A prospective multicenter randomized all-comers trial to assess the safety and effectiveness of the ultra-thin-strut sirolimus-eluting coronary stent Supraflex: 2-year results of the TALENT trial

Azfar Zaman, MD

Freeman Hospital, Newcastle University, and Newcastle upon Tyne Hospitals NHS Trust, Newcastle, UK

Robbert J de Winter, Upendra Kaul, Yoshinobu Onuma, Patrick W. Serruys

On behalf of the TALENT Investigators

Disclosure Statement of Financial Interest

I, (Azfar Zaman) have received lecture/consulting fees/research support from:

- **Abbott Vascular**
- **Boston Scientific**
- **Cardinal Health**
- **Medtronic Corporation**
- **SMT**
- **Merrill**

Background

- **A recent meta-analysis showed that ultra-thin strut DES (<70 μm) reduced the incidence of TLF compared with contemporary thicker strut DES. [1]**

[1] Bangalore S, et al. Circulation. 2018 Nov 13;138(20):2216-2226.

- **TALENT is a prospective, multi-center, all-comers randomized controlled trial (n=1,435), demonstrating non-inferiority of the Supraflex SES vs. the Xience EES in terms of device-oriented composite endpoint (DOCE) up to one years [2].**

[2] Zaman A, et al. Lancet. 2019 Mar 9;393(10175):987-997.

- **The clinical outcomes of Supraflex SES beyond 1 year have not yet been reported in the context of prospective clinical trial.**

Objective

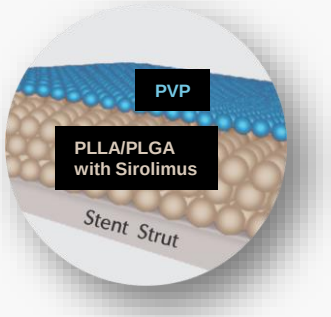
The aim of this study is to investigate whether the comparable outcomes of Supraflex SES to Xience EES are maintained at 2 years follow-up.

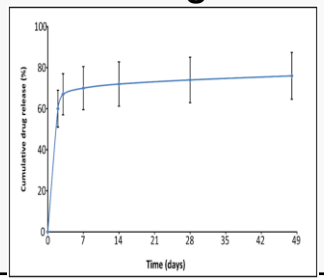
Trial organization (investigator-initiated trial)

- Sponsor: **European Clinical Research Institute** (www.ECRI-trials.com)
- Grant giver:
  - **SMT (Supraflex SES)**
- Clinical Research Organization: **Cardialysis**
- Statistical analysis: **Cardialysis**
- Clinical event committee (CEC)
  - **Prof. W. Rutsch** (Catheterisation Laboratories Charité, University Clinic Berlin, Germany)
  - **Dr. S. Garg** (Central Manchester & Manchester children's Foundation Trust, East Lancashire NHS Trust United Kingdom)
  - **Dr. J-P. R. Herrman** (Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands)
  - **Dr. B. Rensing** (St. Antonius Ziekenhuis, Nieuwegein, the Netherlands)
- Data and Safety Monitoring Board (DSMB)
  - **Prof. S. James** (DSMB Chairman, Uppsala University, Sweden)
  - **Prof. H. Boersma** (DSMB Biostatistician, Erasmus Medical Center, Rotterdam, the Netherlands)
  - **Dr. J. ten Berg** (DSMB member, St. Antonius Hospital, Nieuwegein, the Netherlands)

Supraflex SES

Platform 	**Stent material**	**CoCr (L605) with highly flexible ‘S–link’ interconnector**
	Strut thickness	**60 µm across all stent diameters (2.0 to 4.5mm)**

Carrier 	**Biodegradable polymer matrix**	- **Top layer**
		  • **0% drug**
		  • **Protective layer (PVP: poly-vinylpyrrolidone)**
		- **Base layer**
		  • **100% drug (Sirolimus)**
		  • **PLLA and PLGA**

	Coating	**Circumferential** **The average thickness: 4-5 µm**
Drug 	**Sirolimus**	**1.4 µg/mm^2**

