Supraflex Cruz

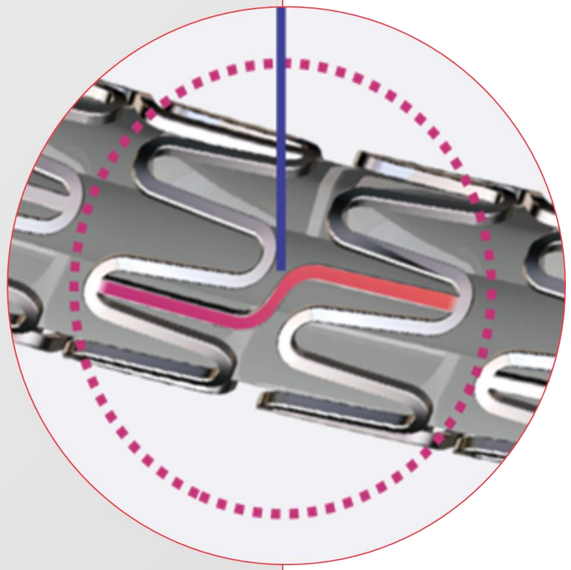
Sirolimus Eluting Cobalt Chromium Coronary Stent System

SUPRAFLEX CRUZ STENT

Main characteristics and studies

FIRE TRIAL

Stent details

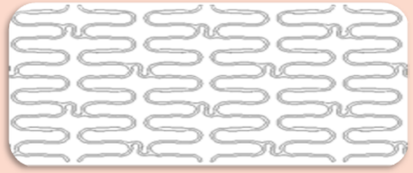


Proprietary LDZ link

*LDZ = Long Dual Z - link

Supraflex Cruz
Sirolimus Eluting Cobalt Chromium Coronary Stent System

Stent details

	Supraflex SES	Supraflex Cruz SES
Drug	Sirolimus (1.4 µg/mm^2)	Sirolimus (1.4 µg/mm^2)
Polymer type	Biodegradable polymers	Biodegradable polymers
Stent design	Open-cell design	Open-cell design
Stent material	L605 Co-Cr alloy	L605 Co-Cr alloy
Stent strut thickness	60 µm	60 µm
No. of crown	4, 6 and 8 crown	4, 6 and 8 crown
No. of interconnectors	Two	Two
Link type	S-link	LDZ link
Stent drawing		

LDZ = Long Dual Z link

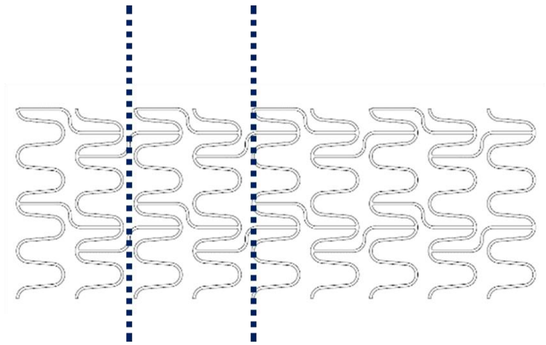
FIRE TRIAL

Supraflex Cruz
Sirolimus Eluting Cobalt Chromium Coronary Stent System

Platform

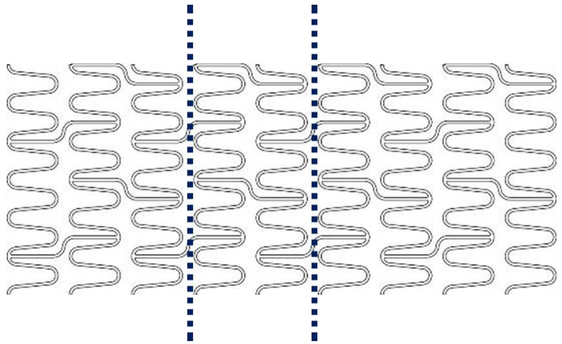
Diameter

2.0 & 2.25



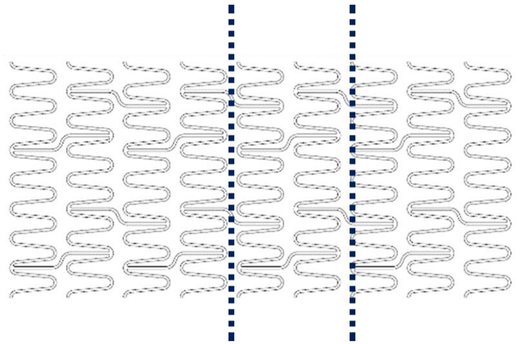
4 Crowns

2.5, 2.75, 3.0 & 3.5



6 Crowns

4.0 & 4.5



8 Crowns

- Open cell design
- 2 connectors between the ringlets
- In-phase design
- Unique LDZ link

FIRE TRIAL

Supraflex Cruz
Sirolimus Eluting Cobalt Chromium Coronary Stent System

Platform – LDZ link

LDZ LINK

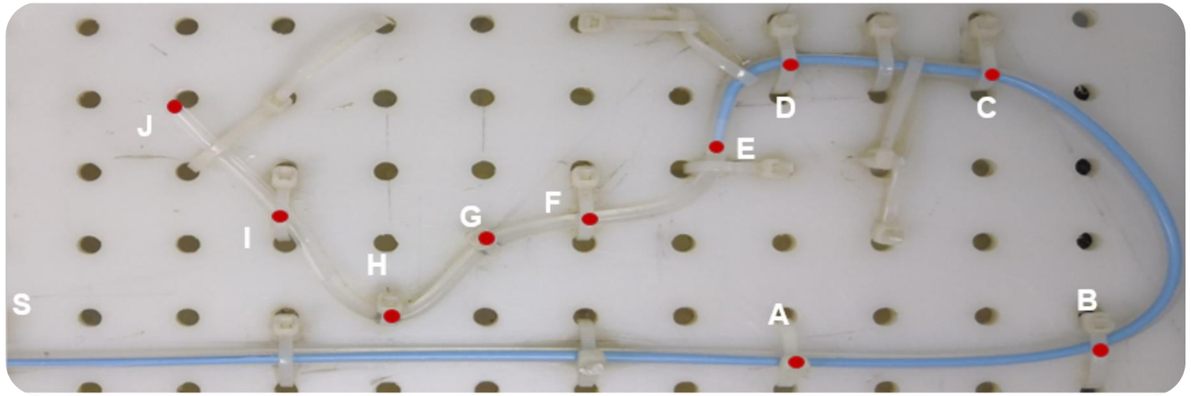
- Long connectors enhance the overall radial strength
- Improves flexibility of the stent
- Transmit ‘Push force’ with higher efficiency
- Resists longitudinal compression

It is more suitable for PCI in tortuous lesions and distal segments

FIRE TRIAL

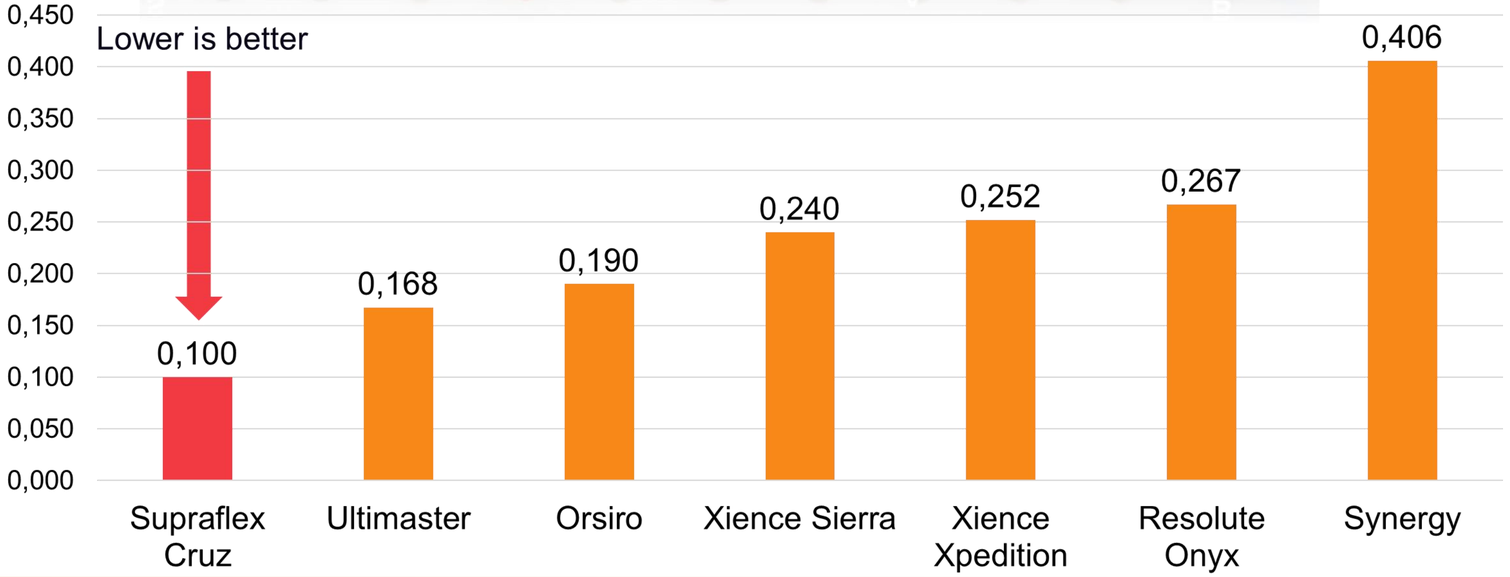
Supraflex Cruz
Sirolimus Eluting Cobalt Chromium Coronary Stent System

Deliverability



- Best deliverability amongst available stents in the market.
- Lowest resistance recorded while maneuvering through complex anatomy.

