TNT session

2018 euro PCR

"Amphilimus™ Eluting Stent: leveraging on innovative technology to go beyond current PCI clinical boundaries in diabetic and HBR patients"

Amphilimus™ eluting stent - clinical results and ongoing clinical plan

Rafael Romaguera, MD

Hospital de Bellvitge

Barcelona - Spain

EAPCI European Society of Cardiology PCR

Speaker's name: **Rafael Romaguera**

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

Receipt of modest speaker honoraria: Alvimedica, Astra Zeneca.

Efficacy:

to reduce new revascularizations

Clinical evidence

SAFETY

Reduced DAPT duration

SPONSORED STUDIES

Randomized trial – Coverage @3m (**Demonstr8**)

INDEPENDENT STUDIES

U-Short registry – DAPT 3m

ASTUTE registry – DAPT 1-3m

Randomized trial Cre8 vs ZES (**ReCre8**) – DAPT 1m in all comers Trop- pts

EFFICACY

Diabetic patients

SPONSORED STUDIES

NEXT randomized trial (sub-group DM)

Real-world study (**Particip8**) (sub-group DM)

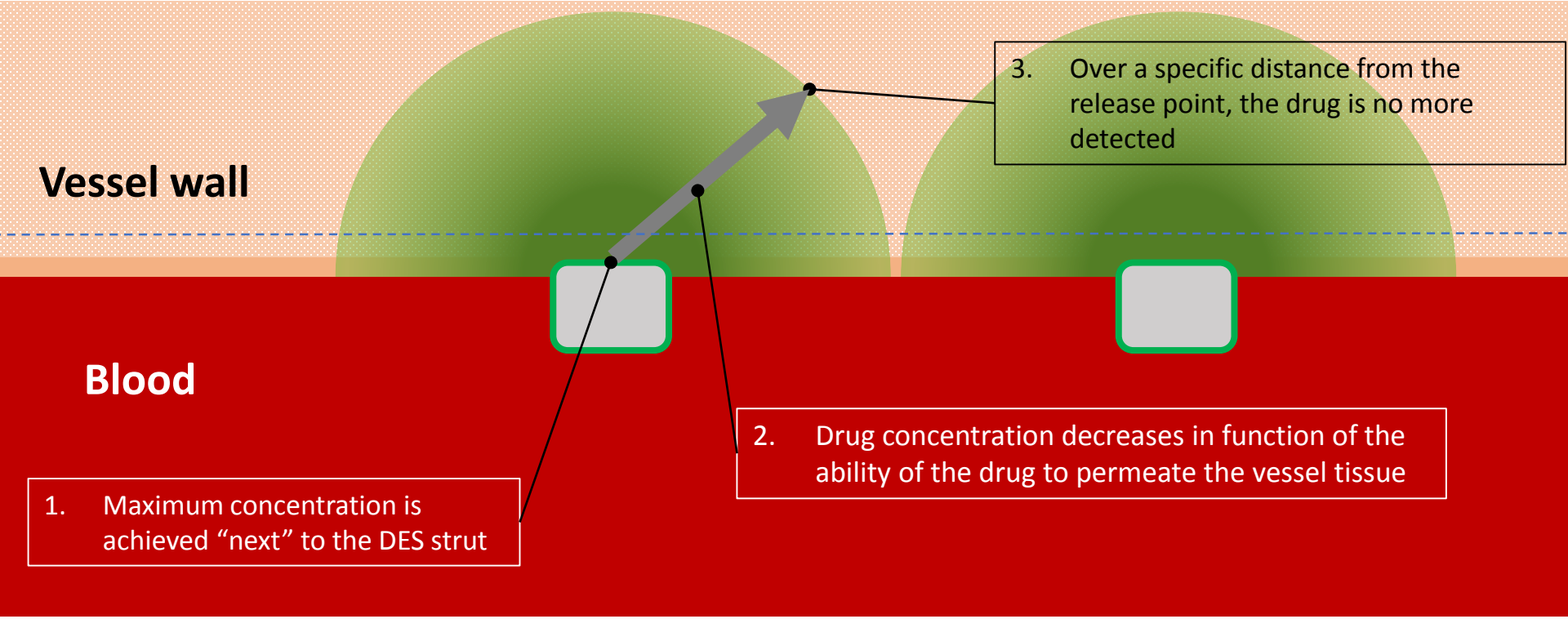
INDEPENDENT STUDIES

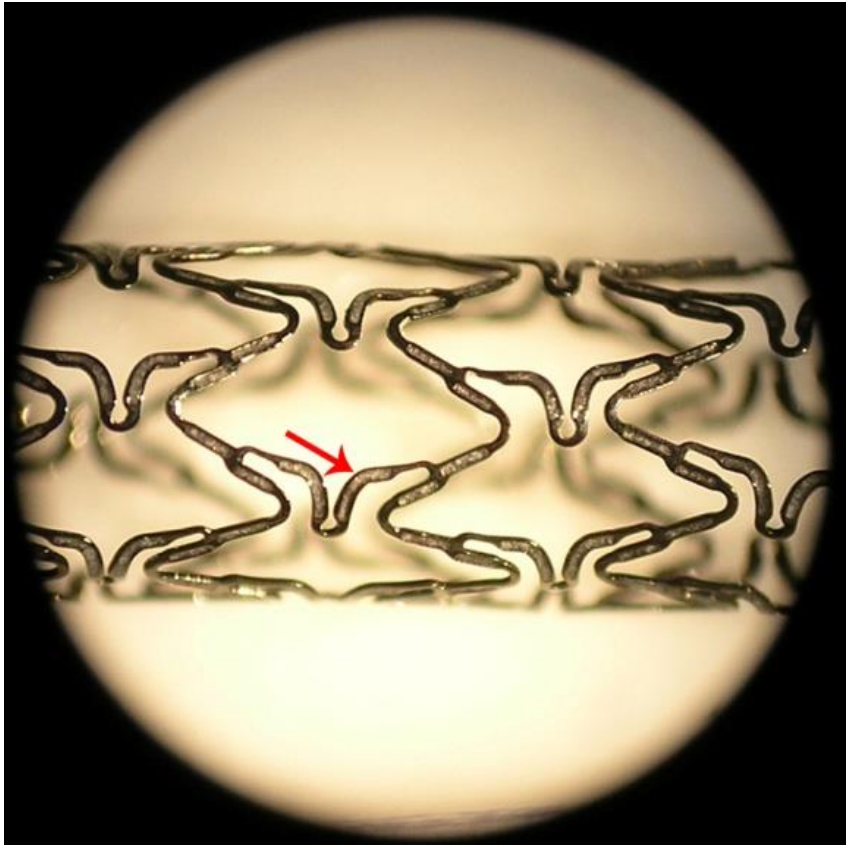
RESERVOIR randomized trial (Cre8 vs EES in DM)

Matched analysis Cre8™ vs EES

ASTUTE registry - Diabetics

Matched analysis Cre8™ vs BES


Vessel wall
Blood
3. Over a specific distance from the release point, the drug is no more detected
2. Drug concentration decreases in function of the ability of the drug to permeate the vessel tissue
1. Maximum concentration is achieved “next” to the DES strut



The NEXT randomized trial

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

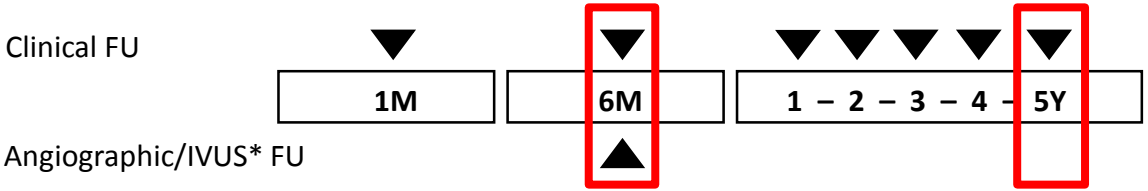
Cre8™ (n=162 pts)

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

TAXUS™ Liberté® (n=161 pts)