	Release profile	**1. Initial burst**
		  - **70% released within 7 days**
		  - **Aiming to prevent excessive cell growth**
		2. Sustained release up to 48 days

TALENT study flow chart up to 2 years

"All-comers" population

- **Any ischemic coronary syndrome (STEMI, NSTEMI, UAP,SAP)**
- **Any type of lesions**
  - ✓ **Left main**
  - ✓ **SVG**
  - ✓ **CTO**
  - ✓ **Bifurcation**
  - ✓ **ISR**
  - ✓ **etc.**
- **Unrestricted use of DES (number, length)**

All-comers patient population
1435 patients from 23 enrolling sites

Randomization (1:1)

Supraflex SES N=720	Xience EES N=715
18 dead 11 withdrew consent 5 lost to follow-up	21 dead 7 withdrew consent 3 lost follow up
704 patients FUP at 720 days (97.8%) - included in ITT analysis	705 patients FUP at 720 days (98.6%) - included in ITT analysis

Primary Endpoint: DOCE
(Device-oriented composite endpoint: cardiac death, TV-MI, and CI-TLR)

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	75.8%	76.5%	-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	24.5%	24.1%	0.4% (-4.0 to 4.9%)
Diabetes mellitus	21.8%	24.9%	-3.1% (-7.5 to 1.3%)
Insulin dependent	6.7%	9.4%	-2.7% (-5.5%, 0.1%)
Hypertension	65.3%	66.1%	-0.8% (-5.7 to 4.1%)
Hypercholesterolemia	61.8%	60.2%	1.6% (-3.4 to 6.7%)
Family history of CAD	46.3%	45.2%	1.2% (-4.1 to 6.5%)
History of			
Previous MI	18.9%	17.9%	1.0% (-3.0 to 5.0%)
PVD	7.1%	9.0%	-1.9% (-4.7 to 0.9%)
Previous PCI	24.3%	21.4%	2.9% (-1.4 to 7.2%)
Previous CABG	4.6%	< 7.7%	-3.1% (-5.6 to -0.6%)
Heart Failure	4.7%	6.9%	-2.1% (-4.5 to 0.3%)
Renal Insufficiency*	2.8%	2.0%	0.8% (-0.8 to 2.4%)
Indication			
Stable angina	40.4%	43.4%	3.0% (-2.1 to 8.1%)
ACS	59.6%	56.6%	
UAP	16.1%	13.8%	2.3% (-1.4 to 6.0%)
NSTEMI	26.9%	26.4%	0.5% (-4.1 to 5.1%)
STEMI	16.5%	16.4%	0.2% (-3.7 to 4.0%)

Data are mean±SD (n) or n (%) *Renal insufficiency is defined as serum creatinine >2.5 mg/dL or creatinine clearance ≤ 30mL/min.

Lesion and procedural characteristics

Lesion characteristics (Patient level)

	Supraflex n=1046 lesions	Xience N=1030 lesions	P-value
Vessel location:			0.070
LAD	44.7%	41.9%	
LCX	21.0%	23.0%	
RCA	32.3%	31.8%	
Left main	1.4%	1.6%	
Bypass graft	0.5%	1.7%	
Number of lesions treated per patient	1.45±0.77	1.44±0.74	0.760
Total stented length per patients (mm)	37.2±27.4	37.2±27.0	0.961
TIMI flow pre			0.122
Flow 0	13.7%	10.9%	
Flow 1	3.8%	4.1%	
Flow 2	6.3%	8.2%	
Flow 3	72.5%	72.2%	
Restenotic lesion	4.2%	4.1%	0.883
Small vessel (≤ 2.75 mm)	40.2%	40.2%	0.999
Long lesion (> 18 mm)	49.7%	49.6%	0.964
Bifurcation involved	16.0%	15.2%	0.650