Mean Track force in N (40 mm)

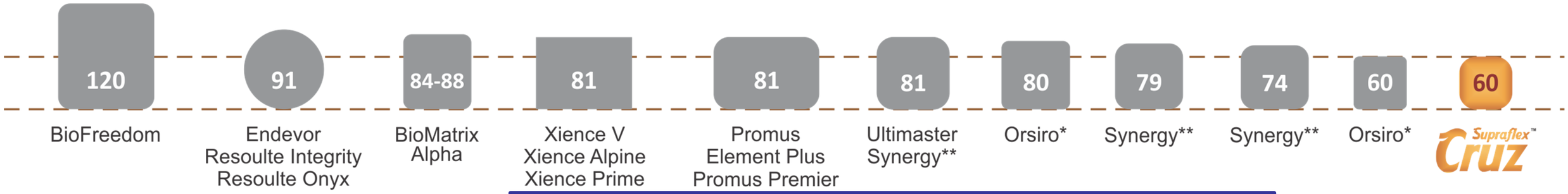


FIRE TRIAL

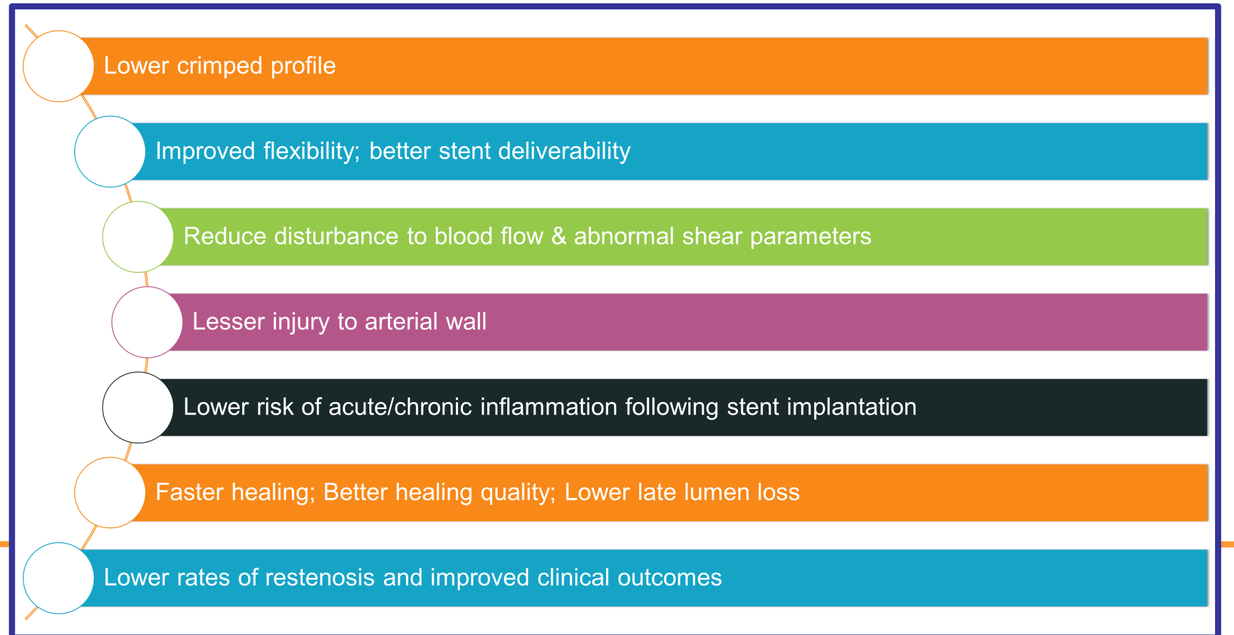
Supraflex Cruz
Sirolimus Eluting Cobalt Chromium Coronary Stent System

Strut thickness

Only stent with ultra-thin 60 µm struts for all diameters.



