2019 euro PCR

MeRes-1 Study:
Three-year clinical and two-year multimodality imaging outcomes of thin-strut sirolimus-eluting bioresorbable vascular scaffold in patients with coronary artery disease

Dr. Praveen Chandra
MD, DM, FACC, FESC, FSCAI, FAPSIC
Chairman- Interventional Cardiology
Medanta-The Medicity, India

On Behalf of MeRes-1 Investigators

Disclosure Statement of Financial Interest

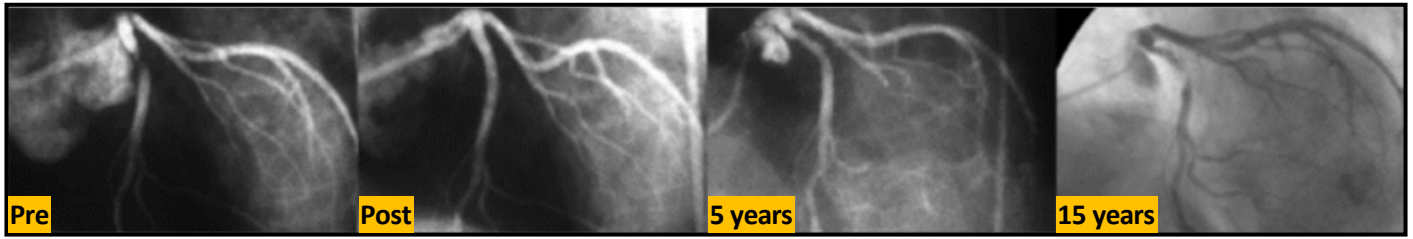
I do have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation, they are:

Affiliation/Financial Interest:	**Name of Organization:**
Grant/ Research support	Meril Life Sciences Pvt. Ltd.

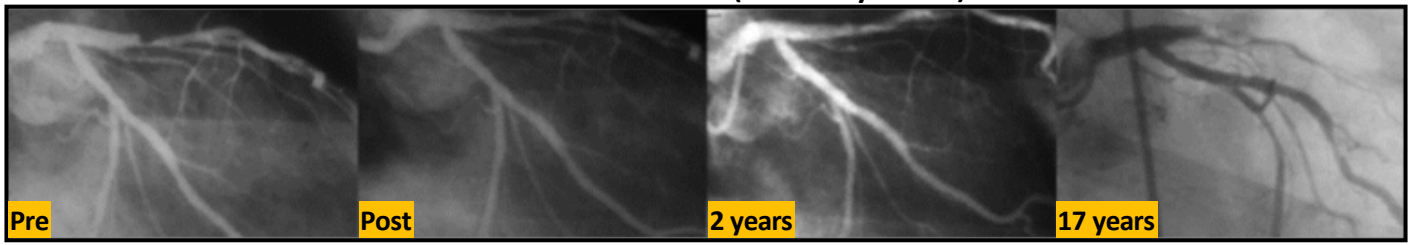
Why do we Need a New Approach for Coronary Artery Disease?

Very late adverse events after metallic stents

In-stent restenosis (at 15 years)



Stent thrombosis (at 17 years)



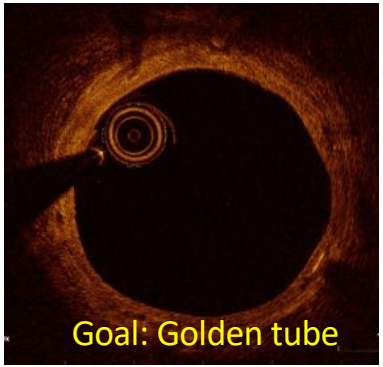
Yamaji K et al. *Circ CV Int* 2010

What are we looking from 2nd Generation BRS?

Acute Performance + Long Term Safety and Efficacy

- Reduced strut thickness, improved profile for better deliverability
- Faster degradation and possibly lower Scaffold Thrombosis
- Large size matrix to cover multitude of morphologies
- Ability to treat lesions across clinical spectrum
- Regular Cath-lab storage conditions & long shelf life

