2019 euro PCR

# Safety and efficacy of sirolimus-eluting stent system in all-comers real-world population with coronary artery stenosis

**Dr. Martin Hudec, MD, PhD, MRCPI, FESC**
**Stredoslovenský ústav srdcových a cievnych chorôb, SÚSCCH, a.s.**
**Slovakia**

**On behalf of MILES-Global Investigators**

# Potential Conflicts of Interest

**Speaker's name : Martin Hudec**

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

Receipt of Grant/ Research support: Meril Life Sciences

# Three Decades of Progress in PCI


Clinical outcomes with contemporary second generation DES, while outstanding, have plateaued and largely remained steady over the past decade

Bangalore et al. Circulation. 2018 Jun 26. pi: CIRCULATIONAHA.118.034456

# The Thin Strut Hypothesis

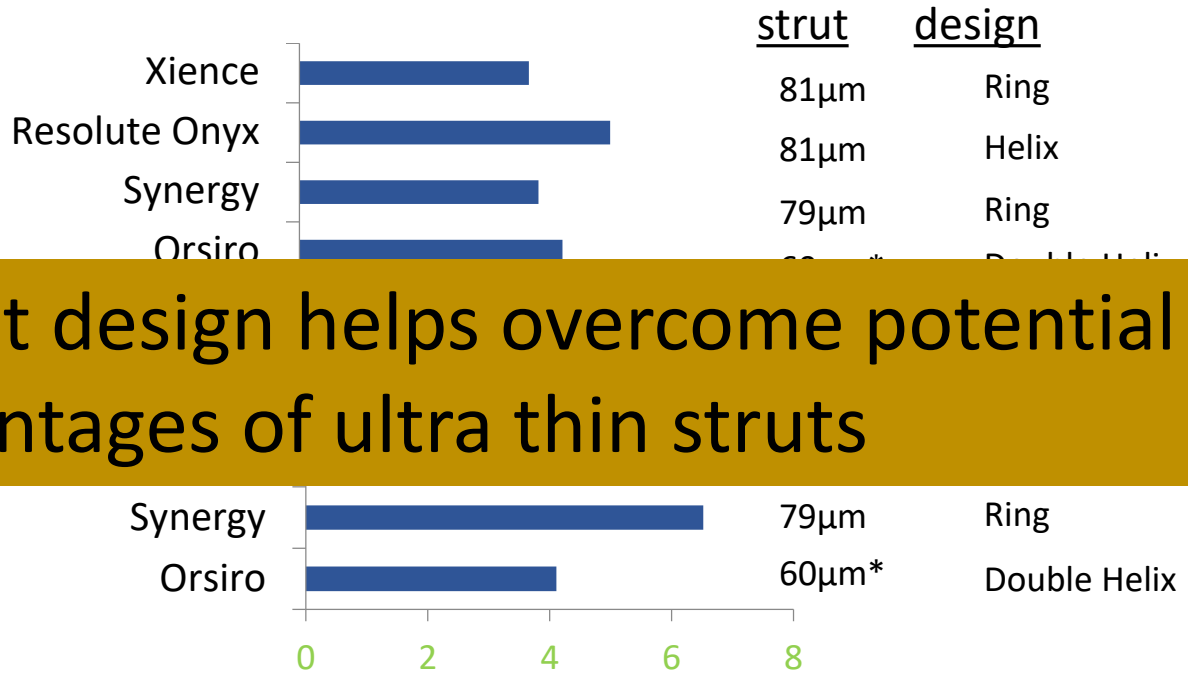
- Short-term: Thinner stent struts produce less vessel injury, inflammation, and thrombus formation compared with thicker struts[1]
- Mid-term: Thinner stent struts results in faster endothelialization and early vascular healing[2]
- Long-term: Thinner stent struts have lower risk of uncovered struts/malapposed struts[2]

[1]Kolandaivelu. Circulation 2011; Soucy. EuroIntervention 2010; Kastrati. Circulation 2001; Pache. JACC 2003

[2]Cassese S et al. Eur Heart J Cardiovasc Imaging. 2018 Jan 2. doi: 10.1093/ehjci/jex334

