Advancing PCI outcome in diabetics with the innovative Cre8™ EVO DES

The latest updates on AES clinical studies

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Disclosure statement

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***
Speaker honoraria, proctor	Medtronik, Biotronik, Boston Scientific, Alvimedica

The NEXT randomized study (FIM)

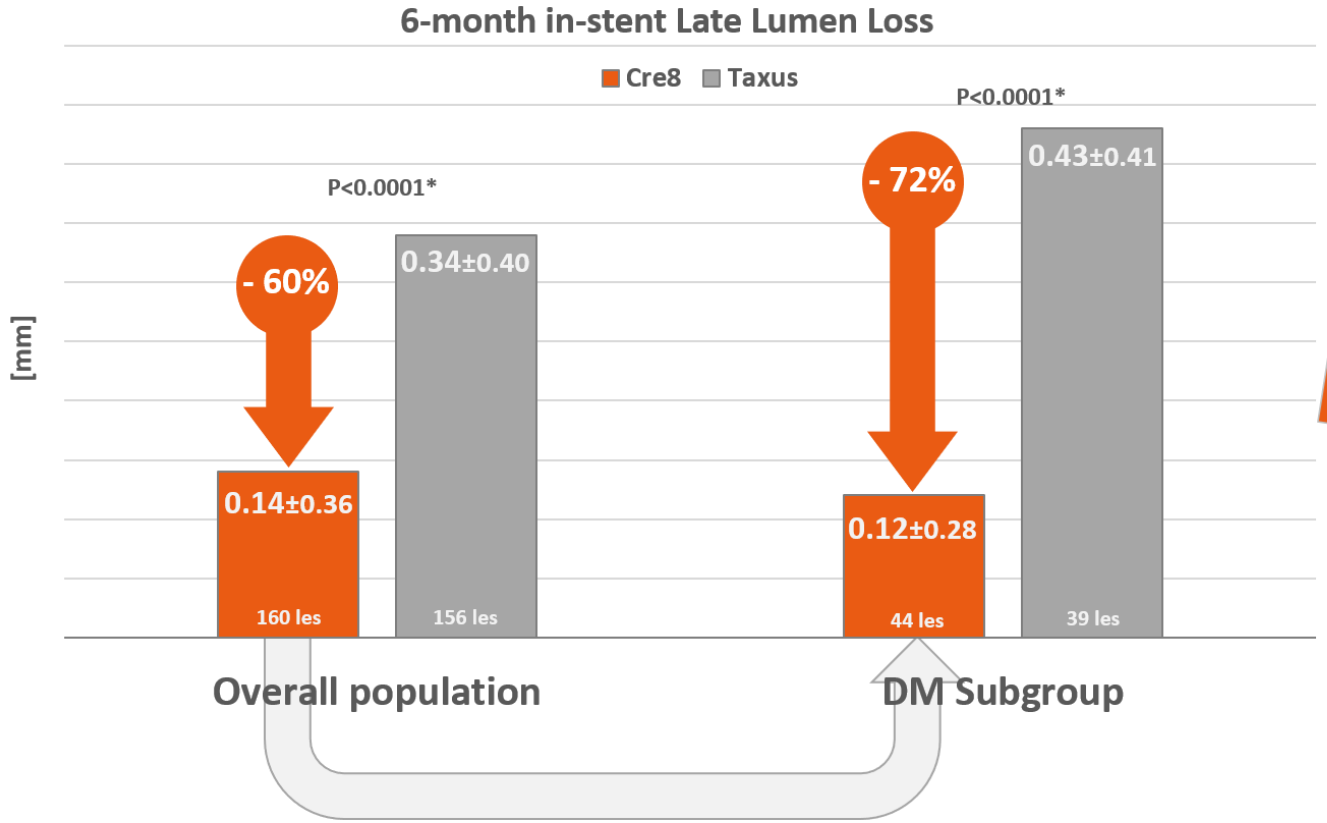
Patients with ischemic myocardial symptoms related to de novo lesions (max 2 in 2 different vessels) in native coronary arteries

323 patients/ 11 European Sites
100% angiographic f-up/ 20% IVUS f-up

Cre8™ (n=162 pts)

TAXUS™ Liberté® (n=161 pts)

Primary Endpoint



*: for superiority

The LLL in the diabetic subgroup is comparable to the LLL obtained in the overall population

Carrié et al JACC, 2012, 59; 1371-76

Reservoir: Independent RCT

Multicenter, randomized, noninferiority trial
in DM patients (receiving glucose-lowering agent) - evaluated with OCT

112 patients/ 89,3% angio f-up/ 87,5% OCT f-up

PI: R. Romaguera, Barcelona, Spain

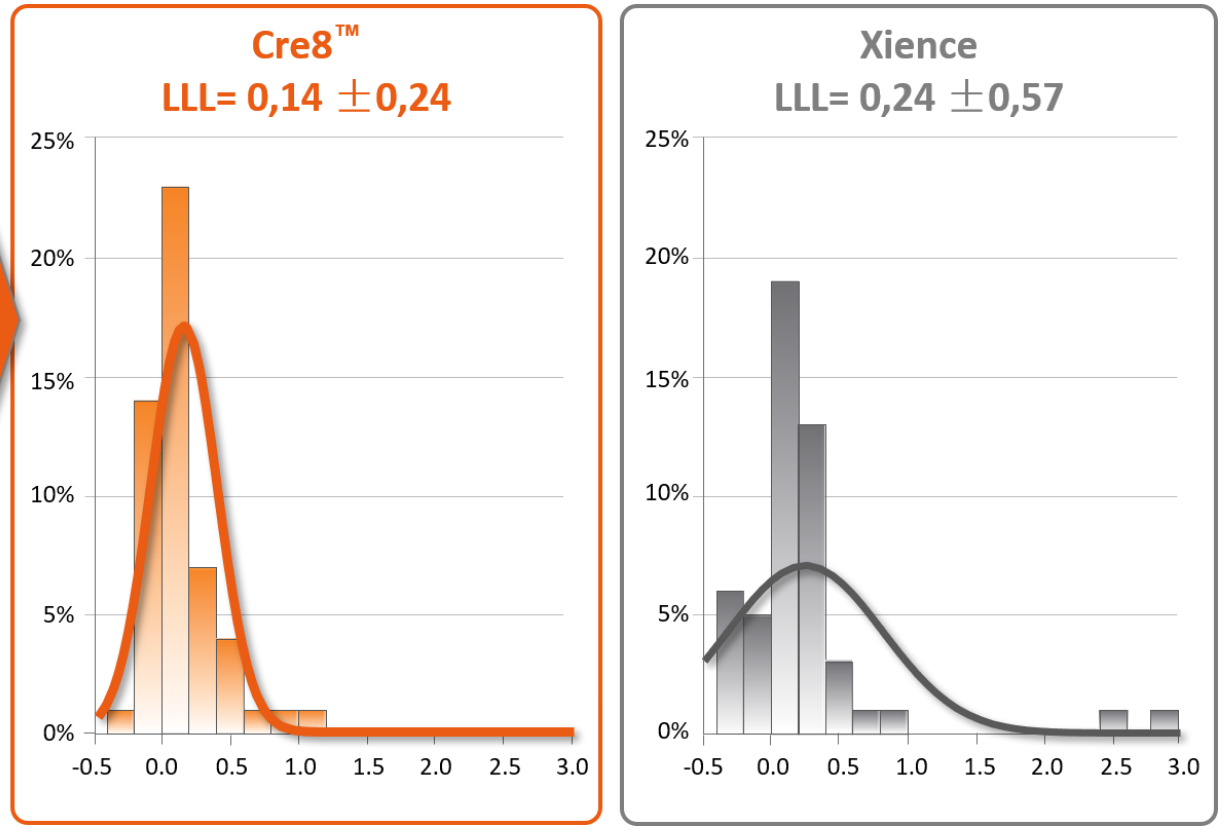
Cre8™ (n=56 pts)

Xience (n=56 pts)

In-stent LLL at 9months

Cre8™ in-stent Late Lumen Loss has resulted very low (0.14mm) confirming the efficacy value seen in FIM study.

The Standard Deviation is really low; it highlights data consistency



JACC Cardiovasc Interv. 2016 Jan 11;9(1):42-50.

