

# **Amphilimus- vs zotarolimus-eluting stents in patients with diabetes and coronary artery disease (SUGAR trial)**

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on behalf of the SUGAR trial investigators

# Disclosure Statement of Financial Interest

Within the past 12 months, I (**Rafael Romaguera**) or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<u>Affiliation/Financial Relationship</u>	<u>Company</u>
Grant/Research Support	-
Consulting Fees/Honoraria	<b>Boston Scientific, Biotronik</b>
Major Stock Shareholder/Equity	-
Royalty Income	-
Ownership/Founder	-
Intellectual Property Rights	-
Other Financial Benefit	-

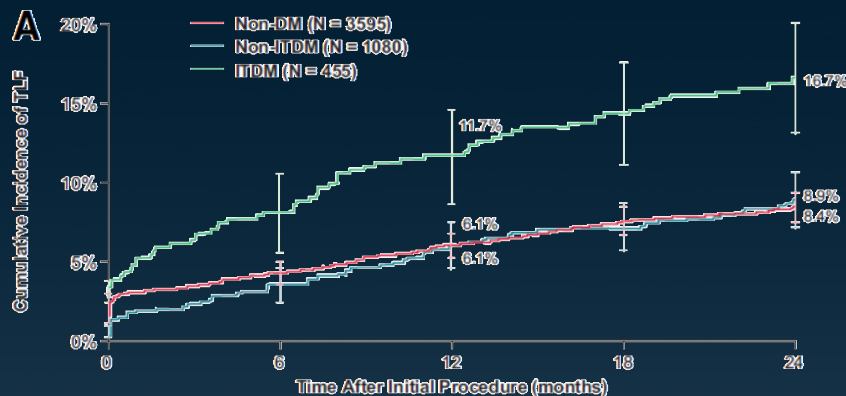
Faculty disclosure information can be found on the app

# Background: overview of the problem



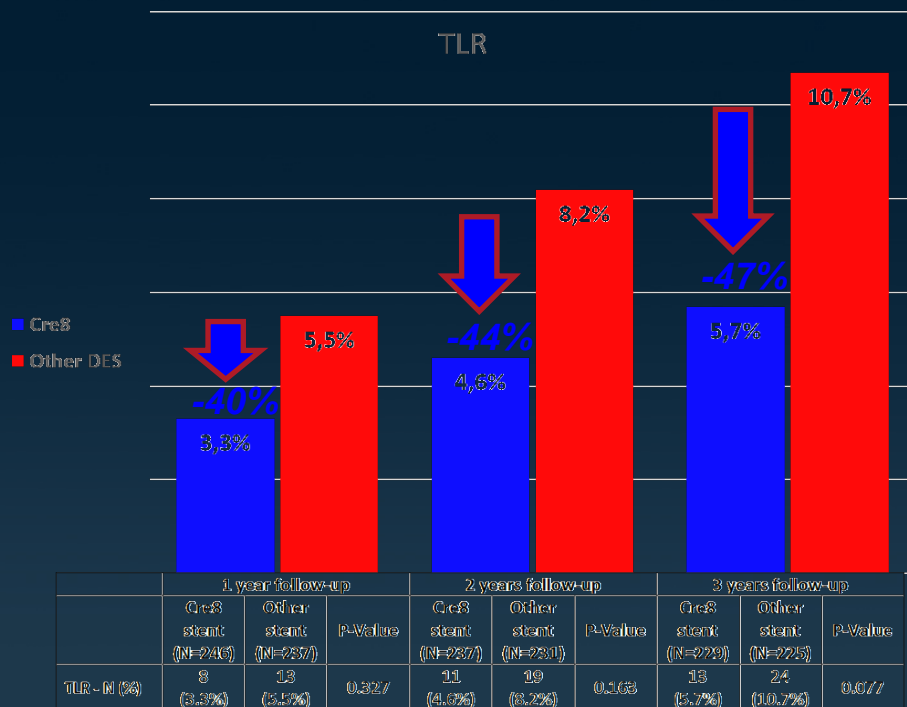
- 463 million patients with DM worldwide
- In US, 38% of PCI have diabetes (~250.000 patients in 2019)

# Background: overview of the problem



- Patients with DM have 2x risk of events with contemporary DES
- Patients with DM & multivessel disease have ↑ mortality compared to CABG when treated with DES

# Background: overview of the problem



- Cre8 EVO stents have shown positive results in non-randomized and small-randomized studies.

