

# Clinical outcomes of everolimus-eluting bioresorbable scaffolds or everolimus-eluting stents in patients with acute myocardial infarction: two-year results of the randomised ISAR-Absorb MI trial

Jens Wiebe<sup>1,2\*</sup>, MD; Robert A. Byrne<sup>3,4</sup>, MB, BCh, PhD; Fernando Alfonso<sup>5</sup>, MD; Michael Maeng<sup>6</sup>, MD; Christian Bradaric<sup>7</sup>, MD; Evgeny Kretov<sup>8</sup>, MD; Javier Cuesta<sup>5</sup>, MD; Constantin Kuna<sup>1</sup>, MD; Tareq Ibrahim<sup>7</sup>, MD; Fernando Rivero<sup>5</sup>, MD; Mira Heugl<sup>1</sup>, cand. med.; Evald H. Christiansen<sup>6</sup>, MD; Michael Joner<sup>1,2</sup>, MD; Heribert Schunkert<sup>1,2</sup>, MD; Karl-Ludwig Laugwitz<sup>2,7</sup>, MD; Adnan Kastrati<sup>1,2</sup>, MD; Salvatore Cassese<sup>1</sup>, MD, PhD

1. Deutsches Herzzentrum München, Department of Cardiology, Technische Universität München, Munich, Germany; 2. DZHK (German Centre for Cardiovascular Research), partner site Munich Heart Alliance, Munich, Germany; 3. Cardiovascular Research Institute, Mater Private Hospital, Dublin, Ireland; 4. School of Pharmacy and Biomolecular Sciences, RCSI University of Medicine and Health Sciences, Dublin, Ireland; 5. Cardiac Department, Hospital Universitario de La Princesa Madrid, Madrid, Spain; 6. Department of Cardiology, Aarhus University Hospital, Aarhus, Denmark; 7. Clinic and Policlinic Internal Medicine I (Cardiology and Angiology), Klinikum rechts der Isar, Technische Universität München, Munich, Germany; 8. E.N. Meshalkin National Medical Research Center, Novosibirsk, Russia

This paper also includes supplementary data published online at: <https://eurointervention.pconline.com/doi/10.4244/EIJ-D-21-00653>

## Introduction

In patients with stable coronary artery disease, drug-eluting bioresorbable scaffolds (BRS) displayed inferior clinical results in comparison to metallic drug-eluting stents<sup>1</sup>. However, initial evidence on BRS implantation in patients with acute myocardial infarction (AMI) was encouraging (Sabaté M. Biodegradable scaffolds in STEMI: rationale, registry outcomes and TROFI II 2-year results. Presented at Transcatheter Therapeutics [TCT], Washington, DC, Oct 31, 2016) and lends support to further investigation. The Intracoronary Scaffold Assessment a Randomized evaluation of Absorb in Myocardial Infarction (ISAR-Absorb MI) trial demonstrated that BRS implanted in the setting of AMI have a similar antirestenotic efficacy compared to everolimus-eluting stents (EES), as assessed by angiographic follow-up after 6-9 months<sup>2</sup>. The aim of the present analysis was to report the two-year clinical follow-up of the ISAR-Absorb MI trial.

## Methods

The ISAR-Absorb MI trial is an investigator-initiated, prospective, randomised, multicentre, non-inferiority, clinical trial. Patients with AMI were randomised in a 2:1 ratio to be treated with either an everolimus-eluting BRS (Absorb; Abbott Vascular) or an EES (XIENCE; Abbott Vascular). A detailed description of the study has been published previously<sup>2</sup>. The endpoints of interest for this analysis were the device-oriented composite endpoint (DOCE) of cardiac death, target vessel myocardial infarction and target lesion revascularisation (TLR), and the patient-oriented composite endpoint (POCE) of all-cause death, any myocardial infarction and any revascularisation. Device thrombosis was defined according to Academic Research Consortium criteria. All events relevant for the primary and secondary endpoints were blindly adjudicated by an independent event adjudication committee.