# Concerns with thinner struts

Radial strength



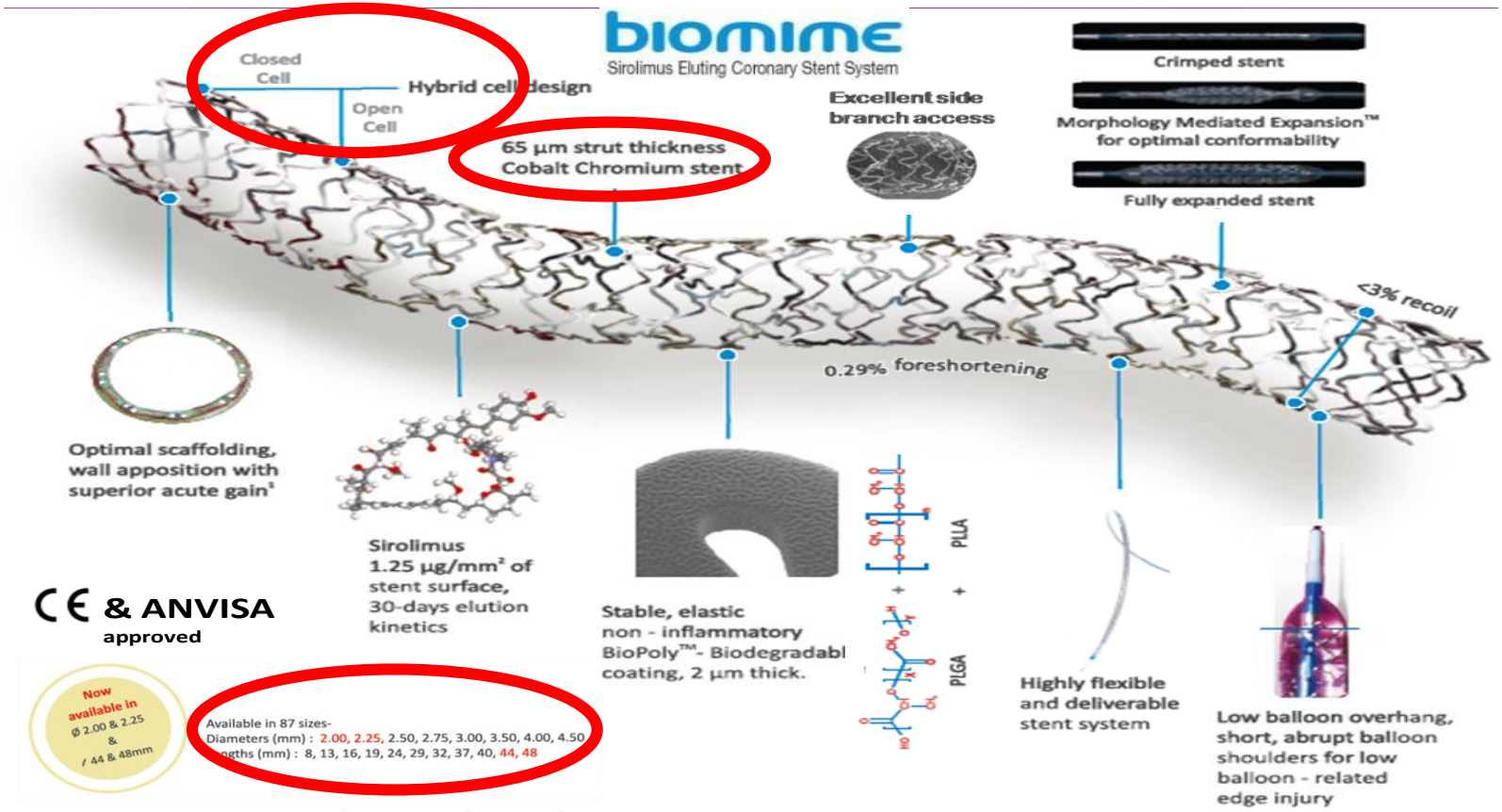

**Advances in stent design helps overcome potential disadvantages of ultra thin struts**

*For 2.25 mm to 3.0 mm Ø stents, 80 µm for > 3.0 mm Ø stents

** Bench test performed by independent laboratory - IIB // BIOTRONIK data on file

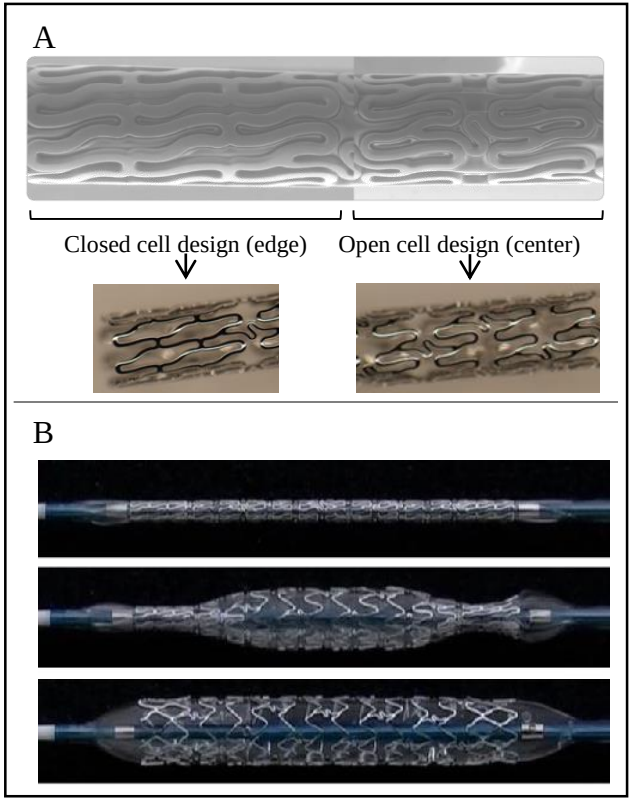
Source: S James, Evaluating the broad clinical utility of ultrathin bioabsorbable polymer DES; Oral presentation; Presented at: EuroPCR 2018; MAY 24

# Device description



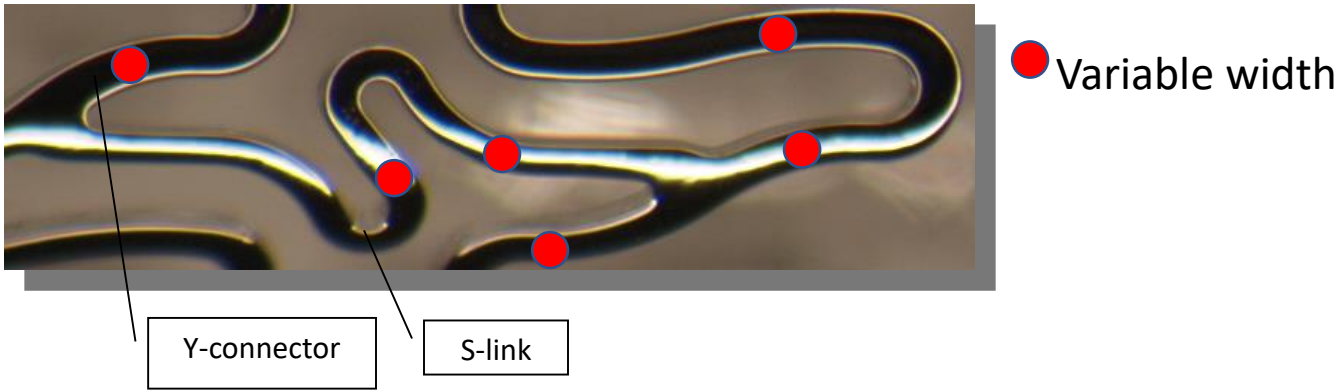
# BioMime Sirolimus-Eluting Stent

- **BioMime™ DES (Meril Life Sciences Pvt. Ltd.,India) – CE Marked**
- **Cobalt-chromium (L605) ultra-thin (65 µm) metallic platform (NexGen™)**
- **Hybrid cell design (A)**
- **Release system with mediated expansion to minimize vascular injury (B)**
- **Proprietary bioabsorbable co-polymer formulation (BioPoly™) – PLLA/PLGA**
- **Polymer coating only 2 µm thick, totally absorbed in < 60 days**
- **Pharmacological agent: Sirolimus**
- **Drug dose: 1.25 µg/mm$^2$ of stent surface area**