# Objective

To compare Cre8 EVO stents to a contemporary DES in patients with DM and coronary artery disease

# Design

- Investigator initiated, randomized (1:1), multicenter (23 centers in Spain), controlled, parallel trial.
- Randomization: web-based, no stratification, blocks of four.
- Masking: event committee.
- Funding: Spanish Society of Cardiology

# Patients

- **INCLUSION CRITERIA:**

- Diabetes mellitus according to ADA
- Indication for PCI

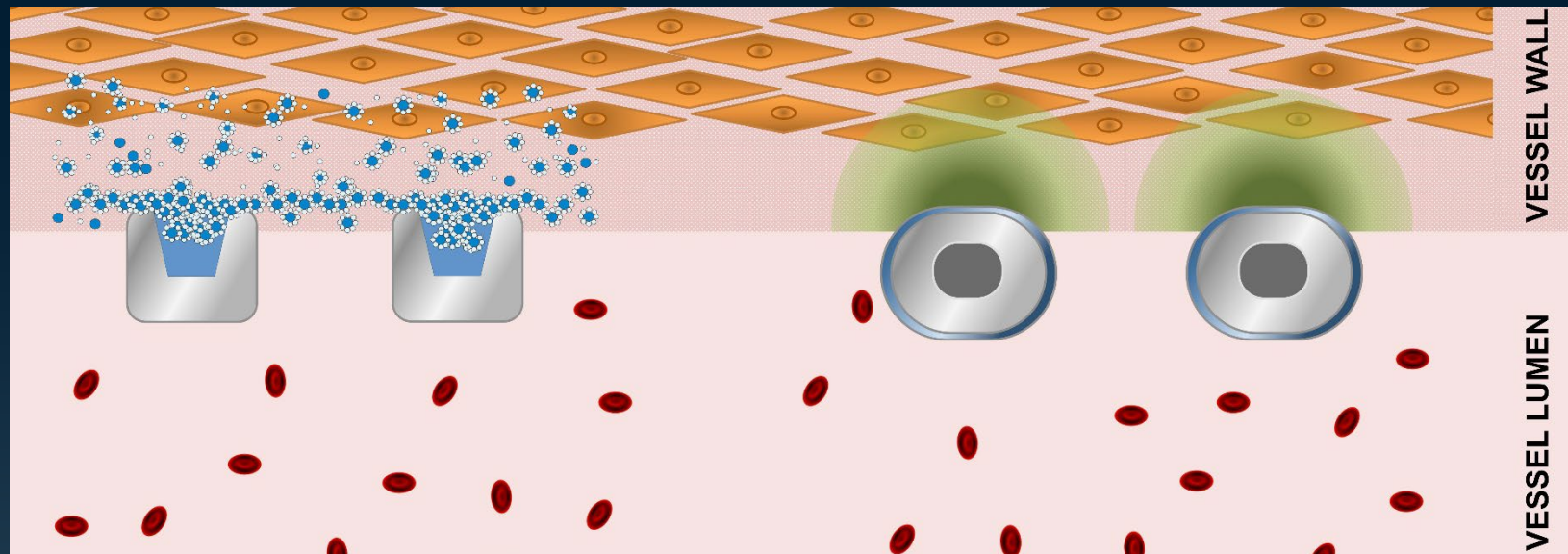
- **EXCLUSION CRITERIA:**

- Life expectancy <2 years
- Cardiogenic shock at presentation
- Mechanical ventilation
- Contraindication for DAPT at least 1 month
- Pregnancy

## **All-comers**

No limitation in clinical presentation, complexity, number of lesions, left main disease, etc.