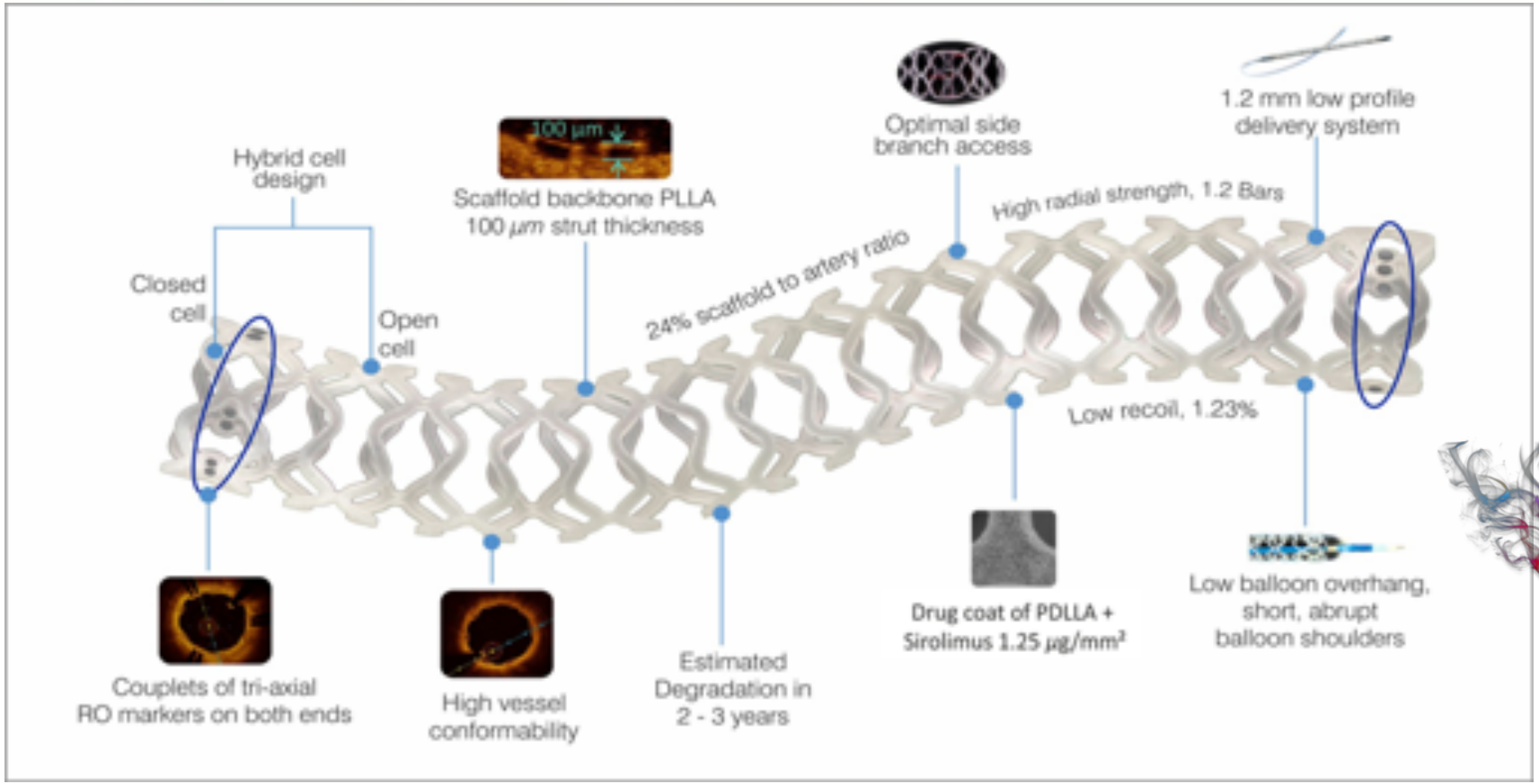
150µm
Strut thickness



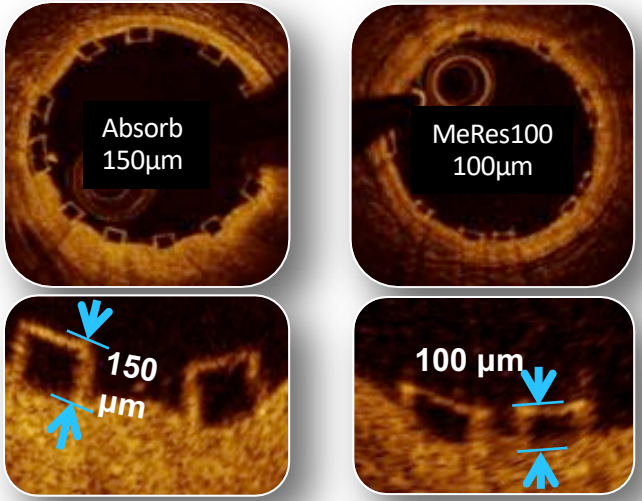
Source: Data on File; 3year f/up of MeRes100 in Porcine coronary arteries, CRF Skirball Centre for Innovation

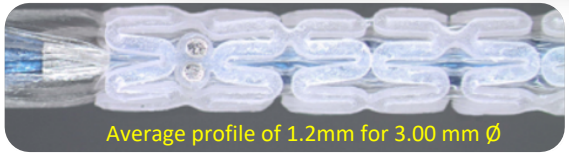
MeRes100 (100µm BRS)