# BioMime Strut Width Variability ensures adequate Radial Strength

- **Bench testing demonstrates Radial Strength with mean collapse pressures of 1.1bar along with <3% recoil and 0.29% foreshortening**
- **Strut-width variability across the design geometry ensure retention of radial strength despite reduction in Strut thickness**
- **Non linear links contribute to flexibility and Closed-cells on the edges lend their radial strength to the entire stent**




Data on file at Meril Lifesciences

# Rationale

- The drug-eluting stents (DES) were developed to overcome the limitations of bare metal stents
- The need for non-thrombogenic and safer stents has encouraged development of next-generation DES with biocompatible and biodegradable polymer, thinner as well as more flexible stent platform, and kinetics of drug release, resulting in a reduction of late and very late stent thrombosis (ST)
- The biodegradable-polymer based ultra-thin strut DES facilitate flexibility and deliverability with reduced arterial injury and inflammation
- The MILES-Global study aimed to evaluate the safety and efficacy of ultra-thin strut BioMime sirolimus-eluting coronary stent system (SES) in all-comers real-world population

Abizaid A, Kedev S, Kedhi E, et al. Randomized Comparison of Biodegradable Polymer Ultra-thin Sirolimus-Eluting Stent Versus Durable Polymer Everolimus-Eluting Coronary Stent in Patients with De Novo Native Coronary Artery Lesions: The meriT-V Trial. EuroIntervention. 2018 Dec 7;14(11):e1207-e1214.

# Major Clinical Endpoints

- **Primary Endpoint**
  - Safety:
    Rate of sub-acute stent thrombosis in presence of dual antiplatelet therapy
  - Efficacy:
    Cumulative major adverse cardiac events (MACE) [composite of cardiac deaths, myocardial infarction (MI), target lesion revascularization (TLR)] at 9 months
- **Secondary Endpoint**
  - MACE at 1, 12 and 24 months
  - TLR at 1, 9, 12 and 24 months
  - ST at 1, 9, 12 and 24 months

# meriT Clinical Trial Series with BioMime SES

## meriT-I

- Single center, FIM
- 30 patients/lesions
- 8-mo. angio FU
- 2-year clinical FU
- Key results (1-yr.):
  - B2/C: 0%
  - LLL: 0.15 mm
  - ABR: 0%
  - MACE: 0%
  - TLR: 0%
  - ST: 0%

Dani S, et al. EuroIntervention 2013;9:493-500

## meriT-II

- Multicenter
- 250 pts/355 les.
- 8-month angio FU
- 5-year clinical FU
- Key results (1-yr.):
  - MACE: 6%
  - TLR: 5.2%
  - ST: 0.4%

Seth A, et al. AsiaIntervention 2016;2:19-27

## meriT-III

- Multicenter
- Post-marketing
- 1161 patients
- 1-year clinical FU
- Key results (1-yr.):
  - MACE: 2.4%
  - Death: 1.4%
  - TLR: 0.5%
  - ST: 0.1%

Jain RK, et al. Indian Heart J 2016;68:599–603

## meriT-V

- Randomized (2:1) Multicenter
- 256 patients (170 BioMime SES and 86 Xience EES )
- 9-month clinical and Angio FU
- Key results (9-month):

| Events | BioMime | Xience |
|---|---|---|
| MACE | 2.98% | 7.14% |
| MI | 0.60% | 4.76% |
| ID-TLR | 2.38% | 2.38% |
| ST | 0.0% | 0.0% |

Abizaid, et al. EuroIntervention 2018; 14(11):e1207-e1214

# Study Design

A prospective, multicenter, single-arm clinical registry

↓

Study enrolled 520 patients was commenced at 19 different sites globally (Bulgaria, Czech Republic, Hungary, Korea, Kuwait, Malaysia, The Netherland, Portugal, Saudi Arabia, Slovakia, Spain, Sri Lanka, Taiwan, Ukraine)