\*Corresponding author: Deutsches Herzzentrum München, Lazarettstraße 36, 80636 Munich, Germany.  
E-mail: [wiebe@dhm.mhn.de](mailto:wiebe@dhm.mhn.de)

## Results

Baseline characteristics were described previously<sup>2</sup>. Two-year clinical follow-up was available for 164 patients in the BRS group and 87 patients in the EES group. DOCE occurred in 10.0% in the BRS group and in 7.9% in the EES group (hazard ratio [HR] 1.28, 95% confidence interval [CI]: 0.53-3.09,  $p=0.58$ ) and POCE occurred in 21.6% and 16.9% (HR 1.28, 95% CI: 0.70-2.33,  $p=0.42$ ), in the BRS group and EES group, respectively. The two-year all-cause mortality rate was not statistically different between patients treated with BRS and EES (5.3% versus 2.2%; HR 2.32, 95% CI: 0.50-10.75,  $p=0.28$ ). The rate of TLR was 7.2% in the BRS group and 6.8% in the EES group (HR 1.06, 95% CI: 0.40-2.82,  $p=0.91$ ). The rate of definite device thrombosis was 2.4% in the BRS group and 2.3% in the EES group (HR 1.04, 95% CI: 0.19-5.65,  $p=0.97$ ). A summary of the clinical outcomes is displayed in **Table 1** and Kaplan-Meier curves are shown on **Supplementary Figure 1**. Data regarding antiplatelet and anticoagulant therapies were available for 98.4% of the patients who were alive at the two-year follow-up. Of these patients, 97.2% were on aspirin, 18.6% on a P2Y<sub>12</sub> inhibitor and 2.4% on oral anticoagulation.

The analysis of clinical outcomes in prespecified subgroups including age, gender, diabetic status, presentation diagnosis and vessel size showed comparable results between BRS and EES regarding DOCE and TLR. With respect to POCE, EES showed more favourable results than BRS in the subgroup of non-ST-elevation myocardial infarction (NSTEMI) patients ( $p_{\text{interaction}}=0.03$ ), without significant differences in other subgroups (**Supplementary Figure 2**).

## Discussion

AMI lesions are typically characterised by predominantly thrombotic, soft, lipid-rich plaques with little calcification and evidence

of plaque rupture and therefore are associated with less resistance to stent expansion<sup>3</sup>. In addition, patients with AMI are also typically younger with fewer comorbidities at the time of diagnosis<sup>4</sup>. Taking into account also the mechanical properties of BRS, with less radial force compared to metallic stents, AMI patients are probably well-suited for interventional treatment with BRS technologies. Thus, further research is justified, and the ISAR-Absorb MI trial aims to address this need.

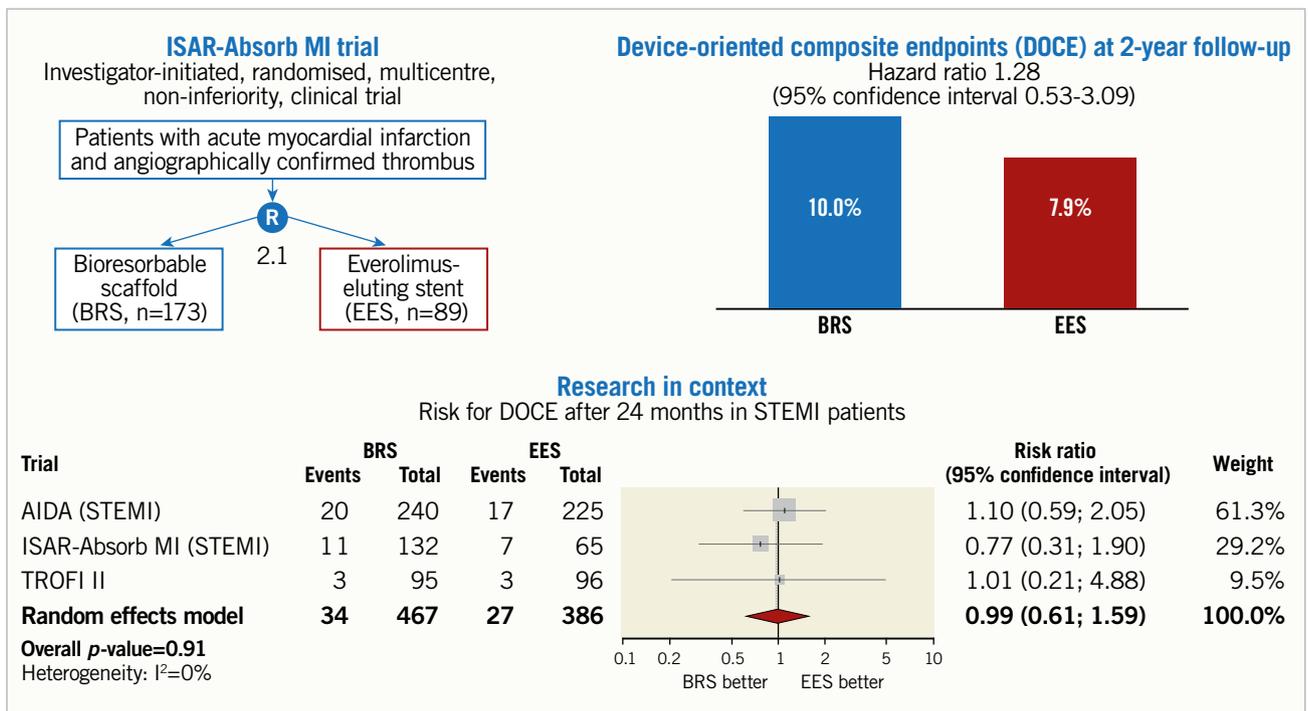
Overall, the two-year clinical outcomes in AMI patients treated with either BRS or EES were comparable in the ISAR-Absorb MI trial. These findings are in line with other randomised studies (**Figure 1**), e.g., the TROFI II study included 191 patients with STEMI and the primary endpoint was a healing score assessed by optical coherence tomography after six months, which was similar in both groups. The two-year clinical outcomes showed statistically comparable rates of DOCE (3.2% versus 3.2%;  $p=0.97$ ), TLR (2.1% versus 1.0%;  $p=0.55$ ) and definite/probable device thrombosis (2.1% versus 1.0%;  $p=0.55$ ) between BRS and EES (Sabaté M. Biodegradable scaffolds in STEMI: rationale, registry outcomes and TROFI II 2-year results. Presented at Transcatheter Therapeutics [TCT]. Washington, D.C., Oct 31, 2016). Furthermore, a prespecified subgroup analysis of the randomised controlled AIDA study did not find statistically relevant differences between patients with STEMI undergoing BRS ( $n=240$ ) or EES ( $n=225$ ) implantation regarding DOCE (8.4% versus 7.7%;  $p=0.722$ ), TLR (6.8% versus 5.0%;  $p=0.394$ ) and definite/probable device thrombosis (5.5% versus 2.7%;  $p=0.135$ ) after two years<sup>4</sup>.