Sirolimus-Eluting Bioresorbable Vascular Scaffold

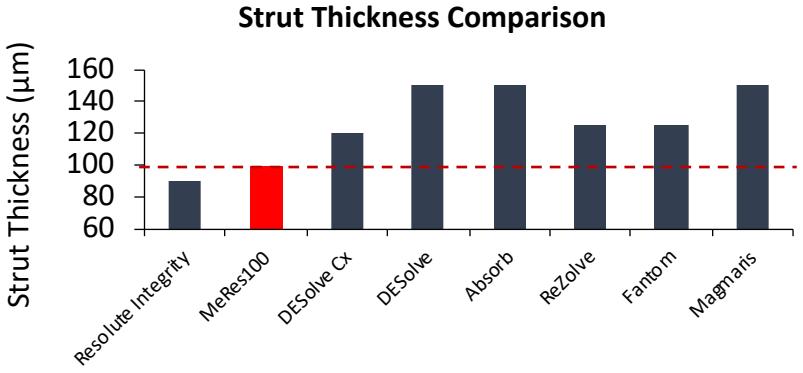


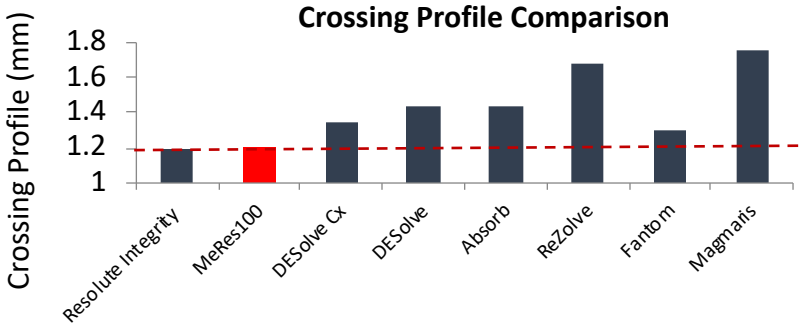
MeRes100 BRS: Strut Thickness & Crossing Profile





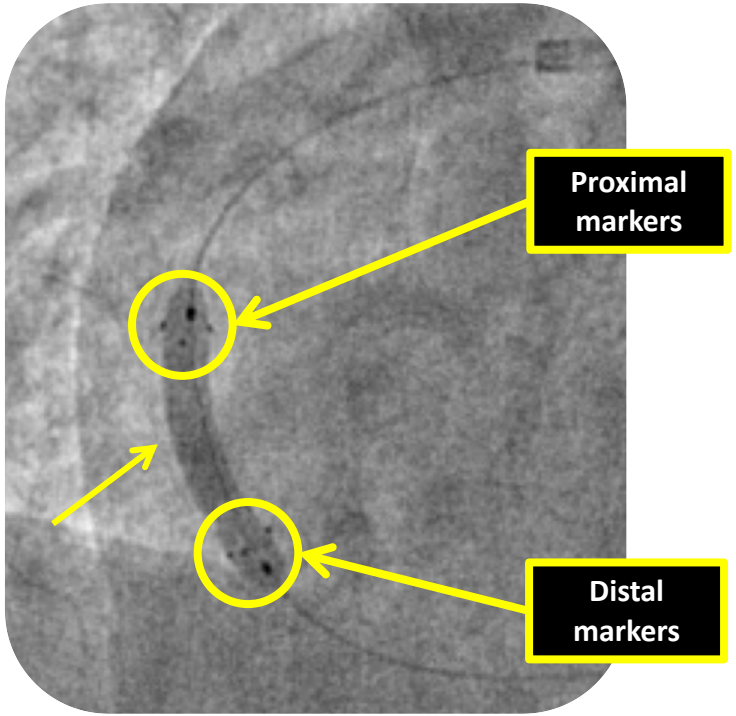
OCT images courtesy of Dr. Daniel Chamié, Dante Pazzanese Institute of Cardiology, Sao Paulo, Brazil. Data on file with Meril Life Sciences Pvt. Ltd.

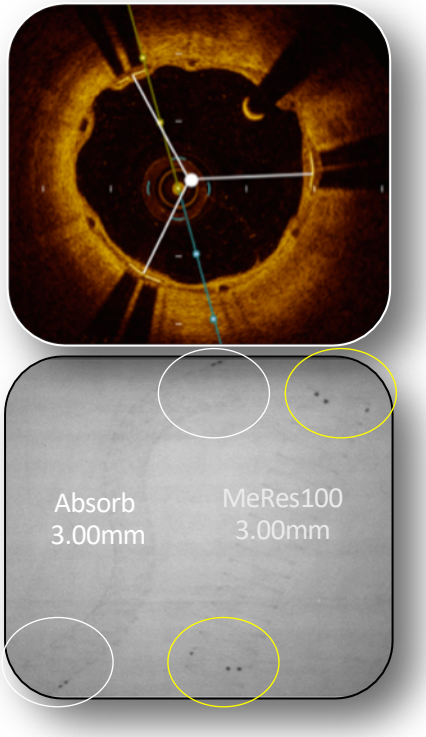




MeRes100 – BRS Radiopacity

- Couplets of **Tri-Axial RO markers** (Pt) at **both ends** of the scaffold
- Enhanced visibility. Gives a sense of **virtual tubing.** High operator comfort