↓

Baseline assessment, informed consent process

↓

Clinical follow-up at 1 month, 9 months, 12 months, and 24 months

# Eligibility Criteria

| Inclusion criteria | Exclusion Criteria |
|---|---|
| • Males and Females more than 18 years of age<br>• Subjects who are able to give voluntary, written informed consent to participate in this clinical investigation and from whom consent has been obtained<br>• The subjects who have been treated with PCI and implantation of BioMime drug eluting stent as a part of their treatment of coronary artery disease, without any further indication for emergent coronary artery bypass graft surgery | • Subjects who were not eligible for a PCI procedure or who were candidates for Urgent or planned elective Coronary Artery Bypass Surgery<br>• Subjects who are treated with stents other than BioMime<br>• Subjects with more than grade III renal insufficiency as indicated by Creatinine > 160 µmol/L<br>• Subjects with short life expectancy less than the trial duration of 2 years (including subjects with cancer, HIV/AIDS), documented LVEF <30%, history of cardiac failure, structural heart disease, myocardiopathies, arrhythmia or other co-morbid conditions |

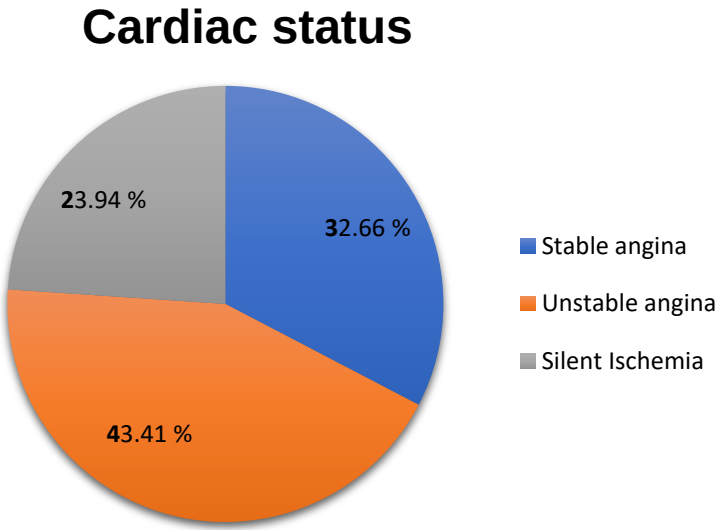
# Investigating Sites

**520 Patients, 19 Investigating Sites**

| Sr. No | Name of Investigator | Name of Hospital (Site) | No. Enrolled Subjects |
|---|---|---|---|
| 1 | Dr. A.J.J. Ijsselmuiden | Albert Schweitzer Hospital | 55 |
| 2 | Dr. Huang | Tiapie Medical University Hospital(TMUH) | 2 |
| 3 | Dr. Hristo Mateev | National Heart Hospital, Sofia, Bulgaria | 4 |
| 4 | Dr. Bela Merkely | University of Semmelweis Hungary | 17 |
| 5 | Dr. Myung Ho Jeong | Chonnam National University | 29 |
| 6 | Dr. In Ho Chae | Seoul National University Bundang Hospital | 31 |
| 7 | Dr. Hyeon-Cheol Gwon | Samsung Medical Center | 50 |
| 8 | Prof. Oteh Maskon | Universiti Kebangsaan Malaysia Medical Centre | 19 |
| 9 | Dr. Jose Maques de Costa | Hospital Santa Maria | 40 |
| 10 | Dr. Rita Cale | Hospital Garcia Orta | 9 |
| 11 | Dr. G K Mayurathan | Teaching Hospital Kandy | 28 |
| 12 | Dr. Martin Hudec | Stredoslovenský ústav srdcových a cievnych chorôb – SUSCCH, a.s. | 88 |
| 13 | Dr. Yi-Chih Wang | National Taiwan University Hospital | 22 |
| 14 | Dr. Min-Ji Charng | Taipei Veterans General Hospital | 24 |
| 15 | Dr. Mar Guang-Yuan | Veteran General Hospital (KVGH) | 1 |
| 16 | Dr. Andriy Khokhlov | Heart Institute of The Ministry of Healthcare of Ukraine | 4 |
| 17 | Dr. Antonio Serra | Hospital de Sant Pau, Barcelona | 15 |
| 18 | Dr. Jose Moreu Burgos | Hospital Virgen de la Salud, Toledo | 29 |
| 19 | Dr. Ramiro Trillo | Complexo Hospitalario Universitario de Santiago de Compostela | 53 |
| | | **Total** | **520** |