Main benefits related to lower strut thickness

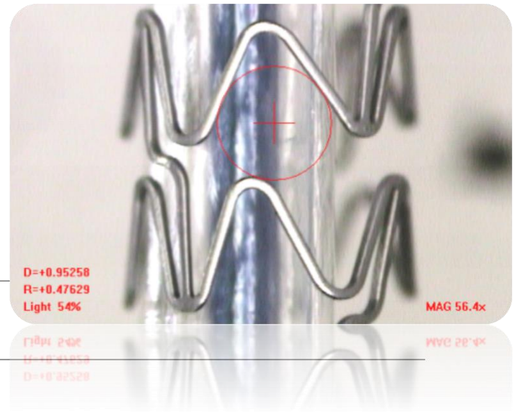


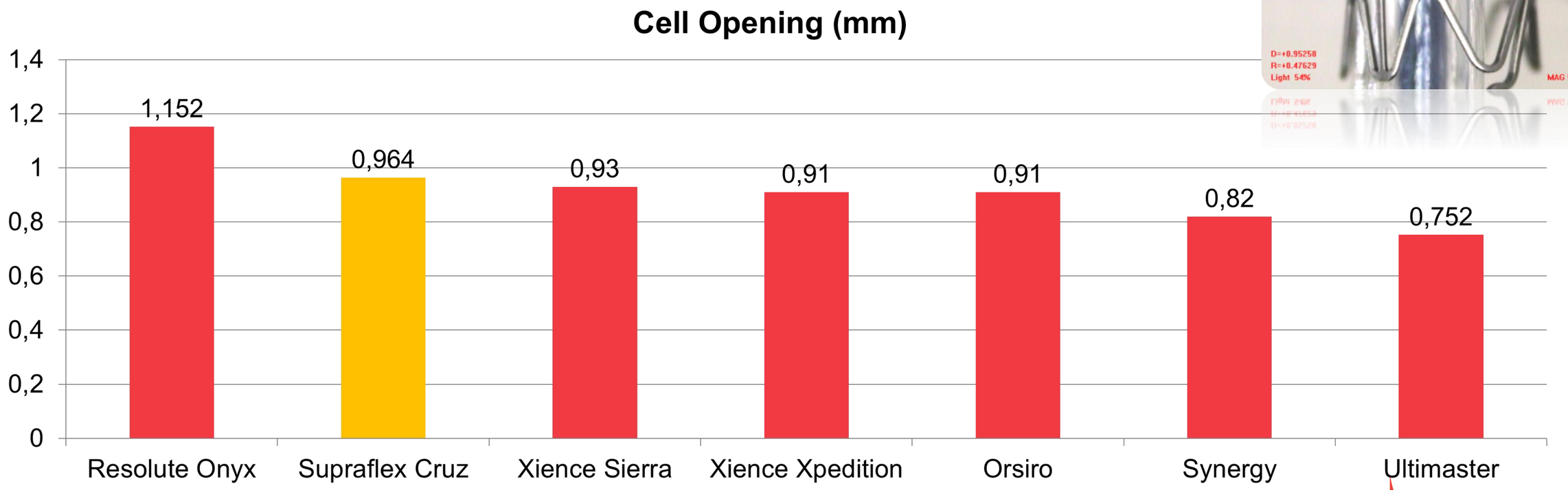
FIRE TRIAL

Supraflex Cruz
Sirolimus Eluting Cobalt Chromium Coronary Stent System

Cell opening

Helps in side branch access





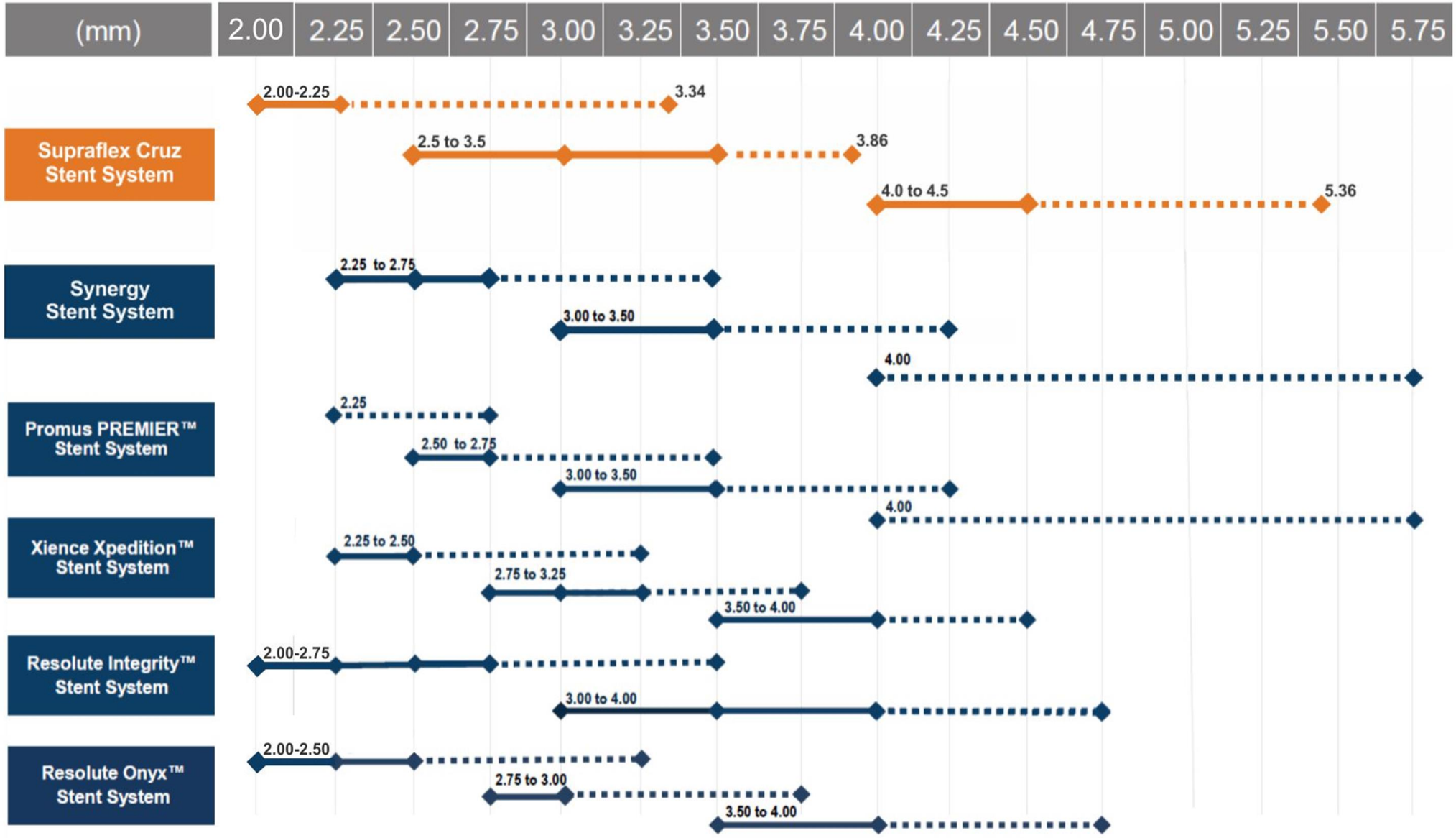
Cell opening is equivalent to side branch access.

FIRE TRIAL

Supraflex Cruz

Sirolimus Eluting Cobalt Chromium Coronary Stent System

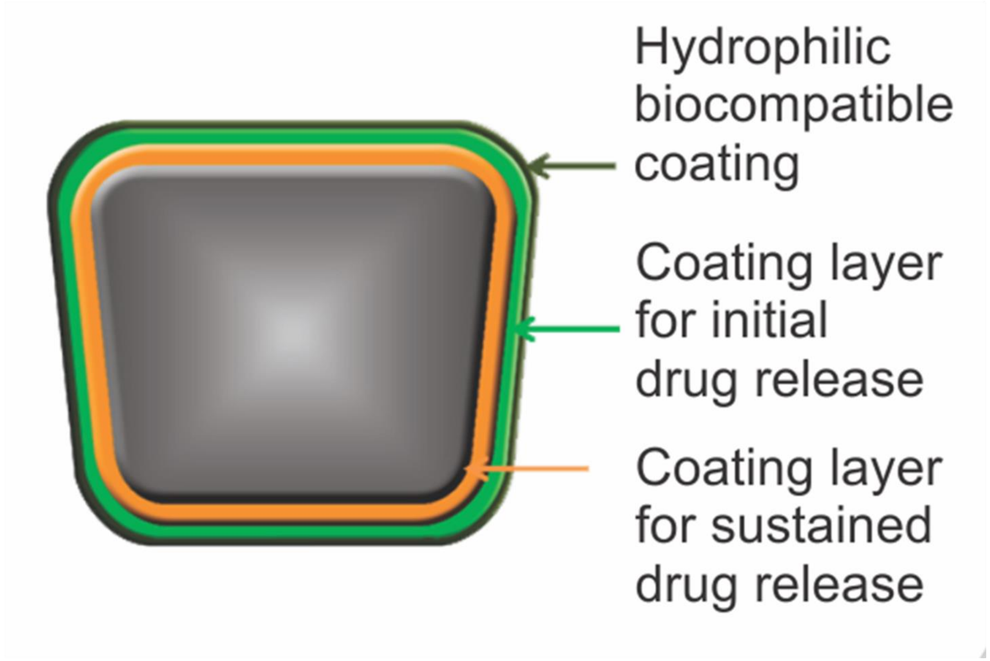
Post-Dilatation



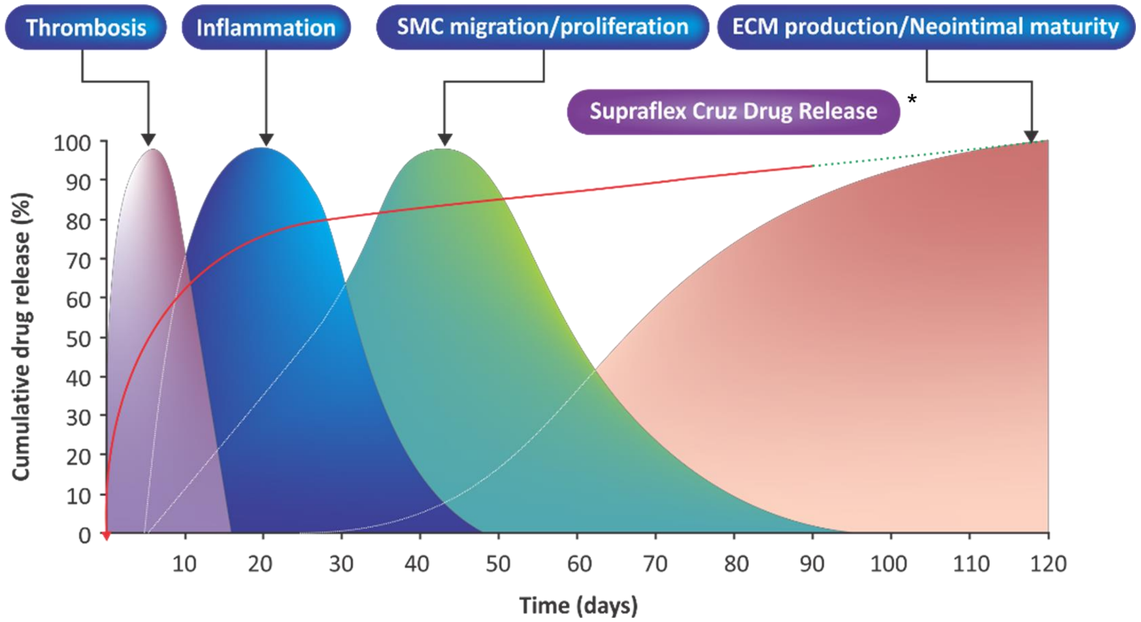
Supraflex Cruz
Sirolimus Eluting Cobalt Chromium Coronary Stent System

Polmer and drug release

Programed to address the entire wound healing cascade in real-world patients.



Sirolimus drug dose: 1.4 μg/mm^2



- Nearly 80% of drug is released within one month **(Initial burst).**
- Remaining drug is programmed to get released for 3 months.
- Designed to cover the entire period of arterial wound healing in real-world patients.

*After 90 days of drug release, the amount of residual drug in the stent is so low that it goes beyond the detection/quantitation limit.

