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Title: Angiographic and clinical outcomes of STEMI patients treated with bioresorbable or metallic everolimus-eluting stents. A pooled analysis of individual patient data from 2 randomized trials.

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Angiographic and clinical outcomes of STEMI patients treated with bioresorbable or metallic everolimus-eluting stents.

A pooled analysis of individual patient data from 2 randomized trials

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Running title: Pooled analysis of Absorb versus EES in STEMI

Clinical Trial Registration:

Both trials were registered at www.clinicaltrials.gov (NCT01942070 and NCT01986803).

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ABBREVIATIONS LIST

BRS: bioresorbable scaffold

DOCE: device-oriented composite endpoint

EES: everolimus-eluting stent

PCI: percutaneous coronary intervention

POCE: patient-oriented composite endpoint

STEMI: ST-elevation myocardial infarction

CONDENSED ABSTRACT

This pooled analysis of two randomized trials investigated angiographic and clinical outcomes of Absorb versus everolimus-eluting metallic stents in STEMI patients treated with percutaneous coronary interventions. After 1 year patients treated with Absorb as compared to those treated with everolimus-eluting metallic stents displayed comparable outcomes.

IMPACT ON DAILY PRACTICE

This study provides evidence for a comparable performance of Absorb and everolimus-eluting metallic stents in STEMI patients undergoing percutaneous revascularization. Although the bioresorbable platform investigated in this analysis is no longer available for clinical use, several scaffolds are in development or under investigation. Thus, the present study may serve as evidence base for future trials investigating improved or new bioresorbable scaffolds in STEMI.

ABSTRACT

Aims: Bioresorbable scaffolds (BRS) were conceived to ensure transient coronary artery support during antiproliferative drug delivery. However, the everolimus-eluting bioresorbable scaffold Absorb (*Abbott Vascular, Santa Clara, CA, USA*) was found inferior to everolimus-eluting metallic stents (EES) in moderately complex coronary anatomies. We sought to investigate whether the Absorb represents a valuable option for the percutaneous treatment of patients with ST-elevation myocardial infarction (STEMI).

Methods and Results: We pooled the individual patient data of two randomized trials specifically designed to investigate the performance of Absorb versus EES in patients with acute myocardial infarction (MI). The primary outcome was lesion (in-segment) diameter stenosis at angiographic follow-up. The main secondary outcome was the device-oriented composite endpoint (DOCE) of cardiac death, target vessel MI and target lesion revascularization at 1 year. A total of 388 patients with STEMI were allocated to Absorb (n=227) or EES (n=161). Angiographic follow-up at 1 year was available for 332 (85.6%) patients. Lesion diameter stenosis was comparable between Absorb and EES (22.8±9.8% versus 23.6±11.2%; mean difference, 95% Confidence intervals= -0.8% [-3.18, 1.48], P= 0.47). DOCE occurred in 21 patients at 1 year, with similar distribution between Absorb and EES groups (5.3% versus 5.6%; hazard ratio, 95% Confidence intervals= 0.95 [0.40, 2.26], P= 0.91).

Conclusions: This pooled analysis provides evidence for a comparable angiographic performance and suggests similar clinical performance of Absorb and EES in STEMI patients undergoing percutaneous revascularization. The long-term durability of Absorb and the extent to which newer BRS platforms might have a potential role in STEMI deserve further investigation.

INTRODUCTION

Bioresorbable scaffolds (BRS) are percutaneous coronary prostheses designed to offer a transient support of the dilated vessel and to dissolve into inert breakdown products overtime, once they antiproliferative function is completed.[1]

The fully-bioresorbable, everolimus-eluting scaffold (Absorb, *Abbott Vascular, Santa Clara, CA, USA*) represents the most studied bioresorbable platform to date. Initial data of percutaneous coronary intervention (PCI) with Absorb in selected patients were encouraging, though not confirmed in subsequent randomized trials.[2] In fact, Absorb displayed out to 1 year a twice as high thrombotic risk in comparison with the metallic everolimus-eluting metallic stents (EES - Xience, *Abbott Vascular, Santa Clara, CA, USA*). More disappointingly, follow-up data beyond 1 year revealed that the risk of failure of Absorb continued to accrue during longer term follow-up.[3] In response to this, in September 2017 the manufacturer withdrew Absorb from the market, though other BRS are approved for clinical use in Europe and available for clinical use.

Although individuals with ST-segment elevation myocardial infarction (STEMI) were excluded from most randomized trials investigating Absorb, these patients may represent a subset that may derive greater benefit from treatment with BRS technology. In fact, lesions of STEMI patients generally consist of soft, lipid-rich, thrombotic plaques located in larger vessel segments, with less resistance to dilation and more favourable healing patterns.[4] To shed more light on the angiographic and clinical performance of Absorb versus EES in patients with STEMI, we performed a pooled-analysis of individual patient data from the Intracoronary Scaffold Assessment a Randomised Evaluation of Absorb in Myocardial Infarction (ISAR-Absorb MI) and from the Comparison of the ABSORB™ Everolimus Eluting Bioresorbable Vascular Scaffold System With a Drug- Eluting Metal Stent

(Xience™) in Acute ST-Elevation Myocardial Infarction (ABSORB STEMI TROFI II) randomized trials.

METHODS

Full details of the study population, methods, endpoints and primary analyses of the ISAR-Absorb MI[5] and ABSORB STEMI TROFI II[4] clinical trials have been reported previously. In brief, both were multicentre, open-label, randomized trials of patients with acute myocardial infarction (MI) undergoing PCI with either Absorb or EES. Between September 2013 and March 2017 the ISAR-Absorb MI trial enrolled 262 patients with STEMI (or NSTEMI with visible thrombus at baseline angiography) in 5 centres: 173 participants were allocated to Absorb and 89 to EES. Between January and September 2014, the ABSORB STEMI TROFI II trial enrolled 191 patients with STEMI in 8 centres: 95 participants received Absorb and 96 received EES.