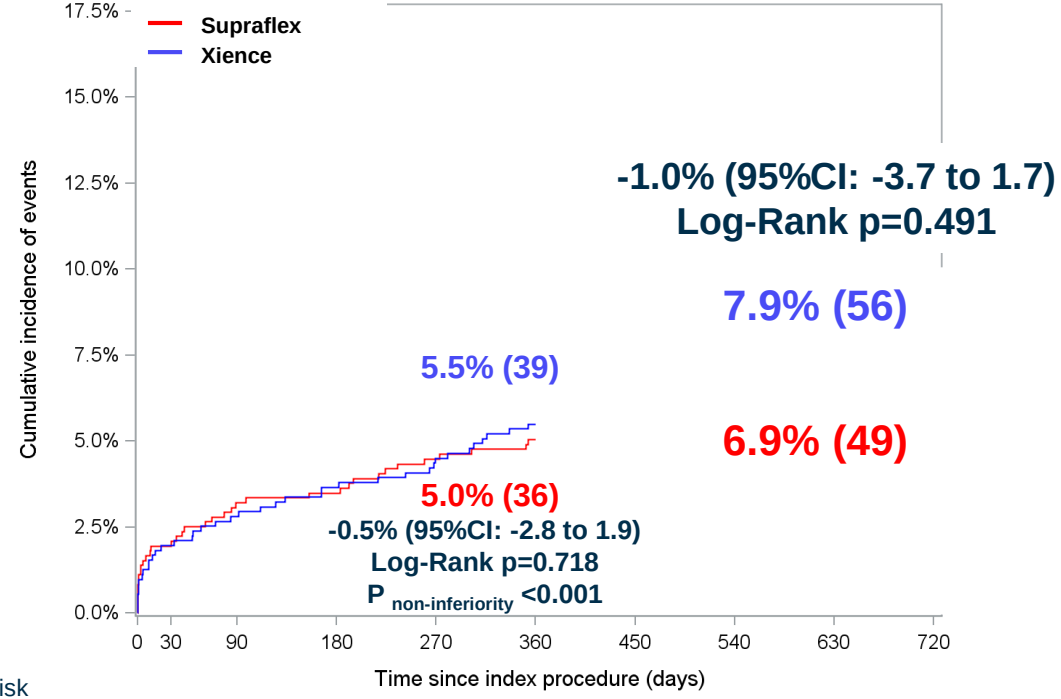
Data are mean±SD (n) or n (%)

Procedural characteristics (Lesion level)

	Supraflex n=1046 lesions		Xience N=1030 lesions	P-value
Pre-dilatation	77.2%		75.9%	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	21.1%		19.5%	0.361
Nominal Stent diameter (mm)	3.0±0.5		3.0±0.5	0.186
Post balloon dilatation	52.0%		52.2%	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

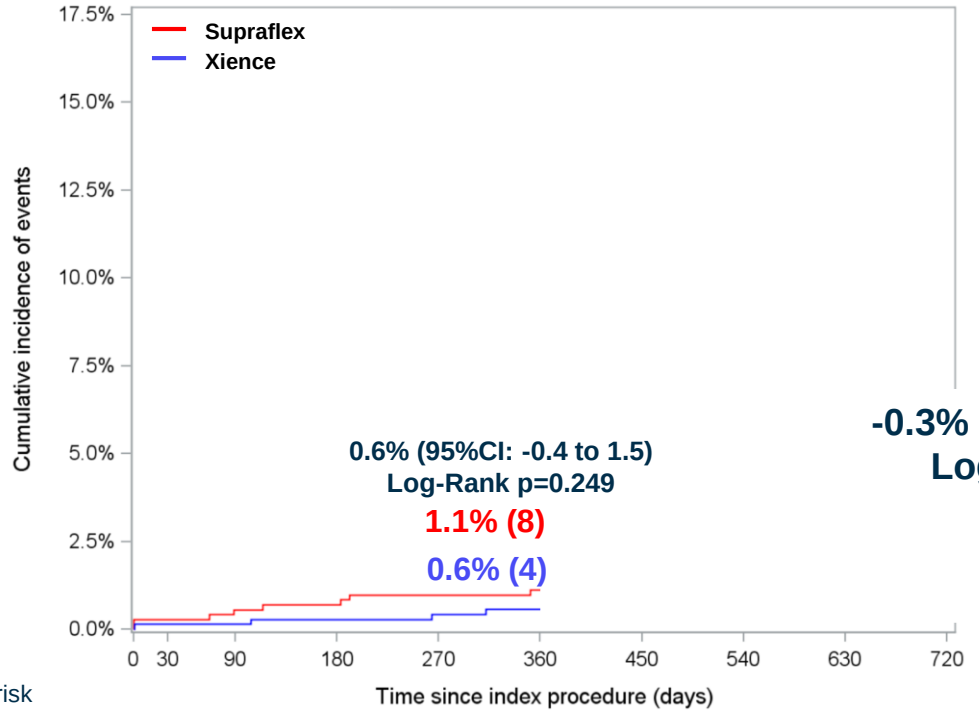
DOCE up to 2 years (ITT)

