

## Supplemental Online Content

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1 **eAppendix 1. STOPDAPT-2 ACS Study Organization**

2 **Steering Committee:**

3 Takeshi Kimura (Principal Investigator), Mitsuru Abe, Kenji Ando, Yuji Ikari, Kazushige Kadota, Kazuya  
4 Kawai, Ken Kozuma, Kengo Tanabe, Keiichi Hanaoka, Koichi Nakao, Yoshihiro Morino.

5 **Clinical Event Committee:**

6 Yoshihisa Nakagawa, Yutaka Furukawa

7 **Statistical Analysis:**

8 Takeshi Morimoto

9 **Coordinating Center:**

10 Research Institute for Production Development, Kyoto, Japan

11 Saori Tezuka, Yumika Fujino, Naoko Okamoto, Risa Kato, Masayo Kitamura, Miyuki Tsumori, Miya

12 Hanazawa, Misato Yamauchi, Itsuki Yamazaki.

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## 1 **eAppendix 2. Participating Centers in the STOPDAPT-2 ACS**

2 Following 74 institutes in Japan screened or enrolled one or more eligible patients.

3 The current analysis included the patients enrolled from 96 centers in Japan including the centers which  
4 participated in the previous STOPDAPT-2 but did not participate in the STOPDAPT-2 ACS.

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6 Teine Keijinkai Hospital, Sapporo, (Mitsugu Hirokami)

7 Megumino Hospital, Eniwa, (Nobuko Makiguchi)

8 Hokko Memorial Hospital, Sapporo, (Yoichi Nozaki)

9 Hirosaki University Hospital, Hirosaki, (Hirofumi Tomita)

10 Iwate Medical University Hospital, Morioka, (Yoshihiro Morino)

11 Sendai Kousei Hospital, Sendai, (Tsuyoshi Isawa)

12 Sendai Cardiovascular Center, Sendai, (Masahiro Yagi)

13 Tohoku Medical and Pharmaceutical University Hospital, Sendai, (Tatsuya Komaru)

14 Mito Saiseikai General Hospital, Mito, (Motoaki Higuchi)

15 Kawaguchi Cardiovascular and Respiratory Hospital, Kawaguchi, (Hideo Tokuyama)

16 Ageo Central General Hospital, Ageo, (Takaaki Isshiki)

17 Mitsui Memorial Hospital, Tokyo, (Kengo Tanabe)

18 Toranomom Hospital, Tokyo, (Takahide Kodama)

19 Showa University Koto Toyosu Hospital, Tokyo, (Kohei Wakabayashi)

20 Kawakita General Hospital, Tokyo, (Atsushi Tosaka)

21 Sakakibara Heart Institute, Fuchu, (Itaru Takamisawa)

22 Tokyo Metropolitan Tama Medical Center, Fuchu, (Hiroyuki Tanaka)

23 Minamino Cardiovascular Hospital, Hachioji, (Yoshiki Hata)

24 Higashiyamato Hospital, Higashiyamato, (Ryuichi Kato)

25 St.Marianna University School of Medicine Hospital, Kawasaki, (Yoshihiro Akashi)

26 Yokohama Rosai Hospital, Yokohama, (Kazuhiko Yumoto)

27 Showa University Fujigaoka Hospital, Yokohama, (Hiroshi Suzuki)

28 Yokohama City University Medical Center, Yokohama, (Kiyoshi Hibi)

29 Fujisawa City Hospital, Fujisawa, (Kengo Tsukahara)

30 Kitasato University Hospital, Sagamihara, (Junya Ako)

31 Hiratsuka Kyosai Hospital, Hiratsuka, (Yuko Onishi)

32 Tokai University Hospital, Isehara, (Yuji Ikari)

33 University of Fukui Hospital, Fukui, (Hiroyasu Uzui)

34 Gifu Prefectural General Medical Center, Gifu, (Toshiyuki Noda)

- 1 Ogaki Municipal Hospital, Ogaki, (Itsuo Morishima)
- 2 Juntendo University Shizuoka Hospital, Izunokuni, (Satoru Suwa)
- 3 Shizuoka General Hospital, Shizuoka, (Hiroki Sakamoto)
- 4 Shizuoka Saiseikai General Hospital, Shizuoka, (Minoru Yamada)
- 5 Nagoya Daini Red Cross Hospital, Nagoya, (Ruka Yoshida)
- 6 Handa City Hospital, Handa, (Susumu Suzuki)
- 7 Ichinomiyanishi Hospital, Ichinomiya, (Takuya Maeda)
- 8 Matsusaka Central General Hospital, Matsusaka, (Takashi Tanigawa)
- 9 Otsu Red Cross Hospital, Otsu, (Kazuaki Kaitani)
- 10 Kyoto University Hospital, Kyoto, (Takeshi Kimura)
- 11 Uji Tokushukai Hospital, Uji, (Shunzo Matsuoka)
- 12 Kyoto Medical Center, Kyoto, (Masaharu Akao)
- 13 Mitsubishi Kyoto Hospital, Kyoto, (Takafumi Yokomatsu)
- 14 Kitano Hospital, Osaka, (Moriaki Inoko)
- 15 Osaka Red Cross Hospital, Osaka, (Tsukasa Inada)
- 16 Osaka General Medical Center, Osaka, (Takashi Morita)
- 17 Kindai University Hospital, Sayama, (Gaku Nakazawa)
- 18 Mimihara General Hospital, Sakai, (Shozo Ishihara)
- 19 Kobe City Medical Center General Hospital, Kobe, (Makoto Kinoshita)
- 20 Tsukazaki Hospital, Himeji, (Takanori Kusuyama)
- 21 Kindai University Nara Hospital, Ikoma, (Kiyonori Togi)
- 22 Tenri Hospital, Tenri, (Toshihiro Tamura)
- 23 Japanese Red Cross Wakayama Medical Center, Wakayama, (Hiroki Watanabe)
- 24 Wakayama Medical University Hospital, Wakayama, (Takashi Akasaka)
- 25 Okayama Medical Center, Okayama, (Isao Tabuchi)
- 26 Kurashiki Central Hospital, Kurashiki, (Kazushige Kadota)
- 27 Hiroshima University Hospital, Hiroshima, (Yasuki Kihara)
- 28 Hiroshima Prefectural Hospital, Hiroshima, (Hironori Ueda)
- 29 Iwakuni Medical Center, Iwakuni, (Yusuke Katayama)
- 30 Tokuyama Central Hospital, Shunan, (Takatoshi Wakeyama)
- 31 Shimonoseki City Hospital, Shimonoseki, (Takeo Kaneko)
- 32 Tokushima University Hospital, Tokushima, (Tetsuzo Wakatsuki)
- 33 Tokushima Red Cross Hospital, Komatsushima, (Koichi Kishi)
- 34 Kagawa Prefectural Central Hospital, Takamatsu, (Masayuki Doi)
- 35 Ehime Prefectural Central Hospital, Matsuyama, (Hideki Okayama)

- 1 Chikamori Hospital, Kochi, (Kazuya Kawai)
- 2 Kokura Memorial Hospital, Kitakyusyu, (Kenji Ando)
- 3 Saiseikai Fukuoka General Hospital, Fukuoka, (Nobuhiro Suematsu)
- 4 Iizuka Hospital, Iizuka, (Shujiro Inoue)
- 5 Saga University Hospital, Saga, (Masahiro Natsuaki)
- 6 Kumamoto University Hospital, Kumamoto, (Kenichi Tsujita)
- 7 Saiseikai Kumamoto Hospital, Kumamoto, (Tomohiro Sakamoto)
- 8 Hitoyoshi Medical Center, Hitoyoshi, (Hirofumi Kurokawa)
- 9 Ibusuki Medical Center, Ibusuki, (Katsuro Kashima)
- 10 Urasoe General Hospital, Urasoe, (Hiroki Uehara)
- 11
- 12

## 1 **eAppendix 3. Definition of Endpoints**

### 2 **1. Death**

3 As classified by Academic Research Consortium (ARC)

- 4 • **Cardiac Death**

5 Any death due to proximate cardiac cause (e.g. MI, low-output failure, fatal arrhythmia),  
6 unwitnessed death and death of unknown cause, all procedure related deaths including those  
7 related to concomitant treatment. All deaths are considered cardiac unless an unequivocal  
8 non-cardiac cause can be established. Specifically, any unexpected death even in subjects with  
9 coexisting potentially fatal non-cardiac disease (e.g. cancer, infection) should be classified as  
10 cardiac.

- 11 • **Vascular Death**

12 Death due to non-coronary vascular causes such as cerebrovascular disease, pulmonary  
13 embolism, ruptured aortic aneurysm, dissecting aneurysm, or other vascular cause.

- 14 • **Non-cardiovascular Death**

15 Any death not covered by the above definitions such as death caused by infection, malignancy,  
16 sepsis, pulmonary causes, accident, suicide or trauma.

### 17 **2. Myocardial Infarction: MI**

18 As classified by Academic Research Consortium (ARC): However, the sensitivity is too high for the  
19 evaluation with Troponin of the peri-procedural MI, thus CKMB will be used.

- 20 • **Preprocedural Adjudication of MI**

21 Myocardial Infarction (MI) is defined by the ARC criteria. However, periprocedural MI will be  
22 evaluated by CKMB, because the evaluation by troponin is too sensitive.

- 23 • **Baseline MI evaluation**

24 ECG showing ST elevation, development of new abnormal Q-wave, clinical symptoms specific  
25 to MI, troponin or CK-MB values exceeding the standard values

- 26 • **Periprocedural MI**

- 27 ○ Occurrence of any of the following events within 48 hours after PCI procedure will be  
28 judged as MI.

- 29 ▪ **CK-MB  $\geq$  3 times Upper Reference Limit (URL)** (CK-MB value exceeding  
30 URL before procedure is not considered as a new MI, but as MI at  
31 enrollment.)

- 32 ▪ Abnormal ECG (new Q-wave, left bundle branch block)

1           ○ Occurrence of troponin  $\geq$  **5 times URL** or CK-MB  $\geq$  **5 times URL** within 72 hours  
2           after CABG procedure accompanied by any of the following criteria will be judged as  
3           MI. (CK-MB value exceeding URL before procedure is not considered as a new MI,  
4           but as MI at enrollment.)

- 5           ▪ Abnormal ECG (new Q-wave, left bundle branch block)
- 6           ▪ New occlusion of coronary autografts or grafts
- 7           ▪ Reduction in living myocardium confirmed by diagnostic imaging

8           • **Spontaneous MI**

9           ○ Occurrence of any of the following events at > 48 hours after PCI or > 72 hours after  
10          CABG will be judged as MI. MI caused by revascularization procedures, such as TLR  
11          and TVR, is defined as periprocedural MI.

- 12          ▪ Abnormal ECG (new Q-wave, left bundle branch block)
- 13          ▪ Troponin or CK-MB value > **URL** (CK-MB value exceeding URL before  
14          procedure is not considered as a new MI, but as MI at enrollment.)

15          • **Sudden Death**

16          ○ When death occurred before blood sampling for biomarker measurements or while  
17          biomarkers appeared to be increasing, MI will be judged according to the following  
18          criteria:

- 19          ▪ Clinical symptoms suggesting ischemia that are accompanied by one of the  
20          following:
  - 21               - New ST elevation or left bundle branch block
  - 22               - Thrombus determined by angiography or at autopsy

23          • **Reinfarction**

24          ○ When after onset of MI stable or decreasing values are confirmed in 2 biomarker  
25          measurements, but 20% increase 3 to 6 hours is observed after the second  
26          measurement.

- 27          ▪ If biomarkers are increasing or have not yet reached the peak, data are insufficient  
28          to diagnose reinfarction.

29 **Electrocardiographic Classification:**

30          • **Classification based on Q-wave**

31          ○ **Q-wave MI (QMI)**

- 32          ▪ Development of abnormal Q-waves confirmed in 2 or more contiguous leads with  
33          or without elevation in cardiac enzymes.

34          ○ **Non-Q-wave MI (NQMI)**

- 35          ▪ All MIs not classified as Q-wave.



1 • **Classification based on ST segment.**

2 ○ **ST-elevation myocardial infarction (MI) (STEMI)**

- 3 ▪ New or presumably new elevation of ST segment at J point in 2 or more  
4 contiguous leads. Cut-off point is  $\geq 0.2$  mV in V1, V2 and V3 leads and  $\geq 0.1$  mV  
5 in other leads.

6 ○ **Non-ST elevation myocardial infarction (MI) (NSTEMI)**

- 7 ▪ MI that is not STEMI

8 **Determination by Infarction Size:**

9 • **Major Infarction**

- 10 ○ CK-MB level is  $\geq 10$  times the upper limit of normal (ULN) (or CK level is  $\geq 10$  times  
11 ULN in case CK-MB level is not measurable).  
12 ▪ Even if the above conditions are not met, fatal MI is determined as large  
13 infarction.

14 • **Minor Infarction**

- 15 ○ All types of MI other than the major infarction

16 • **Classification of MI Size Based on the ARC Classification**

- 17 ○ Increase in the cardiac enzyme (CK-MB, Tn, and total CK) levels  $\geq 10$  times ULN  
18 ○ Increase in the cardiac enzyme (CK-MB, Tn, and total CK) levels  $\geq 5$  times,  $< 10$  times  
19 ULN  
20 ○ Increase in the cardiac enzyme (CK-MB, Tn, and total CK) levels  $\geq 3$  times,  $< 5$  times  
21 ULN  
22 ○ Increase in the cardiac enzyme (CK-MB, Tn, and total CK) levels  $< 3$  times ULN  
23 ○ Increase in the troponin level; no increase in the CK-MB and total CK levels  
24 ○ Increase in the troponin level; no measurements of the CK-MB and total CK levels

25 **The cardiac enzymes should be prioritized in the order of CK-MB, Tn, and total CK.**

26 • **Classification of MI Size Based on the CK-MB Level**

- 27 ○ Increase in the cardiac enzyme (CK-MB) level  $\geq 10$  times ULN  
28 ○ Increase in the cardiac enzyme (CK-MB) level  $\geq 5$  times,  $< 10$  times ULN  
29 ○ Increase in the cardiac enzyme (CK-MB) level  $\geq 3$  times,  $< 5$  times ULN  
30 ○ Increase in the cardiac enzyme (CK-MB) level  $< 3$  times ULN  
31 ○ Increase in the troponin level; no increase in the CK-MB level  
32 ○ Increase in the troponin level; no measurement of the CK-MB level

33 • **Classification of MI Size Based on the Troponin Level**

- 34 ○ Increase in the cardiac enzyme (Tn) level  $\geq 10$  times ULN  
35 ○ Increase in the cardiac enzyme (Tn) level  $\geq 5$  times,  $< 10$  times ULN

- Increase in the cardiac enzyme (Tn) level  $\geq 3$  times,  $< 5$  times ULN
- Increase in the cardiac enzyme (Tn) level  $< 3$  times ULN
- Increase in the troponin level; no increase in the CK-MB level
- Increase in the troponin level; no measurement of the CK-MB level

### 3. Revascularization

#### Classification:

- **Target Lesion Revascularization (TLR)**  
PCI performed in the target lesion (within 5 mm of the stent edges), or CABG performed for restenosis of the target lesion or for treatment of other complications
- **Target Vessel Revascularization (TVR)**  
PCI performed in the target vessel or revascularization by CABG, including TLR
- **Target Vessel Revascularization-Remote (TVR-Remote)**  
Revascularization of a non-target lesion in the target vessel
- **Non Target Vessel Revascularization (Non-TVR)**  
Any revascularization in a vessel other than the target vessel
- **Non Target Lesion Revascularization (Non-TLR)**  
Any revascularization in a lesion other than the target lesion  
Non-TLR = TVR-Remote + Non-TVR

#### Clinically indicated revascularization:

- The revascularization that meets the following criteria is considered as clinically indicated revascularization. Presence/absence of clinical findings is judged by the operator of the procedure before the revascularization.
  - Recurrence of angina pectoris, presumably related to the target vessel;
  - Objective signs of ischemia at rest or during exercise test (or equivalent), presumably related to the target vessel;
  - Signs of functional ischemia revealed by any invasive diagnostic test (e.g., Doppler flow velocity reserve [FVR], fractional flow reserve [FFR]);
  - Revascularization for  $\geq 70\%$  diameter stenosis even in the absence of the above-mentioned ischemic signs or symptoms.

### 4. Stent Thrombosis

Based on the ARC definition, Stent thrombosis is classified into definite, probable and possible according to the “probability”, and into acute, subacute late and very late according to timing of the onset.

