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Final 5-Year Results in Randomized Japanese Patients Implanted With a Thin-Strut, Bioabsorbable, Polymer-Coated, Everolimus-Eluting SYNERGY Stent (From the EVOLVE II Study)

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Background: SYNERGY is a thin-strut, platinum-chromium metal alloy stent with an ultrathin abluminal everolimus-eluting bioabsorbable polymer. EVOLVE II was a global randomized controlled trial that enrolled 1,684 patients treated with either a SYNERGY or durable polymer PROMUS Element Plus (PE+) everolimus-eluting stent, including 155 patients from Japanese sites. This substudy analyzed 5-year clinical outcomes in the Japanese and non-Japanese cohorts.

Methods and Results: Patients aged ≥18 years with ≤3 native coronary artery lesions (reference vessel diameter ≥2.25–≤4.00 mm; length ≤34 mm) in ≤2 major vessels were randomized 1 : 1 to receive either SYNERGY (n=74 patients in Japan) or PE+ (n=81 patients in Japan). Five-year target lesion failure (TLF) was observed in 8.3% SYNERGY- and 11.2% PE+-treated patients (P=0.54). There were no cardiac deaths, and rates of target lesion revascularization and myocardial infarction were comparable between treatment arms. One patient in the SYNERGY arm experienced a very late definite stent thrombosis (ST); no ST occurred in the PE+ arm (P=0.30). Despite differences in baseline clinical and lesion characteristics, the 5-year TLF rates were not significantly different in SYNERGY-treated patients either in (8.3%) or outside (14.8%) Japan (P=0.14).

Conclusions: In Japanese patients with coronary artery disease, SYNERGY showed comparable efficacy to PE+, with low rates of adverse events over 5 years. Similarly, 5-year clinical outcomes were favorable in Japanese vs. non-Japanese patients implanted with SYNERGY.

Key Words: Bioabsorbable polymer; Coronary artery disease; Everolimus-eluting stent

Drug-eluting stents (DES) with antiproliferative drugs delivered from a durable polymer have significantly reduced angiographic and clinical measures of restenosis compared with bare metal stents.[1,2] However, the permanent presence of a durable polymer coating on DES may delay arterial healing, induce local inflammation, and increase the risk of stent thrombosis (ST).[2,3] Recent stent technologies incorporate a biodegradable polymer that leaves behind a bare metal platform after complete resorption, thereby offering the potential of improved arterial healing and reduced occurrence of late or very late ST. Clinical data from these new-generation DES have shown promising results, including reduced rates of revascularization and thrombotic events.[4–7]

The thin-strut platinum-chromium SYNERGY stent (Boston Scientific Corporation, Marlborough, MA, USA) has an abluminal coating of everolimus in an ultrathin bioabsorbable poly-D,L-lactide-proglyolide co-glycolide

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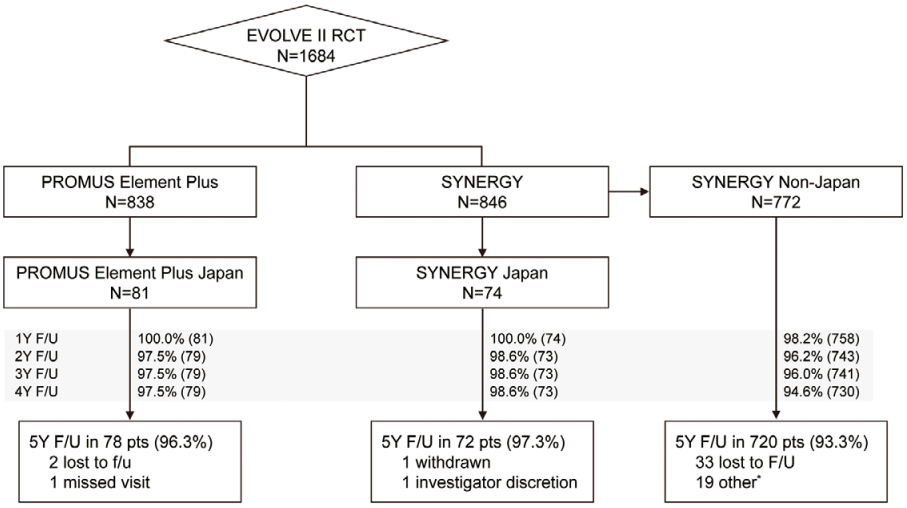

Figure 1. EVOLVE II (Japan) enrollment and follow-up. *Includes investigator discretion, patient withdrew consent, and missed visit. pts, patients; RCT, randomized control trial.

