UMC Utrecht

A Permanent Polymer Zotarolimus-eluting Stent versus a Polymer-Free Amphilimus-eluting Stent in all-comers; Results of the ReCre8 Trial

Pieter Stella, MD, PhD

On behalf of the ReCre8 Study investigators

R Rozemeijer, M Stein, M Voskuil, R van den Bor, P Frambach, B Pereira, S Koudstaal, G Leenders, L Timmers, S Rittersma, A Kraaijeveld, P Agostoni, C Roes, P Doevendans.

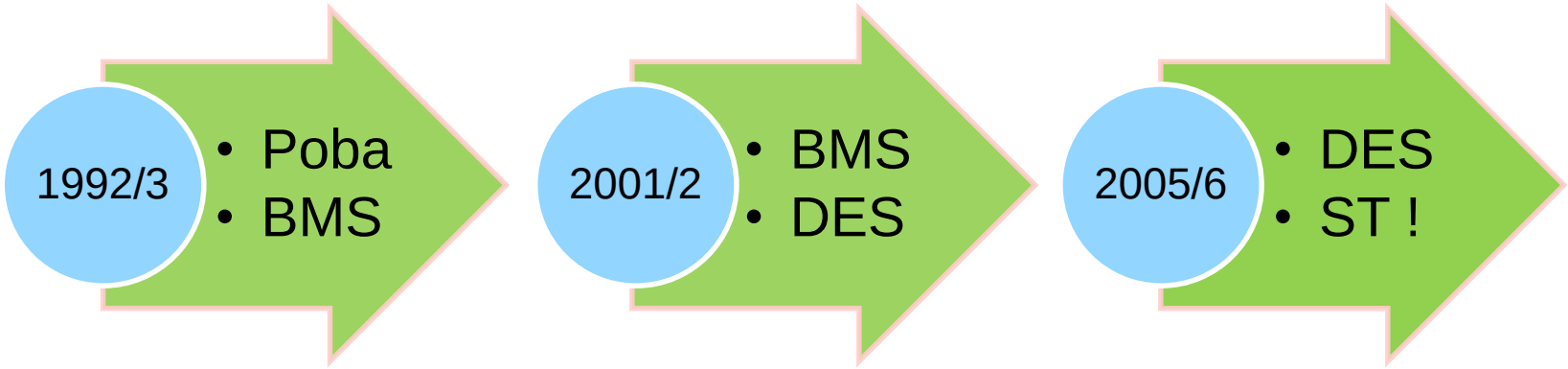
Disclosure Statement

Within the past 12 months, I, Pieter Stella have had a financial interest / arrangement or affiliation with the organization(s) listed below

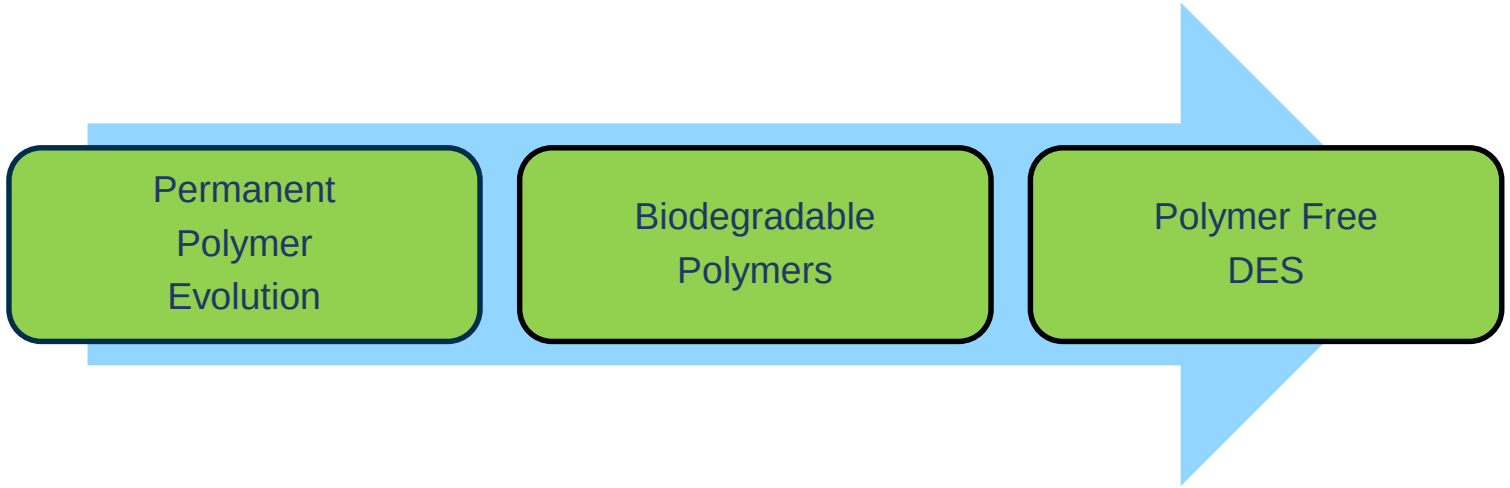
- **Member of speakers bureau Alvimedica**
- **Member advisory board Keystone Heart**
- **Consultant Dekra CE**

UMC Utrecht

Background



PP: Delayed arterial healing / Chronic Inflammation / Aneurysm Formation



UMC Utrecht

Why this study?

- **The clinical safety and efficacy of polymer-free amphilimus-eluting stents (PF-AES) have not yet been compared to latest-generation permanent polymer drug-eluting stents in a large all comers trial.**
  - **Secondary interests (non powered):**
    - **Is a short DAPT duration (1-month) with these devices in troponin-negative patients safe ?**
    - **Does PF-AES shows its promise of positive outcomes in diabetic patients ?**