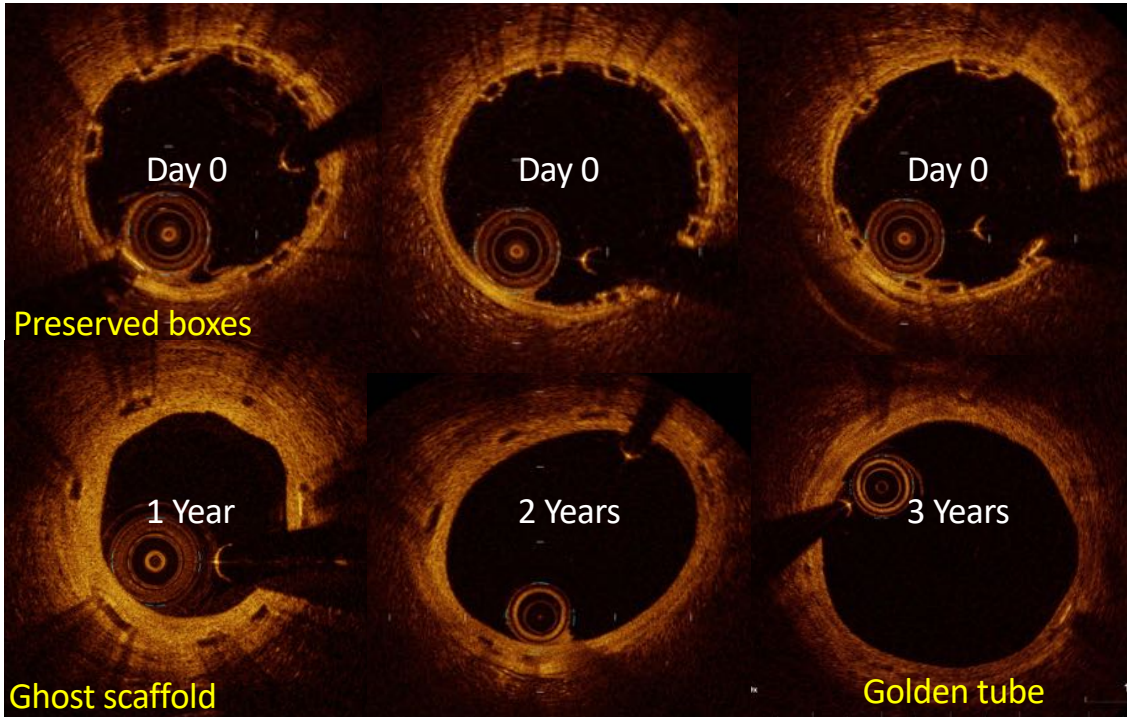




Data on file with Meril Life Sciences Pvt. Ltd.

OCT images illustrating the changes of strut core appearance at Day 0 and at 1 , 2 & 3 Years Follow-up

MeRes100 BRS: Evidence of ‘Golden Tube’

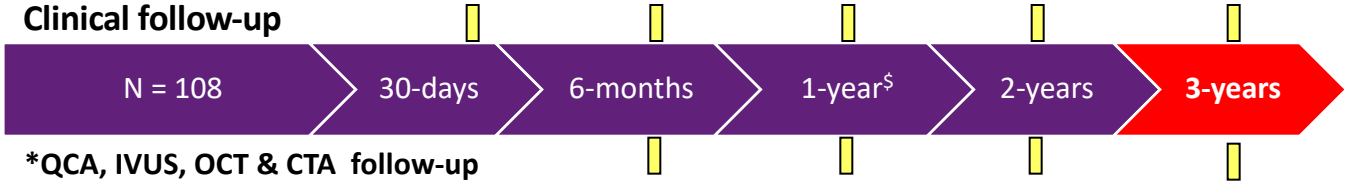


Source: MeRes100 in Porcine coronary arteries, CRF Skirball Centre for Innovation

MeRes-1 Study Design

CTRI/2015/04/005706

First-in-Human ***Safety and Efficacy*** **in Patients with Single,** ***De-novo***
Coronary Lesion (in up to 2 vessels) treated by a Single MeRes100
Scaffold up to 24mm length in 108 pts



CLINICAL FOLLOW-UP	108	108	108	**108**	**108**
ANGIOGRAPHIC FOLLOW-UP	-	37	-	**37**	-
OCT FOLLOW-UP	-	13	-	**13**	-
IVUS FOLLOW-UP	-	12	-	**12**	-
CTA FOLLOW-UP	-	-	12	-	-

