P2Y12 inhibitor monotherapy versus dual antiplatelet therapy in patients with acute coronary syndromes undergoing coronary stenting: rationale and design of the NEOMINDSET Trial

Patricia O. Guimarães[1], MD, PhD; Marcelo Franken[1], MD, PhD; Caio A.M. Tavares[1,2], MD, PhD; Fabio S. Silveira[3], MD; Murillo O. Antunes[4], MD, PhD; Ricardo R. Bergo[5], MD; Rodrigo M. Joaquim[6], MD; Jessica C.S. Hirai[1], PharmD; Pedro B. Andrade[7], MD, PhD; Fabio G. Pitta[1,2], MD; José Mariani Jr[1], MD, PhD; Bruno R. Nascimento[8], MD, PhD; João E.T. de Paula[9], MD; Marcos S. Silveira[3], MD; Tiberio A.O. Costa[4], MD; Frederico T.C. Dall'Orto[5], MD; Renato G. Serpa[10], MD; Fernanda B.A. Sampaio[11], MD; Louis N. Ohe[12], MD; Fernanda M. Mangione[13], MD; Remo H.M. Furtado[2], MD, PhD; Rogério Sarmento-Leite[14], MD, PhD; Frederico Monfardini[1], MSc; Silvia R.L. Assis[1], MS; José C. Nicolau[2], MD, PhD; Andrei C. Sposito[15], MD, PhD; Renato D. Lopes[16], MD, PhD; Yoshinobu Onuma[17], MD, PhD; Marco Valgimigli[18,19], MD, PhD; Dominick J. Angiolillo[20], MD, PhD; Patrick W. Serruys[17], MD, PhD; Otavio Berwanger[1], MD, PhD; Fernando Bacal[1,2], MD, PhD; Pedro A. Lemos[1,2]*, MD, PhD

The authors' affiliations can be found in the Appendix paragraph.

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Abstract

Dual antiplatelet therapy (DAPT) is currently the standard of care after percutaneous coronary intervention (PCI). Recent studies suggest that reducing DAPT to 1-3 months followed by an aspirin-free single antiplatelet therapy (SAPT) strategy with a potent P2Y12 inhibitor is safe and associated with less bleeding. However, to date, no randomised trial has tested the impact of initiating SAPT immediately after PCI, particularly in patients with acute coronary syndromes (ACS). NEOMINDSET is a multicentre, randomised, open-label trial with a blinded outcome assessment designed to compare SAPT versus DAPT in 3,400 ACS patients undergoing PCI with the latest-generation drug-eluting stents (DES). After successful PCI and up to 4 days following hospital admission, patients are randomised to receive SAPT with a potent P2Y12 inhibitor (ticagrelor or prasugrel) or DAPT (aspirin plus a potent P2Y12 inhibitor) for 12 months. Aspirin is discontinued immediately after randomisation in the SAPT group. The choice between ticagrelor and prasugrel is at the investigator's discretion. The primary hypothesis is that SAPT will be non-inferior to DAPT with respect to the composite endpoint of all-cause mortality, stroke, myocardial infarction or urgent target vessel revascularisation, but superior to DAPT on rates of bleeding defined by Bleeding Academic Research Consortium 2, 3 or 5 criteria. NEOMINDSET is the first study that is specifically designed to test SAPT versus DAPT immediately following PCI with DES in ACS patients. This trial will provide important insights on the efficacy and safety of withdrawing aspirin in the early phase of ACS. (ClinicalTrials.gov: NCT04360720)

Corresponding author: Hospital Israelita Albert Einstein, Av. Albert Einstein 627, São Paulo-SP, Brazil 05620-900.
E-mail: pedro.lemos@einstein.br

Abbreviations

ACS   acute coronary syndromes
ASA   acetylsalicylic acid
BARC   Bleeding Academic Research Consortium
DAPT   dual antiplatelet therapy
DES   drug-eluting stents
DSMB   data and safety monitoring board
MI   myocardial infarction
PCI   percutaneous coronary intervention
SAPT   single antiplatelet therapy

Introduction

Acute coronary syndrome (ACS) guidelines suggest that antithrombotic therapies should be tailored to an individual's haemorrhagic and ischaemic risk[1-3]. Single antiplatelet therapy (SAPT) strategies have been proposed that reduce bleeding complications following percutaneous coronary intervention (PCI) without increasing the risk of cardiovascular events[4-11]. Most trials have shown that either acetylsalicylic acid (ASA) or $P2Y_{12}$ receptor antagonists can be safely withdrawn after at least one month of dual antiplatelet therapy (DAPT). The potential benefit of dropping ASA in the early phase of ACS, when more potent $P2Y_{12}$ inhibitors (prasugrel or ticagrelor) are in place, is attractive, especially in terms of preventing gastrointestinal bleeding. However, the optimal timing for ASA withdrawal is still to be determined.

