# Current Status of DES and DES Failure

- The Target study -

Articles

Targeted therapy with a localised abluminal groove, **→**@**†**® low-dose sirolimus-eluting, biodegradable polymer coronary stent (TARGET All Comers): a multicentre, open-label,

randomised non-inferiority trial

Alexandra Lansky, William Wijns, Bo Xu, Henning Kelbæk, Niels van Royen, Ming Zheng, Marie-angèle Morel, Paul Knaapen, Ton Slagboom, Thomas W Johnson, Georgios Vlachojannis, Karin E Arkenbout, Lene Holmvang, Luc Janssens, Andrzej Ochala, Salvatore Brugaletta. Christoph K Naber, Richard Anderson, Harald Rittger, Sergio Berti, Emanuele Barbato, Gabor G Toth, Luc Maillard, Christian Valina, Pawel Buszman, Holger Thiele, Volker Schächinger, Andreas Baumbach, for the TARGET All Comers Investigators

Background The FIREHAWK is a drug-eluting stent with a fully biodegradable sirolimus-containing polymer coating Published Online localised to recessed abluminal grooves on the stent surface. We investigated clinical outcomes with this targeted, September 3, 2018 low-dose, biodegradable polymer, sirolimus-eluting stent compared with XIENCE durable polymer, everolimuseluting stents in an all-comers population.

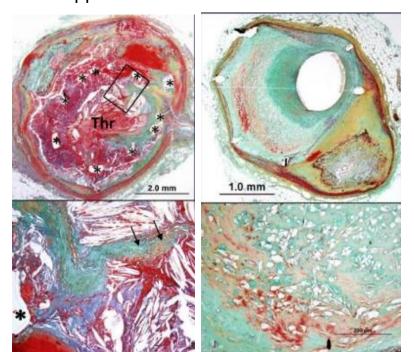
Methods The TARGET All Comers study was a prospective, multicentre, open-label randomised non-inferiority trial done 50140-6736(18)30768-9 at 21 centres in ten European countries. Patients with symptomatic or asymptomatic coronary artery disease and objective Yale University School of evidence of myocardial ischaemia who qualified for percutaneous coronary intervention were randomised 1:1 to undergo Medicine, New Haver, CT, USA implantation of a FIREHAWK or XIENCE. Randomisation was web-based, with random block allocation and stratification
Prof A Baumbach MD); Barts by centre and ST elevation myocardial infarction. Outcome assessors were masked to treatment allocation, but treating physicians and patients were not. The primary endpoint was target lesion failure at 12 months, a composite of cardiac death, target vessel myocardial infarction, or ischaemia-driven target lesion revascularisation. The control event rate for London London UK XIENCE was assumed to be 7%, the non-inferiority margin was 3.5%, and the primary analysis was in the intention-toProf A Baumbach; The Lambe treat population, censoring patients who did not have either an event before 365 days or contact beyond 365 days. Late lumen loss was the primary endpoint of an angiographic substudy designed to investigate the non-inferiority of the Medicine and Curam, National FIREHAWK compared with the XIENCE stent. This trial is registered with ClinicalTrials.gov, number NCT02520180.

SNUH Jeehoon Kang, MD



#### 1<sup>st</sup> generation DES

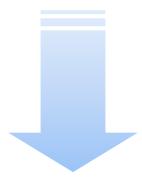
- ✓ Thick strut
- ✓ Uneven/thick polymer distribution
- ✓ High drug dose
- ✓ Uncovered struts
- ✓ Hypersensitivity
- ✓ Malapposition
- ✓ Stent fracture
- ✓ Stent thrombosis
- ✓ Neoatheroscleroisis





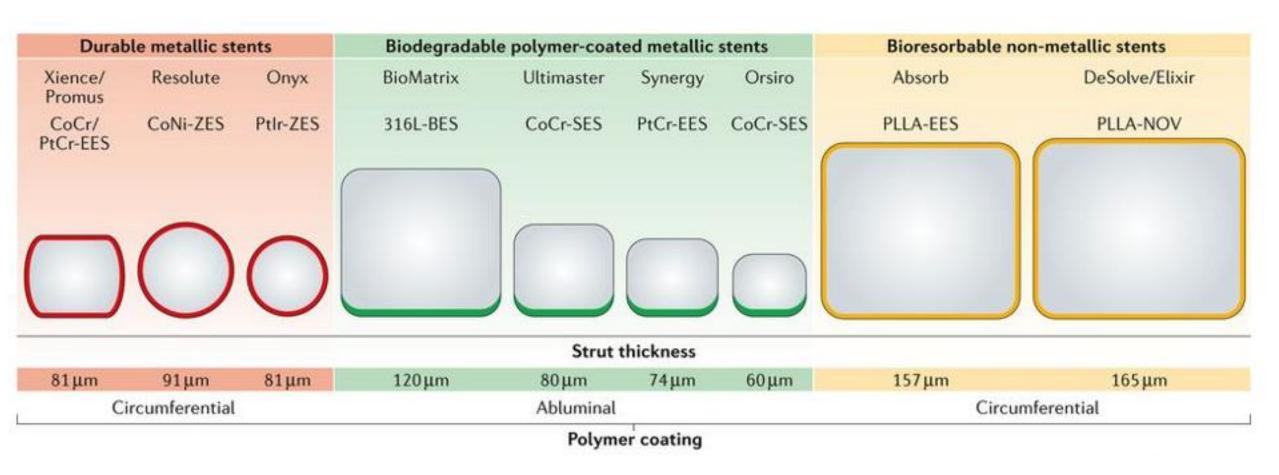
- ✓ Thinner strut
- ✓ Biocompatible / even polymer distribution
- ✓ Reduced drug dose
  - ✓ Improved stent performance
  - ✓ Decreased clinical outcomes



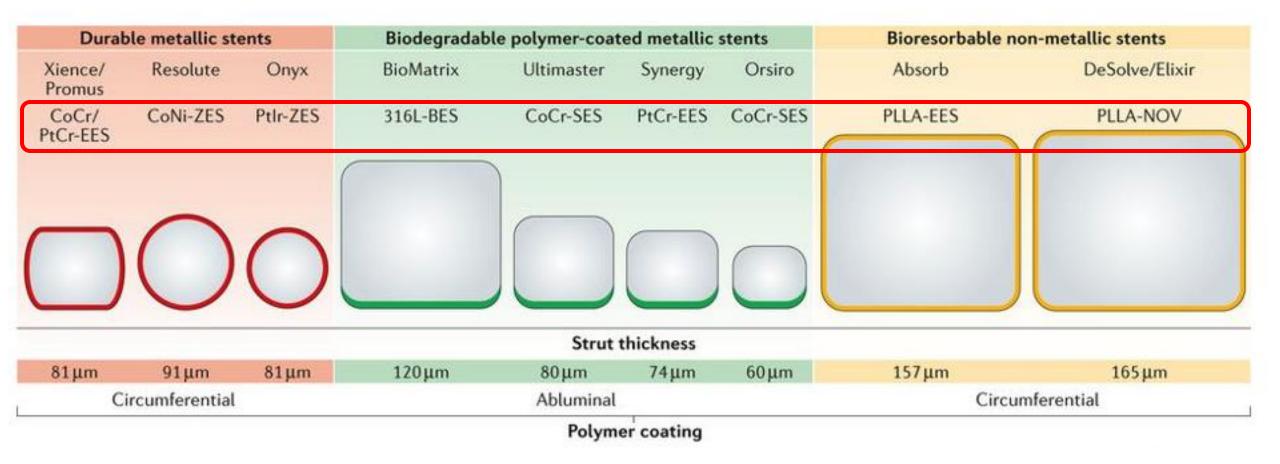


Anything more?