Diameters – 2.25-4.50 mm
Lengths – 13-48 mm
DAPT Rx – 1 year

$Seth A et al., EuroIntervention 2017; 13: 415-423. *Pre-designated sites and patients consents

Key Eligibility Criteria

Key Inclusion Criteria

- Age 18-65 years
- Up to 2 lesions in native arteries
- 1 lesion per target vessel allowed
- **RVD 2.75-3.50 mm**
- **Lesion length ≤ 20 mm**
- Stenosis ≥ 50% & < 100%
- TIMI ≥ 1

Key Exclusion Criteria

- **Acute MI <7 days**
- Creatinine ≥1.3 mg/dL
- Prior revascularization
- LVEF ≤ 30%
- LM and/or Ostial location
- **Significant calcification**
- Bifurcation lesion (SB >2 mm)
- Severe tortuosity/angulation

Major Endpoints

- **Safety**
  - Primary Endpoint:
    - MACE at 6-month (Cardiac death, MI*, ID-TLR)
  - Secondary Endpoints:
    - Device & procedure success
    - Scaffold thrombosis (ARC defined)
- **Efficacy**
  - QCA: Late lumen loss (in-scaffold / in-segment)
  - OCT: Minimum lumen area (flow area), NIH area
  - IVUS: Scaffold & lumen area, %VO
  - CTA: Mean/minimal lumen, plaque & vessel area; Area stenosis; % Cross sections with calcified, mixed & non-calcified plaque

*** Definition of MI – includes all Myocardial Infarction**

Study Organisation

- PI – Dr. Ashok Seth, Fortis Escorts, New Delhi
- Co-PI – Dr. Praveen Chandra, Medanta, Gurugram
- Co-PI – Dr. Vinay K. Bahl, AIIMS, New Delhi

- Core Labs
  - Angiographic – Cardiovascular Research Center, Sao Paulo
  - IVUS / OCT /CTA – Cardialysis, Rotterdam

- CRO
  - Data Management – JSS, New Delhi

Investigating Sites

108 Patients, 13 Investigating Sites

Investigating Site	City	Investigator	# Enrolled
Jayadeva	Bangalore	Dr. C. N. Manjunath	23
LTMG	Mumbai	Dr. Ajay Mahajan	20
Max	New Delhi	Dr. Viveka Kumar	13
SGPGI	Lucknow	Dr. P. K. Goel	11
Medanta The Medicity	Gurugram	Dr. Praveen Chandra	10
AIIMS	New Delhi	Dr. Vinay K. Bahl Dr. Sundeep Mishra	07
Hero DMC	Ludhiana	Dr. G. S. Wander	07
Fortis Escorts	New Delhi	Dr. Ashok Seth	06
Apollo	Chennai	Dr. Samuel Mathew Dr. G. Sengottuvelu	04
Sree Chitra	Trivandrum	Dr. Ajit Kumar V. K.	03
Fortis Vasant Kunj	New Delhi	Dr. Upendra Kaul	02
GB Pant	New Delhi	Dr. Vijay Trehan	01
Apollo Jubilee Hills	Hyderabad	Dr. P. C. Rath	01

Baseline Demographics

Clinical characteristics of the patients	n = 108
Age, Years, (mean±SD)	50.1±8.8
Male, n (%)	77 (71.3)
Smokers, n (%)	**18 (16.7)**
Diabetes mellitus, n (%)	**30 (27.8)**
Dyslipidemia, n (%)	14 (13.0)
Hypertension, n (%)	45 (41.7)
Previous Myocardial Infarction (>7 days), n (%)	**37 (34.3)**
Clinical Presentation, n (%)	
Stable Angina	56 (51.9)
Unstable Angina	37 (34.3)
Silent Ischemia/Asymptomatic	15 (13.9)
Left ventricular ejection fraction, %, (mean±SD)	50.6±9.9
Type B1/B2/C Lesions	93.1%