# Baseline and Demographic Characteristics

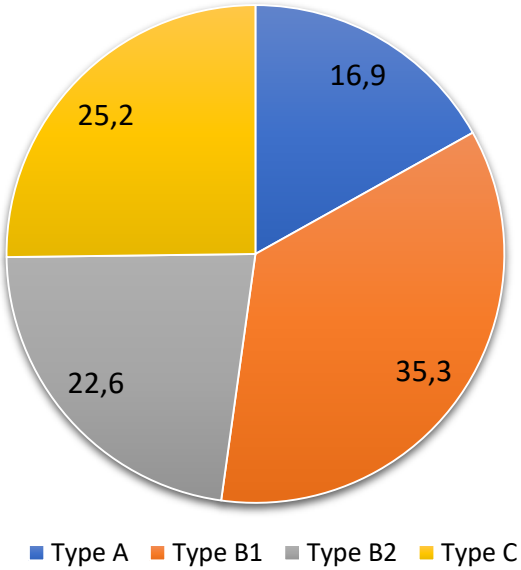
| Characteristics | n = 520 |
|---|---|
| Age, Years, mean±SD | 64.12±11.14 |
| **Gender, n (%)** | |
| Male | 385 (74) |
| Female | 135 (26) |
| BMI, Mean ± SD | 27.10 ± 4.44 |
| **Medical history, n (%)** | |
| Diabetes | 151 (29.0) |
| Hypertension | 326 (62.7.0) |
| Hyperlipidaemia | 267 (51.3) |
| Renal insufficiency | 33 (6.3) |
| Previous MI | 95 (18.3) |
| Previous PCI | 73 (14.0) |
| Family history of CAD | 155 (29.8) |
| Smokers | 265 (51.0) |
| Alcoholic | 106 (20.4) |



# Lesion Characteristics

| Lesion characteristic's, (n=615) | |
|---|---|
| **Total no. of lesion** | 684 |
| **Total no. of lesion treated with study device** | 615 |
| **Stenosis, n (%)** | |
| De novo | 604 (98.2) |
| In-stent | 6 (1.0) |
| Bifurcation | 5 (0.8) |
| **Lesion Location, n (%)** | |
| RCA | 203 (33.0) |
| LAD | 252 (41.0) |
| LCx | 96 (15.6) |
| LM | 6 (1.0) |
| Diagonal | 29 (4.7) |
| Obtuse Marginal | 29 (4.7) |
| **TIMI flow** | **Pre-procedure, n (%)** |
| 0 | 76 (12.4) |
| 1 | 26 (4.2) |
| 2 | 122 (19.8) |
| 3 | 391 (63.6) |

**Lesion Characteristics (%)**
**American College of Cardiology/**
**American Heart Association**



# Cumulative Major cardiac clinical events up to 9 months follow-up

| Events, n (%) | In-hospital (n =520)* | 1-month FU (n =520) | 9-month FU (n =518) |
|---|---|---|---|
| **All cause death** | 0 (0.0) | 0 (0.0) | 2 (0.39) |
| Cardiac death | 0 (0.0) | 0 (0.0) | 1 (0.19) |
| Non-cardiac death | 0 (0.0) | 0 (0.0) | 1 (0.19) |
| **MI** | 0 (0.0) | 0 (0.0) | 3 (0.58) |
| **ID-TLR** | 0 (0.0) | 2 (0.38) | 5 (0.97) |
| **ST** | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| **MACE** | 0 (0.0) | 2 (0.38) | 9 (1.74) |

Values are presented in n (%), MACE=Major adverse cardiac event, MI=Myocardial infarction, ST=Stent thrombosis, TLR=Target lesion revascularization, TVR=Target vessel revascularization

* ongoing Follow-up

# Conclusions

- Study to evaluate the safety and efficacy of BioMime SES in all-comers real-world population
- Safety endpoints were rate of sub-acute ST in presence of dual antiplatelet therapy
- Other endpoints were occurrence of TLR and MACE at 1 and 9 months; frequency of ST at each time point
- Prospective, multicenter, open-label, all-comers real world, clinical study at 19 different sites globally
- MACE occurred in 9 (2.0) subjects at 9-month follow-up which composed of one cardiac death, and two patients had MI with no TVR
- Based on **the lower rate of MACE at 1 and 9 months follow-up**, it can be suggested that BioMime SES is safe and effective in all-comers real-world population
- Novel BioMime SES demonstrated promising performance in treating coronary artery lesions showing high procedural success in real-world population

2019 euro PCR

# Thank You