- **Definite Stent Thrombosis**

- 1           ○ Angiographic confirmation of stent thrombosis\*:
- 2           ▪ The presence of a thrombus† that originates in the stent segment (including 5 mm
- 3           of the stent edges) is revealed by angiography, and presence of at least one of the
- 4           following criteria within a 48-hour time window is observed:
- 5           - Acute onset of ischemic symptoms at rest
- 6           - New ECG changes that suggest acute ischemia
- 7           - Typical rise and fall in cardiac biomarkers (refer to definition of spontaneous
- 8           MI)
- 9           - Nonocclusive thrombus
- 10          ▪ Intracoronary thrombus is defined as a noncalcified filling defect
- 11          (spherical, ovoid, or irregular) or lucency surrounded by contrast material
- 12          (on 3 sides or within a coronary stenosis) seen in multiple projections, or
- 13          persistence of contrast material within the lumen, or a visible
- 14          embolization
- 15          - Occlusive thrombus
- 16          ▪ TIMI 0 or TIMI 1 intrastent or proximal to a stent up to the most adjacent
- 17          downstream side branch or main branch
- 18          ○ Pathological confirmation of stent thrombosis:
- 19          ▪ Evidence of recent thrombus within the stent determined at autopsy or via
- 20          examination of tissue retrieved following thrombectomy
- 21      • **Probable Stent Thrombosis**
- 22          ○ When the following cases occurred after intracoronary stenting:
- 23          ▪ Any unexplained death within the first 30 days after procedure‡
- 24          ▪ Irrespective of the time after the index procedure, any MI in the territory of the
- 25          implanted stent in the absence of any other obvious cause such as angiography or
- 26          other lesions
- 27      • **Possible Stent Thrombosis**
- 28          ○ Any unexplained death from 30 days after intracoronary stenting
- 29      \*          The incidental angiographic documentation of stent occlusion in the absence of
- 30      clinical signs is not considered to be a confirmed stent thrombosis (silent occlusion)
- 31      †          Intracoronary thrombus
- 32      • **Acute Stent Thrombosis**
- 33      0-24 hours post stent implantation (Time 0 is defined as the time of removal of the guiding
- 34      catheter).
- 35      • **Subacute Stent Thrombosis**

1 > 24 hours-30 days post stent implantation

2 • **Late Stent Thrombosis \***

3 > 30 days-1 year post stent implantation

4 • **Very Late Stent Thrombosis \***

5 > 1 year post stent implantation

6 \* Including “primary” as well as “secondary” stent thrombosis after stented segment  
7 revascularization.

8 **5. Surgery**

9 • Including endoscopic surgeries and therapies

10 • Including CABG

11 • Excluding percutaneous intravascular treatments

12 • Including aortic aneurysm stent graft procedure

13 • Excluding tooth extraction

14 **6. Bleeding/Hemorrhagic Complications**

15 Bleeding/Hemorrhagic Complications will be evaluated using the TIMI, GUSTO and BARC definitions

16 **TIMI bleeding classification:**

17 Bleeding is classified by the Thrombosis in Myocardial Infarction (TIMI). Measurement of  
18 hemoglobin and hematocrit values at baseline is required for the severity rating.

19 • **Major Bleeding**

20 ○ When any of the following criteria is met.

21 ▪ Intracranial hemorrhage

22 ▪ Decrease in hemoglobin to  $\geq 5$  g/dL decrease in the hemoglobin concentration

23 ▪ Absolute drop in hematocrit to  $\geq 15\%$  (Baseline – Onset of the event)

24 • **Minor Bleeding**

25 ○ When blood loss is observed, and any of the following criteria is met:

26 ▪ Decrease in hemoglobin to  $\geq 3$  g/dL

27 ▪ Decrease in hematocrit to  $\geq 10\%$  (Baseline – Onset of the event)

28 ○ When no blood loss is observed, but any of the following criteria is met:

29 ▪ Decrease in hemoglobin to  $\geq 4$  g/dL

30 ▪ Decrease in hematocrit to  $\geq 12\%$  (Baseline – Onset of the event)

31 • **Minimal Bleeding**

32 ○ Any clinically overt sign of hemorrhage that is associated with a fall in hemoglobin to  
33  $< 3$  g/dL.

34 (Microscopical urine occult blood and fecal occult blood are not defined as Minimal

bleeding.)

## **GUSTO bleeding classification:**

### **Severe Bleeding**

- Life-threatening bleeding
- Intracranial hemorrhage
- Hemorrhage or bleeding that causes drop in blood pressure and requires interventions, such as infusion, blood transfusion, administration of a hypertensor, surgical interception.

### **Moderate Bleeding**

- Bleeding that requires blood transfusion but does not meet criteria for severe bleeding

## **BARC bleeding classification:**

Bleeding is classified based on definitions by the Bleeding Academic Research Consortium (BARC).

Measurement of hemoglobin concentration is required for severity rating.

- **Type 0:** No bleeding
- **Type 1:** Bleeding that is not medically significant and does not cause the patient to seek unscheduled performance of studies, hospitalization, or treatment by a health care professional.
- **Type 2:** Any overt sign of hemorrhage that should be treated and does not fit the criteria for Types 3, 4, or 5, but does meet at least one of the following criteria:
  - (1) requiring non-surgical, medical intervention by a health care professional, (2) leading to hospitalization or increased level of care, (3) prompting evaluation.
- **Type 3:**
  - Type 3a
    - Overt bleeding plus hemoglobin drop of 3-5 g/dL
    - Transfusion with overt bleeding
  - Type 3b
    - Overt bleeding plus hemoglobin drop of  $\geq 5$  g/dL
    - Cardiac tamponade
    - Bleeding requiring surgical intervention (excluding dental/nasal/skin/hemorrhoid)
    - Bleeding requiring intravenous vasoactive drugs
  - Type 3c
    - Intracranial hemorrhage
    - Intraocular bleeding compromising vision
- **Type 4:** CABG-related bleeding
  - Perioperative intracranial hemorrhage within 48 hours
  - Reoperation following closure of sternotomy for the purpose of controlling bleeding
  - Transfusion of  $\geq 5$  units of whole blood or concentrated red blood cell within 48 hours

- Chest tube output  $\geq 2$  L within 24 hours

- **Type5:** Fatal bleeding

- Type 5a

Probable Fatal bleeding: no autopsy or imaging confirmation, but clinically suspicious

- Type 5b

Definite fatal bleeding: overt bleeding or autopsy or imaging confirmation

## 7. Composite Endpoint

Composite endpoint of secondary endpoints will be defined as follows:

- **TLF: Target Lesion Failure**

Cardiac death, myocardial infarction (MI) of target vessels, Clinically-indicated TLR

- **TVF:Target Vessel Failure**

Cardiac death, MI or Clinically-indicated TVR.

- **MACE: Major Adverse Cardiac Events**

Cardiac death, MI or Clinically-indicated TVR

## 8. Stroke or Cerebrovascular Accident

Acute onset of a neurological deficit that persists for at least 24 hours and is the result of a disturbance of the cerebral circulation due to ischemia or hemorrhage. Deficits that last  $\leq 24$  hours are due to transient ischemic neurological attack and are not classified in this category.

## 9. Classification of Angina

- **Braunwald Classification of Unstable Angina**

- **Class I :** New onset of severe or accelerated angina: Patients with new onset ( $< 2$  months in duration) exertional angina pectoris that is severe or frequent ( $> 3$  episodes/day) or patients with chronic stable angina who develop accelerated angina (angina distinctly more frequent, severe, longer in duration, or precipitated by distinctly less exertion than previously) but who have not experienced pain at rest during the preceding 2 months.

- **Class II :** Angina at rest, subacute: Patients with 1 or more episodes of angina at rest during the preceding month but not within the preceding 48 hours

- **Class III :** Angina at rest, acute: Patients with 1 or more episodes of angina at rest within the preceding 48 hours

- **Canadian Cardiovascular Society (CCS) Classification of Stable Angina**

- **Class I :** Ordinary physical activity does not cause angina, such as walking or climbing stairs. Angina occurs with strenuous, rapid or prolonged exertion at work or recreation.

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- **Class II** : Slight limitation of ordinary activity. Angina occurs on walking or climbing stairs rapidly, walking uphill, walking or stair climbing after meals, or in cold, in wind, under emotional stress or only during the few hours after awakening. Angina occurs on walking more than two blocks on the level and climbing more than one flight of ordinary stairs at a normal pace and in normal condition.
- **Class III** : Marked limitation of ordinary physical activity. Angina occurs on walking one to two blocks on the level and climbing one flight of stairs in normal conditions and at a normal pace.
- **Class IV** : Inability to carry on any physical activity without discomfort – angina symptoms may be present at rest.

# 1 **eMethods**

## 2 **Statistical analysis**

3           For the primary and major secondary endpoints, hierarchical testing was predefined in the  
4 following order: 1) noninferiority test on the primary endpoint; 2) noninferiority test for the major secondary  
5 cardiovascular composite endpoint; 3) superiority test for the major secondary bleeding endpoint; and 4)  
6 superiority test for the primary endpoint. The main results were described on basis of the intention-to-treat  
7 analysis. The noninferiority of the experimental arm to the control arm for the primary outcome was also  
8 tested in per-protocol population, as-treated population, and worst-case scenario, as defined in the statistical  
9 analysis plan. The interaction tests were made to confirm the consistency of the treatment effect for the  
10 primary endpoint for the following pre-specified subgroups: age over 75, sex, diabetes, severe chronic kidney  
11 disease (estimated glomerular filtration rate less than 30 ml/min/1.73m<sup>2</sup> or dialysis), prior MI and acute  
12 myocardial infarction at presentation of the current study, ST-segment elevated MI, total stent length over 28  
13 mm, two or more target vessels, Paris thrombotic/bleeding risk scores, CREDO-Kyoto thrombotic/bleeding  
14 risk scores, and the study (STOPDAPT-2 ACS or the ACS patients in STOPDAPT-2). Results for the other  
15 secondary endpoints were described only in the form of HRs with their confidence intervals (CIs) without  
16 P-values.



1 **eTables**

2 **eTable 1. Clinical and procedural characteristics compared between enrolled patients and eligible but non-enrolled**  
 3 **patients among overall ACS patients, ACS patients in STOPDAPT-2, and patients in STOPDAPT-2 ACS.**

	Overall			STOPDAPT-2			STOPDAPT-2 ACS		
	Enrolled	Non-enrolled	P	Enrolled	Non-enrolled	P value	Enrolled	Non-enrolled	P
	N=4136	N=2305	value	N=1148	N=1257		N=2988	N=1048	value
Age, yr	66.8±11.9	70.1±13.1	<0.001	66.6±11.6	69.2±13.0	<0.001	66.9±12.0	71.2±13.2	<0.001
Men, no (%)	3280 (79.3)	1707 (74.1)	<0.001	914 (79.6)	943 (75.0)	0.01	2366 (79.2)	764 (72.9)	<0.001
Body-mass index, kg/m <sup>2</sup>	24.1±3.6	23.7±3.7	<0.001	24.2±3.5	23.8±3.6	0.005	24.1±3.6	23.6±3.9	<0.001
Acute coronary syndrome, no (%)	4136 (100)	2305 (100)		1148 (100)	1257 (100)		2988 (100)	1048 (100)	
STEMI, no. (%)	2324 (56.2)	1346 (58.4)	0.001	561 (48.9)	702 (55.9)	0.001	1763 (59.0)	644 (61.5)	0.01
NSTEMI, no. (%)	826 (20.0)	375 (16.3)		180 (15.7)	192 (15.3)		646 (21.6)	183 (17.5)	
Unstable angina, no. (%)	986 (23.8)	584 (25.3)		407 (35.5)	363 (28.9)		579 (19.4)	221 (21.1)	
Hypertension, no (%)	2810 (67.9)	1596 (69.2)	0.28	802 (69.9)	862 (68.6)	0.50	2008 (67.2)	734 (70.0)	0.09
Diabetes, no (%)	1229	765 (33.2)	0.004	358 (31.2)	400 (31.8)	0.74	871	365 (34.8)	<0.001

	(29.7)						(29.2)		
Treated with insulin, no (%)	125 (3.0)	117 (5.1)	<0.001	40 (3.5)	47 (3.7)	0.74	85 (2.8)	70 (6.7)	<0.001
Smoking, no (%)	2698 (65.2)	1388 (60.2)	<0.001	745 (64.9)	762 (60.6)	0.03	1953 (65.4)	626 (59.7)	0.001
Current smoking, no (%)	1420 (34.3)	682 (29.6)	<0.001	367 (32.0)	377 (30.0)	0.30	1053 (35.2)	305 (29.1)	<0.001
Prior myocardial infarction, no (%)	244 (5.9)	240 (10.4)	<0.001	70 (6.1)	144 (11.5)	<0.001	174 (5.8)	96 (9.2)	<0.001
Prior stroke, no (%)	193 (4.7)	155 (6.7)	<0.001	57 (5.0)	78 (6.2)	0.19	136 (4.6)	77 (7.4)	<0.001
Prior PCI, no (%)	559 (13.5)	395 (17.1)	<0.001	271 (23.6)	229 (18.2)	0.001	288 (9.6)	166 (15.8)	<0.001
Prior 1st generation DES implantation, no (%)	75 (1.8)	85 (3.7)	<0.001	31 (2.7)	47 (3.7)	0.15	44 (1.5)	38 (3.6)	<0.001
Heart failure, no (%)	308 (7.5)	91 (4.0)	<0.001	62 (5.4)	44 (3.5)	0.02	246 (8.2)	47 (4.5)	<0.001
Peripheral artery disease, no (%)	82 (2.0)	75 (3.3)	0.002	35 (3.1)	38 (3.0)	0.97	47 (1.6)	37 (3.5)	<0.001
Severe CKD, no (%)	138 (3.3)	212 (9.2)	<0.001	33 (2.9)	103 (8.2)	<0.001	105 (3.5)	109 (10.4)	<0.001
Dialysis, no (%)	49 (1.2)	106 (4.6)	<0.001	13 (1.1)	54 (4.3)	<0.001	36 (1.2)	52 (5.0)	<0.001
Atrial fibrillation, no (%)	51 (1.2)	64 (2.8)	<0.001	11 (1.0)	33 (2.6)	0.002	40 (1.3)	31 (3.0)	0.001
Number of treated lesions	1.27±0.59	1.20±0.49	<0.001	1.27±0.61	1.19±0.48	<0.001	1.27±0.59	1.22±0.51	0.004
Number of stents	1.40±0.78	1.24±0.54	<0.001	1.39±0.77	1.23±0.52	<0.001	1.41±0.78	1.25±0.55	<0.001
Minimal stent diameter, mm	3.02±0.51	3.02±0.49	0.79	3.01±0.49	3.03±0.47	0.51	3.02±0.52	3.01±0.50	0.78
Total stent length, mm	34.5±23.0	29.9±16.9	<0.001	32.9±21.0	28.4±15.2	<0.001	35.1±23.7	31.8±18.5	<0.001
Target lesion location									
Left main coronary artery, no. (%)	110 (2.7)	120 (5.2)	<0.001	18 (1.6)	53 (4.2)	<0.001	92 (3.1)	67 (6.4)	<0.001

Left anterior descending coronary artery, no. (%)	2497 (60.4)	1254 (54.4)	<0.001	701 (61.1)	680 (54.1)	<0.001	1796 (60.1)	574 (54.8)	0.003
Left circumflex coronary artery, no. (%)	825 (20.0)	368 (16.0)	<0.001	241 (21.0)	218 (17.3)	0.02	584 (19.5)	150 (14.3)	<0.001
Right coronary artery, no. (%)	1486 (35.9)	720 (31.7)	<0.001	394 (34.3)	386 (30.7)	0.06	1092 (36.6)	344 (32.8)	0.03
Bypassed graft, no. (%)	3 (0.1)	6 (0.3)	0.08	1 (0.1)	5 (0.4)	0.22	2 (0.1)	1 (0.1)	1.00
Target of 2 vessels or more, no. (%)	734 (17.8)	221 (9.6)	<0.001	184 (16.0)	105 (8.4)	<0.001	550 (18.4)	116 (11.1)	<0.001
Target of 3 vessels or more, no. (%)	133 (3.2)	9 (0.4)	<0.001	32 (2.8)	5 (0.4)	<0.001	101 (3.4)	4 (0.4)	<0.001

- 1 Among the 1282 ACS patients who were eligible but not enrolled in the STOPDAPT-2, complete screening data was available in 1257 patients. The data on baseline characteristics were obtained in
- 2 all the 1048 ACS patients who were eligible but not enrolled into STOPDAPT-2 ACS.
- 3 ACS denotes acute coronary syndrome, CKD chronic kidney disease, DES drug-eluting stents, NSTEMI non-ST-segment elevation myocardial infarction, PCI percutaneous coronary intervention,
- 4 and STEMI ST-segment elevation myocardial infarction.