SAPT with a potent $P2Y_{12}$ receptor antagonist, without ASA, may reduce the risk of bleeding while preserving efficacy regarding ischaemic events when compared with traditional DAPT shortly after PCI in ACS patients. To test this hypothesis, we designed the "PercutaNEOus coronary intervention followed by Monotherapy INstead of Dual antiplatelet therapy in the SETting of acute coronary syndromes: The NEO-MINDSET Trial" (NEOMINDSET) to evaluate the efficacy and safety of withdrawing ASA immediately after PCI with the latest generation of drug-eluting stents (DES) in ACS patients (ClinicalTrials.gov: NCT04360720).

Methods

STUDY ORGANISATION AND DESIGN

NEOMINDSET is an investigator-initiated, multicentre, randomised, open-label trial with blinded outcome assessment funded by the Institutional Development Support Program of the Brazilian Unified Health System (PROADI-SUS). The trial is ongoing and aims to test the comparative efficacy and safety of SAPT with a potent $P2Y_{12}$ inhibitor versus DAPT with ASA plus a potent $P2Y_{12}$ inhibitor in ACS patients undergoing PCI with DES **(Figure 1)**. The executive committee is responsible for the scientific and operational conduct of the study, integrity of data analysis and reporting of results. The trial is being conducted in accordance with the Good Clinical Practice guidelines. Ethical committees at each participating site have approved the study protocol, and all patients must provide informed consent before enrolment in the trial.

STUDY OBJECTIVE

The primary objective of the NEOMINDSET Trial is to evaluate the efficacy and safety of SAPT with a potent $P2Y_{12}$ inhibitor compared with traditional DAPT for 12 months following PCI with DES in ACS patients. The primary hypothesis of the study is that SAPT is non-inferior for ischaemic events and superior for bleeding events compared with DAPT.

STUDY POPULATION – ENROLMENT AND RANDOMISATION

A full list of inclusion and exclusion criteria are presented in **Table 1**. Briefly, we will include 3,400 patients aged 18 years or older with atherosclerotic coronary disease presenting with ST-elevation or non-ST-elevation ACS, whose last symptoms occurred within 24 hours prior to hospital admission. To be included, patients must undergo successful PCI of one or more coronary artery stenoses with DES implantation (culprit and non-culprit vessels) within 96 hours of hospitalisation and should have no further planned additional revascularisation. Successful PCI is determined per the treating physician based on criteria relating to the combination of optimum stent results in the target lesion(s) (no significant residual intra-stent or border residual stenosis or dissection and no occurrence of thrombosis, distal embolism, occlusion of a major side branch, or "no-reflow" phenomenon). Patients undergoing staged PCI are enrolled after completion of all planned procedures; these must be completed within the 96-hour time frame from hospital admission.

Key exclusion criteria are the following: ACS treated conservatively, surgically or with unsuccessful PCI; an intended DAPT duration of less than 12 months; presence of residual coronary stenosis with a high likelihood of future revascularisation in the next year; indication for oral anticoagulation; index event of a presumed non-atherothrombotic cause; major active or recent bleeding; ischaemic stroke in the prior month; and any previous haemorrhagic stroke.

Randomisation is performed centrally through an electronic data capture system, in blocks of permutable sizes, stratified by study site.

STUDY TREATMENT AND FOLLOW-UP

After hospital admission for ACS, investigators have up to 96 hours to include the participant in the study. Prior to randomisation, patients can receive any combination of antiplatelet agents as per local practice **(Figure 2)**. If a participant undergoes staged PCI, standard DAPT will be administered between the initial PCI and the staged procedure, as per standard of practice. Randomisation is performed after the last PCI, when the coronary revascularisation plan is considered finished and has been successfully accomplished. The treating physician selects either ticagrelor or prasugrel as the $P2Y_{12}$ inhibitor to be given immediately after randomisation. Patients are then randomised in an open-label 1:1 fashion to receive low-dose ASA (80-100 mg) plus the chosen $P2Y_{12}$ antagonist (DAPT group) or to withdraw ASA and maintain monotherapy with only the selected $P2Y_{12}$ inhibitor (SAPT

Table 1. Study enrolment criteria.

