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

Potential Conflicts of Interest

Speaker's name : Praveen Chandra

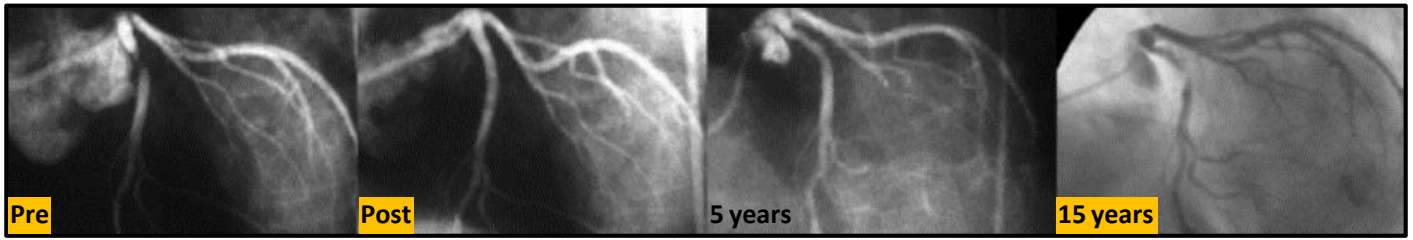
☑ I have the following potential conflicts of interest to declare:

Grant/ Research support: Meril Life Sciences

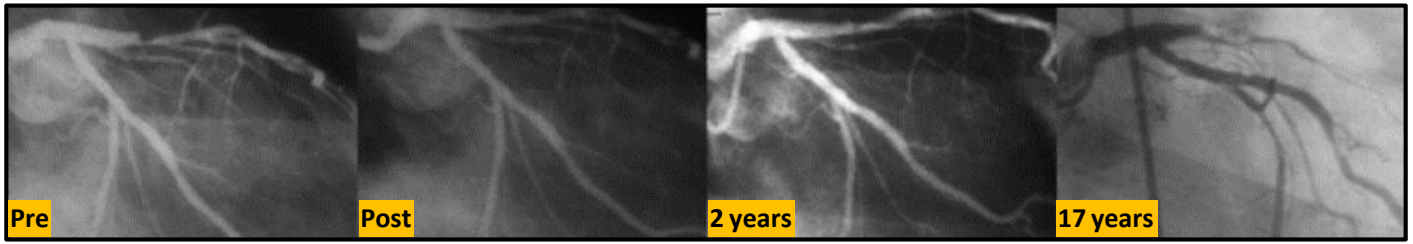
Why do we Need a New Approach for Coronary Artery Disease?

Very late adverse events after metallic stents

In-stent restenosis (at 15 years)

