

1           **Short-term Dual Antiplatelet Therapy after Deployment of**  
2           **Bioabsorbable Polymer Everolimus-eluting Stent: SHARE trial**

3

4

5

6

7

8

9

10

11

12

13

14

15

16   **Principal Investigator:**

17   Bum-Kee Hong, MD, PhD

18   Cardiology Division, Department of Internal Medicine, Gangnam Severance Hospital, Yonsei  
19   University College of Medicine

20   20, Eonju-ro 63-gil, Gangnam-gu, Seoul 06229, South Korea

21   Tel: 82-2-2019-3310

22   Fax: 82-2-3463-3882

23   E-mail: bkhong@yuhs.ac

24

25

<b>0. Protocol Summary</b>	3
<b>1. Background</b>	6
<b>2. Study Objectives</b>	8
2.1. Primary Outcome	8
2.2. Secondary Outcome	8
2.3. Safety Assessment	8
<b>3. Study Design</b>	9
3.1. Patient Enrollment and Informed Consent	9
3.1.1. Inclusion Criteria	9
3.1.2. Exclusion Criteria	9
3.2. Sample Size Calculation and Statistical Analyses	10
3.2.1. Sample Size Calculation	10
3.2.2. Statistical Analyses	11
<b>4. Study Procedure</b>	12
4.1. Enrollment and Randomization	12
4.2. Study Drug and Study Device	12
4.3. Schedule of Measurements	12
4.4. Guidelines for Standard Care	14
4.5. Definition of adverse events/serious adverse events/unanticipated adverse device effect	14
4.6. Responding to adverse events and discontinuing treatment	15
4.7. Patient Discontinuation (Withdrawal Criteria)	16
<b>5. Study Algorithm</b>	17
<b>6. Confidentiality</b>	18
<b>7. Data Safety Monitoring Board</b>	19
7.1. Data safety monitoring	19
7.2. Frequency of Data Safety Monitoring	20
7.3. Content of Data Safety Monitoring Report	20

7.4. Informed Consent	20
<b>8. Reporting of Adverse Events</b>	21
<b>9. References</b>	22
26	
27	
28	
29	

30 **Protocol Summary**

Title of Study	Short-term Dual Antiplatelet Therapy after Deployment of Bioabsorbable Polymer Everolimus-eluting Stent: SHARE trial
Study Center	Gangnam Severance Hospital, Yonsei University College of Medicine
Study Phase	Others
Objective	To compare the efficacy and safety of P2Y12 inhibitor monotherapy versus aspirin plus P2Y12 inhibitor following 3 months of DAPT in patients PCI with new generation EES.
Method	Prospective, open-label, multicenter, randomized trial
Sample size	A total of 1,452 subjects who received percutaneous coronary intervention using bioresorbable polymer everolimus-eluting stent (Competitive enrollment)
Study design	<ul style="list-style-type: none"> <li>● Prospective, open-label, multicenter, randomized trial</li> <li>● Patients who received bioresorbable polymer everolimus-eluting stent (the SYNERGY stent) implantation within 3 months</li> <li>● Patients who meet the inclusion and exclusion criteria will be selected, informed consent will be obtained, and randomized 1:1 into two groups: those who will maintain DAPT for up to 1 year, and 3 months of DAPT followed by P2Y12 inhibitor monotherapy</li> <li>● The primary outcome is a net adverse clinical event, defined as a composite of major adverse cardiac and cerebrovascular events and major bleeding between 3 and 12 months after the index procedure.</li> </ul>
Inclusion criteria	<ul style="list-style-type: none"> <li>● Age <math>\geq</math> 19 years</li> <li>● Patients who received bioresorbable polymer everolimus-eluting stent (the SYNERGY stent) implantation within 3 months</li> <li>● Patients who can understand the contents of the informed consent document and have voluntarily signed the informed consent form</li> </ul>
Primary & secondary outcomes	<p><b>Primary outcome</b></p> <p>The primary outcome is a net adverse clinical event (NACE), defined as a composite of major adverse cardiac and cerebrovascular events (MACCE) and major bleeding between 3 and 12 months after the index PCI. MACCE is defined as cardiac death, myocardial infarction (MI), stent thrombosis, stroke, or target lesion revascularization (TLR). Major bleeding is defined as Bleeding Academic Research</p>