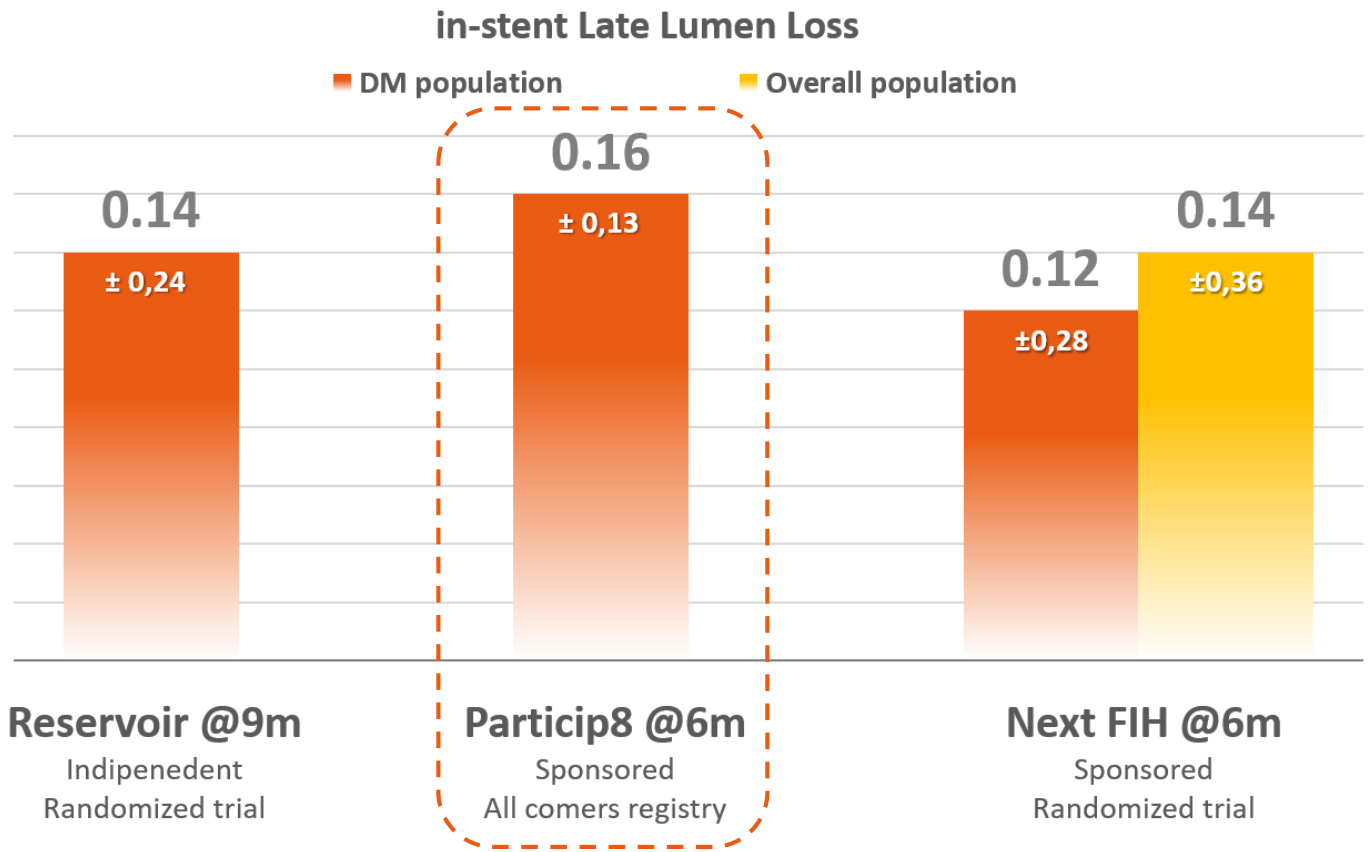
Particip8: Prospective all-comers study

Multicentric Registry on Cre8™ in “Real-World” patients with a specific focus on diabetics subjects

1186 patients/ 30 European Sites/ 8 Countries/ DM prespecified subgroup with angiographic f-up

PI: A. Colombo, Milan, Italy

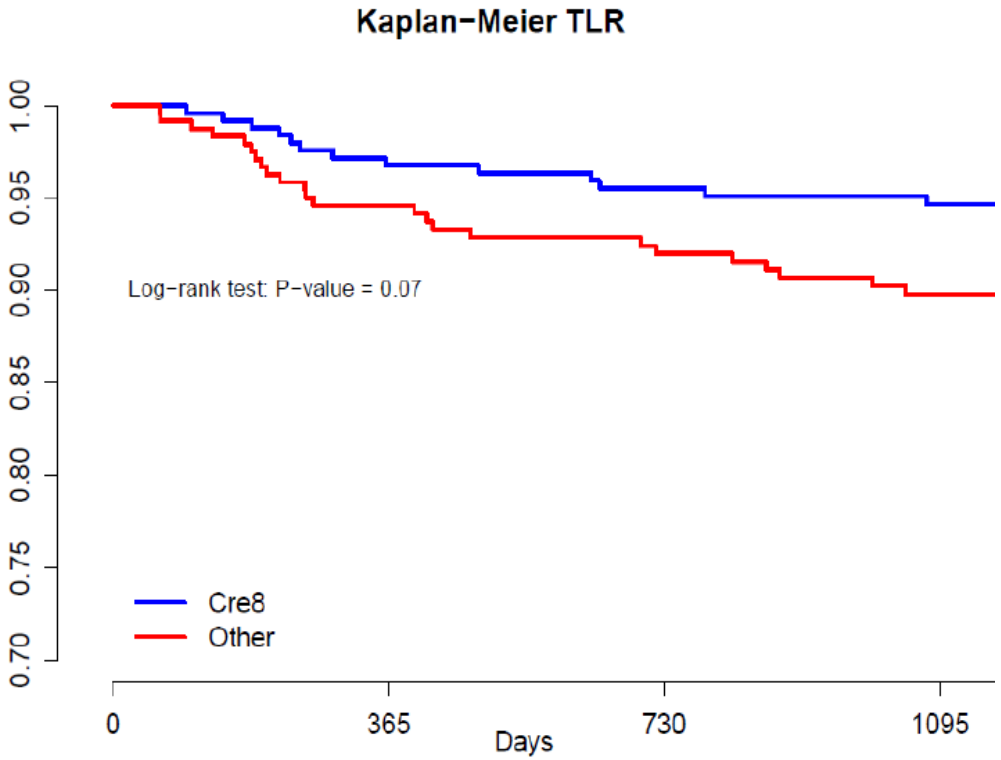
3 different studies
3 different core labs
EQUIVALENT OUTCOME

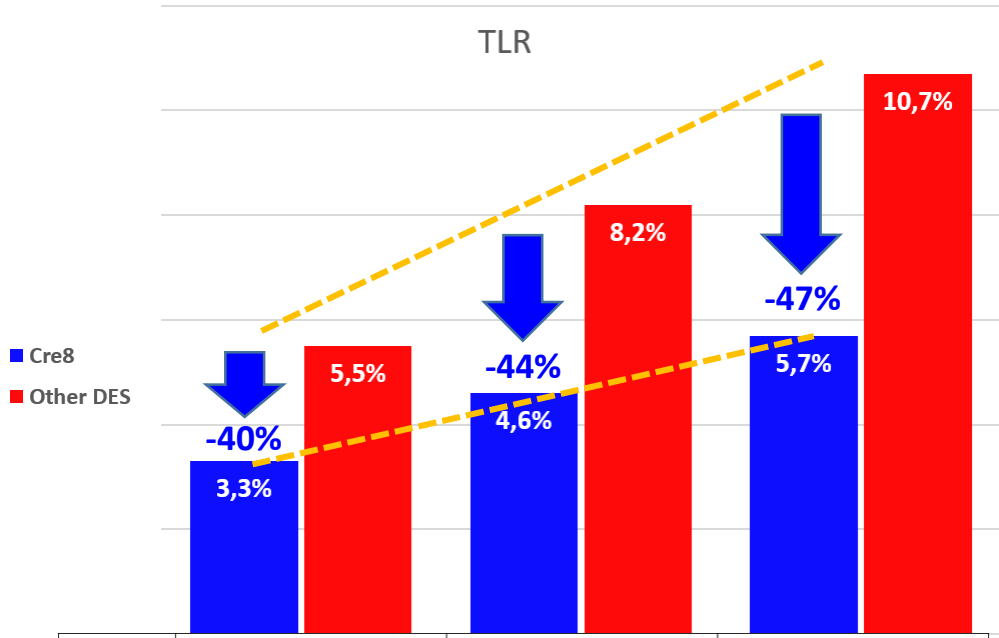


Data released @ TCT 2015

Pulled RCTs analysis @ 3years (DM pts)