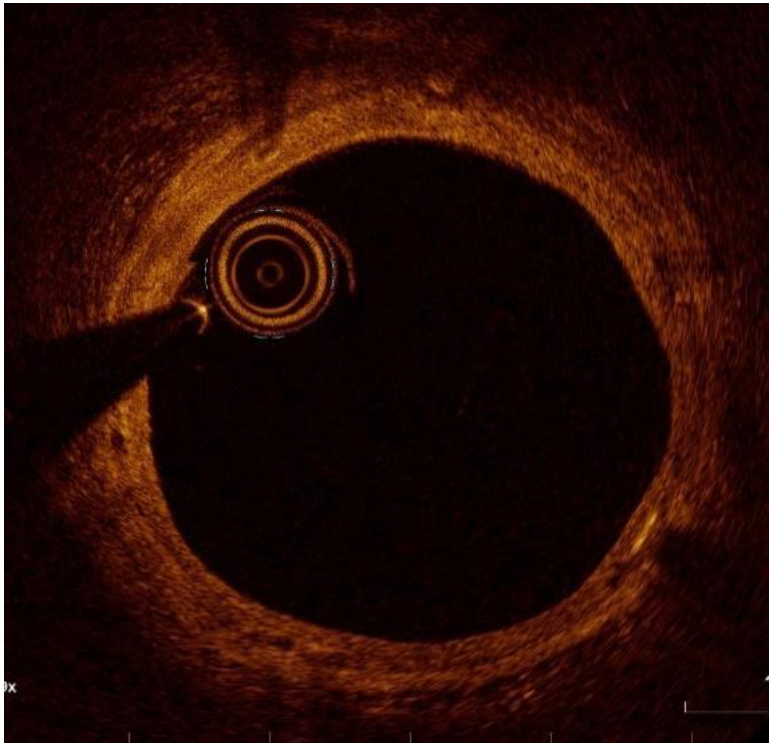


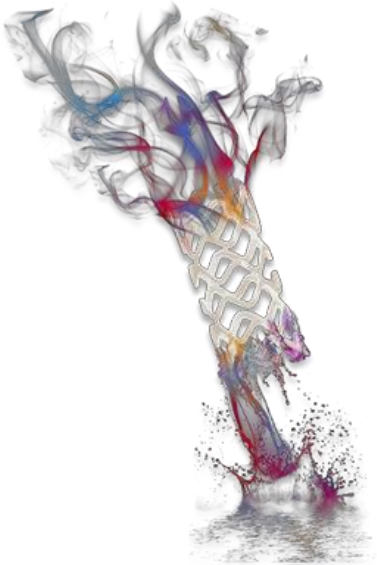
Stent thrombosis (at 17 years)



Yamaji K et al. *Circ CV Int* 2010

Leave no permanent implant behind – Future Tx Possibilities





The Promise of 1st Gen BVS– 'Golden Tube'

Initial Results of BVS were promising

Clinical outcomes

Data are present in %

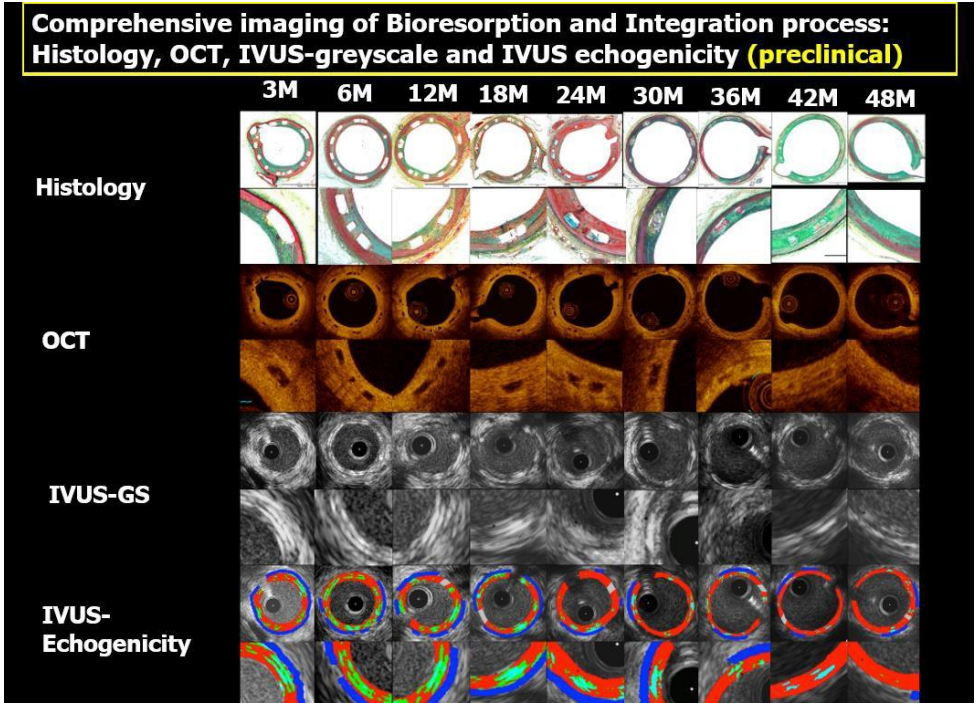
Non-hierarchial	30 days N=101	1 year N=101	2 years N=100	3 years N=100	4 years N=100*	5 years N=100
All death	0	0	0	1.0	3.0	3.0
Cardiac death	**0**	**0**	**0**	**0**	**0**	**0**
Myocardial Infarction	**2.0**	**3.0**	**3.0**	**3.0**	**3.0**	**3.0**
Non Q-wave MI	2.0	3.0	3.0	3.0	3.0	3.0
All-TLR	0	5.0	9.0	10.0	10.0	11.0
ID-TLR	**0**	**4.0**	**6.0**	**7.0**	**7.0**	**8.0**
ID-TVR	0	4.0	8.0	10.0	10.0	11.0
MACE	**2.0**	**6.9**	**9.0**	**10.0**	**10.1**	**11.0**
TVF	2.0	6.9	11.0	13.0	13.1	14.0