Supraflex Cruz
Sirolimus Eluting Cobalt Chromium Coronary Stent System

Clinical studies

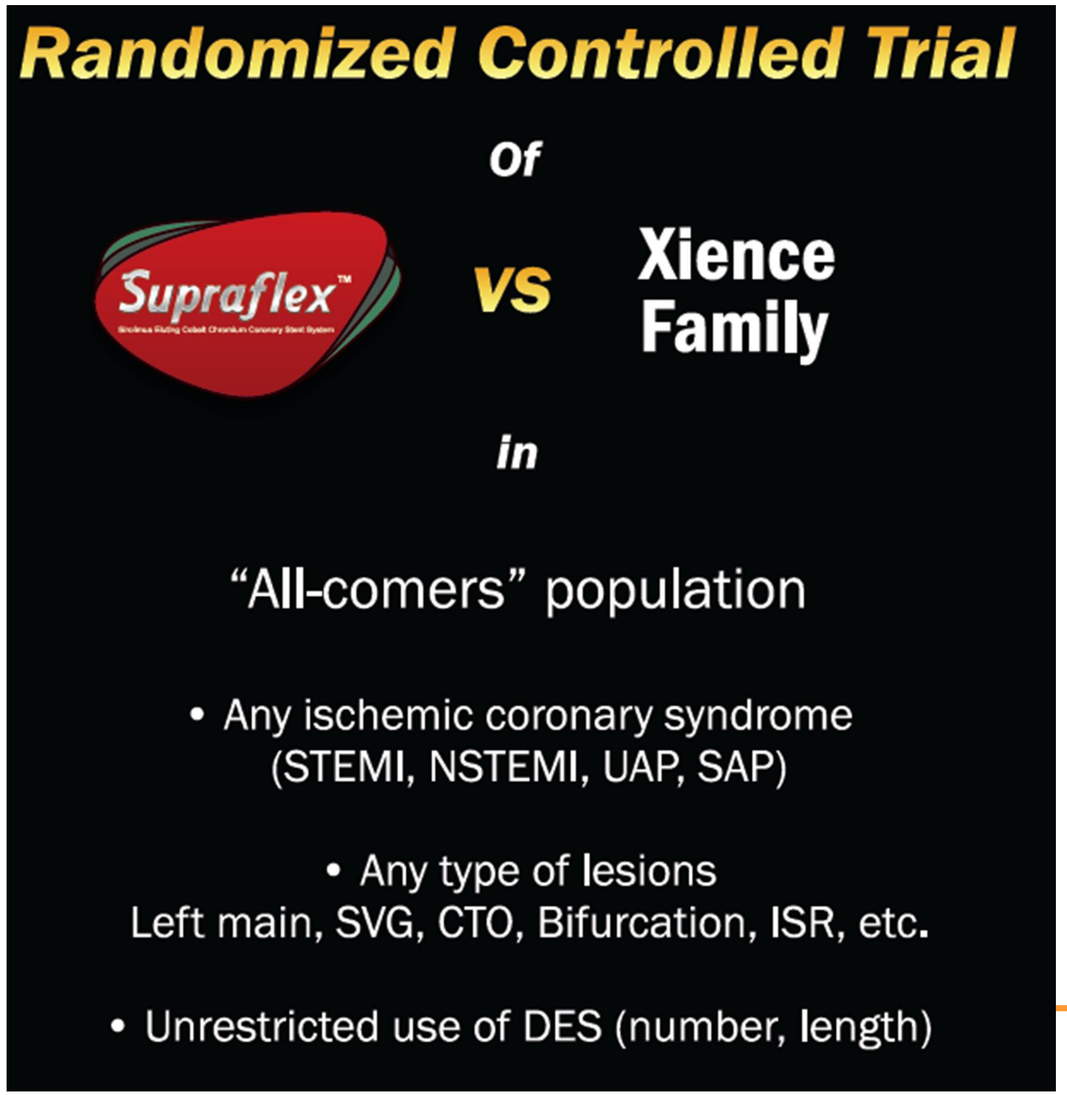
Levels of Evidence

Talent

Thin strut sirolimus-eluting stent in All comers population vs Everolimus-eluting stent

FIRE TRIAL

General details of the study

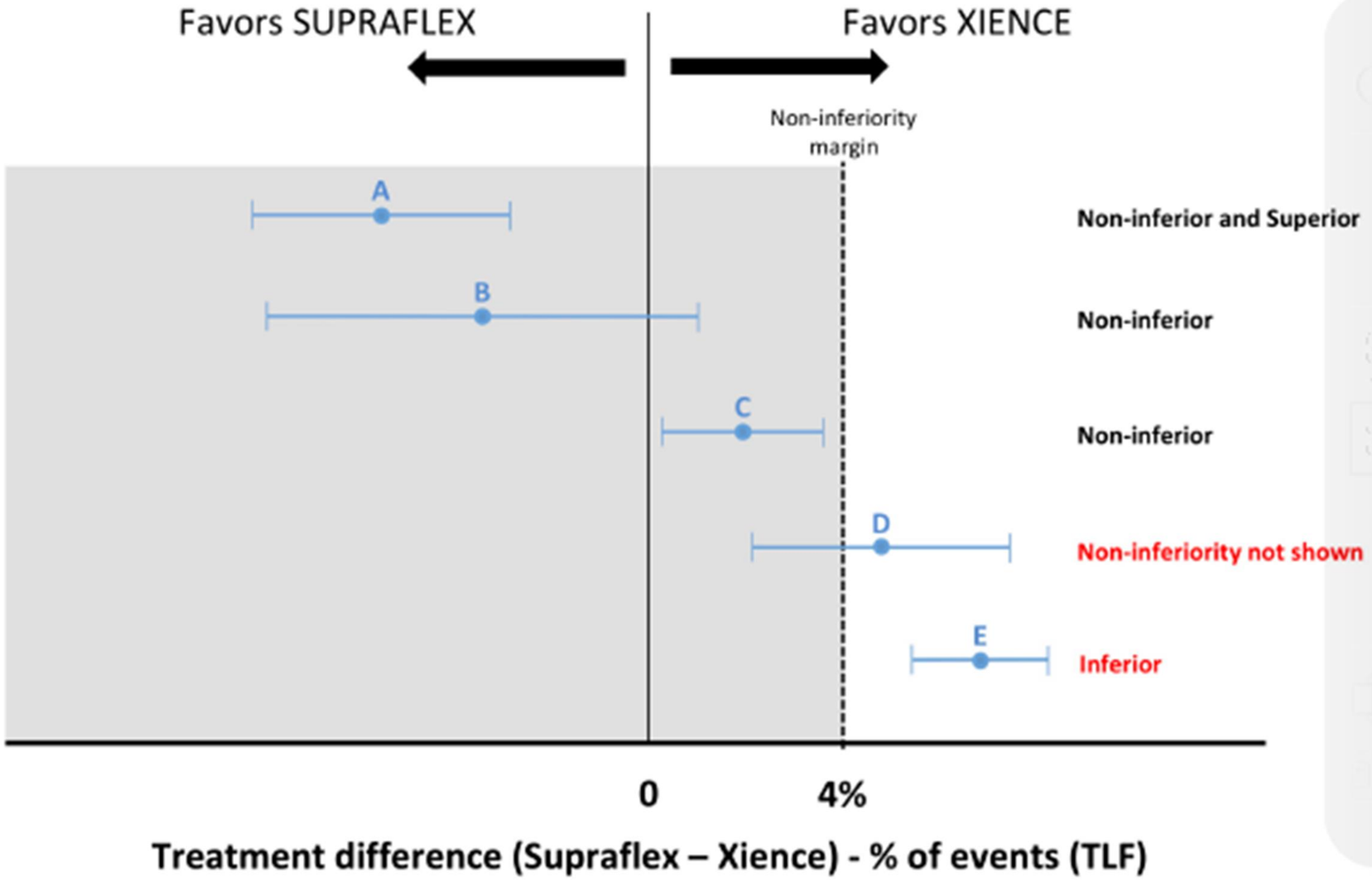


- **Hypothesis**
  - Non-inferiority of device-oriented endpoint (DOCE) – a composite of cardiac death, target vessel myocardial infarction, and clinically-indicated target lesion revascularization – in the Supraflex arm compared with the Xience arm at 12 months post-procedure.

- **Sample size calculation**
  - Expected DOCE rate of Xience at 12 months: 8.3% (Resolute All-comers (Xience arm)*
  - Non-inferiority margin of 4.0%
  - One-sided type I error of 0.05
  - 85% power to detect non-inferiority
  - Assume lost to follow-up of 3%

- **A total of 1435 subjects were to be randomized.**

Non inferiority



EuroIntervention 2018; Jaa-421 2018, doi: 10.4244/EIJ-D-18-00499

Baseline Characteristics

Characteristic	Supraflex (n=720)	Xience (n=715)	Percentage difference (95% CI)
Age (years)	65.0±10.3	64.7±10.1	0.3 (-0.8 to 1.3)
Male	75.80%	76.50%	-0.7% (-5.1 to 3.7%)
BMI (kg/m^2)	28.3±4.8	28.3±4.6	0.0% (-0.5 to 0.5%)
Risk factors			
Current smoker	24.50%	24.10%	0.4% (-4.0 to 4.9%)
Diabetes mellitus	21.80%	24.90%	-3.1% (-7.5 to 1.3%)
Insulin dependent	6.70%	9.40%	-2.7% (-5.5%, 0.1%)
Hypertension	65.30%	66.10%	-0.8% (-5.7 to 4.1%)
Hypercholesterolemia	61.80%	60.20%	1.6% (-3.4 to 6.7%)
Family history of CAD	46.30%	45.20%	1.2% (-4.1 to 6.5%)
History of			
Previous MI	18.90%	17.90%	1.0% (-3.0 to 5.0%)
PVD	7.10%	9.00%	-1.9% (-4.7 to 0.9%)
Previous PCI	24.30%	21.40%	2.9% (-1.4 to 7.2%)
Previous CABG	4.60%	7.70%	-3.1% (-5.6 to -0.6%)
Heart Failure	4.70%	6.90%	-2.1% (-4.5 to 0.3%)
Renal Insufficiency	2.80%	2.00%	0.8% (-0.8 to 2.4%)
Indication			
Stable angina	40.40%	43.40%	3.0% (-2.1 to 8.1%)
ACS	59.60%	56.60%	
UAP	16.10%	13.80%	2.3% (-1.4 to 6.0%)
NSTEMI	26.90%	26.40%	0.5% (-4.1 to 5.1%)
STEMI	16.50%	16.40%	0.2% (-3.7 to 4.0%)

