

# Three-year follow-up of the randomised comparison between an everolimus-eluting bioresorbable scaffold and a durable polymer everolimus-eluting metallic stent in patients with ST-segment elevation myocardial infarction (TROFI II trial)



Yuki Katagiri<sup>1</sup>, MD; Yoshinobu Onuma<sup>2</sup>, MD, PhD; Taku Asano<sup>1</sup>, MD; Andres Iniguez<sup>3</sup>, MD, PhD; Lisette Okkels Jensen<sup>4</sup>, MD, PhD; Àngel Cequier<sup>5</sup>, MD, PhD; Sjoerd H. Hofma<sup>6</sup>, MD, PhD; Evald H. Christiansen<sup>7</sup>, MD, PhD; Maarten Suttorp<sup>8</sup>, MD, PhD; Salvatore Brugaletta<sup>9</sup>, MD, PhD; Lorenz Räber<sup>10</sup>, MD, PhD; Manel Sabaté<sup>9</sup>, MD, PhD; Stephan Windecker<sup>10</sup>, MD; Patrick W. Serruys<sup>11\*</sup>, MD, PhD

1. Amsterdam University Medical Center, Amsterdam, the Netherlands; 2. Thoraxcenter, Erasmus Medical Center, Rotterdam, the Netherlands; 3. Complejo Hospitalario Universitario, Hospital Alvaro Cunqueiro, Vigo, Spain; 4. Department of Cardiology, Odense University Hospital, Odense C, Denmark; 5. Bellvitge University Hospital, Bellvitge Biomedical Research Institute (IDIBELL), University of Barcelona, Barcelona, Spain; 6. Department of Cardiology, Medical Centre Leeuwarden, Leeuwarden, the Netherlands; 7. Department of Cardiology, Aarhus University Hospital, Aarhus, Denmark; 8. Department of Cardiology, St. Antonius Hospital, Nieuwegein, the Netherlands; 9. Hospital Clinic, Institut Clinic Cardiovascular, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona, Barcelona, Spain; 10. Department of Cardiology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland; 11. NHLI, Imperial College London, London, United Kingdom

GUEST EDITOR: Alec Vahanian, MD, PhD; Department of Cardiology, Hôpital Bichat-Claude Bernard, and University Paris VII, Paris, France

This paper also includes supplementary data published online at: [http://www.pcronline.com/eurointervention/144th\\_issue/220](http://www.pcronline.com/eurointervention/144th_issue/220)

## Introduction

Previous midterm follow-up reports after implantation of the Absorb™ everolimus-eluting bioresorbable scaffold (BRS; Abbott Vascular, Santa Clara, CA, USA) in stable coronary artery disease and acute coronary syndrome have shown an increase of scaffold thrombosis leading to an excess of the device-oriented composite endpoint (DOCE: a composite of cardiac death, target vessel myocardial infarction [TVMI], and clinically driven target lesion revascularisation [CD-TLR])<sup>1</sup>. In contrast, in the six-month primary report of ABSORB STEMI: the TROFI II Study (NCT01986803)<sup>2</sup>, which randomised patients with ST-elevation myocardial infarction (STEMI) to receive either the Absorb BRS or the XIENCE metallic everolimus-eluting stent (EES; Abbott Vascular), optical frequency domain imaging (OFDI)-derived healing score was comparable between the BRS arm and the EES arm. The aim of this report was to present the three-year clinical outcome results of the BRS and the metallic EES at the time when full resorption of the scaffold device can be expected.