	<p>Consortium (BARC) type 3 or 5 bleeding.</p> <p><b>Secondary outcome</b></p> <p>The major secondary outcomes are MACCE and major bleeding. Other secondary outcomes are cardiac death, MI, stent thrombosis, stroke, TLR, target vessel revascularization (TVR), and all-cause death.</p> <p><b>Safety Assessment</b></p> <p>Major bleeding</p> <p>Adverse drug reaction</p>
Statistical analyses	<p>Cumulative incidence using Kaplan-Meier method</p> <p>Log-rank test</p> <p>Cox proportional hazard model</p>
Product name	Everolimus-eluting stent (Synergy®, Boston Scientific, Marlborough, MA, USA)
Drug name	Aspirin, clopidogrel, ticagrelor
Study duration	Expected duration for the completion of the study: Total 66 months (Enrollment 48 months, follow-up duration 12 months, data analyses 6 months)
Participating sites	<ol style="list-style-type: none"> <li>1. Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul</li> <li>2. Severance Cardiovascular Hospital, Yonsei University Health System</li> <li>3. Wonju Christian Hospital, Wonju</li> <li>4. Yongin Severance Hospital, Yongin</li> <li>5. Kyung Hee University Hospital at Gangdong, Seoul</li> <li>6. NHIC Ilsan Hospital, Goyang</li> <li>7. Seoul National University Bundang Hospital, Seongnam</li> <li>8. Hallym University Kangnam Sacred Heart Hospital, Seoul</li> <li>9. Myongji Hospital, Hanyang University College of Medicine, Goyang</li> <li>10. Chungang University Hospital, Seoul</li> <li>11. Dankook University Hospital, Cheonan</li> <li>12. Kangwon National University School of Medicine, Chuncheon</li> </ol>

	13. Inha University Hospital, Incheon 14. Yeungnam University Medical Center, Daegu 15. Ewha Womans University Mokdong Hospital, Seoul 16. Konkuk University Chungju Hospital, Chungju 17. Soon Chun Hyang University Cheonan Hospital, Cheonan 18. Kangbuk Samsung Hospital, Seoul 19. Nowon Eulji Medical Center, Eulji University, Seoul 20. Hallym University Chuncheon Sacred Heart Hospital, Chuncheon 21. Ajou University Hospital, Suwon 22. Gangneung Asan Hospital, University of Ulsan College of Medicine, Gangneung 23. Kangdong Sacred Heart Hospital, Seoul 24. Gachon Gil University Hospital, Incheon 25. Hallym University Sacred Heart Hospital, Anyang 26. Ilsan Paik Hospital, University of Inje College of Medicine, Seoul 27. Chungnam National University Hospital, Daejeon 28. Inje University Sanggye Paik Hospital, Seoul 29. Gyeongsang National University Hospital, Jinju 30. Ulsan University Hospital, Ulsan 31. Daejeon Eulji Medical Center, Eulji University, Daejeon
Angiographic core lab	Gangnam Severance Hospital, Seoul

31

32

33 **1. Background**

34 Despite the wide use of drug-eluting stents (DES) in percutaneous coronary intervention  
35 (PCI), there is still controversy over the optimal duration of dual antiplatelet therapy (DAPT)  
36 with aspirin and P2Y12 inhibitors after PCI. The current guidelines recommend DAPT for at  
37 least 6 to 12 months after DES implantation.<sup>1</sup> In patients with stable coronary artery disease  
38 (CAD), DAPT for at least 6 months is recommended based on the results of recent  
39 randomized trials<sup>2-6</sup> that showed no increase in cardiovascular events, including stent  
40 thrombosis, after 3 to 6 months of DAPT compared with 12 months of DAPT, and in patients  
41 with ACS, DAPT for at least 12 months. However, the current guidelines are mostly based on  
42 the results from clinical trials using first- or second-generation DES, and further studies are  
43 needed because they do not include studies using new generations of DES with bioabsorbable  
44 polymers. In addition, clopidogrel was mainly used as a P2Y12 inhibitor in these trials, but  
45 the use of a new P2Y12 inhibitor such as ticagrelor in patients with ACS has been reported to  
46 reduce major cardiovascular events (MACE) without increasing major bleeding compared to  
47 clopidogrel.<sup>7</sup> Therefore, the optimal duration and regimen of DAPT after PCI are still being  
48 debated.