# Procedures



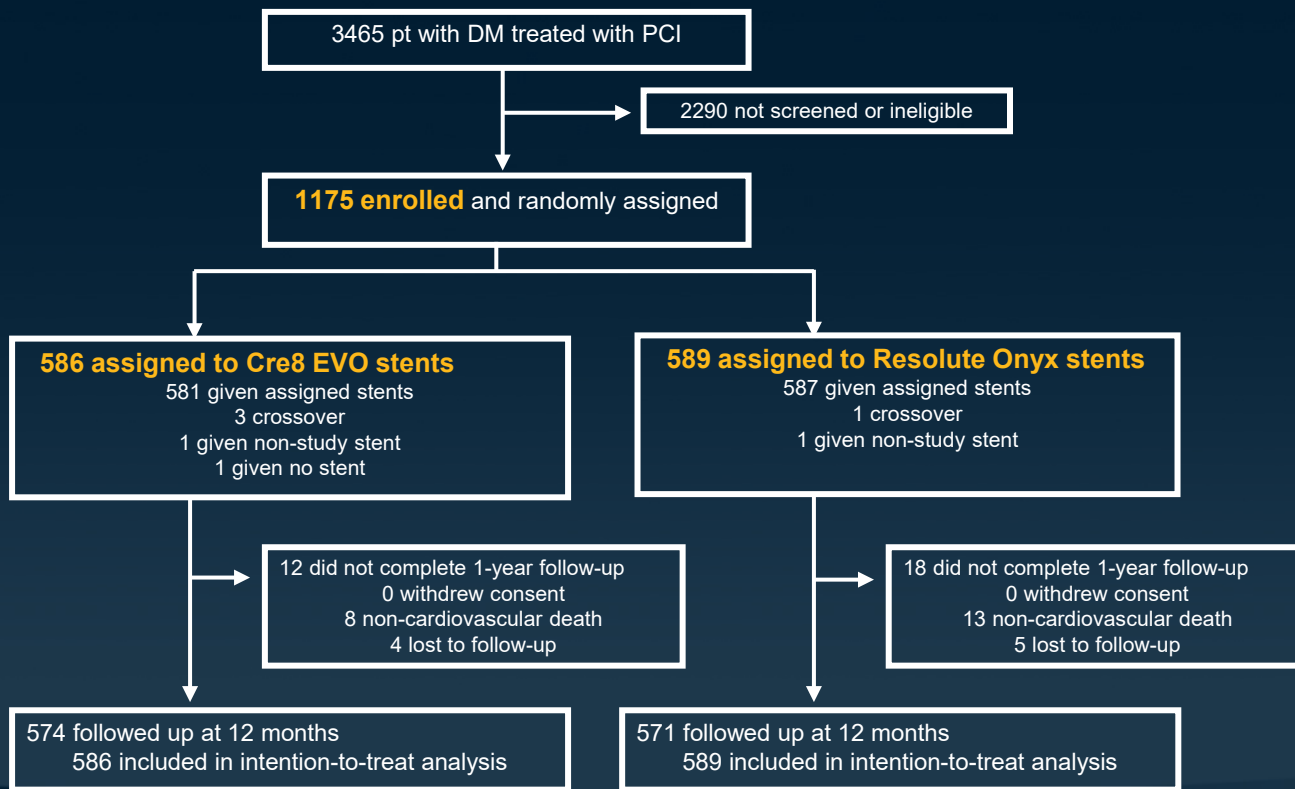
70-80  $\mu\text{m}$   
No polymer  
Sirolimus + carrier

92-102  $\mu\text{m}$   
Permanent polymer  
Zotarolimus alone

# Events and assumptions

- Primary endpoint: **TLF at 1-year** (cardiac death + target-vessel MI + target-lesion failure)
- Adjudication by independent CEC & Barcore-Lab.
- Hypothesis at 1-year: **Non-inferiority at 1-year**.  $\alpha=0.025$ ,  $\beta=80\%$ , 8% events in Resolute Onyx group, 4% NI margin (1.5 RR).  
**Prespecified superiority analysis if NI is met.**

# Trial profile



# Baseline characteristics

	Cre8 EVO (n=586)	Resolute Onyx (n=589)
Age (years)	68.6 (9.8)	67.2 (10.6)
Male sex	449 (76.6%)	439 (74.5%)
LVEF	56.6 (11.3)	56.7 (10.8)
<b>Indication index procedure</b>		
Chronic coronary syndromes	243 (41.5%)	229 (38.9%)
NSTEACS	277 (47.3%)	280 (47.5%)
STEMI	66 (11.3%)	80 (13.6%)
<b>Diabetes and metabolic characteristics</b>		
Diabetes type 2	565 (96.4%)	557 (94.6%)
Years with known diabetes	10.6 (8.7)	11.4 (9.2)
Insulin-treated diabetes at randomization	183 (31.2%)	194 (32.9%)
Waist circumference (cm)	103.1 (13.5)	102.5 (12.4)
LDL cholesterol (mg/dL)	78.8 (44.7)	80.9 (45.5)
HbA1c (%)	7.4 (1.5)	7.5 (1.5)
Creatinine clearance (mL/min)	70.0 (25.4)	73.1 (24.0)

