EuroIntervention 2021;17:e332-e334 published online jqq June 2020 ■ published online e-edition July 2021

Abluminal groove-filled biodegradable polymer sirolimus-eluting stent versus durable polymer everolimus-eluting stent: three-year results of the TARGET All Comers trial

Yuichi Saito[1], MD; Henning Kelbæk[2], MD; Bo Xu[3], MD; Yasin Hussain[1], MD; Richard Anderson[4], MD; Volker Schächinger[5], MD; Ming Zheng[6], MD; William Wijns[7], MD; Andreas Baumbach[1,8], MD; Alexandra Lansky[1,8]*, MD; on behalf of the TARGET AC Investigators

1. Yale University School of Medicine, New Haven, CT, USA; 2. Department of Cardiology, Roskilde University Hospital, Roskilde, Denmark; 3. Fu Wai Hospital, National Centre for Cardiovascular Diseases, Chinese Academy of Medical Sciences, Beijing, China; 4. Department of Cardiology, University Hospital of Wales, Heath Park, Cardiff, United Kingdom; 5. Medizinische Klinik I, Herz-Thorax Zentrum, Klinikum Fulda, Fulda, Germany; 6. Shanghai MicroPort Medical (Group) Co., Ltd., Shanghai, China; 7. The Lambe Institute for Translational Medicine and Curam, National University of Ireland, Galway, and Saolta University Healthcare Group, Galway, Ireland; 8. Barts Heart Centre, London, and Queen Mary University of London, London, United Kingdom

This paper also includes supplementary data published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-20-00344

Introduction

New-generation drug-eluting stents (DES), including both biodegradable and durable polymer stents, are currently recommended as a default strategy in percutaneous coronary intervention (PCI). A meta-analysis of 16 contemporary randomised DES trials demonstrated similar safety and efficacy of biodegradable polymer DES with respect to stent-related coronary events up to a mean follow-up period of 26 months compared to current-generation durable polymer DES, suggesting no clinical benefit of biodegradable polymer at least at two-year follow-up[1]. The Firehawk® (Shanghai MicroPort® Medical (Group), Co., Ltd., Shanghai, China) is a thin-strut coronary stent with sirolimus and biodegradable polymer complex localised in abluminal grooves on the strut surface. The TARGET All Comers study recently reported the non-inferiority of target lesion failure (TLF) at one and two years with the Firehawk stent compared to the XIENCE, a durable polymer everolimus-eluting stent (Abbott Vascular, Santa Clara, CA, USA)[2,3]. Nevertheless, the clinical outcomes of the Firehawk stent might further improve at a later stage. The present paper reports the three-year results of the TARGET All Comers study.

Methods

STUDY POPULATION AND PROCEDURES

TARGET All Comers was a prospective, multicentre, open-label, non-inferiority trial with 1:1 randomisation conducted at 21 centres in 10 European countries (NCT02520180). The study protocol was approved by the ethics committee at each participating site, and written informed consent was obtained from all participants. The detailed study design has been reported previously[2,3].

CLINICAL OUTCOMES

The primary endpoint of the TARGET All Comers study was TLF, a composite of cardiac death, target vessel myocardial infarction (MI), or ischaemia-driven target lesion revascularisation at 12 months. The patient-oriented composite endpoint (PoCE) was defined as a composite of all-cause death, any MI, and any revascularisation. Clinical follow-up was scheduled at 1, 6, and 12 months, and annually thereafter up to 5 years by the study protocol. We report the main endpoints of interest including TLF, PoCE, and stent thrombosis at three-year follow-up.

STATISTICAL ANALYSIS

The Kaplan-Meier analysis was used to assess time to clinical events, and the log-rank test was applied to compare between-group differences. Cox proportional hazards regression analysis was used for hazard ratio calculations with 95% confidence intervals. Landmark analyses were performed using the one-year landmark.