(PLGA) polymer.[8,9] Everolimus is released over a period of approximately 90 days and the polymer is completely degraded shortly thereafter (~120 days),[10] which may promote rapid arterial healing. The EVOLVE II randomized controlled trial (RCT) demonstrated non-inferiority of SYNERGY to the durable polymer PROMUS Element everolimus-eluting stent for 1-year target lesion failure (TLF).[11] Comparable outcomes were maintained through 5 years of follow-up, including a favorably low incidence of ST.[11]

Previous studies have reported differences in stent deployment techniques and medical management in Japan, particularly greater use of post-dilatation and higher balloon pressure than in other countries.[12,13] In addition, due to potential differences in lifestyle (medical history, food, weight, body mass index [BMI]), ethnicities and patient demographics, it is important to investigate the clinical impact of bioabsorbable polymer DES in a Japanese population. This paper describes the final 5-year outcomes in the Japanese cohort of the EVOLVE II RCT after implantation of either the SYNERGY or PROMUS Element Plus stents.

Methods

Study Design and Patient Selection

EVOLVE II was a prospective multicenter single-blinded non-inferiority RCT that enrolled patients worldwide. Detailed methods of the RCT have been described previously.[14] Briefly, patients aged ≥18 years with ≤3 native coronary lesions in ≤2 major epicardial vessels (reference vessel diameter ranging from ≥2.25 to ≤4.0 mm and lesion length ≤34 mm) were enrolled. Eligible patients had target lesion stenosis ≥50% and <100% with Thrombolysis in Myocardial Infarction (TIMI) flow >1 and/or a stenosis ≥70%, abnormal fractional flow reserve, elevated cardiac biomarkers, or an abnormal stress or imaging stress test. Patients with left main disease, chronic total occlusion, ST-elevation myocardial infarction (STEMI), vein graft disease, or in-stent restenosis were excluded. After meeting the study selection criteria, patients were randomized 1:1 to SYNERGY or PROMUS Element Plus stents.

This study was approved by the institutional review board at each site prior to enrollment and complied with the principles of the Declaration of Helsinki, the US Food and Drug Administration's Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance, and all applicable local and federal regulations. The EVOLVE II RCT is registered with Clinicaltrials.gov (ID: NCT01665053).

Device Description and Procedure

The SYNERGY stent consists of a thin strut (74–81 μm), platinum-chromium platform coated abluminally with an ultrathin (4 μm) bioabsorbable everolimus-eluting (100 μm/cm^2) PLGA polymer. Everolimus is eluted within 3 months and PLGA degrades within 4 months, leaving behind the biologically inert bare metal platform.[10] The control stent used in the EVOLVE II RCT was a durable polymer PROMUS Element Plus everolimus-eluting platinum-chromium coronary stent.[15] The study device and implantation procedure have been described previously.[8]

Dual antiplatelet therapy (DAPT) with aspirin and a $P2Y_{12}$ inhibitor was prescribed for a minimum of 6 months after the procedure (1 year in patients not at high risk of bleeding). An independent core laboratory evaluated all baseline and follow-up angiograms (Beth Israel Deaconess Medical Center, Boston, MA, USA). Clinical follow-up was required in hospital and 30 days and 6, 12, and 18 months after PCI, and then annually between 2 and 5 years.

Study Endpoints

The primary endpoint of the EVOLVE II RCT was 12-month TLF (ischemia-driven target lesion revascularization [TLR], target vessel-related myocardial infarction [TV-MI], or cardiac death).[14,16] Additional prespecified clinical endpoints of target vessel revascularization (TVR),