5

1 **eTable 2. Complete baseline characteristics**

	All	1-2 month DAPT	12 months DAPT
	N=4136	N=2058	N=2078
<b>Patient demographics</b>			
Age, yr	66.8±11.9	67.0±11.9	66.6±11.9
>=75, no. (%)	1183 (28.6)	585 (28.4)	598 (28.8)
Men, no. (%)	3280 (79.3)	1631 (79.3)	1649 (79.4)
Women, no. (%)	856 (20.7)	427 (20.8)	429 (20.6)
Body mass index, kg/m <sup>2</sup>	24.1±3.6	24.1±3.7	24.2±3.5
Body mass index <25, no. (%)	2599 (62.8)	1301 (63.2)	1298 (62.5)
<b>Clinical presentation</b>			
Acute coronary syndrome, no. (%)	4136 (100)	2058 (100)	2078 (100)
Acute myocardial infarction, no. (%)	3150 (76.2)	1578 (76.7)	1572 (75.7)
ST segment elevation, no. (%)	2324 (56.2)	1179 (57.3)	1145 (55.1)
Non-ST segment elevation, no. (%)	826 (20.0)	399 (19.4)	427 (20.6)
Treated =< 24 hours, no. (%)	2734 (86.8)	1386 (87.8)	1348 (85.8)
> 24 hours, no. (%)	416 (13.2)	192 (12.2)	224 (14.3)
Onset to door time, hour	3.0 (1.3-10.0)	3.0 (1.3-9.4)	3.0 (1.3-10.1)
Door to wire crossing time (STEMI within 24 hours), min	60 (44-78)	60 (44-81)	60 (44-77)
Killip class			
1	2717 (86.3)	1351 (85.6)	1366 (87.1)
2	263 (8.4)	140 (8.9)	123 (7.8)
3	66 (2.1)	34 (2.2)	32 (2.0)
4	101 (3.2)	53 (3.4)	48 (3.1)
Location of STEMI <sup>1)</sup>			
Anterior, no. (%)	1241 (53.5)	628 (53.3)	613 (53.6)
Inferior, no. (%)	925 (39.9)	466 (39.6)	459 (40.2)
Posterolateral, no. (%)	286 (12.3)	154 (13.1)	132 (11.6)
Peak CK/ULN	6.4 (2.3-13.3)	6.5 (2.4-13.2)	6.3 (2.2-13.4)
Peak CKMB/ULN	8.5 (2.3-21.9)	8.6 (2.3-22.1)	8.2 (2.2-21.3)
Unstable angina, no. (%)	986 (23.8)	480 (23.3)	506 (24.4)

Braunwald class			
I	411 (41.7)	206 (42.9)	205 (40.5)
II	137 (13.9)	75 (15.6)	62 (12.3)
III	438 (44.4)	199 (41.5)	239 (47.2)
Culprit vessels <sup>2)</sup>			
Left anterior descending coronary artery	2208 (53.6)	1108 (54.0)	1100 (53.2)
Left circumflex coronary artery	554 (13.5)	284 (13.8)	270 (13.1)
Right coronary artery	1309 (31.8)	632 (30.8)	677 (32.7)
Left main coronary artery	46 (1.1)	27 (1.3)	19 (0.9)
Saphenous vein graft	3 (0.1)	1 (0.1)	2 (0.1)
CPAOA	40 (1.0)	22 (1.1)	18 (0.9)
ECMO use	13 (0.3)	7 (0.3)	6 (0.3)
Impella use	3 (0.1)	2 (0.1)	1 (0.1)
IABP use	148 (3.6)	84 (4.1)	64 (3.1)
<b>Past history and comorbidities</b>			
Prior PCI, no. (%)	427 (10.3)	225 (10.9)	202 (9.7)
Prior first-generation DES, no. (%)	75 (1.8)	43 (2.1)	32 (1.5)
Prior CABG, no. (%)	27 (0.7)	9 (0.4)	18 (0.9)
Prior myocardial infarction, no. (%)	244 (5.9)	135 (6.6)	109 (5.3)
Prior stroke, no. (%)	193 (4.7)	98 (4.8)	95 (4.6)
Prior bleeding events, no. (%)	32 (0.8)	18 (0.9)	14 (0.7)
Heart failure, no. (%)	308 (7.5)	157 (7.6)	151 (7.3)
Atrial fibrillation, no. (%)	51 (1.2)	35 (1.7)	16 (0.8)
Anemia, no. (%) <sup>3)</sup>	247 (6.0)	117 (5.7)	130 (6.3)
Thrombocytopenia, no. (%) <sup>4)</sup>	21 (0.5)	9 (0.4)	12 (0.6)
Chronic obstructive pulmonary disease, no. (%)	87 (2.1)	34 (1.7)	53 (2.6)
Cirrhosis, no. (%)	10 (0.2)	5 (0.2)	5 (0.2)
Cancer, no. (%)	272 (6.6)	135 (6.6)	137 (6.6)
Active cancer, no. (%)	43 (1.0)	22 (1.1)	21 (1.0)
Peripheral artery disease, no. (%)	82 (2.0)	40 (1.9)	42 (2.0)
Moderate or Severe chronic kidney disease, no. (%) <sup>5)</sup>	1227 (29.7)	622 (30.2)	605 (29.1)

Severe chronic kidney disease, no. (%) <sup>5)</sup>	138 (3.3)	68 (3.3)	70 (3.4)
eGFR <30 mL/min/1.73m <sup>2</sup> not on dialysis, no. (%) <sup>5)</sup>	89 (2.2)	42 (2.0)	47 (2.3)
Dialysis, no. (%)	49 (1.2)	26 (1.3)	23 (1.1)
Hypertension, no. (%)	2810 (67.9)	1396 (67.8)	1414 (68.1)
Hyperlipidemia, no. (%)	2764 (66.8)	1373 (66.7)	1391 (66.9)
Diabetes, no. (%)	1229 (29.7)	608 (29.5)	621 (29.9)
Diabetes with insulin, no. (%)	125 (3.0)	51 (2.5)	74 (3.6)
Smoker, no. (%)	2698 (65.2)	1346 (65.4)	1352 (65.1)
Current Smoker, no. (%)	1420 (34.3)	718 (34.9)	702 (33.8)
Left ventricular ejection fraction, % <sup>6)</sup>	56.8±10.6	56.7±10.6	56.9±10.5
<40%, no. (%) <sup>6)</sup>	171 (4.5)	95 (5.0)	76 (4.0)
Mitral regurgitation grade 3/4, no. (%)	63 (1.5)	29 (1.4)	34 (1.6)
<b>Risk scores</b>			
PARIS Thrombotic Risk Score	3 (2-4)	3 (2-4)	3 (2-4)
High ≥5	685 (16.6)	347 (16.9)	338 (16.3)
Intermediate 3-4	2127 (51.4)	1076 (52.3)	1051 (50.6)
Low 0-2	1324 (32.0)	635 (30.9)	689 (33.2)
PARIS Bleeding Risk Score	5 (3-7)	5 (3-7)	5 (3-7)
High ≥8	747 (18.1)	380 (18.5)	367 (17.7)
Intermediate 4-7	2138 (51.7)	1071 (52.0)	1067 (51.4)
Low 0-3	1251 (30.3)	607 (29.5)	644 (31.0)
CREDO-Kyoto Thrombotic Risk Score	1 (0-1)	1 (0-1)	1 (0-1)
High ≥4	171 (4.1)	78 (3.8)	93 (4.5)
Intermediate 2-3	694 (16.8)	355 (17.3)	339 (16.3)
Low 0-1	3271 (79.1)	1625 (79.0)	1646 (79.2)
CREDO-Kyoto Bleeding Risk Score	0 (0-0)	0 (0-0)	0 (0-0)
High ≥3	132 (3.2)	71 (3.5)	61 (2.9)
Intermediate 1-2	800 (19.3)	402 (19.5)	398 (19.2)
Low 0	3204 (77.5)	1585 (77.0)	1619 (77.9)
<b>Procedural characteristics</b>			

Emergent procedure, no. (%)	3372 (81.5)	1691 (82.2)	1681 (80.9)
Radial approach, no. (%)	3695 (89.3)	1832 (89.0)	1863 (89.7)
Brachial approach, no. (%)	106 (2.6)	50 (2.4)	56 (2.7)
Femoral approach, no. (%)	494 (11.9)	257 (12.5)	237 (11.4)
Only radial approach, no. (%)	3541 (85.6)	1751 (85.1)	1790 (86.1)
Invasive fractional flow reserve, no. (%)	137 (3.3)	60 (2.9)	77 (3.7)
Staged procedure, no. (%) <sup>7)</sup>	597 (14.4)	280 (13.6)	317 (15.3)
Number of procedures	1.16±0.40	1.15±0.39	1.17±0.41
Number of target lesions <sup>7)</sup>	1.27±0.59	1.27±0.60	1.28±0.59
Target lesion location			
Left main coronary artery, no. (%)	110 (2.7)	52 (2.5)	58 (2.8)
Left anterior descending coronary artery, no. (%)	2497 (60.4)	1242 (60.4)	1255 (60.4)
Left circumflex coronary artery, no. (%)	825 (20.0)	408 (19.8)	417 (20.1)
Right coronary artery, no. (%)	1486 (35.9)	719 (34.9)	767 (36.9)
Bypassed graft, no. (%)	3 (0.1)	1 (0.1)	2 (0.1)
Chronic total occlusion, no. (%)	128 (3.1)	66 (3.2)	62 (3.0)
Bifurcation lesions, no. (%)	1101 (26.6)	552 (26.8)	549 (26.4)
Final 2 stents implantation, no. (%)	25 (0.6)	15 (0.7)	10 (0.5)
Target of 2 vessels or more, no. (%)	734 (17.8)	344 (16.7)	390 (18.8)
Target of 3 vessels or more, no. (%)	133 (3.2)	60 (2.9)	73 (3.5)
Use of IVUS or OCT, no. (%)	4023 (97.3)	1994 (96.9)	2029 (97.6)
IVUS, no. (%)	3588 (86.8)	1796 (87.3)	1792 (86.2)
OCT, no. (%)	589 (14.2)	279 (13.6)	310 (14.9)
Number of implanted stents	1.40±0.78	1.40±0.77	1.41±0.79
Minimal stent diameter, mm	3.02±0.51	3.01±0.51	3.02±0.50
<3.0 mm, no. (%)	1599 (38.7)	817 (39.7)	782 (37.6)
Total stent length, mm	34.5±23.0	34.3±22.6	34.6±23.5
>=28mm, no. (%)	2238 (54.1)	1111 (54.0)	1127 (54.2)
<b>Length of hospital stay</b>			
Admission to discharge, day	9 (6-12)	9 (6-12)	9 (5-12)

Index PCI to discharge, day	7 (3-11)		8 (3-11)	7 (3-11)
Admission to staged PCI, day	7 (4-11)		7 (4-11)	7 (3-11)
<b>Medication at discharge</b>				
Aspirin, no. (%)	4131 (99.9)		2055 (99.9)	2076 (99.9)
200mg/day, no. (%)	2 (0.1)		1 (0.1)	1 (0.1)
100mg/day, no. (%)	4070 (98.5)		2027 (98.6)	2043 (98.4)
81mg/day, no. (%)	59 (1.4)		27 (1.3)	32 (1.5)
P2Y <sub>12</sub> inhibitors, no. (%)	4131 (99.9)		2055 (99.9)	2076 (99.9)
Ticlopidine, no. (%)	0 (0)		0 (0)	0 (0)
Clopidogrel, no. (%)	2170 (52.5)		1062 (51.6)	1108 (53.3)
75mg/day, no. (%)	2170 (100)		1062 (100)	1108 (100)
Prasugrel, no. (%)	1962 (47.4)		994 (48.3)	968 (46.6)
3.75mg/day, no. (%)	1931 (98.4)		982 (98.8)	949 (98.0)
2.5mg/day, no. (%)	31 (1.6)		12 (1.2)	19 (2.0)
Ticagrelor, no. (%)	0 (0)		0 (0)	0 (0)
Anticoagulation, no. (%) <sup>8)</sup>	23 (0.56)		10 (0.5)	13 (0.6)
Novel oral anticoagulants, no. (%)	13 (0.3)		6 (0.3)	7 (0.3)
Warfarin, no. (%)	10 (0.2)		4 (0.2)	6 (0.3)
Beta-blockers, no. (%)	2436 (58.9)		1246 (60.5)	1190 (57.3)
Angiotensin converting enzyme inhibitors, no. (%)	2152 (52.0)		1071 (52.0)	1081 (52.0)
Angiotensin-2 receptor blockers, no. (%)	988 (23.9)		488 (23.7)	500 (24.1)
Calcium channel blockers, no. (%)	902 (21.8)		434 (21.1)	468 (22.5)
Nitrates, no. (%)	198 (4.8)		107 (5.2)	91 (4.4)
Statin, no. (%)	3989 (96.5)		1981 (96.3)	2008 (96.6)
High-intensity statin, no. (%) <sup>9)</sup>	1407 (34.0)		710 (34.5)	697 (33.6)
Proton pump inhibitors, no. (%)	3808 (92.1)		1875 (91.1)	1933 (93.0)

1 Categorical variables were presented as number and percentage. Continuous variables are presented as mean ± SD or

2 median with interquartile range.

3 1) Some patients had two or more location of myocardial infarction.

4 2) The culprit vessels are missing in 6 patients in 1-2 month DAPT group and 10 patients in 12 months DAPT group.

5 These 16 patients were enrolled in STOPDAPT-2.

6 3) Anemia was defined as hemoglobin <11 g/dl. Hemoglobin values were missing in 3 patients, who were included in the



- 1 no anemia group.
- 2 4) Thrombocytopenia was defined as platelet counts  $<100 \times 10^9/L$ . Platelet counts were missing in 12 patients, who were  
3 included in the no thrombocytopenia group.
- 4 5) Moderate chronic kidney disease is defined as estimated glomerular filtration rate  $<60$  and  $\geq 30$  ml/min/1.73m<sup>2</sup>. Severe  
5 chronic kidney disease is defined as estimated glomerular filtration rate  $<30$  ml/min/1.73m<sup>2</sup> or maintenance dialysis  
6 therapy. Preprocedural creatinine values were missing in 11 patients. One of these patients on dialysis was included in  
7 severe chronic kidney disease, while the remaining 10 patients were regarded as having neither moderate nor severe  
8 chronic kidney disease.
- 9 6) Left ventricular ejection fraction was missing in 312 patients, who were excluded for the calculation of left ventricular  
10 ejection fraction  $<40\%$ .
- 11 7) Lesions treated at the staged procedure(s) preceding the index PCI procedure were included as the target lesions.  
12 Clinical diagnosis and baseline characteristics were defined based on the findings at the time of first PCI for the index  
13 ACS event.
- 14 8) Concomitant oral anticoagulant use was one of the exclusion criteria, but some patients started anticoagulation after  
15 enrollment (e.g., new onset of atrial fibrillation or venous thrombosis).
- 16 9) High-intensity statin therapy was defined by the maximum approved dose of strong statin in Japan (e.g., rosuvastatin  
17 10mg, atorvastatin 20mg, or pitavastatin 4mg).
- 18 CABG coronary artery bypass grafting, CK creatine kinase, CKMB creatine kinase-MB, CPAOA cardiopulmonary arrest on  
19 arrival, CREDO-Kyoto The Coronary Revascularization Demonstrating Outcome Study in Kyoto, DAPT dual antiplatelet  
20 therapy, DES drug eluting stents, ECMO extracorporeal membrane oxygenation, eGFR estimated glomerular filtration rate,  
21 IVUS intravascular ultrasound, IABP intra-aortic balloon pumping, OCT optical coherence tomography, PARIS Patterns of  
22 Non-Adherence to Anti-Platelet Regimen in Stented Patients, PCI percutaneous coronary intervention, STEMI ST segment  
23 elevation myocardial infarction, and ULN upper limit of normal.