Results

A total of 1,653 patients with 2,400 lesions were randomised 1:1 to receive either Firehawk or XIENCE stent implantation, of whom 1,549 (93.7%) patients completed three-year follow-up or

**Corresponding author: Division of Cardiovascular Medicine, Yale School of Medicine, 135 College Street, Suite 101, New Haven, CT 06510, USA. E-mail: alexandra.lansky@yale.edu*

SUBMITTED ON 29/03/2020 - REVISION RECEIVED ON 15/05/2020 - ACCEPTED ON 26/05/2020

DOI: 10.4244/EIJ-D-20-00344

had died **(Supplementary Figure 1)**. Baseline patient and lesion characteristics were matched; post-PCI angiographic results were not significantly different between the two groups, as shown previously.

The primary endpoint of TLF occurred similarly in the Firehawk and XIENCE groups at three years **(Figure 1)**. The rates of PoCE, stent thrombosis, individual components of the primary endpoint and other secondary endpoints were comparable between the groups **(Supplementary Table 1)**. Landmark analyses between one and three years demonstrated no significant differences in TLF, PoCE, and definite or probable stent thrombosis **(Figure 2)**. Very late definite or probable stent thrombosis beyond one year occurred in 6 (0.8%) Firehawk-treated patients and in 11 (1.4%) XIENCE-treated patients (p=0.24).

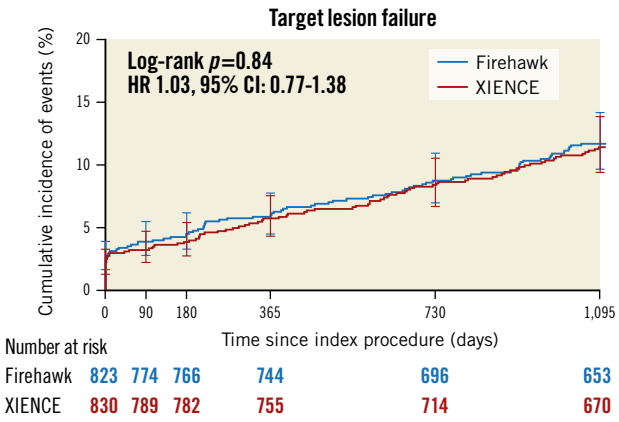


Figure 1. *Target lesion failure up to three years.*

Discussion

At three-year follow-up, the TARGET All Comers study demonstrated that the abluminal groove-filled biodegradable polymer sirolimus-eluting Firehawk stent had no significant difference in the major clinical endpoints compared with the benchmark durable polymer everolimus-eluting XIENCE stent.

Very late stent-related adverse events continue to accrue even in PCI with contemporary DES. In a recent, large-scale, individual patient data pooled study (n=25,032), very late stent-related events (defined as TLF) occurred at an annual rate of around 2% with all stent types between one and five years after PCI. The only

