Two-Year Outcomes Of The Randomized Second-Generation Drug-Eluting Stents In Diabetes (SUGAR) Trial

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and Rafael Romaguera on behalf of the SUGAR investigators

Disclosure Statement of Financial Interest

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

Affiliation/Financial Relationship	Company
Consulting fees/Honoraria	Boston Scientific, Abbott Vascular, Biomenco, Medtronic

Faculty disclosure information can be found on the app

Background (i)

- Diabetes Mellitus (DM) global prevalence is estimated at 450 M
- PCI in patients with DM has an increased risk of adverse events, but few studies address specifically this population
- Previous evidence suggested improved PCI outcomes in DM with the amphillimus eluting stent in observational or small randomized trials
- The Sugar Trial aims to confirm these findings with clinical outcomes

WHO global burden of disease study 2019

The SUGAR Trial

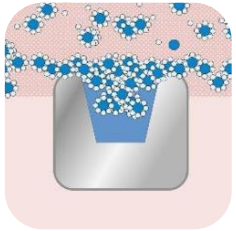
Second-generation drUg-elutinG stents in diAbetes: a Randomized trial

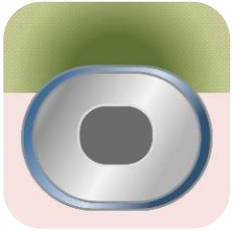
1175 all comers patients with diabetes mellitus eligible for PCI were randomized (1:1)

NCT03321032

Cre8 EVO

Polymer-free stent eluting Amphillimus
70 – 80 µm thickness
(laser-dug wells)





Resolute Onyx

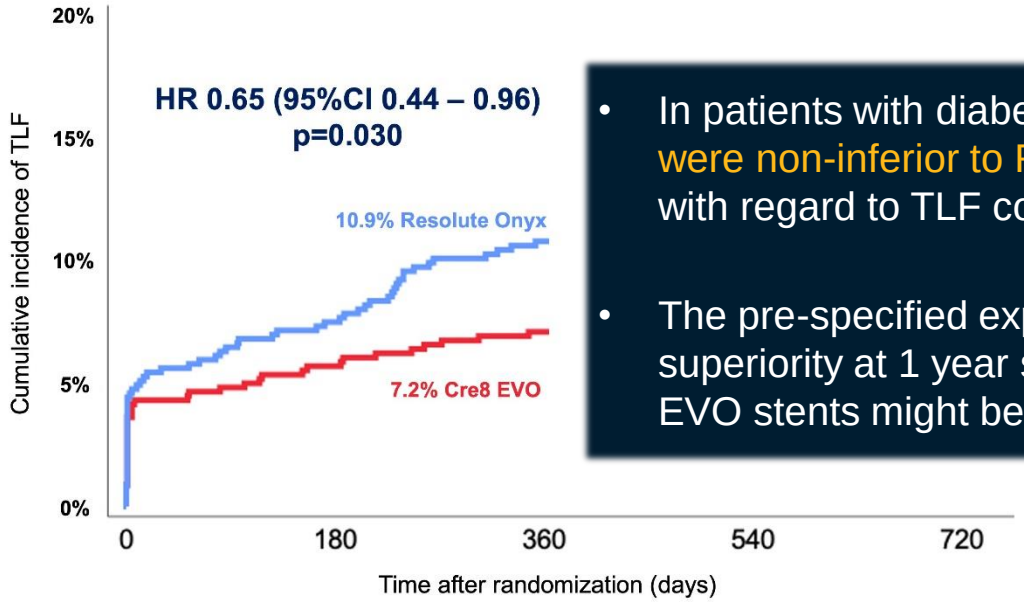
Durable polymer stent eluting Zotarolimus
92 – 102 µm thickness
(including metal + polymer)

Primary endpoint Target lesion failure (TLF)
(cardiac death, target vessel MI, or target lesion revascularization)

Romaguera, Salinas et al. SUGAR Trial rationale and study design. Am Heart J 2020;222:174-82