PI: Prof D. Carrié, Toulouse, France

Primary Endpoint: In-stent LLL at 6 months

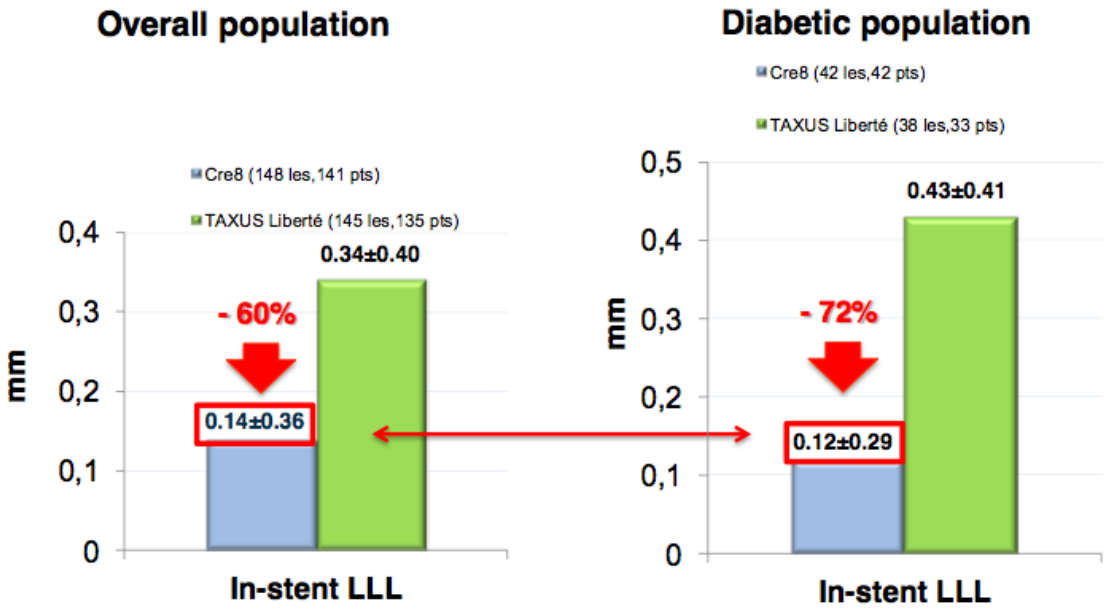


*Angiographic/IVUS Core Lab: BioClinica Leiden, The Netherlands

Carrié et al JACC, 2012, 59; 1371-76

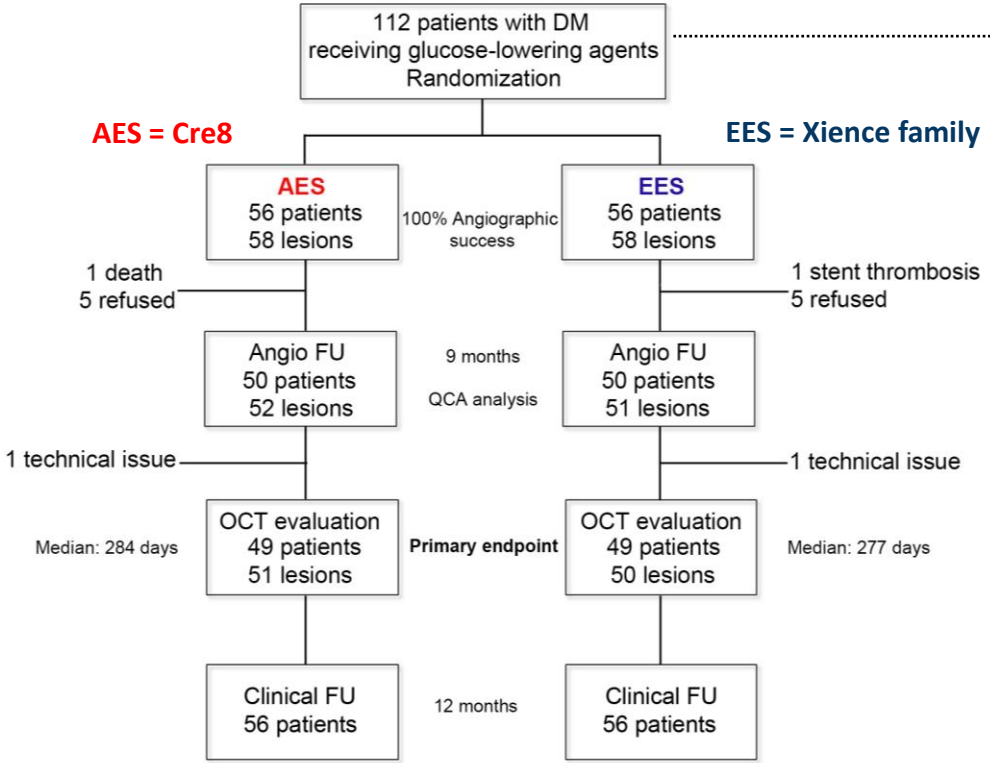
The NEXT randomized trial

Primary Endpoint: 6month in-stent LLL



The in-stent LLL in DM subgroup is comparable to that obtained in overall population

The RESERVOIR randomized trial



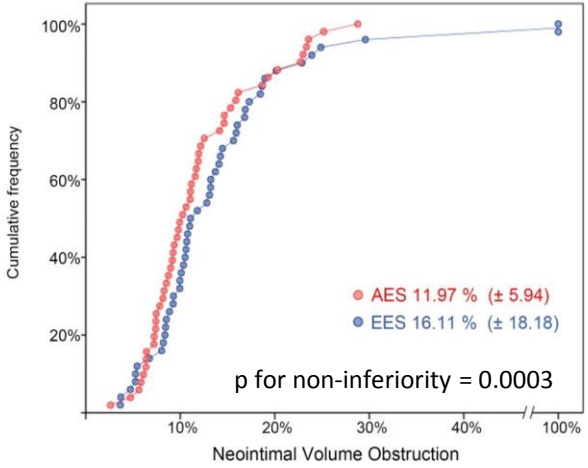
Exclusion criteria

- Life-style changes only
- STEMI
- Bifurcation>2.5mm
- Left Main/ostial LAD
- 3V with CABG indication
- GFR<30 ml/min
- LVEF < 30%
- Contraindication DAPT