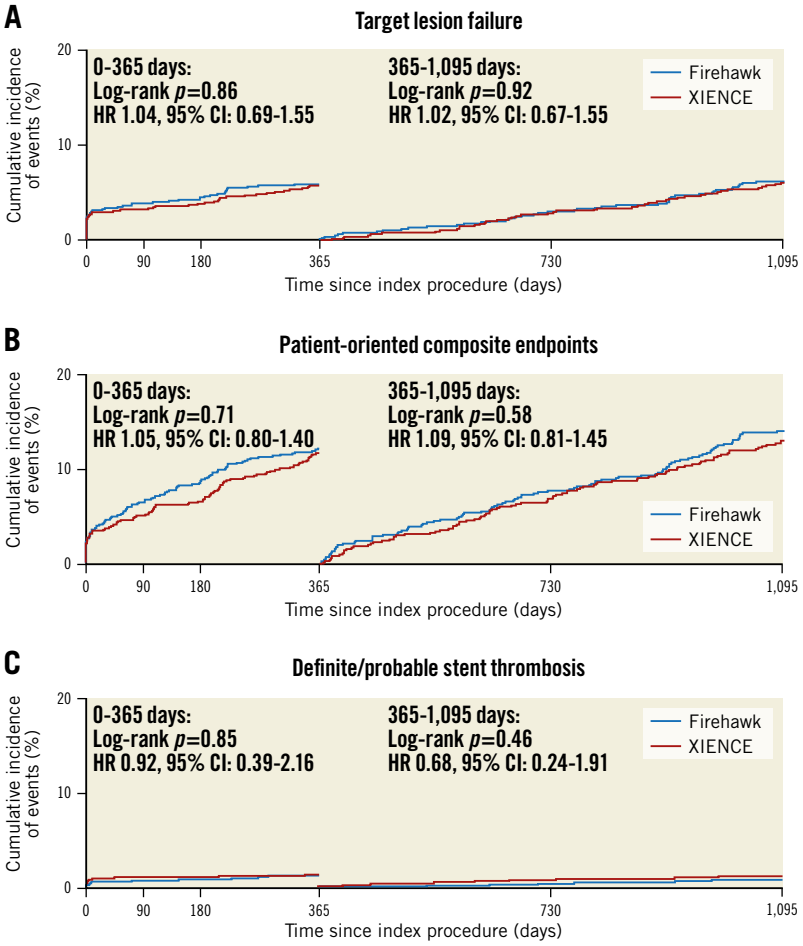


Figure 2. *Time-to-event curve for endpoints up to three years. A landmark was set at one year. A) Target lesion failure. B) Patient-oriented composite endpoints. C) Definite/probable stent thrombosis.*

difference was a decrease in the rate of TLF within one year as coronary stents evolved from bare metal stents to first-generation DES, and from first- to second-generation DES (17.8% vs 8.1% vs 5.0%, p<0.0001)[4]. Therefore, novel approaches are required to improve long-term outcomes after current-generation DES implantation.

The Firehawk stent has been established as being as safe and effective as the XIENCE stent with similar TLF rates at one and two years[2,3]. In addition, a sub-analysis of the TARGET All Comers study showed that outcomes with the Firehawk were comparable to the XIENCE stent across the spectrum of patient and lesion risk profiles[5]. The present study demonstrated that, during the third year of follow-up, the Firehawk continued to perform as well as the XIENCE stent but has not yet demonstrated an advantage of the low polymer density and drug concentration. Continued longer-term observations are needed and are planned up to five years.

Limitations

This study was powered for the primary composite endpoint of TLF at one year. The analysis therefore remained underpowered to detect differences in the individual components of the primary endpoint and stent thrombosis. The TARGET All Comers study will continue to evaluate clinical outcomes up to five years to address the potential benefits of the unique technology, although this follow-up period may not be sufficient.

Conclusion

The TARGET All Comers three-year outcomes confirm the continued safety and efficacy of the Firehawk compared to the XIENCE stent.

Impact on daily practice

Long-term data with the abluminal groove-filled biodegradable polymer sirolimus-eluting Firehawk stent have not been reported in a randomised all-comers population. The present three-year results of the TARGET All Comers study confirm similar safety and efficacy profiles of the Firehawk stent compared with the XIENCE stent. Further long-term follow-up and real-world data are needed to address potential benefits of the Firehawk stent.

Funding

This research was funded by Shanghai MicroPort Medical.

Conflict of interest statement

M. Zheng is a MicroPort employee. W. Wijns has received research grant and speaker fees from MicroPort. A. Baumbach has received speaker fees from MicroPort. A. Lansky has received research grant and speaker fees from MicroPort. The other authors have no conflicts of interest to declare.

References

1. El-Hayek G, Bangalore S, Casso Dominguez A, Devireddy C, Jaber W, Kumar G, Mavromatis K, Tamis-Holland J, Samady H. Meta-Analysis of Randomized Clinical Trials Comparing Biodegradable Polymer Drug-Eluting Stent to Second-Generation Durable Polymer Drug-Eluting Stents. *JACC Cardiovasc Interv.* 2017;10:462-73.