Inclusion criteria were broadly comparable between studies. To be included, patients should be aged ≥18 years, present with MI and planned to receive a stent in *de novo* lesions in native vessels or coronary bypass grafts with reference vessel diameter ≥2.25 mm and ≤3.9 mm in diameter. Patients were considered ineligible for the studies if they had a target lesion located in an unprotected left main trunk, cardiogenic shock, malignancies or other co-morbid conditions with life expectancy <12 months or that may result in protocol non-compliance or had contraindications or known allergy to antiplatelet therapy, stent components or pregnancy (present, suspected or planned). Patient allocation to each of the treatment groups was in a 2:1 proportion in the ISAR-Absorb MI trial and in equal proportion in the ABSORB STEMI TROFI II trial. The primary endpoints of the ISAR-Absorb MI and ABSORB STEMI TROFI II trials were percentage diameter stenosis at 6- to 8-month coronary angiography and neointimal healing score at 6-month optical coherence tomography, respectively. In both trials, a non-inferiority design served to test the primary study hypothesis.

For patients treated with Absorb, the protocol of ISAR-Absorb MI had no explicit recommendation for lesion preparation, vessel- and device-sizing and for scaffold post-dilation, though pre-dilation was strongly encouraged. In the ABSORB STEMI TROFI II trial manual thrombus aspiration with at least two passages was mandatory to reduce thrombus burden. All patients were pre-treated with aspirin (250 to 500 mg) before PCI in both trials. In all cases, anticoagulation during PCI was accomplished by intra-arterial or intravenous administration of heparin up to a total amount of 100 U/kg body weight or bivalirudin (intravenous bolus of 0.75 mg/kg prior to the start of the intervention, followed by infusion of 1.75 mg/kg per hour for the duration of the procedure). After the intervention, all patients received dual antiplatelet therapy (DAPT) according to recommendation of guidelines-writing authorities.[6] Other cardioactive drugs were prescribed according to standard practice.

Collection of patient-level data

For the purpose of this study, the principal investigators of the ABSORB STEMI TROFI II trial were contacted to provide individual data of participants. After agreement, anonymized data was transferred to the *Deutsches Herzzentrum München, Technische Universität München - Munich, Germany* and merged with that of ISAR-Absorb MI in a single dedicated database. The final dataset was checked for completeness and consistency and compared with the results from prior publications. Principal investigators were directly contacted in case of inconsistencies with the original publications or requirement for additional data. Divergences were resolved by consensus. Data were analysed according to the intention-to-treat principle. The institutional review board or ethics committee at each participating centre approved the studies included in the present analysis, and all patients signed informed, written consent before receiving the assigned treatment in each trial.

Outcome variables

The primary outcome of this analysis was lesion (in-segment) percentage diameter stenosis at repeat coronary angiography 6-8 months after intervention. The main secondary outcome was the device-oriented composite endpoint (DOCE) of cardiac death/target vessel MI/target lesion revascularization (TLR). Other angiographic endpoints of interest were in-device percentage diameter stenosis, late lumen loss (LLL) and binary restenosis. Other clinical endpoints of interest were the composite of death/any MI/all revascularization (patient-oriented composite endpoint, POCE), each individual component of the main secondary outcome and the incidence of definite/probable scaffold or stent thrombosis. Study definitions have been described in detail previously.[4, 5] Clinical follow-up was up to 12 months.

Statistical analysis

See **Appendix**.

RESULTS

A total of 453 patients were enrolled in the two trials (**Supplemental Figure 1**). Of these, 65 patients with NSTEMI and visible thrombus at coronary angiography enrolled in the ISAR-Absorb MI trial were excluded, leaving a number of 388 individuals with STEMI (227 assigned to Absorb and 161 to EES) available for final analyses. Baseline characteristics were well balanced between the treatment groups and matched those typically associated with STEMI patients. In fact, participants were relatively young, overweight, the overwhelming majority being male, and a high proportion having hyperlipidaemia and smoke habit (**Table 1**).

Baseline lesion and procedural characteristics are shown in **Table 2** and were well balanced between the treatment groups. The infarct related vessels comprised more frequently the left anterior descending or the right coronary artery. A complete occlusion of infarct related vessel

was observed in circa 60% of patients. Pre-dilation (78.3% and 63.1%, P= 0.001) and post-dilation (53.3% and 32.3%, P< 0.001) were more common in patients treated with Absorb versus EES. After PCI the minimal lumen diameter was non-significantly smaller with Absorb versus EES (2.54±0.41 mm versus 2.60±0.43 mm, P= 0.22) whilst the residual percentage diameter stenosis was significantly higher with Absorb compared with EES (14.1±8.6% versus 12.6±5.5%, P= 0.03). Six (2.6%) patients allocated to Absorb did not receive the assigned stent and were treated with EES. Two (1.2%) patients allocated to EES did not receive the assigned stent and were treated with Absorb. At discharge, all patients received thienopyridines (ticagrelor: 219 [56.7%]; prasugrel: 128 [33.2%]; clopidogrel: 39 [10.1%]). The discharge therapy was unknown in 2 (0.5%) patients.

Angiographic follow-up was available for 332 (85.6%) patients without significant difference between treatment groups (P= 0.72). The median time to angiographic follow-up was shorter with Absorb - 230 (208, 278) days - as compared to EES - 241 (211, 307) days - (P= 0.03). The **Table 3** resumes the angiographic outcomes of the study. The primary outcome of lesion diameter stenosis was 22.8±9.8% with Absorb versus 23.6±11.2% with EES, with a mean difference of -0.8% [-3.18, 1.48], P= 0.47 (**Figure 1**). The analysis stratified by trial revealed a significant interaction between the treatment effect and the primary angiographic outcome (P= 0.002). In fact, lesion diameter stenosis was 23.7±11.4% with Absorb versus 29.3±12.1% with EES (P= 0.006) in the ISAR-Absorb MI trial, and 21.6±7.3% with Absorb versus 20.2±9.0% with EES (P= 0.27) in the ABSORB STEMI TROFI II trial.

Absorb was associated with a higher degree in-device diameter stenosis as compared to EES (17.3±9.9% versus 15.9±11.1%, mean difference -1.4% [-0.89, 3.78], P= 0.019). LLL was comparable at in-segment (0.20±0.36 mm with Absorb versus 0.24±0.35 mm with EES, P= 0.37; **Supplemental Figure 2A**) and in-device measurements (0.16±0.26 mm with Absorb versus 0.13±0.36 mm with EES, P= 0.43). Overall, binary restenosis was observed in 9

patients (4 patients with Absorb and 5 patients with EES, P= 0.40). There were no cases of complete restenotic occlusion at follow-up.