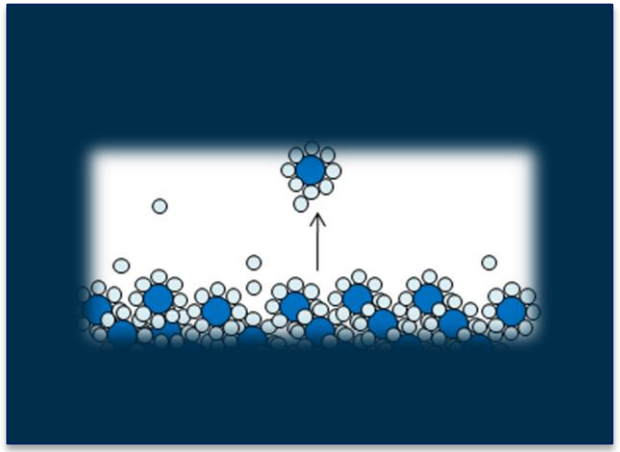
Introduction – PF AES

Thin-strut (80 µm) Co-Cr alloy

Polymer-free platform

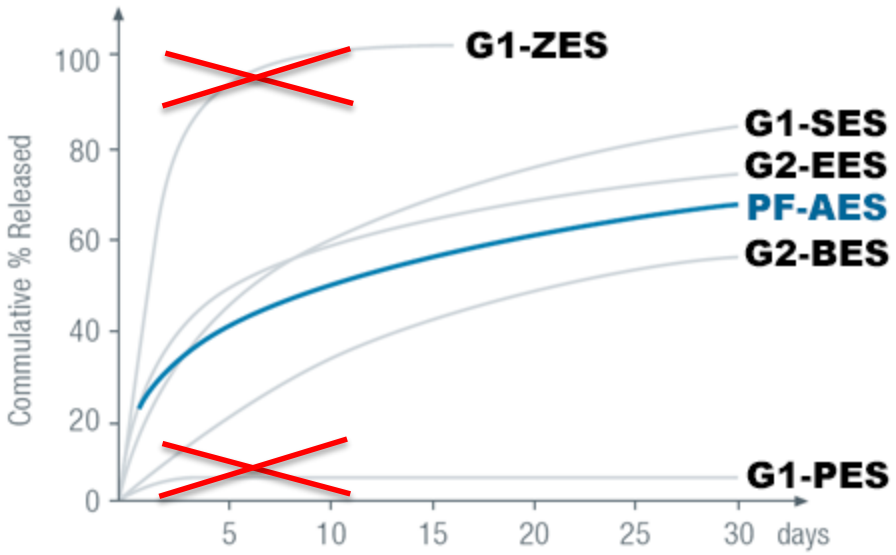
Abluminal Reservoir Technology

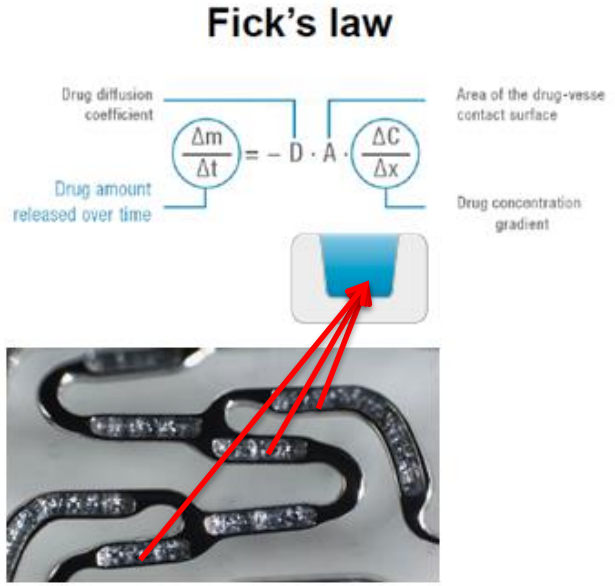
Amphilimus™ Formulation: Sirolimus + organic acid (fatty acid)



BIS: Bio Inducer Surface

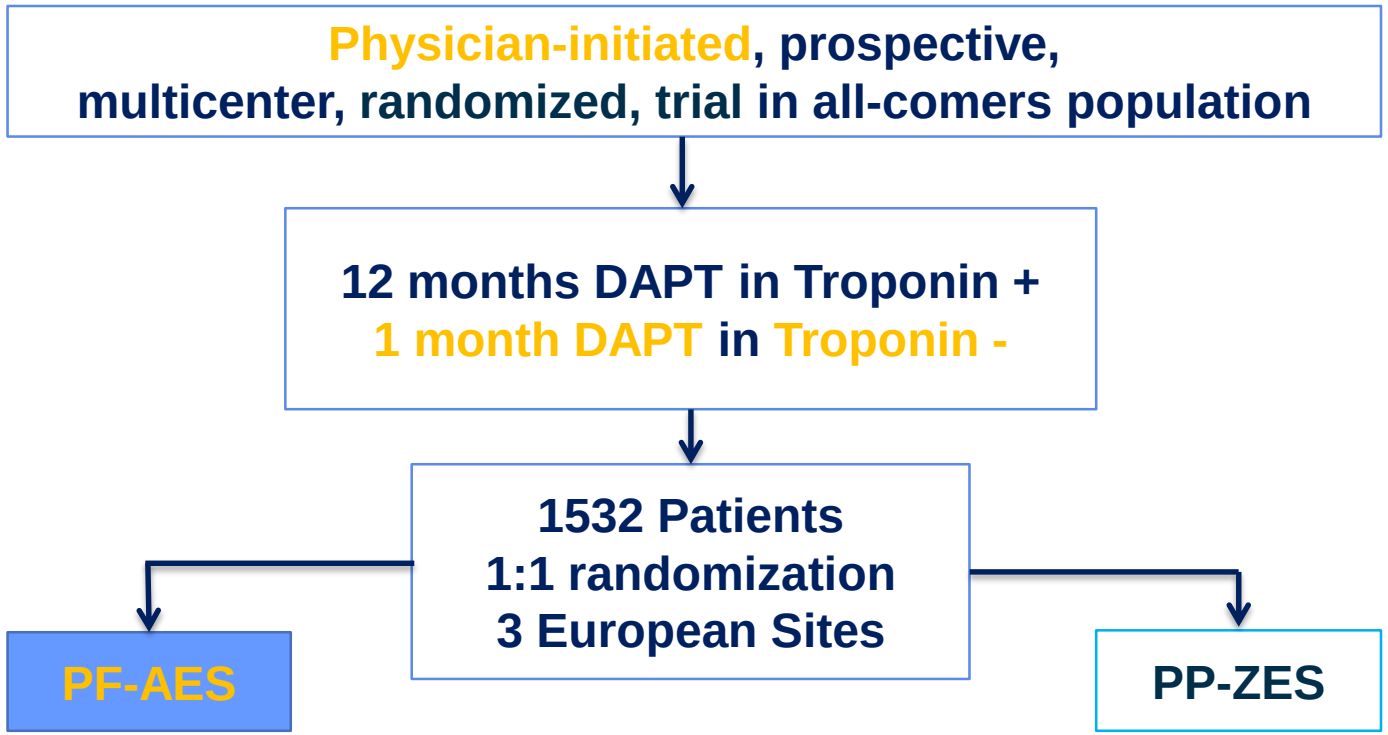
Introduction – PF AES





- ***Peak tissue concentration during first days***
- ***50% drug-elution in 18 days***
- ***65-70% drug-elution in 30 days***
- ***100% drug-elution in 90 days***

How was the study executed?