24  
25

1 **eTable 3. Comparison of baseline characteristics between STOPDAPT-2**  
 2 **and STOPDAPT-2 ACS**

	<b>STOPDAPT-2 ACS</b>	<b>STOPDAPT-2</b>	
	<b>N=2988</b>	<b>N=1148</b>	<b>P value</b>
<b>Patient demographics</b>			
Age, yr	66.9±12.0	66.6±11.6	0.39
≥75, no. (%)	885 (29.6)	298 (26.0)	0.02
Men, no. (%)	2366 (79.2)	914 (79.6)	0.76
Women, no. (%)	622 (20.8)	234 (20.4)	
Body mass index, kg/m <sup>2</sup>	24.1±3.6	24.2±3.5	0.59
Body mass index <25, no. (%)	1895 (63.4)	704 (61.3)	0.21
<b>Clinical presentation</b>			
Acute coronary syndrome, no. (%)	2988 (100)	1148 (100)	-
Acute myocardial infarction, no. (%)	2409 (80.6)	741 (64.6)	<0.001
ST segment elevation, no. (%)	1763 (73.2)	561 (75.7)	0.17
Non-ST segment elevation, no. (%)	646 (26.8)	180 (24.3)	
Treated ≤ 24 hours, no. (%)	2093 (86.9)	641 (86.5)	0.79
> 24 hours, no. (%)	316 (13.1)	100 (13.5)	
Onset to door time, hour	3.0 (1.3-10.0)	3.0 (1.3-10.2)	0.72
Door to wire crossing time (STEMI within 24 hours), min	60 (42-77)	60 (46-82)	<0.001
Killip class			0.003
1	2055 (85.3)	662 (89.7)	
2	209 (8.7)	54 (7.3)	
3	57 (2.4)	9 (1.2)	
4	88 (3.7)	13 (1.8)	
Location of STEMI <sup>1)</sup>			
Anterior, no. (%)	958 (54.3)	283 (50.7)	0.14
Inferior, no. (%)	697 (39.5)	228 (40.9)	0.58
Posterolateral, no. (%)	213 (12.1)	73 (13.1)	0.53
Peak CK/ULN	6.5 (2.2-13.4)	6.2 (2.6-12.7)	0.98
Peak CKMB/ULN	7.9 (2.1-20.8)	9.6 (2.8-23.6)	0.009
Unstable angina, no. (%)	579 (19.4)	407 (35.5)	<0.001
Braunwald class			<0.001

I	229 (39.6)	182 (44.7)	
II	66 (11.4)	71 (17.4)	
III	284 (49.1)	154 (37.8)	
Culprit vessels <sup>2)</sup>			0.06
Left anterior descending coronary artery	1600 (53.6)	608 (53.7)	
Left circumflex coronary artery	390 (13.1)	164 (14.5)	
Right coronary artery	955 (32.0)	354 (31.3)	
Left main coronary artery	41 (1.4)	5 (0.4)	
Saphenous vein graft	2 (0.1)	1 (0.1)	
CPAOA	26 (0.9)	14 (1.2)	0.30
ECMO use	10 (0.3)	3 (0.3)	1.00
Impella use	3 (0.1)	0 (0)	0.57
IABP use	128 (4.3)	20 (1.8)	<0.001
<b>Past history and comorbidities</b>			
Prior PCI, no. (%)	288 (9.6)	139 (12.1)	0.02
Prior first-generation DES, no. (%)	44 (1.5)	31 (2.7)	0.01
Prior CABG, no. (%)	18 (0.6)	9 (0.8)	0.52
Prior myocardial infarction, no. (%)	174 (5.8)	70 (6.1)	0.74
Prior stroke, no. (%)	136 (4.6)	57 (5.0)	0.57
Prior bleeding events, no. (%)	22 (0.7)	10 (0.9)	0.66
Heart failure, no. (%)	246 (8.2)	62 (5.4)	0.001
Atrial fibrillation, no. (%)	40 (1.3)	11 (1.0)	0.31
Anemia, no. (%) <sup>3)</sup>	165 (5.5)	82 (7.1)	0.053
Thrombocytopenia, no. (%) <sup>4)</sup>	11 (0.4)	10 (0.9)	0.053
Chronic obstructive pulmonary disease, no. (%)	63 (2.1)	24 (2.1)	0.97
Cirrhosis, no. (%)	6 (0.2)	4 (0.4)	0.48
Cancer, no. (%)	198 (6.6)	74 (6.5)	0.83
Active cancer, no. (%)	32 (1.1)	11 (1.0)	0.75
Peripheral artery disease, no. (%)	47 (1.6)	35 (3.1)	0.004
Moderate chronic kidney disease, no. (%) <sup>5)</sup>	914 (30.6)	313 (27.3)	0.04
Severe chronic kidney disease, no. (%)	105 (3.5)	33 (2.9)	0.30

5)			
eGFR <30 mL/min/1.73m <sup>2</sup> not on dialysis, no. (%) <sup>5)</sup>	69 (2.3)	20 (1.7)	0.25
Dialysis, no. (%)	36 (1.2)	13 (1.1)	0.85
Hypertension, no. (%)	2008 (67.2)	802 (69.9)	0.10
Hyperlipidemia, no. (%)	2001 (67.0)	763 (66.5)	0.76
Diabetes, no. (%)	871 (29.2)	358 (31.2)	0.20
Diabetes with insulin, no. (%)	85 (2.8)	40 (3.5)	0.29
Smoker, no. (%)	1953 (65.4)	745 (64.9)	0.78
Current Smoker, no. (%)	1053 (35.2)	367 (32.0)	0.046
Left ventricular ejection fraction, % <sup>6)</sup>	56.4±10.9	57.8±9.7	<0.001
<40%, no. (%) <sup>6)</sup>	133 (4.8)	38 (3.6)	0.09
Mitral regurgitation grade 3/4, no. (%)	40 (1.3)	23 (2.0)	0.13
<b>Risk scores</b>			
PARIS Thrombotic Risk Score	3 (2-4)	3 (2-4)	0.56
High ≥5	453 (15.2)	232 (20.2)	
Intermediate 3-4	1589 (53.2)	538 (46.9)	<0.001
Low 0-2	946 (31.7)	378 (32.9)	
PARIS Bleeding Risk Score	5 (3-7)	5 (3-7)	0.09
High ≥8	553 (18.5)	194 (16.9)	
Intermediate 4-7	1542 (51.6)	596 (51.9)	0.43
Low 0-3	893 (29.9)	358 (31.2)	
CREDO-Kyoto Thrombotic Risk Score	1 (0-1)	1 (0-1)	0.19
High ≥4	124 (4.2)	47 (4.1)	
Intermediate 2-3	499 (16.7)	195 (17.0)	0.97
Low 0-1	2365 (79.2)	906 (78.9)	
CREDO-Kyoto Bleeding Risk Score	0 (0-0)	0 (0-0)	0.48
High ≥3	98 (3.3)	34 (3.0)	
Intermediate 1-2	582 (19.5)	218 (19.0)	0.80
Low 0	2308 (77.2)	896 (78.1)	
<b>Procedural characteristics</b>			
Emergent procedure, no. (%)	2652 (88.8)	720 (62.7)	<0.001
Radial approach, no. (%)	2736 (91.6)	959 (83.5)	<0.001
Brachial approach, no. (%)	70 (2.3)	36 (3.1)	0.16

Femoral approach, no. (%)	293 (9.8)	201 (17.5)	<0.001
Only radial approach, no. (%)	2627 (87.9)	914 (79.6)	<0.001
Invasive fractional flow reserve, no. (%)	93 (3.1)	44 (3.8)	0.25
Staged procedure, no. (%) <sup>7)</sup>	447 (15.0)	150 (13.1)	0.12
Number of procedures	1.16±0.41	1.14±0.38	0.10
Number of target lesions <sup>7)</sup>	1.27±0.59	1.27±0.61	0.80
Target lesion location			
Left main coronary artery, no. (%)	92 (3.1)	18 (1.6)	0.004
Left anterior descending coronary artery, no. (%)	1796 (60.1)	701 (61.1)	0.57
Left circumflex coronary artery, no. (%)	584 (19.5)	241 (21.0)	0.30
Right coronary artery, no. (%)	1092 (36.6)	394 (34.3)	0.18
Bypassed graft, no. (%)	2 (0.1)	1 (0.1)	1.00
Chronic total occlusion, no. (%)	100 (3.4)	28 (2.4)	0.12
Bifurcation lesions, no. (%)	811 (27.1)	290 (25.3)	0.22
Final 2 stents implantation, no. (%)	17 (0.6)	8 (0.7)	0.64
Target of 2 vessels or more, no. (%)	550 (18.4)	184 (16.0)	0.07
Target of 3 vessels or more, no. (%)	101 (3.4)	32 (2.8)	0.33
Use of IVUS or OCT, no. (%)	2916 (97.6)	1107 (96.4)	0.046
IVUS, no. (%)	2592 (86.8)	996 (86.8)	0.99
OCT, no. (%)	446 (14.9)	143 (12.5)	0.04
Number of implanted stents	1.41±0.78	1.39±0.77	0.57
Minimal stent diameter, mm	3.02±0.52	3.01±0.49	0.78
<3.0 mm, no. (%)	1173 (39.3)	426 (37.1)	0.20
Total stent length, mm	35.1±23.7	32.9±21.0	0.004
>=28mm, no. (%)	1651 (55.3)	587 (51.1)	0.02
<b>Medication at discharge</b>			
Aspirin, no. (%)	2984 (99.9)	1147 (99.9)	1.00
200mg/day, no. (%)	2 (0.1)	0 (0)	
100mg/day, no. (%)	2936 (98.4)	1134 (98.9)	0.50
81mg/day, no. (%)	46 (1.5)	13 (1.1)	
P2Y <sub>12</sub> receptor blockers, no. (%)	2985 (99.9)	1146 (99.8)	0.56

Ticlopidine, no. (%)	0 (0)	0 (0)	-
Clopidogrel, no. (%)	1578 (52.8)	592 (51.6)	0.47
75mg/day, no. (%)	1578 (100)	592 (100)	
Prasugrel, no. (%)	1408 (47.1)	554 (48.3)	0.51
3.75mg/day, no. (%)	1386 (98.4)	545 (98.4)	0.92
2.5mg/day, no. (%)	22 (1.6)	9 (1.6)	
Ticagrelor, no. (%)	0 (0)	0 (0)	-
Anticoagulation, no. (%) <sup>8)</sup>	16 (0.5)	7 (0.6)	0.78
Novel oral anticoagulants, no. (%)	9 (0.3)	4 (0.4)	0.76
Warfarin, no. (%)	7 (0.2)	3 (0.3)	1.00
Beta-blockers, no. (%)	1802 (60.3)	634 (55.2)	0.003
Angiotensin converting enzyme inhibitors, no. (%)	1594 (53.4)	558 (48.6)	0.006
Angiotensin-2 receptor blockers, no. (%)	706 (23.6)	282 (24.6)	0.53
Calcium channel blockers, no. (%)	575 (19.2)	327 (28.5)	<0.001
Nitrates, no. (%)	104 (3.5)	94 (8.2)	<0.001
Statin, no. (%)	2921 (97.8)	1068 (93.0)	<0.001
High-intensity statin, no. (%) <sup>9)</sup>	1321 (44.2)	86 (7.5)	<0.001
Proton pump inhibitors, no. (%)	2790 (93.4)	1018 (88.7)	<0.001

1 Categorical variables were presented as number and percentage. Continuous variables are presented as mean ± SD or  
2 median with interquartile range.

3 1) Some patients had two or more location of myocardial infarction.

4 2) The culprit vessels are missing in 16 patients enrolled in STOPDAPT-2.

5 3) Anemia was defined as hemoglobin <11 g/dl. Hemoglobin values were missing in 3 patients, who were included in the  
6 no anemia group.

7 4) Thrombocytopenia was defined as platelet counts <100\*10<sup>9</sup>/L. Platelet counts were missing in 12 patients, who were  
8 included in the no thrombocytopenia group.

9 5) Moderate chronic kidney disease is defined as estimated glomerular filtration rate <60 and ≥30 ml/min/1.73m<sup>2</sup>. Severe  
10 chronic kidney disease is defined as estimated glomerular filtration rate <30 ml/min/1.73m<sup>2</sup> or maintenance dialysis  
11 therapy. Preprocedural creatinine values were missing in 11 patients. One of these patients on dialysis was included in  
12 severe chronic kidney disease, while the remaining 10 patients were regarded as having neither moderate nor severe  
13 chronic kidney disease.

14 6) Left ventricular ejection fraction was missing in 312 patients, who were excluded for the calculation of left ventricular

1           ejection fraction <40%.

2    7)   Lesions treated at the staged procedure(s) preceding the index PCI procedure were included as the target lesions.

3           Clinical diagnosis and baseline characteristics were defined based on the findings at the time of first PCI for the index  
4           ACS event.

5    8)   Concomitant oral anticoagulant use was one of the exclusion criteria, but some patients started anticoagulation after  
6           enrollment (e.g. new onset of atrial fibrillation or venous thrombosis).

7    9)   High-intensity statin therapy was defined by the maximum approved dose of strong statin in Japan (e.g., rosuvastatin  
8           10mg, atorvastatin 20mg, or pitavastatin 4mg).

9    CABG coronary artery bypass grafting, CK creatine kinase, CKMB creatine kinase-MB, CPAOA cardiopulmonary arrest on  
10   arrival, CREDO-Kyoto The Coronary Revascularization Demonstrating Outcome Study in Kyoto, DAPT dual antiplatelet  
11   therapy, DES drug eluting stents, ECMO extracorporeal membrane oxygenation, eGFR estimated glomerular filtration rate,  
12   IVUS intravascular ultrasound, IABP intra-aortic balloon pumping, OCT optical coherence tomography, PARIS Patterns of  
13   Non-Adherence to Anti-Platelet Regimen in Stented Patients, PCI percutaneous coronary intervention, STEMI ST segment  
14   elevation myocardial infarction, and ULN upper limit of normal.

15

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17

1 **eTable 4. Per-protocol and as-treated population according to the mode of**  
 2 **antithrombotic therapy at 60-day**

	<b>1-2 month DAPT</b>	<b>12 months DAPT</b>	
	<b>N=2058</b>	<b>N=2078</b>	
1. Follow-up at 60-day	2046 (99.4)	2064 (99.3)	
2. Aspirin on treatment at 60-day	98 (4.8)	2046 (99.1)	
3. Aspirin off treatment at 60-day	1948 (95.2)	18 (0.9)	
4. P2Y <sub>12</sub> inhibitors on treatment at 60-day	2029 (99.2)	2048 (99.2)	
5. Clopidogrel on treatment at 60-day	1992 (98.2)	1953 (95.4)	
6. no OAC at 60-day	2018 (98.6)	2038 (98.7)	
7. No other exclusion criteria (prior BVS/Hemorrhagic stroke/Other APT)	2048 (99.5)	2064 (99.3)	
<b>Per protocol population</b>			
3, 5, 6, and 7 (1-2 month DAPT)	1898 (92.2)	0 (0)	
2, 5, 6, and 7 (12 months DAPT)	0 (0)	1908 (91.8)	
<b>As-treated population</b>			<b>subtotal</b>
1, 3, 5, and 6 (Clopidogrel monotherapy)	1908 (92.7)	7 (0.3)	1915 (49.2)
1, 2, 5, and 6 (DAPT with Aspirin + Clopidogrel)	58 (2.8)	1921 (92.4)	1979 (50.8)

3 DAPT denotes dual antiplatelet therapy, OAC oral anticoagulation, BVS bioresorbable vascular scaffold, and APT antiplatelet  
 4 therapy.