Clinical follow-up out to 12 months was available in all patients, with a similar duration among treatment groups (P= 0.59). The clinical outcomes are resumed in **Table 4**. DOCE occurred in 12 (5.3%) patients treated with Absorb versus 9 (5.6%) with EES (HR, 95% CIs= 0.95 [0.40, 2.26], P= 0.91; **Figure 2**). Findings were consistent in the analysis stratified by trial (P= 0.67).

POCE occurred in 36 (15.9%) patients treated with Absorb versus 24 (14.9%) with EES (HR, 95% CIs= 1.08 [0.64, 1.81], P= 0.76; **Supplemental Figure 2B**). Cardiac death occurred in 5 (2.2%) patients treated with Absorb versus 2 (1.2%) with EES (HR, 95% CIs= 1.77 [0.35, 8.96], P= 0.49). Target vessel MI occurred in 2 (1.1%) patients treated with Absorb versus 2 (1.2%) with EES (HR, 95% CIs= 0.71 [0.10, 4.99], P= 0.73). TLR occurred in 7 (3.1%) patients with Absorb versus 7 (4.4%) patients with EES (HR, 95% CIs= 0.71 [0.25, 2.03], P= 0.53; **Supplemental Figure 2C**). Definite/probable stent or scaffold thrombosis occurred in 4 (1.8%) patients with Absorb versus 2 (1.2%) patients with EES (HR, 95% CIs= 1.41 [0.26, 7.63], P= 0.69).

The treatment effect for primary angiographic and main secondary clinical outcomes had no interaction with age (P for interaction - $P_{int} \geq 0.24$), gender ($P_{int} \geq 0.37$), diabetic status ($P_{int} \geq 0.15$), thienopyridines at discharge ($P_{int} \geq 0.66$), presence or absence of TIMI 0 flow pre PCI ($P_{int} \geq 0.26$), thrombus aspiration ($P_{int} \geq 0.51$), pre-dilation ($P_{int} \geq 0.06$), post-dilation ($P_{int} \geq 0.19$) and total stented length ($P_{int} \geq 0.69$; **Supplemental table**).

DISCUSSION

In this analysis, we pooled the largest cohort of STEMI patients receiving a PCI with either Absorb or EES among randomized trials with angiographic follow-up. The main findings were that: i) Absorb was comparable to EES in terms of angiographic outcomes at 6 to 8 months and in terms of clinical outcomes at 12 months; ii) in the subgroup analysis there was no evidence of interaction between several clinical, angiographic and procedural features and treatment effect for primary angiographic and main secondary outcomes. However, some issues need to be considered when interpreting the data.

Lesion diameter stenosis was chosen as the primary angiographic outcome. Previous investigations have shown that this surrogate endpoint represents a reliable parameter of device efficacy.[7] In this regard, the overall comparable angiographic performance of Absorb and EES observed in this study is noteworthy. Indeed, earlier trials including patients with predominantly stable CAD and/or moderately complex anatomies found inferior angiographic efficacy of Absorb versus EES after a follow-up duration comparable to that accumulated for the present study.[2] The mechanical properties of Absorb are likely to play a major role: in particular, the expansion capability of current Absorb could not approximate that of metallic stents,[8] failing more often in complex coronary anatomies.[9] In contrast, STEMI lesions typically consist of less bulky, lipid-rich plaques with a necrotic core and superimposed thrombi, without relevant calcifications. By expanding more easily, these lesions appear more suitable to scaffolding with BRS. Consistent with previous data [10] we found a lower minimum lumen diameter after PCI with Absorb as compared to EES, reflecting the intrinsic limitation of this technology. However, the treatment groups did not differ for this parameter at angiographic follow-up, suggesting a relatively stable mechanical behaviour of Absorb in STEMI patients, without instances of late recoil as previously observed.[11]

Second, the risk for DOCE at 12 months was similar with Absorb or EES. However, this analysis is underpowered to detect potential clinical differences between the treatment groups. Previous registry data demonstrated a poor 1-year clinical performance with Absorb in STEMI, mainly attributable to more frequent scaffold thrombosis within 30 days after implantation.[12] The lack of optimized technique for Absorb implantation (pre-dilation, appropriate vessel sizing, and high-pressure post-dilation) was deemed responsible for this increased risk.[13] At the same time, some experts proposed to intensify DAPT after Absorb implantation.[14] Although we recognize the importance of proper implantation technique to improve the acute and late performance of stents and scaffolds, this pooled analysis of randomized trials did not find a significant interaction between pre- and post-deployment dilation rates and the treatment effect for main outcomes. Moreover, the use of more potent ADP-receptor antagonists did not impact angiographic and clinical efficacy of Absorb versus EES in this study, though approximately 90% of our cohort received highly effective antiplatelet drugs as standard treatment for STEMI.

Third, our data lends support to device iteration and appropriate lesion selection as prerequisite for future BRS technologies. Indeed, two recent randomized trials[15, 16] including patients with higher anatomical complexity found Absorb associated with higher risk of thrombosis at 1 year despite the adoption of specific implantation protocols and relatively high proportions of DAPT after PCI. In this regard, although the platform investigated in this analysis is no longer available for clinical use, several BRS are in development or under investigation.[17] Thus, the present study may serve as evidence base for future trials investigating improved or new BRS in STEMI, pending the demonstration of at least non-inferiority in comparison with current high-performance metallic DES.[18]

Study limitations: The current study presents a number of limitations. First, this analysis has limitations inherent to pooled analyses and reflects the flaws of the original trials. Amongst others, the studies included were open label, which represents a source of bias. In addition they focused on a single BRS platform. Second, angiographic data was collected by two different core labs and this may partially account for the significant interaction observed between treatment effect and primary angiographic outcome. Third, this study was not powered to evaluate the performance of Absorb versus EES in specific subgroups of patients; in this regard, the present analysis remains exploratory in nature. Finally, the clinical follow-up was limited to 1 year and longer follow-up remains crucial for two reasons: to definitively ascertain the durability of Absorb and to address whether BRS technology has late advantages compared to current metallic DES in STEMI.