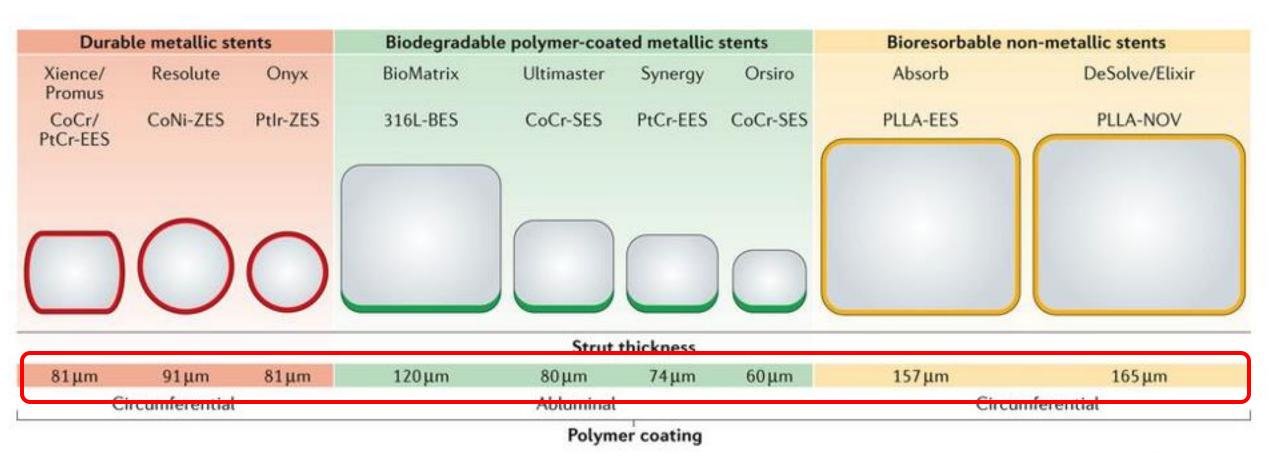
Various designs of current stents



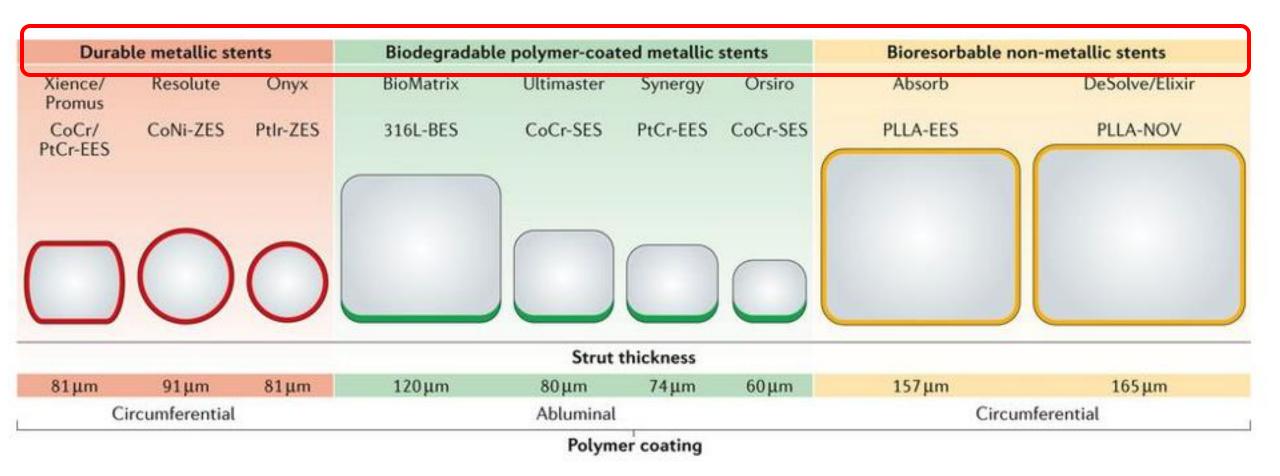
- Various designs of current stents
  - Backbone / Drug



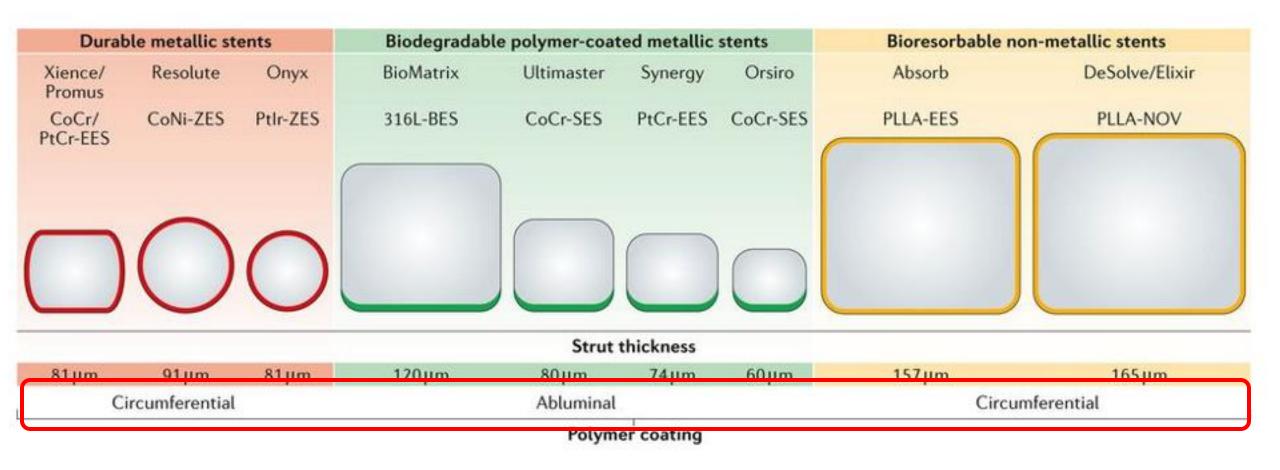
- Various designs of current stents
  - Strut thickness



- Various designs of current stents
  - Polymer

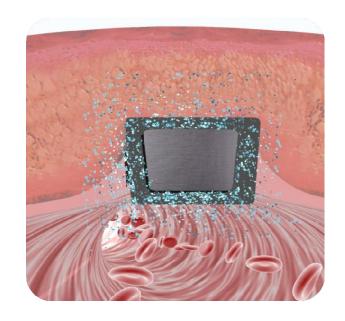


- Various designs of current stents
  - Drug coating

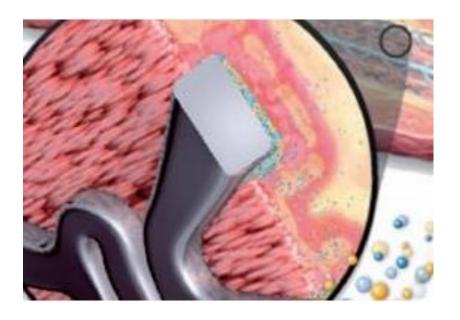


### **Fundamental limitations of current stents**

Drug concentration should be maximal at the abluminal side



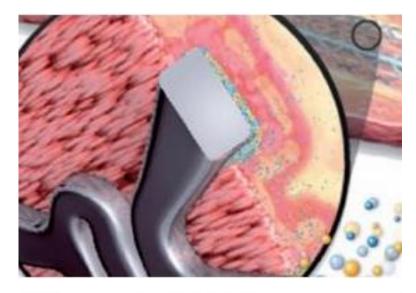
- ✓ Multi-directional Eluting
- ✓ The drug used on DES currently inhibits both SMC and EC
- ✓ The drug not only releases to vessel, but also to the blood.

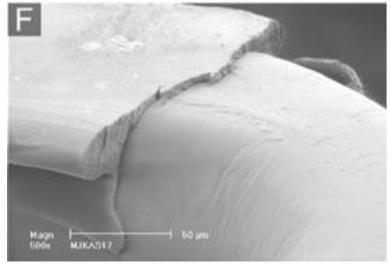


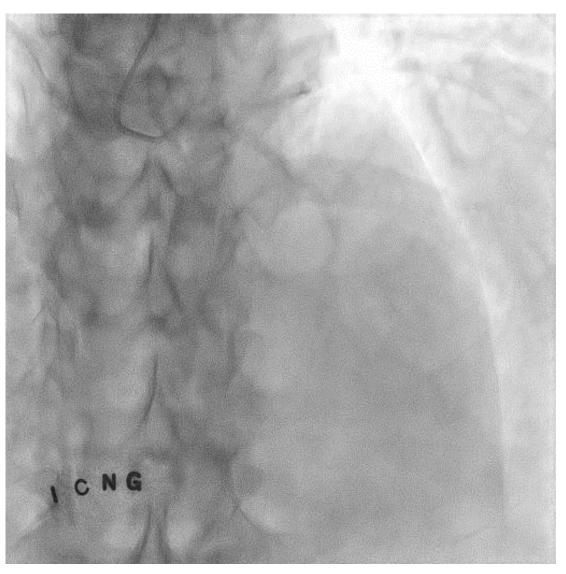
- ✓ Abluminal Eluting
- ✓ No direct antiproliferative drug on the EC side