TLR results of a pooling analysis of three different Cre8™ RCTs, considering DM patients only, have been taken into account. Specifically those vs Xience[1], Resolute[2] and Taxus[3]





	1 year follow-up			2 years follow-up			3 years follow-up		
	Cre8 stent (N=246)	Other stent (N=237)	P-Value	Cre8 stent (N=237)	Other stent (N=231)	P-Value	Cre8 stent (N=229)	Other stent (N=225)	P-Value
TLR - N (%)	8 (3.3%)	13 (5.5%)	0.327	11 (4.6%)	19 (8.2%)	0.163	13 (5.7%)	24 (10.7%)	0.077

Presented by Dr. R. Romaguera at EuroPCR 2021

1: Romaguera R. JACC Intv 2016/ 2:Stella P. Circulation 2019/ 3: Carrie D. JACC 2012

Matched analysis: Astute vs Inspire-1

ASTUTE registry

AmphilimuS iTalian mUlticenTer rEgistry

1216 patients (1637 lesions)

August 2011 - January 2015
San Raffaele Scientific Institute, Milan
Clinica Mediterranea, Naples
IRCCS Policlinico San Donato, San Donato M.se, Milan
Ospedale San Pietro FBF, Rome
Ospedale San Giovanni di Dio, Agrigento
Ospedali Riuniti Marche Nord, Pesaro
Ospedale Santa Corona, Pietra Ligure
Istituto Clinico Città Studi, Milan
EMO-GVM Centro Cuore Columbus, Milan

Int J Cardiol. 231 (2017) 54–60
Int J Cardiol. 214 (2016) 113–120

INSPIRE-1 registry

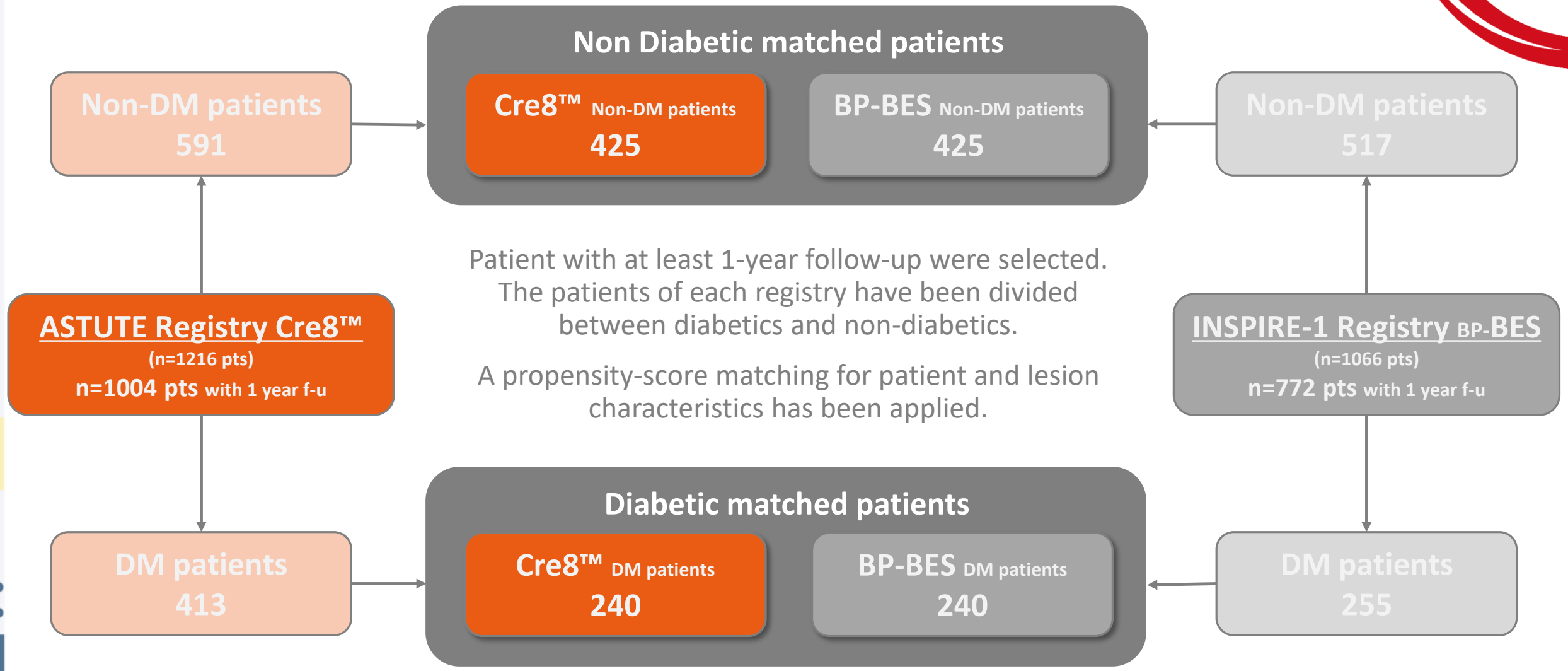
Italian Nobori Stent ProspectIve REgistry-1

1066 patients (1589 lesions)

February 2008 - July 2012
San Raffaele Scientific Institute,Milan
Humanitas Clinical Institute, Milan
Ospedale San Paolo, Bari, Italy
Policlinico Umberto I, "La Sapienza" University of Rome
Clinica Mediterranea, Naples
Ospedali Riuniti Marche Nord, Pesaro
EMO-GVM Centro Cuore Columbus, Milan

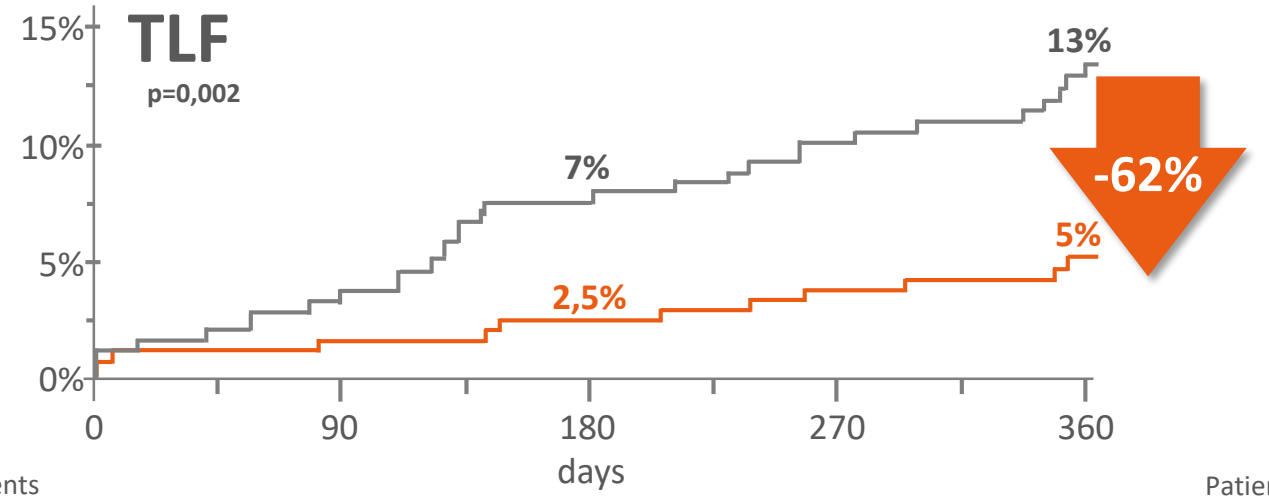
Int J Cardiology 177 (2014)