MACE: Cardiac death, any MI, ID-TLR; TVF:Cardiac death, any MI, ID-TVR

***=backfilled**

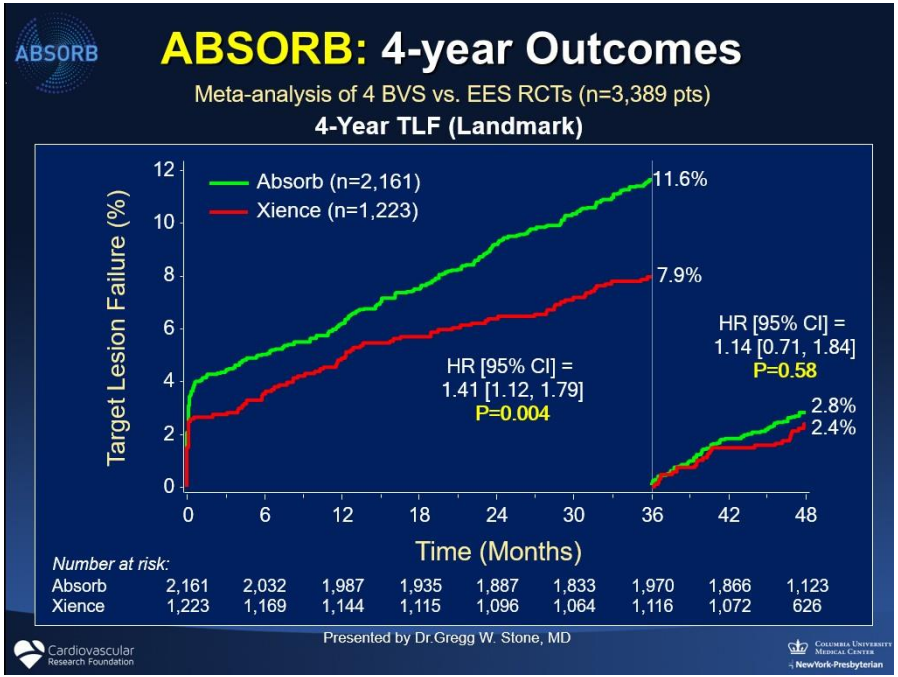
Absorb 5-Year Cohort B Presented by Patrick W. Serruys

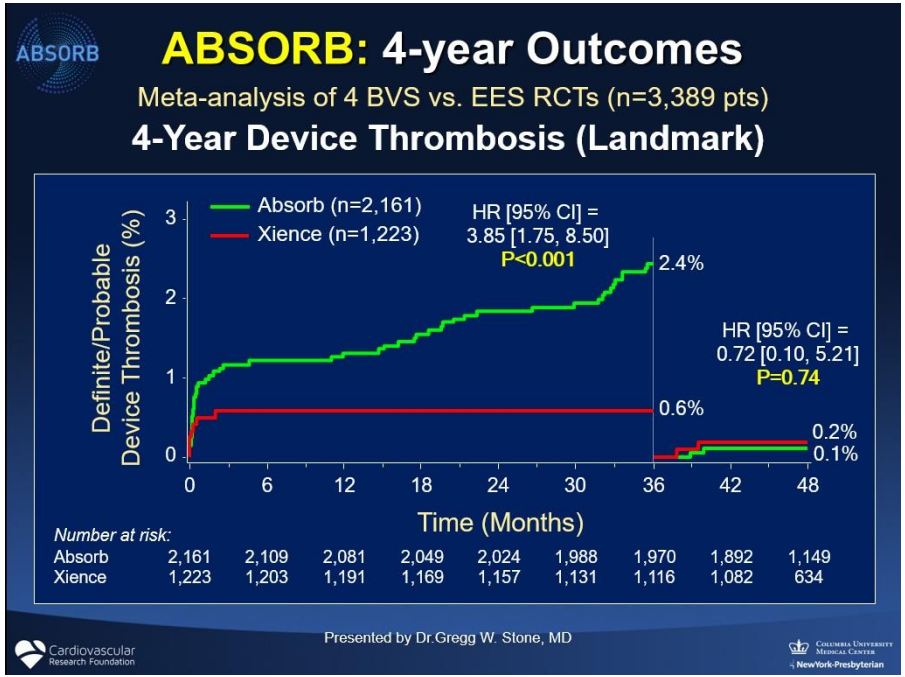
tct2015 CRF CARDIOVASCULAR RESEARCH FOUNDATION At the heart of innovation



Absorb 5-Year Cohort B Presented by Patrick W. Serruys

But, Reality was presenting differently & we learnt from the same





- ✓ **BVS specific procedures/techniques – lesion selection, dilatation, sizing**
- ✓ **2nd Generation device required**

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

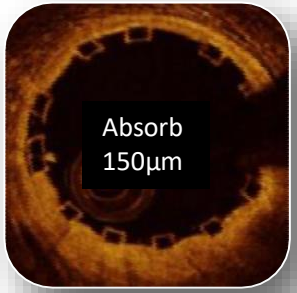
Ability to **treat lesions across clinical spectrum**