Table 1. Baseline Characteristics

	PROMUS Element Plus (n=81 patients)	SYNERGY (n=74 patients)	P value
Baseline characteristics			
Male sex	74.1 (60/81)	77.0 (57/74)	0.67
Age (years)	66.83±9.91 (81)	67.42±12.02 (74)	0.74
BMI (kg/m²)	24.75±3.37 (81)	25.07±3.40 (74)	0.56
Medical history			
Current smoker	23.5 (19/81)	14.9 (11/74)	0.18
Diabetes	29.6 (24/81)	29.7 (22/74)	0.99
Hyperlipidemia	82.7 (67/81)	75.7 (56/74)	0.28
Hypertension	72.8 (59/81)	79.7 (59/74)	0.31
Unstable angina	11.1 (9/81)	12.2 (9/74)	0.84
Myocardial infarction	16.0 (13/81)	14.9 (11/74)	0.84
Congestive heart failure	19.8 (16/81)	18.9 (14/74)	0.89
Multivessel disease	28.8 (23/80)	29.7 (22/74)	0.89
Previous PCI	38.3 (31/81)	41.9 (31/74)	0.65
Peripheral vascular disease	1.2 (1/81)	5.4 (4/74)	0.19
Silent ischemia	21.8 (17/78)	23.3 (17/73)	0.83
Target vessel treated[A]			
No. lesions	99	85	
LAD	46.5 (46/99)	47.1 (40/85)	0.94
LCx	17.2 (17/99)	20.0 (17/85)	0.62
RCA	36.4 (36/99)	32.9 (28/85)	0.63
Target lesions treated	1.22±0.42 (81)	1.15±0.36 (74)	0.24
2 lesions	22.2 (18/81)	14.9 (11/74)	0.24
Target lesion characteristics[A]			
RVD (mm)	2.65±0.49 (99)	2.71±0.44 (85)	0.32
<2.25 mm	22.2 (22/99)	15.3 (13/85)	0.23
MLD (mm)	0.86±0.31 (99)	0.91±0.27 (85)	0.23
Diameter stenosis (%)	67.16±11.18 (99)	66.19±9.08 (85)	0.53
Lesion length (mm)	15.85±7.05 (99)	16.86±8.28 (85)	0.37
Modified ACC/AHA Type B2/C	76.8 (76/99)	87.1 (74/85)	0.07

Intent-to-treat analysis. Values are given as percentages (n/N) or as the mean ± SD. P values were calculated using Student's t-tests for continuous variables and the Chi-squared test for discrete variables. [A]Per lesion. ACC/AHA, American College of Cardiology/American Heart Association; BMI, body mass index; LAD, left anterior descending; LCx, left circumflex; MLD, minimum lumen diameter; PCI, percutaneous coronary intervention; RVD, reference vessel diameter.

target vessel failure (TVF; composite of ischemia-driven TVR, TV-MI, or cardiac death related to the target vessel), all-cause death, myocardial infarction (MI; third universal definition),[17] and Academic Research Consortium (ARC)-defined ST[17] were evaluated over a 5-year follow-up period. A clinical events committee reviewed and adjudicated all major adverse events. Technical success rate was defined as successful delivery and deployment of the study stent to the target vessel, without balloon rupture or stent embolization, with a post-procedure diameter stenosis of <30% and TIMI 3 flow in the target lesion (as assessed visually by the treating physician). Clinical procedural success was defined as post-procedural diameter stenosis <30%, TIMI 3 flow in all target lesions, and the absence of in-hospital MI, TVR, or cardiac death.

Statistical Analysis

Clinical outcomes were evaluated by the Kaplan-Meier method. Hazard ratios (HRs) and P values were evaluated using the Wald confidence interval (CI) and log-rank test, respectively. Discrete variables are reported as percentages (%), and the significance of differences was assessed using Chi-squared or Fisher exact tests. Continuous variables are provided as the mean±SD and were compared using Student's t-test. Statistical analyses were conducted using SAS® Version 9.0 (SAS Institute, Cary, NC, USA).

Results

Patients and Clinical Follow-up

The EVOLVE II RCT enrolled 1,684 patients at 125 sites globally. Of these patients, 155 were Japanese: 74 randomized to the SYNERGY arm and 81 randomized to the PROMUS Element Plus arm (**Figure 1**). Clinical follow-up at 5 years was completed in 97% SYNERGY- and 96% PROMUS Element Plus stent-treated patients. In all, 772 non-Japanese patients were implanted with the SYNERGY stent and 720 patients had follow-up data available at 5 years (**Figure 1**).