2. Lansky A, Wijns W, Xu B, Kelbæk H, van Royen N, Zheng M, Morel MA, Knaapen P, Slagboom T, Johnson TW, Vlachojannis G, Arkenbout KE, Holmvang L, Janssens L, Ochala A, Brugaletta S, Naber CK, Anderson R, Rittger H, Berti S, Barbato E, Toth GG, Maillard L, Valina C, Buszman P, Thiele H, Schächinger V, Baumbach A; TARGET All Comers Investigators. 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. *Lancet.* 2018;392:1117-26.

3. Xu B, Saito Y, Baumbach A, Kelbaek H, van Royen N, Zheng M, Morel MA, Knaapen P, Slagboom T, Johnson TW, Vlachojannis G, Arkenbout KE, Holmvang L, Janssens L, Ochala A, Brugaletta S, Naber CK, Anderson R, Rittger H, Berti S, Barbato E, Toth GG, Maillard L, Valina C, Buszman P, Thiele H, Schachinger V, Lansky A, Wijns W; TARGET AC Investigators. 2-Year Clinical Outcomes of an Abluminal Groove-Filled Biodegradable-Polymer Sirolimus-Eluting Stent Compared With a Durable-Polymer Everolimus-Eluting Stent. *JACC Cardiovasc Interv.* 2019;12:1679-87.

4. Madhavan MV, Kirtane AJ, Redfors B, Généreux P, Ben-Yehuda O, Palmerini T, Benedetto U, Biondi-Zoccai G, Smits PC, von Birgelen C, Mehran R, McAndrew T, Serruys PW, Leon MB, Pocock SJ, Stone GW. Stent-Related Adverse Events >1 Year After Percutaneous Coronary Intervention. *J Am Coll Cardiol.* 2020;75:590-604.

5. Saito Y, Baumbach A, Wijns W, Xu B, Kelbaek H, Zheng M, Morel MA, Anderson R, Schächinger V, Lansky A; TARGET AC Investigators. Clinical outcomes of complex lesions treated with an abluminal groove-filled biodegradable polymer sirolimus-eluting stent and durable polymer everolimus-eluting stent. *Catheter Cardiovasc Interv.* 2020;96:1023-8.