Matched analysis: Astute vs Inspire-1

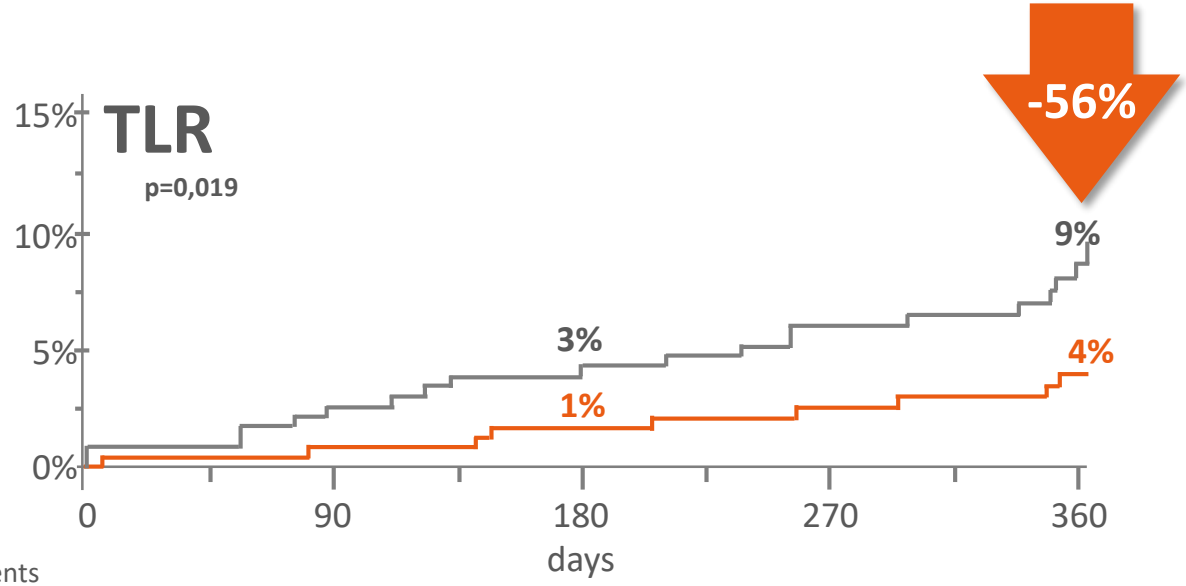


Matched analysis: Cre8™ vs BP-BES (Nobori)

Diabetic cohort – TLF/TLR



Patients at risk					
BP-BES	240	231	221	214	164
Cre8™	240	236	232	226	191



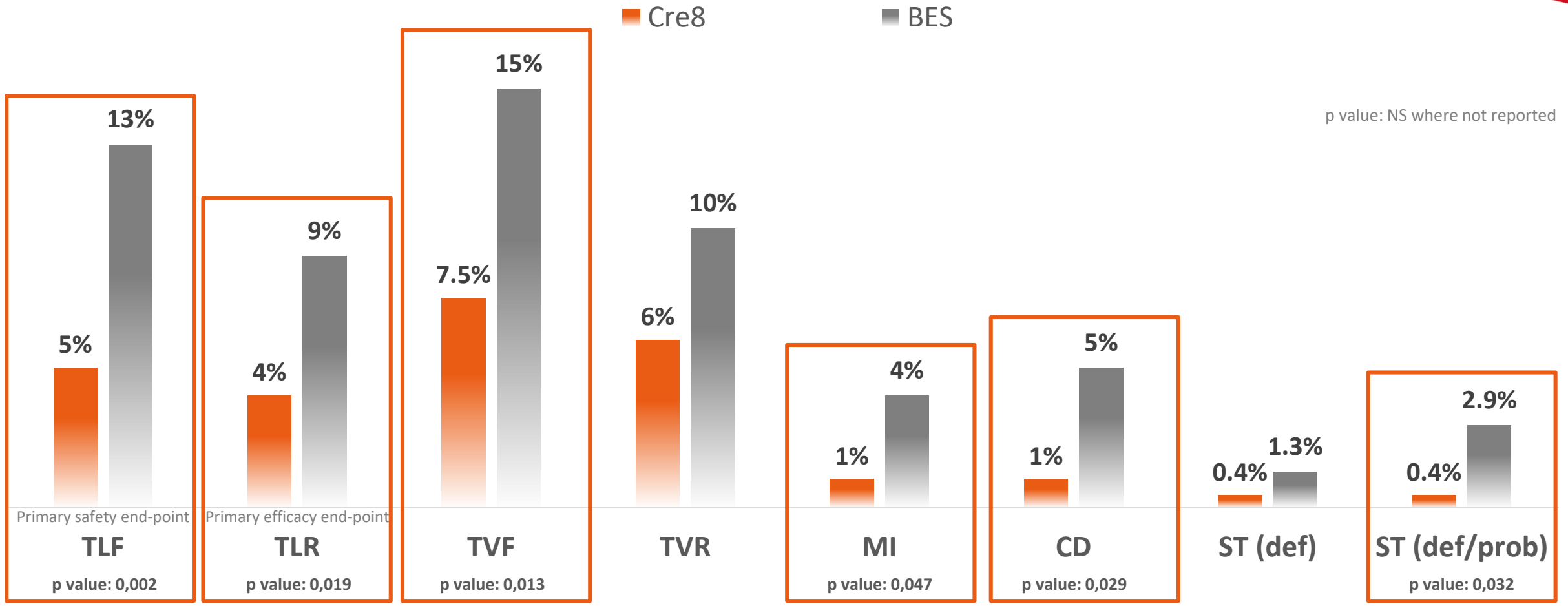
Patients at risk					
BP-BES	240	232	223	216	166
Cre8™	240	236	232	226	191

Cre8™ is always statistically superior to BP-BES:
TLF = 5% vs. 13% (-62%; p=0.002)
TLR = 4% vs. 9% (-57%; p=0.019)

Int J Cardiology 245 (2017) 69–76

Matched analysis: Cre8™ vs BP-BES (Nobori)

DM-matched population - Clinical Endpoints at 12 months follow-up.



Int J Cardiology 245 (2017) 69–76

The latest evidence

The SUGAR randomized trial

Study promoted and funded by the Spanish Society of Cardiology

SECOND GENERATION DRUG ELUTING STENT IN DIABETES: A RANDOMIZED TRIAL (SUGAR)

Multicenter, randomized
in all-comer DM patients undergoing PCI

1175 patients
26 Spanish sites
Randomization 1:1

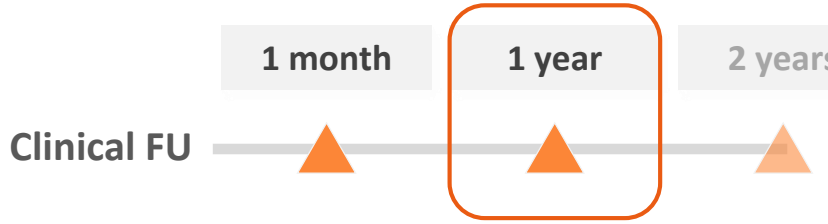
PIs: R. Romaguera, Barcelona, Spain
P. Salinas, Madrid, Spain

Cre8™ EVO
PF AES

ONYX
DP ZES

Primary Endpoint: TLF (composite of CD, TV-MI and cl-TLR) at 1 year (non inferiority - NI) and prespecified superiority analysis if NI is met

Co-Primary Endpoint: TLF at 2 years (**superiority**)