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



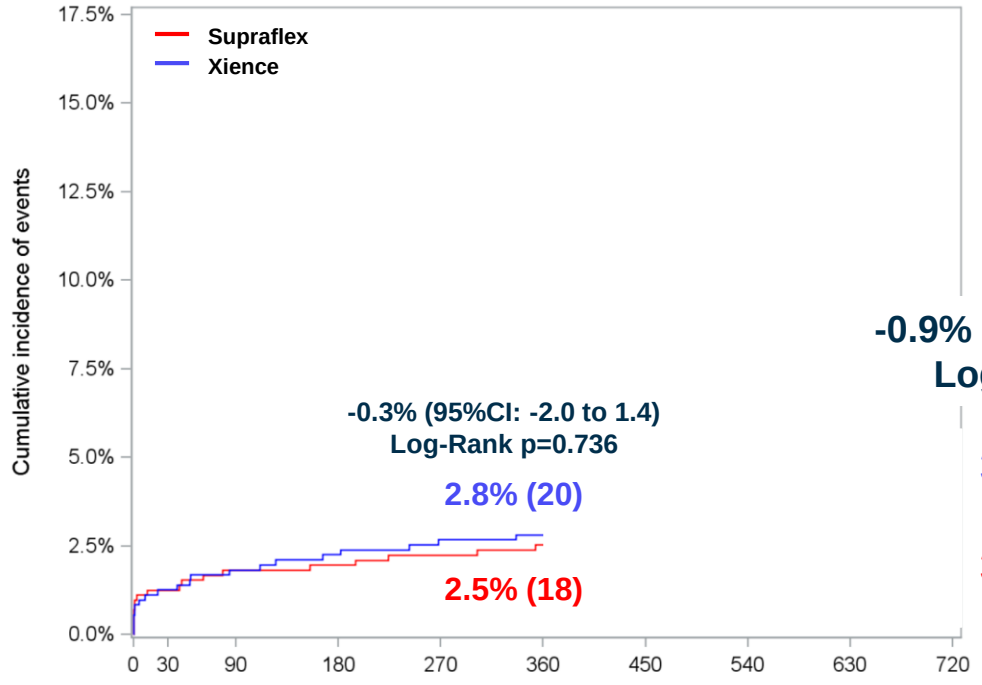
At risk			
Supraflex	720	686	668
Xience	715	682	667

Cardiac death up to 2 years (ITT)



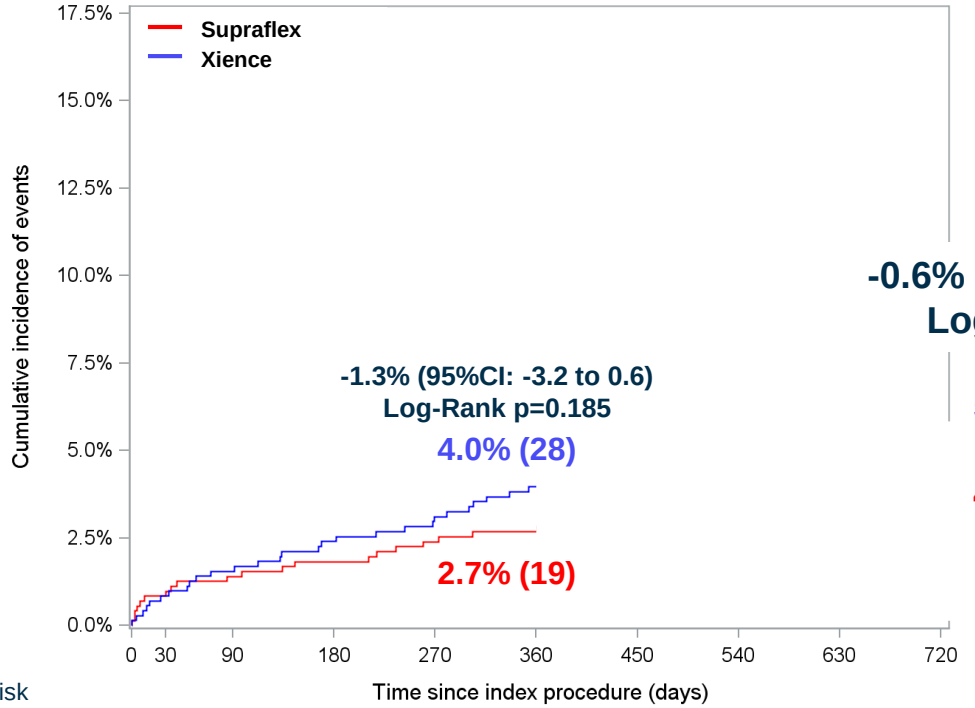
At risk			
Supraflex	720	706	695
Xience	715	705	700