## Methods

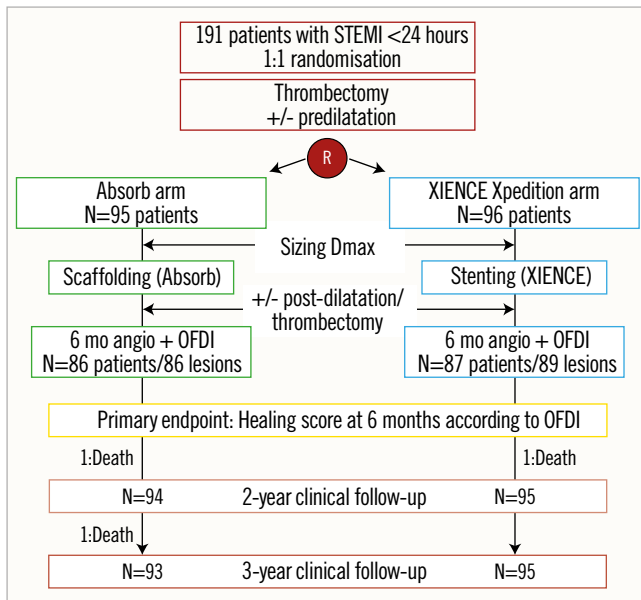
The trial design and methods, as well as the study population, have been described in previous reports<sup>2</sup>. Follow-up information at three years was available in 100% of the study population (**Figure 1**). All clinical events were adjudicated by an independent clinical events adjudication committee. Time-to-event variables were compared by log-rank test.

## Results

Clinical outcomes at three years are tabulated in **Table 1**. At three years, the rates of DOCE were 5.3% (5/95) in the BRS arm and 3.1% (3/96) in the EES arm without a statistically significant difference (p=0.465).

There were two cardiac deaths (2.1%) in the BRS arm: one was adjudicated as cardiac death on day 280 since no information was available as the patient died overseas. The autopsy of the second patient who died on day 999 revealed no evidence of scaffold thrombosis. There were no cardiac deaths in the EES arm.

\*Corresponding author: Cardiovascular Science Division of the NHLI within Imperial College of Science, Technology and Medicine, South Kensington Campus, London, SW7 2AZ, United Kingdom. E-mail: [patrick.w.j.c.serruys@gmail.com](mailto:patrick.w.j.c.serruys@gmail.com)



**Figure 1.** Study flow chart. OFDI: optical frequency domain imaging; STEMI: ST-segment elevation myocardial infarction

Definite/probable very late scaffold/stent thrombosis (VLST) occurred in 1.1% (1/95) and 1.0% (1/96) in the BRS and EES arm, respectively (**Supplementary Figure 1**).

**Table 1. Clinical outcomes at 3 years.**

Variables	BRS (N=95 patients) % (n/N)	EES (N=96 patients) % (n/N)	p-value
<b>Clinical outcomes – non-hierarchical events at 3 years</b>			
Device-oriented composite endpoint	5.3% (5/95)	3.1% (3/96)	0.465
Death (all causes)	2.1% (2/95)	1.0% (1/96)	0.558
Cardiac death	2.1% (2/95)	0.0% (0/96)	NA
Vascular death	0.0% (0/95)	1.0% (1/96)	NA
Non-cardiovascular death	0.0% (0/95)	0.0% (0/96)	NA
Myocardial infarction	3.2% (3/95)	4.2% (4/96)	0.737
Q-wave	0.0% (0/95)	1.0% (1/96)	NA
Non-Q-wave	3.2% (3/95)	3.1% (3/96)	0.969
Target vessel MI	2.1% (2/95)	3.1% (3/96)	0.327
All TLR	4.2% (4/95)	3.1% (3/96)	0.678
Clinically driven TLR	3.2% (3/95)	1.0% (1/96)	0.327
Definite/probable ST	2.1% (2/95)	1.0% (1/96)	0.55
Very late (after 360 days)	1.1% (1/95)	1.0% (1/96)	0.98

BRS: bioresorbable scaffold; EES: everolimus-eluting stent; MI: myocardial infarction; NA: not applicable; ST: scaffold/stent thrombosis; TL: target lesion; TLR: target lesion revascularisation; TVR: target vessel revascularisation

## Discussion

Three years after implantation of BRS or EES, in the setting of primary PCI, the rates of DOCE and ST were low and not significantly different between both arms. It is of note that there were no cases of ST after two years, while most of the patients in both arms discontinued dual antiplatelet therapy between one and two years (**Supplementary Table 1**). The three-year clinical results are in line with the comparable OFDI-derived healing scores<sup>2</sup> and neointimal quality<sup>3</sup> at six months. In addition, the recent report in the subpopulation of the current cohort showed a better vasomotion in BRS than in EES and similar microcirculatory function as well as healing score at three years<sup>4</sup>.