In Japanese patients, the baseline clinical and quantitative coronary angiographic lesion characteristics were well balanced between the treatment arms (**Table 1**). The mean

Table 2. Procedural and Post-Procedural Characteristics

	PROMUS Element Plus (n=99 lesions, n=81 patients)	SYNERGY (n=86 lesions, n=74 patients)	P value
Procedural characteristics			
Technical success[A] (%)	99.0	100	1.00
Clinical procedural success[B] (%)	96.3	97.3	1.00
No. stents per patient[B]	1.23±0.43	1.19±0.39	0.49
No. stents per target lesion[A]	1.01±0.10	1.02±0.15	0.48
Total stent length implanted[A] (mm)	23.31±8.08	23.28±7.93	0.97
Predilatation[A] (%)	100.0	100.0	Undefined
Post-dilatation[A] (%)	78.8	62.8	0.02
Maximum pressure overall[A] (atm)	16.11±3.00	14.93±3.57	0.02
Post-procedural characteristics			
MLD (mm)			
In-stent	2.47±0.44	2.52±0.40	0.42
In-segment	2.11±0.46	2.18±0.41	0.28
Diameter stenosis (%)			
In-stent	6.63±8.61	7.24±7.95	0.62
In-segment	20.85±7.91	20.13±8.14	0.55
Acute gain (mm)			
In-stent	1.61±0.46	1.61±0.41	0.98
In-segment	1.25±0.48	1.27±0.43	0.79

Intent-to-treat analysis. Unless indicated otherwise, data are given as the mean±SD. P values were calculated using Student's t-tests for continuous variables and the Chi-squared test for discrete variables. [A]Per lesion. [B]Per patient. MLD, minimum lumen diameter.

Table 3. Antiplatelet Medications Throughout the 5-Year Follow-up

	PROMUS Element Plus (n=81 patients)	SYNERGY (n=74 patients)	P value
Aspirin			
At discharge	100.0 (81/81)	100.0 (74/74)	Undefined
1 year	100.0 (81/81)	100.0 (73/73)	Undefined
2 years	96.2 (76/79)	97.2 (70/72)	1.00*
3 years	96.2 (76/79)	100.0 (71/71)	0.25*
4 years	97.4 (76/78)	100.0 (70/70)	0.49*
5 years	94.7 (72/76)	100.0 (69/69)	0.12*
Dual antiplatelet therapy			
At discharge	100.0 (81/81)	100.0 (74/74)	Undefined
1 year	91.4 (74/81)	86.3 (63/73)	0.32
2 years	49.4 (39/79)	48.6 (35/72)	0.93
3 years	43.0 (34/79)	45.1 (32/71)	0.80
4 years	38.5 (30/78)	44.3 (31/70)	0.47
5 years	30.3 (23/76)	40.6 (28/69)	0.19

Intent-to-treat subjects. Values show the percentage (n/N). *P values derived from Fisher's exact test; all other P values are derived from Chi-square tests. Dual antiplatelet therapy consisted of aspirin and one of clopidogrel, ticlopidine, prasugrel, or ticagrelor.

age was 67 years, approximately 75% were male, 30% had diabetes, and 16% had prior MI. More than 15% of patients in each treatment group had 2 target lesions treated and approximately 82% were classified as American Heart Association/American College of Cardiology Type B2 or C lesions by core laboratory-adjudicated angiography (**Table 1**). The rates of technical and clinical procedural success were similar between treatment groups (**Table 2**). Other procedural variables and post-procedural angiographic outcomes were well matched between the subgroups (**Table 2**). As indicated in **Table 3**, DAPT (aspirin plus a $P2Y_{12}$ inhibitor) and aspirin use at 5 years was similar between the SYNERGY (41% and 100%, respectively) and PROMUS Element Plus (30% and 95%, respectively) arms.

Baseline and lesion characteristics were well matched between Japanese and non-Japanese patients implanted with SYNERGY, except that Japanese patients were older