Procedural details

	Supraflex (n=1046 lesions)	Xience (n=1030 lesions)	p-value
Pre-dilatation	77.20%	75.90%	0.509
Max pressure (atm)	13.6±4.3	13.5±4.1	0.677
Max balloon diameter (mm)	2.52±0.43	2.46±0.43	0.006
Stent characteristics (per lesion)			
Number of stents used	1.2±0.5	1.2±0.5	0.592
Total stent length (mm)	25.7±14.5	26.0±14.5	0.623
Overlapping stents	21.10%	19.50%	0.361
Stent length (mm)	21.3±8.3	21.8±8.8	0.12
Nominal Stent diameter (mm)	3.0±0.5	3.0±0.5	0.186
Post balloon dilatation	52.00%	52.20%	0.918
Max pressure (atm)	17.1±4.3	17.5±3.9	0.096
Max balloon diameter (mm)	3.30±0.58	3.29±0.60	0.804

Lesion details

	Supraflex (n=1046 lesions)	Xience (n=1030 lesions)	p-value
Vessel location:			0.07
LAD	44.70%	41.90%	
LCX	21.00%	23.00%	
RCA	32.30%	31.80%	
Left main	1.40%	1.60%	
Bypass graft	0.50%	1.70%	
Number of lesions treated per patient	1.45±0.77	1.44±0.74	0.76
Total stented length per patients (mm)	37.2±27.4	37.2±27.0	0.961
TIMI flow pre			0.122
Flow 0	13.70%	10.90%	
Flow 1	3.80%	4.10%	
Flow 2	6.30%	8.20%	
Flow 3	72.50%	72.20%	
Restenotic lesion	4.20%	4.10%	0.883
Small vessel (≤ 2.75 mm)	40.20%	40.20%	0.999
Long lesion (> 18 mm)	49.70%	49.60%	0.964
Bifurcation involved	16.00%	15.20%	0.65

Device success

	Supraflex n=720 patients n=1046 lesions		Xience n=715 patients n=1030 lesions	Difference (95% CI)	p value
Operators attempted to implant the allocated stent	997 lesions		1003 lesions	-2.1% (-3.7 to -0.5%)	0.014
No stent was able to cross the lesion	1 (0.1%)		3 (0.3%)	- 0.2% (-0.6 to 0.2%)	0.371
Stent dislodgement and failure to retrieve	1 (0.1%)		0 (0.0%)	0.1% (-0.1 to 0.3%)	1.000
Cross over Allocated stent did not cross the lesion	21 (2.0%)	>	1 (0.1%)	1.9% (1.0 to 2.8%)	<0.0001
In-stent residual stenosis ≥30%	1 (0.1%)		1 (0.1%)	-0.0% (-0.3 to 0.3%)	1.000
Device success (per lesion)	97.6% (973/997)	<	99.5% (998/1003)	-1.9% (-3.0 to -0.9%)	0.0003

- The crossovers to non-allocated stent - in total 21 lesions out of 1046 in the Supraflex arm (12 lesions crossovered to the Xience arm, 9 lesions crossovered to non-study stents) - were **clustered in 7 out of the 23 centers.**
- **Some investigators had a tendency to quickly crossover to a familiar stent technology.**

Device success

	Supraflex n=720 patients n=1046 lesions	Xience n=715 patients n=1030 lesions	Difference (95% CI)	p value
Device success (per lesion)	97.6% (973/997)	99.5% (998/1003)	-1.9% (-3.0 to -0.9%)	0.0003
In-hospital DOCE	1.5% (11/720)	1.4% (10/715)	0.1% (-1.2 to 1.5%)	0.837
Procedure success (per patient)	95.6% (673/704)	98.3% (695/707)	-2.7% (-4.5 to -0.9%)	0.003

- In spite of the slight difference in device success rates between groups, the device success rates in the Supraflex (**97.6%**) are comparable or even superior to other current DES in all-comers trials.

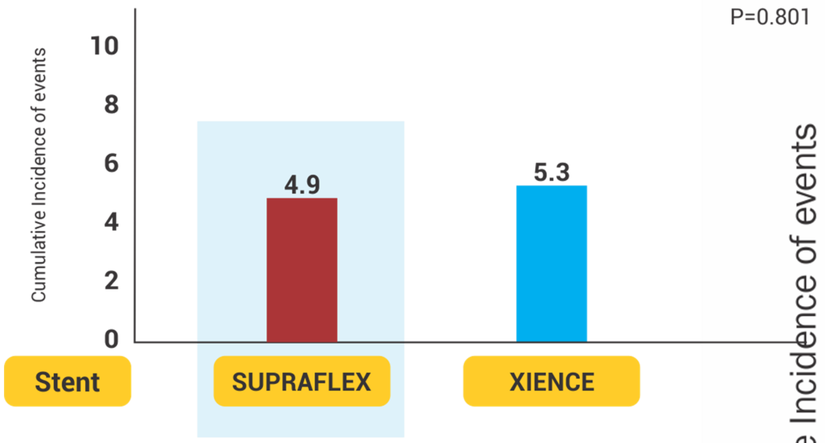
  ✓ RESOLUTE All-comers: **97**% in each group (Xience and Resolute)
  ✓ TWENTE: **98**% in Resolute vs. **98.4**% in Xience
  ✓ DESSOLVE III*: **98.3**% in Mistent vs. **98.6**% in Xience
  ✓ TARGET AC: **92.4**% in Firehawk vs. **94.8**% in Xience
  ✓ BIOFLOW V**: **98**% in Orsiro vs. **97**% in Xience

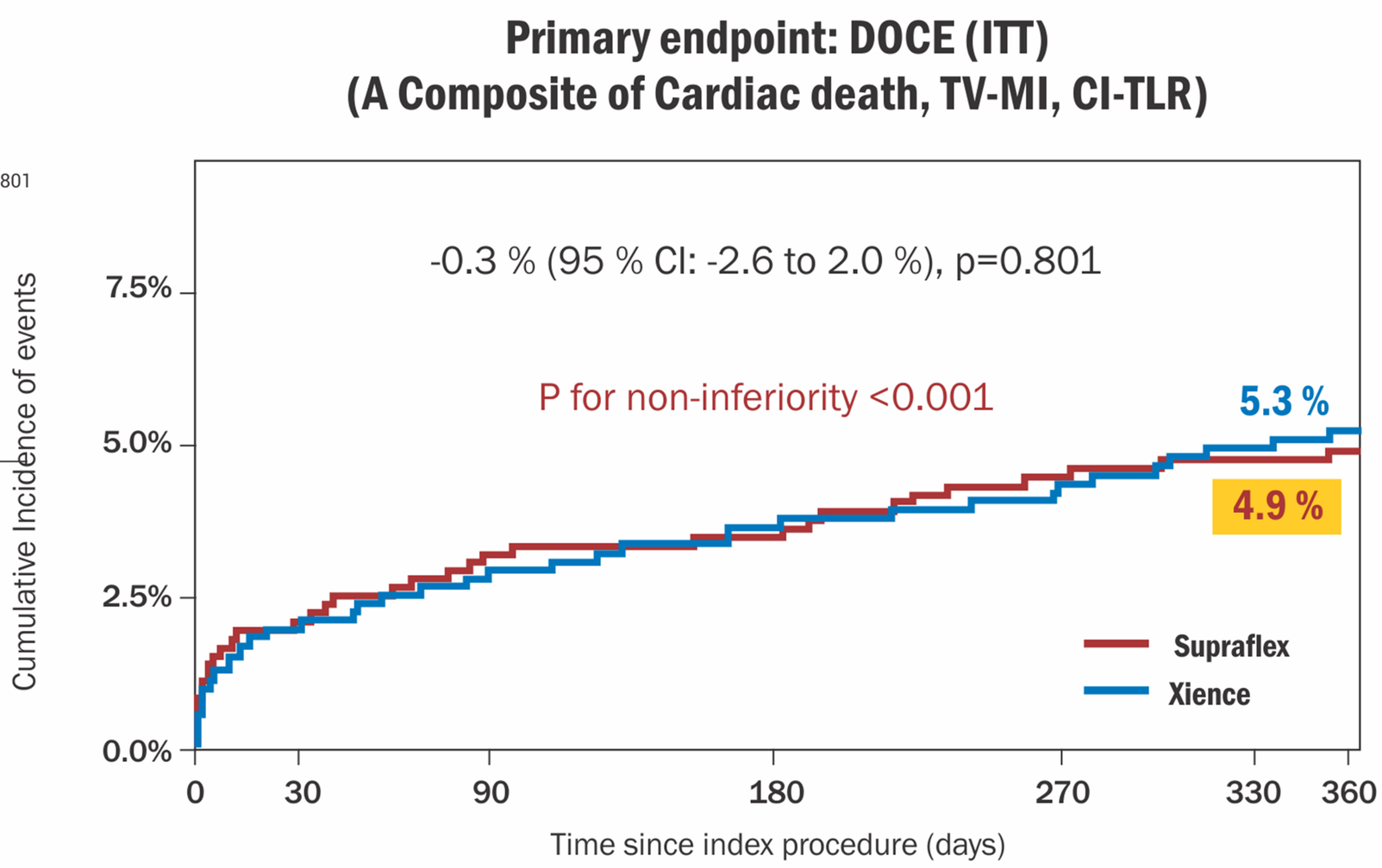
- The difference of device success rate did not have any bearing on patient outcomes.