Although routine thrombectomy is not recommended in the recent guidelines, in treating STEMI patients with BRS, thrombectomy could facilitate better scaffold sizing to achieve better long-term outcome.

In the substudy of the present trial<sup>4</sup>, intraluminal dismantling was observed by OCT in 26.3%. However, the fact that the substudy only included event-free patients precludes the understanding of the clinical implication of intraluminal dismantling.

## Limitations

The trial was not powered to evaluate clinical endpoints. The implantation technique reflects the state of the art at the time of enrolment in 2014 and did not take into account the more recent findings on BRS usage in terms of size selection, lesion preparation and deployment technique. It remains to be elucidated whether the comparative clinical outcomes in this study performed in STEMI patients will be maintained after three years.

## Conclusions

Three years after implantation of BRS or EES, in the setting of primary PCI, the rates of DOCE and ST were low and not significantly different between both arms. The three-year clinical results are in line with the comparable healing scores observed at six months. However, the study was not powered to assess clinical endpoints.

## Impact on daily practice

Previous midterm follow-up reports after BRS implantation have shown an increase of ST leading to an excess of DOCE. The three-year follow-up of the TROFI II trial is the first observation of midterm clinical outcomes in a STEMI population treated with BRS in the context of a randomised trial. The rates of DOCE and ST were low and not different between BRS and EES, and no excess risk in BRS was observed.

## Guest Editor

This paper was guest edited by Alec Vahanian, MD, PhD; Department of Cardiology, Hôpital Bichat-Claude Bernard, and University Paris VII, Paris, France.

## Funding

The TROFI II trial was sponsored by the ECRI and supported with unrestricted grants from Terumo Europe N.V. and Abbott Vascular.

## Conflict of interest statement

Y. Onuma is a member of the Advisory Board for Abbott Vascular and has received speaker honoraria from Terumo. L. Jensen has received research grants to the institution from Terumo, Biotronik and Biosensors. S. Hofma declares non-study-related unrestricted educational research grants from Abbott Vascular to the institution. L. Räber has received grants to the institution from Abbott, Sanofi and Regeneron and speaker or consulting fees from Abbott, Amgen, AstraZeneca, Biotronik, and CSL Behring. M. Sabaté reports personal fees from Abbott Vascular. S. Windecker reports having received research contracts to the institution from Abbott, Amgen, Bayer, Biotronik, Boston Scientific, Medtronic, Edwards, Terumo and St. Jude. P.W. Serruys is a member of the Advisory Board for Abbott Vascular. The other authors have no conflicts of interest to declare. The Guest Editor is a consultant for Edwards Lifesciences.

## References

1. Ali ZA, Gao R, Kimura T, Onuma Y, Kereiakes DJ, Ellis SG, Chevalier B, Vu MT, Zhang Z, Simonton CA, Serruys PW, Stone GW. Three-Year Outcomes With the Absorb Bioresorbable Scaffold: Individual-Patient-Data Meta-Analysis From the ABSORB Randomized Trials. *Circulation*. 2018;137:464-79.
2. Sabaté M, Windecker S, Iniguez A, Okkels-Jensen L, Cequier A, Brugaletta S, Hofma SH, Räber L, Christiansen EH, Suttrop M, Pilgrim T, Anne van Es G, Sotomi Y, Garcia-Garcia HM, Onuma Y, Serruys PW. Everolimus-eluting bioresorbable stent vs.

durable polymer everolimus-eluting metallic stent in patients with ST-segment elevation myocardial infarction: results of the randomized ABSORB ST-segment elevation myocardial infarction-TROFI II trial. *Eur Heart J*. 2016;37:229-40.