Inclusion criteria
1. Aged ≥18 years old
2. ACS with last symptoms <24 hours from hospital admission
3. Successful PCI of all target lesions with latest-generation drug-eluting stents (culprit and non-culprit vessels)
4. Hospitalisation for less than 96 hours
5. Signed written informed consent

Exclusion criteria
1. ACS at index hospitalisation treated conservatively, with unsuccessful percutaneous coronary intervention, or undergoing coronary artery bypass graft surgery
2. Impossible, according to the judgment of the investigator, to treat the patient with dual antiplatelet therapy for 12 months
3. Presence of residual lesions with a high likelihood of future intervention within the next 12 months
4. Received fibrinolytic therapy <24 hours from randomisation
5. Need for oral anticoagulation with warfarin or non-vitamin K antagonist anticoagulants
6. Chronic bleeding diathesis
7. Major active or recent bleeding (in-hospital)
8. Previous intracranial haemorrhage
9. Ischaemic stroke in the prior 30 days
10. Presence of brain arteriovenous malformation
11. Index event of non-atherothrombotic cause (e.g., stent thrombosis, coronary embolism, spontaneous coronary dissection, myocardial ischaemia due to supply/demand imbalance)
12. Scheduled or potential cardiac or non-cardiac surgery within the next 12 months
13. Platelet count <100,000 cells/mm^3 or >700,000 cells/mm^3
14. Total white blood count <3,000 cells/mm^3
15. Suspected or documented active liver disease (including laboratory evidence of hepatitis B or C)
16. Heart transplant recipient
17. Known allergies or intolerance to ASA, clopidogrel, ticlopidine, ticagrelor, prasugrel, heparin or -limus family antiproliferative agents
18. Life expectancy lower than 1 year
19. Any significant medical condition that, in the investigator's opinion, may interfere with optimal patient participation in this study
20. Participation in another trial within the last 12 months, unless the subject is deemed to benefit from participation in this study
ACS: acute coronary syndrome; ASA: acetylsalicylic acid; PCI: percutaneous coronary intervention

group) for 12 months. Protocol-mandated therapy begins directly after randomisation, and ASA is discontinued immediately in the SAPT group **(Supplementary Figure 1)**. Details on study treatment administration are presented in **Supplementary Appendix 1**.

Patients have in-person follow-up visits at 1, 6 and 12 months after randomisation to assess for adverse events, study endpoints and treatment adherence. Telephone calls occur at 3, 9 and 13 months after randomisation for the same purpose. Study drug adherence will be assessed using the Non-adherence Academic Research Consortium (NARC) consensus[12]. Non-compliance will be categorised per type of non-adherence, the decision-making process, reasons and timing of non-adherence. After 12 months of study treatment, the antiplatelet regimen will be chosen at the investigator's discretion.

STUDY ENDPOINTS
PRIMARY ENDPOINT
The co-primary endpoints are an ischaemic endpoint (composed of all-cause mortality, stroke, myocardial infarction or urgent target vessel revascularisation) and a bleeding endpoint (major or clinically relevant non-major bleeding defined by Bleeding Academic Research Consortium [BARC] 2, 3 or 5 criteria)[13]. In brief, BARC Type 2, 3 and 5 bleeds are defined as follows: clinically overt haemorrhage requiring medical attention (Type 2); requiring transfusion, surgical correction or associated with a haemoglobin drop of at least 3 g/dl (Type 3); or fatal events (Type 5). Detailed definitions of the ischaemic endpoints are presented in **Supplementary Appendix 2**.

The co-primary endpoints are assessed between randomisation and 12 months (equalling 365 days). All clinical endpoints are adjudicated by an external independent clinical event classification committee, whose members are unaware of the treatment-group assignments.
### SECONDARY ENDPOINTS
Secondary endpoints include all-cause death, cardiovascular death, non-cardiovascular death, myocardial infarction, stroke, sudden death at 30 days, stent thrombosis, unplanned invasive coronary intervention, BARC 1-5 bleeding, and net efficacy and safety outcomes. Primary and secondary endpoints are shown in **Supplementary Table 1**.