## Limitations

1) Although we found no significant differences between the treatment groups, the trial was not powered to assess clinical outcomes.

**Table 1. Clinical results at two years.**

	BRS	EES	Hazard ratio (95% CI)	$p$ -value
<b>Device-oriented outcomes</b>				
Composite of cardiac death, target vessel myocardial infarction, target lesion revascularisation (device-oriented composite endpoint)	17 (10.0)	7 (7.9)	1.28 (0.53-3.09)	0.58
Cardiac death	5 (2.9)	2 (2.2)	1.29 (0.25-6.63)	0.76
Target vessel myocardial infarction	3 (1.8)	1 (1.1)	1.58 (0.16-15.1)	0.69
Target lesion revascularisation	12 (7.2)	6 (6.8)	1.06 (0.40-2.82)	0.91
Definite device thrombosis	4 (2.4)	2 (2.3)	1.04 (0.19-5.65)	0.97
Probable device thrombosis	1 (0.6)	0	NA	0.91
Definite or probable device thrombosis	5 (3.0)	2 (2.3)	1.29 (0.25-6.64)	0.76
<b>Patient-oriented outcomes</b>				
Composite of death, myocardial infarction, any revascularisation (patient-oriented composite endpoint)	37 (21.6)	15 (16.9)	1.28 (0.70-2.33)	0.42
All-cause death	9 (5.3)	2 (2.2)	2.32 (0.50-10.75)	0.28
Any myocardial infarction	6 (3.6)	4 (4.6)	0.78 (0.22-2.77)	0.70
Any revascularisation	26 (15.7)	12 (13.7)	1.10 (0.53-2.25)	0.71
Target vessel revascularisation	23 (13.8)	11 (12.5)	1.10 (0.53-2.25)	0.80
Non-target vessel revascularisation	21 (12.6)	12 (13.8)	0.91 (0.45-1.86)	0.80
Data shown as numbers (percentages are Kaplan-Meier estimates). $p$ -values are derived from superiority testing. NA: not applicable				