*procedure success
**Non-all-comers

Primary endpoint

(A composite of cardiac death, TV-MI, CI-TLR)



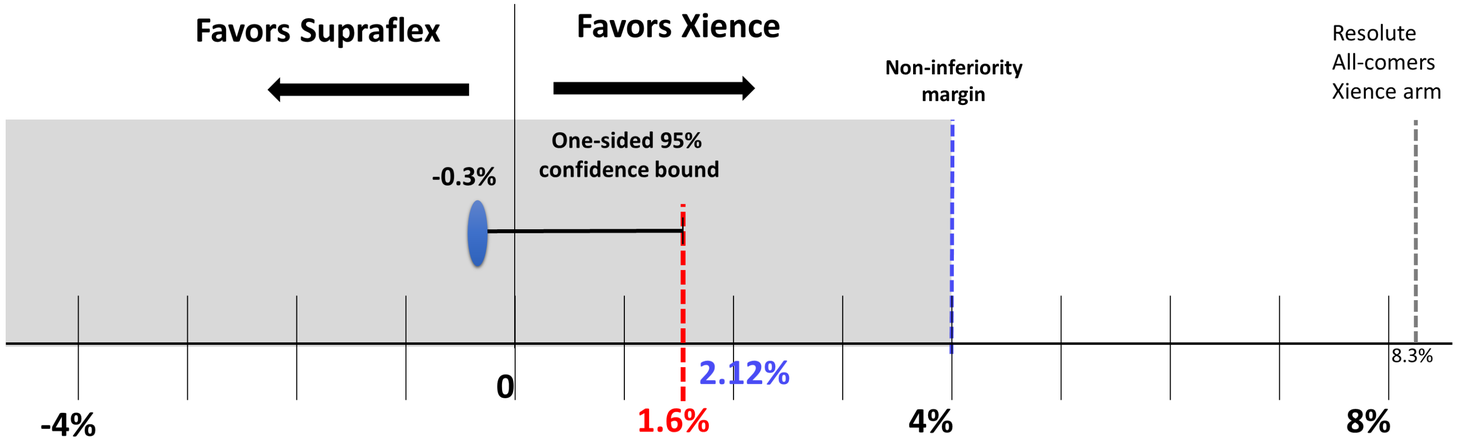


Supraflex	At risk	720	689	684	665	655
Xience	At risk	715	686	679	665	653

Non inferiority

Original Hypothesis

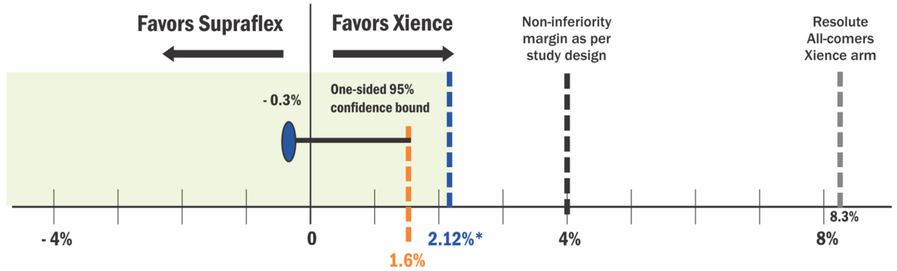
Primary endpoint	Supraflex n=720	Xience n=715	Difference	One sided 95% upper confidence bound	Non-inferiority margin	P-value for non-inferiority
DOCE	4.9% (35)	5.3% (37)	-0.3%	1.6%	2.12%	<0.001



Post-Hoc Hypothesis

Primary endpoint: DOCE (ITT)
(A composite of cardiac death, TV-MI, CI-TLR)

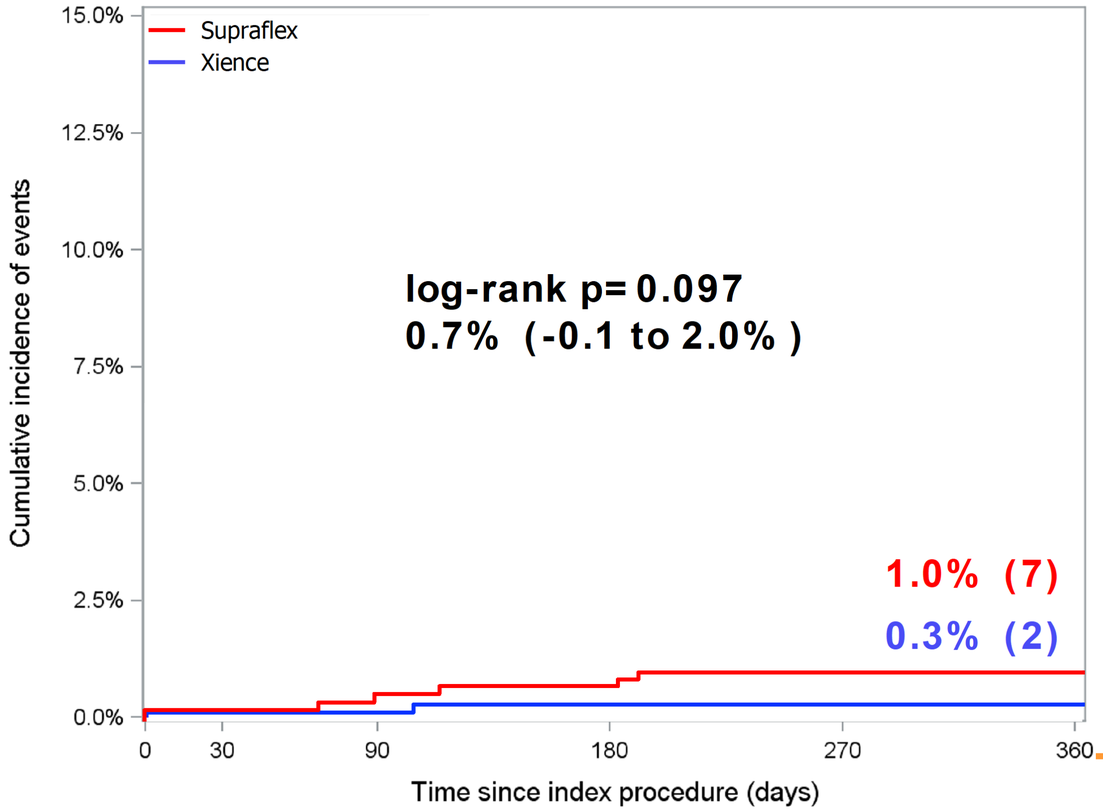
Primary endpoint	Supraflex n=720	Xience n=715	Difference	One sided 95% upper confidence bound	Non-inferiority margin*	P-value for non-inferiority
DOCE	4.9%	5.3%	- 0.3%	1.6%	2.12%	= 0.019



Treatment difference (Supraflex - Xience) -% of events (DOCE)

* non inferiority margin re calculated as per the results of Xience and Hazard Ratio 40%