CONCLUSIONS

In STEMI patients undergoing a percutaneous revascularization, this pooled analysis of individual participant data from two randomized trials suggests comparable performance of Absorb and EES at angiographic and clinical follow-up. The results remained consistent across several subgroups of patients. The long-term durability of Absorb and the extent to which newer BRS platforms might have a potential role in STEMI remains to be further studied.

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TABLES

Table 1. Baseline clinical characteristics

	Absorb	EES	P value
Patients	227	161	
Age	60.0±10.9	60.3±10.0	0.76
Body mass index, kg/m^2	27.0±3.9	27.4±4.0	0.21
Female gender	43 (18.9)	31 (19.2)	0.94
Diabetes mellitus	45 (19.8)	25/159 (15.7)	0.30
Insulin dependent	32 (14.1)	14/159 (8.8)	
Hypertension	104/224 (46.4)	72/159 (45.3)	0.82
Hyperlipidemia	110/224 (49.1)	85/158 (53.8)	0.36
Smoking	136 (59.9)	98/159 (61.6)	0.73
Prior MI	12/226 (5.3)	6 (3.7)	0.62
Prior PCI	4/226 (1.7)	3 (1.8)	>0.99
Killip class			0.92
I	214 (94.3)	155 (96.3)	
II	9 (3.9)	4 (2.5)	
III	2 (0.9)	1 (0.6)	
IV	2 (0.9)	1 (0.6)	

Data shown as mean±SD or number (percentage); denominators are provided when they differ from the total number of patients. MI: myocardial infarction; PCI: percutaneous coronary intervention

Table 2. Baseline angiographic and procedural characteristics

	Absorb	EES	P value
Culprit lesions	227	161	
Target vessel			0.30
Left anterior descending	99 (43.6)	71 (44.1)	
Left circumflex	35 (15.9)	18 (11.2)	
Right coronary artery	92 (40.5)	72 (44.7)	
Bifurcation	23/225 (10.2)	18 (11.2)	0.76
TIMI flow, pre PCI			0.61
0	131/226 (57.9)	103/160 (64.4)	
1	11/226 (4.9)	6/160 (3.7)	
2	30/226 (13.3)	20/160 (12.5)	
3	54/226 (23.9)	31/160 (19.4)	
Procedural anticoagulation therapy			0.40
Heparin	196 (86.3)	136 (84.5)	
Bivalirudin	7 (3.1)	10 (6.2)	
Heparin plus bivalirudin	18 (8.0)	13 (8.1)	
Not specified	6 (2.6)	2 (1.2)	
Pre-dilation	177/226 (78.3)	101/160 (63.1)	0.001
Nominal diameter of first balloon (mm)	2.7±0.5	2.6±0.5	0.15
Balloon pressure, max (atm)	14.0±3.8	13.5±3.4	0.29
Thrombusaspiration	127 (55.9)	98 (60.9)	0.33
Stent diameter, max (mm)	3.2±0.3	3.2±0.4	0.28
Number of primary stents used	1.08±0.3	1.08±0.3	0.79
Total stented length (mm)	24.8±11.3	26.7±14.0	0.17
Post-dilation	121 (53.3)	52 (32.3)	<0.001
Nominal diameter of largest balloon (mm)	3.3±0.4	3.3±0.5	0.95
Balloon pressure, max (atm)	16.8±3.9	16.8±4.1	0.99
TIMI flow, post PCI			0.50
0	-	1 (0.6)	
1	-	-	
2	5/226 (2.2)	5 (3.1)	
3	221/226 (97.8)	155 (96.3)	

Quantitative coronary angiography analysis

Pre-intervention			
Reference diameter (mm)	2.90±0.43	2.92±0.47	0.72
Minimal lumen diameter (mm)	0.28±0.39	0.25±0.40	0.39
Diameter stenosis (%)	89.8±13.7	91.1±14.1	0.40
Post-intervention			
Minimal lumen diameter (mm)	2.54±0.41	2.60±0.43	0.22
Diameter stenosis (%)	14.1±8.6	12.6±5.5	**0.03**

Data shown as mean±SD or number (percentage); denominators are provided when they differ from the total number of patients. EES: everolimus-eluting stent; PCI: percutaneous coronary intervention; TIMI: Thrombolysis in Myocardial Infarction

Table 3. Angiographic follow-up at 6-8 months

	Absorb	EES	P value
Lesions/patients assessed	193	139	
Days to angiographic follow-up	230 (208, 278)	241 (211, 307)	**0.03**
In-segment analysis			
late lumen loss (mm)	0.20±0.36	0.24±0.35	0.37
minimal lumen diameter (mm)	2.21±0.44	2.17±0.47	0.42
diameter stenosis (%)	22.8±9.8	23.6±11.2	0.47
binary restenosis	4 (2.1)	5 (3.5)	0.40
In-device analysis			
late lumen loss (mm)	0.16±0.26	0.13±0.36	0.43
minimal lumen diameter (mm)	2.40±0.46	2.43±0.51	0.49
diameter stenosis (%)	17.3±9.9	15.9±11.1	**0.019**

Data shown as mean±SD or median (IQR) or number (percentage). EES: everolimus-eluting stent

Table 4. Clinical results at 12 months

	Absorb	EES	Hazard ratio [95% Confidence intervals]	P value
Patients	227	161		
Death	6 (2.6)	2 (1.2)	2.12 [0.44, 10.14]	0.36
Cardiac death	5 (2.2)	2 (1.2)	1.77 [0.35, 8.96]	0.49
Device-oriented outcomes				
definite or probable device thrombosis	4 (1.8)	2 (1.2)	1.41 [0.26, 7.63]	0.69
definite device thrombosis	3 (1.3)	2 (1.2)	1.05 [0.17, 6.33]	0.95
probable device thrombosis	1 (0.5)	0	N/A	0.89
target vessel myocardial infarction	2 (1.1)	2 (1.2)	0.71 [0.10, 4.99]	0.73
target lesion revascularization	7 (3.1)	7 (4.4)	0.71 [0.25, 2.03]	0.53
composite of cardiac death, target-vessel myocardial infarction, target lesion revascularization (device-oriented composite endpoint)	12 (5.3)	9 (5.6)	0.95 [0.40, 2.26]	0.91
Patient-oriented outcomes				
myocardial infarction	5 (2.2)	4 (2.5)	0.88 [0.23, 3.31]	0.86
target vessel revascularization	13 (5.8)	12 (7.5)	0.77 [0.35, 1.69]	0.52
non target vessel revascularization	20 (9.0)	13 (8.2)	1.10 [0.55, 2.22]	0.77
all revascularization	29 (13.0)	22 (13.7)	0.95 [0.54, 1.66]	0.87

composite of death, myocardial infarction, any revascularization (patient-oriented composite endpoint)	36 (15.9)	24 (14.9)	1.08 [0.64, 1.81]	0.76

Data shown as number (percentages are Kaplan-Meier estimates). EES: everolimus-eluting stent; N/A: not applicable

FIGURE LEGENDS

Figure 1. Primary outcome: lesion percentage diameter stenosis at 6- to 8-month angiographic follow-up. Cumulative frequency distribution for lesion diameter stenosis at follow-up angiography. P-values are presented unadjusted and stratified by trial.