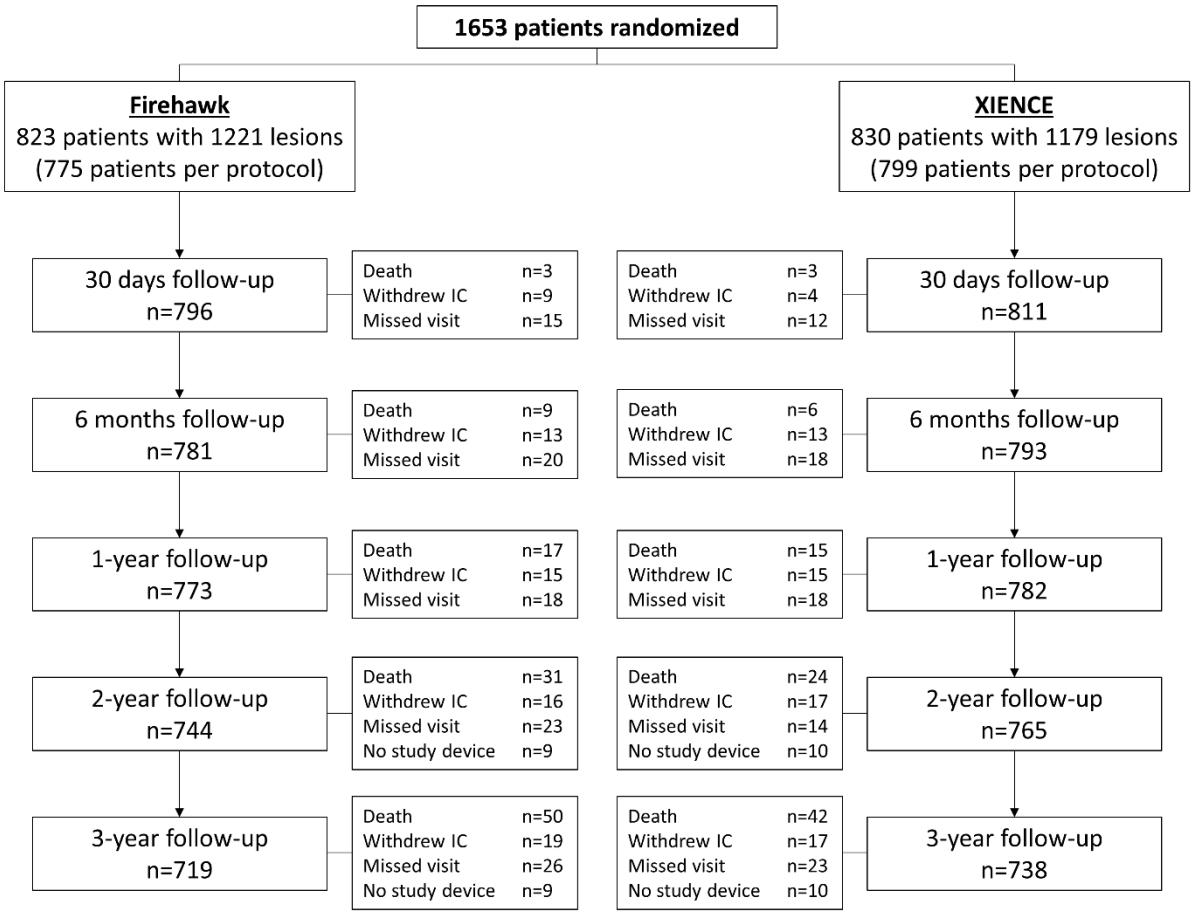
Supplementary data

Supplementary Figure 1. Study patient flow.

Supplementary Table 1. Clinical outcomes at 3-year follow-up.

The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-20-00344

Supplementary data



Supplementary Figure 1. Study patient flow.

A total of 1,549 of 1,653 (93.7%) patients completed 3-year follow-up or had died.

IC: informed consent

Supplementary Table 1. Clinical outcomes at 3-year follow-up.

Variable	Firehawk (n=823)	XIENCE (n=830)	Risk difference (95% CI)	*p*-value
Target lesion failure	92/775 (11.9%)	91/789 (11.5%)	0.3% (−2.8% to 3.5%)	0.84
Cardiac death	19/775 (2.5%)	15/789 (1.9%)	0.6% (−0.9% to 2.0%)	0.46
Target vessel MI	58/775 (7.5%)	62/789 (7.9%)	−0.4% (−3.0% to 2.3%)	0.78
Ischaemia-driven TLR	30/775 (3.9%)	39/789 (4.9%)	−1.1% (−3.1% to 1.0%)	0.30
PoCE	195/775 (25.2%)	187/789 (23.7%)	1.5% (−2.8% to 5.7%)	0.50
All-cause death	49/775 (6.3%)	42/789 (5.3%)	1.0% (−1.3% to 3.3%)	0.40
Any MI	77/775 (9.9%)	83/789 (10.5%)	−0.6% (−3.6% to 2.4%)	0.70
Any revascularisation	117/775 (15.1%)	121/789 (15.3%)	−0.2% (−3.8% to 3.3%)	0.90
Definite or probable ST	16/775 (2.1%)	20/789 (2.5%)	−0.5% (−2.0% to 1.0%)	0.54
Very late ST	6/775 (0.8%)	11/789 (1.4%)	−0.6% (−2.0% to 1.0%)	0.24

MI: myocardial infarction; PoCE: patient-oriented composite endpoint; ST: stent thrombosis; TLR: target lesion revascularisation