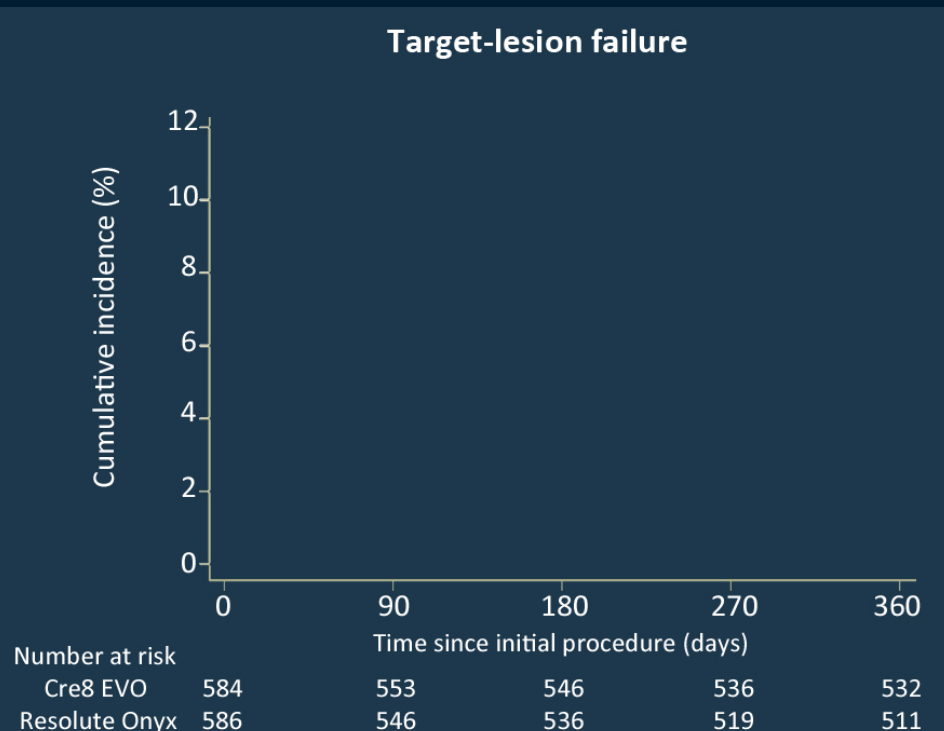
# Procedural characteristics

	Cre8 EVO (patients=586) (lesions=879)	Resolute Onyx (patients=589) (lesions=950)
Syntax Score at randomization	13.0 (9.7)	13.0 (8.7)
Number of vessel diseased		
2	189 (32.3%)	200 (34.0%)
3	102 (17.4%)	107 (18.2%)
Number of stents per patient	1.63 (1.02)	1.75 (1.07)
Complete revascularization	397 (67.7%)	389 (66.0%)
Staged procedures	21 (3.6%)	30 (5.1%)
Target vessel Left Main	28 (3.7%)	25 (3.2%)
Chronic total occlusion	16 (2.1%)	19 (2.4%)
Bifurcation with 2-stents	43 (5.6%)	38 (4.9%)
Reference vessel diameter	2.98 (0.51)	2.96 (0.50)
Total stented length (mm)	26.5 (13.7)	27.4 (14.9)
Postdilation	286 (37.4%)	226 (28.9%)
Rotational atherectomy	22 (2.9%)	11 (1.4%)