Primary endpoint TLF at 12 months

Secondary endpoint NACE at 12 months

Clinical FU *1m* *1y* *3y*

Rozemeijer et al. *Catheter Cardiovasc Interv.* 2018;91:410–416.

How did we study?

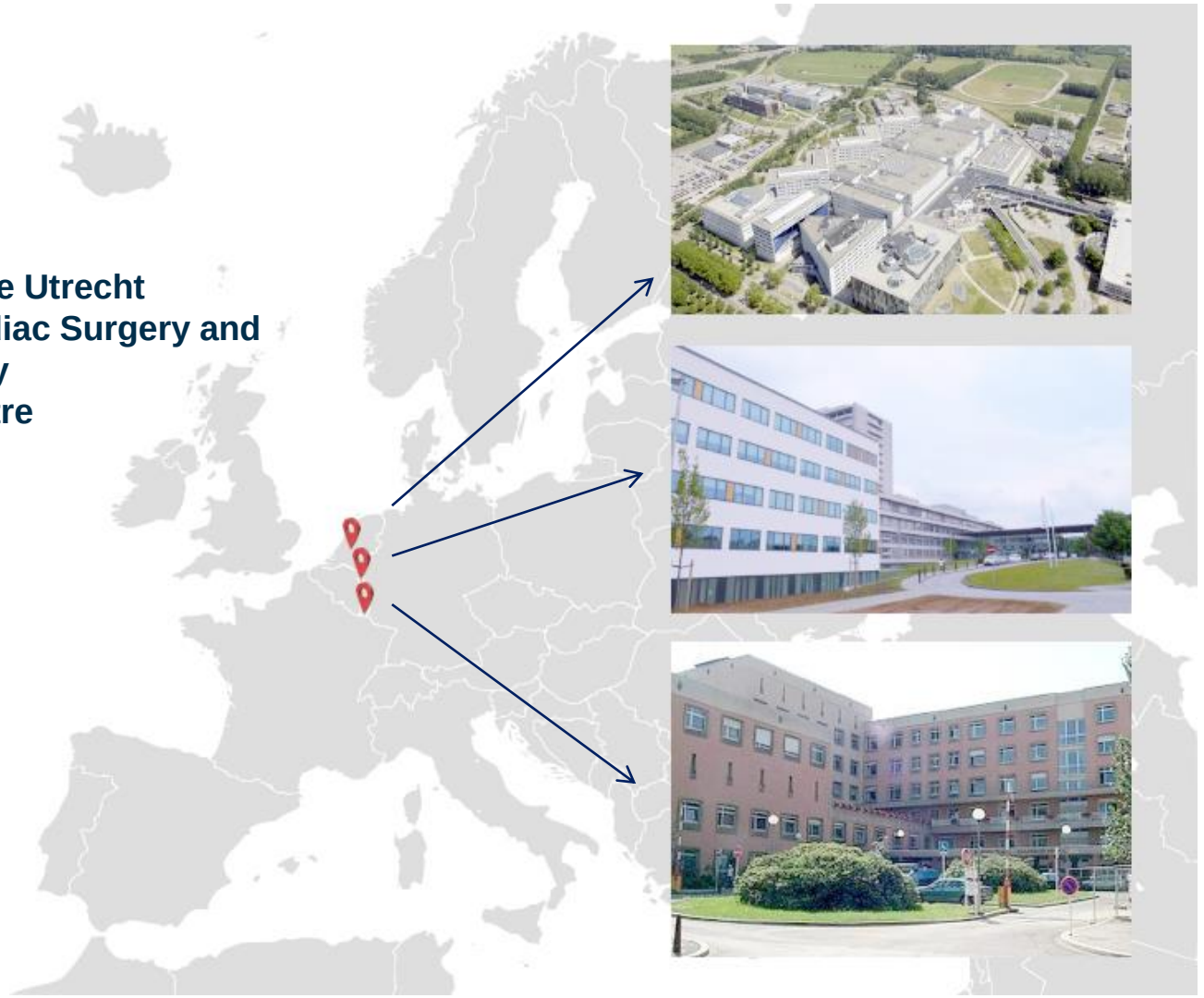
Steering committee:
- Mera Stein
- Pierfrancesco Agostoni
- Pieter Stella

Participating centres:
- University Medical Centre Utrecht
- National Institute of Cardiac Surgery and Interventional Cardiology
- Zuyderland Medical Centre

CEC:
- dr. Bart de Smet
- dr. Willem Agema
- dr. Marc Buijsrogge

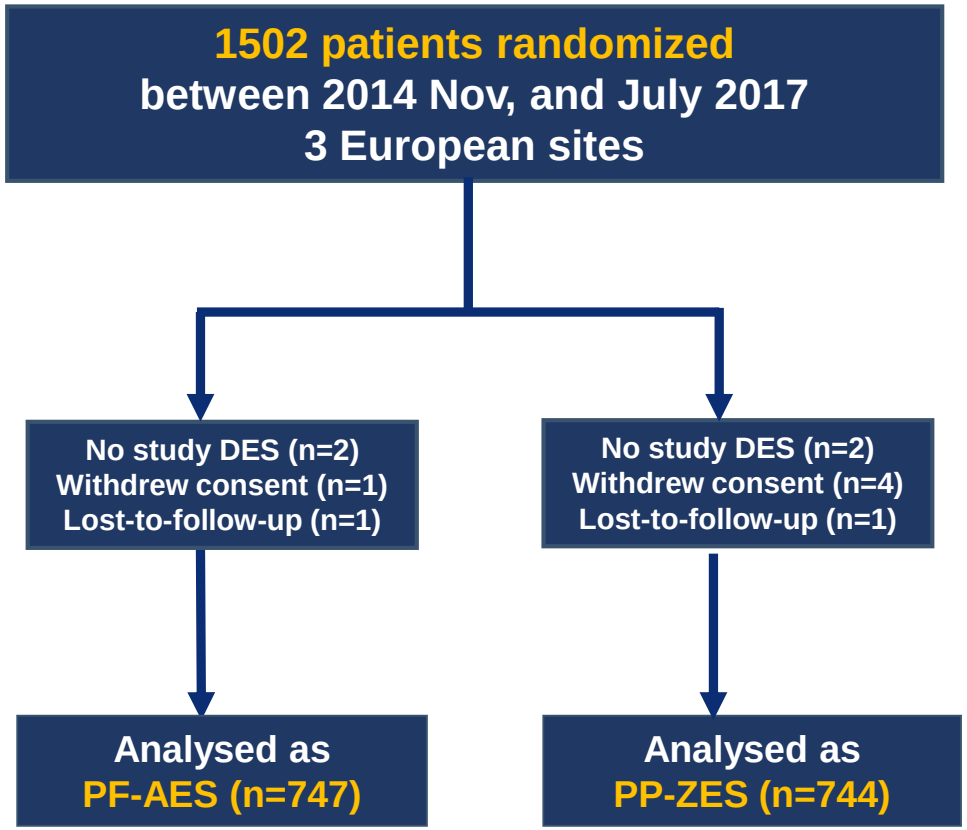
Data monitoring:
- Julius Clinical Research