**Figure 1.** Design, clinical outcome and research in the context of the ISAR-Absorb MI trial. Only data from randomised studies were considered for the meta-analysis. Risk ratio with 95% confidence intervals was used as summary statistic to compare the risk of device-oriented composite endpoints (DOCE) in patients receiving a coronary revascularisation with either bioresorbable scaffolds (BRS) or everolimus-eluting stents (EES). The random effects model with the Hartung-Knapp adjustment served for overall calculations. A  $p$ -value  $<0.05$  was considered statistically significant. The  $I^2$  statistic tested the heterogeneity across trials. In all trials, risk estimates refer to the 24-month follow-up time point (Sabat  M. Biodegradable scaffolds in STEMI: rationale, registry outcomes and TROFI II 2-year results. Presented at Transcatheter Therapeutics [TCT]. Washington, D.C., Oct 31, 2016)<sup>4</sup>. For the AIDA and ISAR-Absorb MI trials, summary estimates were obtained from patients with ST-elevation myocardial infarction (STEMI). AIDA: Amsterdam Investigator-initiated Absorb Strategy All-comers Trial; ISAR-Absorb MI: Intracoronary Scaffold Assessment a Randomized evaluation of Absorb in Myocardial Infarction trial

2) According to the trial protocol, the clinical follow-up was limited to two years. A longer follow-up is desirable to address the risk of late adverse events associated with BRS.

## Conclusion

The ISAR-Absorb MI trial found that, in patients with AMI, PCI with either BRS or EES is associated with a comparable clinical performance at two-year follow-up. The potential role of contemporary BRS technology for AMI patients needs to be assessed in future trials.

## Funding

The trial was sponsored by the Deutsches Herzzentrum M nchen. The study was predominantly funded by the Deutsches Herzzentrum M nchen and in part by a grant from Abbott Vascular.

## Conflict of interest statement

R.A. Byrne reports research funding to the institution of prior employment from CeloNova BioSciences, and research or educational funding to the institution of current employment from Abbott Vascular, Biosensors, Biotronik and Boston Scientific. M. Joner

reports grants and personal fees from Edwards, personal fees from Recor, AstraZeneca, Amgen, Biotronik, Orbus Neich, Boston Scientific and Abbott, and grants from Boston Scientific. J. Wiebe reports other from AstraZeneca, outside the submitted work. H. Schunkert reports personal fees from Amgen, grants and personal fees from AstraZeneca, personal fees from Bayer Vital GmbH, Boehringer Ingelheim, Bristol Myers Squibb, Daiichi Sankyo, MSD Sharp & Dohme, Novartis, Sanofi-Aventis, Servier and SYNLAB. The other authors have no conflicts of interest to declare.

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## Supplementary data

**Supplementary Figure 1.** Clinical outcomes after two years.

**Supplementary Figure 2.** Subgroup analysis.

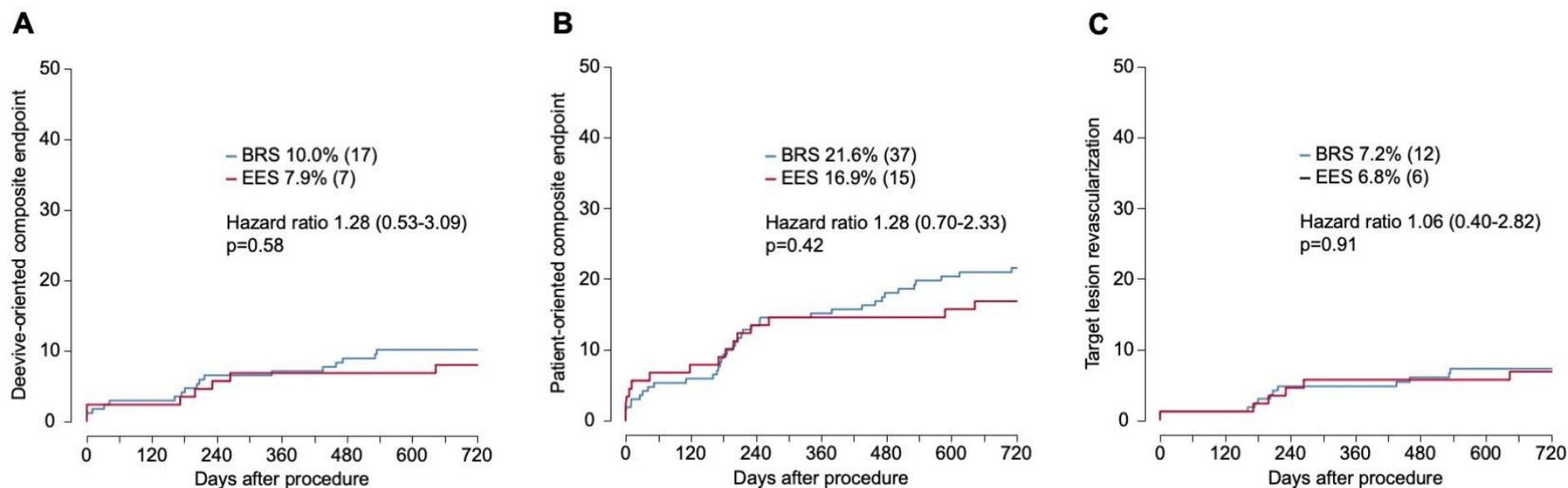
*The supplementary data are published online at:*