Primary endpoint:
Neointimal volume obstruction by OCT

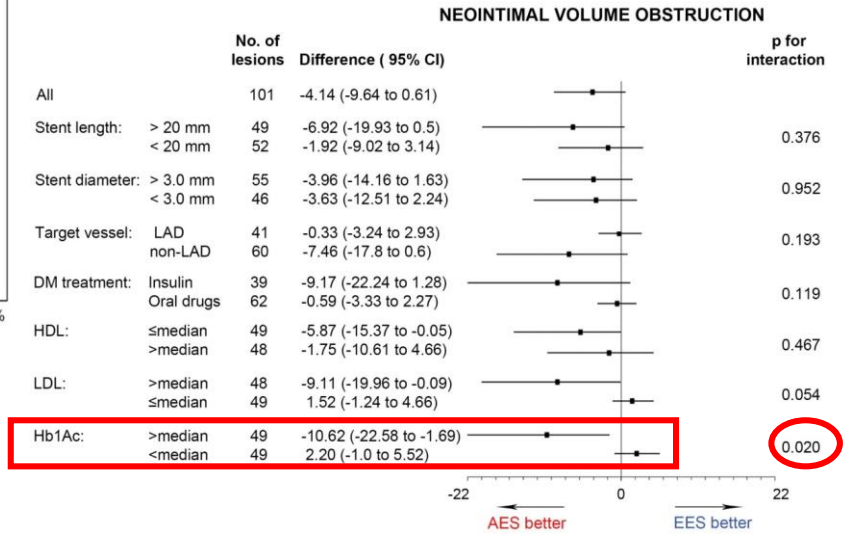
The RESERVOIR randomized trial

Primary endpoint: Neointimal Volume Obstruction



AES = Cre8

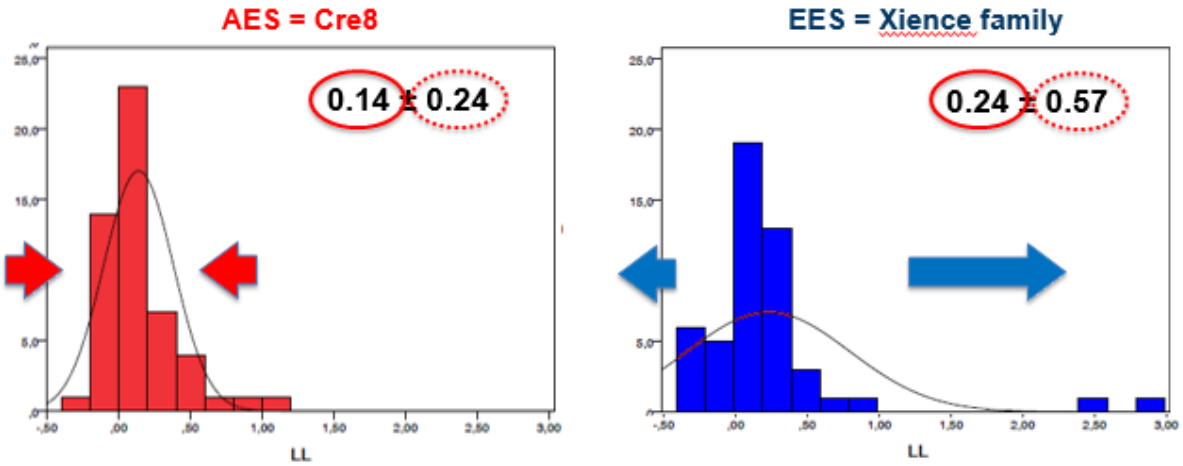
EES = Xience family



Romaguera R, et al. JACC Cardiovasc Interv. 2016; 9: 42-50.

The RESERVOIR randomized trial

Late Lumen Loss (9months)



	AES	EES	p value
MLD (mm)			
In-stent	2.38 ± 0.44	2.19 ± 0.59	0.07
In-segment	2.09 ± 0.45	1.84 ± 0.61	0.02

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

Particip8 trial Design

"Real world" patients with ischemic myocardial symptoms related to de novo coronary artery lesions, treated with Cre8