Background (ii) Sugar Trial at 1 year

Co-primary endpoint powered for non-inferiority



- In patients with diabetes, Cre8 EVO stents were non-inferior to Resolute Onyx stents with regard to TLF composite outcome
- The pre-specified exploratory analysis for superiority at 1 year suggested that Cre8 EVO stents might be superior

TLF is a composite of cardiac death, target vessel MI, or target lesion revascularization

Romaguera, Salinas et al. *Eur Heart J* (2022) 43, 1320–1330

The SUGAR Trial: study design

Trial organization

- **Design:** Randomized, controlled, single-blind, multi-center, investigator-initiated trial
- **Funding:** Spanish Society of Cardiology
- **Randomization:** patient-based, blocks of four, no stratification
- **Independent & blinded event adjudication:** BARCICORE Lab, Barcelona, Spain
- **Independent statistical board:** Clinical Trials Coordination Unit at CNIC, Madrid, Spain
- **Principal investigators**
  Rafael Romaguera. (H. Bellvitge, Barcelona)
  Pablo Salinas (H. Clinico, Madrid)

23 centers in Spain

Romaguera, Salinas et al. SUGAR Trial rationale and study design. Am Heart J 2020;222:174-82

The SUGAR Trial: study design

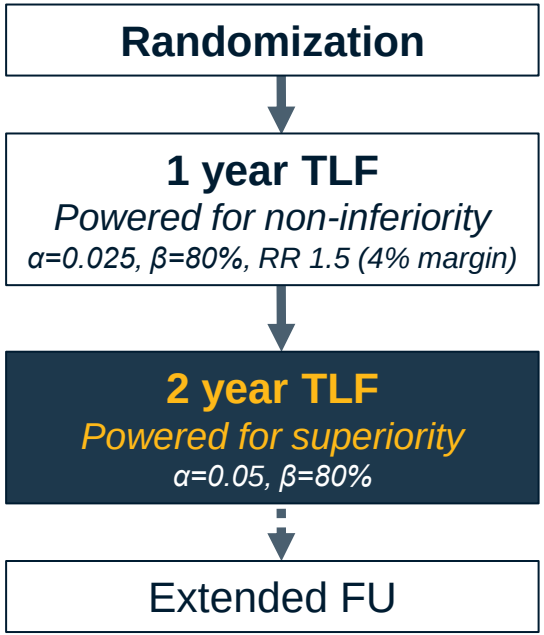
Inclusion criteria

- Diabetes mellitus according to ADA definition
- Indication for PCI (local Heart Team)