49 On the other hand, few studies have been performed on which drug should be maintained as a  
50 single antiplatelet therapy after completion of DAPT. Currently, guidelines recommend  
51 aspirin monotherapy as maintenance therapy after DAPT. However, strategies to discontinue  
52 aspirin after a brief period of DAPT and continue P2Y12 inhibitor monotherapy have  
53 recently emerged as an attractive alternative. In CAPRIE Study, clopidogrel has shown a  
54 superior effect on preventing cardiovascular events while reducing the frequency of  
55 gastrointestinal bleeding compared to aspirin.<sup>8</sup> However, no randomized study has compared  
56 aspirin and P2Y12 inhibitors as a single antiplatelet therapy. According to a recent  
57 retrospective observational study, the group using clopidogrel as a single maintenance

58 therapy after DAPT reduced the incidence of ischemic events without increasing bleeding  
59 compared to the aspirin monotherapy group.<sup>9</sup>

60 A new generation of everolimus-eluting stent (EES), the SYNERGY stent (Boston Scientific,  
61 Marlborough, MA, USA) is a bioabsorbable polymer (BP) EES designed to promote rapid  
62 reendothelialization by combining a thin-strut (74-81  $\mu\text{m}$ ) platinum-chromium platform with  
63 an abluminally coated ultrathin (4  $\mu\text{m}$ ) bioabsorbable polymer.<sup>10,11</sup> At around 90 days, drug  
64 release was completed and followed by complete bioabsorption of polymer. Therefore, these  
65 features may shorten the duration of DAPT compared with the older generation of DES.

66 Therefore, the Short-term Dual Antiplatelet Therapy After Deployment of Bioabsorbable  
67 Polymer Everolimus-eluting Stent (SHARE) trial will test the noninferiority of P2Y12  
68 inhibitor monotherapy to DAPT in patients undergoing PCI with the SYNERGY stent and  
69 receiving 3 months of DAPT.

70

71

72



73 **2. Study Objectives**

74 To compare the efficacy and safety of P2Y12 inhibitor monotherapy versus aspirin plus  
75 P2Y12 inhibitor following 3 months of DAPT in patients PCI with new generation EES.

76 **2.1 Primary outcome**

77 The primary outcome is a net adverse clinical event (NACE), defined as a composite of major  
78 adverse cardiac and cerebrovascular events (MACCE) and major bleeding between 3 and 12  
79 months after the index PCI. MACCE is defined as cardiac death, myocardial infarction (MI),  
80 stent thrombosis, stroke, or target lesion revascularization (TLR). Major bleeding is defined  
81 as Bleeding Academic Research Consortium (BARC) type 3 or 5 bleeding.

82 **2.2 Secondary outcome**

83 The major secondary outcomes are MACCE and major bleeding. Other secondary outcomes  
84 are cardiac death, MI, stent thrombosis, stroke, TLR, target vessel revascularization (TVR),  
85 and all-cause death.

86 **2.3 Safety Assessment**

87 Major bleeding

88 Adverse drug reaction

89

90 **3. Study Design**

91 3.1. Patient Enrollment and Informed Consent

92 Patients undergoing PCI and stent implantation for CAD are eligible to participate in this  
93 study. Patients who meet all inclusion criteria and do not meet any exclusion criteria will be  
94 considered for inclusion. Written informed consent will be obtained after the procedure and  
95 prior to drug assignment. The Principal Investigator (or a physician authorized by the  
96 Principal Investigator) will explain the study sufficiently for the subject to understand the  
97 study in an independent location and obtain voluntary written informed consent. Even after  
98 participating in the study, it will be confirmed whether or not to continue to agree to the  
99 research progress.

100 **3.1.1. Inclusion Criteria**

- 101 ● Age  $\geq$  19 years
- 102 ● Patients who received bioresorbable polymer everolimus-eluting stent (the  
103 SYNERGY stent) implantation within 3 months
- 104 ● Patients who can understand the contents of the informed consent document and  
105 have voluntarily signed the informed consent form

106 **3.1.2. Exclusion Criteria**

- 107 ● Age  $\geq$  86 years
- 108 ● Hemodynamically unstable patients
- 109 ● History of severe hypersensitivity to aspirin, clopidogrel, ticagrelor, everolimus, or  
110 contrast media
- 111 ● Patients at high risk of bleeding, anemia, or thrombocytopenia
- 112 ● Patients requiring oral anticoagulation
- 113 ● Pregnancy or women of childbearing potential
- 114 ● Life expectancy less than 1 year