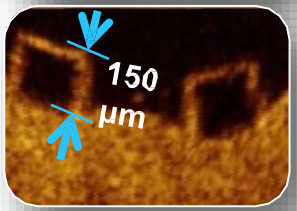
Regular Cath-lab storage conditions & long shelf life

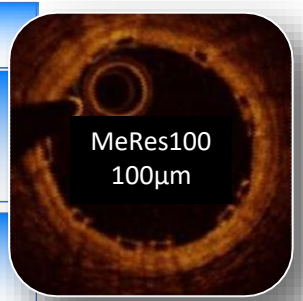
Source: Data on File; 3year f/up of MeRes100 in Porcine coronary arteries, CRF Skirball Centre for Innovation

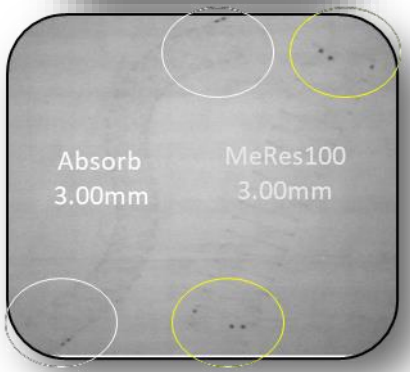
MeRes100 – The 2nd Generation BRS

Features	1st Gen BVS	MeRes100
Cell Design	Multi-link design platform	Hybrid Geometry
Scaffold to Artery Ratio	35-40%	24%
Strut Thickness	150µm	100µm
Crossing Profile	1.4mm	1.2mm
RO Markers	Pair of RO markers at opposite end	Couplets of 3 RO markers on each end
Size Matrix	14 SKUs D 2.50-3.50 mm & L 8-28 mm	63 SKUs D 2.50 – 4.00 mm & L 8-40 mm
Storage	Prefer Refrigeration	Cath-Lab Temperature





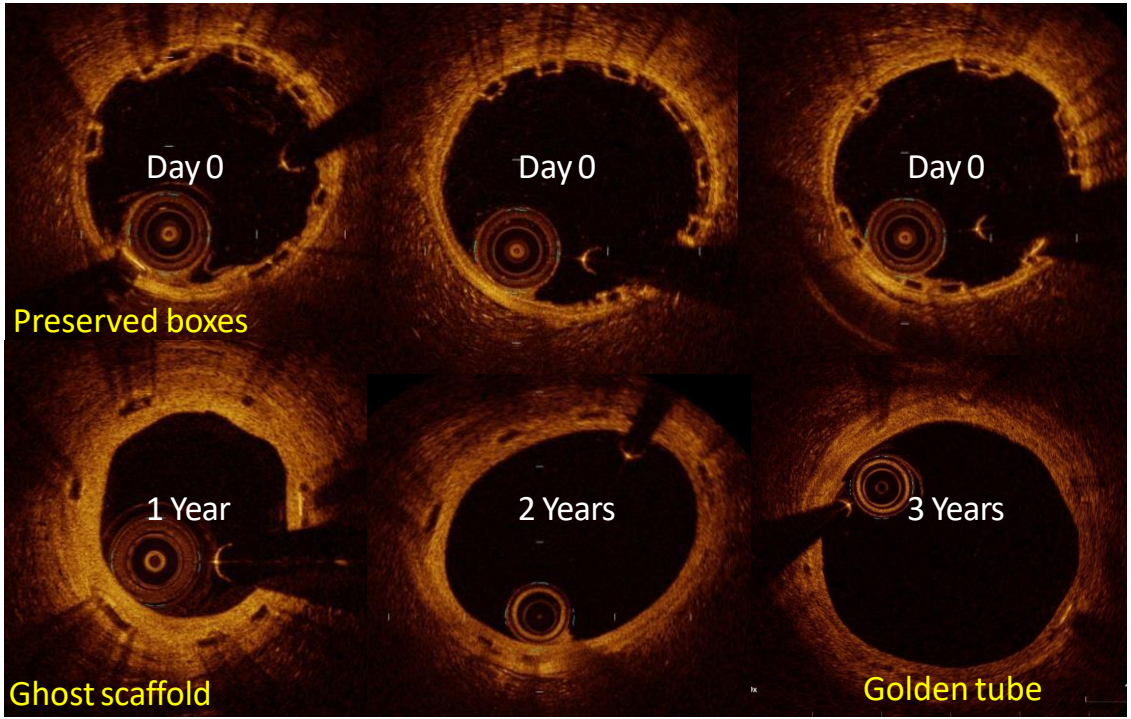




OCT images illustrating the changes of strut core appearance at Day 0 and at 1 , 2 & 3 Years Follow-up