TV-MI up to 2 years (ITT)



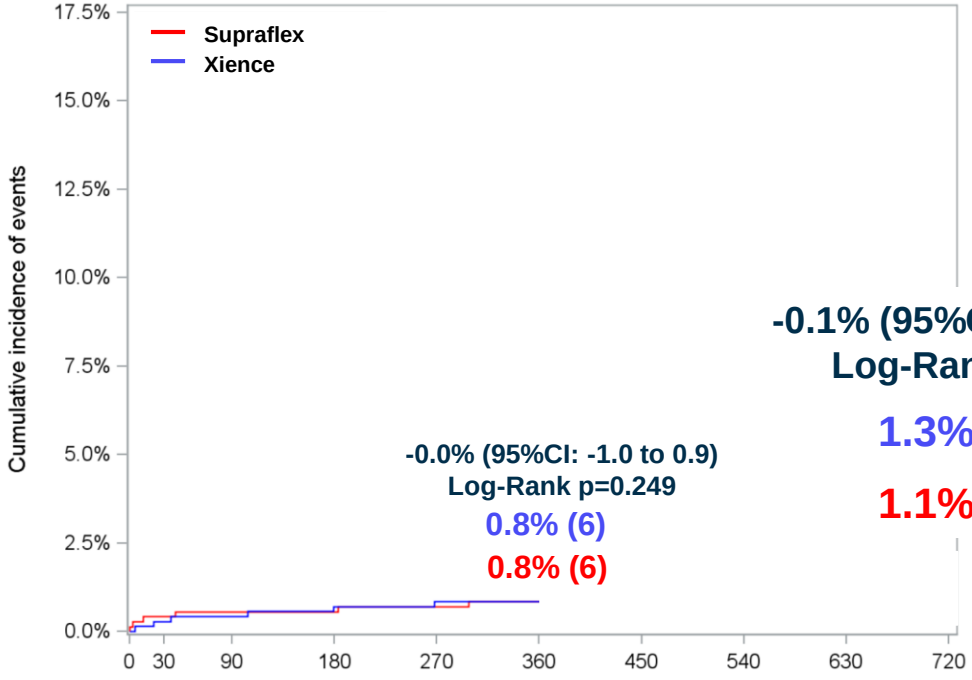
At risk			
Supraflex	720	694	680
Xience	715	691	682

CI-TLR up to 2 years (ITT)



At risk			
Supraflex	720	693	677
Xience	715	688	673

Definite or probable ST up to 2 years (ITT)



-0.1% (95%CI: -1.3 to 1.0)
Log-Rank p=0.813

1.3% (9)

1.1% (8)

-0.0% (95%CI: -1.0 to 0.9)
Log-Rank p=0.249

0.8% (6)

