



Appendix A. Investigator and Trial Personnel List

The following persons participated in the enrollment of patients, data collection, or study coordination. Number of patients enrolled per site is indicated following the site name in parentheses.

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Appendix B. Endpoint definitions

Death

Cardiac death: Any death due to proximate cardiac cause (e.g., myocardial infarction, low-output failure, fatal arrhythmia), unwitnessed death, death of unknown cause, and all procedure-related deaths, including those related to concomitant treatment, will be classified as cardiac death.

Vascular death: Death due to noncoronary vascular causes, such as cerebrovascular disease, pulmonary embolism, ruptured aortic aneurysm, dissecting aneurysm, or other vascular diseases.

Non-cardiovascular death: Any death not covered by the above definitions, such as death caused by infection, malignancy, sepsis, pulmonary causes, accident, suicide, or trauma.

Myocardial infarction

CABG-related myocardial infarction (MI) is arbitrarily defined as elevation of cardiac biomarker values ($>10 \times 99\text{th percentile upper reference limit, URL}$) in patients with normal baseline cTn values ($\leq 99\text{th percentile URL}$). In addition, either (i) new pathological Q waves or new LBBB, or (ii) angiographically documented new graft or new native coronary artery occlusion, or (iii) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.

The term *acute MI* should be used when there is evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischemia. Under these conditions any one of the following criteria meets the diagnosis for MI:

- Detection of a rise and/or fall of cardiac biomarker values [preferably cardiac troponin (cTn)] with at least one value above the 99th percentile URL and with at least one of the following: Symptoms of ischemia.

New or presumed new significant ST-segment-T wave (ST-T) changes or new left bundle branch block (LBBB).

Development of pathological Q waves in the ECG. Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality. Identification of an intracoronary thrombus by angiography or autopsy.

- Cardiac death with symptoms suggestive of myocardial ischemia and presumed new ischaemic ECG changes or new LBBB, but with death occurring before cardiac biomarkers were obtained, or before cardiac biomarker values would be increased.

• *Percutaneous coronary intervention (PCI)-related MI* is arbitrarily defined by elevation of cTn values ($>5 \times 99\text{th percentile URL}$) in patients with normal baseline values ($\leq 99\text{th percentile URL}$) or a rise of cTn values $>20\%$ if the baseline values are elevated and are stable or falling. In addition, either (i) symptoms suggestive of myocardial ischemia, or (ii) new ischemic ECG

changes, or (iii) angiographic findings consistent with a procedural complication, or (iv) imaging demonstration of new loss of viable myocardium or new regional wall motion abnormality are required.

- Stent thrombosis associated with MI when detected by coronary angiography or autopsy in the setting of myocardial ischemia and with a rise and/or fall of cardiac biomarker values with at least one value above the 99th percentile URL.

Repeat revascularization

Any ischaemia-driven repeat PCI or bypass surgery

Stroke:

Acute neurological event of at least 24 hours of duration with focal signs and symptoms and without evidence supporting any alternative explanation

Etiology:

Haemorrhagic stroke (with diagnosis of intracerebral bleeding by CT or MRI):

Including intraparenchymal, subarachnoid hemorrhage, and subdural hematomas)

Ischemic stroke (without diagnosis of intracerebral bleeding by CT or MRA):

Unknown cause:

In cases where there was no brain imaging or autopsy.

Degree of severity:

Non-disabling stroke:

If the patient had no sequelae or only a minor deficit (with the functional status unchanged).

Modified Rankin scale grade of ≤ 3 (see below).

Disabling stroke:

If at the time of hospital discharge the patient had a moderate deficit (substantial limitation of activity and capabilities) or a severe deficit (inability to live independently or work). Modified Rankin scale grade of ≥ 4 (see below)

Modified Rankin scale - Stroke severity assessment scale

Scale 0

No symptoms at all

Scale 1

No significant disability despite symptoms: able to carry out all usual duties and activities

Scale 2

Slight disability: unable to carry out all previous activities but able to look after own affairs without assistance

Scale 3

Moderate disability: requiring some help, but able to walk without assistance

Scale 4

Moderately severe disability: unable to walk without assistance, and unable to attend to own bodily needs without assistance

Scale 5

Severe disability: bedridden, incontinent, and requiring constant nursing care and attention

Bleeding

Bleeding definition for secondary endpoints:

Major bleeding: Periprocedural CABG and hospital stay-related: BARC Type 4 and 5

Post- discharge: BARC \geq Type 3

Definition in accordance with BARC (Bleeding Academic Research Consortium)⁴⁷:

Type 0: no bleeding

Type 1: bleeding that is not actionable and does not cause the patient to seek unscheduled performance of studies, hospitalization, or treatment by a healthcare professional; may include episodes leading to self-discontinuation of medical therapy by the patient without consulting a healthcare professional

Type 2: any overt, actionable sign of haemorrhage (e.g., more bleeding than would be expected for a clinical circumstance, including bleeding found by imaging alone) that does not fit the criteria for types 3, 4, or 5 but does meet at least one of the following criteria: ⁴⁶ requiring nonsurgical, medical intervention by a healthcare professional, (2) leading to hospitalization or increased level of care, or (3) prompting evaluation.

Type 3

Type 3a

Overt bleeding plus haemoglobin drop of 3 to <5 g/dL* (provided haemoglobin drop is related to bleed)

Any transfusion with overt bleeding

Type 3b

Overt bleeding plus haemoglobin drop ≥ 5 g/dL* (provided haemoglobin drop is related to bleed)

Cardiac tamponade

Bleeding requiring surgical intervention for control (excluding dental/intraspinal/skin/hemorrhoid)

Bleeding requiring intravenous vasoactive agents

Type 3c

Intracranial hemorrhage (does not include microbleeds or haemorrhagic transformation, does include intraspinal bleeds)

Subcategories confirmed by autopsy or imaging or lumbar puncture

Intraocular bleed compromising vision

Type 4: CABG-related bleeding

Perioperative intracranial bleeding within 48 h

Reoperation after closure of sternotomy for the purpose of controlling bleeding

Transfusion of ≥ 5 U whole blood or packed red blood cells within a 48-h period†

Chest tube output ≥ 2 L within a 24-h period

Type 5: 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

Appendix C. Supplementary data

Supplementary Results

Supplemental Figure:

Cumulative Kaplan–Meier Curves for cardiovascular death, myocardial infarction, stroke, revascularization and the composite of cardiovascular death and myocardial infarction

Pretreatment and Outcome

The majority of patients received aspirin before randomization (ticagrelor group 78.1%, aspirin group 78.8%). We found no significant difference for the primary outcome after one year between both groups ($p=0.17$), i.e. those who did – or did not – take aspirin prior to surgery. Interestingly, there was a tendency for more primary endpoints in patients that were switched from aspirin (before) to ticagrelor (after) surgery compared to patients that continued with aspirin (9.8% vs 7.8%).

In aspirin naïve patients there was no significant difference regarding the primary endpoint after one year between both groups (ticagrelor 7.4% vs. aspirin 8.1%).

Atrial Fibrillation at discharge and Outcomes

The rate of atrial fibrillation at discharge did not show significant differences between the ticagrelor (2.4%) vs aspirin group (2.5%). Patients with atrial fibrillation at discharge carried a higher risk of adverse events in both groups compared to patients without this rhythm disorder. Regarding the primary endpoint in patients with atrial fibrillation in the ticagrelor (6/22) vs aspirin group (2/23), there was no significant difference ($p=0.22$). No significant interaction was found in patients in the ticagrelor group between intake of ticagrelor and occurrence of adverse events ($p=0.36$).