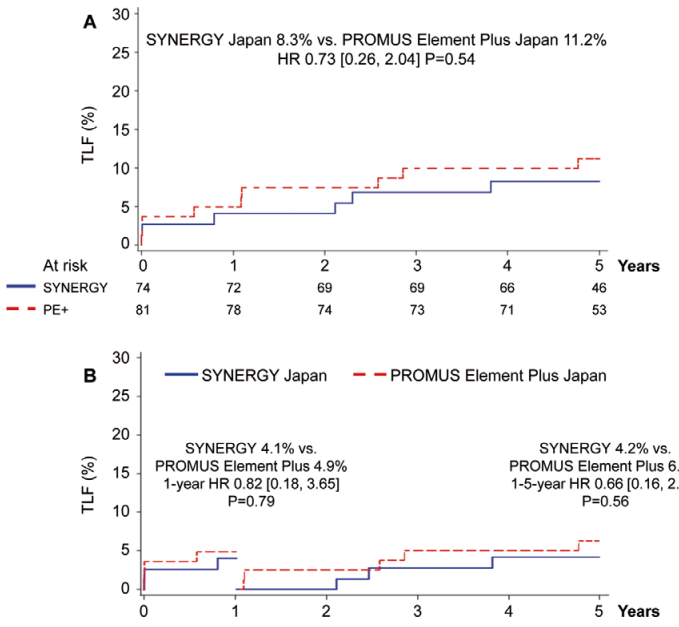

Figure 2. Target lesion failure (TLF) in the EVOLVE II (Japan) randomized control trial. (**A**) Cumulative Kaplan-Meier curves for TLF over the 5-year follow-up period. (**B**) Landmark analysis of TLF at 1 year and between 1 and 5 years. P values were calculated using log-rank tests. Hazard ratios (HRs) are given with 95% confidence intervals in square brackets. PE+, PROMUS Element Plus.

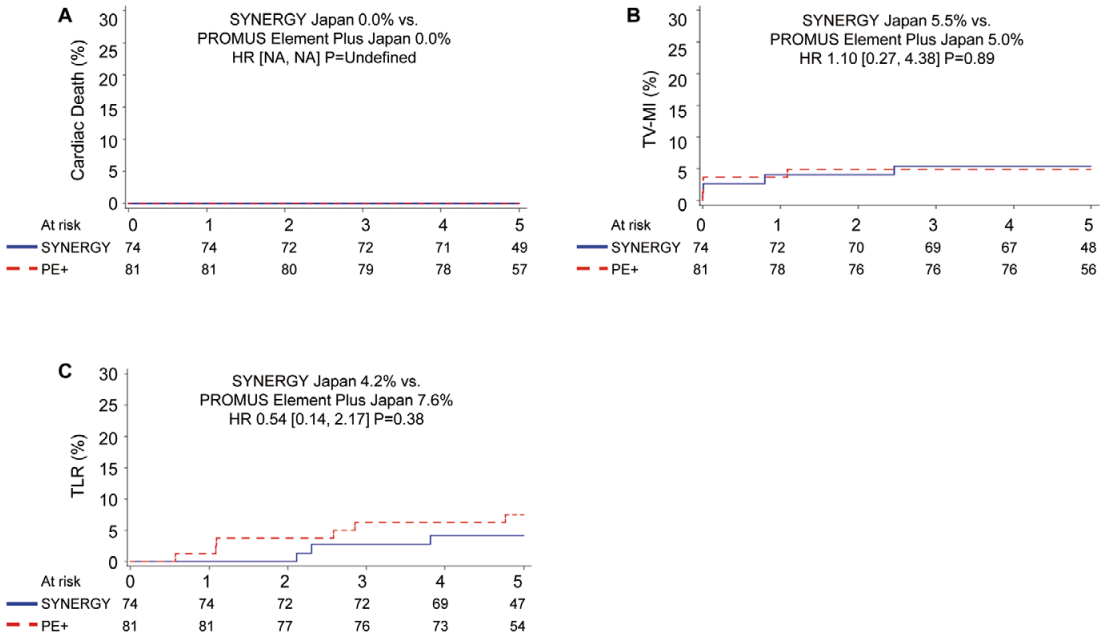

Figure 3. Kaplan-Meier curves for individual components of target lesion failure (TLF) in the EVOLVE II (Japan) randomized control trial. (**A**) Cardiac death, (**B**) target vessel-related myocardial infarction (TV-MI), and (**C**) target lesion revascularization (TLR) over the 5-year follow-up period. P values were calculated using log-rank tests. Hazard ratios (HRs) are given with 95% confidence intervals in square brackets. PE+, PROMUS Element Plus.