Figure 2. Main secondary outcome: device-oriented composite endpoint. Survival analysis curves for the composite of cardiac death, target vessel myocardial infarction and target lesion revascularization. P-values are derived from Cox proportional hazards models and are presented unadjusted and stratified by trial.

Figure 1.

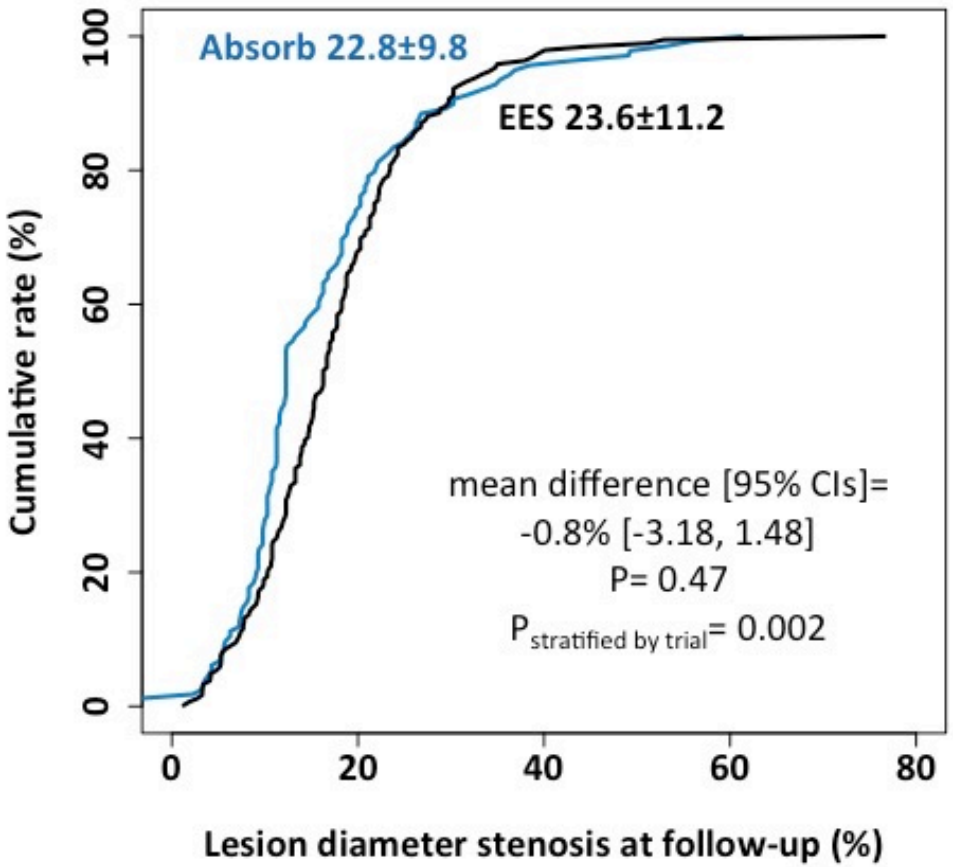
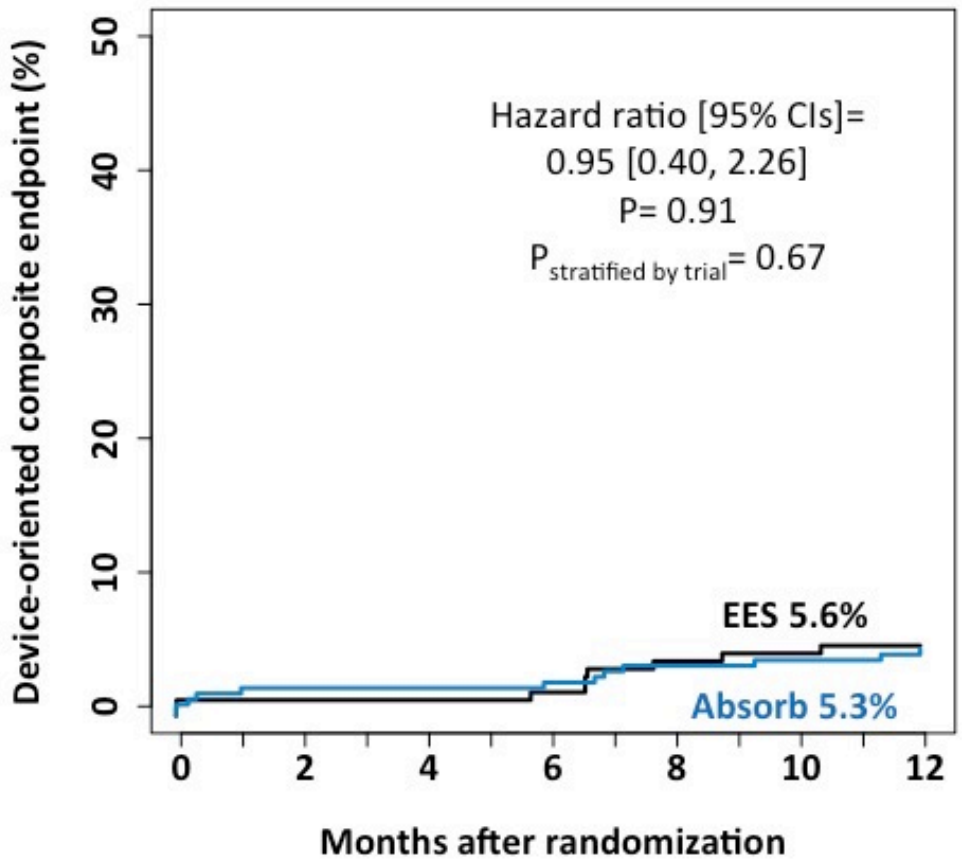


Figure 2.