Statistical Analysis:
- Dep. of Biostatistics



UMC Utrecht

Flow Chart



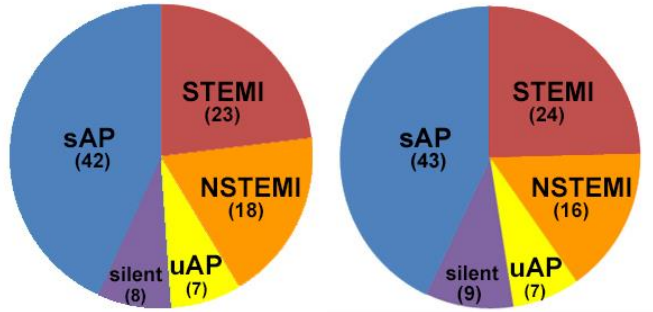
Baseline Characteristics -1

Patient demographics

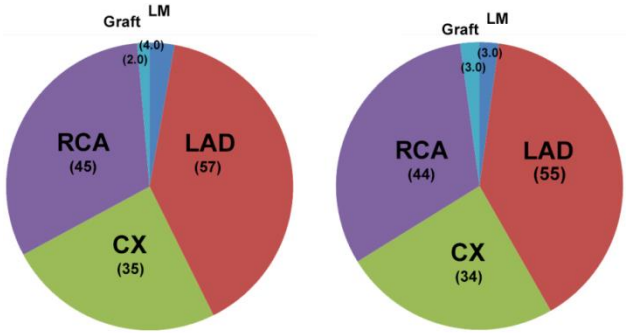
	PF-AES (n=747)	PP-ZES (n=744)
Age (years)	64·7 ± 11·3	65·1 ± 10·6
Hypertension	412 (55·2)	411 (55·2)
Hypercholesterolemia	325 (43·5)	340 (45·8)
Diabetes Mellitus	155 (20·8)	149 (20·0)
Current smoker	193 (25·9)	191 (25·7)
Family history of CAD	291 (39·0)	275 (37·0)
eGFR<60 ml/min	84 (17·3)	80 (16·3)
Previous MI	139 (18·6)	158 (21·2)
Previous PCI	138 (18·5)	166 (22·3)
Previous CABG	67 (9·0)	71 (9·5)

PF-AES **PP-ZES**

Clinical presentation



Target vessels



Baseline characteristics were well-balanced

UMC Utrecht

Baseline Characteristics -2

	PF-AES (n=747)	PP-ZES (n=744)
De-novo coronary lesions	710 (95·0)	704 (94·6)
At least one complex lesion	436 (58·4)	437 (58·7)
At least one bifurcation lesion	176 (23·6)	147 (19·8)
At least one chronic total occlusion	51 (6·8)	47 (6·3)
At least one ostial lesion	23 (3·1)	20 (2·7)
At least one restenotic lesion	24 (3·2)	24 (3·2)
At least one moderate or severely calcified lesion	196 (26·3)	205 (27·7)
At least one venous graft lesion	13 (1·7)	16 (2·2)
At least one small vessel (RVD < 2·75 mm)	200 (26·9)	199 (26·9)
At least one long lesion (length >20 mm)	329 (44·3)	415 (56·1)

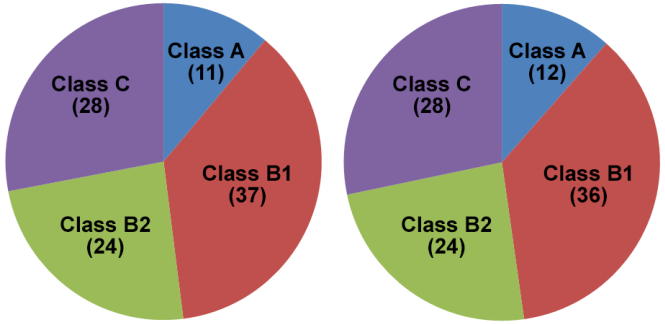
True *"all-comers"* population

Procedural Data

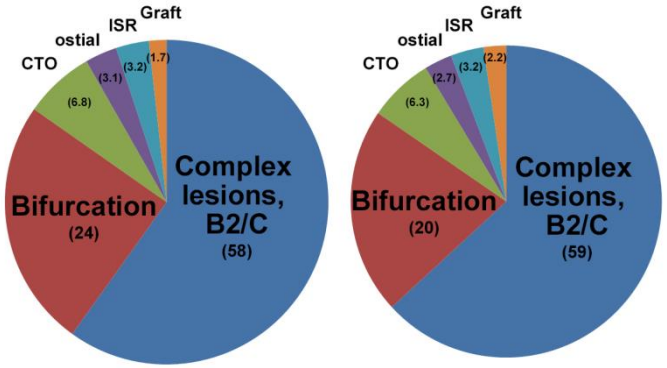
	PF-AES (n=747)	PP-ZES (n=744)
No of stents per lesion	1·29±0·59	1·25±0·57
No of stents per patient	1·89 ± 1·25	1·73 ± 1·09
Total stent length (mm)	47·7 ± 21·2	47·7 ± 21·4
Stent diameter (mm)	3·03 ± 0·45	3·01 ± 0·45
Multi overlapping stents	219 (20·02)	177 (17·4)
Pre-dilatation	973 (69·2)	904 (70·5)
Direct stenting	427 (30·3)	376 (29·3)
Post-dilatation	942 (68·0)	757 (59·6)
ACC/AHA class B2	261 (24·0)	244 (24·0)
ACC/AHA class C	304 (28·0)	288 (28·3)
Procedural success	1008 (99·3)	1068 (98·5)