(67 vs. 63 years; P=0.0007), had a lower BMI (25 vs. 30 kg/m^2; P<0.0001), a lower frequency of unstable angina (12% vs. 36%; P<0.0001), a greater history of congestive heart failure (18.9% vs. 7.3%; P=0.0005), highly complex lesions (87.1% vs. 75.9%; P=0.02), and longer lesions (17 vs. 14 mm; P=0.0004; **Supplementary Table 1**). Procedural and post-procedural characteristics were similar in Japanese and non-Japanese patients (**Supplementary Table 2**). However, Japanese patients had significantly longer stents (23.3 vs. 21.3 mm; P=0.05), a greater number of stents (1.3

Table 4. Clinical Outcomes at 5 Years

	PROMUS Element Plus (n=81 patients)	SYNERGY (n=74 patients)	HR (95% CI)	P value
All-cause death/MI	7.5 (6)	15.0 (11)	2.05 (0.76, 5.55)	0.15
Death	2.5 (2)	4.1 (3)	1.67 (0.28, 9.98)	0.57
Cardiac death	0.0 (0)	0.0 (0)	NA (NA, NA)	Undefined
Non-cardiac death	2.5 (2)	4.1 (3)	1.67 (0.28, 9.98)	0.57
MI	7.5 (6)	11.1 (8)	1.49 (0.52, 4.30)	0.45
TV-MI	5.0 (4)	5.5 (4)	1.10 (0.27, 4.38)	0.89
Q-wave	0.0 (0)	2.7 (2)	NA (NA, NA)	0.14
TV-Q-wave	0.0 (0)	2.7 (2)	NA (NA, NA)	0.14
Non-Q-wave	7.5 (6)	8.4 (6)	1.10 (0.35, 3.40)	0.87
TV-non-Q-wave	5.0 (4)	2.7 (2)	0.54 (0.10, 2.94)	0.47
TVR	8.8 (7)	12.7 (9)	1.43 (0.53, 3.84)	0.47
TLR	7.5 (6)	4.2 (3)	0.54 (0.14, 2.17)	0.38
TLF	11.2 (9)	8.3 (6)	0.73 (0.26, 2.04)	0.54
TVF	12.5 (10)	15.4 (11)	1.21 (0.52, 2.86)	0.66
Definite or probable ST	0.0 (0)	1.4 (1)	NA (NA, NA)	0.29
Definite ST	0.0 (0)	1.4 (1)	NA (NA, NA)	0.29
Probable ST	0.0 (0)	0.0 (0)	NA (NA, NA)	Undefined

Intent-to-treat subjects. Unless indicated otherwise, values show the percentage (n). Time-to-event analysis. P values are derived from long-rank tests. Target vessel failure (TVF) was defined as target vessel revascularization (TVR), target vessel-related myocardial infarction (TV-MI), or death related to the target vessel. CI, confidence interval; HR, hazard ratio; MI, myocardial infarction; NA, not available; ST, stent thrombosis; TLF, target lesion failure; TV, target vessel related.