# **Fundamental limitations of current stents**

• ...which is the most vulnerable, open site in a stent

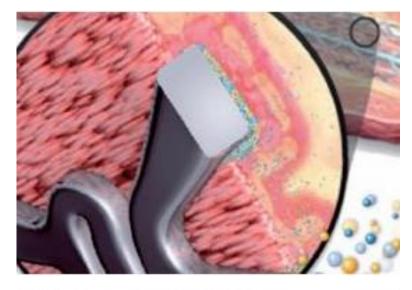


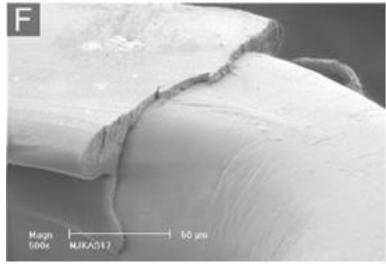


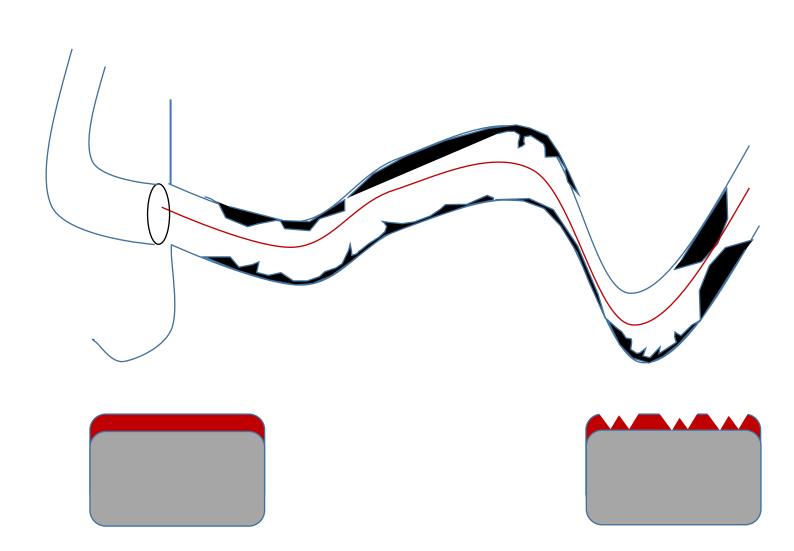


# **Fundamental limitations of current stents**

• ...which is the most vulnerable, open site in a stent

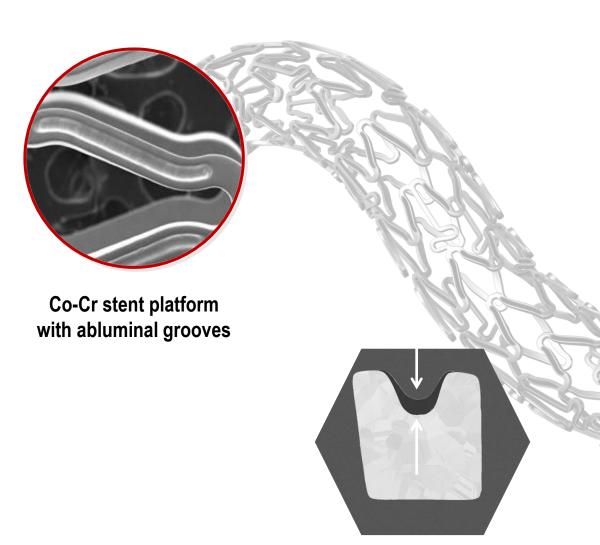






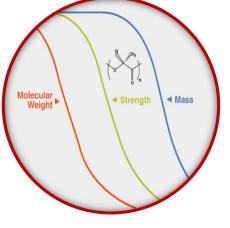
# The Firehawk<sup>™</sup> DES



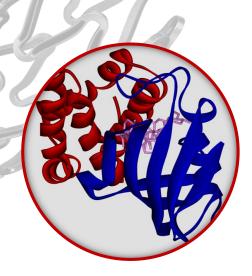


Depth of the groove is

1/3 of the strut

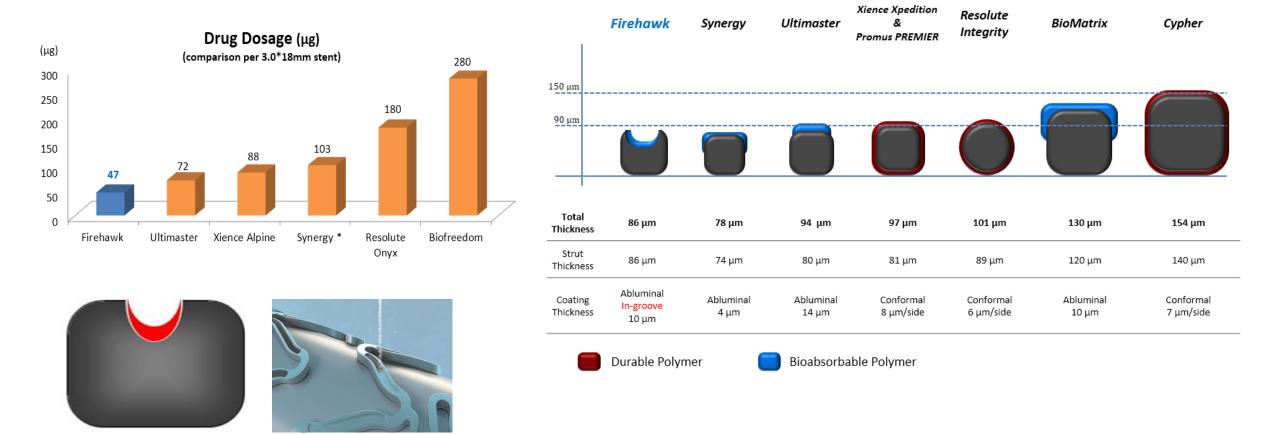


DL PLA absorbed after 6-9 months



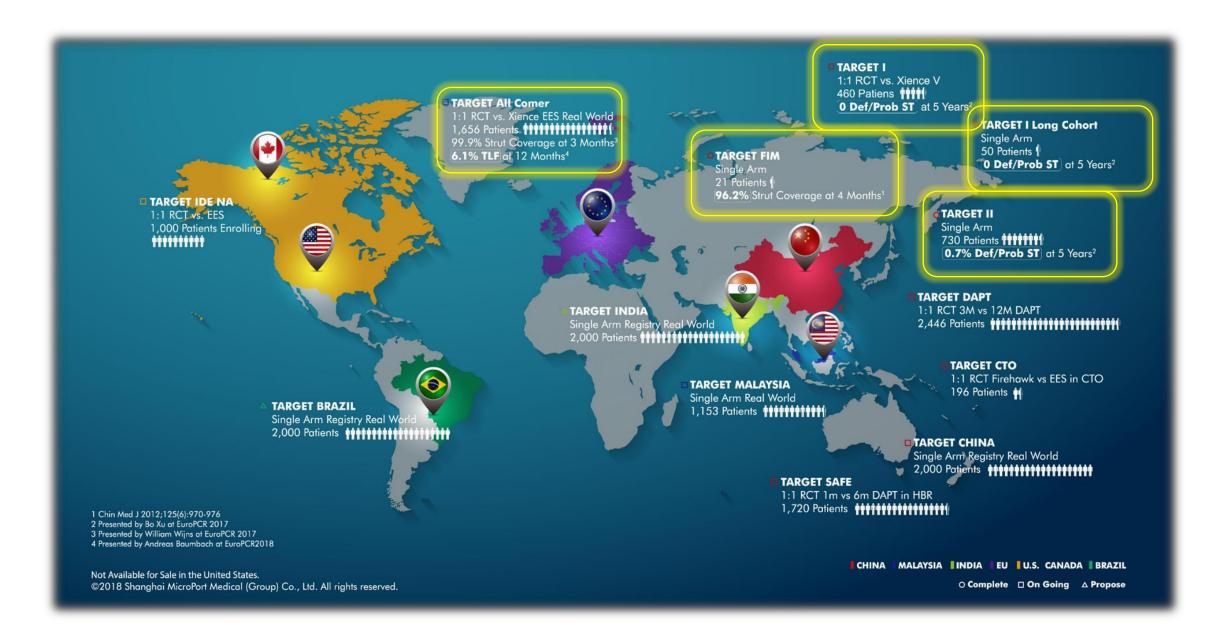
**Sirolimus** 

## The Firehawk<sup>™</sup> DES



- ✓ Lower drug dosage enables fast healing and increase safety of the device potentially
- ✓ Shorter DAPT duration may be more feasible.





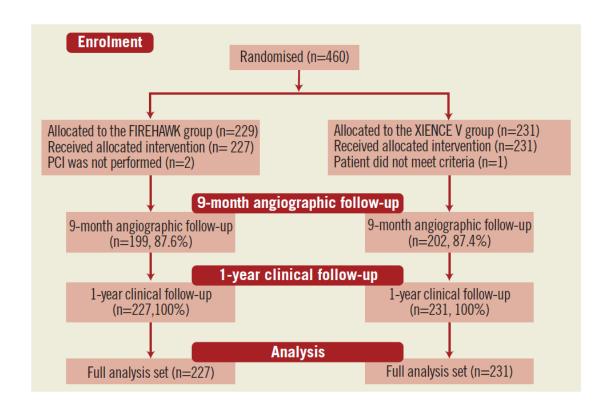
## Target I study

 Prospective, multicenter RCT with single de novo coronary artery lesions in a 1:1 ratio to receive either the FIREHAWK stent or the XIENCE V in China.

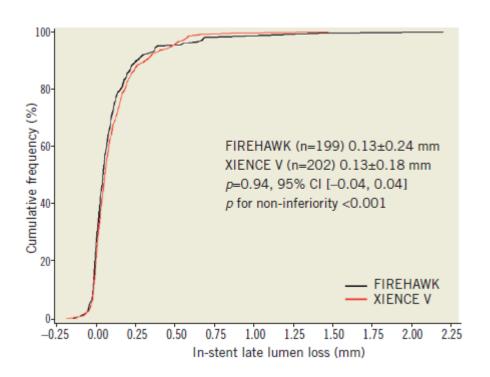
A randomised comparison of a novel abluminal groove-filled biodegradable polymer sirolimus-eluting stent with a durable polymer everolimus-eluting stent: clinical and angiographic follow-up of the TARGET I trial

Run-Lin Gao<sup>1\*</sup>, MD; Bo Xu<sup>1</sup>, MBBS; Alexandra J. Lansky<sup>2</sup>, MD; Yue-Jin Yang<sup>1</sup>, MD; Chang-Sheng Ma<sup>3</sup>, MD; Ya-Ling Han<sup>4</sup>, MD; Shao-Liang Chen<sup>5</sup>, MD; Hui Li<sup>6</sup>, MD; Rui-Yan Zhang<sup>7</sup>, MD; Guo-Sheng Fu<sup>8</sup>, MD; Zu-Yi Yuan<sup>9</sup>, MD; Hong Jiang<sup>10</sup>, MD; Yong Huo<sup>11</sup>, MD; Wei Li<sup>1</sup>, PhD; Yao-Jun Zhang<sup>5</sup>, MD; Martin B. Leon<sup>12</sup>, MD; on behalf of the TARGET I Investigators

1. Fu Wai Hospital, National Center for Cardiovascular Diseases of China, Beijing, China; 2. Yale University School of Medicine, New Haven, CT, USA; 3. Affiliated An zhen Hospital of Capital Medical University, Beijing, China; 4. Shenyang Northern Hospital, Shenyang, China; 5. Nanjing First Hospital, Nanjing Medical University, Nanjing, China; 6. Daqing Oil Field General Hospital, Daqing, China; 7. Affiliated Ruijin Hospital of Shanghai Jiao Tong University School of Medicine, Shanghai, China; 8. Affiliated SRRS Hospital of Zhejiang University School of Medicine, Hangzhou, China; 9. 1st Affiliated Hospital of Xi'an Jiaotong University School of Medicine, Xi'an, China; 10. Wuhan University People's Hospital, Wuhan, China; 11. Peking University First Hospital, Beijing, China; 12. Columbia University Medical Center, New York, NY, USA