Cardiac death

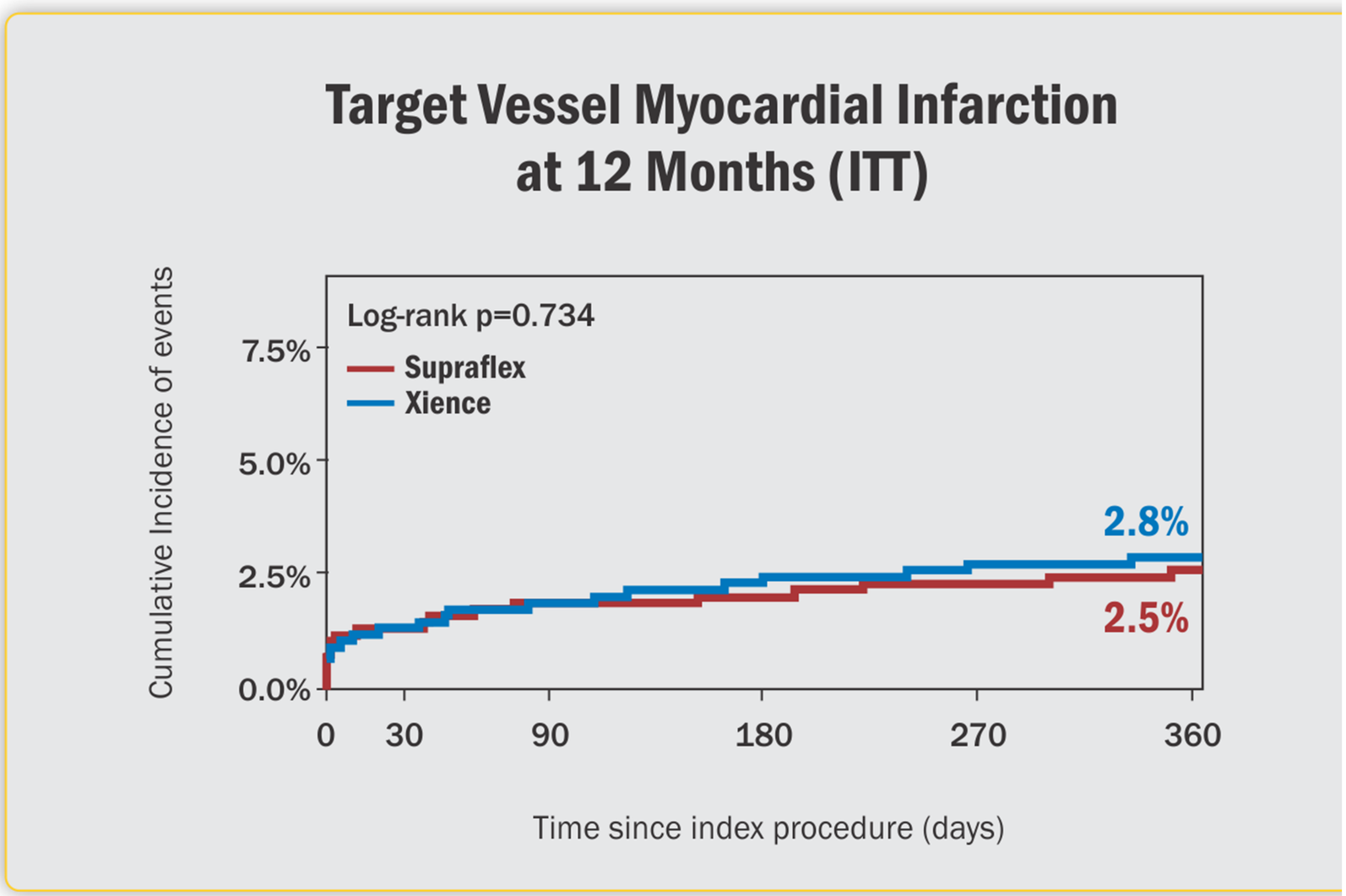


ID and allocation	Days after index procedure	Type of death	Comments
Supraflex Case 1	0 days	• Explained • Witnessed	• Patient died 15 minutes after the procedure in the Cath Lab • Cardiac death due to residual significant lesion at proximal LAD with heavy calcification • No stent thrombosis
Supraflex Case 2	0 days	• Explained • Witnessed	• Patient underwent PCI with a stent in the proximal LAD. • Cardiac death due to STEMI occurred after index procedure due to linear dissection at the proximal edge of stent. • No stent thrombosis confirmed with CAG
Supraflex Case 3	67 days	• Unexplained • Witnessed	• Unexplained death more than 30 days after PCI → **Possible ST**
Supraflex Case 4	89 days	• Explained • Witnessed	• Patient died due to decompensation of HF. • No stent thrombosis
Supraflex Case 5	114 days	• Unexplained • Witnessed	• Unexplained death more than 30 days after PCI → **Possible ST**
Supraflex Case 6	183 days	• Explained • Unwitnessed	• Found dead in a car. • Autopsy confirmed complete occlusion of the stent vessel. • **Definite stent thrombosis.**
Supraflex Case 7	191 days	• Explained • Witnessed	• Patient died due to decompensation of HF. • No stent thrombosis
Xience Case 1	1 day	• Explained • Witnessed	• Cardiac death due to STEMI presentation and no reflow phenomenon (final TIMI 1 flow after index PCI) • No stent thrombosis
Xience Case 2	104 days	• Explained • Unwitnessed	• Patient collapsed at home. • Autopsy confirmed complete occlusion of the stent vessel. • **Definite stent thrombosis.**

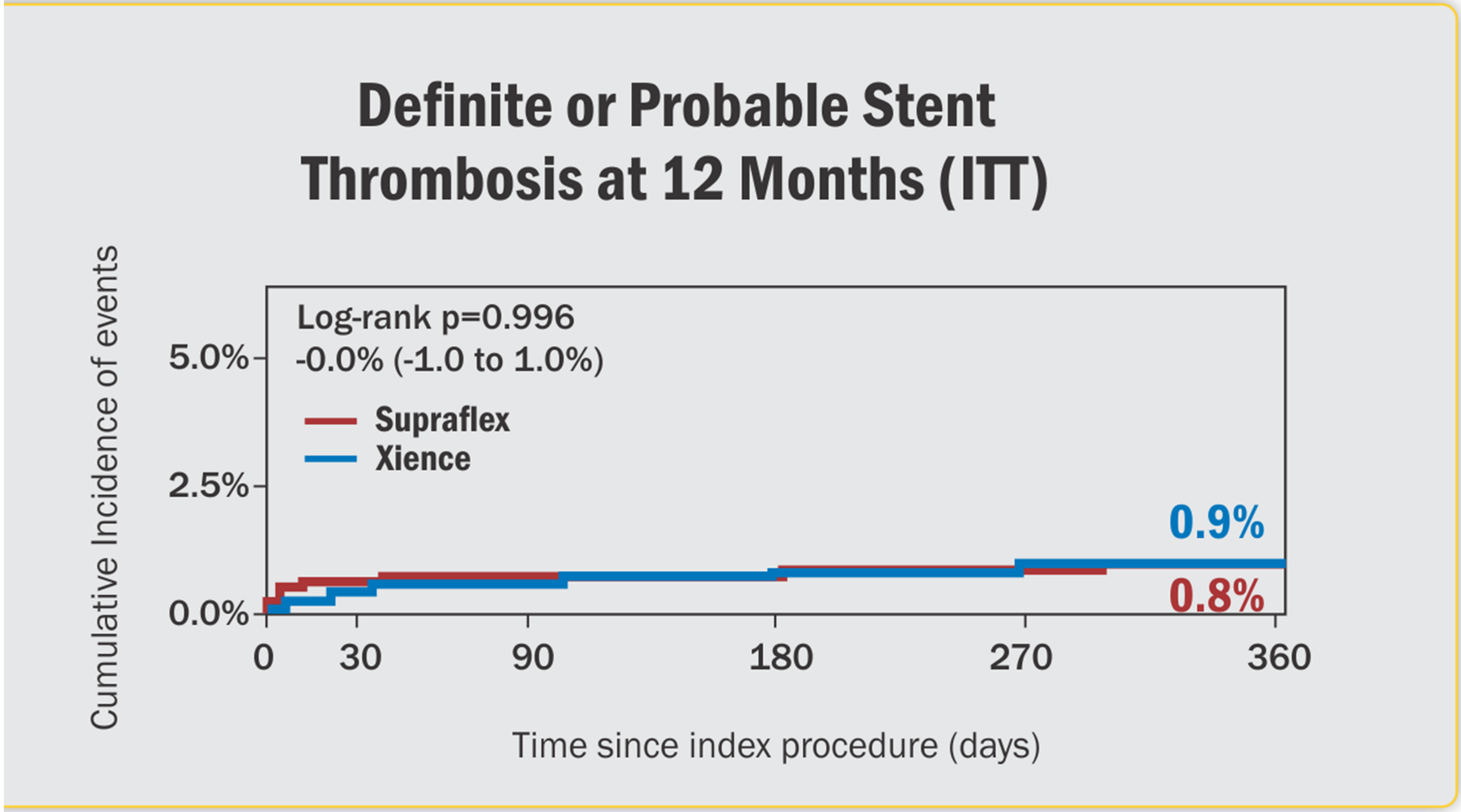
Cardiac death

TALENT All-comers	Supraflex n=720 patients n=1046 lesions	Xience n=715 patients n=1030 lesions	p value
	2·0%	0·6%	0·019
TARGET All-comers	Firehawk n=823 patients n=1221 lesions	Xience n=830 patients n=1179 lesions	p value
	2·2%	2·2%	0·98
BIOSCIENCE All-comers	Orsiro n=1063 patients n=1594 lesions	Xience n=1056 patients n=1545 lesions	p value
	3·3%	2·6%	0·360
TWENTE All-comers	Resolute n=697 patients n=1080 lesions	Xience n=694 patients n=1036 lesions	p value
	2·1%	2·2%	0·86
RESOLUTE All-comers	Resolute n= 1140 patients n= 1876 lesions	Xience n= 1152 patients n= 1954 lesions	
	1·6%	2·8%	0·08
BIOFlOW V (not all comers)	Orsiro n=884 patients n= 1111 lesions	Xience n=450 patients n= 589 lesions	p value
	1·0%	1·0%	0·382