1 **eTable 5. Details of cases with definite or probable stent thrombosis <sup>1)</sup>**

Assigned group	Days after index PCI	ARC definition of stent thrombosis	Medication at the event	Study	Age, gender	Index presentation, other risk factors
1-2 month DAPT	4	Definite	DAPT: aspirin +prasugrel	STOPDAPT-2 ACS	60 yr Male	STEMI, Peak CK/CKMB 9705/923(ng/ml), Current smoker, OAC, EF 30%, PARIS-T ARC-HBR
1-2 month DAPT	6	Probable	DAPT: aspirin +prasugrel	STOPDAPT-2	70 yr Male	UA, Braunwald III HTN, Current smoker PARIS-T/B 2/7, CREDO-Kyoto T/B 0/0
1-2 month DAPT	30	Definite	DAPT: aspirin +clopidogrel	STOPDAPT-2 ACS	47 yr Male	NSTEMI, Peak CK/CKMB 933/101, Prior PCI, Dialysis, HTN, HL, Diabetes, Current PARIS-T/B; 8/9, CREDO-Kyoto-T/B; 3/2 ARC-HBR

1-2 month DAPT	40	Definite	Clopidogrel monotherapy. Day 8 since discontinuation of aspirin	STOPDAPT-2 ACS	68 yr Female	STEMI, Peak CK/CKMB 2271/323, PARIS-T/B; 2/7, CREDO-Kyoto-T/B; 2/0, ARC-HBR
1-2 month DAPT	51	Definite	Clopidogrel monotherapy. Day 22 since discontinuation of aspirin	STOPDAPT-2	64 yr Male	STEMI, Peak CK/CKMB 3055/259 HL, Current Smoker PARIS-T/B; 3/4, CREDO-Kyoto-T/B: 0/0
1-2 month DAPT	56	Definite	Clopidogrel monotherapy. Day 17 since discontinuation of aspirin	STOPDAPT-2 ACS	76 yr Male	STEMI, Peak CK/CKMB 940/103, HTN, HL, Diabetes, PARIS-T/B; 5/7, CREDO-Kyoto-T/B; 3/0 ARC-HBR

1-2 month DAPT	105	Definite	Clopidogrel monotherapy. Day 78 since discontinuation of aspirin	STOPDAPT-2 ACS	64 yr Male	NSTEMI, Peak CK/CKMB 2055/182, HTN, HL, Dialysis, PARIS-T/B; 4/9, CREDO-H ARC-HBR
1-2 month DAPT	112	Definite	Clopidogrel monotherapy. Day 76 since discontinuation of aspirin	STOPDAPT-2	51 yr Female	UA, Braunwald II HTN, HL, past smoker, Prior PCI (-5y): G1-DES implanted in LCx PARIS-T/B; 4/1, CREDO-Kyoto-T/B; 1/0
1-2 month DAPT	352	Definite	Clopidogrel monotherapy. Day 312 since discontinuation of aspirin	STOPDAPT-2 ACS	70 yr Male	UA, Braunwald III HL, Diabetes, PARIS-T/B; 2/5, CREDO-Kyoto-T/B; 1/0
1-2 month DAPT	359	Definite	No APT Day 23 since discontinuation of clopidogrel by self-judgement, and Day 310	STOPDAPT-2 ACS	40 yr Male	STEMI, Peak CK/CKMB 5658/452(ng/ml), Current smoker, PARIS-T/B; 3/4, CREDO-H ARC-HBR

			since scheduled discontinuation of aspirin			
12 months DAPT	3	Definite	DAPT: aspirin +clopidogrel	STOPDAPT-2 ACS	84 yr Male	UA, Braunwald III, Diabetes, current smoker, PARIS-T/B; 5/10, CREDO-Kyoto-T/B; Complex PCI, ARC-HBR
12 months DAPT	148	Definite	DAPT: aspirin +clopidogrel	STOPDAPT-2	69 yr Male	UA, Braunwald I HTN, HL, Diabetes, Prior PCI (-5 months); LAD G2-DES implanted (different site from the index PCI). PARIS-T/B: 4/4, CREDO-Kyoto-T/B: 1/0

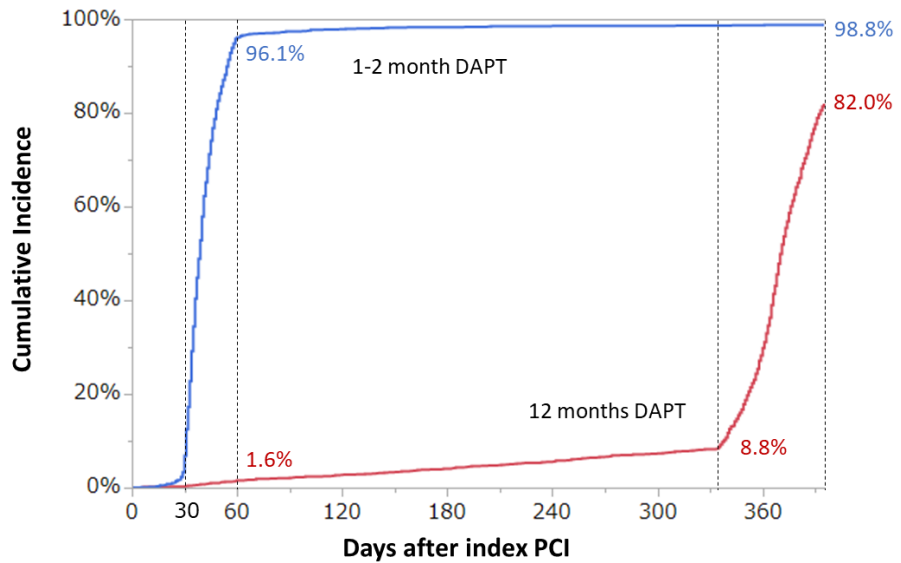
12 months DAPT	160	Definite	DAPT: aspirin +clopidogrel	STOPDAPT-2 ACS	73 yr Female	UA, Braunwald I, Prior CABG, PCI, Dialysis, HTN, HL, Diabetes, PARIS-T/B; 8/5, C ARC-HBR
12 months DAPT	362	Definite	No APT by self-judgement. Day 7 from discontinuation of both aspirin and clopidogrel	STOPDAPT-2 ACS	75 yr Male	STEMI, Peak CK/CKMB 302/39, PARIS-T/B; 2/5, CREDO-Kyoto-T/B; 1/0

1) The cases are sorted by the days after index PCI.

PARIS-T/B, and CREDO-Kyoto T/B indicate PARIS thrombotic/bleeding risk score and CREDO-Kyoto thrombotic/bleeding risk scores. APT denotes antiplatelet therapy, ARC academic research consortium, CK creatine kinase, CKD chronic kidney disease, CKMB creatine kinase-MB, CoCr-EES, cobalt-chromium everolimus-eluting stents, DAPT dual antiplatelet therapy, DCB drug coated balloon, DES drug-eluting stents, DM diabetes mellitus, EF ejection fraction, G1 first generation, G2 second generation, HBR high bleeding risk, HTN hypertension, HL hyperlipidemia, ISR in-stent restenosis, IVUS intravascular ultrasound, KBT kissing balloon technique, LAD left anterior ascending coronary artery, LCx left circumflex coronary artery, NSTEMI non-ST -segment elevation myocardial infarction, OCT optical coherence tomography, PCI percutaneous coronary intervention, POBA plain old balloon angioplasty, RCA right coronary artery, SCD sudden cardiac death, SES sirolimus-eluting stents, STEMI ST-segment elevation myocardial infarction, and UA unstable angina.

1 **eFigures**

2 **eFigure 1. The rate of persistent DAPT discontinuation rate**



1-2 month DAPT	0	30	60	120	180	240	300	335	395
N of patients with DAPT discontinuation		140	1972	2010	2019	2023	2025	2025	2028
N of patients with DAPT	2058	1986	86	42	33	29	27	27	17
Cumulative incidence (%)		6.8	96.1	97.9	98.4	98.6	98.7	98.7	98.8
12 months DAPT	0	30	60	120	180	240	300	335	395
N of patients with DAPT discontinuation		8	32	58	84	115	151	181	1567
N of patients with DAPT	2078	2070	2033	2004	1974	1941	1903	1879	299
Cumulative incidence (%)		0.4	1.6	2.8	4.1	5.6	7.3	8.8	82.0

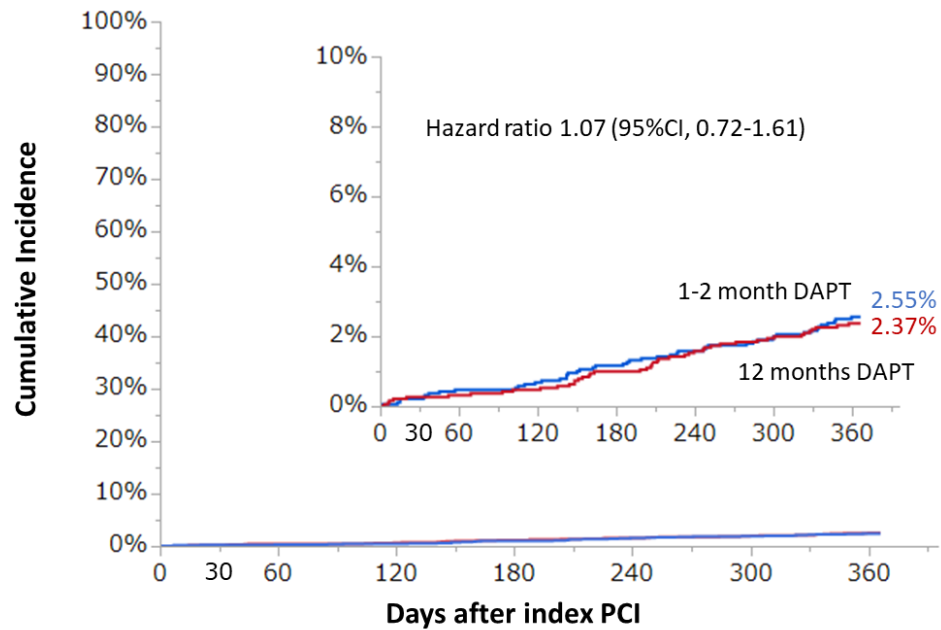
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5 Within the first month after the index PCI, patients in both groups were to receive DAPT with aspirin (doses determined by  
6 sites) and a P2Y<sub>12</sub> inhibitor (clopidogrel 75 mg/day or prasugrel 3.75mg/day at the discretion of the attending physicians). At  
7 1 month (30 to 59 days) after the index PCI, patients in the 1-month DAPT group were to stop aspirin and to receive  
8 clopidogrel monotherapy, while patients in the 12-month DAPT group were to receive DAPT with aspirin and clopidogrel up  
9 to 12 months. In patients who had received prasugrel, it was switched to clopidogrel at 1 month in both groups. In the  
10 12-month DAPT group, clopidogrel was to be discontinued at 12-month with the allowance period between 335- and 394-day  
11 after index PCI. We collected data for discontinuation, change, or restart of antithrombotic therapy including anticoagulation  
12 on daily basis. Persistent DAPT discontinuation was defined as stopping of either aspirin or P2Y<sub>12</sub> inhibitor by the study  
13 protocol or stopping >60 days for any reasons.

14

1 **eFigure 2. Per-protocol analysis for the primary endpoint**



1-2 month DAPT	0	30	60	120	180	240	300	365
Number of patients with event		4	9	13	22	30	38	48
Number of patients at risk	1898	1894	1888	1884	1872	1859	1848	1495
Cumulative incidence (%)		0.21	0.47	0.69	1.16	1.58	2.01	2.55
12 months DAPT	0	30	60	120	180	240	300	365
Number of patients with event		5	6	9	19	30	38	45
Number of patients at risk	1908	1903	1902	1897	1886	1873	1864	1465
Cumulative incidence (%)		0.26	0.31	0.47	1.00	1.57	1.99	2.37

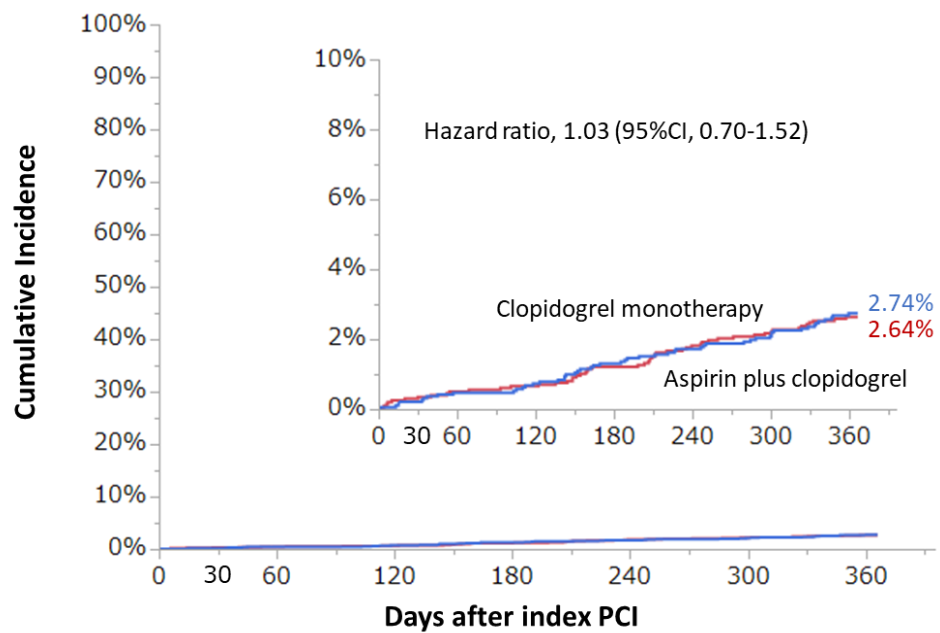
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Time-to-event curves were presented for the primary endpoint in the per-protocol population. This analysis included the patients in the 1-month DAPT group receiving clopidogrel monotherapy without aspirin, and the patients in the 12-month DAPT group receiving both aspirin and clopidogrel at 60 days after index PCI. Patients with oral anticoagulants use, use of other antiplatelet therapy, history of hemorrhagic stroke, and history of implantation of bioabsorbable vascular scaffolds were excluded according to the protocol defined exclusion criteria.

DAPT denotes dual antiplatelet therapy and PCI percutaneous coronary intervention.

1 **eFigure 3. As-treated analysis for the primary endpoint**

2



	0	30	60	120	180	240	300	365
<b>Clopidogrel monotherapy</b>								
Number of patients with event		4	9	14	25	33	42	52
Number of patients at risk	1915	1911	1905	1900	1886	1873	1862	1506
Cumulative incidence (%)		0.21	0.47	0.73	1.31	1.73	2.20	2.74
<b>Aspirin plus clopidogrel</b>	<b>0</b>	<b>30</b>	<b>60</b>	<b>120</b>	<b>180</b>	<b>240</b>	<b>300</b>	<b>365</b>
Number of patients with event		7	10	13	24	36	44	52
Number of patients at risk	1979	1973	1969	1964	1952	1938	1929	1521
Cumulative incidence (%)		0.35	0.51	0.66	1.21	1.82	2.23	2.64

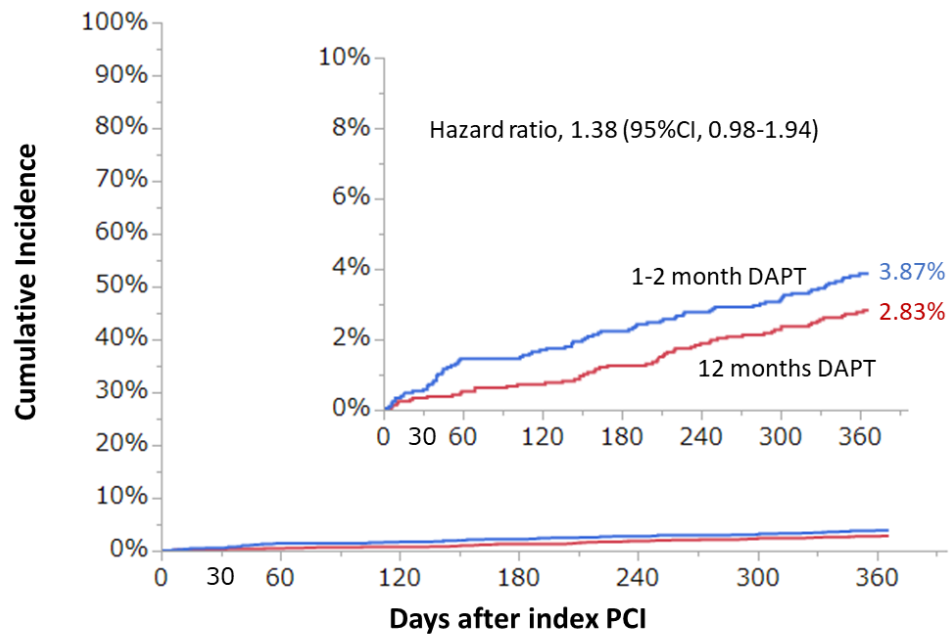
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4 Time-to-event curves were presented for the primary endpoint in the as-treated population. In this analysis, regardless of the  
 5 randomly assigned groups, 1) the patients receiving clopidogrel monotherapy without oral anticoagulants at 60-day were set  
 6 as clopidogrel monotherapy group, and 2) the patients receiving both aspirin and clopidogrel without anticoagulants at  
 7 60-day were set as aspirin plus clopidogrel group. We did not consider other exclusion criteria (history of hemorrhagic stroke,  
 8 oral anticoagulants use, use of other antiplatelet therapy, history of implantation of bioabsorbable vascular scaffolds).  
 9 PCI denotes percutaneous coronary intervention.