## Target I study



1 month		6 months		12 months				
FIREHAWK (n=227)	XIENCE V (n=231)	<i>p</i> -value	FIREHAWK (n=227)	XIENCE V (n=231)	<i>p</i> -value	FIREHAWK (n=227)	XIENCE V (n=231)	<i>p</i> -value
3 (1.3%)	4 (1.7%)	1.00	3 (1.3%)	4 (1.7%)	1.00	5 (2.2%)	5 (2.2%)	1.00
3 (1.3%)	4 (1.7%)	1.00	3 (1.3%)	5 (2.2%)	0.72	8 (3.5%)	17 (7.4%)	0.07
0 (0.0%)	0 (0.0%)	NA	0 (0.0%)	1 (0.4%)	1.00	1 (0.4%)	2 (0.9%)	1.00
0 (0.0%)	0 (0.0%)	NA	0 (0.0%)	0 (0.0%)	NA	1 (0.4%)	0 (0.0%)	NA
3 (1.3%)	4 (1.7%)	1.00	3 (1.3%)	4 (1.7%)	1.00	3 (1.3%)	5 (2.2%)	0.72
0 (0.0%)	0 (0.0%)	NA	0 (0.0%)	0 (0.0%)	NA	0 (0.0%)	0 (0.0%)	NA
3 (1.3%)	4 (1.7%)	1.00	3 (1.3%)	4 (1.7%)	1.00	3 (1.3%)	5 (2.2%)	0.72
3 (1.3%)	4 (1.7%)	1.00	3 (1.3%)	4 (1.7%)	1.00	3 (1.3%)	4 (1.7%)	1.00
0 (0.0%)	0 (0.0%)	NA	0 (0.0%)	0 (0.0%)	NA	1 (0.4%)	1 (0.4%)	1.00
0 (0.0%)	0 (0.0%)	NA	0 (0.0%)	0 (0.0%)	NA	1 (0.4%)	1 (0.4%)	1.00
0 (0.0%)	0 (0.0%)	NA	0 (0.0%)	0 (0.0%)	NA	1 (0.4%)	3 (1.3%)	0.62
0 (0.0%)	0 (0.0%)	NA	0 (0.0%)	0 (0.0%)	NA	4 (1.8%)	11 (4.8%)	0.07
0 (0.0%)	0 (0.0%)	NA	0 (0.0%)	0 (0.0%)	NA	0 (0.0%)	0 (0.0%)	NA
	(n=227) 3 (1.3%) 3 (1.3%) 0 (0.0%) 0 (0.0%) 3 (1.3%) 0 (0.0%) 3 (1.3%) 0 (0.0%) 0 (0.0%) 0 (0.0%) 0 (0.0%)	FIREHAWK (n=227) (n=231)  3 (1.3%) 4 (1.7%)  3 (1.3%) 4 (1.7%)  0 (0.0%) 0 (0.0%)  3 (1.3%) 4 (1.7%)  0 (0.0%) 0 (0.0%)  3 (1.3%) 4 (1.7%)  0 (0.0%) 0 (0.0%)  3 (1.3%) 4 (1.7%)  3 (1.3%) 4 (1.7%)  0 (0.0%) 0 (0.0%)  0 (0.0%) 0 (0.0%)  0 (0.0%) 0 (0.0%)  0 (0.0%) 0 (0.0%)	FIREHAWK (n=227)	FIREHAWK (n=227)         XIENCE V (n=231)         p-value (n=227)         FIREHAWK (n=227)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)	FIREHAWK (n=227)         XIENCE V (n=231)         p-value (n=227)         FIREHAWK (n=227)         XIENCE V (n=231)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         5 (2.2%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         1 (0.4%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         0 (0.0%)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         0 (0.0%)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         0 (0.0%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         0 (0.0%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         0 (0.0%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         0 (0.0%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         0 (0.0%) <td>FIREHAWK (n=227)         XIENCE V (n=231)         p-value         FIREHAWK (n=227)         XIENCE V (n=231)         p-value           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         5 (2.2%)         0.72           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         1 (0.4%)         1.00           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         0 (0.0%)         NA           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         0 (0.0%)         NA           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00           3 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         NA</td> <td>FIREHAWK (n=227)         XIENCE V (n=231)         p-value (n=227)         FIREHAWK (n=227)         XIENCE V (n=231)         p-value (n=227)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00         5 (2.2%)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         5 (2.2%)         0.72         8 (3.5%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         1 (0.4%)         1.00         1 (0.4%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         0 (0.0%)         NA         1 (0.4%)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         0 (0.0%)         NA         0 (0.0%)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)           3 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)           0 (0.0%)         0 (0.0%)         0 (0.0%)</td> <td>FIREHAWK (n=227)         XIENCE V (n=231)         p-value (n=227)         FIREHAWK (n=227)         XIENCE V (n=231)         p-value (n=227)         FIREHAWK (n=227)         XIENCE V (n=231)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00         5 (2.2%)         5 (2.2%)         5 (2.2%)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         5 (2.2%)         0.72         8 (3.5%)         17 (7.4%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         1 (0.4%)         1.00         1 (0.4%)         2 (0.9%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         0 (0.0%)         NA         1 (0.4%)         0 (0.0%)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         5 (2.2%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         NA         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0</td>	FIREHAWK (n=227)         XIENCE V (n=231)         p-value         FIREHAWK (n=227)         XIENCE V (n=231)         p-value           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         5 (2.2%)         0.72           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         1 (0.4%)         1.00           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         0 (0.0%)         NA           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         0 (0.0%)         NA           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00           3 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         NA	FIREHAWK (n=227)         XIENCE V (n=231)         p-value (n=227)         FIREHAWK (n=227)         XIENCE V (n=231)         p-value (n=227)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00         5 (2.2%)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         5 (2.2%)         0.72         8 (3.5%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         1 (0.4%)         1.00         1 (0.4%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         0 (0.0%)         NA         1 (0.4%)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         0 (0.0%)         NA         0 (0.0%)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)           3 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)           0 (0.0%)         0 (0.0%)         0 (0.0%)	FIREHAWK (n=227)         XIENCE V (n=231)         p-value (n=227)         FIREHAWK (n=227)         XIENCE V (n=231)         p-value (n=227)         FIREHAWK (n=227)         XIENCE V (n=231)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00         5 (2.2%)         5 (2.2%)         5 (2.2%)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         5 (2.2%)         0.72         8 (3.5%)         17 (7.4%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         1 (0.4%)         1.00         1 (0.4%)         2 (0.9%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         0 (0.0%)         NA         1 (0.4%)         0 (0.0%)           3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         4 (1.7%)         1.00         3 (1.3%)         5 (2.2%)           0 (0.0%)         0 (0.0%)         NA         0 (0.0%)         NA         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0

Patient-oriented composite endpoint: all-cause death, all myocardial infarction, or any revascularisation; Device-oriented composite endpoint (TLF): cardiac death, target vessel myocardial infarction, or ischaemia-driven target lesion revascularisation; MI: myocardial infarction; NA: not available; ST: stent thrombosis; TLR: target lesion revascularisation; TVR: target vessel revascularisation; TLF: target lesion failure

The novel abluminal groove-filled biodegradable polymer SES FIREHAWK was non-inferior to the durable polymer EES XIENCE V for 9-month in-stent LLL.

# Clinical studies using the Firehawk DES: The Target All-comer trial

Targeted therapy with a localised abluminal groove, low-dose sirolimus-eluting, biodegradable polymer coronary stent (TARGET All Comers): a multicentre, open-label, randomised non-inferiority trial

Alexandra Lansky, William Wijns, Bo Xu, Henning Kelbak, Niels van Royen, Ming Zheng, Marie-angèle Morel, Paul Knoapen, Ton Slagboom, Thomas W Johnson, Georgios Vlachojannis, Karin E Arkenbout, Lene Holmvang, Luc Janssens, Andrzej Ochala, Salvatore Brugaletta, Christoph K Naber, Richard Anderson, Harald Rittger, Sergio Berti, Emanuele Barbata, Gabor G Toth, Luc Maillard, Christian Valina, Pawel Buszman, Holger Thiele, Volker Schächinger, Andreas Baumbach, for the TARGET All Corners Investigators

#### Summary

Background The FIREHAWK is a drug-eluting stent with a fully biodegradable sirolimus-containing polymer coating localised to recessed abluminal grooves on the stent surface. We investigated clinical outcomes with this targeted, low-dose, biodegradable polymer, sirolimus-eluting stent compared with XIENCE durable polymer, everolimus-eluting stents in an all-comers population.