Exclusion criteria

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

Follow-up



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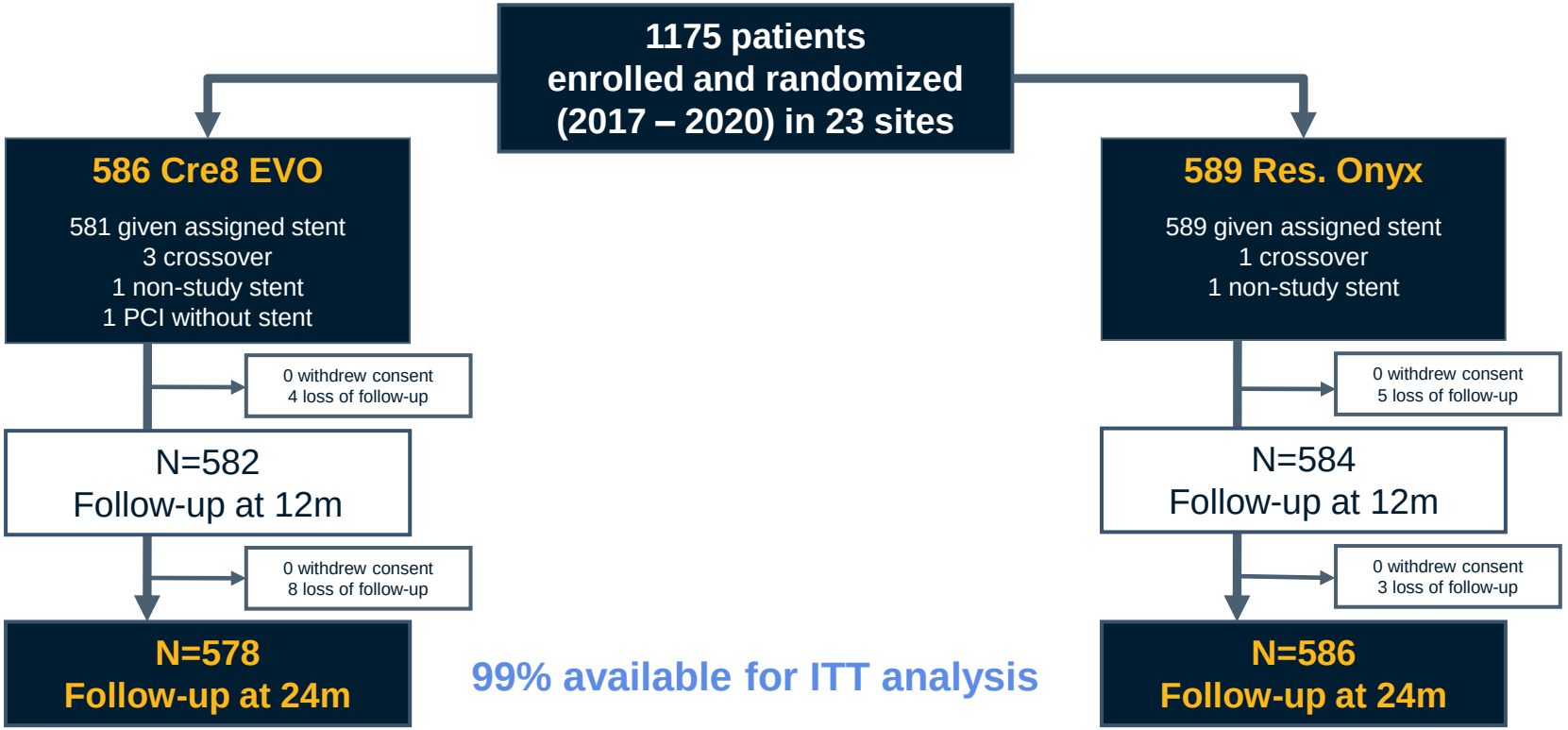
Study Flow


1175 patients
enrolled and randomized
(2017 – 2020) in 23 sites
586 Cre8 EVO
581 given assigned stent
3 crossover
1 non-study stent
1 PCI without stent
0 withdrew consent
4 loss of follow-up
N=582
Follow-up at 12m
0 withdrew consent
8 loss of follow-up
N=578
Follow-up at 24m
589 Res. Onyx
589 given assigned stent
1 crossover
1 non-study stent
0 withdrew consent
5 loss of follow-up
N=584
Follow-up at 12m
0 withdrew consent
3 loss of follow-up
N=586
Follow-up at 24m
99% available for ITT analysis

Main baseline characteristics at randomization

	Cre8 EVO 586 pts	Resolute Onyx 589 pts
Age (years)	68.6 ± 9.8	67.2 ± 10.6
Male Sex	449 (76.6%)	439 (74.5%)
Hypertension	493 (84.1%)	488 (82.9%)
Dyslipidemia	485 (82.8%)	471 (80.0%)
LDL cholesterol (mg/dL)	78.8 ± 44.7	80.9 ± 45.5
BMI (kg/m^2)	29.4 ± 5.0	29.0 ± 4.5
Creatinine clear. (mL/min)	70.0 ± 25.4	73.1 ± 24.0
LVEF	56.6 ± 11.3	56.7 ± 10.8
Current smoker	111 (18.9%)	144 (24.4%)
Previous MI	105 (17.9%)	95 (16.1%)
Previous PCI	136 (23.2%)	122 (20.7%)
Previous CABG	21 (3.6%)	15 (2.5%)