Pre-Clinical

MeRes100 BRS: Evidence of ‘Golden Tube’

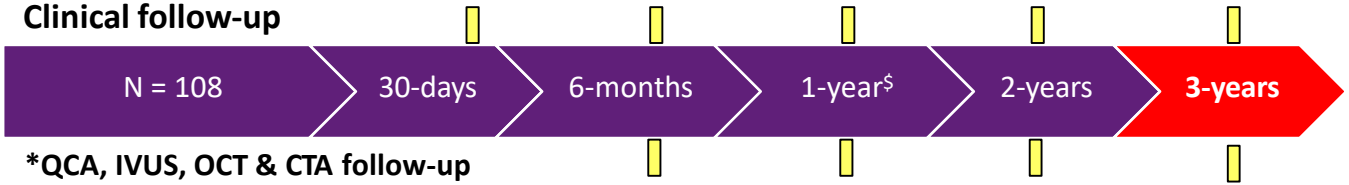


Source: MeRes100 in Porcine coronary arteries, CRF Skirball Centre for Innovation

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

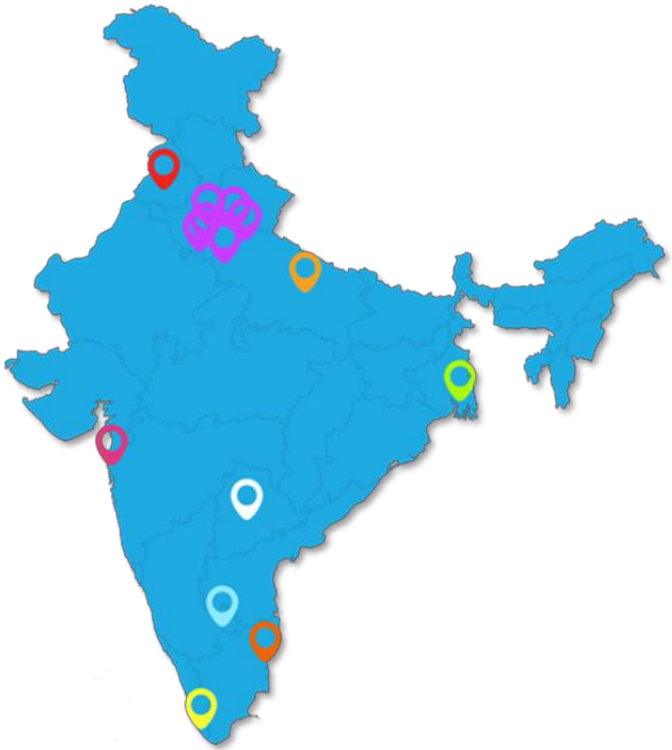
- PI – Dr. Ashok Seth, Fortis Escorts, New Delhi
- Co-PI – Dr. Praveen Chandra, Medanta, Gurugram
- Co-PI – Dr. Vinay K. Bahl, AIIMS, New Delhi

- 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 Clinical Outcomes up to 3-year Follow-up

Clinical outcomes

Data are present in %

Non-hierarchial	30 days N=101	1 year N=101	2 years N=100	3 years N=100
All death	0	0	0	1.0
Cardiac death	**0**	**0**	**0**	**0**
Myocardial Infarction	**2.0**	**3.0**	**3.0**	**3.0**
Non Q-wave MI	2.0	3.0	3.0	3.0
All-TLR	0	5.0	9.0	10.0
ID-TLR	**0**	**4.0**	**6.0**	**7.0**
ID-TVR	0	4.0	8.0	10.0
MACE	**2.0**	**6.9**	**9.0**	**10.0**
TVF	2.0	6.9	11.0	13.0