3. Sotomi Y, Onuma Y, Liu S, Asano T, Eggermont J, Katagiri Y, Cavalcante R, de Winter RJ, Wykrzykowska JJ, Brugaletta S, Räber L, Sabaté M, Windecker S, Dijkstra J, Serruys PW. Quality difference of neointima following the implantation of everolimus-eluting bioresorbable scaffolds and metallic stents in patients with ST-elevation myocardial infarction: quantitative assessments by light intensity, light attenuation, and backscatter on optical coherence tomography in the TROFI II trial. *EuroIntervention*. 2018; 14:678-85.

4. Gomez-Lara J, Brugaletta S, Ortega-Paz L, Vandelloo B, Moscarella E, Salas M, Romaguera R, Roura G, Ferreiro JL, Teruel L, Gracida M, Windecker S, Serruys PW, Gomez-Hospital JA, Sabaté M, Cequier A. Long-Term Coronary Functional Assessment of the Infarct-Related Artery Treated With Everolimus-Eluting Bioresorbable Scaffolds or Everolimus-Eluting Metallic Stents: Insights of the TROFI II Trial. *JACC Cardiovasc Interv*. 2018;11:1559-71.

## Supplementary data

**Supplementary Figure 1.** Very late scaffold/stent thrombosis cases in BRS and EES.

**Supplementary Table 1.** Proportion of patients on dual antiplatelet therapy at 1-, 2-, and 3-year follow-up.

The supplementary data are published online at:  
[http://www.pronline.com/eurointervention/144th\\_issue/220](http://www.pronline.com/eurointervention/144th_issue/220)