- 115 ● Patients receiving strong CYP3A4 inhibitors (e.g., ketoconazole, clarithromycin,  
116 nefazodone, ritonavir, atazanavir)
- 117 ● Patients with a history of intracranial hemorrhage.
- 118 ● Patients with moderate to severe hepatic impairment.
- 119 ● Patients unable to take aspirin, clopidogrel, or ticagrelor due to contraindications of  
120 each agent

### 121 **Coronary angiographic exclusion criteria**

- 122 ● Patients who have undergone coronary stent implantation within 1 year
- 123 ● Patients with left main disease requiring intervention
- 124 ● Patients with chronic total occlusion lesion requiring intervention
- 125 ● Patients with in-stent restenosis requiring intervention
- 126 ● Patients with bifurcation lesions requiring stenting in the side branches
- 127 ● Patients with lesions requiring overlap of 3 or more stents

## 128 **3.2. Sample Size Calculation and Statistical Analyses**

### 129 **3.2.1. Sample Size Calculation**

130 The annual event rate of the primary endpoint is expected to be around 5% based on the  
131 results from several randomized trials that compared short-term DAPT versus 12-month  
132 DAPT after coronary PCI using DES implantation<sup>2-5</sup>. A noninferiority margin of 3  
133 percentage points is chosen with a consideration that this is not clinically different between  
134 the 2 groups in terms of primary endpoint. The number of subjects is determined by  
135 assuming that the experimental group is not inferior when the upper limit of 95%  
136 confidence interval of the difference in the event rate between the 2 groups do not exceed  
137 the event rate for the control group. When the significance level is 5% and the power is  
138 80%, a total of 1,306 subjects, or 653 subjects per group are required. Assuming a 10%

139 dropout rate, a total of 1,452 subjects, or 726 subjects per group, are required to prove our  
140 hypothesis.

### 141 **3.2.2. Statistical Analyses**

142 Analyze categorical variables with the  $\chi^2$  test or Fisher's exact test, and continuous variables  
143 with the student t-test. Evaluate the cumulative incidence of events at 12-month follow-up.  
144 Kaplan-Meier will be used to analyze overall and between-group survival, and comparisons  
145 between groups will be made using the log-rank test. If necessary, hazard ratios between  
146 groups will be presented using the Cox proportional hazard model. A P-value < 0.05 is  
147 considered statistically significant.

148 The primary analysis will be performed in the randomized group regardless of the actual  
149 patient's treatment status but excluding patients with a major cardiac and cerebrovascular  
150 event or major bleeding within 3 months of index procedure (modified intention-to-treatment  
151 analysis). Perform a comparative analysis of the two arms with stratification factors (fixed  
152 effect and/or random effect model) and subgroup analysis. In case of missing, patients are  
153 excluded from analyses involving the missing variable but included in analyses not involving  
154 the missing variable. Additional analysis can be performed (per-protocol analysis or as-  
155 treated analysis).

156

157

158 **4. Study Procedure**

159 **4.1. Enrollment and Randomization**

160 Patients presenting with CAD and undergoing PCI with a new generation EES (Synergy®)  
161 are eligible for this study. Patients who meet the inclusion and exclusion criteria will be  
162 selected, informed consent will be obtained, and randomized 1:1 into two groups: those  
163 who will maintain DAPT for up to 1 year, and 3 months of DAPT followed by P2Y12  
164 inhibitor monotherapy. Patients will be randomized at enrollment by the electronic case  
165 record file (e-CRF) computerized system and obtaining informed consent and  
166 randomization will be permitted from the time of the PCI until the first follow-up, 3 months  
167 after the procedure. As a P2Y12 inhibitor, Clopidogrel will be used as a P2Y12 inhibitor in  
168 patients with SCAD. For patients with ACS, ticagrelor will be recommended as a P2Y12  
169 inhibitor, but clopidogrel will be also allowed according to the physician’s discretion.  
170 Randomization will be stratified by site and clinical diagnosis (stable CAD or ACS).  
171 Baseline clinical status, angiographic characteristics, and blood test findings will be  
172 assessed at randomization. Informed consent will be obtained from all subjects.