MACE: Cardiac death, any MI, ID-TLR; TVF:Cardiac death, any MI, ID-TVR

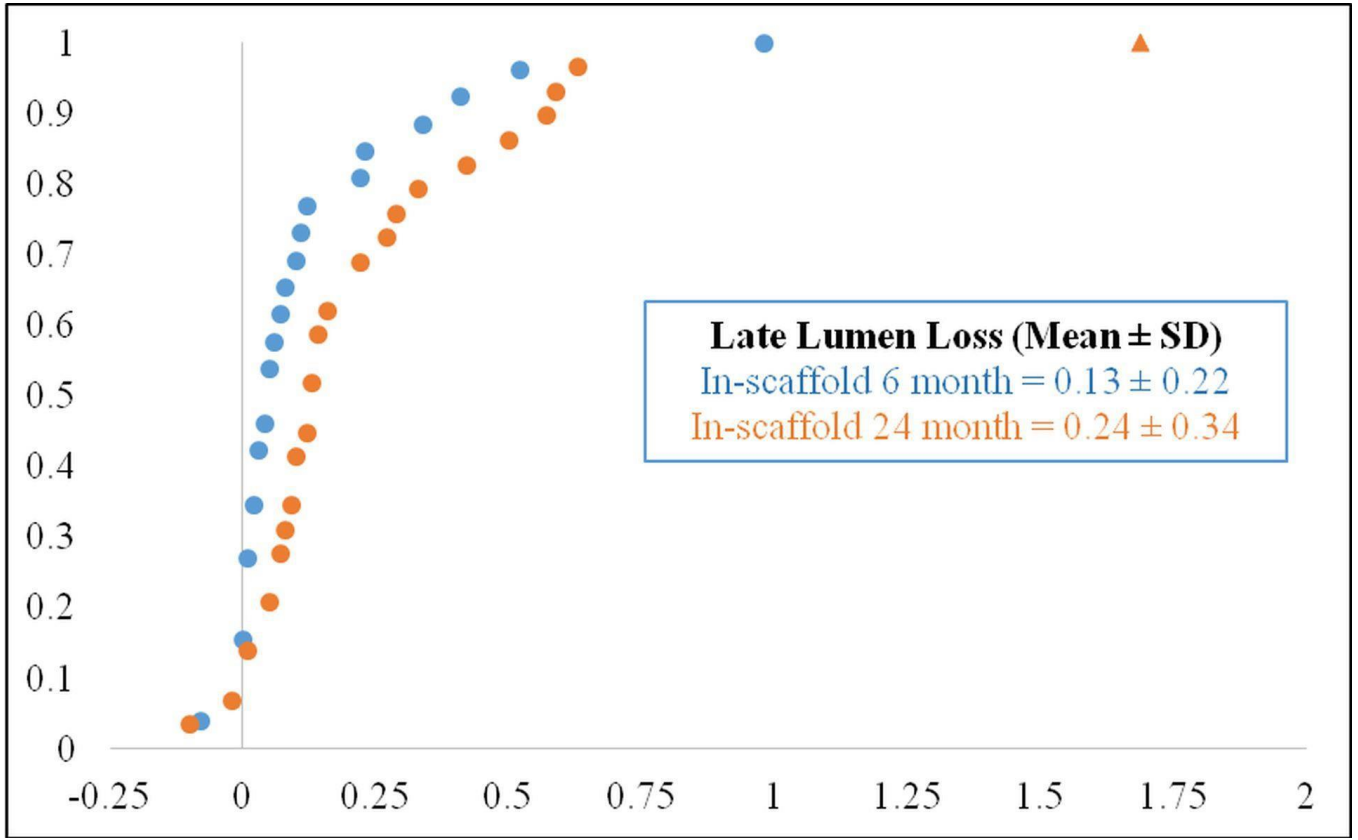
*=backfilled

Absorb 5-Yr Cohort-B

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)**

MeRes-1 Study

Cumulative Frequency Distribution Curve for In-scaffold Late Lumen Loss



Angio QCA – CRC, Sao Paulo, Brazil

Paired OCT analysis

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**

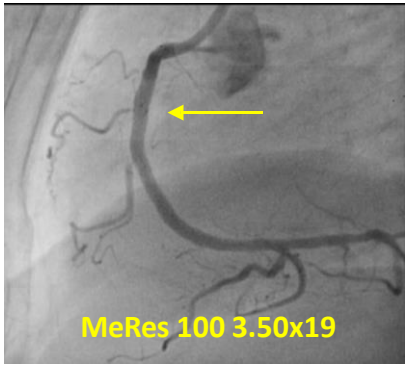
Paired IVUS Analysis

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**

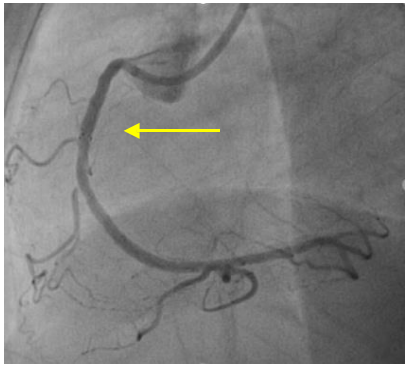
MeRes100 Case + OCT F/up out to 2yrs

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

