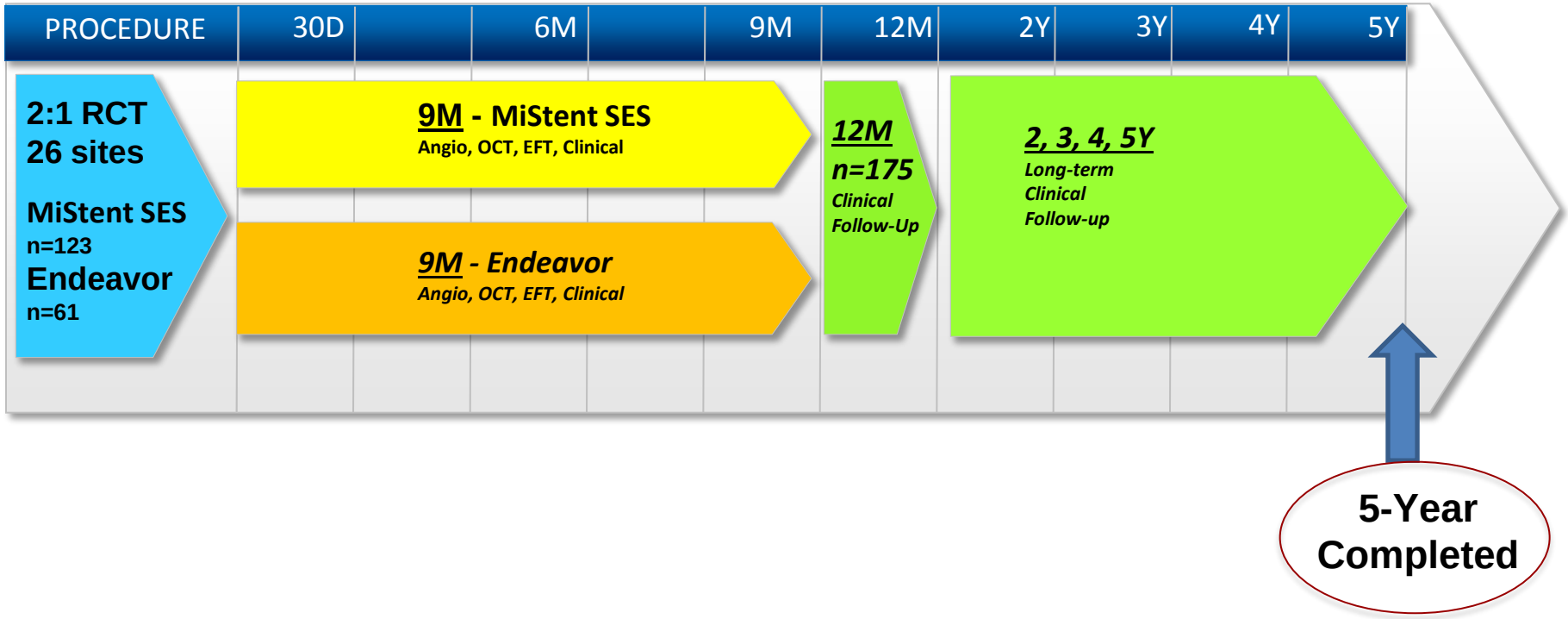
Data represents matched cases for each time point with serial 3D analysis: 4M n=9, 6M n=9, 8M n=9, 18M n=27

CD-TLR Over Time



DESSOLVE II
Study Design

2:1 RCT design for superiority of in-stent LLL at 9 months vs Endeavor
184 patients at 26 sites



Wijns W et al. EuroInterv 2015;10:1383-90

DESSOLVE II: Inclusion / Exclusion Criteria

Key Criteria

Patient

- stable or unstable angina pectoris (Class I, II, III or IV), documented ischemia, or documented silent ischemia
- no recent Q wave MI (<72 hrs) or no elevated cardiac biomarkers