10



1 **eFigure 4. Worst-case scenario for the primary endpoint**

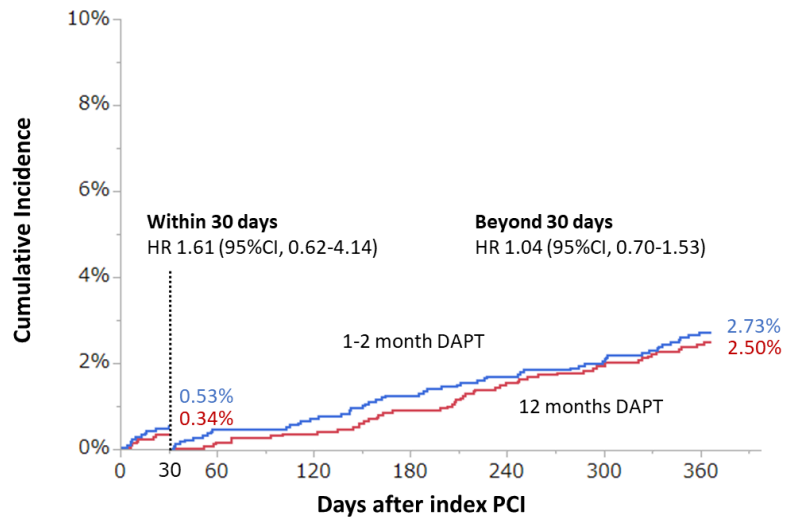


	0	30	60	120	180	240	300	365
<b>1-2 month DAPT</b>								
Number of patients with event		12	30	35	46	57	65	79
Number of patients at risk	2058	2047	2028	2021	2007	1993	1982	1606
Cumulative incidence (%)		0.58	1.46	1.70	2.24	2.77	3.16	3.87
<b>12 months DAPT</b>								
Number of patients with event		7	11	15	26	39	49	58
Number of patients at risk	2078	2070	2055	2048	2036	2021	2010	1581
Cumulative incidence (%)		0.34	0.53	0.72	1.26	1.89	2.37	2.83

3 Time-to-event curves were presented for the primary endpoint in a sensitivity analysis assuming that patients lost to  
 4 follow-up in the experimental arm had the primary endpoint event, while those in the control arm did not have the event.  
 5  
 6 DAPT denotes dual antiplatelet therapy, PCI percutaneous coronary intervention.  
 7

1 **eFigure 5. Landmark analysis at 30 days**

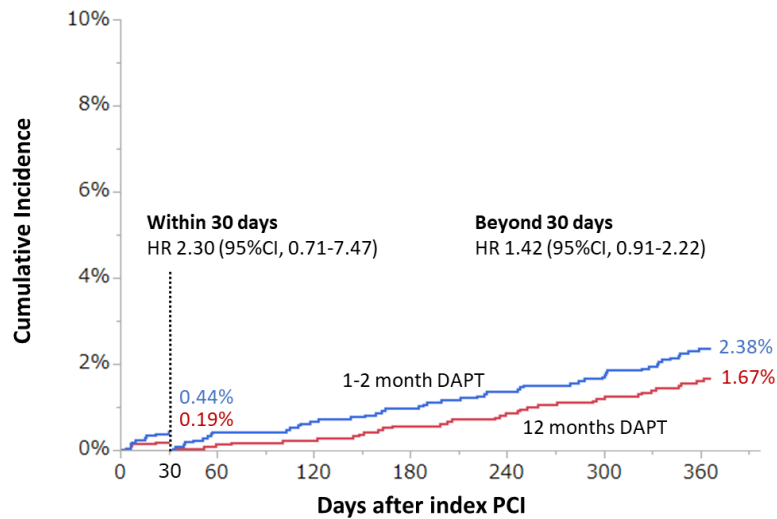
2 **(a) Primary endpoint**



1-2 month DAPT	0	30	60	120	180	240	300	365
Number of patients with event		11	10	15	26	35	43	55
Number of patients at risk	2058	2047	2028	2021	2007	1993	1982	1606
Cumulative incidence (%)		0.53	0.49	0.74	1.28	1.72	2.11	2.73
12 months DAPT	0	30	60	120	180	240	300	365
Number of patients with event		7	4	8	19	32	42	51
Number of patients at risk	2078	2070	2055	2048	2036	2021	2010	1581
Cumulative incidence (%)		0.34	0.19	0.39	0.92	1.56	2.04	2.50

3

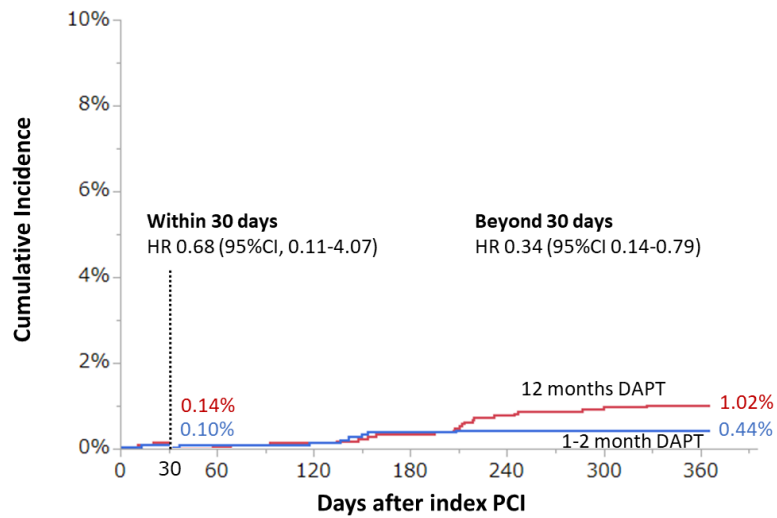
4 **(b) Major secondary cardiovascular endpoint**



1-2 month DAPT	0	30	60	120	180	240	300	365
Number of patients with event		9	9	14	20	28	36	48
Number of patients at risk	2058	2049	2031	2024	2015	2002	1991	1614
Cumulative incidence (%)		0.44	0.44	0.69	0.98	1.37	1.77	2.38
12 months DAPT	0	30	60	120	180	240	300	365
Number of patients with event		4	3	5	12	18	26	34
Number of patients at risk	2078	2073	2059	2054	2046	2038	2028	1597
Cumulative incidence (%)		0.19	0.15	0.24	0.58	0.87	1.26	1.67

5

1 (c) Major secondary bleeding endpoint



1-2 month DAPT	0	30	60	120	180	240	300	365
Number of patients with event		2	2	3	8	9	9	9
Number of patients at risk	2058	2052	2041	2038	2030	2023	2015	1642
Cumulative incidence (%)		0.10	0.10	0.15	0.39	0.44	0.44	0.44
12 months DAPT	0	30	60	120	180	240	300	365
Number of patients with event		3	1	3	7	16	20	21
Number of patients at risk	2078	2073	2060	2054	2045	2033	2027	1603
Cumulative incidence (%)		0.14	0.05	0.15	0.34	0.78	0.97	1.02

2

3

4 Time-to-event curves were presented for the primary and major secondary endpoints in a landmark analysis at 30 days. See  
5 text and eAppendix 3 for the definition of each endpoint.

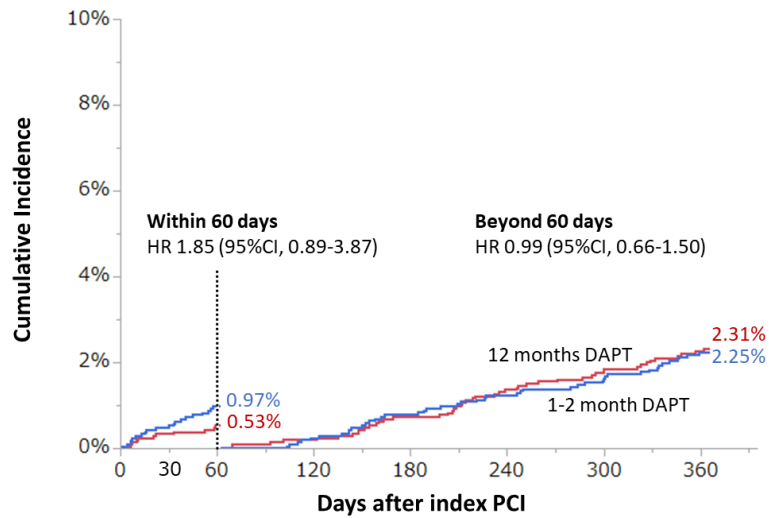
6 DAPT denotes dual antiplatelet therapy, PCI percutaneous coronary intervention.

7

8

1 **eFigure 6. Landmark analysis at 60 days**

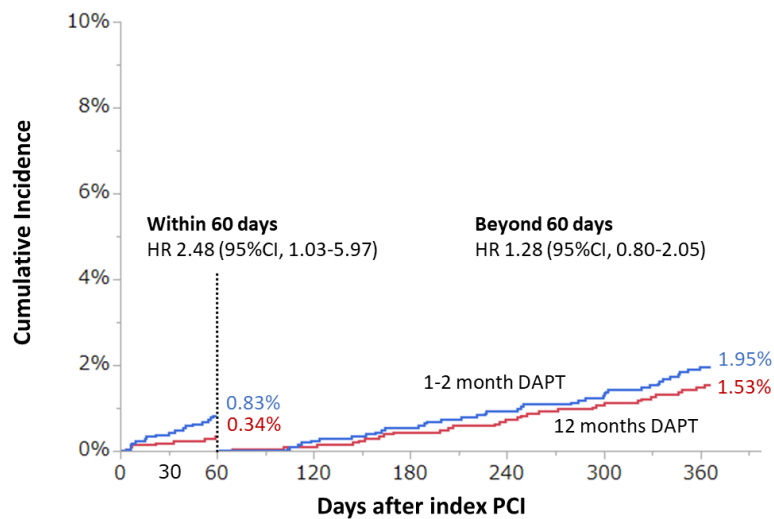
2 **(a) Primary endpoint**



1-2 month DAPT	0	30	60	120	180	240	300	365
Number of patients with event		11	20	5	16	25	33	45
Number of patients at risk	2058	2047	2028	2021	2007	1993	1982	1606
Cumulative incidence (%)		0.53	0.97	0.25	0.79	1.24	1.63	2.25
12 months DAPT	0	30	60	120	180	240	300	365
Number of patients with event		7	11	4	15	28	38	47
Number of patients at risk	2078	2070	2055	2048	2036	2021	2010	1581
Cumulative incidence (%)		0.34	0.53	0.19	0.73	1.37	1.85	2.31

3

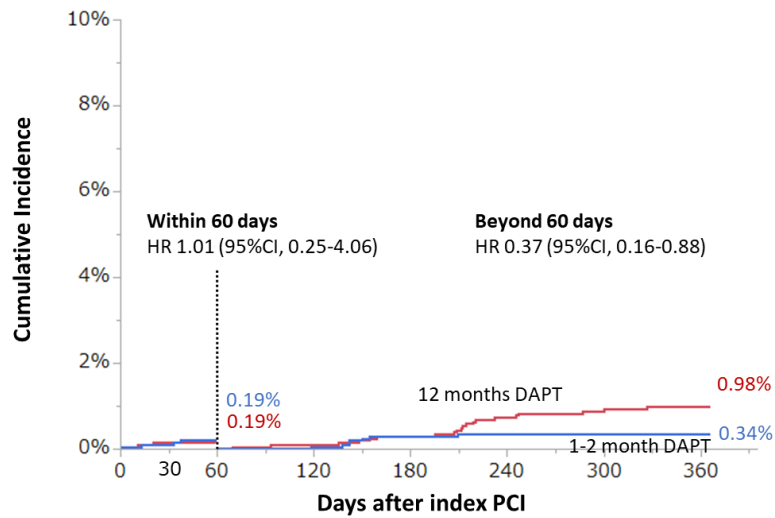
4 **(b) Major secondary cardiovascular endpoint**



1-2 month DAPT	0	30	60	120	180	240	300	365
Number of patients with event		9	17	5	11	19	27	39
Number of patients at risk	2058	2049	2031	2024	2015	2002	1991	1614
Cumulative incidence (%)		0.44	0.83	0.25	0.54	0.94	1.33	1.95
12 months DAPT	0	30	60	120	180	240	300	365
Number of patients with event		4	7	2	9	15	23	31
Number of patients at risk	2078	2073	2059	2054	2046	2038	2028	1597
Cumulative incidence (%)		0.19	0.34	0.10	0.44	0.73	1.12	1.53

5

1 (c) Major secondary bleeding endpoint



1-2 month DAPT	0	30	60	120	180	240	300	365
Number of patients with event		2	4	1	6	7	7	7
Number of patients at risk	2058	2052	2041	2038	2030	2023	2015	1642
Cumulative incidence (%)		0.10	0.19	0.05	0.29	0.34	0.34	0.34
12 months DAPT	0	30	60	120	180	240	300	365
Number of patients with event		3	4	2	6	15	19	20
Number of patients at risk	2078	2073	2060	2054	2045	2033	2027	1603
Cumulative incidence (%)		0.14	0.19	0.10	0.29	0.73	0.93	0.98

2

3

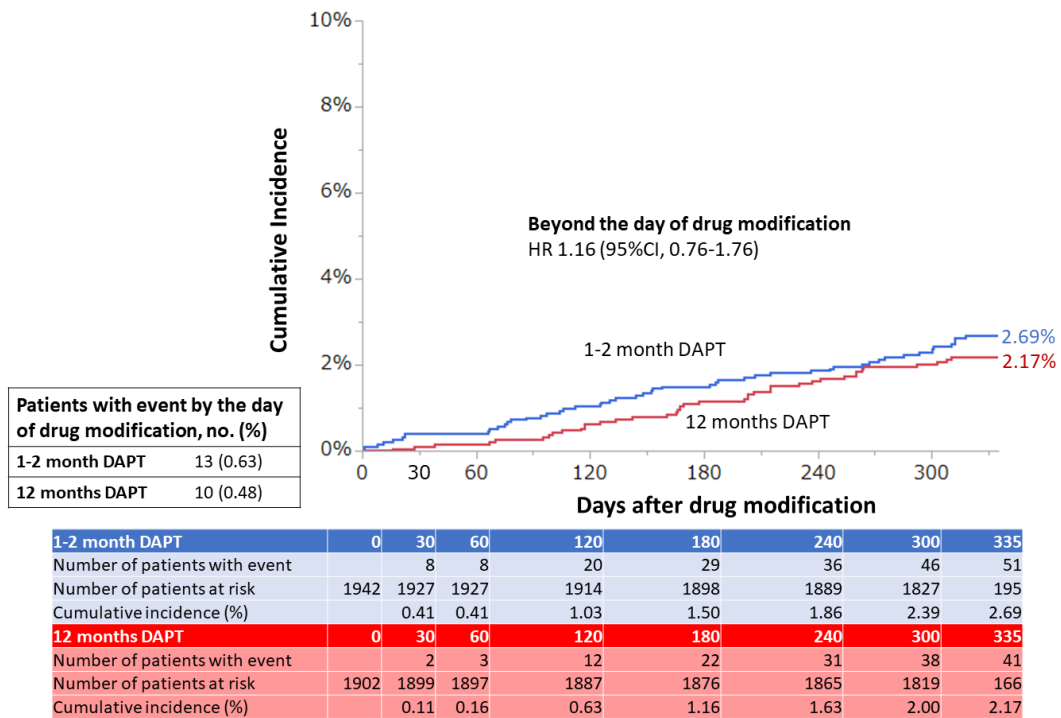
4 Time-to-event curves were presented for the primary and major secondary endpoints in a landmark analysis at 60 days. See  
 5 text and eAppendix 3 for the definition of each endpoint.