173 **4.2. Study Drug and Study Device**

<b>Drug or Device</b>		<b>Company</b>
Clopidogrel	Tablet, 75mg, once a day	Unrestricted
Ticagrelor (Brilinta <sup>®</sup> )	Tablet, 90mg, twice a day	ASTRAZENECA
Synergy <sup>®</sup>	Everolimus-eluting bioabsorbable polymer stent	Boston Scientific

174

175 **4.3. Schedule of Measurements**

176 Clinical follow-up will be performed at 3 ( $\pm$  1), 6 ( $\pm$  1), and 12 ( $\pm$  1) months after the  
177 index PCI.

178

179 **Table1. Schedule of Measurements**

	Screening	3M <sup>9</sup>	6M <sup>9</sup>	12M <sup>9</sup>
	& Baseline	3 Months ±30 days	6 Months ±30 days	12 Months ±30 days
Informed consent	X <sup>1</sup>			
Inclusion/exclusion criteria	X			
Medical history	X <sup>2</sup>			
Randomization	X			
Antiplatelet therapy	X	X	X	X
Check compliance		X	X	X
Adverse event <sup>4</sup>		X	X	X
Serious adverse event		X	X	X
12 lead ECG	X <sup>5</sup>			
Coronary angiography	X			
CBC	X	X <sup>8</sup>		
Creatinine, BUN,	X	X <sup>8</sup>		
hs-CRP	X	X <sup>8</sup>		
Total cholesterol, TG, HDL cholesterol, LDL cholesterol	X	X <sup>8</sup>		
AST, ALT		X <sup>8</sup>		
Fasting glucose level	X <sup>6</sup>	X <sup>8</sup>		
HbA1c	X			
Pregnancy test, Urine (if applicable)	X			
CPK, CK-MB, Troponin I, Troponin T	X <sup>7</sup>			
Echocardiography	X			

180

181 <sup>1</sup> The informed consent should be signed within 3 months after the coronary intervention.

182 <sup>2</sup> Assessment of age, sex, risk factors, clinical diagnosis, angina status, cardiac history, cardiac and  
183 cerebrovascular event, and bleeding

184 <sup>3</sup> For patients undergoing stent implantation

185 <sup>4</sup> Assessment of cardiac and cerebrovascular event and bleeding, especially

186 <sup>5</sup> ECG at follow up visits will only be obtained when clinically indicated such as recurrent chest pain,  
187 ischemia, or significant arrhythmias, heart failure or other signs or symptoms of clinical instability.

188 <sup>6</sup> It may be done later, before discharge when the patient is in a fasting state

189 <sup>7</sup> Optional in selected centers and if baseline lab is done, enzymes must be followed every 8-hours for  
190 24 hours post-index procedure

191 <sup>8</sup> These tests are subject to change at the discretion of the attending physician, and the results of other  
192 tests, if any, are available at that time.

193 <sup>9</sup> If the patient is unable to attend within the visit window specified in the protocol, a telephone visit  
194 may be conducted to confirm adverse events, serious adverse events, and medication status.

195

196 **4.4. Guidelines for Standard Care**

197 Other antiplatelet or anticoagulant agents: The use of prasugrel or cilostazol is not allowed.

198 Lipid lowering agents: Statins are recommended in all patients unless contraindicated.  
199 Fibrates, omega-3 polyunsaturated fatty acids or nicotinic acids may be used when other  
200 lipid profiles are abnormal.

201 **4.5. Definition of adverse event/serious adverse event/unanticipated adverse device**  
202 **effect**

203 ● Adverse event

204 An adverse event is defined as an undesirable, unintended condition that occurs in a subject  
205 during a clinical trial and is not necessarily causally related to the study treatment.

206 Therefore, an adverse event is any undesirable, unintended condition (e.g., abnormal test  
207 result) or illness that occurs during the study that is temporally related to the study  
208 procedure, regardless of whether it is caused by the study device or procedure.

209 ● Serious adverse event (SAE)

210 An adverse event caused by a medical device used in a clinical trial is considered serious if  
211 it meets one or more of the following criteria

212 - Causes death

213 - Is life-threatening

214 For example, a clinician determines that there is a risk of death immediately following the  
215 occurrence of the adverse event (does not include a serious form of an adverse event that  
216 occurred in the past that could have resulted in death).

217 - Causes persistent or meaningful disabilities or diminished function (subject's physical  
218 function/structure, physical activity, and quality of life).