Target Lesion

- planned single, de novo, types A, B1 or B2 coronary lesions (according to the ACC/AHA classification) in the native coronary artery with >50% diameter stenosis
- vessel diameter 2.5 to 3.5 mm - maximum **30** mm long stent
- exclude if highly calcified, tortuous, thrombus present, proximal angulation
- exclude if located at side branch >2.5mm, ostial location, previously treated vessel

Non-Target Lesion

- may treat one critical non-target lesion in another vessel prior to target lesion

DESSOLVE II
9-Month Results

Angiography

The MiStent SES was superior to Endeavor for the primary endpoint analysis of in-stent late lumen loss

Measure (Mean)	**MiStent SES** N=103	**Endeavor ZES** N=52	
Late Lumen Loss	0.27 ± 0.46	0.58 ± 0.41	$P < 0.001$

OCT

The proportion of uncovered struts and % strut malapposition was remarkably low in both groups

Measure (Median)	**MiStent SES** N=24	**Endeavor ZES** N=10
% Uncovered Struts	0.34	0.00
% Strut Malapposition	0.00	0.00

Endothelial Function Testing

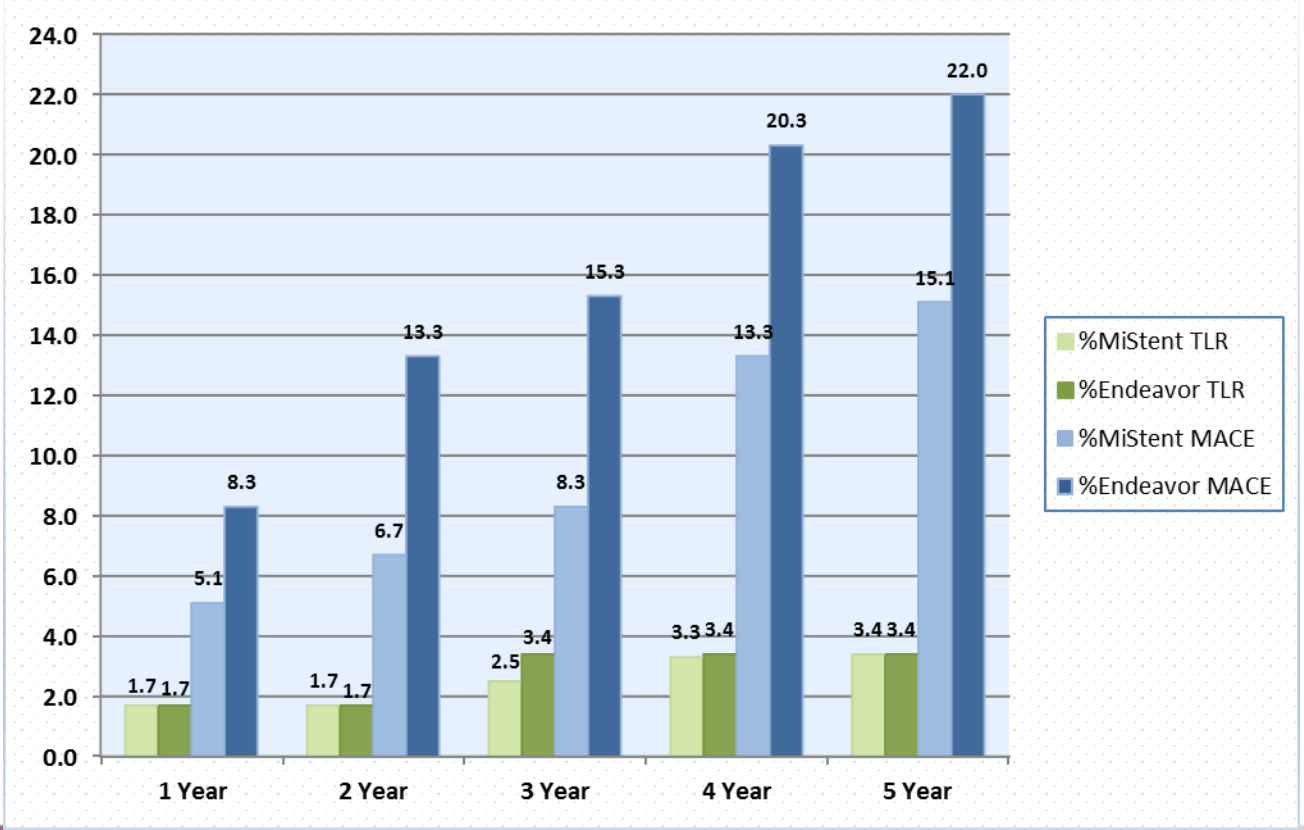
Dilation of the reference vessel segments after pacing indicating normal vasomotor function for both MiStent SES and Endeavor at 9 months