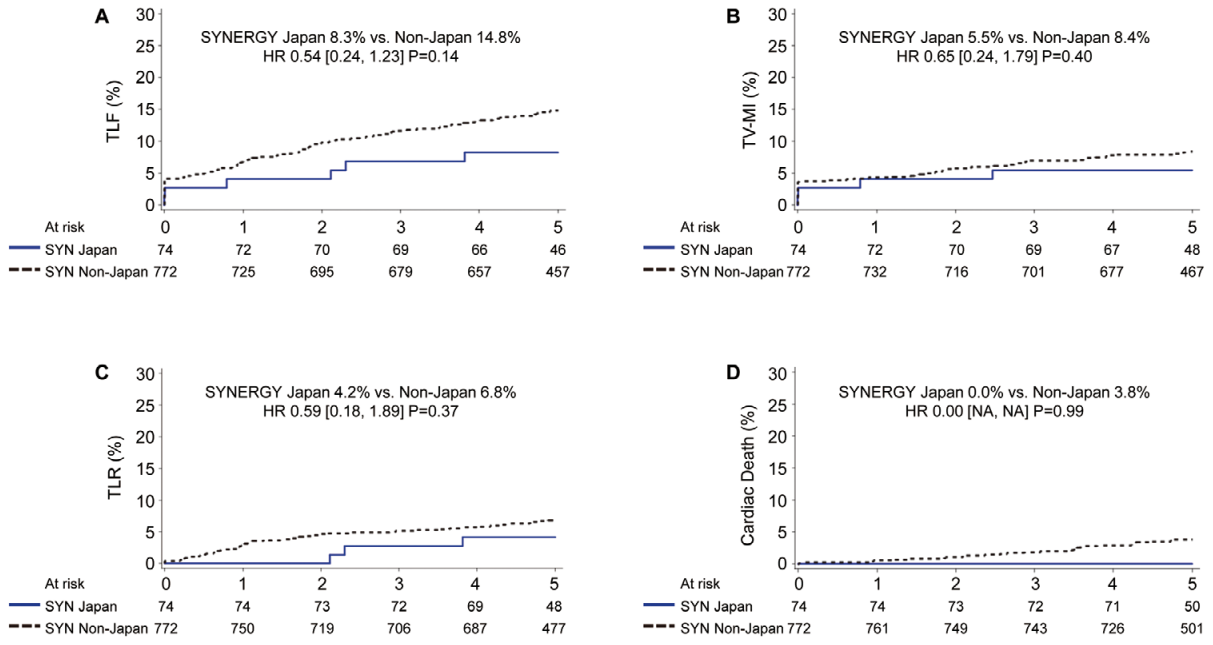

Figure 4. Kaplan-Meier curves for target lesion failure (TLF) and individual components over the 5-year follow-up period in SYNERGY Japanese and non-Japanese patients. (**A**) TLF, (**B**) target vessel-related myocardial infarction (TV-MI), (**C**) target lesion revascularization (TLR), and (**D**) cardiac death. P values were calculated using log-rank tests. Hazard ratios (HRs) are given with 95% confidence intervals in square brackets.

vs. 1.2; P=0.05), and lower maximum overall pressure (14.9 vs. 16.1 atm; P=0.0009) than non-Japanese patients (**Supplementary Table 2**). There were no significant between-group differences in the use of DAPT and aspirin at 5 years (**Supplementary Table 3**).

Clinical Events

As reported previously, the primary endpoint of 12-month TLF was met in the EVOLVE II RCT: SYNERGY was non-inferior to PROMUS Element Plus for 1-year TLF (6.7% vs. 6.5%, respectively; $P_{non\text{-}inferiority}$=0.0005).[14] Kaplan-Meier curves for TLF over the 5-year period were similar for both the SYNERGY and PROMUS Element Plus stents (8.3% vs. 11.2%, respectively; HR 0.73; 95% CI 0.26–2.04; P=0.54; **Figure 2A**) in the EVOLVE II Japanese patients. Landmark analyses demonstrated comparable TLF rates at 1 year, as well as between 1 and 5 years (**Figure 2B**). There were no differences in the rates of individual components of TLF at the 5-year follow-up (**Figure 3**). Additional clinical endpoints listed in **Table 4** were low and comparable between arms. One patient in the SYNERGY arm experienced a very late (>1 year) definite ST; no ST occurred in the PROMUS Element Plus arm (P=0.30).

Kaplan-Meier curves for TLF occurrence throughout the 5-year follow-up were similar between SYNERGY Japanese and non-Japanese patients (8.3% vs. 14.8%, respectively; HR 0.54; 95% CI 0.24–1.23; P=0.14; **Figure 4**). The individual rates of cardiac death, TV-MI, and TLR were similar between groups (**Figure 4**). Additional prespecified outcomes throughout the 5-year follow-up are provided in **Supplementary Table 4**. Definite ST occurred in 1 SYNERGY Japanese and 4 SYNERGY non-Japanese patients (P=0.38; **Supplementary Table 4**).

Discussion

The present study describes outcomes in the Japanese cohort of the EVOLVE II RCT that compared the SYNERGY and PROMUS Element Plus stents. The data are in line with those reported previously for the overall EVOLVE II RCT,[11] where both stents exhibited similar clinical efficacy and safety. The principle outcomes of the present subanalysis are that rates of the primary clinical endpoint, TLF, were relatively low and comparable for both stent types at 1 and 5 years. Second, there were no cardiac deaths and the rates of TV-MI and TLR were not significantly different between treatment arms. Third, no ST was observed in Japanese patients treated with PROMUS Element Plus and only 1 very late ST was seen with SYNERGY. Fourth, despite baseline differences in patient and lesion characteristics, clinical events, including TLF, mortality, MI and ST, throughout the 5-year follow-up were comparable in Japanese and non-Japanese patients implanted with SYNERGY.