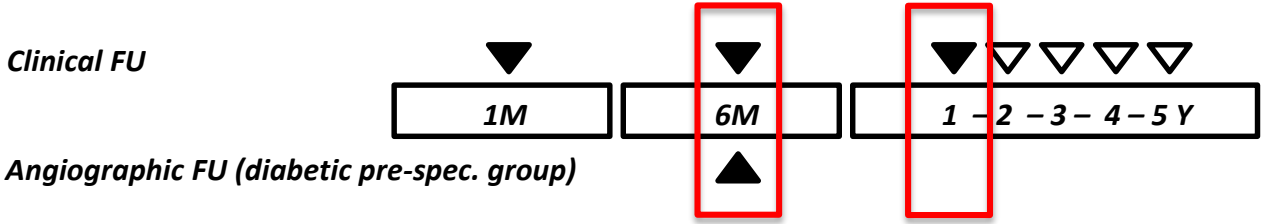
1186 patients
30 European Sites

→ Pre-specified diabetic subgroup

↓ Diabetics patients submitted to angio FU

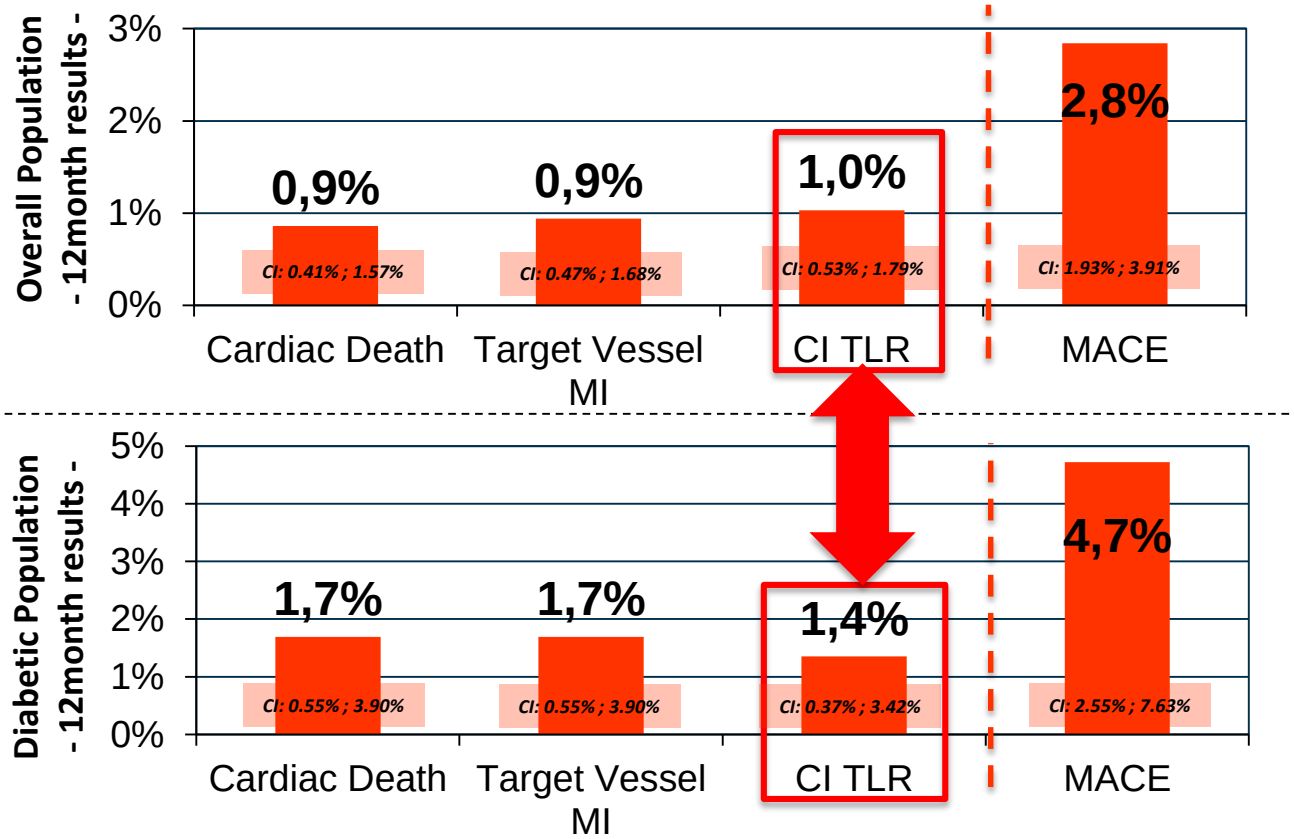
PI: A. Colombo - Italy

- **<u>OBJECTIVE</u>:** evaluate the safety and efficacy performances of Cre8, in patients comparable to the everyday's clinical practice population, with a specific focus on diabetics subjects
- **<u>PRIMARY ENDPOINT</u>: 6-month incidence of clinical composite endpoint: Cardiac death/ Target Vessel MI/ Clinically indicated TLR**



Particip8 trial

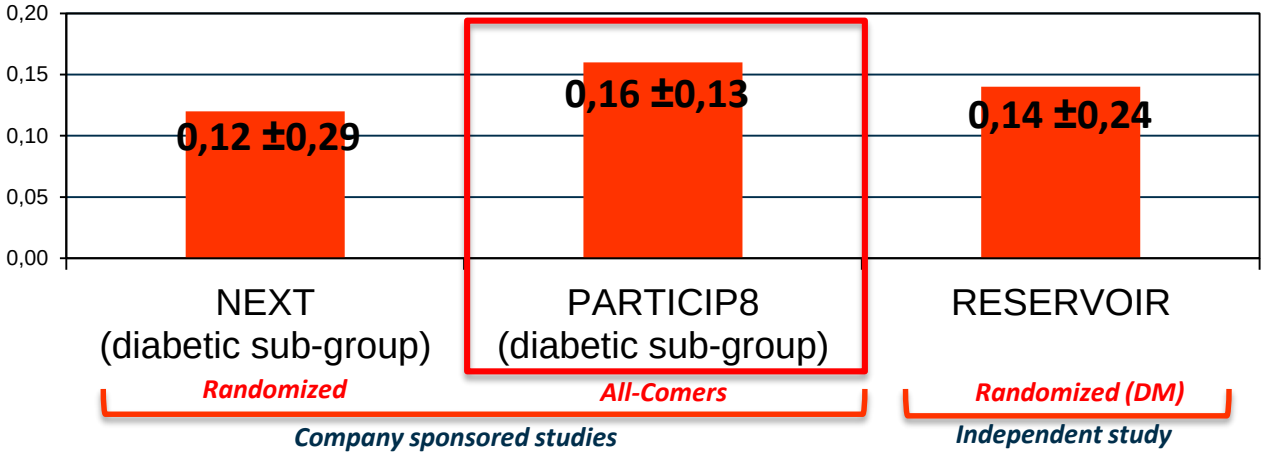
12month MACE* = CD + TV MI + CI LLR



*MACE as percent frequencies of the device–oriented clinical composite of CD, TV MI, CI TLR up to 12 months - ITT population - Diabetic population (N = 296) - Adjudicated events