100% device and 99% procedural success

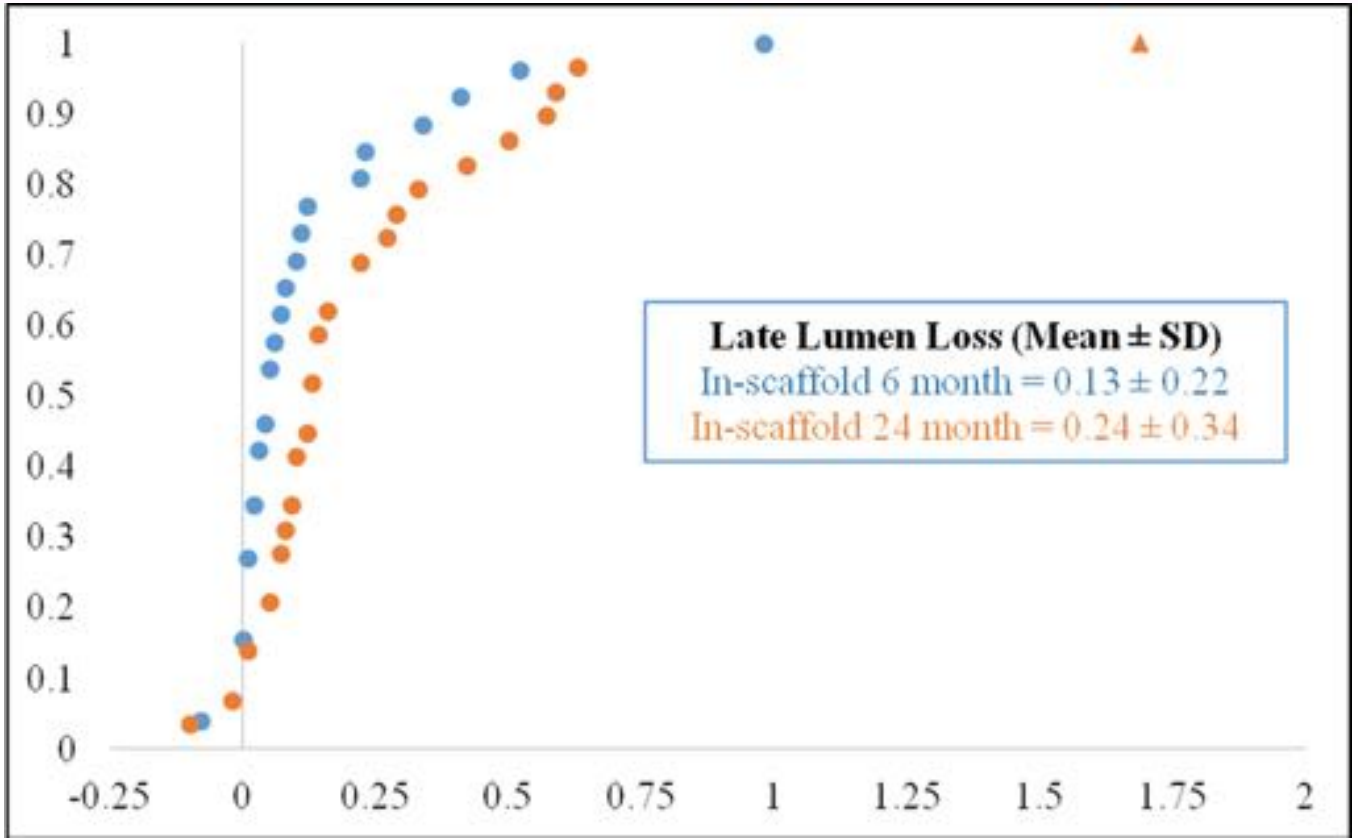
Cumulative Clinical Outcomes up to 3-year Follow-up

Events, n (%)	In-Hospital n =108	6-month n =108	1-year n = 107	2-year n = 107	3-year n=107
Cumulative MACE	**0 (0)**	**0 (0)**	**1 (0.93)**	**2 (1.87)**	**2 (1.87)**
Cardiac Death	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Myocardial Infarction	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
ID-TLR	0 (0)	0 (0)	1 (0.93)	2 (1.87)	2 (1.87)
Non-cardiac death	**0 (0)**	**1 (0.93)***	**1 (0.93)**	**1 (0.93)**	**1 (0.93)**
Scaffold Thrombosis	**0 (0)**	**0 (0)**	**0 (0)**	**0 (0)**	**0 (0)**

*Death due to Aminophylline-induced anaphylactic shock. @ Myocardial Infarction defined as per WHO criteria. $ ARC defined criteria.

Sustained successful clinical outcomes up to 3 years

Cumulative Frequency Distribution Curve for In-scaffold Late Lumen Loss



Angio QCA – CRC, Sao Paulo, Brazil

Paired OCT analysis

MeRes-1

Characteristic	Post-procedure (n=9)	6-Month (n=9)	2- year (n=9)	Friedman p-value
Mean flow area, (mm^2)	7.33±2.28	6.99±2.75	6.49±2.79	0.032
Mean lumen area, (mm^2)	7.69±2.36	6.99±2.75	6.49±2.79	0.008
Minimum lumen area, (mm^2)	6.59±2.12	4.99±1.65	4.29±2.00	<0.01
Mean scaffold area, (mm^2)	8.06±2.51	8.64±3.05	8.39±3.19	0.121
Minimum scaffold area, (mm^2)	7.13±2.29	7.05±2.02	6.29±2.43	0.120
Mean strut area, (mm^2)	0.14±0.04	0.11±0.03	0.06±0.02	0.001
Covered struts (%)	-	98.99±1.59	99.24±2.27	0.102