6 DAPT denotes dual antiplatelet therapy, PCI percutaneous coronary intervention.

7

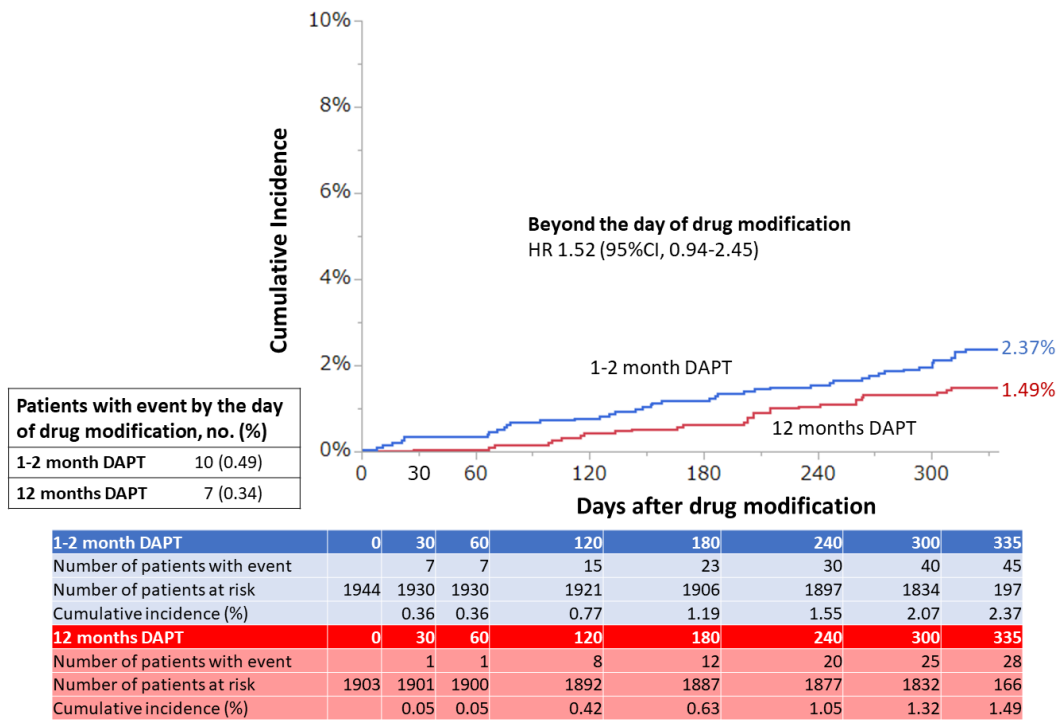
1 **eFigure 7. Landmark analysis at the day of drug modification**

2 **(a) Primary endpoint**



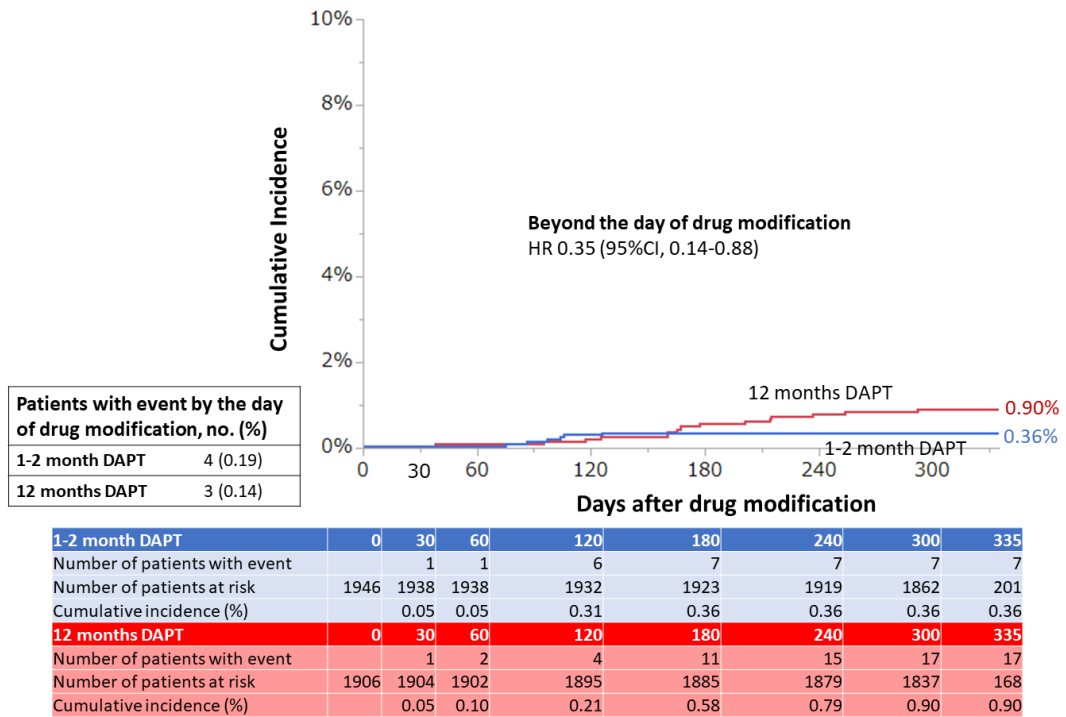
3

4 **(b) Major secondary cardiovascular endpoint**



5

1 (c) Major secondary bleeding endpoint



2

3

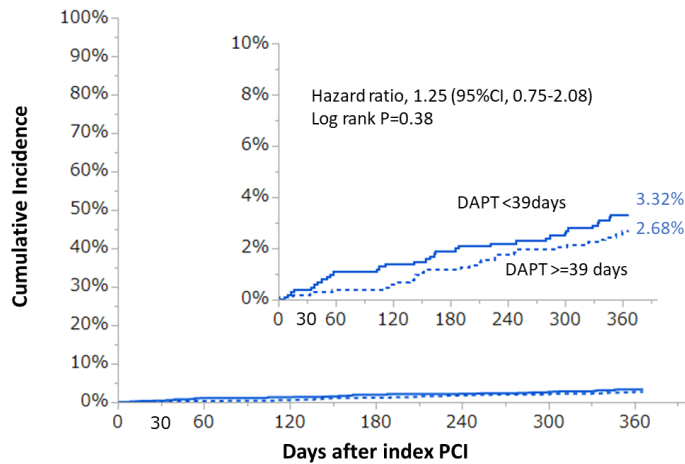
4 Time-to-event curves were presented for the primary and major secondary endpoints in a post-hoc landmark analysis at the  
 5 day of drug modification on the scheduled 1-month visit. In this analysis, the patients were excluded who did not change  
 6 their antiplatelet therapy on the day of 1-month visit in the 1-month DAPT arm or who did not visit at 1 month. In patients who  
 7 did not change their antiplatelet therapy at 1-month visit, the day of 1-month visit was regarded as the day of drug  
 8 modification. See text and eAppendix 3 for the definition of each endpoint.

9 DAPT denotes dual antiplatelet therapy, PCI percutaneous coronary intervention.

10

1 **eFigure 8. Time-to-event curves for the primary and major secondary**  
 2 **cardiovascular and bleeding endpoints in the 1-2 month DAPT group**  
 3 **stratified by the median value of DAPT duration**

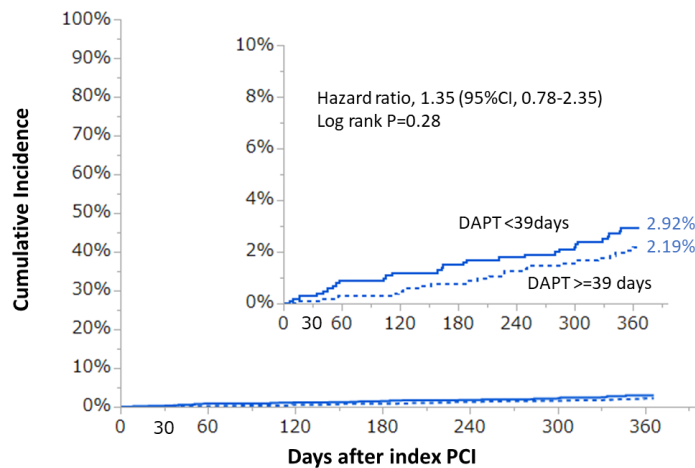
4 **(a) Primary endpoint**



DAPT <39days	0	30	60	120	180	240	300	365
Number of patients with event		4	11	14	19	22	27	33
Number of patients at risk	1003	999	988	985	977	972	966	781
Cumulative incidence (%)		0.40	1.10	1.40	1.90	2.20	2.70	3.32
DAPT >=39days	0	30	60	120	180	240	300	365
Number of patients with event		2	4	6	12	18	21	27
Number of patients at risk	1025	1023	1017	1014	1008	999	994	805
Cumulative incidence (%)		0.20	0.39	0.59	1.17	1.76	2.06	2.68

5

6 **(b) Major secondary cardiovascular endpoint**

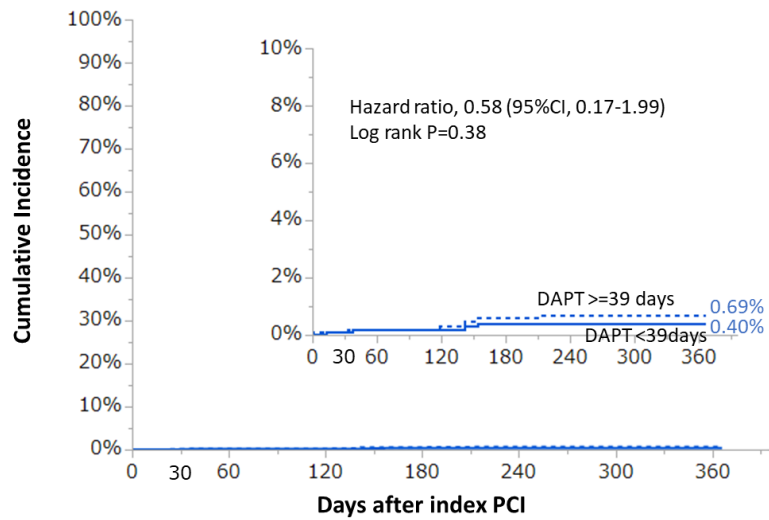


DAPT <39days	0	30	60	120	180	240	300	365
Number of patients with event		3	9	12	15	18	23	29
Number of patients at risk	1003	1000	990	987	981	976	970	785
Cumulative incidence (%)		0.30	0.90	1.20	1.50	1.80	2.31	2.92
DAPT >=39days	0	30	60	120	180	240	300	365
Number of patients with event		1	3	5	8	13	16	22
Number of patients at risk	1025	1024	1018	1015	1012	1004	999	809
Cumulative incidence (%)		0.10	0.29	0.49	0.78	1.27	1.57	2.19

7



1 (c) Major secondary bleeding endpoint



DAPT <39days	0	30	60	120	180	240	300	365
Number of patients with event		1	2	2	4	4	4	4
Number of patients at risk	1003	1002	997	997	992	990	986	802
Cumulative incidence (%)		0.10	0.20	0.20	0.40	0.40	0.40	0.40
DAPT >=39days	0	30	60	120	180	240	300	365
Number of patients with event		1	2	3	6	7	7	7
Number of patients at risk	1025	1024	1019	1017	1014	1009	1005	818
Cumulative incidence (%)		0.10	0.20	0.29	0.59	0.69	0.69	0.69

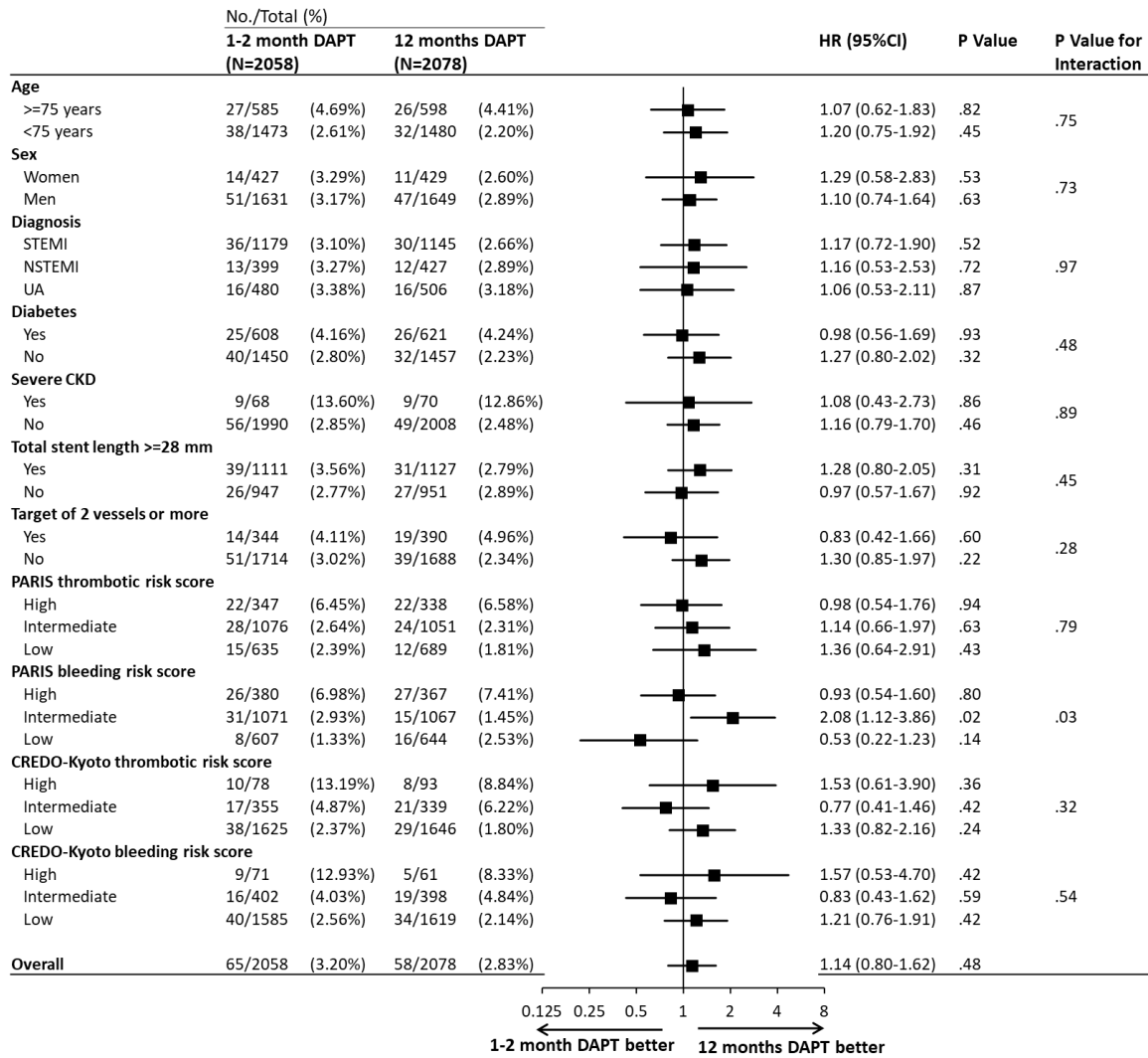
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9

Time-to-event curves for (a) the primary endpoint, (b) major secondary cardiovascular endpoint, and (c) major secondary bleeding endpoint in the 1-2 month DAPT group stratified by the median value of the DAPT duration (39 days). See text and eAppendix 3 for the definition of each endpoint.

DAPT denotes dual antiplatelet therapy and PCI percutaneous coronary intervention.