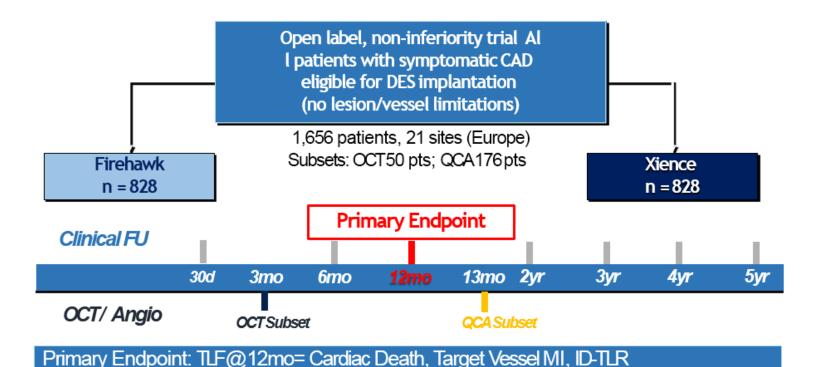
Methods The TARGET All Comers study was a prospective, multicentre, open-label randomised non-inferiority trial done at 21 centres in ten European countries. Patients with symptomatic or asymptomatic coronary artery disease and objective evidence of myocardial ischaemia who qualified for percutaneous coronary intervention were randomised 1:1 to undergo implantation of a FIREHAWK or XIENCE. Randomisation was web-based, with random block allocation and stratification by centre and ST elevation myocardial infarction. Outcome assessors were masked to treatment allocation, but treating physicians and patients were not. The primary endpoint was target lesion failure at 12 months, a composite of cardiac death, target vessel myocardial infarction, or ischaemia-driven target lesion revascularisation. The control event rate for XIENCE was assumed to be 7%, the non-inferiority margin was 3.5%, and the primary analysis was in the intention-to-treat population, censoring patients who did not have either an event before 365 days or contact beyond 365 days. Late lumen loss was the primary endpoint of an angiographic substudy designed to investigate the non-inferiority of the FIREHAWK compared with the XIENCE stent. This trial is registered with ClinicalTrials.gov, number NCT02520180.

Findings From Dec 17, 2015, to Oct 14, 2016, 1653 patients were randomly assigned to implantation of the FIREHAWK (n=823) or XIENCE (n=830). 65 patients in the FIREHAWK group and 66 in the XIENCE group had insufficient follow-up data and were excluded from the analyses. At 12 months, target lesion failure occurred in 46 (6-196) of 758 patients in the FIREHAWK group and in 45 (5-96) of 764 patients in the XIENCE group (difference 0-296, 90% CI –1-9 to 2-2, p\_moladom\_=0-004, 95% CI –2-2 to 2-6, p\_moladom\_=0-88). There were no differences in ischaemina-driven revascularisation or stent thrombosis rates at 12 months. 176 patients were included in the angiographic substudy, in which in-stent late lumen loss was 0-17 mm (SD 0-48) in the FIREHAWK group and 0-11 mm (0-52) in the XIENCE group (p=0-48), with an absolute difference of 0-05 mm (95% CI –0-09 to 0-18, p\_moladom=0-024).

Interpretation In a broad all-comers population of patients requiring stent implantation for myocardial ischaemia, the FIREHAWK was non-inferior to the XIENCE as assessed with the primary endpoint of target lesion failure at 12 months and in-stent late lumen loss at 13 months. The FIREHAWK is a safe and effective alternative stent to treat patients with ischaemic coronary artery disease in clinical practice.

Funding Shanghai Microport Medical

- Prospective, multicenter, open label, RCT
- Non-inferiority trial



Secondary Endpoints: TLF30d, 6mo, 2-5 yr; Composite (all death, all MI, anyrevasc)

DAPT:ASAand P2Y<sub>12</sub>inhibitor > 6 months (perguidelines)

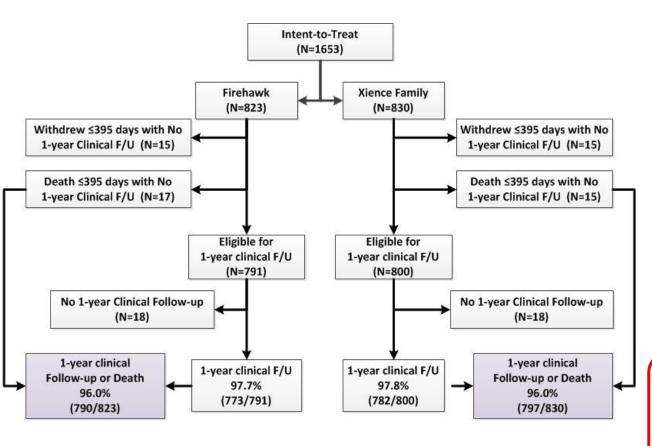
- Statistical Assumptions
- A total of 1654 randomized subjects (1572 evaluable) will provide 85% power to demonstrate non inferiority based on the following assumptions:
  - 1:1 Randomization
  - Primary Endpoint TLFControl event rate: 7%
  - Non Inferiority Margin: 3.5% (50% relative)
  - One sided alpha: 0.05
  - Lossto follow-up: 5%
  - Intention-to-treat population



P(Xience) – P(Firehawk)

Executive Operations Committee	TARGETAII Comers Trial Chair:  • William Wijns, MD (Galway, Ireland) CO-Pl's:  • Andreas Baumbach, MD (Bristol, UK)  • Alexandra Lansky, MD (New Haven, US)
	<ul> <li>Other Committee Members:</li> <li>XUBo, MBBS (Beijing, China)</li> <li>Zheng Ming, MD (Shanghai, China)</li> <li>Laure Artus-Jacenko, D.E.S.S. (Paris, France)</li> </ul>
Clinical Events Committee	CONplc, (Dublin, Ireland.) Chair: Michael Gibson, MD (Boston, US)
Data Safety Monitoring Board	Cardialysis, (Rotterdam, The Netherlands) Chair: Stefan James, MD (Uppsala, Sweden)
Angiographic Core Lab	Cardialysis, (Rotterdam, The Netherlands) CCRF,(Beijing, China)
OCT Core Lab	Cardialysis, (Rotterdam, The Netherlands) Dr Y.Onuma and team
Data Management	CONplc, (Dublin, Ireland.)





	Firehawk (N = 823 Pts)	Xience (N = 830 Pts)	P-value
Age (yrs)	64.9±9.8	65.3±10.5	0.40
Male	78.1% (641/821)	76.4% (634/830)	0.41
Diabetes mellitus	24% (197/820)	23% (191/830)	0.89
Hypertension	59.9% (492/821)	62.5% (519/830)	0.28
Hypercholesterolemia	53.0% (435/821)	51.2% (425/830)	0.47
Family history of CAD	42.8% (286/669)	43.4% (297/684)	0.80
Previous M I	21.7% (178/821)	24.8% (206/830)	0.13
Peripheral vessel disease	5.4% (44/821)	5.7% (47/830)	0.79
Previous PCI	28.7% (236/821)	31.6% (262/830)	0.21
Previous CABG	8.4% (69/821)	7.5% (62/830)	0.48
Renal insufficiency	5.5% (45/821)	7.0% (58/830)	0.21
Neurological events	8.1% (62/768)	7.7% (59/770)	0.76
Vessel location			
ROA	36.6% (299/817)	33.8% (280/829)	0.23
LAD	52.1% (426/817)	51.9% (430/829)	0.91
LCX	32.2% (263/817)	32.1% (266/829)	0.96
LMCA	3.1% (25/817)	2.1% (17/829)	0.19
Bypass graft	1.5% (12/817)	1.8% (15/829)	0.59
Any small vessel (<3.0mm)	74.4% (571/767)	71.0%(552/777)	0.13
Any long lesion	62.1% (439/707)	57.6% (411/713)	0.09
Any bifurcation lesions	39.1% (300/767)	38.2%(297/777)	0.72
Any total occlusion	14.2% (109/767)	12.0% (93/777)	0.19
Any coronary occlusion (>72 hrs)	6.0% (47/789)	6.4% (51/792)	0.69
Any in-stent restenosis	5.6% (43/766)	7.3% (57/777)	0.17

	Biodegradable polymer, sirolimus-eluting stent (FIREHAWK)	Durable polymer, everolimus-eluting stent (XIENCE)	p value
Lesions treated	1221	1179	
Stent implantation characteristics			
Number of stents per lesion, mean (SD), range	1.1 (0.5), 0-6	1.2 (0.6), 0-4	0.10
Stent length per lesion (mm), mean (SD), range	26.7 (15.3), 8-149	27.1 (16.9), 8-134	0.46
Stent diameter, mm	3.07 (0.47)	3.07 (0.50)	0.88
Procedure characteristics			
Assigned study stent implanted	1148 (94-2%)	1127 (95.6%)	0.013
Non-assigned stent implanted	26 (2.1%)	26 (2.2%)	0.90
Crossover	9 (0.7%)	0	0.004
No stent implanted	30 (2.5%)	23 (2.0%)	0.40
Any overlapping stent	179 (16.7%)	187 (17.7%)	0.91
Pre-dilation	859 (71%)	841 (71.8%)	0.68
Maximum pressure (atm)	14-4 (3-3)	14.3 (3.7)	0.85
Post-dilation	565 (46.7%)	541 (46-2%)	0.79
Maximum pressure (atm)	16.9 (3.5)	17-2 (3-6)	0.20
Lesions with core lab analysis	1074	1058	
Target vessel location*			
Left anterior descending	453 (42·2%)	463 (43-8%)	0.46
Left circumflex	272 (25·3%)	269 (25.4%)	0.96
Right coronary artery	313 (29·1%)	288 (27-2%)	0.32
Left main	19 (1.8%)	18 (1.7%)	0.90
Bypass graft	17 (1-6%)	20 (1.9%)	0.59