The use of DES in percutaneous coronary intervention (PCI) has shown improved clinical outcomes; however, the presence of a permanent polymer is associated with local inflammation and impaired stent healing.[18,19] New stent technologies incorporate antiproliferative drugs eluting from a bioabsorbable polymer, offering the potential of enhanced arterial healing, improved clinical outcomes, and a reduced incidence of late or very late ST. The SYNERGY stent incorporates platinum-chromium metal alloy struts with an ultrathin PLGA everolimus-eluting polymer applied only to the abluminal surface. Animal studies have shown that drug release and PLGA absorption from the SYNERGY stent are completed within 4 months, leaving behind a biocompatible bare metal platform.[10] Preclinical data have shown facilitated endothelial recovery and reduced thrombogenicity following SYNERGY stent implantation compared with the thick-strut bioabsorbable biolimus-eluting stent.[20] These preclinical benefits further translate into clinical benefits, as seen in the EVOLVE series of trials demonstrating low and comparable event rates with permanent vs. bioabsorbable polymer DES over 5 years.[11,21]

The short-term safety and efficacy of bioabsorbable polymer DES compared with durable polymer DES have been well established in recent large-scale "all-comers" randomized trials. The BIO-RESORT trial demonstrated non-inferiority of bioabsorbable polymer SYNERGY (everolimus-eluting) and Orsiro (sirolimus-eluting) stents compared with the durable polymer Resolute Integrity (zotarolimus-eluting) stent for the occurrence of 1-year TVF.[6] Furthermore, 3-year results from the BIO-RESORT trial showed a similar trend regarding the rate of the primary composite endpoint of TVF.[7] The incidence of definite ST was <1.0% in the SYNERGY arm of both trials. In addition, an analysis from the Swedish Coronary Angiography and Angioplasty Registry (SCAAR) comparing SYNERGY-treated patients with those treated with a new-generation DES showed a low rate of ST at 1 year (0.4% vs. 0.5%; P=0.17).[4] In the SORT-OUT VIII trial, SYNERGY was non-inferior to the bioabsorbable polymer Biomatrix NeoFlex (biolimus-eluting) stent with respect to the primary endpoint of 1-year TLF (4.0% vs. 4.4%; P<0.001).[22] In a recently conducted meta-analysis that included data from the EVOLVE first in human[21] and EVOLVE II[11] randomized trials, bioabsorbable stents demonstrated similar safety and efficacy compared with durable stents.[23] The rate of definite or probable ST was numerically lower with bioabsorbable than durable polymer stents (0.98% vs. 1.15%), although this difference was not statistically significant (P=0.19).[23]

The potential clinical benefits of a bioabsorbable polymer stent would be expected to accrue slowly over time (>1 year). Therefore, long-term follow-up of trials using this new stent technology is important. Five-year outcomes between bioabsorbable polymer and durable polymer DES were similar in the EVOLVE,[21] COMPARE II,[24] ISAR-TEST 4,[25] and LEADERS[26] trials. Importantly, data from the present analysis are consistent with the overall EVOLVE II RCT, demonstrating no significant differences between the 2 stent types in the 5-year rates of revascularization, MI, death, and ST.

Despite similar inclusion and exclusion criteria, there were some baseline differences between Japanese and non-Japanese patients treated with SYNERGY, which may be attributed to differences in lifestyle, race, and/or nationality. Consistent with prior reports, Japanese patients in this study tended to be older and had a lower BMI and lower incidence of unstable angina than non-Japanese patients.[12,13] In addition, Japanese patients had a greater history of congestive heart failure and highly complex and longer lesions than non-Japanese patients. Regardless of these observed differences, the 5-year clinical outcomes did not differ significantly between cohorts.

Study Limitations

Although the present substudy is a RCT, it only included a small cohort of patients in Japan. Patients with high complexity were excluded, and therefore this analysis does not fully represent real-world clinical practice. Analysis in the Japanese cohort was prespecified, but the sample size may have limited the ability to assess clinical complications like ST. Moreover, differences in baseline and procedural characteristics between Japanese and non-Japanese cohorts may have affected the 5-year outcomes. Finally, this substudy was not powered to detect differences between Japanese and non-Japanese cohorts.

Conclusions

This substudy provides the longest follow-up data in Japanese patients implanted with the SYNERGY stent. Final 5-year data demonstrate low and comparable clinical outcomes between the SYNERGY and PROMUS Element Plus stents. Japanese and non-Japanese patients implanted with the SYNERGY stent experienced similarly low rates of adverse events at 5 years. These data support the long-term safety and efficacy of SYNERGY in Japanese patients undergoing PCI.

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Disclosures

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IRB Information

This study was approved by the Western Institutional Review Board (Reference no. IRB00000533).

Data Availability

The data for this clinical trial, including any deidentified patient data, will not be shared.

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Supplementary Files

Please find supplementary file(s);
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