PF-AES **PP-ZES**

Lesion Complexity



Individual Complex lesions



Procedural details were well-balanced, except post-dilatation

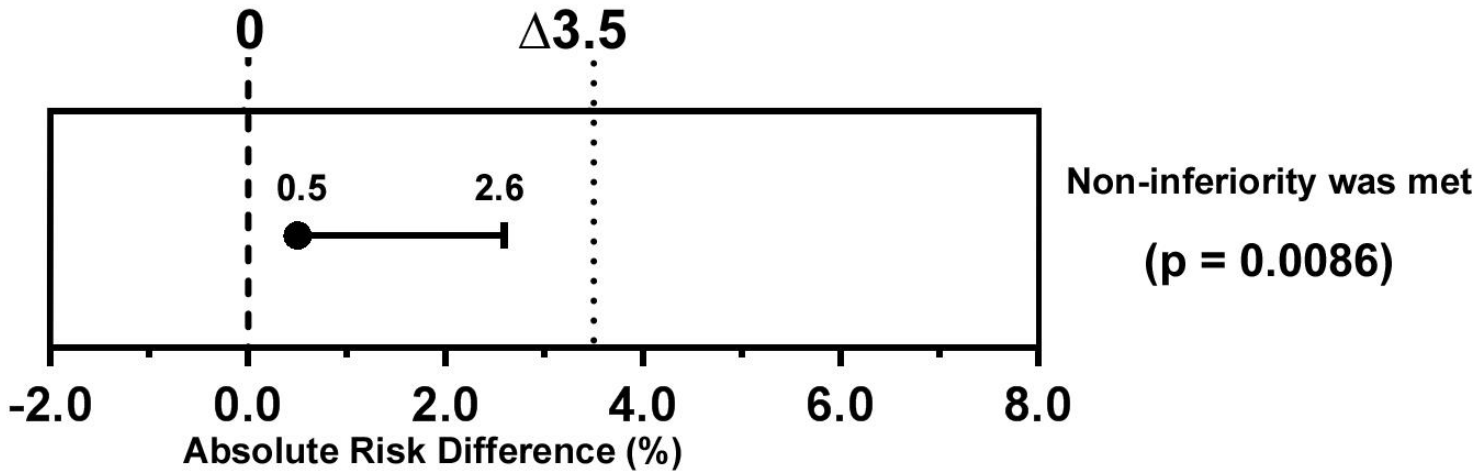
ClinicalTrials.gov NCT02328898

UMC Utrecht

What are the results?

Target Lesion Failure at 12-months

	PF-AES	PP-ZES	Risk Diff	One sided 95% CI	NI-margin	$p_{non\text{-}inferiority}$
TLF at 12 months	6.2	5.6	0.5%	2.6%	3.5%	0.0086

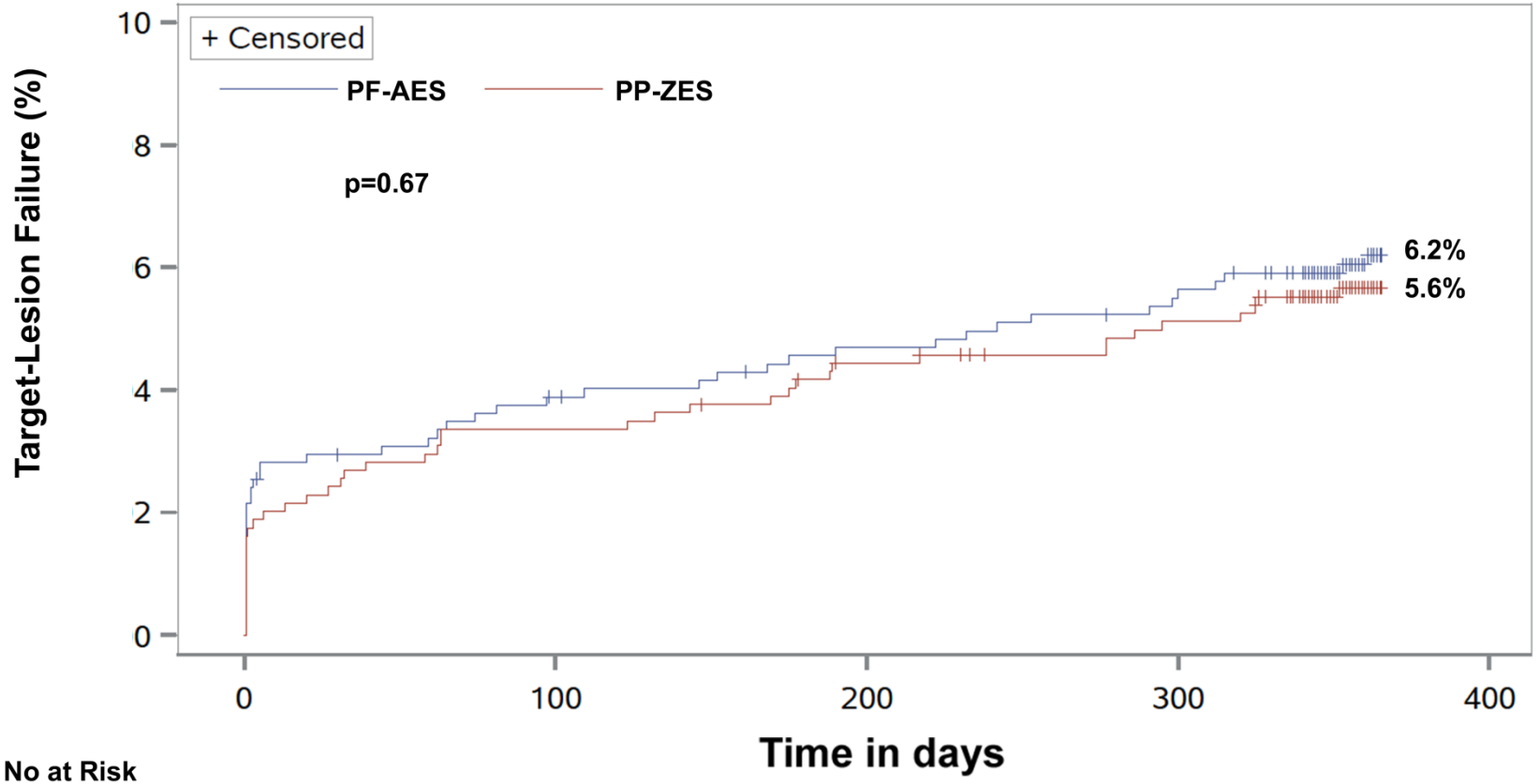


Clinical non-inferiority of PF-AES was met!

UMC Utrecht

What are the results?