Particip8 trial

In-stent LLL results in diabetics

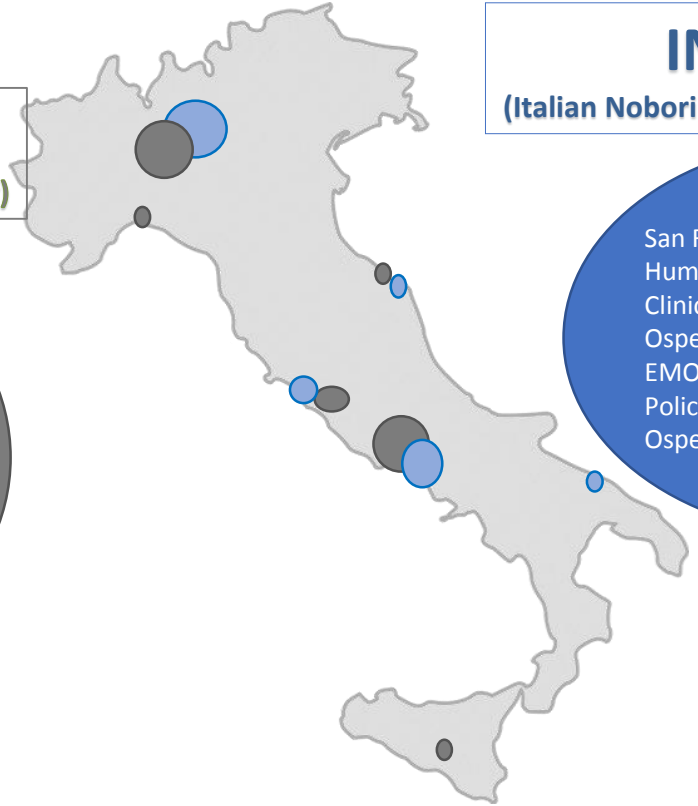


Matched analysis: Cre8 vs. BES

ASTUTE

(AmphilimuS iTalian mUlticenTre rEgistry)

San Raffaele Scientific Institute
Clinica Mediterranea
Istituto Clinico Città Studi
IRCCS Policlinico san Donato
EMO-GVM Centro Cuore Columbus
Ospedali Riuniti Marche Nord
Ospedale San Giovanni di Dio
Ospedale San Pietro, FBF
Ospedale Santa Corona



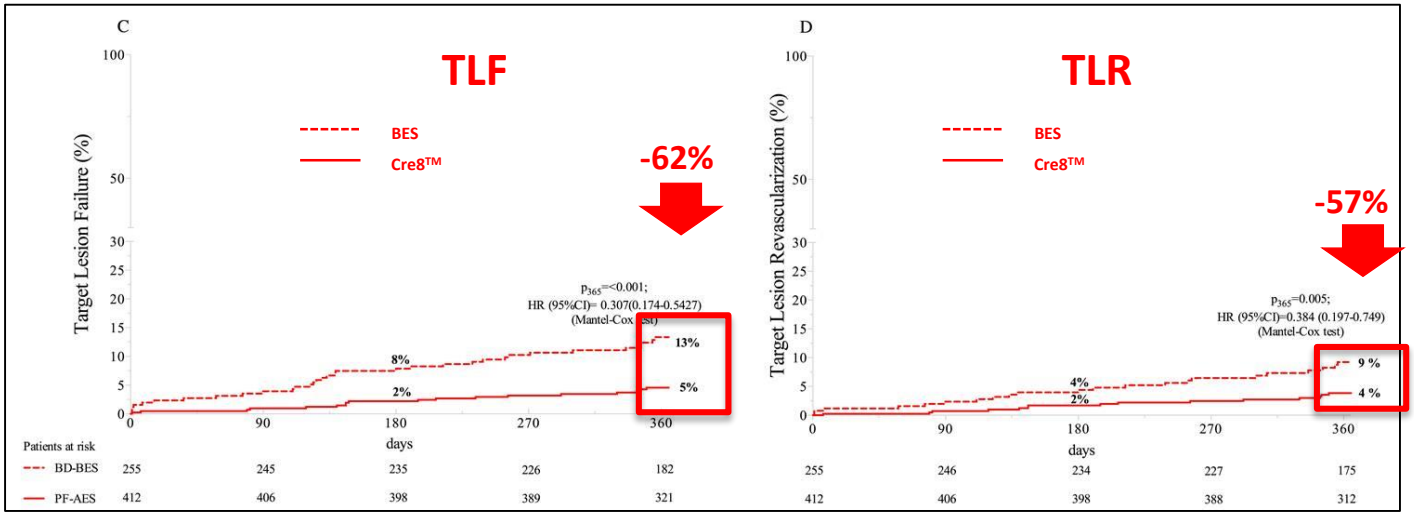
INSPIRE-1

(Italian Nobori Stent Prospectlve REgistry-1)