Patients at risk								
	Absorb	227	221	220	219	215	214	214
	EES	161	159	159	158	154	153	152

APPENDIX

Angiographic and clinical outcomes of STEMI patients treated with bioresorbable or metallic everolimus-eluting stents.

A pooled analysis of individual patient data from 2 randomized trials

Statistical analysis

The data is presented as counts (proportions), means±SD or median (interquartile range). Categorical variables were compared between treatment groups using chi-squared test or Fisher's exact test (where at least one expected cell value <5). Continuous variables were compared using t-test's or Wilcoxon rank sum test in case of skewed distribution. Time-to-event analyses are displayed as counts and rates computed according to the Kaplan-Meier method, with risk estimates presented as hazard ratios (HRs) with 95% Confidence intervals [CIs]. Two-way analysis of variance stratified by trial for the primary outcome and Cox proportional hazards models stratified by trial for the main secondary outcomes served to evaluate the consistency of the treatment effect across several subgroups of patients defined by age (under versus above the median value), gender, diabetic status, thienopyridines at discharge, Thrombolysis In Myocardial Infarction (TIMI) 0 flow pre PCI, thrombus aspiration, pre-dilation, post-dilation and total stented length (under versus above the median value). All analyses were performed in R (*version 3.5.0; R Foundation for Statistical Computing, Vienna, Austria*).

Supplemental table. Subgroup analysis for primary angiographic and main secondary clinical outcomes

	Lesion diameter stenosis Mean difference [95% Confidence intervals]			DOCE Hazard ratio [95% Confidence intervals]		
	Absorb versus EES	**P value**	**P value $_{int}$**	**Absorb versus EES**	**P value**	**P value $_{int}$**
Trial			**0.002**			0.43
ISAR-Absorb MI	-5.6 [-9.62, -1.67]	0.006		0.65 [0.23, 1.87]		
ABSORB STEMI TROFI II	1.4 [-1.09, 3.85]	0.27		1.37 [0.31, 6.08]		
Age			0.49			0.24
Young (≤59 years)	-0.8 [-4.04, 2.44]	0.63		0.50 [0.11, 2.21]	0.38	
Old (>59 years)	-0.7 [-4.08, 2.81]	0.72		1.35 [0.45, 4.00]	0.59	
Gender			0.37			0.49
Female	-5.2 [-10.90, 0.61]	0.08		0.47 [0.08, 2.70]	0.41	
Male	-0.1 [-2.58, 2.54]	0.98		1.19 [0.43, 3.29]	0.73	
Diabetes status			0.50			0.15
Diabetic	-2.3 [-8.72, 3.94]	0.45		3.61 [0.50, 26.13]	0.23	
Non-diabetic	-0.4 [-2.81, 2.04]	0.75		0.63 [0.21, 1.86]	0.41	
Thienopyridines at discharge			0.99			0.66
Prasugrel/ticagrelor	-1 [-3.42, 1.50]	0.44		1.18 [0.48, 2.88]	0.71	
Clopidogrel	-1.2 [-7.62, 5.39]	0.72		N/A	0.92	
TIMI 0, pre PCI			0.26			0.57
Yes	-2.2 [-4.94, 0.65]	0.13		1.11 [0.35, 3.51]	0.85	
No	1.2 [-2.79, 5.32]	0.54		0.74 [0.20, 2.77]	0.66	
Thrombus aspiration			0.56			0.51
Yes	-0.7 [-3.37, 2.14]	0.66		1.32 [0.32, 5.51]	0.70	
No	-1.7 [-5.68, 2.32]	0.41		0.72 [0.24, 2.15]	0.56	
Pre-dilation			0.06			0.73