Target Lesion Failure at 12-months

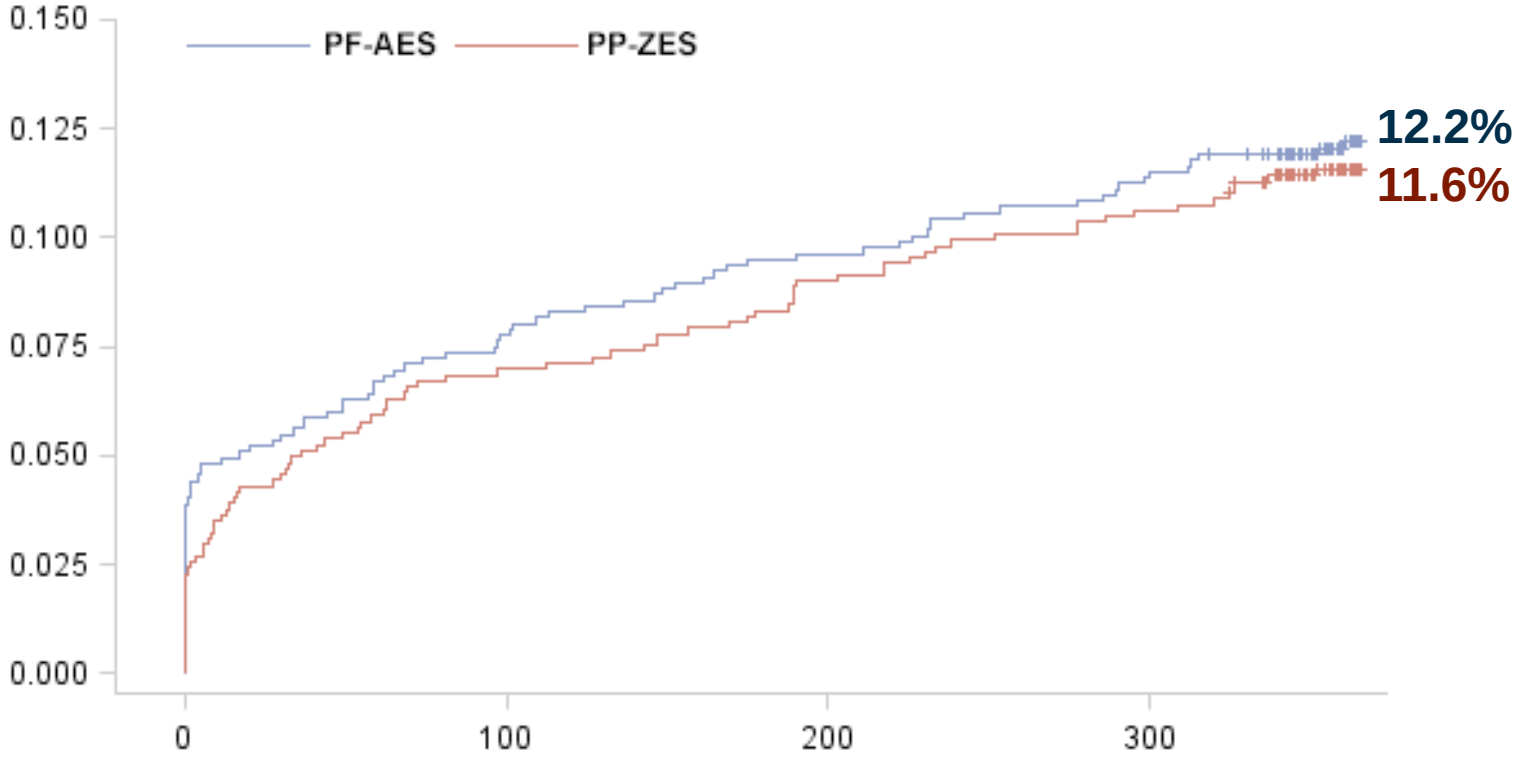


No at Risk					
PF-AES	747	715	707	700	0
PP-ZES	744	719	708	699	0

UMC Utrecht

What are the results?

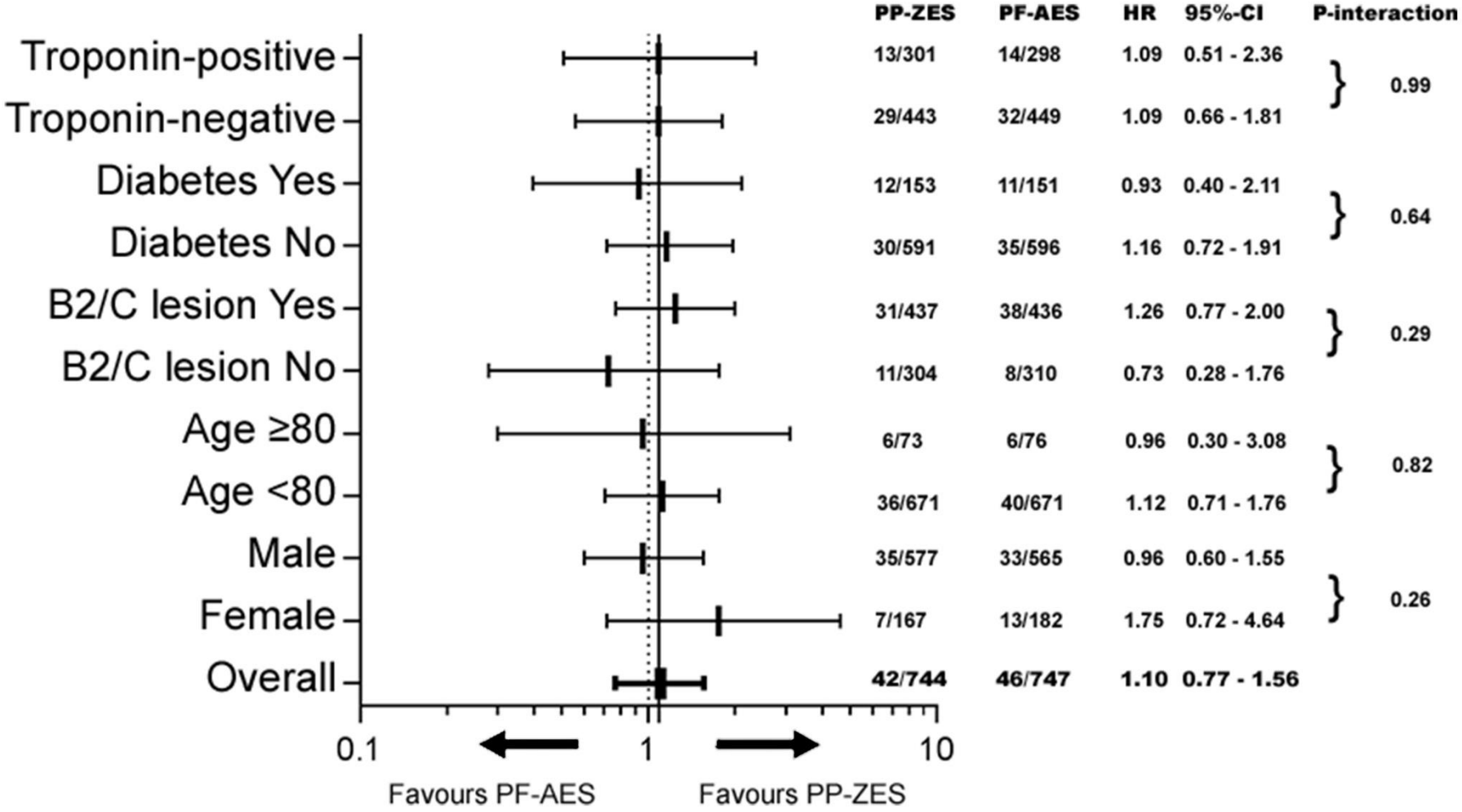
Net Adverse Clinical Events at 12-months