# Treatment

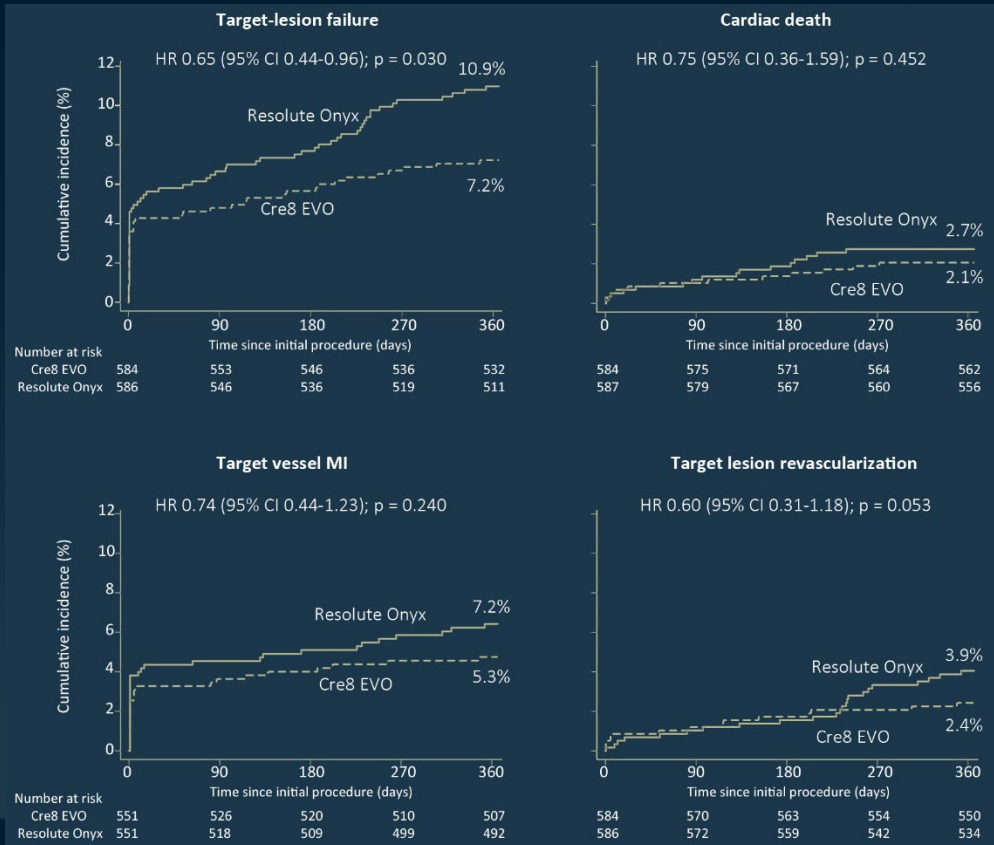
	Cre8 EVO (n=586)	Resolute Onyx (n=589)	p-value
<b>Medication at discharge</b>			
Acetylsalicylic acid	560 (95.6%)	567 (96.3%)	0.54
P2Y12-inhibitors			0.98
Clopidogrel	282 (48.1%)	278 (47.2%)	
Prasugrel	47 (8%)	47 (8%)	
Ticagrelor	241 (41.1%)	249 (42.3%)	
<b>Glucose-lowering drugs</b>			
Insulin	200 (34.1%)	219 (37.2%)	0.28
SGLT2 inhibitors	119 (20.3%)	107 (18.2%)	0.35
GLP1 agonists	18 (3.1%)	14 (2.4%)	0.46
<b>Dual antiplatelet therapy</b>			
At 1 month	552 (94.2%)	554 (94.1%)	0.919
At 6 months	504 (86%)	504 (85.6%)	0.830
At 12 months	314 (53.6%)	349 (59.3%)	0.050

# Primary endpoint



- Difference -3.73%  
(95% CI -7.01 to -0.45)  
 $p < 0.001$  for noninferiority
- HR 0.65 (95% CI 0.44 to 0.96)  
 $p = 0.030$  for superiority

# Individual components of the primary endpoint



# Other secondary endpoints

	Cre8 EVO (n=586)	Resolute Onyx (n=589)	HR (95% CI)	p-value
All-cause mortality	20 (3.4%)	29 (5.0%)	0.69 (0.39-1.22)	0.201
Any MI	34 (6.2%)	43 (7.7%)	0.78 (0.50-1.23)	0.289
Any revascularizations	29 (5.0%)	37 (6.3%)	0.78 (0.48-1.27)	0.314
Target vessel revascularization	18 (3.1%)	24 (4.1%)	0.75 (0.40-1.37)	0.346
Definite stent thrombosis	6 (1.0%)	5 (0.9%)	1.20 (0.37-3.94)	0.760
Probable or definite stent thrombosis	8 (1.4%)	8 (1.4%)	1.00 (0.38-2.67)	0.994
Acute	3 (0.5%)	2 (0.3%)	-	
Subacute	4 (0.7%)	4 (0.7%)	-	
Late	1 (0.2%)	2 (0.3%)	-	
Target vessel failure	44 (7.5%)	65 (11.1%)	0.67 (0.46-0.99)	0.042
MACE	64 (11.7%)	88 (15.7%)	0.74 (0.53-1.02)	0.067

# Conclusions

- SUGAR is the first powered trial to compare new-generation DES in patients with diabetes, and also the first to include a broad population of patients with diabetes (all-comers design).
- **Cre8 EVO stents were non-inferior to Resolute Onyx stents** with regards to TLF composite outcome.
- In the prespecified superiority analysis, **Cre8 EVO stents were also superior** to Resolute Onyx stents with regards to the same outcome (35% risk reduction of TLF at 1-year).