LBT @ TCT2021

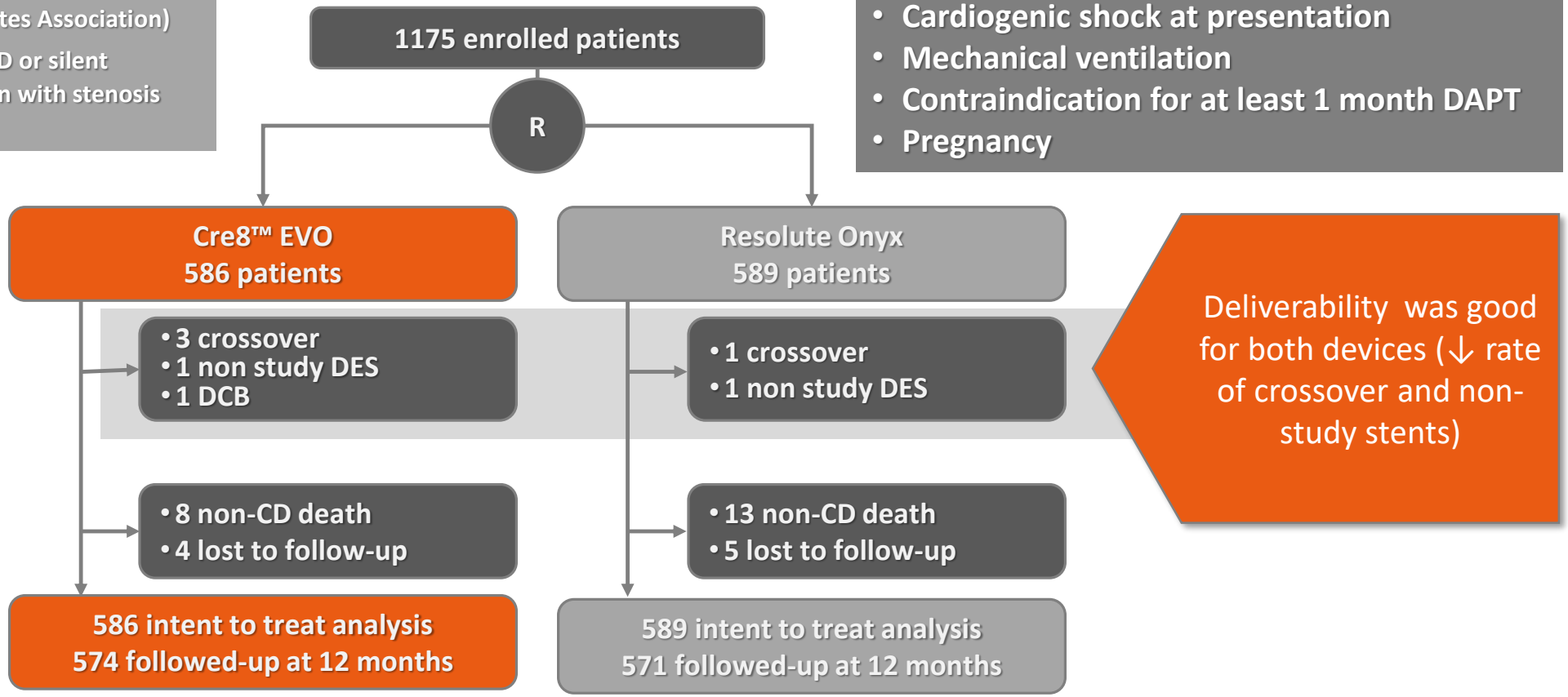
Romaguera R. European Heart Journal. 2021

The SUGAR randomized trial

ALL COMERS DESIGN

INCLUSION CRITERIA
- Patient age ≥18 years
- Diabetes Mellitus (American Diabetes Association)
- Indication for PCI (symptomatic CAD or silent ischemia with at least one coronary lesion with stenosis >50%)

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



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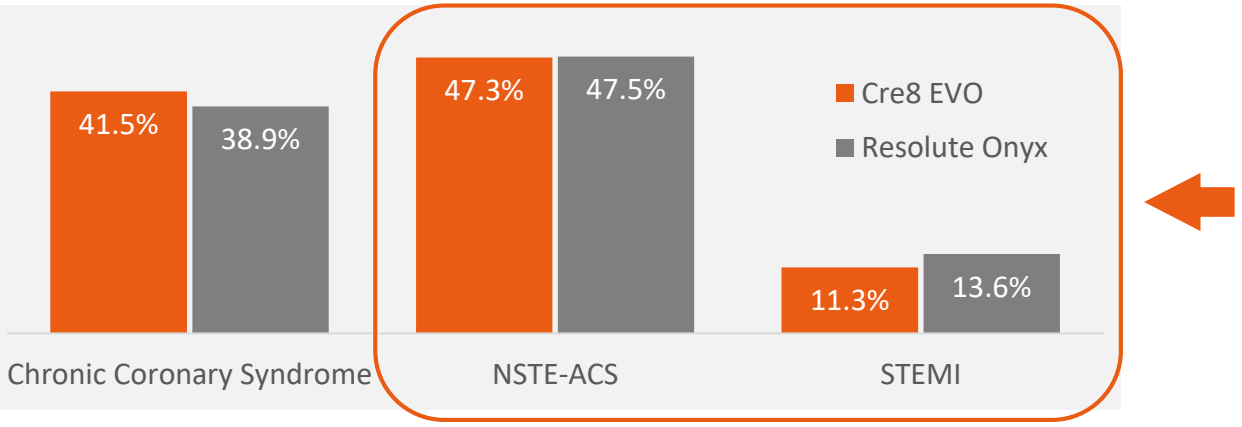
The SUGAR randomized trial

BASELINE CHARACTERISTICS

Baseline characteristic	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%)
Indication Index Procedure		
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 clearance (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%)

ACS ~60%



Diabetes characteristics	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 at randomization	183 (31.2%)	194 (32.9%)
HbA1c (%)	7.4 ± 1.5	7.5 ± 1.5

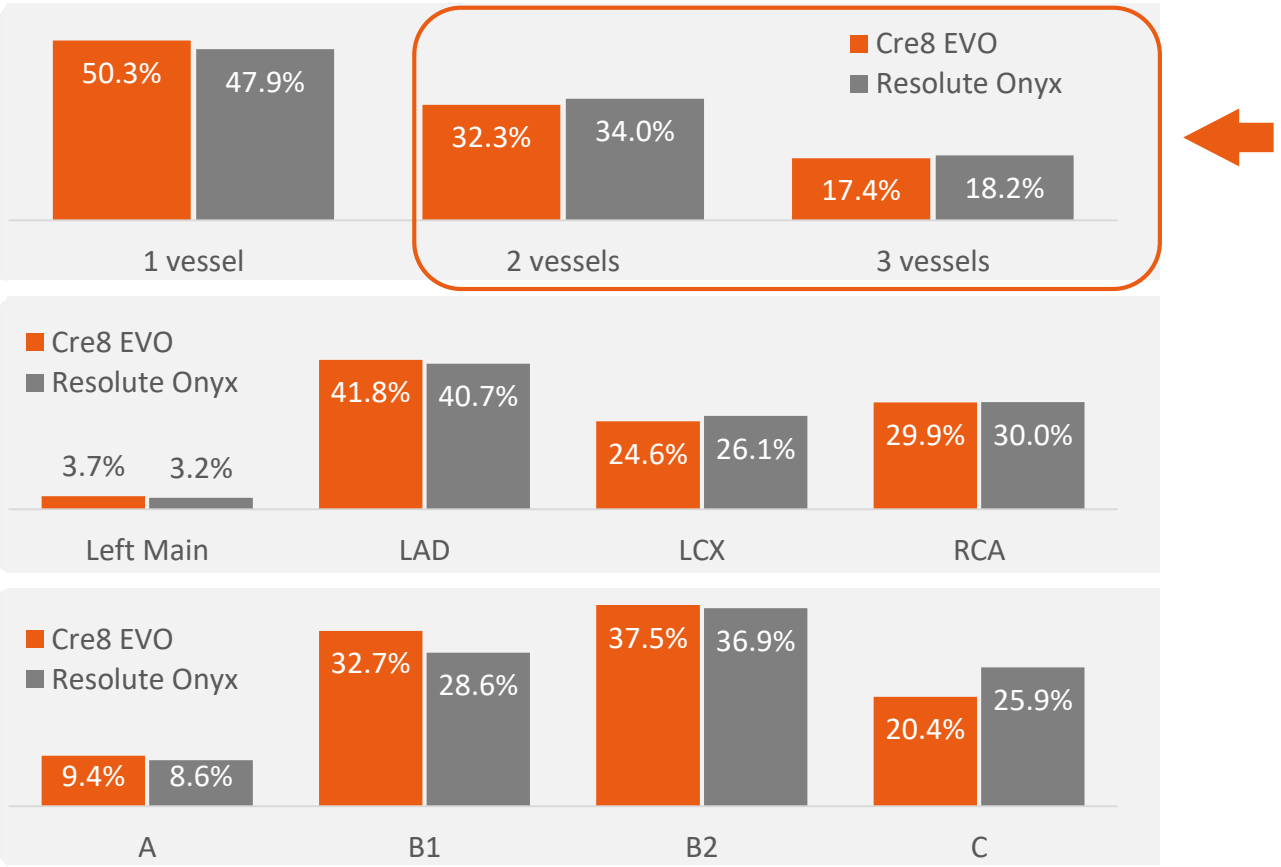
1/3 ID-DM

The SUGAR randomized trial

PROCEDURAL CHARACTERISTICS

Procedural characteristic	Cre8™ EVO 586 pts 879 lesions	Resolute™ Onyx 589 pts 950 lesions
Syntax score at randomization	13.0 ± 9.7	13.0 ± 8.7
Number of diseased vessel		
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 at randomization		
Chronic total occlusion	16 (2.1%)	19 (2.4%)
Bifurcation with 2 stents	43 (5.6%)	38 (4.9%)
Aorto-ostial lesion	13 (1.7%)	12 (1.5%)
AHA/ACC complexity		
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%)