	Cre8 EVO 586 pts	Resolute Onyx 589 pts
Diabetes type 2	565 (96.4%)	557 (94.6%)
Years with known diabetes	10.6 ± 8.7	11.4 ± 9.2
Insulin-treated diabetes	183 (31.2%)	194 (32.9%)
HbA1c (%)	7.4 ± 1.5	7.5 ± 1.5

Clinical presentation	Cre8 EVO 586 pts	Resolute Onyx 589 pts
Chronic coronary syndrome	243 (41.5%)	229 (38.9%)
Acute coronary syndrome		
Non ST elevation ACS	277 (47.3%)	280 (47.5%)
ST elevation MI	66 (11.3%)	80 (13.6%)

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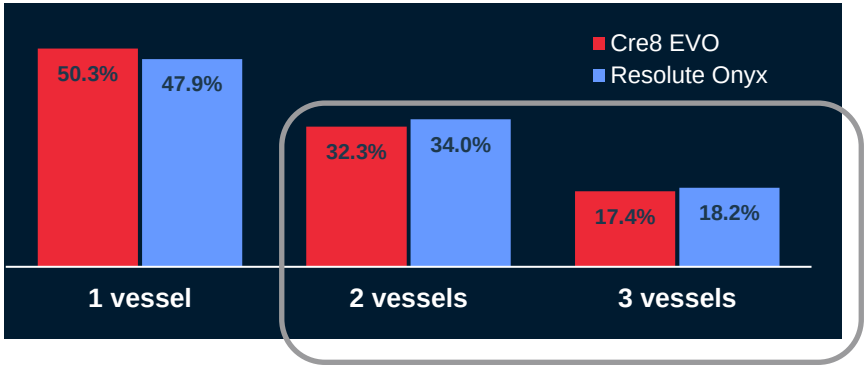
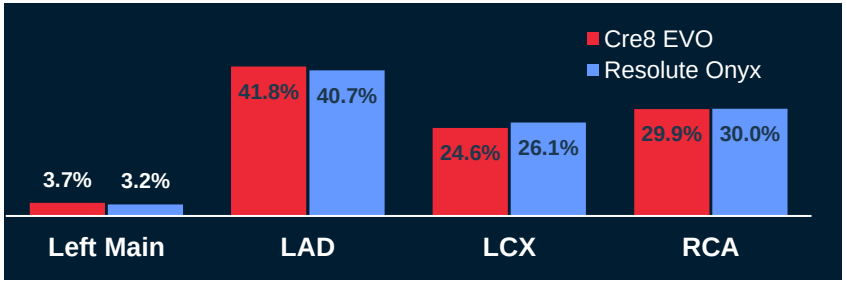
Main procedural characteristics at randomization

	Cre8 EVO 586 pts	Resolute Onyx 589 pts
Syntax score at randomization	13.0 ± 9.7	13.0 ± 8.7
Number of lesions per patient	1.50 ± 0.83	1.61 ± 1.88
Number of stents per patient	1.63 ± 1.02	1.75 ± 1.07
Complete revascularization	397 (67.7%)	389 (66.0%)
Diameter stenosis (%)	83.3 ± 17.1	84.7 ± 15.1
RVD by visual estimation (mm)	2.98 ± 0.51	2.96 ± 0.50
Total stented length (mm)	26.5 ± 13.7	27.4 ± 14.9
Post-dilation	286 (37.4%)	226 (28.9%)
Rotational atherectomy	22 (2.9%)	11 (1.4%)
Chronic total occlusion	16 (2.1%)	19 (2.4%)
Bifurcation with 2 stents	43 (5.6%)	38 (4.9%)
Intracoronary imaging	41 (5.2%)	41 (5.4%)