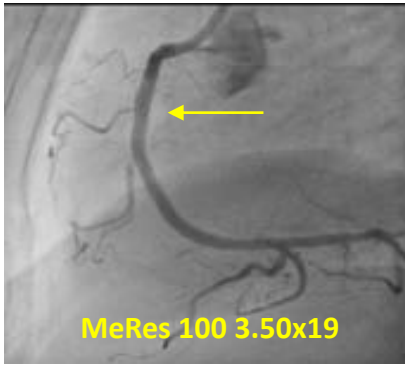
Paired IVUS Analysis

Parameters	Post-procedure (n=10)	6-month (n=10)	2- year (n=10)	Friedman p-value
Mean lumen area, (mm^2)	6.17±1.28	6.28±1.28	5.47±1.50	0.30
Minimum lumen area, (mm^2)	5.14±1.19	4.88±1.05	4.05±1.42	0.741
Mean scaffold area, (mm^2)	6.20±1.27	6.54±1.29	5.94±1.34	0.122
Mean vessel area, (mm^2)	12.91±4.05	13.05±3.30	11.98±3.03	0.061
Neointimal hyperplasia area, (mm^2)	-	0.14±0.16	0.40±0.35	0.002
Volume obstruction (%)	-	**2.59±3.10**	**7.50±6.08**	**0.002**

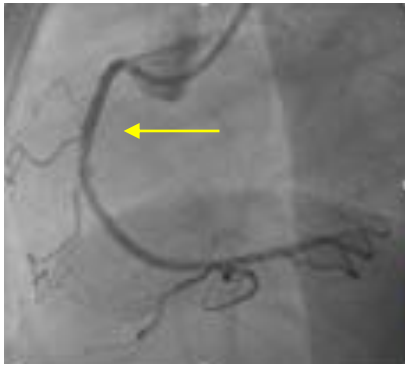
MeRes100 Case + OCT F/up out to 2yrs

47y/F | Diabetic | Hypertensive | No family history | Non-smoker | Stable angina

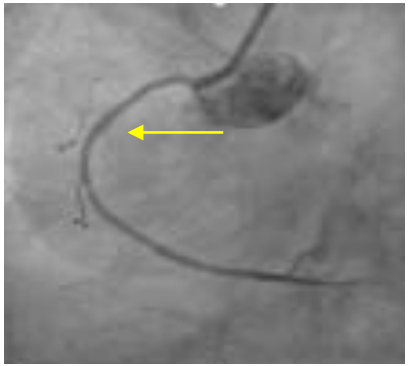
Post-Procedure



6-Month FU

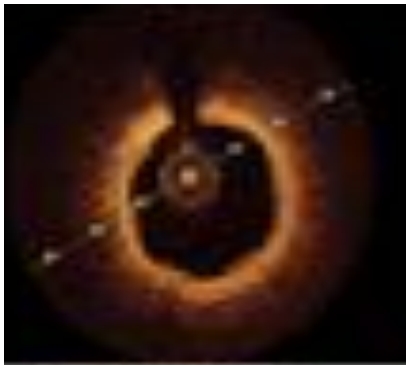


2-Year FU



Post-Procedure

6-month OCT f/up



2-Year OCT f/up

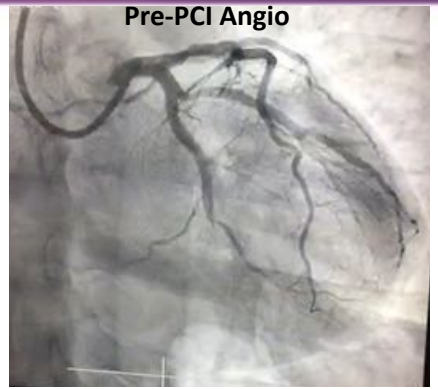
Data on file at Meril Life Sciences, Pvt. Ltd.

MeRes100 Case with Tapered balloon/delivery system

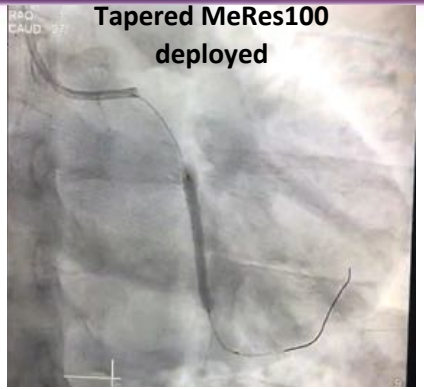
Patient details:

- 37 Y/male with CAD
- CAG: 100% Occlusion in mid LCX
- Focal moderate 50% Stenosis in Prox. LAD
- PCI with MeRes100 (3.0-2.5X30mm)