Multi-vessel ~50%



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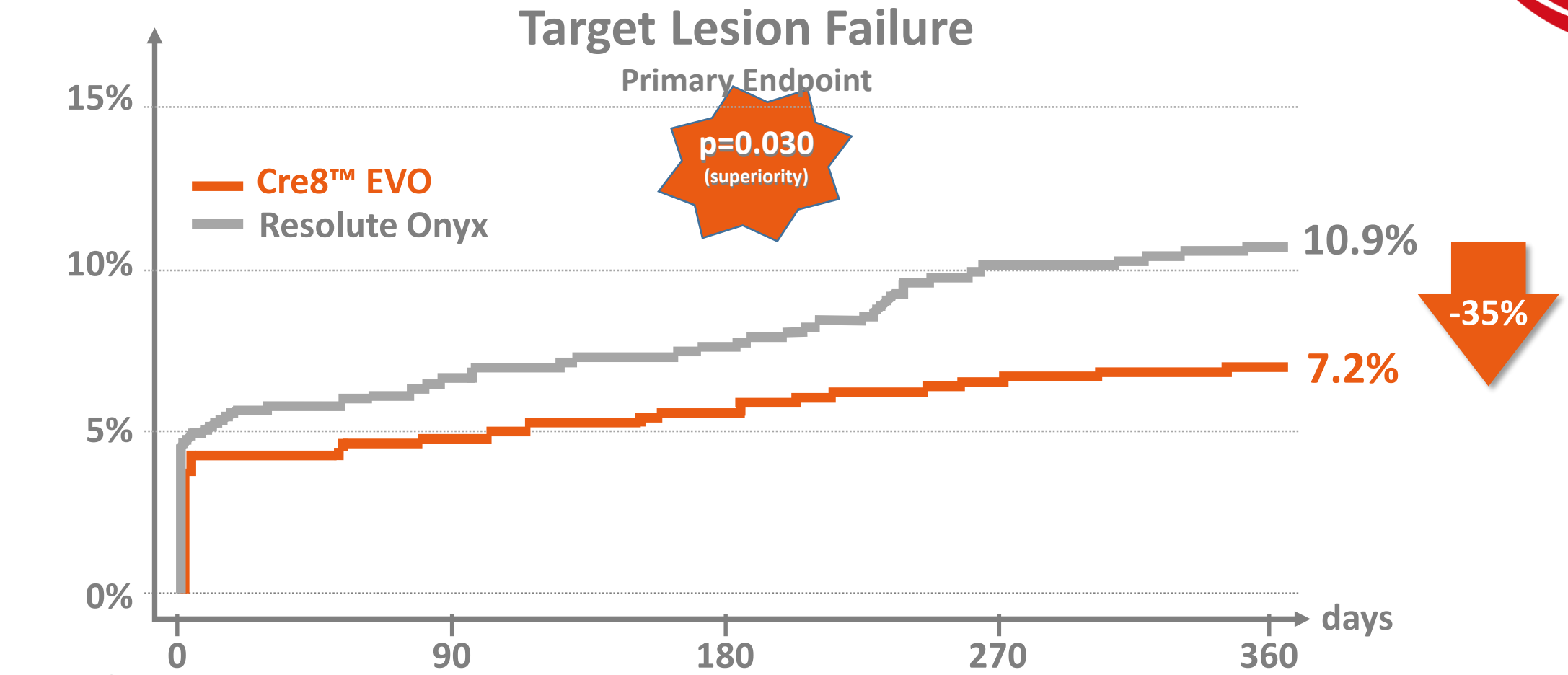
The SUGAR randomized trial



N. at risk					
Cre8™ EVO	584	553	546	536	532
Onyx	586	546	536	519	511

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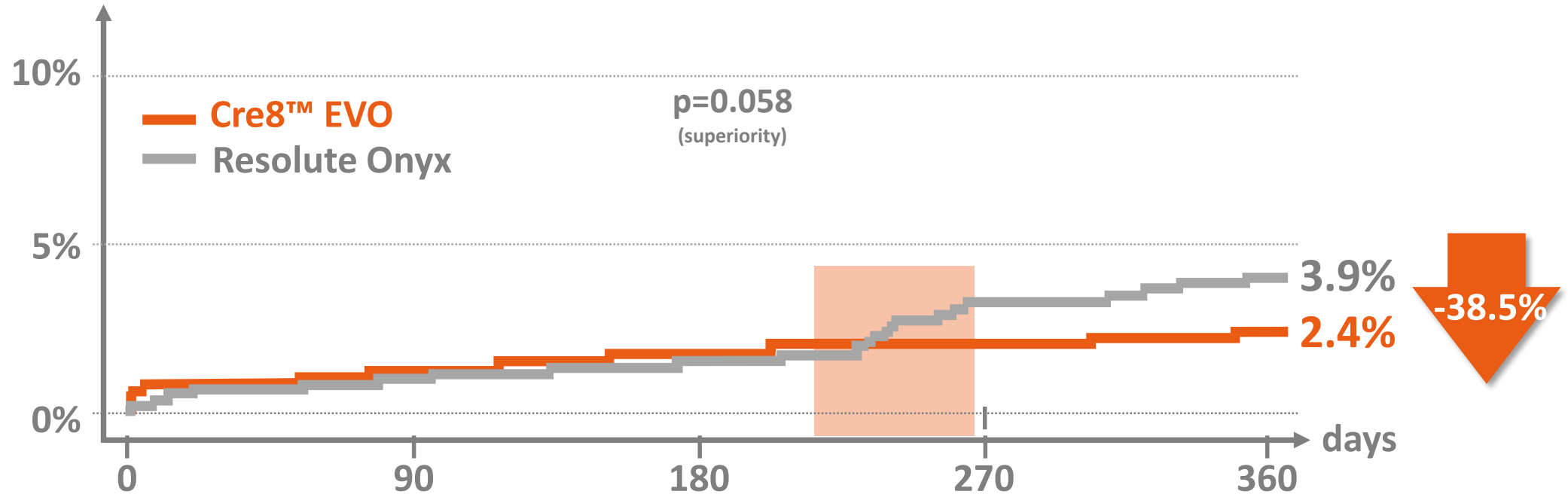
Target Lesion Revascularization



N. at risk

Cre8™ EVO	584	570	563	554	550
Onyx	586	572	559	442	434

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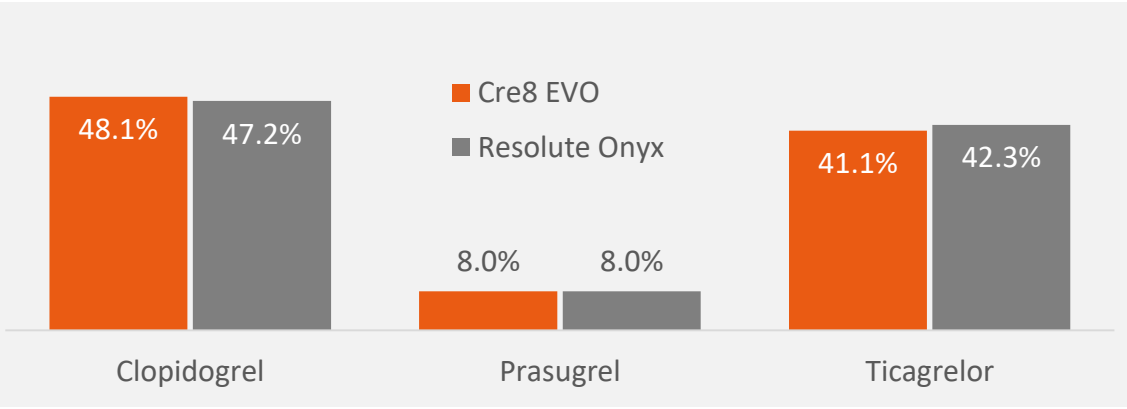
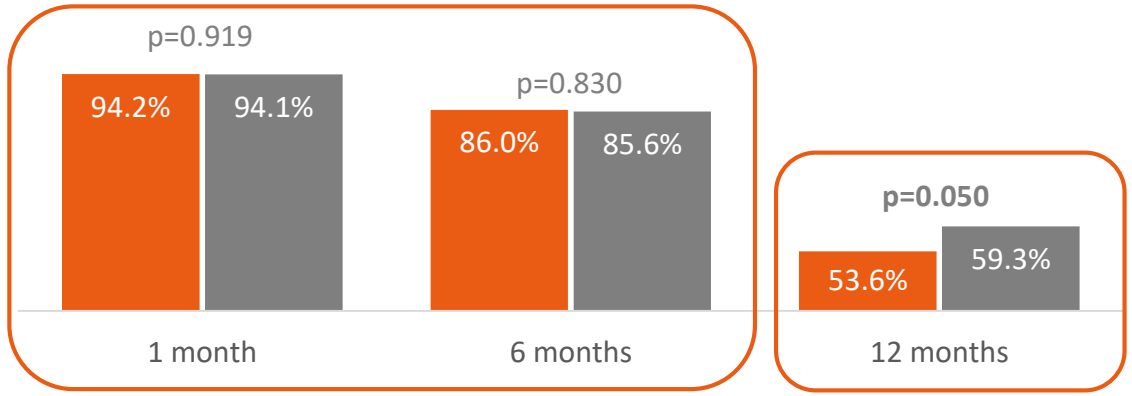
MEDICATION TREATMENT