San Raffaele Scientific Institute
Humanitas Clinical Institute
Clinica Mediterranea
Ospedali Riuniti Marche Nord
EMO-GVM Centro Cuore Columbus
Policlinico Umberto I
Ospedale San Paolo

Matched analysis: Cre8 vs. BES

Diabetic cohort – TLF/TLR



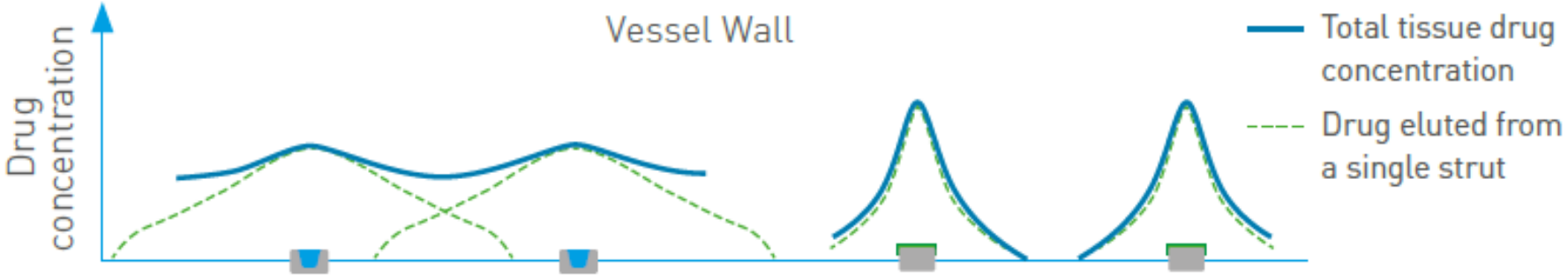
Cre8 is always statistically superior to BES:

- TLF = 5% vs. 13% (-62%; p<0.001)
- TLR = 4% vs. 9% (-57%; p=0.005)

C. Godino et al /International Journal of Cardiology 245 (2017) 69–76

Safety:

to avoid an excess of risk of cardiac death, MI or ST



Carrier-based

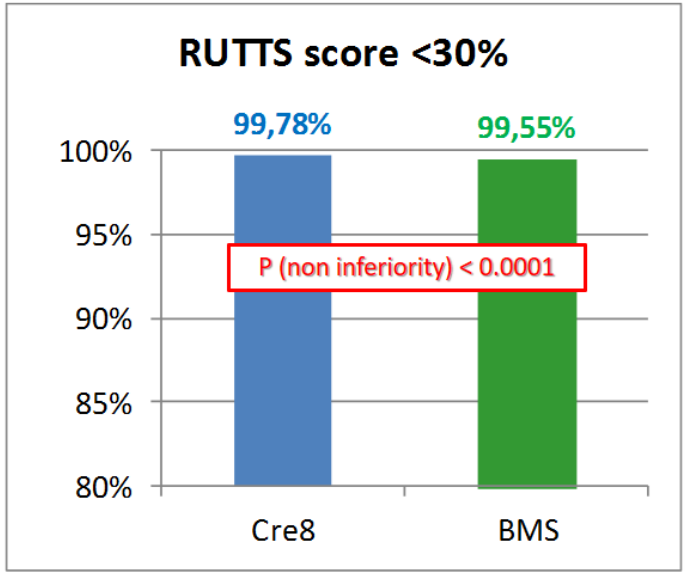
Simple-diffusion

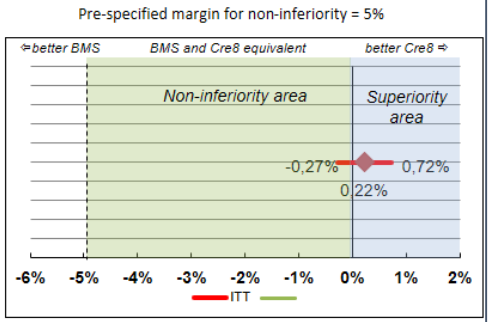
Demonstr8 trial

euro PCR

Primary endpoint: Results - I

- Analyzed patients: 35 (Cre8:17pts; BMS:18pts)
- Total analyzed struts = +17000
- Total analyzed sections = +2000