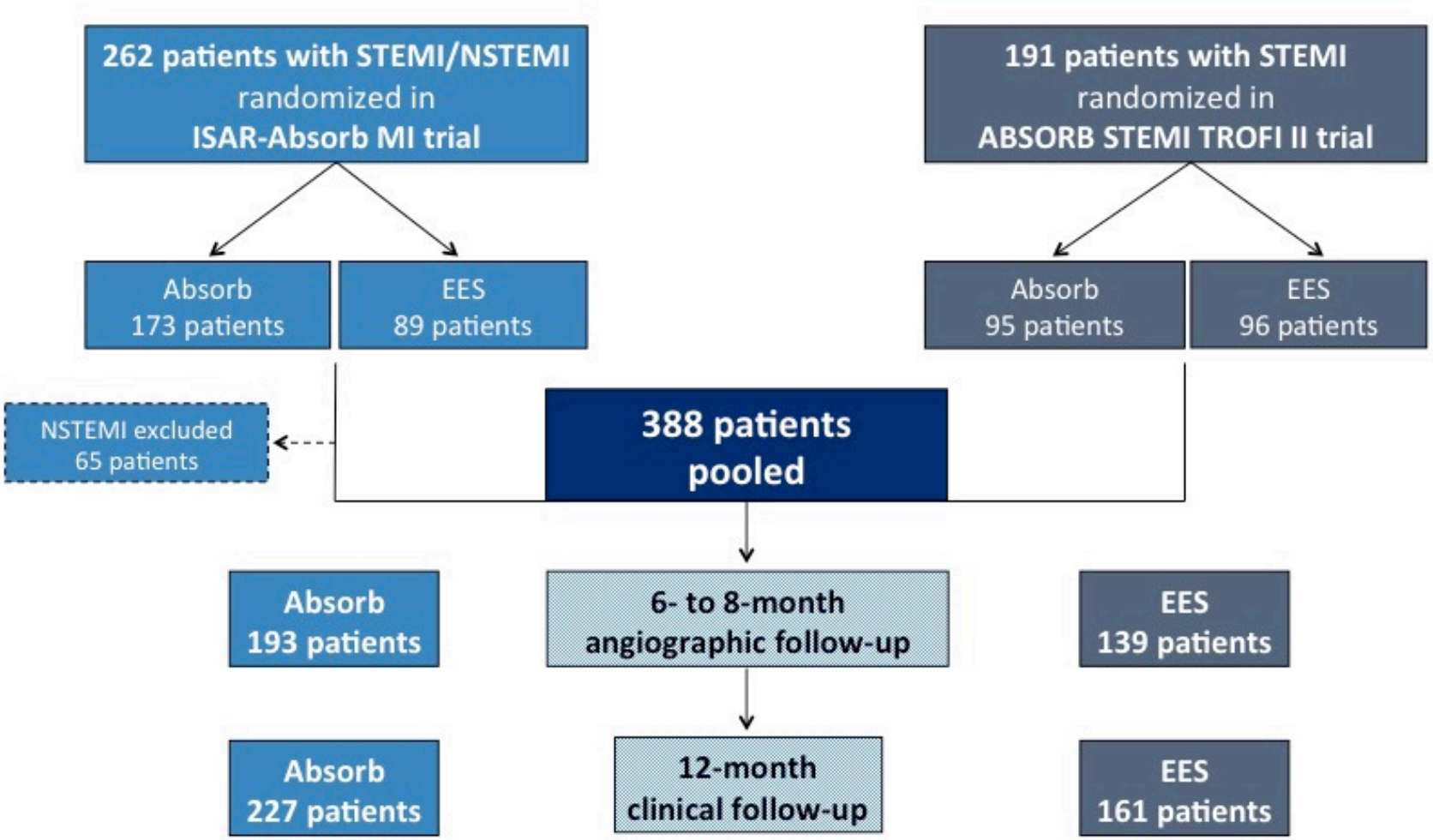
Yes	-2.8 [-5.82, 0.21]	0.07		0.79 [0.32, 1.96]	0.61	
No	0.9 [-2.42, 4.28]	0.58		1.18 [0.07, 18.85]	0.90	
Post-dilation			0.19			0.23
Yes	-3.8 [-8.20, 0.70]	0.10		0.50 [0.16, 1.61]	0.25	
No	-0.3 [-2.84, 2.20]	0.80		1.58 [0.45, 5.55]	0.48	
Total stented length			0.82			0.69
Short (≤23 mm)	-0.2 [-3.18, 2.80]	0.90		1.21 [0.29, 5.07]	0.79	
Long (>23 mm)	-1.7 [-5.45, 1.99]	0.36		0.98 [0.31, 3.10]	0.98	

P value $_{int}$: P value for interaction. ABSORB STEMI TROFI II: Comparison of the ABSORB^{TM} Everolimus Eluting Bioresorbable Vascular Scaffold System With a Drug- Eluting Metal Stent (Xience^{TM}) in Acute ST-Elevation Myocardial Infarction; DOCE: device-oriented clinical endpoint; EES: everolimus-eluting stent; ISAR-Absorb MI: Intracoronary Scaffold Assessment a Randomised Evaluation of Absorb in Myocardial Infarction; PCI: percutaneous coronary intervention; TIMI: Thrombolysis in Myocardial Infarction.

SUPPLEMENTAL FIGURE LEGENDS

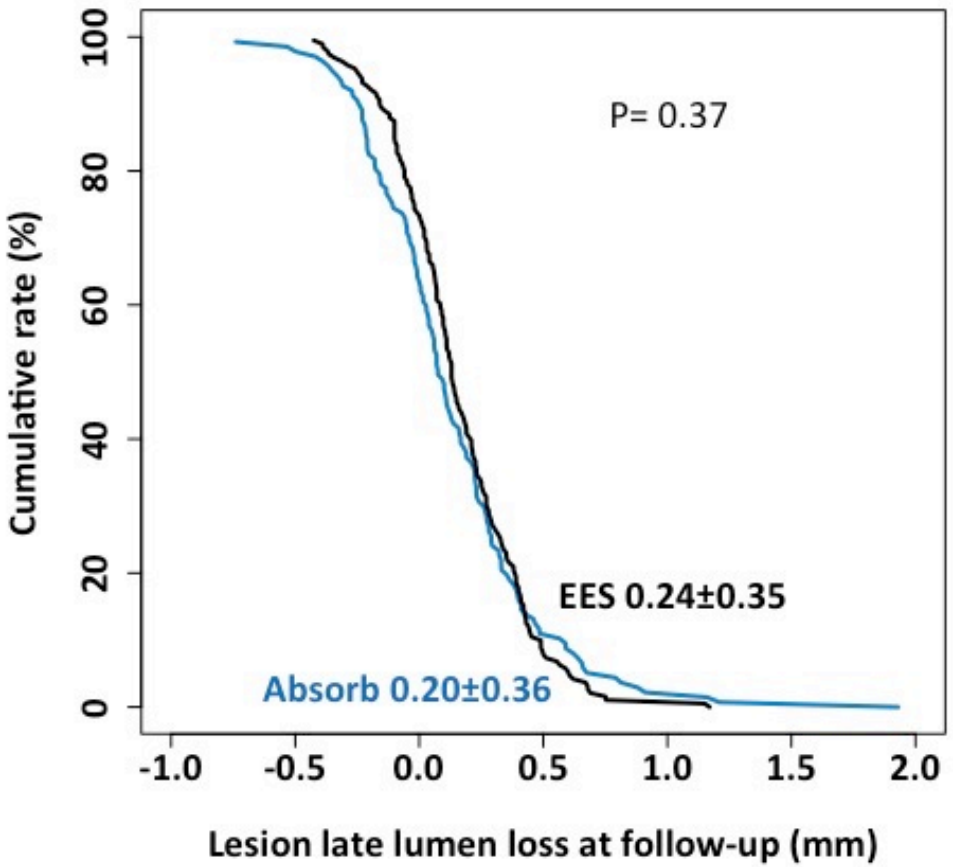
S-Figure 1. Flow chart of the analysis. ABSORB STEMI TROFI II: Comparison of the ABSORB^{TM} Everolimus Eluting Bioresorbable Vascular Scaffold System With a Drug- Eluting Metal Stent (Xience^{TM}) in Acute ST-Elevation Myocardial Infarction randomized trials; ISAR-Absorb MI: Intracoronary Scaffold Assessment a Randomised Evaluation of Absorb in Myocardial Infarction; EES: everolimus-eluting stent; (N)STEMI: (Non) ST-segment elevation myocardial infarction.