Treatment	Cre8™ EVO 586 pts	Resolute™ Onyx 589 pts
Medication at discharge		
ASA	560 (95.6%)	567 (96.3%)
P2Y12 inhibitors		
Insulin	200 (34.1%)	219 (37.2%)



DAPT - Dual Antiplatelet Therapy

Equal percentage of patients under DAPT



Statistically higher # of patients under DAPT for ONYX

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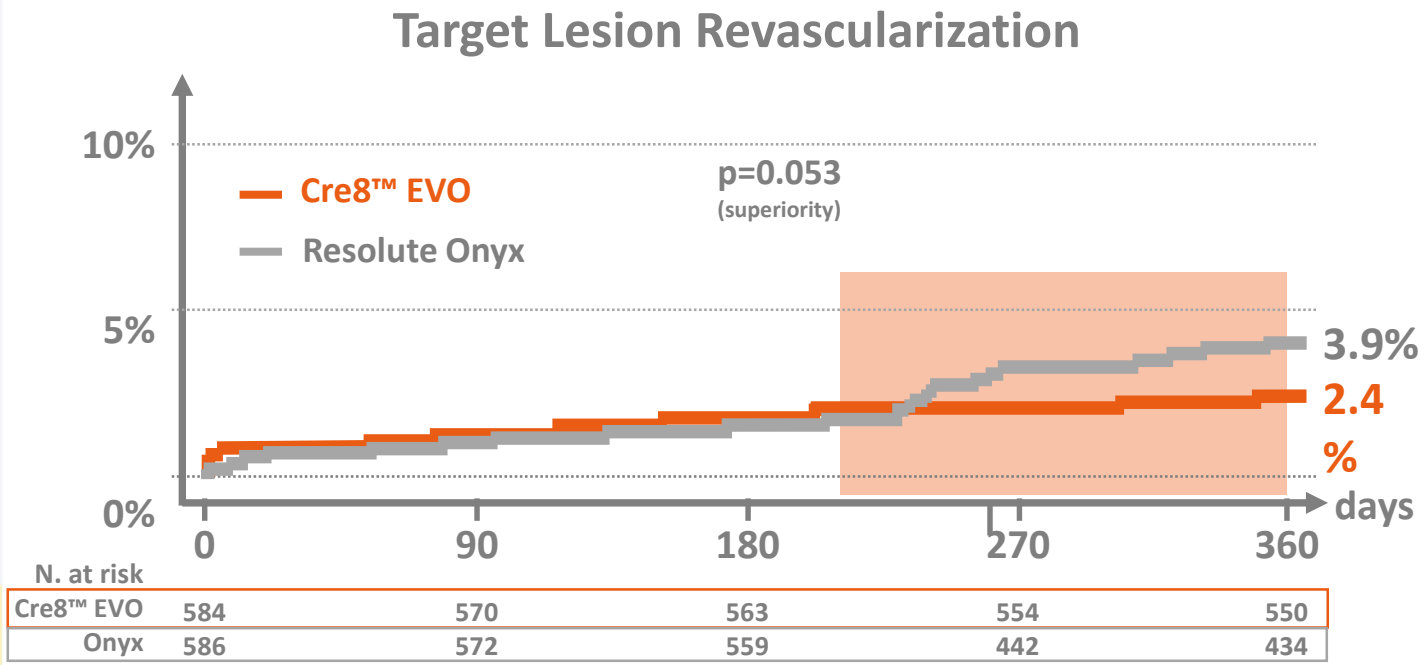
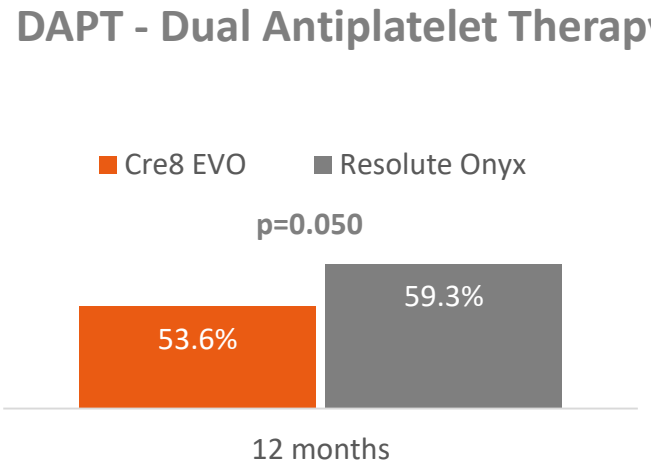
The SUGAR randomized trial

Efficacy & Safety are interconnected!

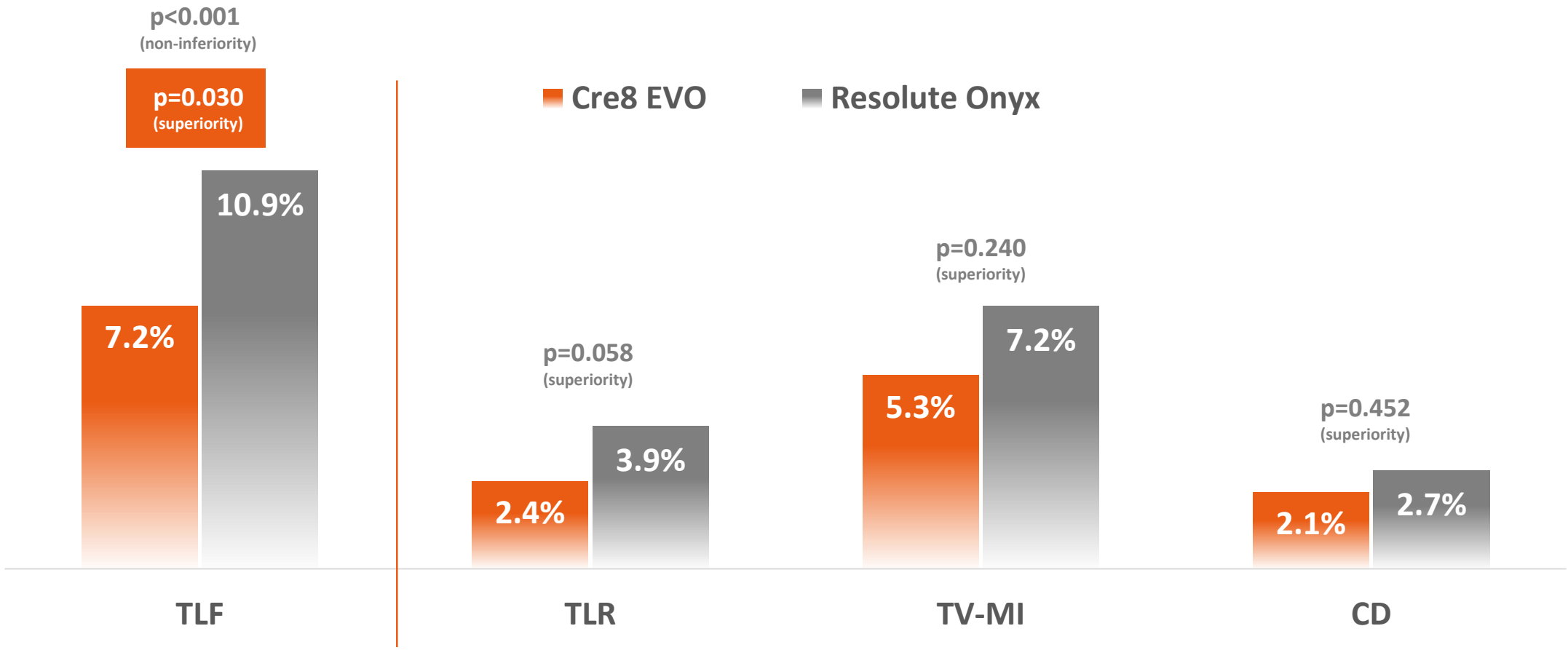




- When a DES is implanted in a high bleeding risk patient and then that patient has a TLR, this patient will need to prolong DAPT due to the re-intervention.
- “Efficacy and safety are very interconnected when it comes to DES outcomes.” “If you have less-efficient DES, you have to restart DAPT, and thus you could have more bleeding.”