~50% multivessel disease



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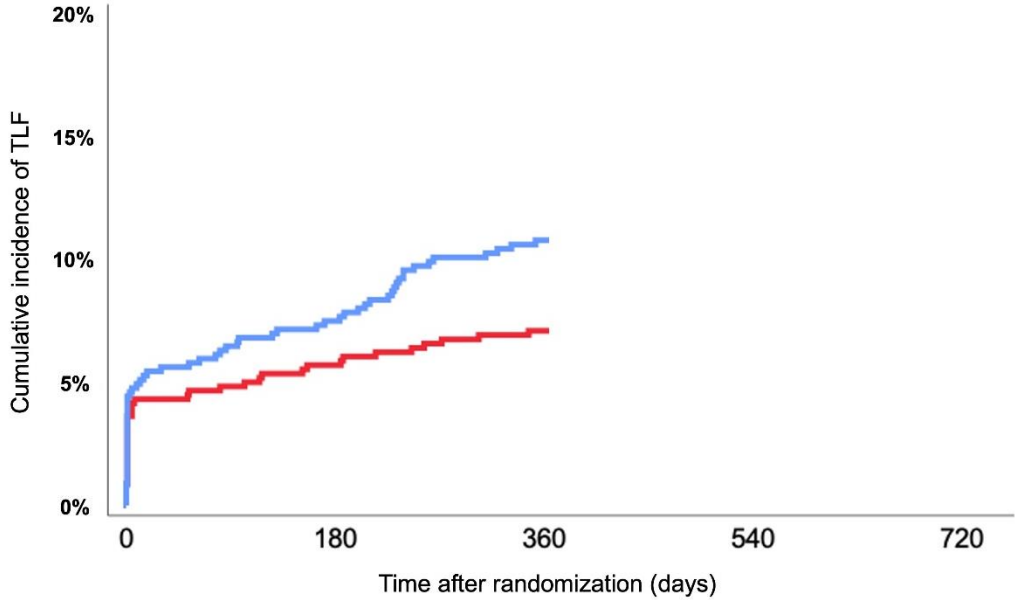
Target Lesion Failure at 2 years

primary endpoint powered for superiority

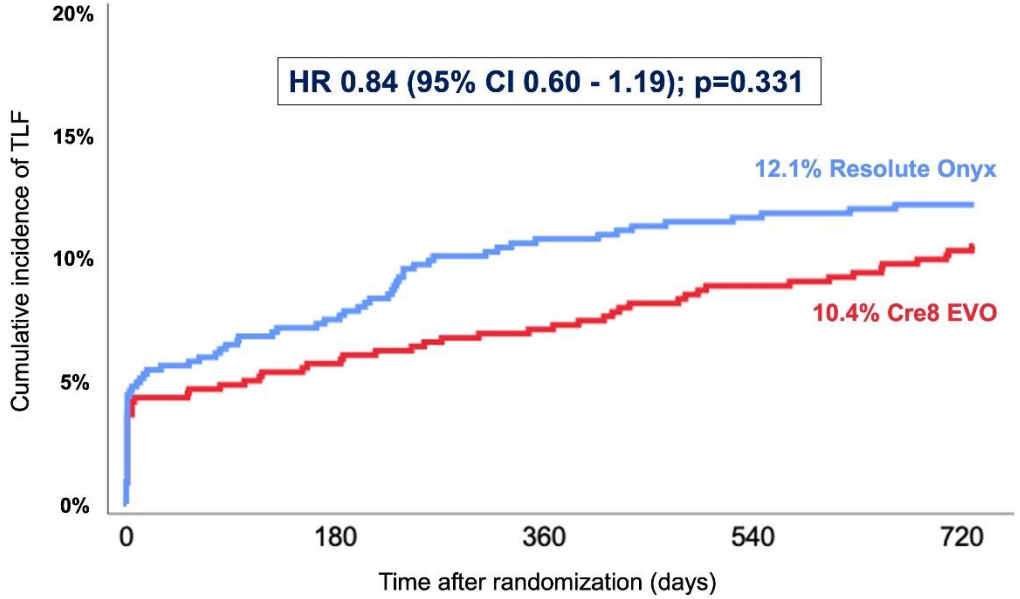


Number at risk					
Cre8 EVO	578	541	529	512	496
Res. Onyx	586	537	512	502	497

TLF is a composite of cardiac death, target vessel MI, or target lesion revascularization