ACC/AHA lesion class*			0.80
A	24 (2.2%)	30 (2.8%)	
B1	157 (14.6%)	155 (14.7%)	
B2	432 (40.2%)	432 (40.8%)	
C	461 (42.9%)	441 (41.7%)	
Total occlusion (TIMI 0/1)	102 (9.5%)	86 (8-1%)	0.27
Calcification (moderate or severe)	65 (6· <b>1</b> %)	65 (6.2%)	0.41
Thrombus	25 (2.3%)	18 (1.7%)	0.30
In-stent restenosis	46 (4.3%)	58 (5.5%)	0.20
Bifurcation	359 (33·4%)	344 (32.5%)	0.65
Bifurcation side branch treatment			0.96
Side branch stent	79 (22.5%)	73 (21.7%)	
Side branch balloon only	23 (6.6%)	22 (6.5%)	
Baseline QCA results*			
Reference diameter (mm)	2.77 (0.49)	2.77 (0.52)	0.77
Minimal lumen diameter (mm)	0.78 (0.47)	0.79 (0.48)	0.83
Diameter stenosis	71.7% (15.9)	71.5% (16.1)	0.76
Lesion length (mm)	19.0 (11.8)	18.8 (12.4)	0.76
Final QCA results			
In-stent minimum lumen diameter (mm)	2.56 (0.45)	2.55 (0.47)	0.54
In-stent diameter stenosis	7.4% (6.9)	7.6% (6.5)	0.54
In-stent acute gain (mm)	1.77 (0.55)	1.76 (0.57)	0.50
Segment minimal lumen diameter (mm)	2.23 (0.49)	2.24 (0.51)	0.64
Segment diameter stenosis	16.2% (11.5)	15.7% (10.7)	0.31
Segment acute gain (mm)	1.45 (0.57)	1.45 (0.59)	0.82
Data are n, n (%), or mean (SD), unless noted otherw Association. TIMI=Thrombolysis In Myocardial Infarcanalysis. QCA=quantitative coronary analysis.  Table 2: Angiographic and procedural character	tion. *Results reported bas		

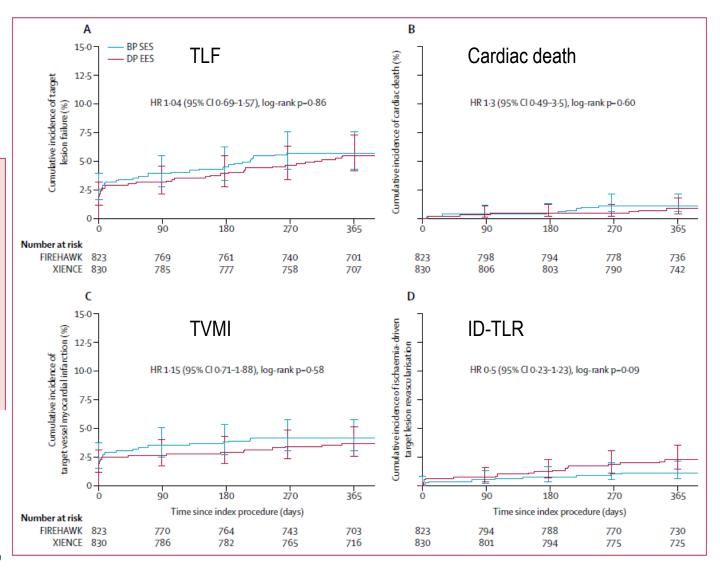
- 12 month fu
  - Mean fu: 373 days (SD 95.7 days)

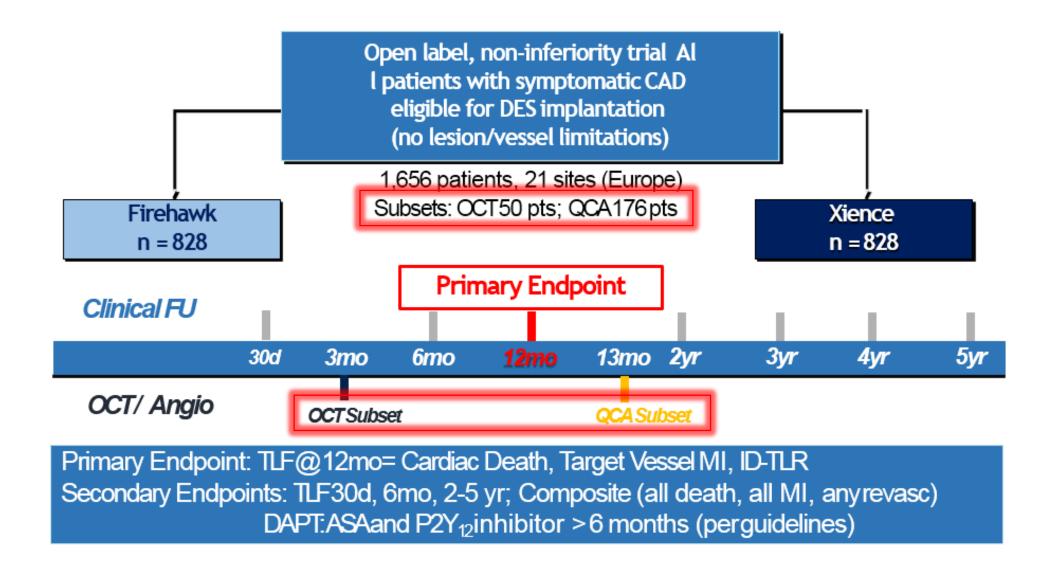
	Biodegradable polymer, sirolimus-eluting stent (FIREHAWK; n=823)	Durable polymer, everolimus-eluting stent (XIENCE; n=830)	Difference (95% CI)	pvalue
Primary outcome				
Target lesion failure	6.1% (46/758)	5.9% (45/764)	0·2% (-2·2 to 2·6)	0.88
Primary outcome compo	nents			
Cardiac death	1.2% (9/758)	0.9% (7/764)	0·3% (-0·8 to 1·3)	0.60
Target vessel myocardial infarction	4.5% (34/758)	3.9% (30/764)	0.6% (-1.5 to 2.6)	0.59
Ischaemia-driven target lesion revascularisation	1.2% (9/758)	2.4% (18/764)	-1·2% (-2·5 to 0·2)	0.08

#### • TLF

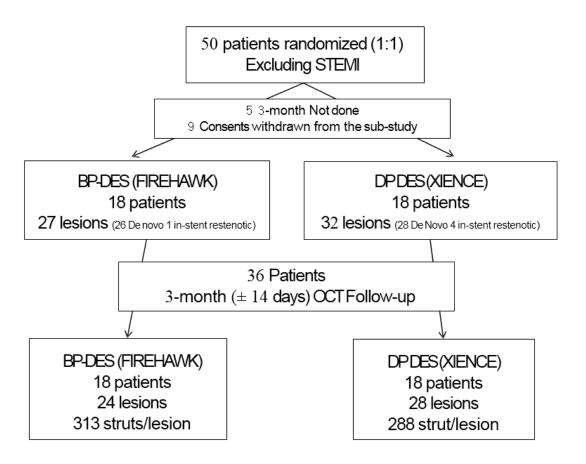
• Absolute: 0.2%

• 90% CI: 1·9 - 2·2,  $p_{\text{non-inferiority}} = 0.004$ , 95% CI: 2·2 - 2·6,  $p_{\text{superiority}} = 0.88$ )

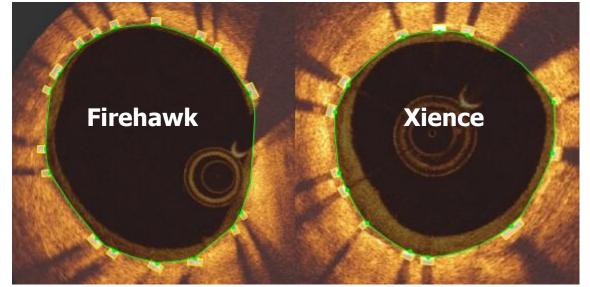




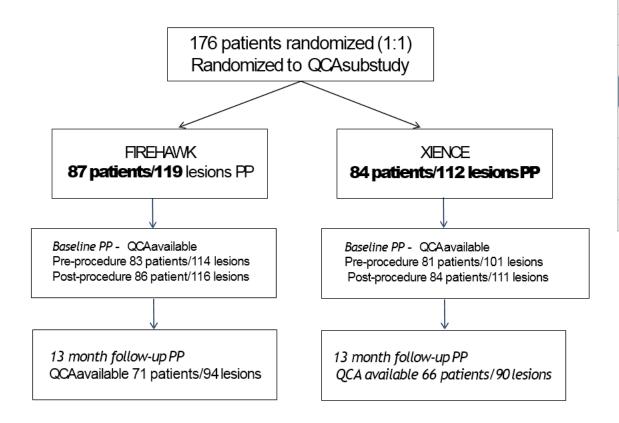
OCT subset



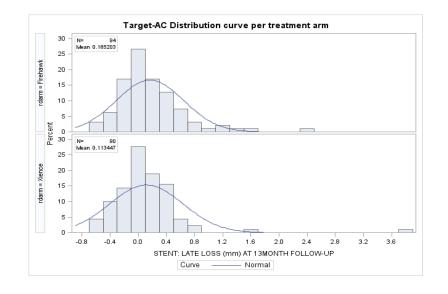
Characteristic	Firehawk (N=24les.)	Xience (N=28les.)	P-value
Mean neointimalthickness/strut coverag e(μm)	75.5 ± 25.8	82.3 ± 31.1	P <sub>noninf</sub> *:<0.001 P <sub>t-test</sub> *: 0.40
Length stented region(mm)	28.85 ± 20.86	27.28 ± 12.18	0.75
Mean stent diameter(mm)	3.07 ± 0.51	2.92 ± 0.50	0.29
Minimum stent diameter(mm)	2.71 ± 0.40	2.53 ± 0.51	0.17
Mean stent area(mm²)	7.63 ± 2.78	6.92 ± 2.46	0.33
Minimum stent area(mm²)	5.88 ± 1.71	5.23 ± 2.25	0.25