219 - Requires hospitalization or an extended period of hospitalization

220 - Causes a congenital malformation or abnormality

221 - A significant medical event that is classified as a serious adverse event, based on medical  
222 judgment, that does not result in death, is not life-threatening, or requires hospitalization. A

223 medical event that threatens the safety of the subject and/or requires intervention to prevent  
224 an adverse event as defined above and/or requires immediate medical or surgical  
225 intervention to prevent permanent body function/structure damage or to mitigate  
226 unforeseen damage.

227 Allergic bronchospasm, blood disorders, or seizures that require intensive care in the  
228 emergency room or at home without causing hospitalization or drug dependence or abuse.

229 There is a clear distinction between severe and serious adverse events. The difference  
230 between severe and serious adverse reactions is distinguishable. A severe adverse event is  
231 not always a serious adverse event, and a serious adverse event is not always severe. The  
232 term "severe" is used to describe the severity of a particular adverse event (mild, moderate,  
233 or severe). However, there are cases where the adverse event itself is mild (e.g., a severe  
234 headache). This is different from a "serious adverse event", which is an adverse event that  
235 causes life-threatening damage to a patient's life or body functions.

236 Notes: An adverse event involving an efficacy endpoint is considered a serious adverse  
237 event.

238 (Unplanned revascularization events are considered SAEs).

239 ● Unanticipated adverse device effect

240 An unanticipated adverse device effect is a serious adverse event associated with a medical  
241 device that adversely affects the health or safety of a subject or is fatal or results in death.

242 - Its nature, severity, or occurrence was not identified in a previous protocol or clinical trial  
243 (including a supplemental protocol or clinical trial)

244 - Defined as an unexpected serious adverse event caused by an investigational medical  
245 device that is relevant to the rights, safety, or welfare of the subject.

246 Note: "effect" implies a causal relationship to the medical device.

247 **4.6 Responding to adverse events and discontinuing treatment**



248 In the event of a SAE, such as stent thrombosis or major bleeding, appropriate action  
249 should be taken based on symptoms. Subjects should be questioned in detail about SAE-  
250 related symptoms at outpatient visits in accordance with the above measurement schedule.  
251 If myocardial infarction due to stent thrombus is suspected, emergency coronary  
252 angiography should be performed, medications should be adjusted, and safety reporting  
253 should be expedited. In the event of major bleeding, antiplatelet therapy should be  
254 discontinued, and the patient should be treated according to their condition. In addition, if  
255 adverse drug reactions occur, such as dyspnea, hypotension, or hyperuricemia, consult with  
256 the patient to determine whether to continue treatment.

#### 257 **4.7. Patient Discontinuation (Withdrawal Criteria)**

##### 258 ● Criteria

- 259 - Subject or representative withdraws consent
- 260 - The subject cannot be followed up
- 261 - The researcher determines that it is not feasible to continue for any other reason.