The SUGAR randomized trial

Primary Endpoints and its components at 1-year follow-up.



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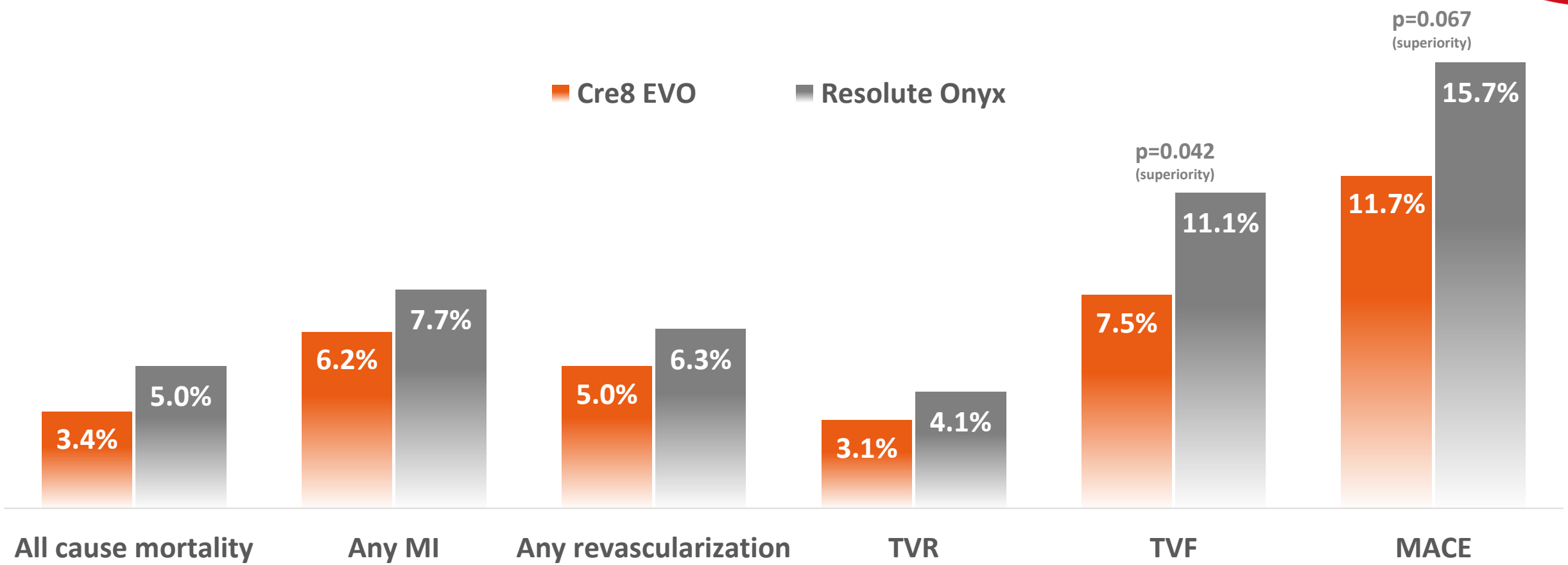
Secondary Endpoints at 1-year follow-up.



p value: NS for all parameters, where not reported

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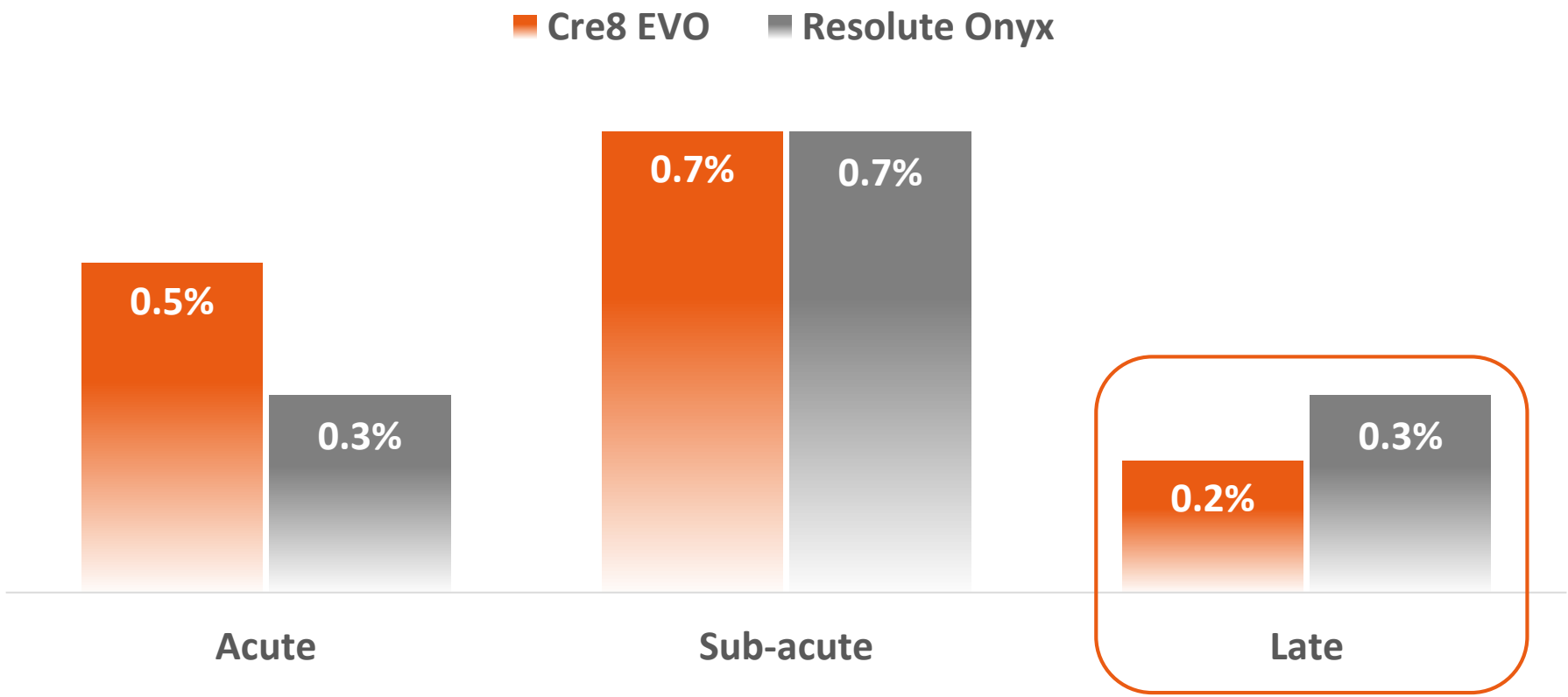
Secondary Endpoints at 1-year follow-up.

Probable or definite stent thrombosis



p value: NS for all parameters

Romaguera R. European Heart Journal. 2021

Conclusions

- Patients with DM had metabolic traits that put them at high risk of stent failure.
- There is a large evidence suggesting that the unique features of Cre8 EVO could be more effective than other DES in DM.
- The SUGAR trial confirms that Cre8EVO is superior than othe polymer-based DES (Resolute Onyx), and therefore it should be considered to reduce the risk of adverse events in patients with DM.