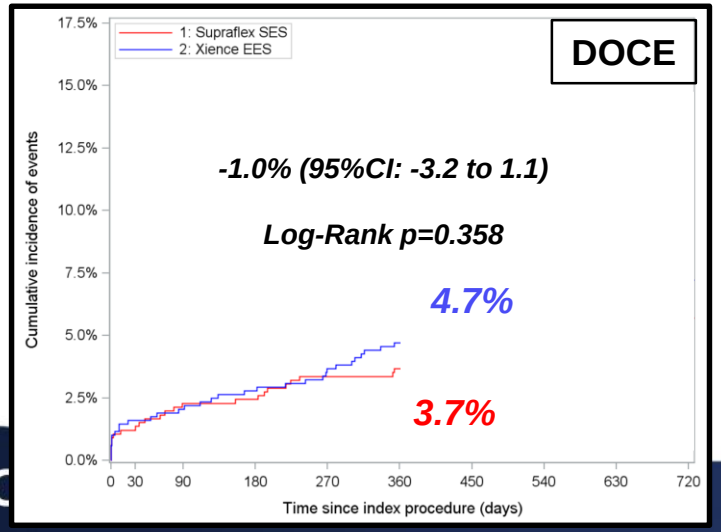
0.8% (6)

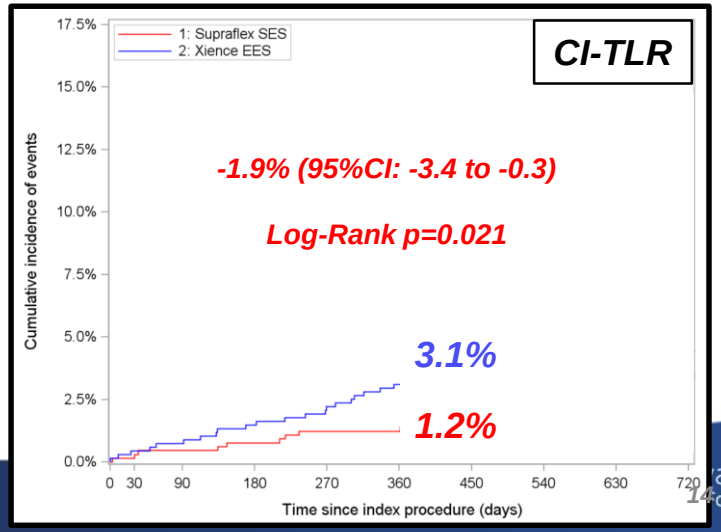
At risk			
Supraflex	720	706	695
Xience	715	705	700

Per-protocol analysis at 1 years

(including patients who have received only the assigned study stent)

	Supraflex	Xience		
	n=660	n=685	Percentage difference (95% CI)	p value
DOCE	3.7% (24)	4.7% (32)	-1.0% (-3.2 to 1.1%)	0.358
Cardiac death	1.2% (8)	0.6% (4)	0.6% (-0.4 to 1.7%)	0.217
TV-MI	2.1% (14)	2.8% (19)	-0.6% (-2.3 to 1.0%)	0.450
CI-TLR	1.2% (8)	3.1% (21)	-1.9% (-3.4 to -0.3%)	0.021