##### 262 ● Process

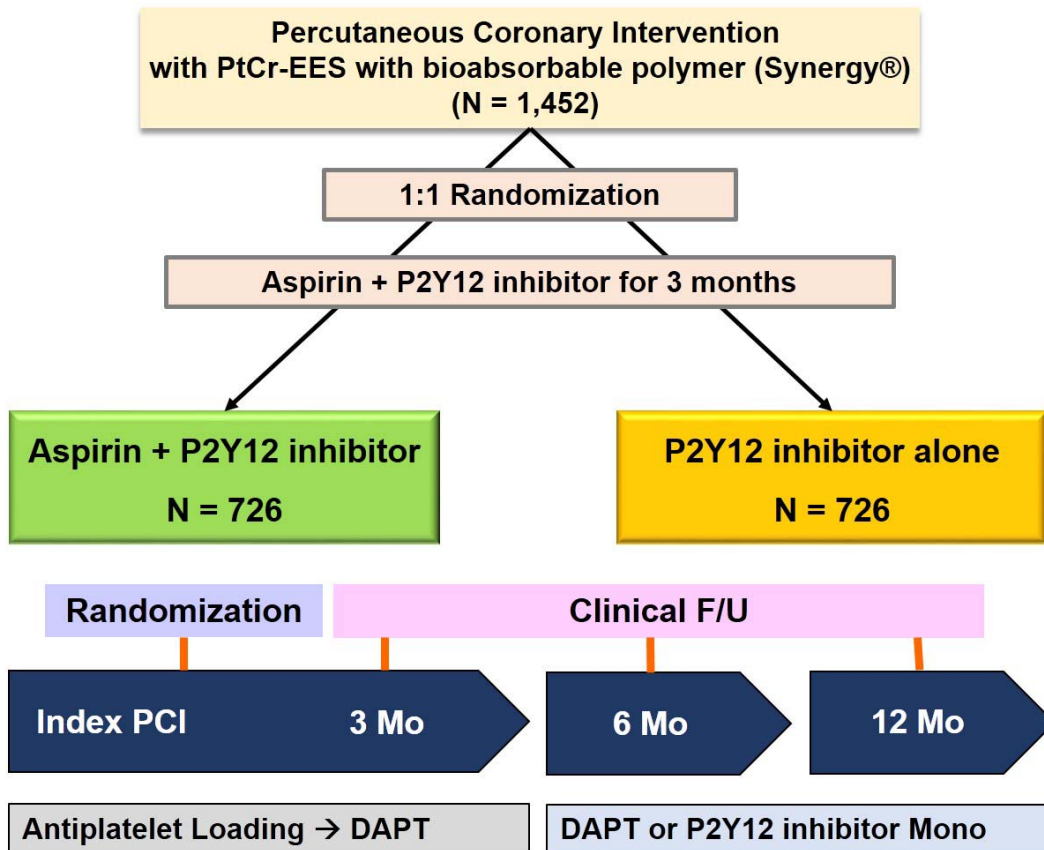
- 263 - Record and retain the reason for discontinuation or withdrawal and the data related to the  
264 study up to that point.
- 265 - Subjects who drop out will be included in the statistical analysis unless there is a valid  
266 reason.

267

268

269 **5. Study Algorithm**

270



271

272

273

274 **6. Confidentiality**

275 All data will be collected in an e-CRF, which will be inaccessible except to authorized  
276 personnel. Subject identifiers will be coded and identified by a unique study number and will  
277 not contain any identifiable personal information about the subjects. Study-related documents  
278 will be stored in a separate, locked location in the lab, and documents stored on computers  
279 will also be password protected to limit access by outsiders. The collected information will be  
280 kept for the duration of the study and for three years after the end of the study and will be  
281 properly managed and disposed of in accordance with the Personal Information Protection  
282 Act. However, the storage period may be extended if the principal investigator deems it  
283 necessary.

284

285

286 **7. Data Safety Monitoring Board**

287 The Data Safety Monitoring Board (DSMB) will be composed of general and  
288 interventional cardiologists and a biostatistician. The names of the actual members will not  
289 be published but will be made available to the governing body upon request. The DSMB  
290 will function in accordance with applicable administrative guidelines.

291 Members of the committee will not participate in the trial and will be independent.

292 The DSMB will review safety data from clinical trials and make recommendations based  
293 on safety analyses, including unexpected adverse device effect (UADEs), serious adverse  
294 events (SAEs), protocol biases, device failures, and 30-day observation reports.

295 The frequency of DSMB meetings will be determined prior to study initiation. In addition,  
296 a Data Safety Review Committee meeting will be convened at any time if there is reason to  
297 suspect safety. This committee is responsible for advising on any safety or complaints  
298 throughout the trial and may recommend to the Steering Committee that the trial be  
299 adjusted or stopped. However, the Steering Committee has the final decision authority on  
300 all study manipulations.

301 All cumulative safety results will be reported to the DSMB and will be reviewed during the  
302 follow-up and recruitment periods to ensure patient safety. The committee will be allowed  
303 to make every effort to conduct an unbiased review of patient safety information.

304 All DSMB reports will be made publicly available upon request to appropriate  
305 organizations but will otherwise be strictly confidential.

306 A draft Data Safety Review Committee charter will be prepared prior to the Data Safety  
307 Review Committee's first data review. The DSMB will develop agreement on the  
308 definitions used to assess the validity of all clinical trials and the decision to proceed. All  
309 DSMB reports will be strictly confidential but may be made public upon request by  
310 regulatory authorities.

311 **7.1. Data safety monitoring**

312 The Principal Investigator will be responsible for the safety of human subjects. The DSMB  
313 will have a detailed role in reviewing the safety of subjects, study progress, procedures to  
314 maintain valid data, and the quality of data collection, processing, and analysis.