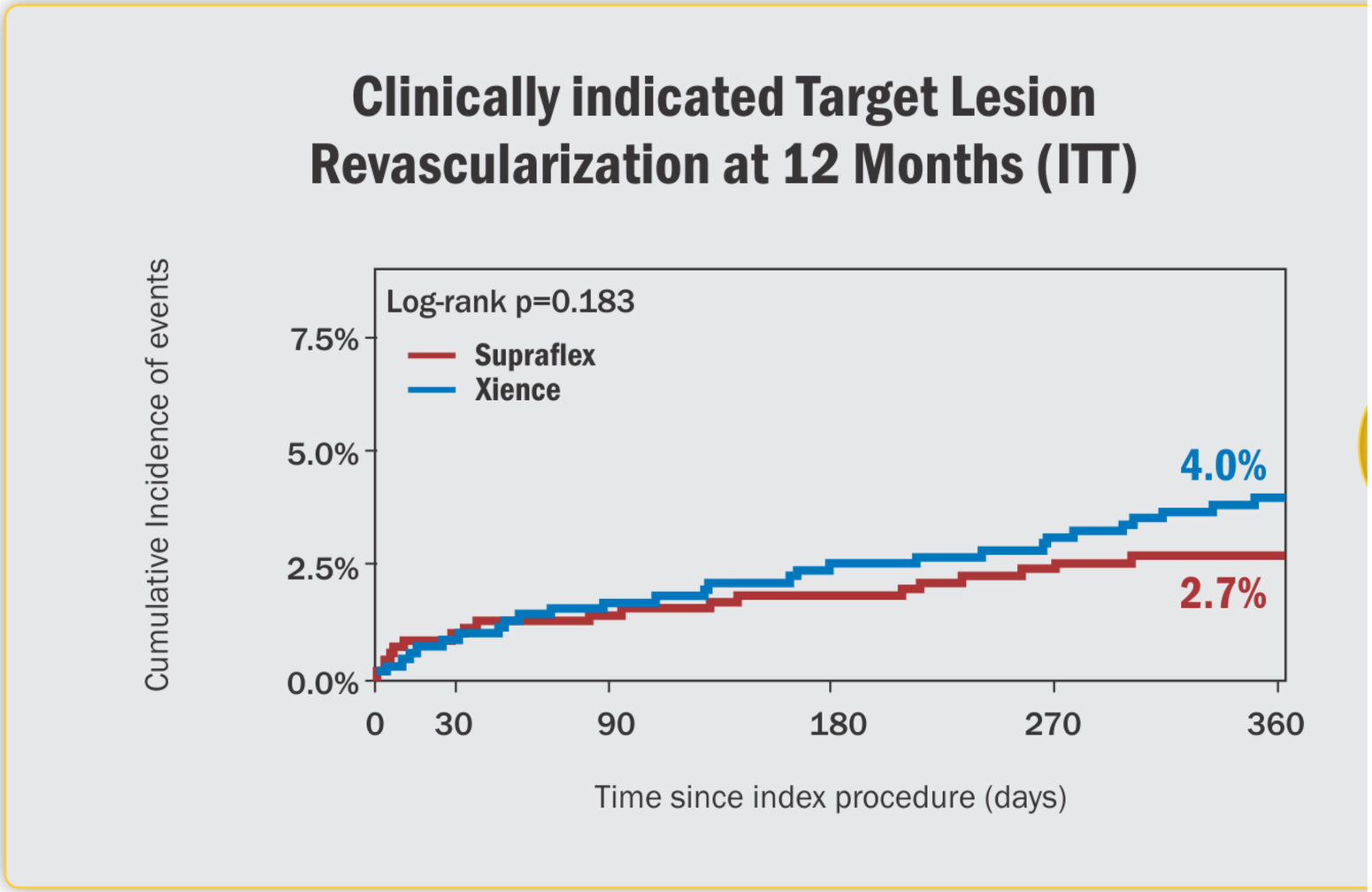
Target vessel MI



Stent thrombosis

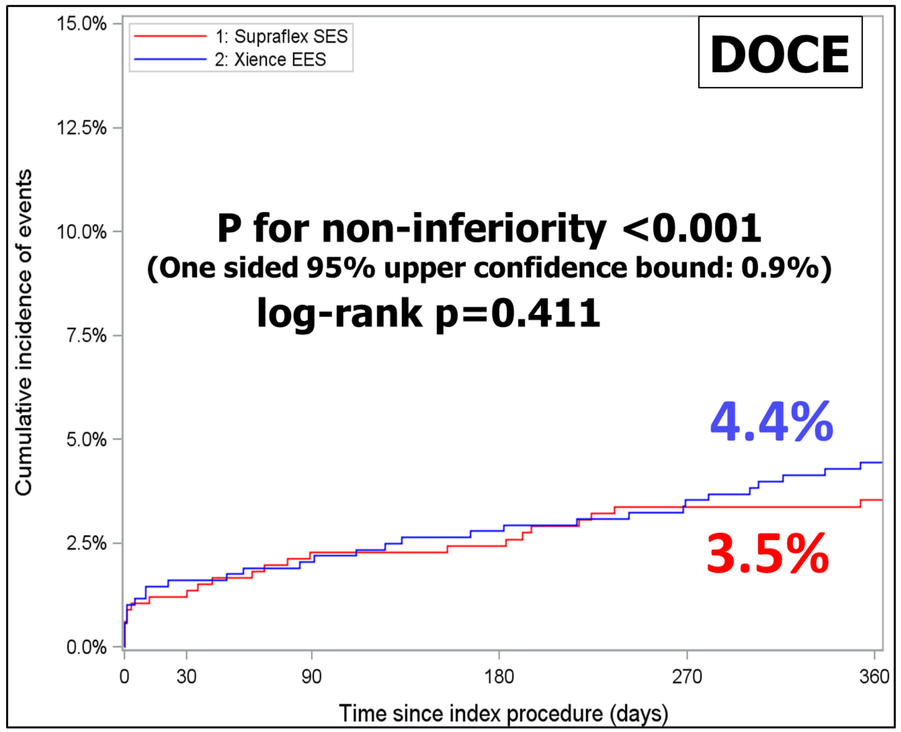


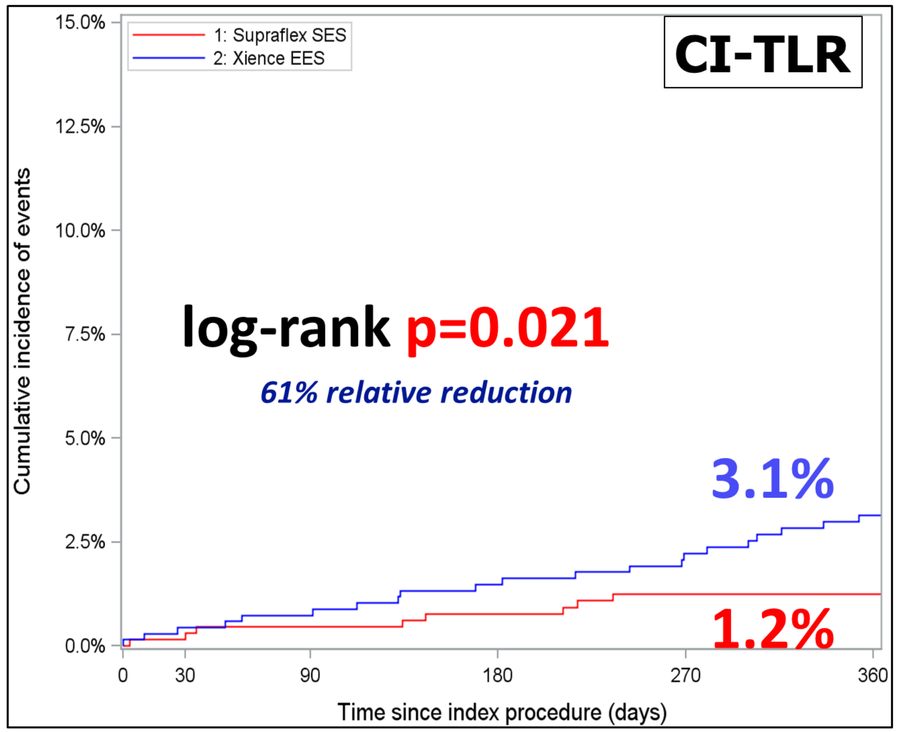
Clinically indicated TLR



Per protocol analysis

	Supraflex	Xience		
	n=660	n=685	Percentage difference (95% CI)	p value
DOCE	3.5% (23)	4.4% (30)	-0.9% (-3.0 to 1.2%)	0.411
Cardiac death	1.1% (7)	0.3% (2)	0.8% (-0.1 to 1.7%)	0.084
TV-MI	2.2% (14)	2.8% (19)	-0.6% (-2.3 to 1.0%)	0.447
CI-TLR	1.2% (8)	3.1% (21)	-1.9% (-3.5 to -0.3%)	0.021





Supraflex Cruz
Sirolimus Eluting Cobalt Chromium Coronary Stent System

Future clinical studies

Multi Talent Trial

- European RCT
- 3VD, lesion treatment based on physiology guidance with IVUS stent optimization
- 1550 patients; Everolimus DES vs Supraflex Cruz

Diabetic RCT

- Indian RCT
- Diabetic patients with multi-vessel disease
- Xience family vs Supraflex Cruz

Supraflex Cruz
Sirolimus Eluting Cobalt Chromium Coronary Stent System

Future clinical studies

Cruz HBR registry

- Post-market study in Germany, France, Switzerland
- 1120 all-comers patients, including 400 patients at high bleeding risk (HBR)

FIRE Trial

- RCT in Italy and Spain
- >75 year old patients with MI (STE or NSTE) with multi-vessel disease, physiological assessment for non-culprit lesion, 1400 patients; 1 Month DAPT

ACS DAPT study

- Study in Latin America + Europe + Asia
- 3 month vs 6 month DAPT in ACS patients