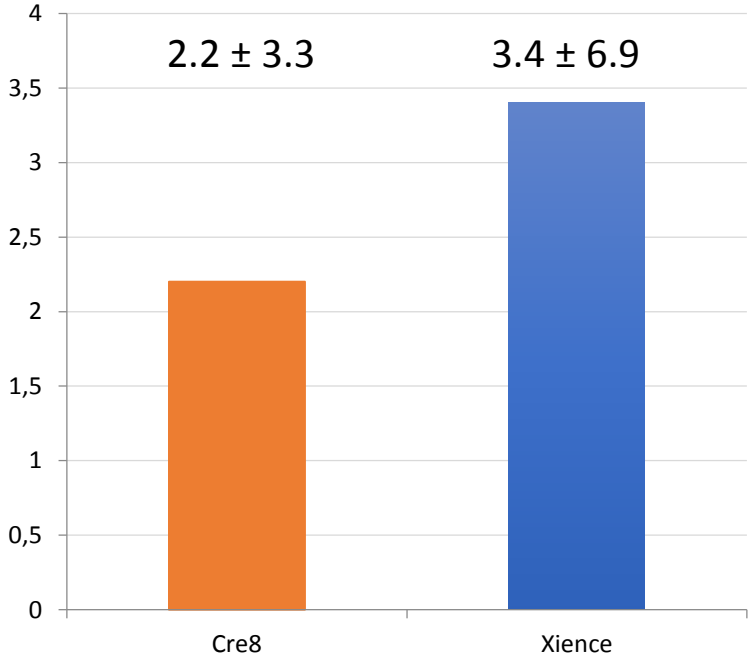




RHR

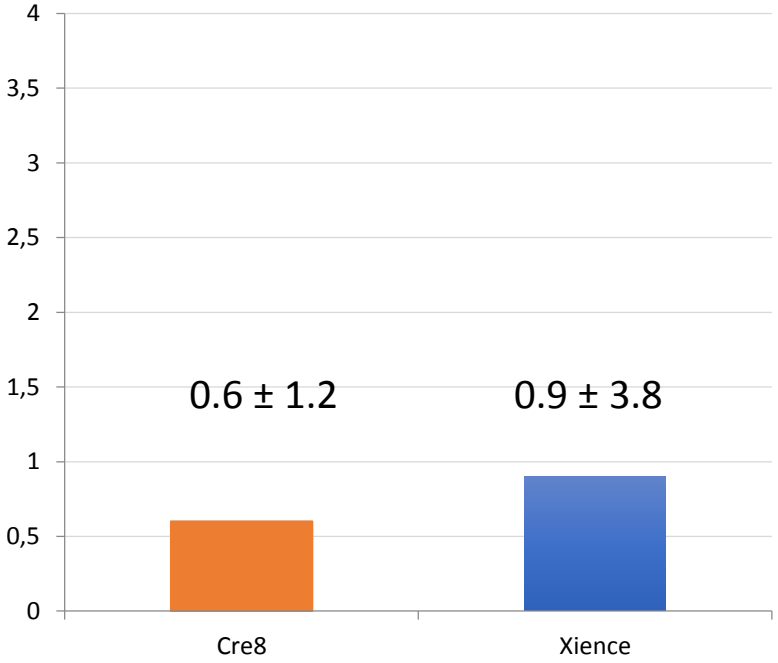
RESERVOIR trial

Uncovered struts @9m



p = 0.83

Uncovered & malapposed



p = 0.46

Large-scale randomized trials

ReCre8 randomized trial*

All-comer patients requiring PCI stratified by DM and troponin status.
- 1 month DAPT in troponin-negative patients
- 12 months DAPT in troponin-positive patients

Cre8™

1532 patients
3 European Sites
Randomization 1:1

Resolute Integrity

PI: P. Stella – The Netherlands

Primary Endpoint
- 12 months Target Lesion Failure (TLF: Cardiac Death + lesion related MI + TLR)

Secondary Endpoint
- 12 months Net Adverse Clinical Events (NACE: any Death + any stroke + any MI + any Revasc. + any Bleeding BARC≥3)

Clinical FU

1month	1Y	3Y

***Enrollment completed**

Ongoing/ Planned studies

Diab8 randomized trial

All-comer patients with diabetes mellitus undergoing PCI

Cre8™ EVO

3040 patients
55 International Sites
Randomization 1:1

Everolimus Eluting Stent (EES)

PI: Antonio Colombo

Primary Endpoint

- **EFFICACY** = 12 months Target Lesion Revascularization (TLR)
  Sequential check for Non-inferiority (first step) and then for **Superiority** (second step)

Secondary main Endpoints

- **EFFICACY** = 24 months TLR for **Superiority**
- SAFETY = 12 months Cardiac Death + Target Vessel MI (CD + TVMI)

Clinical FU

1 year | **2 years** | **3 years**

Ongoing/ Planned studies

Second-generation drUg-elutinG stents in diAbetes: a Randomized trial (the SUGAR trial*)

All-comers DM patients undergoing PCI

Amphilimus-Eluting Stents (AES)

1164 patients

26 Spanish Centers

Randomization 1:1

Zotarolimus-Eluting Stent (ZES)

Primary Endpoint: 12 months **TLF** (non-inferiority)

Co-Primary Endpoint: 24 months **TLF** (Superiority)

PI: Rafael Romaguera
Hospital de Bellvitge

Co-PI: Pablo Salinas
Hosp. Clínico San Carlos

* Study funded by the Spanish Society of Cardiology

Conclusions

- The Cre8™ EVO stent represents **a "different DES technology"** vs. classic polymer-based DES because of its design which allows formulation of the drug with carriers.

- This technology has shown in several registries and RCT to be **highly effective preventing target lesion failure in patients with DM**, with a very low late loss (0.12-016) and a very low rate of events in this population.

- The ongoing large-scale RCT **SUGAR** and **Diab8** trials will further add evidences to the Cre8 Evo™ efficacy in the challenging patient population represented by diabetics. **ReCre8** trial will also add evidence of safety with short DAPT.