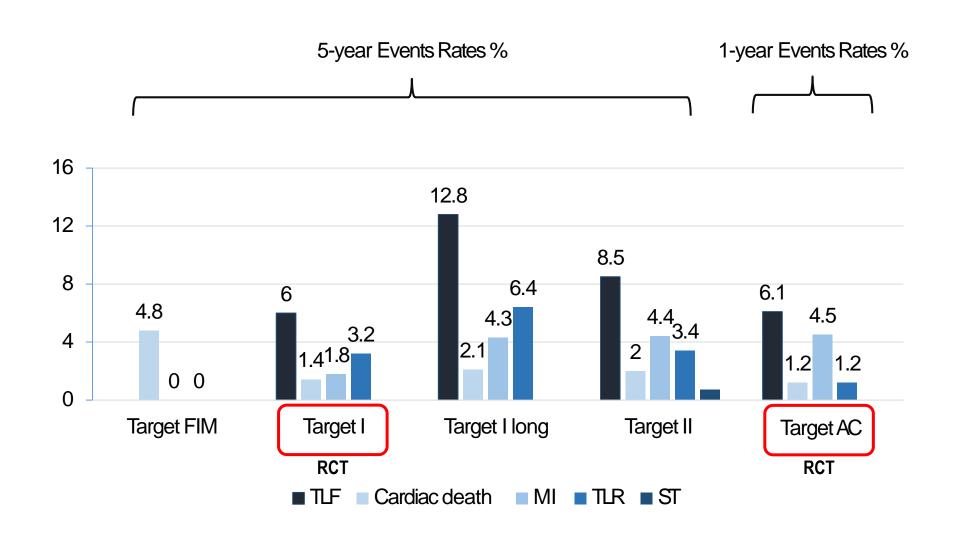
QCA subset



	Firehawk (N =87Pts/119 lesions)	Xience (N =84Pts/112 lesions)	P-value
In-stent			
MLD (mm)	2.40±0.45	2.33±0.43	0.23
Acutegain (mm)	1.57±0.64	1.45±0.50	0.12
Diameter stenosis(%)	12.3±7.2	12.1±6.7	0.80
In-segment			
MLD (mm)	2.05±0.46	1.99±0.52	0.38
Acute gain (mm)	1.22±0.65	1.09±0.55	0.13
Diameter stenosis(%)	22.3±9.2	22.0±9.2	0.86
In-stent Late Loss (mm)	0.17±0.05	0.11±0.05	P <sub>non-inf</sub> =0.024

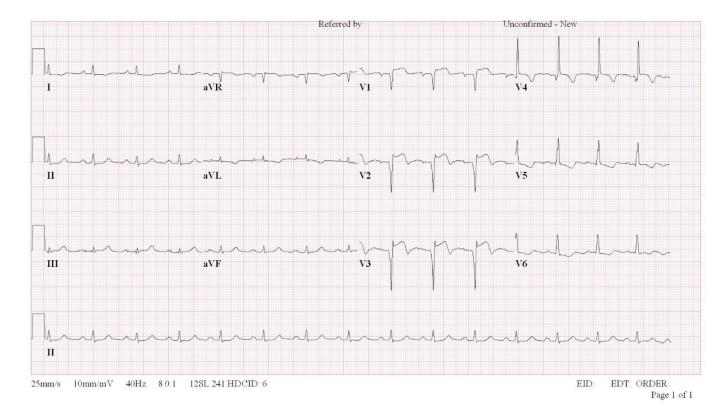


# Results of all 5 Clinical studies using the Firehawk DES

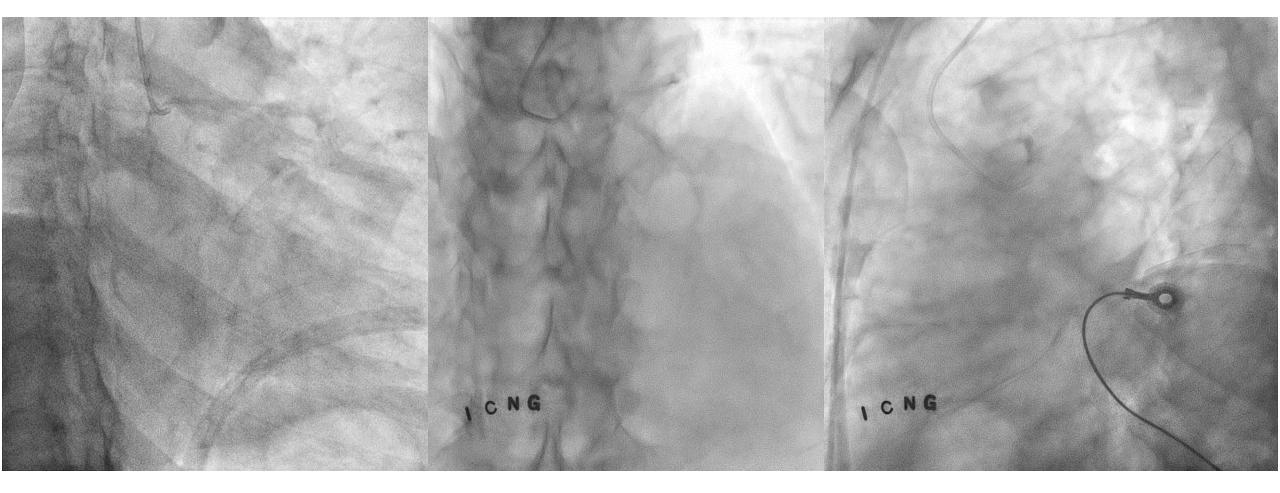


### **Case Presentation**

- 76/M, 160cm, 49kg, BMI 19.2 kg/m2
  - Recurrent DOE since 2MA
  - GB polyp & stone, s/p LC ('17.5.2), Ex-smoker: 30PY, quit 20YA
  - Visited the OPD clinic (Friday) due to severely aggravated chest discomfort at 4P30
  - Sent to the ER for further evaluation

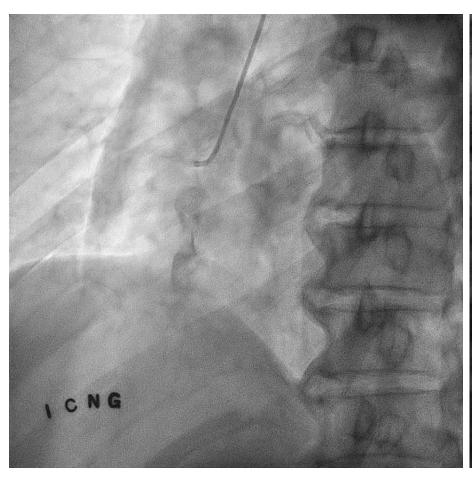


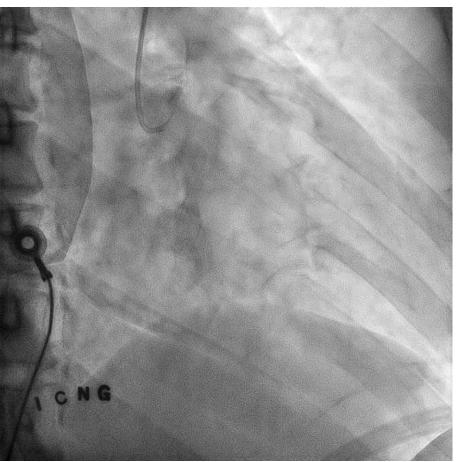
## **Case Presentation: Initial CAG**



LAD: pLAD tubular near total occlusion with heavy calcification m-dLAD diffuse upto 90% stenosis
LCx: os focal 80% stenosis, pLCx near total occlusion