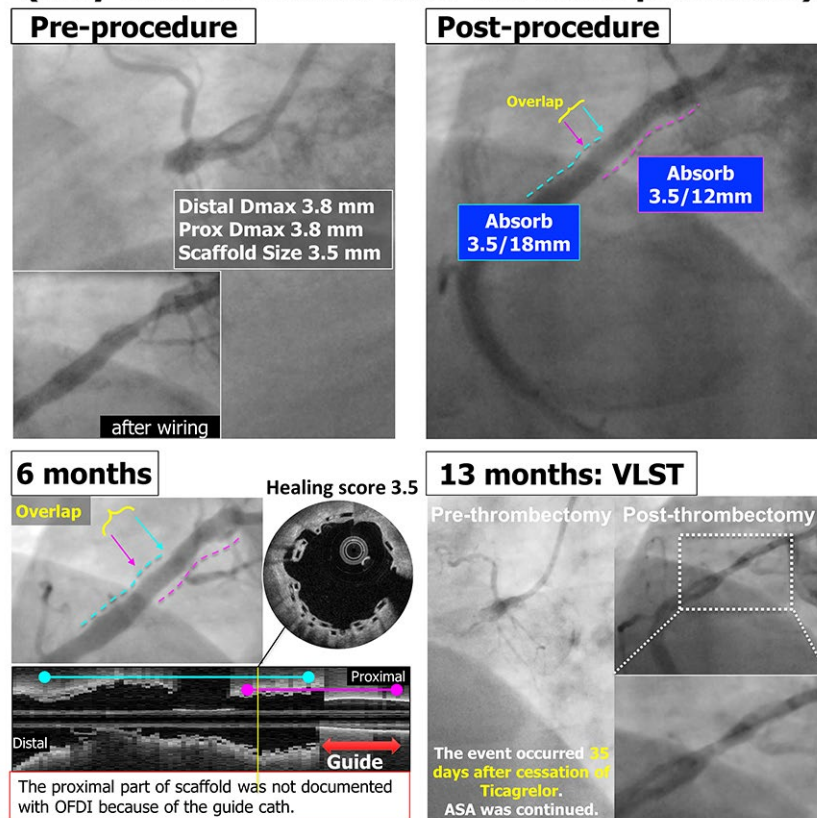


## Supplementary data

**Supplementary Figure 1.** Very late scaffold/stent thrombosis cases in BRS and EES. The VLST case in the BRS arm (panel A) occurred 13 months after the index procedure using overlapping scaffolds (3.5/18 and 3.5/12 mm) and following the cessation of ticagrelor 35 days before the event. The VLST in the EES arm (panel B) occurred at 24 months after the index procedure. At the time of ST, the patient was receiving single antiplatelet therapy with aspirin. The light attenuation analysis at 6-month OFDI in panel B shows high attenuation in orange and low attenuation in dark blue. ASA: acetylsalicylic acid; BRS: bioresorbable scaffold; EES: everolimus-eluting stent; OFDI: optical frequency domain imaging; ST: scaffold/stent thrombosis; VLST: very late scaffold/stent thrombosis

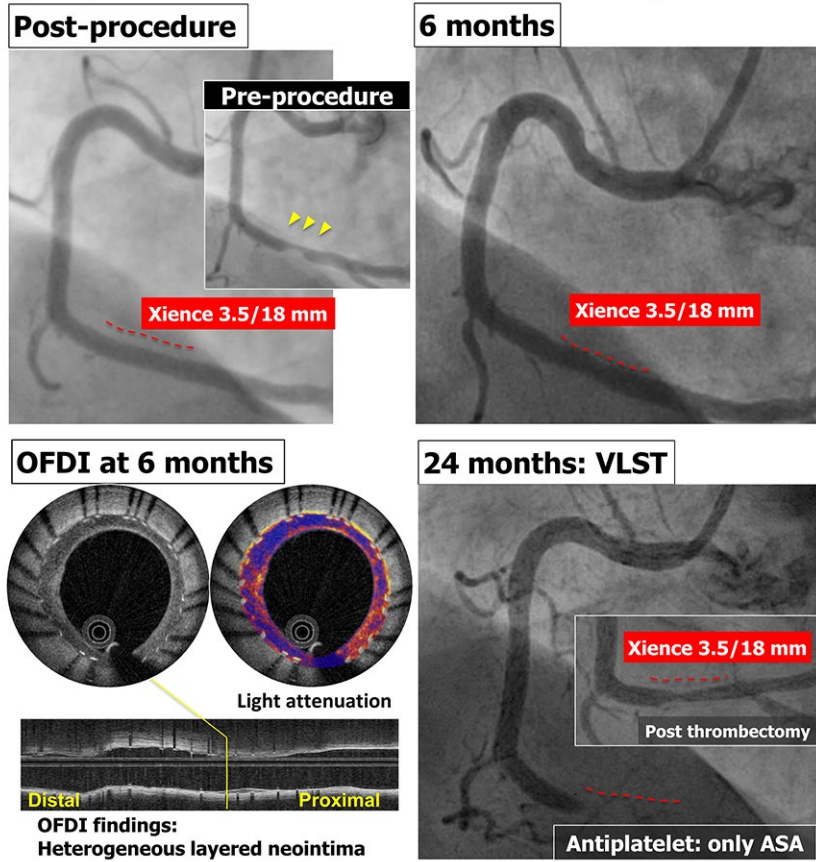
A.

### Scaffold thrombosis in the **BRS** arm (very late: 13 months after the index procedure)



B.

### Stent thrombosis in the **EES** arm (very late: 24 months after the index procedure)



**Supplementary Table 1. Proportion of patients on dual antiplatelet therapy at 1-, 2-, and 3-year follow-up.**

	<b>BRS</b>	<b>EES</b>	<b><i>p</i>-value</b>
At 1-year follow-up	78.5% (73/93)	78.1% (75/96)	0.951
At 2-year follow-up	15.1% (14/93)	10.4% (10/96)	0.338
At 3-year follow-up	10.8% (10/93)	6.3% (6/95)	0.276

BRS: bioresorbable scaffold; EES: everolimus-eluting stent