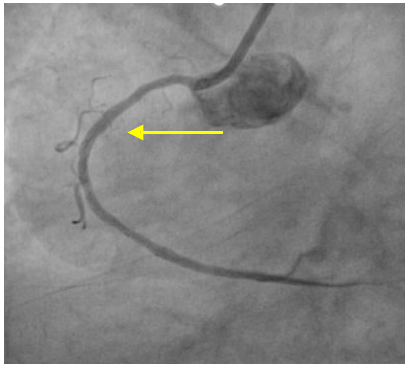
Post-Procedure



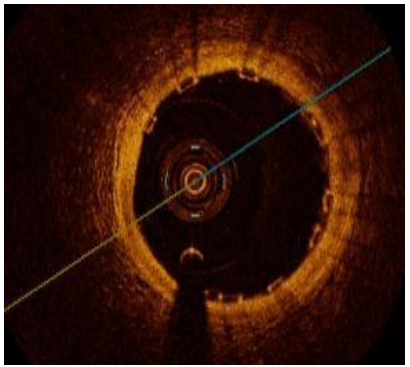
6-Month FU



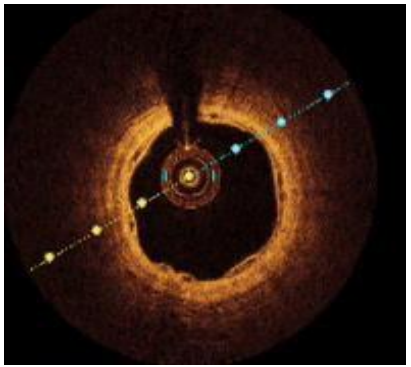
2-Year FU



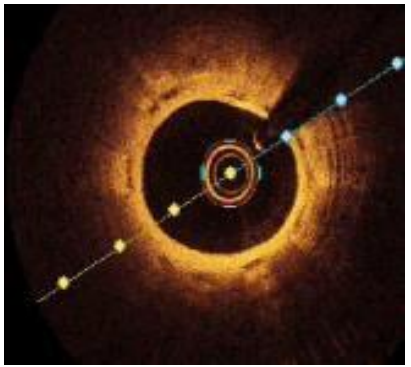
Post-Procedure



6-month OCT f/up



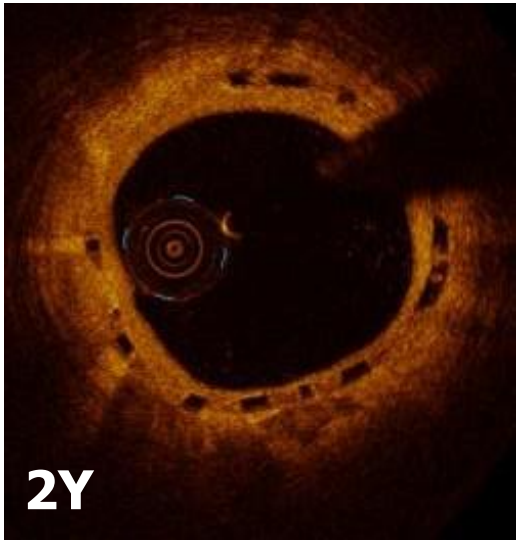
2-Year OCT f/up



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

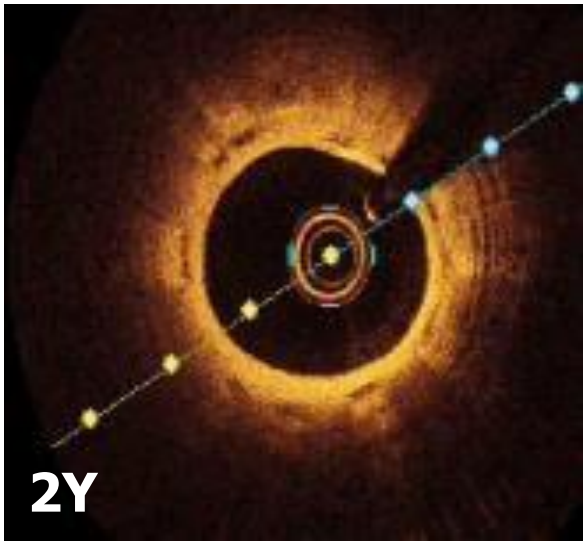
2nd Generation BRS holds promise

Absorb



Absorb 5-Year Cohort B Presented by Patrick W. Serruys

MeRes100



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

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).
- 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.