## **Case Presentation: Initial CAG**

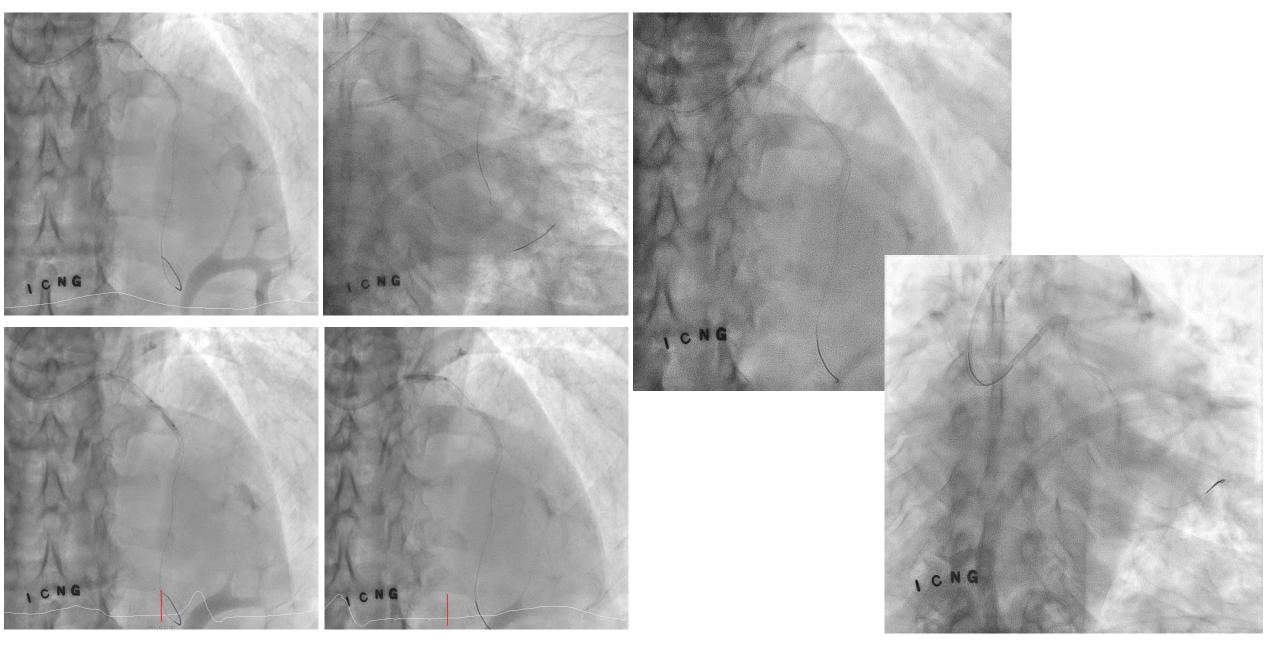




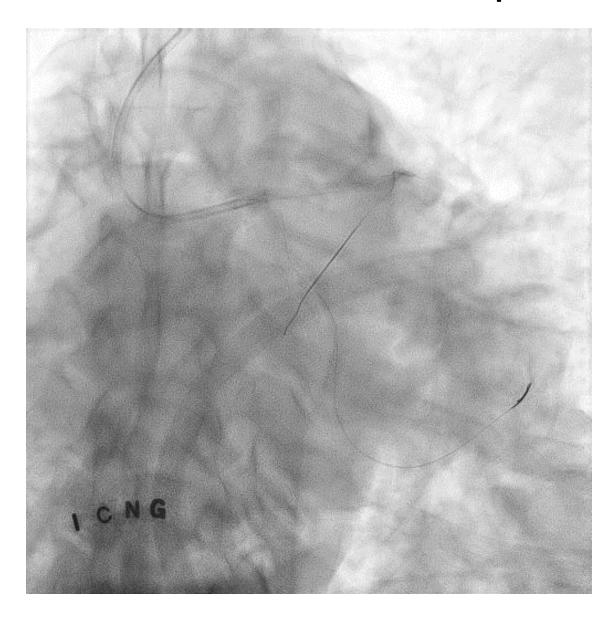
Which is the culprit?

One stage PCI? Or two staged?

RCA: pRCA focal 20% stenosis mRCA diffuse upto 50% stenosis



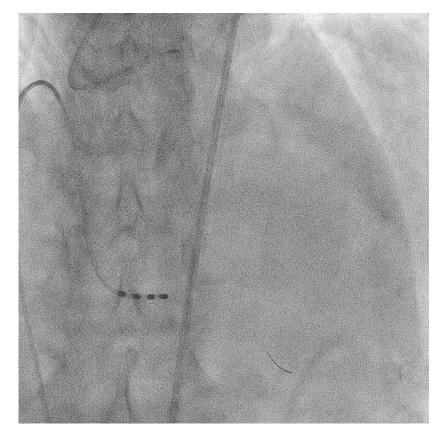
# **Case Presentation: PCI #1..and proceed?**



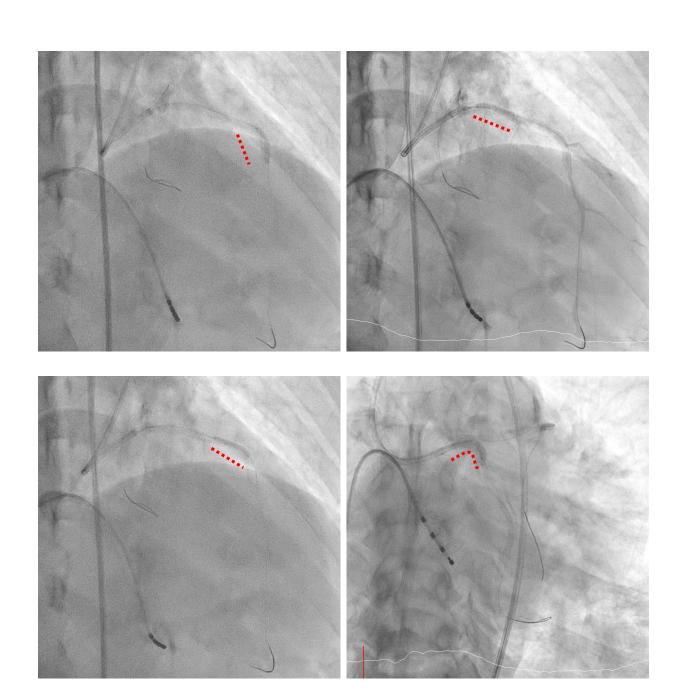
PCI for the LCX lesion without difficulty (Resolute Onyx 2.75mm x 30mm)

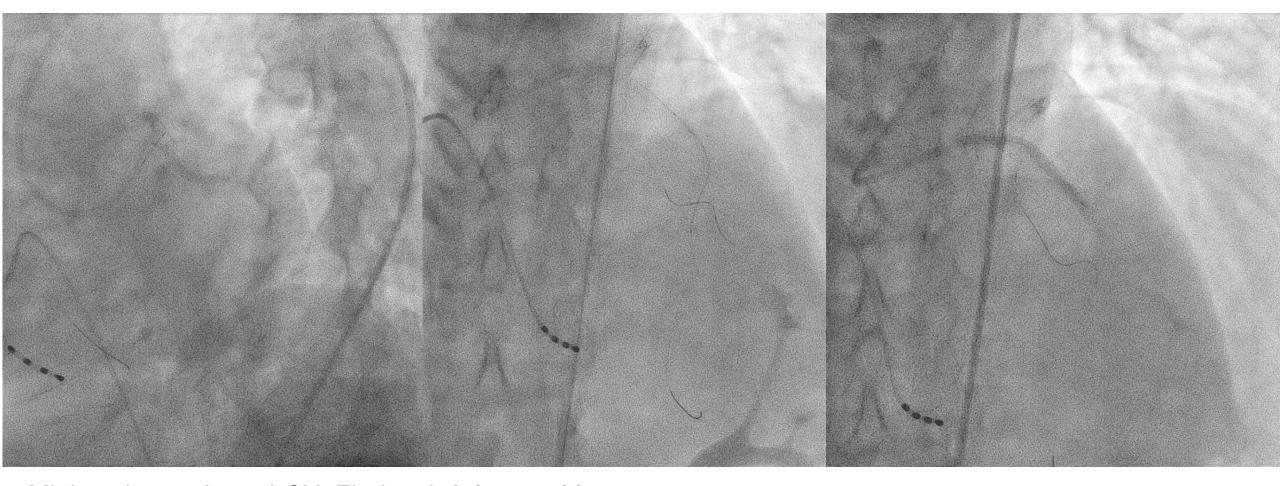
Vital sign stable

LAD PCI may need....
Rota-ablation needed
which is not appropriate on Friday night?



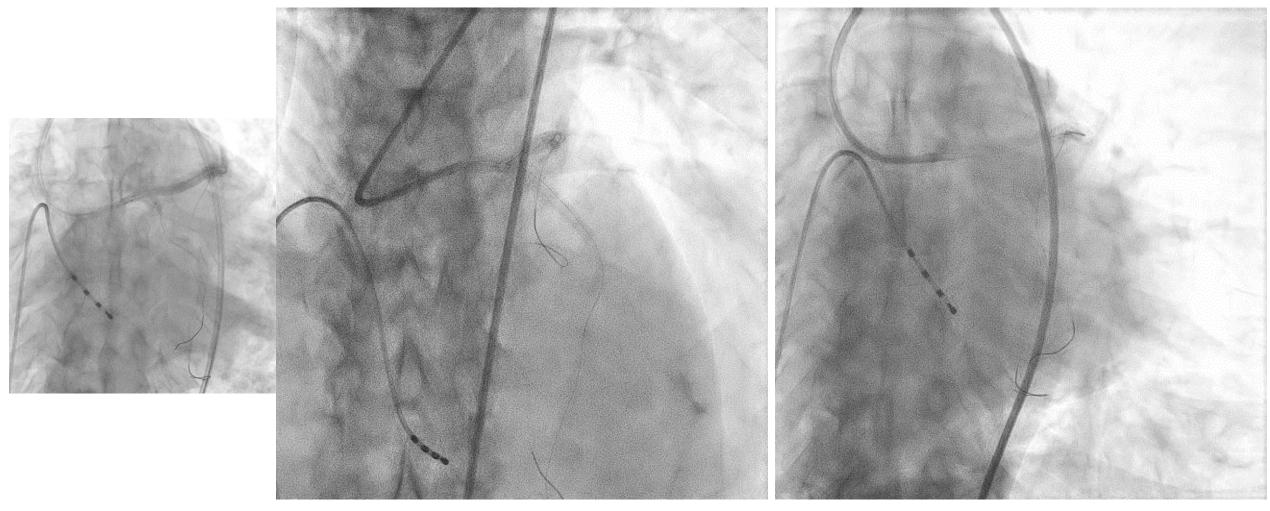
Rota-ablation with 1.5 burr Successful ballooning to LM-pLAD





Minicrush stenting: pLCX: Firehawk 3.0mm x 23mm

LM-pLAD: Firehawk 3.5mm x 38mm, Firehawk 3.0mm x 38mm



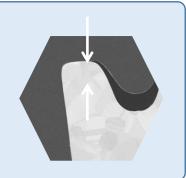
Final results after, kissing balloon to LM-LAD / LCX

#### **Case Presentation**

- EchoCG
  - Dilated LV (LVEDD 59mm) with depressed LVEF (33%)
  - RWMA: LAD/LCX territory akinesia
- Discharged 2 days after the 2<sup>nd</sup> PCI, free from cardiac symptoms
- Medication >
  - Aspirin+Plavix, Rosuvastatin 20mg, Bisoprolol 1.25mg, Valsartan 49mg 0.5T qd, Isoket 40mg bid



Successful PCI for a heavily calcified coronary artery using the localized abluminal groove Sirolimus-eluting DES



# **Thank You For Your Attention**

For any comments, questions, suggestions, please contact <a href="mailto:medikang@gmail.com">medikang@gmail.com</a>