315 **7.2. Frequency of Data Safety Monitoring**

316 The Principal Investigator must report any serious adverse events to the DSMB as soon as  
317 possible and within 24 hours. The DSMB will meet regularly once a year to assess study  
318 progress, data management, and safety. The DSMB may convene at any time if a  
319 significant issue related to subject safety arises.

320 **7.3. Content of Data Safety Monitoring Report**

321 The data safety review report shall include information on human subjects, safety  
322 information, and the quality of the research.

323 **7.4 Informed Consent**

324 The investigator shall provide and obtain the signature of an approved informed consent  
325 form to each subject in each prospective clinical trial prior to recruitment. Variations may  
326 be made to suit the circumstances of each clinical trial site.

327

328

329 **8. Reporting of Adverse Events**

330 The Principal Investigator will evaluate all adverse events for severity, seriousness, and  
331 causality to the study drug and study procedures. All adverse events should be documented  
332 on the appropriate page of the clinical case record, regardless of their association with the  
333 study drug or severity. SAEs corresponding to the efficacy endpoints should be reported in  
334 accordance with the reporting criteria of each institution's Clinical Research Protection Center.

335

336

337

## 338 9. References

- 339 1. Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA Guideline Focused Update on Duration  
340 of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease: A Report of the  
341 American College of Cardiology/American Heart Association Task Force on Clinical Practice  
342 Guidelines. *J Am Coll Cardiol*. 2016;68(10):1082-1115.
- 343 2. Kim BK, Hong MK, Shin DH, et al. A new strategy for discontinuation of dual antiplatelet  
344 therapy: the RESET Trial (REal Safety and Efficacy of 3-month dual antiplatelet Therapy  
345 following Endeavor zotarolimus-eluting stent implantation). *J Am Coll Cardiol*.  
346 2012;60(15):1340-1348.
- 347 3. Gwon HC, Hahn JY, Park KW, et al. Six-month versus 12-month dual antiplatelet therapy  
348 after implantation of drug-eluting stents: the Efficacy of Xience/Promus Versus Cypher to  
349 Reduce Late Loss After Stenting (EXCELLENT) randomized, multicenter study. *Circulation*.  
350 2012;125(3):505-513.
- 351 4. Feres F, Costa RA, Abizaid A, et al. Three vs twelve months of dual antiplatelet therapy after  
352 zotarolimus-eluting stents: the OPTIMIZE randomized trial. *JAMA*. 2013;310(23):2510-2522.
- 353 5. Colombo A, Chieffo A, Frasheri A, et al. Second-generation drug-eluting stent implantation  
354 followed by 6- versus 12-month dual antiplatelet therapy: the SECURITY randomized  
355 clinical trial. *J Am Coll Cardiol*. 2014;64(20):2086-2097.
- 356 6. Schulz-Schupke S, Byrne RA, Ten Berg JM, et al. ISAR-SAFE: a randomized, double-blind,  
357 placebo-controlled trial of 6 vs. 12 months of clopidogrel therapy after drug-eluting stenting.  
358 *Eur Heart J*. 2015;36(20):1252-1263.
- 359 7. Wallentin L, Becker RC, Budaj A, et al. Ticagrelor versus clopidogrel in patients with acute  
360 coronary syndromes. *N Engl J Med*. 2009;361(11):1045-1057.
- 361 8. Committee CS. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of  
362 ischaemic events (CAPRIE). CAPRIE Steering Committee. *Lancet*. 1996;348(9038):1329-  
363 1339.
- 364 9. Park TK, Song YB, Ahn J, et al. Clopidogrel Versus Aspirin as an Antiplatelet Monotherapy

365 After 12-Month Dual-Antiplatelet Therapy in the Era of Drug-Eluting Stents. *Circ Cardiovasc*  
366 *Interv.* 2016;9(1):e002816.

367 10. Wilson GJ, Marks A, Berg KJ, et al. The SYNERGY biodegradable polymer everolimus  
368 eluting coronary stent: Porcine vascular compatibility and polymer safety study. *Catheter*  
369 *Cardiovasc Interv.* 2015;86(6):E247-257.

370 11. de la Torre Hernandez JM, Tejedor P, Camarero TG, et al. Early healing assessment with  
371 optical coherence tomography of everolimus-eluting stents with bioabsorbable polymer  
372 (synergy) at 3 and 6 months after implantation. *Catheter Cardiovasc Interv.* 2016;88(3):E67-  
373 73.

374

375