1 **eFigure 9. Subgroup Analyses for the Relative Effect of 1-2 Month DAPT on**  
 2 **the Primary and Major Secondary Endpoints**

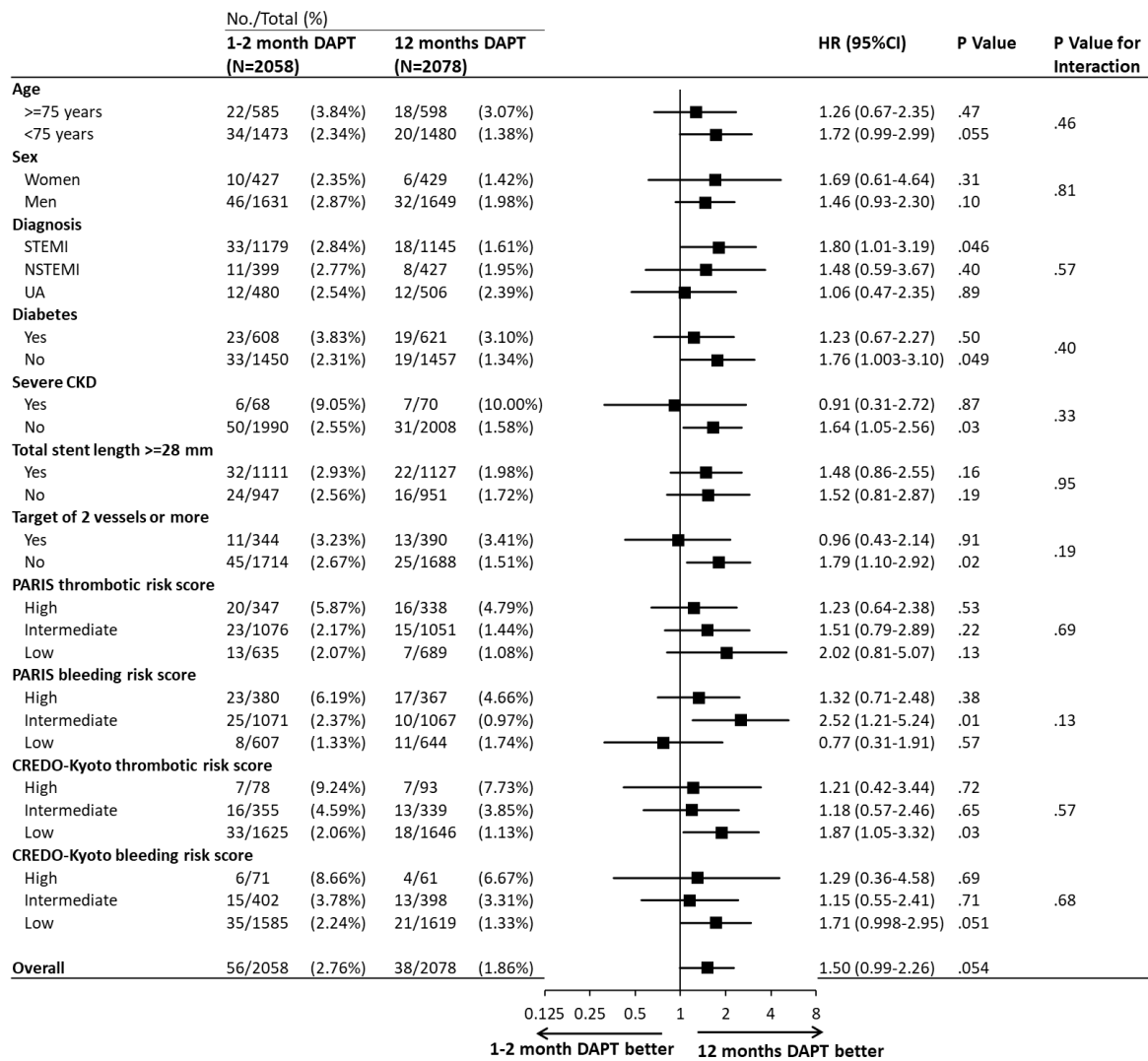
3 **(a) Primary endpoint**



4

5

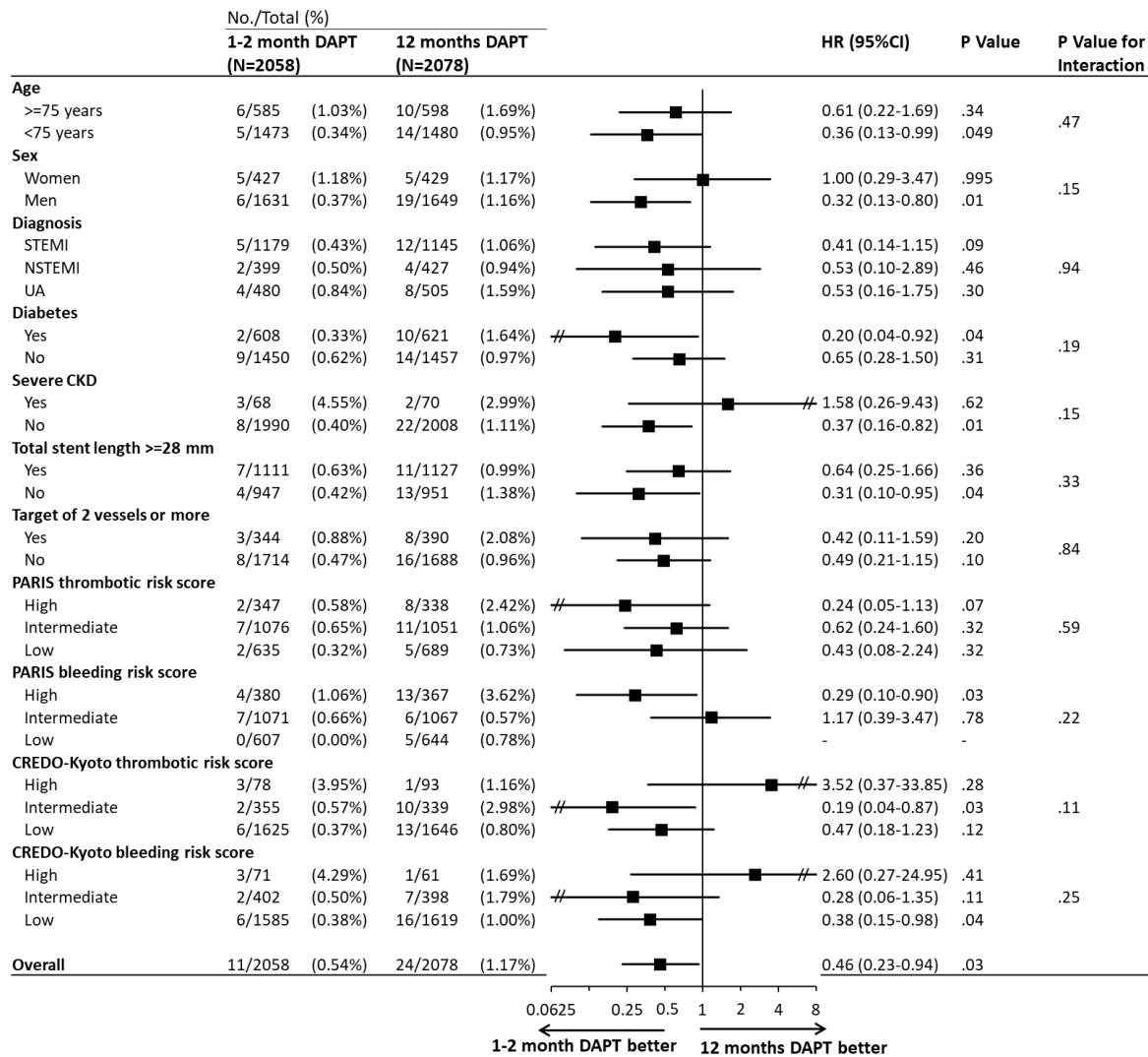
1 (b) Major secondary cardiovascular endpoint



2

3

1 (c) Major secondary bleeding endpoint



2  
3 The subgroup analyses on (A) primary endpoint, (B) major secondary cardiovascular endpoint, and (C) major bleeding  
4 endpoint. Numbers indicate number of patients with event/number of patients at risk.

5 Severe CKD was defined as pre-procedural eGFR <30 mL/min/1.73m<sup>2</sup> or on maintenance dialysis.

6 DAPT denotes dual antiplatelet therapy, HR hazard ratio, CI confidence interval, ACS acute coronary syndrome, STEMI

7 ST-segment elevation myocardial infarction, NSTEMI non-ST-segment elevation myocardial infarction, UA unstable angina,

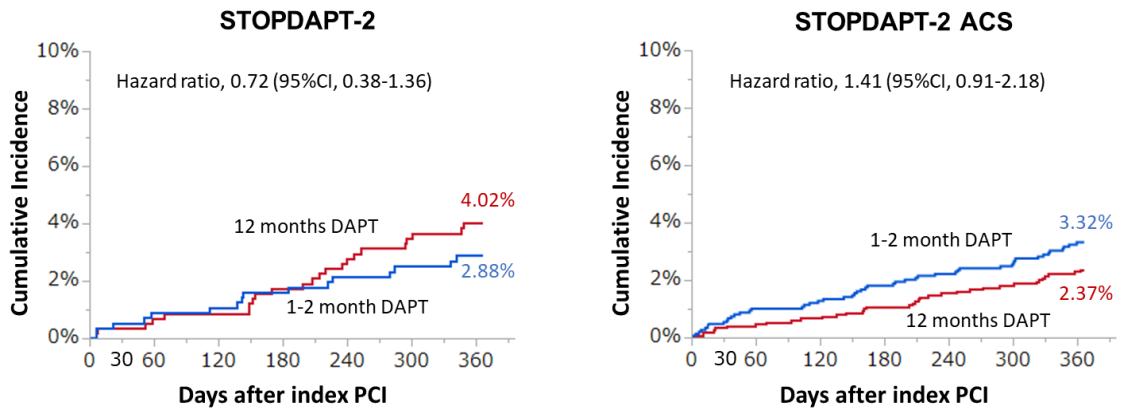
8 CKD chronic kidney disease, PARIS Patterns of Non-Adherence to Anti-Platelet Regimen in Stented Patients, CREDO-Kyoto

9 Coronary REvascularization Demonstrating Outcome study in Kyoto, and eGFR estimated glomerular filtration rate.

10

1 **eFigure 10. Time-to-event curves for the primary and major secondary**  
 2 **cardiovascular and bleeding endpoints stratified by the study (patients in**  
 3 **STOPDAPT-2 and STOPDAPT-2 ACS)**

4 **(a) Primary endpoint**

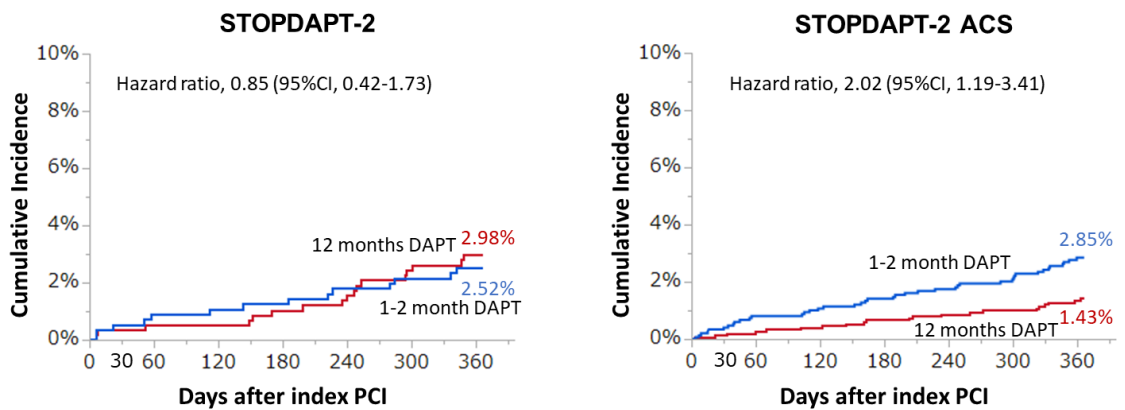


1-2 month DAPT	0	30	60	120	180	240	300	365	1-2 month DAPT	0	30	60	120	180	240	300	365
N with event		3	5	6	9	12	14	16	N with event		8	15	19	27	33	39	49
N at risk	565	561	551	550	547	541	538	439	N at risk	1493	1486	1477	1471	1460	1452	1444	1167
Incidence (%)		0.53	0.89	1.07	1.61	2.15	2.51	2.88	Incidence (%)		0.54	1.00	1.27	1.81	2.21	2.62	3.32
<b>12 months DAPT</b>	<b>0</b>	<b>30</b>	<b>60</b>	<b>120</b>	<b>180</b>	<b>240</b>	<b>300</b>	<b>365</b>	<b>12 months DAPT</b>	<b>0</b>	<b>30</b>	<b>60</b>	<b>120</b>	<b>180</b>	<b>240</b>	<b>300</b>	<b>365</b>
N with event		2	4	5	10	16	21	23	N with event		5	7	10	16	23	28	35
N at risk	583	580	571	570	564	558	551	447	N at risk	1495	1490	1484	1478	1472	1463	1459	1134
Incidence (%)		0.34	0.69	0.87	1.74	2.78	3.65	4.02	Incidence (%)		0.33	0.47	0.67	1.07	1.54	1.88	2.37

5

6

7 **(b) Major secondary cardiovascular endpoint**

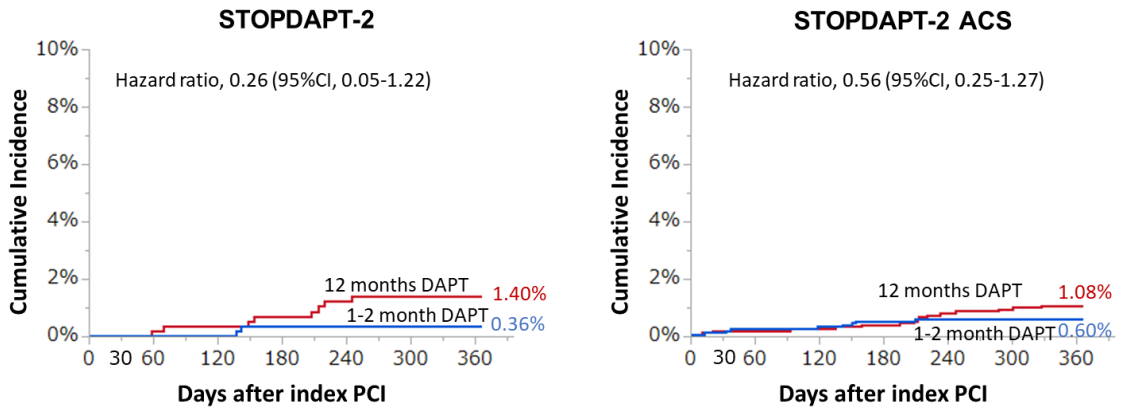


1-2 month DAPT	0	30	60	120	180	240	300	365	1-2 month DAPT	0	30	60	120	180	240	300	365
N with event		3	5	6	7	10	12	14	N with event		6	12	16	21	26	32	42
N at risk	565	561	551	550	549	543	540	441	N at risk	1493	1488	1480	1474	1466	1459	1451	1173
Incidence (%)		0.53	0.89	1.07	1.25	1.79	2.15	2.52	Incidence (%)		0.40	0.80	1.07	1.41	1.74	2.15	2.85
<b>12 months DAPT</b>	<b>0</b>	<b>30</b>	<b>60</b>	<b>120</b>	<b>180</b>	<b>240</b>	<b>300</b>	<b>365</b>	<b>12 months DAPT</b>	<b>0</b>	<b>30</b>	<b>60</b>	<b>120</b>	<b>180</b>	<b>240</b>	<b>300</b>	<b>365</b>
N with event		2	3	3	6	9	15	17	N with event		2	4	6	10	13	15	21
N at risk	583	580	572	572	568	565	557	452	N at risk	1495	1493	1487	1482	1478	1473	1471	1145
Incidence (%)		0.34	0.52	0.52	1.04	1.56	2.61	2.98	Incidence (%)		0.13	0.27	0.40	0.67	0.87	1.01	1.43

8

1

2 (c) Major secondary bleeding endpoint



1-2 month DAPT	0	30	60	120	180	240	300	365	1-2 month DAPT	0	30	60	120	180	240	300	365
N with event		0	0	0	2	2	2	2	N with event		2	4	5	8	9	9	9
N at risk	565	562	554	554	552	549	546	448	N at risk	1493	1490	1487	1484	1478	1474	1469	1194
Incidence (%)		0.00	0.00	0.00	0.36	0.36	0.36	0.36	Incidence (%)		0.13	0.27	0.34	0.54	0.60	0.60	0.60
<b>12 months DAPT</b>	<b>0</b>	<b>30</b>	<b>60</b>	<b>120</b>	<b>180</b>	<b>240</b>	<b>300</b>	<b>365</b>	<b>12 months DAPT</b>	<b>0</b>	<b>30</b>	<b>60</b>	<b>120</b>	<b>180</b>	<b>240</b>	<b>300</b>	<b>365</b>
N with event		0	1	2	4	7	8	8	N with event		3	3	4	6	12	15	16
N at risk	583	582	574	573	568	564	560	457	N at risk	1495	1491	1486	1481	1477	1469	1467	1146
Incidence (%)		0.00	0.17	0.35	0.70	1.22	1.40	1.40	Incidence (%)		0.20	0.20	0.27	0.40	0.81	1.01	1.08

3

4

5 Time-to-event curves for (a) the primary endpoint, (b) major secondary cardiovascular endpoint, and (c) major secondary  
 6 bleeding endpoint compared between the 1-2 month and 12 months DAPT groups stratified by the study (ACS patients  
 7 enrolled in STOPDAPT-2 and STOPDAPT-2 ACS). See text and eAppendix 3 for the definition of each endpoint.

8 DAPT denotes dual antiplatelet therapy, PCI percutaneous coronary intervention, STOPDAPT-2 Short and Optimal duration  
 9 of Dual AntiPlatelet Therapy after everolimus-eluting cobalt-chromium stent-2.

10

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