S-Figure 2. Main secondary outcomes. A) Lesion late lumen loss at 6- to 8-month angiographic follow-up: cumulative frequency distribution for lesion late lumen loss at follow-up angiography. **B) Patient-oriented composite endpoint** and **C) Target lesion revascularization:** survival analysis curves for the composite of death, any myocardial infarction and all revascularization. P-values are derived from Cox proportional hazards models. Other abbreviations are as in the **Supplemental Figure 1**.

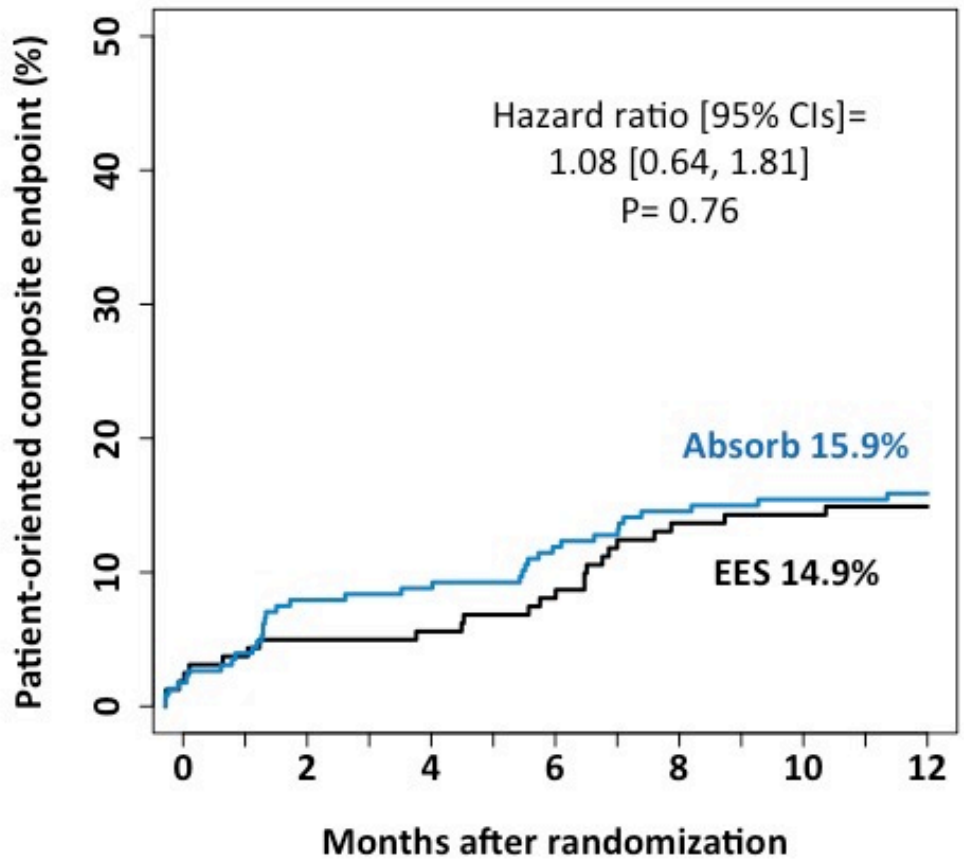


S-Figure 1.

S-Figure 2A.

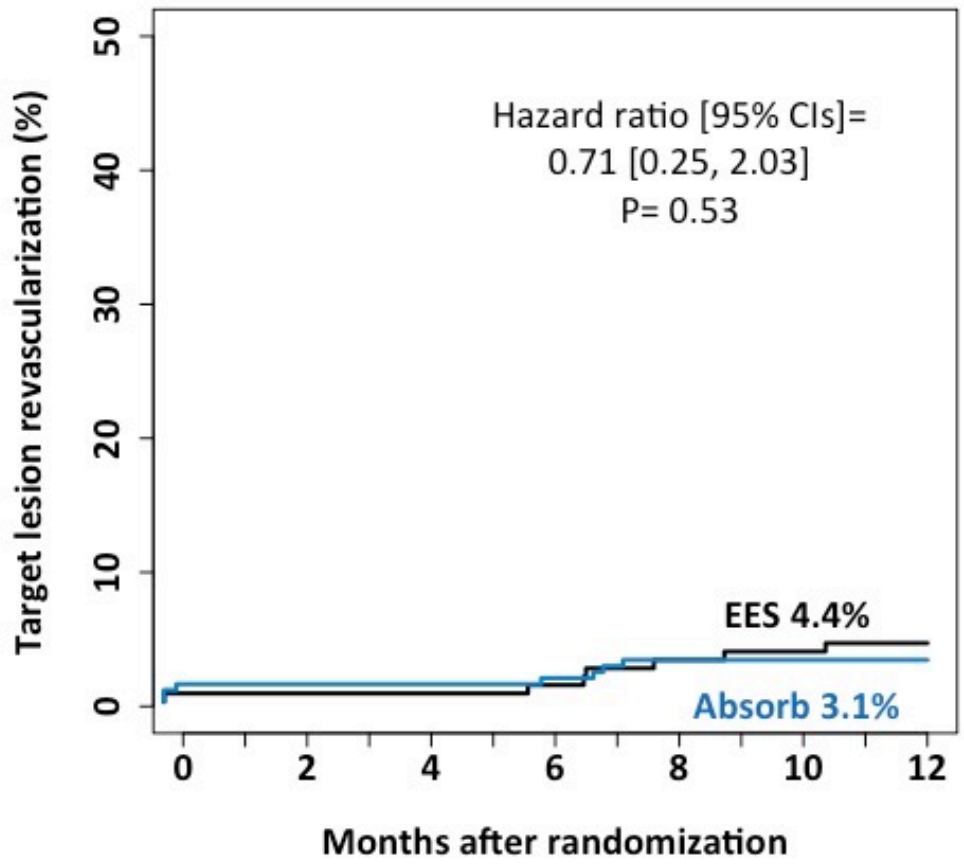


S-Figure 2B.



Patients at risk	Absorb	227	209	207	201	193	191	191
	EES	161	153	152	148	139	138	137

S-Figure 2C.



Patients at risk	Absorb	227	221	220	219	215	214	214
	EES	161	159	159	158	155	154	153