Pre-PCI Angio

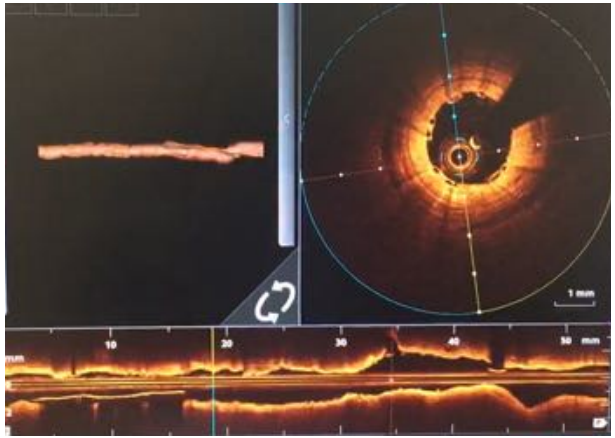


Tapered MeRes100 deployed

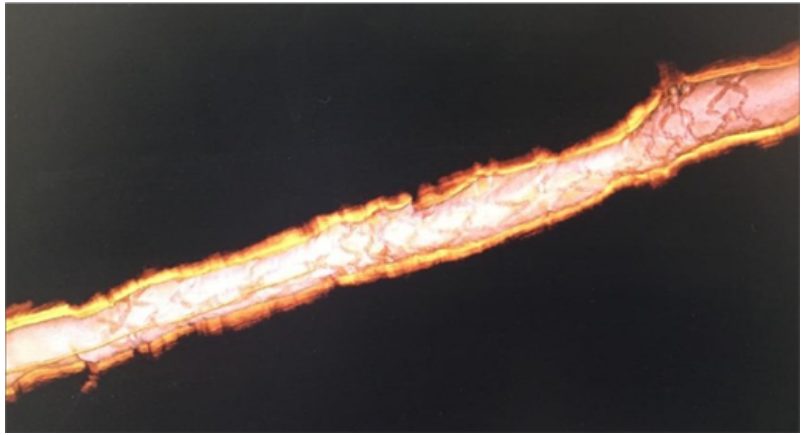


Post-PCI Angio

Post-PCI OCT



3D OCT View of MeRes100 post-PCI



Data on file at Meril Life Sciences, Pvt. Ltd

MeRes100 – Global Clinical Program

>5,000 Patients
Global Clinical Program

MeRes-1[1] (n=108)
FiM, Single, denovo lesions.
13 Indian Sites

MeRes-1 Extend[2] (n=64
Single, denovo lesions
8 Global Sites

MeRes100 Global[3] (n=2,000)
All comers, real world registry.
100 participating sites global.

MeRes-Evolve[4] (n=800)
RCT MeRes100 Vs XIENCE
30 participating sites global

MeRes100-China[5] (n=1,242)
RCT 242:242 MeRes100 Vs XIENCE
+ 800 MeRes100. 1 year MACE, ST

MeRes100-US/JPN[6] (n=2,000)
RCT MeRes100 Vs XIENCE
1 year MACE, ST

1-2. Achieved Primary Objective **3-6. Planning phase.**

Excellent Clinical Safety & Efficacy	MeRes-1 N=107^	MeRes-1 Extend N=62 ^
Follow-up	3-year	2-year
MACE	2 (1.87%)	1 (1.61%)
ST	0%	0%
Late Lumen Loss	2-year 0.24± 0.34 mm	6-month 0.18±0.31mm

^MeRes-1 One-Year Results: Seth A. et al. EuroIntervention 2017;13:415-423
^MeRes-1 Ext presented at EuroPCR'2018

Conclusion & Future Directions

- MeRes-1 trial, the 1st human evaluation of novel 2nd generation MeRes100 BRS with 100µm struts demonstrated high acute success as well as long term clinical success up to 3-year follow-up with **very low MACE rate of 1.87% (2, ID-TLR)** and **Zero Scaffold Thrombosis** (ST). [ABSORB II @ 3 Year MACE: BVS – 10.5%, XIENCE – 5%; ST: BVS - 2.5% including very late thrombosis (>1 year): 1.8%][1]
- All four imaging modalities are consistent in demonstrating high efficacy of MeRes100 – BRS:
  - QCA at 2-years: **Low late lumen loss (0.24± 0.34 mm)**
  - OCT at 2-years: Virtually **complete strut coverage (99.24%)**
  - IVUS at 2- years: Sustained mean flow area and **very low %VO (7.50%)**
- These encouraging results of MeRes-1 study provide the basis for further studies, using a wider range of lengths and sizes in more complex and larger patient population.

1. https://www.acc.org/latest-in-cardiology/clinical-trials/2014/09/14/19/17/absorb-ii

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Thank You