*<https://eurointervention.pcronline.com/>*

*[doi/10.4244/EIJ-D-21-00653](https://doi.org/10.4244/EIJ-D-21-00653)*



## Supplementary data

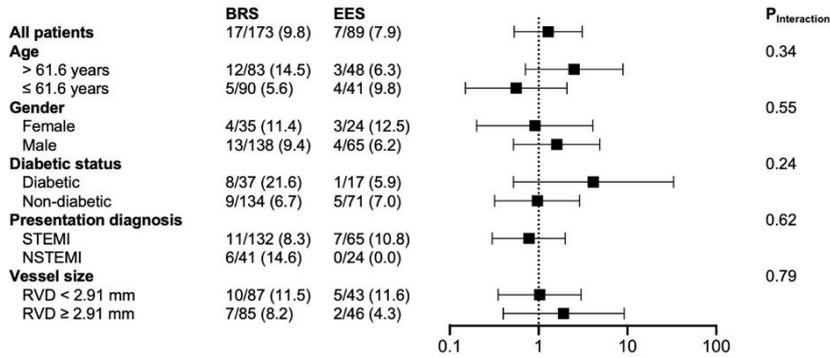


### Supplementary Figure 1. Clinical outcomes after two years.

This figure shows the Kaplan-Meier curves for (A) the device-oriented composite endpoint of cardiac death/target vessel myocardial infarction/target lesion revascularisation, (B) the patient-oriented composite endpoint of death/any myocardial infarction/all revascularisation, and (C) target lesion revascularisation. Data is displayed as Kaplan-Meier event rates and hazard ratios with 95% confidence intervals.

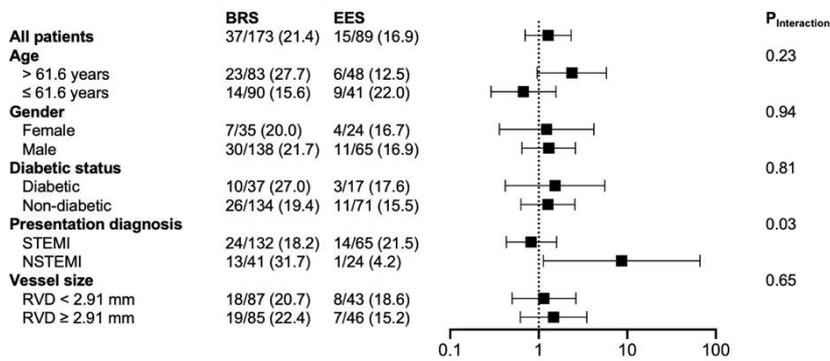
**A**

**Device-oriented composite endpoint**



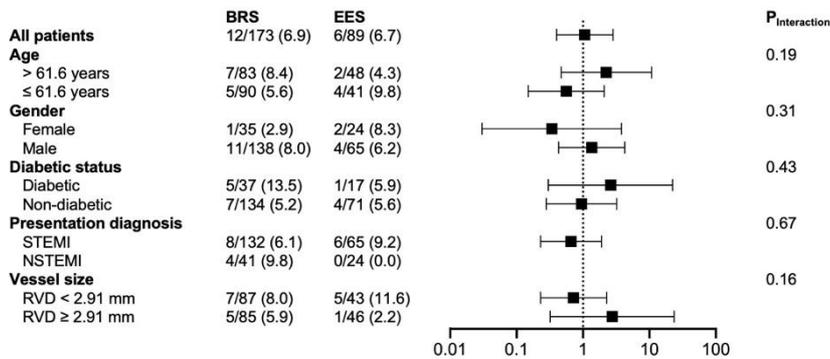
**B**

**Patient-oriented composite endpoint**



**C**

**Target lesion revascularization**



**Supplementary Figure 2. Subgroup analysis.**

This Figure illustrates an analysis of pre-specified subgroups regarding (A) the device-oriented composite endpoint of cardiac death/target vessel myocardial infarction/target lesion revascularisation, (B) the patient-oriented composite endpoint of death/any myocardial infarction/all revascularisation, and (C) target lesion revascularisation. Data are shown as numbers and percentage. Hazard ratios with 95% confidence intervals are shown graphically. RVD: reference vessel diameter