Measure (%)	**MiStent SES** N=19	**Endeavor ZES** N=10
Responders	100%	100%
Non-Responders	0%	0%
Vasoconstrictors	0%	0%

DESSOLVE II
5-Year Clinical Outcomes

Sustained clinical outcomes though 5 years for MiStent SES

- **3.4% TLR rate**
- **No Definite/Probable Stent Thrombosis for MiStent SES**



DESSOLVE I and II Conclusions

MiStent appears to provide outcomes indicative of optimized healing

- **High rate of early strut coverage by OCT**
- **Maintenance of vasomotor function out to 9 months**
- **Absence of late "Catch-Up" in lumen loss out to 18 months**
- **Minimal progression of NIH out to 18 months**
- **No definite / probable Stent Thrombosis through 5 years**
- **Low MACE and TLR rates, stable up to 5 years**

Pooled analysis of patients treated with MiStent SES, which has a unique bioabsorbable coating that provides continued drug delivery in the absence of polymer, suggests long term (5-years) safety and continued efficacy of this novel coronary stent

DESSOLVE Clinical Trials Program

DESSOLVE I ***First-in-Human*** ***N = 30 pts***	Study Initiation: Q4 2010 Five-year follow-up completed: Q1 2016 -In-Stent LLL	***Completed***
DESSOLVE II ***CE Mark Approval*** ***N = 184 pts [vs. Endeavor DES]***	Study Initiation: Q1 2011 Five-year follow-up completed: Q2 2016 -Superiority in-stent LLL at 9M	***Completed***
DESSOLVE III ***Outcomes Trial*** ***N = 1,400 pts [vs. Xience]***	Study Initiation: Q1 2015 Enrollment completed: Q4 2015 -Non-inferiority of TLF at 12M	***Results 2017***
DESSOLVE III ***OCT Sub-study*** ***N = 60 pts [vs. Xience]***	Study Initiation: Q1 2015 Enrollment completed: Q1 2016 -Superiority intimal hyperplasia progression	
DESSOLVE CHINA ***CFDA Approval*** ***N = 428 pts [vs. Tivoli DES]***	Study Initiation: Q2 2015 Enrollment to complete: Q1 2017 -Non-inferiority in-stent LLL at 9M	
DESSOLVE CHINA ***Angiographic Sub-study*** ***N = 170 pts [vs. Tivoli DES]***	Study Initiation: Q2 2015 Endpoint Report: Late 2019 -Superiority LLL progression at 3 years	

DESSOLVE Clinical Trials Program

DESSOLVE JAPAN
PMDA Approval
N = 120 pt study supportive of the DESSOLVE III [vs. Xience]

- Initiated November 2016
- Prospective, balanced, randomized
- Five-year follow-up
- Non-inferiority of TLF at 12 months

CRYSTAL *
U.S. IDE
N = ~2000 pts
[vs. Xience or Promus]

- Prospective, balanced, randomized
- Five-year follow-up
- Non-inferiority of TLF at 12 months

**** Pending review with the FDA***