Target Lesion Failure at 2 years

primary endpoint powered for superiority



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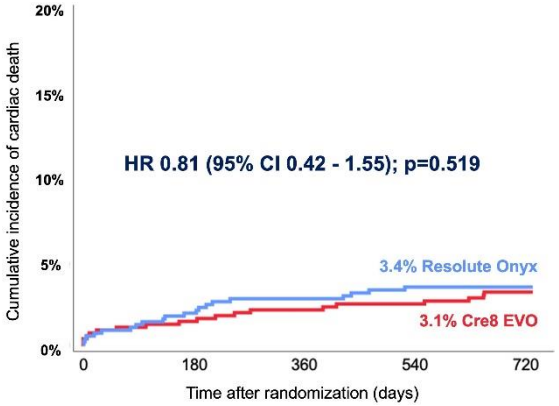
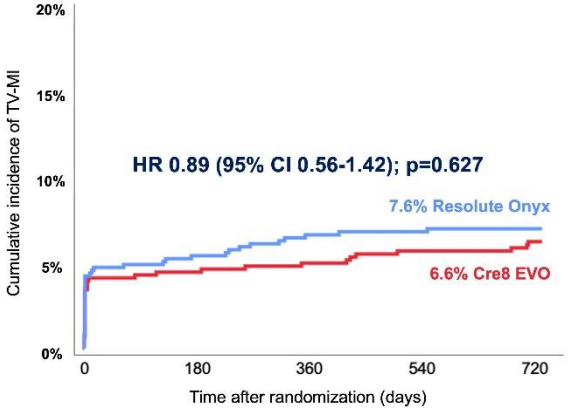
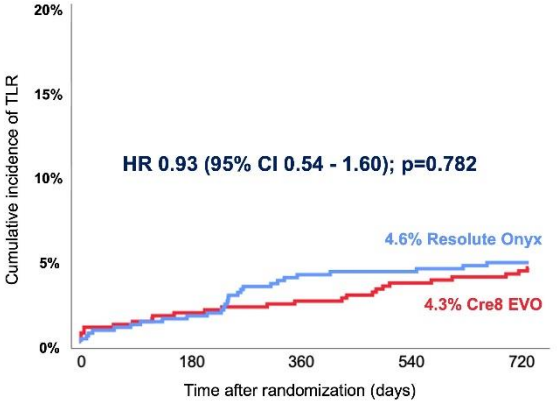
Individual components of the primary endpoint



Cardiac death



Target vessel Myocardial Infarction



Target Lesion Revascularization

TVMI defined as per the third universal definition
TLR was clinically indicated (no angiographic FU)

Secondary endpoints

	Cre8 EVO n = 578	Res. Onyx n = 578	HR (95% CI)	*P* Value
All cause mortality	41 (7.1%)	40 (6.8%)	1.03 (0.67-1.59)	0.890
Any MIs	44 (9.0%)	51 (9.2%)	0.89 (0.59-1.36)	0.595
Target vessel revascularization	32 (5.5%)	30 (5.1%)	1.07 (0.65-1.76)	0.790
All new revascularizations	44 (7.6%)	55 (9.4%)	0.79 (0.54-1.19)	0.265
Definite stent thrombosis	6 (1.0%)	7 (1.2%)	0.87 (0.29-2.58)	0.795
Probable or definite stent thrombosis	8 (1.4%)	10 (1.7%)	0.81 (0.32-2.05)	0.655
Target vessel failure	64 (11.1%)	73 (12.5%)	0.88 (0.63-1.23)	0.440
Major adverse cardiac events	101 (18.3%)	116 (20.8%)	0.88 (0.68-1.16)	0.371

No difference in as-treated analysis. No differences in pre-specified subgroup analyses

Conclusion

- SUGAR is the first randomized trial to compare second-generation DES in patients with diabetes and an all-comers pragmatic design
- **At two years, there is insufficient evidence that Amphilimus-eluting stents (Cre8 EVO) are superior to Zotarolimus-eluting stents (Resolute Onyx) with regard to target lesion failure in patients with diabetes undergoing PCI**
- Extended follow-up until 5 years is warranted