No At Risk					
PF-AES	747	689	675	662	0
PP-ZES	744	692	677	665	0

ClinicalTrials.gov NCT02328898

What are the results?



Consistency* across all subgroups, with *no significant statistical interactions

UMC Utrecht

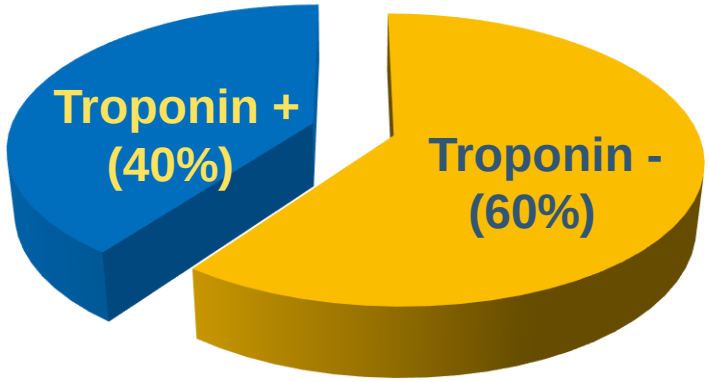
Sub-study 1

To assess clinical safety of 1-month DAPT in troponin-negative patients

UMC Utrecht

Sub-study: 1-month DAPT

12-months DAPT *1-month DAPT*



n=892!

Definite Stent Thrombosis according to ARC

DES type	Sex, (age)	Timing (days)	DM	LVEF (%)	Stratification	Lesion complexity†	Special Lesion	Post-dilatation	No of DES
PP-ZES	M (71)	37	No	45-54	1-month, CCS IV	C	De novo	Yes	6
PP-ZES	M (65)	84	No	NA	1-month, CCS II*	C	Ostial, Bif	Yes	1
PP-ZES	M (61)	200	No	>55	1-month, CCS II*	C	Restenotic	No	1
PP-ZES	F (68)	295	No	30-44	1-month, CCS III*	C	De novo	Yes	1
PF-AES	M (91)	1	No	NA	1-month, CCS II*	B1	De novo	Yes	1
PF-AES	M (78)	2	No	55	1-month, CCS II*	C	CTO	Yes	1
PF-AES	M (73)	45	No	45-54	1-month, CCS II*	C	CTO	No	2
PF-AES	M (71)	320	Yes	30-44	1-month, CCS II*	B1	De novo	Yes	1

Overall ST 8/892 (0·9%)