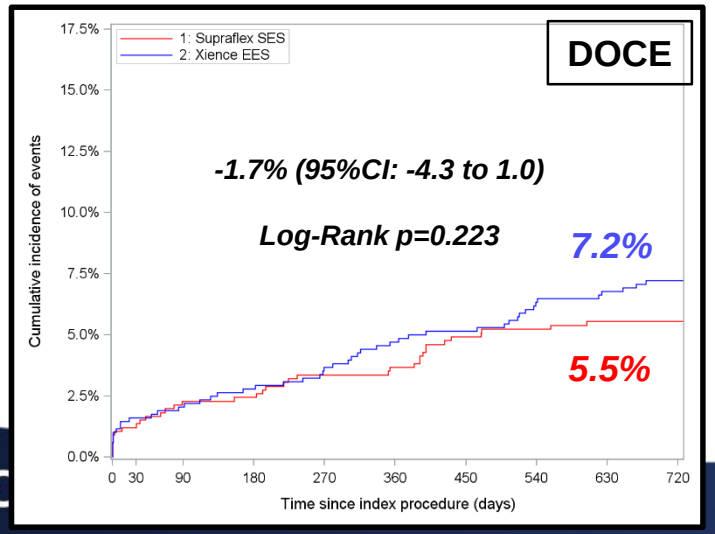


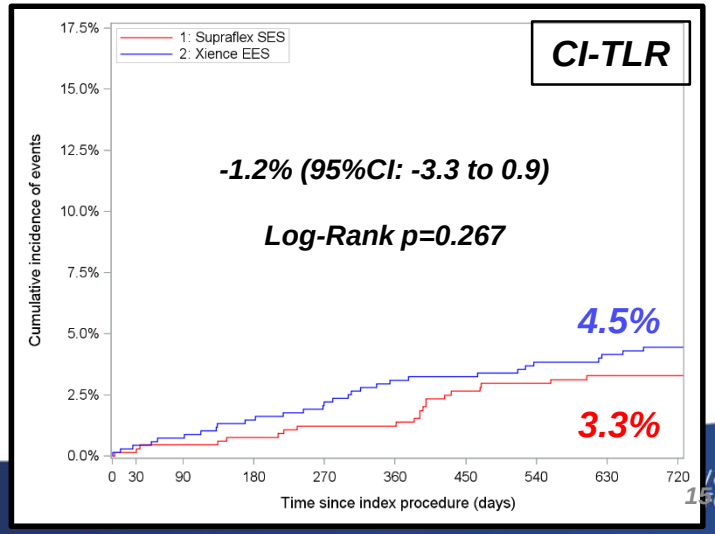


Per-protocol analysis at 2 years

(including patients who have received only the assigned study stent)

	Supraflex	Xience		
	n=660	n=685	Percentage difference (95% CI)	p value
DOCE	5.5% (36)	7.2% (49)	-1.7% (-4.3 to 1.0%)	0.223
Cardiac death	1.4% (9)	1.6% (11)	-0.2% (-1.6 to 1.1%)	0.736
TV-MI	2.6% (17)	3.8% (26)	-1.2% (-3.1 to 0.7%)	0.216
CI-TLR	3.3% (21)	4.5% (30)	-1.2% (-3.3 to 0.9%)	0.267





Conclusion

- The Supraflex biodegradable polymer SES demonstrated comparable 2-year clinical outcomes to Xience EES in all-comer population.

- Lower rate of CI-TLR in the Supraflex arm up to 1 year in per-protocol analysis was subsided beyond 1 year.

TALENT participating 23 sites

Thank you for your contribution!

	Number of enrollment
Amsterdam University Medical Center **Prof. R-J. de Winter**	224
Catharina hospital **Dr. P. Tonino**	217
Medisch Centrum Leeuwarden **Dr. S. Hofma**	154
PAKS Chrzanów **Dr. A. Zurakowski**	116
Maasstad ziekenhuis **Dr. P. Smits**	100
PAKS Kędzierzyn- Koźle **Dr. J. Prokopczuk**	94
Hospital La Paz **Dr. R. Moreno**	69
University Hospital of Wales **Dr. A. Choudhury**	65
Freeman Hospital **Prof. A. Zaman**	63
City Clinic Heart and Vascular Institute **Prof. I. Petrov**	61
Bellvitge University Hospital **Dr. A. Cequier**	53
Lister Hospital **Dr. N. Kukreja**	36
Castle Hill Hospital **Dr. A. Hoye**	33
Hospital alvaro Cunqueiro University Hospital of Vigo **Dr. A. Iniguez**	29
Invasive Cardiology Unit, Cardiology Center **Dr. I. Ungi**	27
Hospital de Sant Pau **Dr. A. Serra**	23
Central Hospital of the Internal and Administration Ministry **Prof. R. Gil**	13
Royal Victoria Hospital **Dr. S. Walsh**	12
St. George's University Multi-profile Hospital for Active Treatment **Dr. G. Tonev**	11
Ospedale San Raffaele **Prof. A. Colombo**	10
Semmelweis University Heart and Vascular Center **Prof. B. Merkely**	10
St Bartholomew's Hospital **Prof. A. Mathur**	10
Amphia Ziekenhuis **Dr. S. IJsselmuiden**	5

From 7 countries in Europe