MeRes-1 trial (3 years follow-up) simultaneous publication in EuroIntervention

CORONARY INTERVENTIONS
CLINICAL RESEARCH

EuroIntervention 2019;15:1-9 published onlin

euro PCR 2019 LATE BREAKING TRIALS

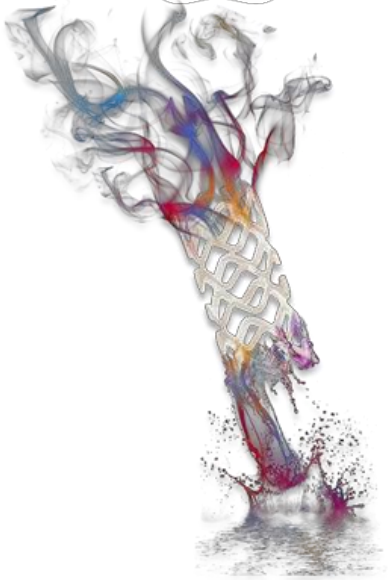
Three-year clinical and two-year multimodality imaging outcomes of a thin-strut sirolimus-eluting bioresorbable vascular scaffold: MeRes-1 trial

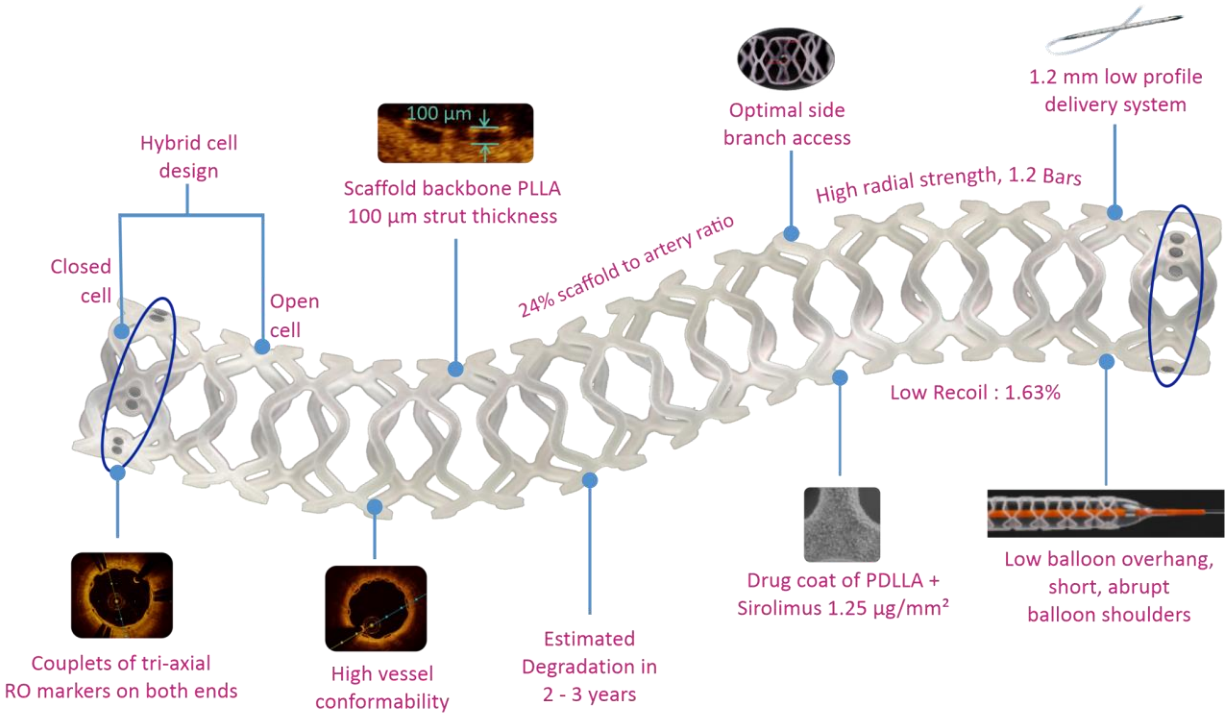
Ashok Seth[1*], FRCP, FESC, D.Sc; Yoshinobu Onuma[2,3], MD, PhD; Praveen Chandra[4], MD, DM; Vinay K. Bahl[5], MD, DM; Cholenahally N. Manjunath[6], MD, DM; Ajaykumar U. Mahajan[7], MD, DM; Viveka Kumar[8], MD, DM; Parvin K. Goel[9], MD, DM; Gurpreet S. Wander[10], MD, DM; Upendra Kaul[11], MD, DM; V.K. Ajit Kumar[12], MD, DM; Alexandre Abizaid[13], MD, PhD; Patrick W. Serruys[14], MD, PhD

MeRes100 (100µm BRS)

Sirolimus-Eluting Bioresorbable Vascular Scaffold

CE APPROVED





2019 euro PCR

Thank You