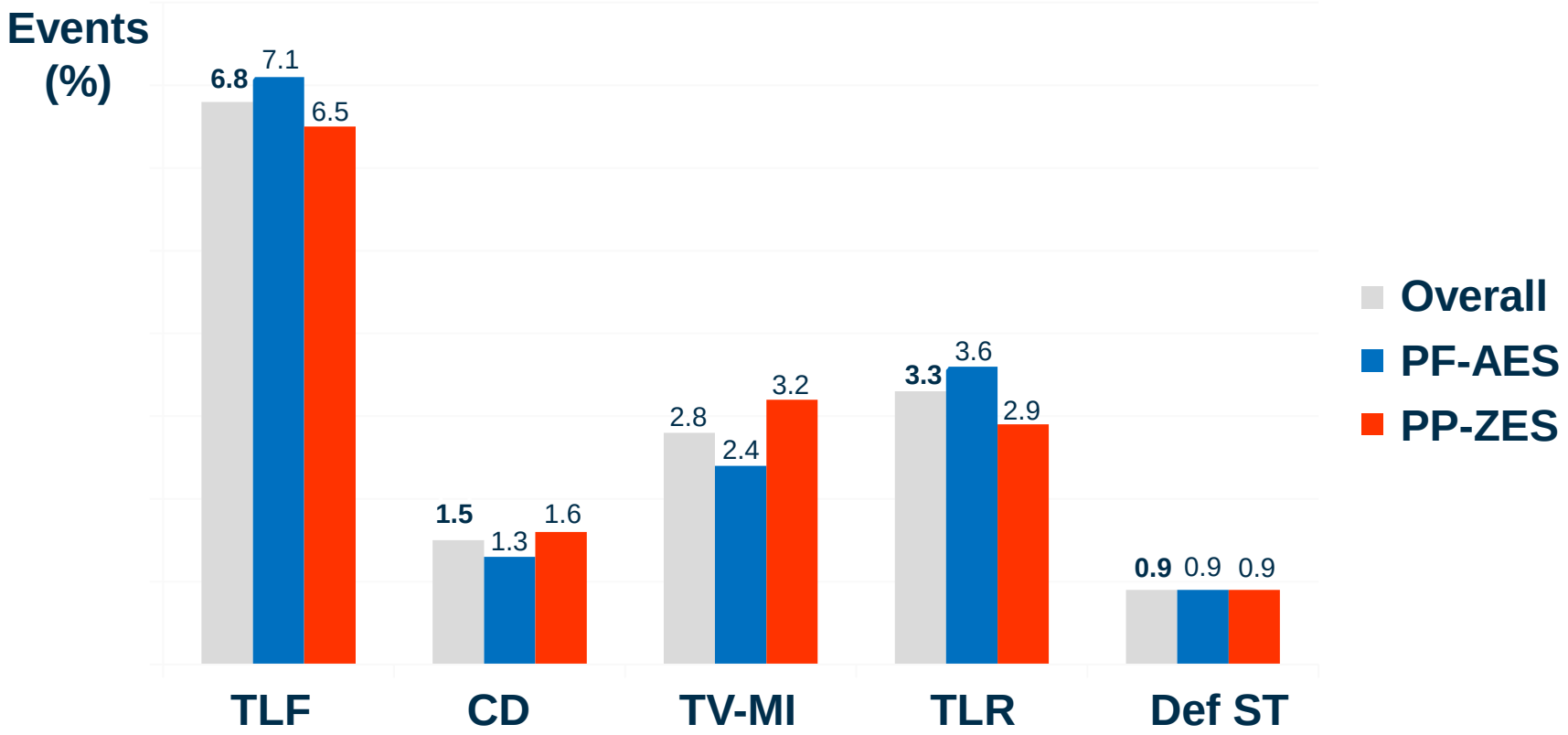
6/8 (0.7%) after DAPT

4/8 in complex lesions

ClinicalTrials.gov NCT02328898

Sub-study: 1-month DAPT

Individual outcomes at 12-months



No statistical significant differences between stents at the p<0.05 level

UMC Utrecht

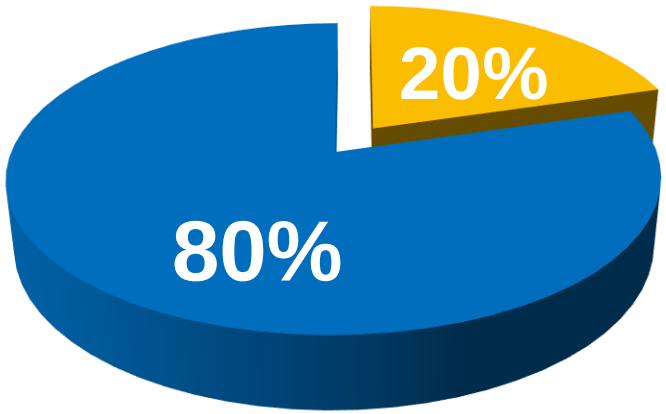
Sub-study 2

To assess clinical outcomes of PF-AES in patients with diabetes

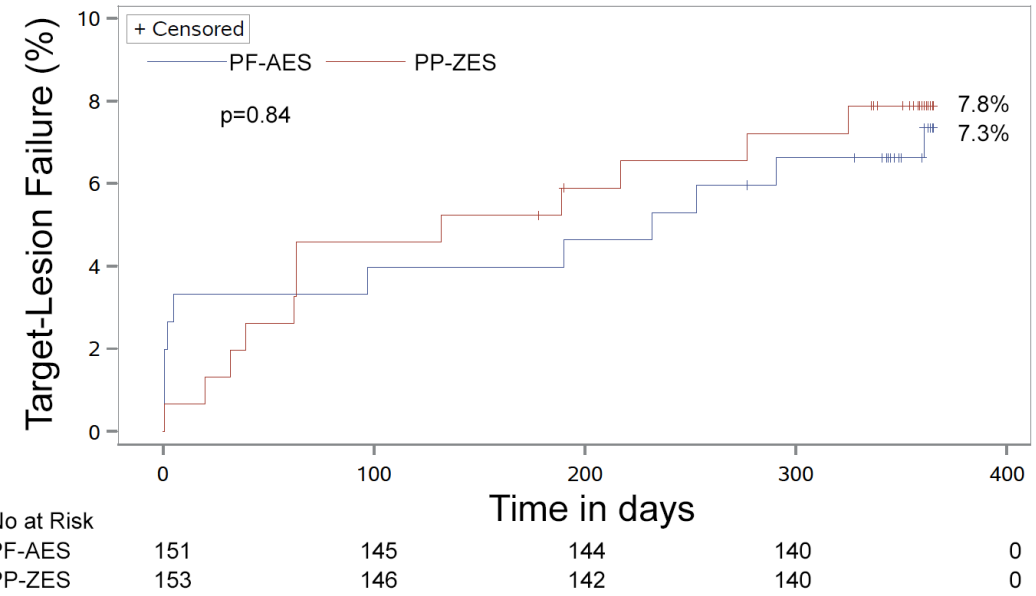
ClinicalTrials.gov NCT02328898

Sub-study: PF-AES in DM

Diabetes



TLF at 12-months



No at Risk					
PF-AES	151	145	144	140	0
PP-ZES	153	146	142	140	0

***No differences** the primary endpoint of PF-AES as compared to PP-ZES in DM*

UMC Utrecht

Conclusions

- ReCre8 was the first RCT comparing PF-AES versus latest gen PP ZES in an all comers PCI population.
- Main finding was that clinical non-inferiority of PF-AES as compared to PP-ZES in terms of TLF at 12 months was met.
- Findings regarding the secondary endpoint and pre-specified subgroups were generally consistent with the primary endpoint.
- Short DAPT following these latest-generation drug-eluting stents in troponin-negative patients needs further evaluation (*not powered!*).
- Future trials need to investigate efficacy of PF-AES in patients with diabetes

Acknowledgements

Co-investigators

- R. Rozemeijer, MD, MSc, PharmD
- M. Stein, MD, PhD
- M. Voskuil, MD, PhD
- R. van den Bor, MSc, PhD
- P. Frambach, MD
- B. Pereira, MD
- S. Koudstaal, MD, PhD
- G. Leenders, MD, PhD
- L. Timmers, MD, PhD
- S. Rittersma, MD, PhD
- A. Kraaijeveld, MD, PhD
- P. Agostoni MD, PhD
- K. Roes, MSc, PhD
- P. Doevendans, MD, PhD

Study enrolment

- Nurses, technicians, and personnel
- Fellows, participating centres
- Physicians, participating centres

Clinical Event Committee

- B. de Smet, Meander Medical Centre
- W. Agema Diakonessen Hospital
- M. Buijsrogge, UMCU

Data completion

- Y. Breuer , R&D UMCU
- A. Links, R&D UMCU
- B. Camus, R&D INCCI

UMC Utrecht

Thank you for your attention,
have a great TCT 2018 Conference!

Back-up slides

RE: CIRCULATIONAHA/2018/037707R1
Randomised All-comers Evaluation of a Permanent Polymer Zotarolimus-eluting Stent Versus a Polymer-Free Amphilimus-eluting Stent: (ReCre8) a Multicentre, Non-inferiority Trial.