POWER, SAMPLE SIZE AND STATISTICAL CONSIDERATIONS
This trial was designed to test hierarchically whether SAPT as compared with DAPT would be non-inferior with regard to ischaemic events and superior with respect to major or non-major clinically relevant bleeding. The GLASSY study[14], a dedicated analysis of adjudicated events from the GLOBAL LEADERS Study[6], indicated that the composite of all-cause death, non-fatal MI, non-fatal stroke, or urgent target vessel revascularisation was 9.6% in ACS patients after 2 years of DAPT, with approximately two-thirds of the events occurring during the first year. Based on these assumptions, we calculated that the enrolment of 3,400 patients would provide 80% power to establish non-inferiority regarding ischaemic events, assuming an 8.0% cumulative incidence at 1 year in the DAPT group and an absolute non-inferiority margin of 2.5%. If non-inferiority is demonstrated, the analysis for the bleeding endpoint will be performed to assess the superiority of SAPT over DAPT, with an estimated 88% power of demonstrating superiority with an assumed 8.0% occurrence of bleeding events[4] in the DAPT group and 5.0% in the SAPT group (37.5% relative risk reduction). The final sample size takes into account an anticipated 4% loss to follow-up.
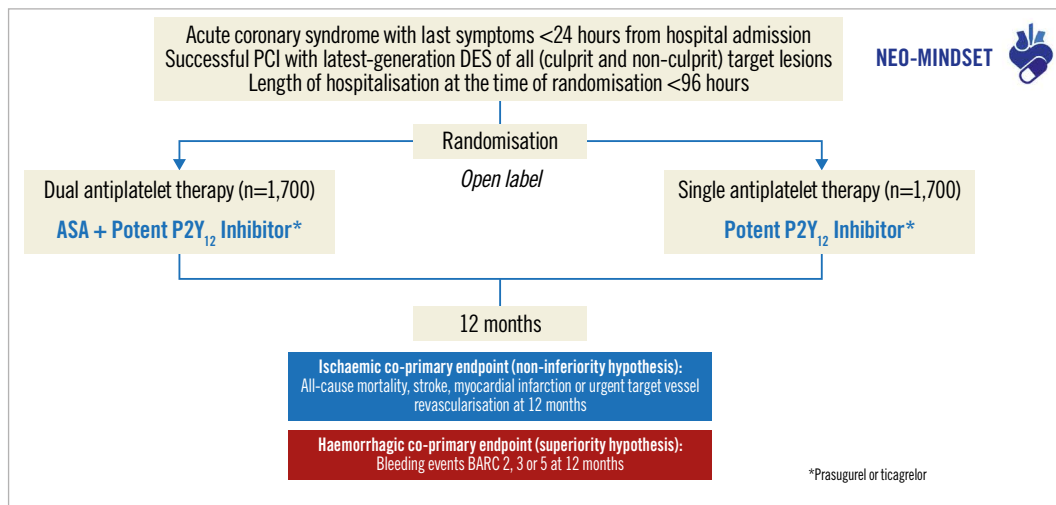
Figure 1. *NEOMINDSET Trial design. Patient selection starts after successful percutaneous coronary intervention with latest-generation drug-eluting stents, and patients can be consented within 96 hours of hospital admission due to acute coronary syndromes. Patients will be randomised in a 1:1 ratio to receive dual antiplatelet therapy with aspirin and a potent P2Y$_{12}$ inhibitor or single antiplatelet therapy with a potent P2Y$_{12}$ inhibitor. The choice between prasugrel or ticagrelor will be made at the investigator's discretion. The 2 co-primary endpoints will be assessed at 1-year follow-up. ASA: acetylsalicylic acid; BARC: Bleeding Academic Research Consortium; DES: drug-eluting stent; PCI: percutaneous coronary intervention*
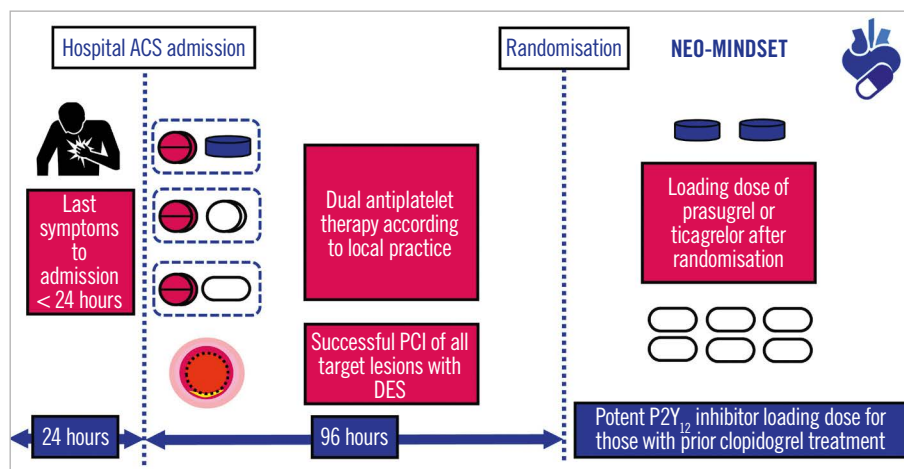
Figure 2. *Study protocol timelines. To be included, patients should present with last symptoms occurring within 24 hours of hospital admission. Once hospitalised, investigators will have up to 96 hours to include the participant in the study. Randomisation will be performed after coronary revascularisation is considered complete. A loading dose of prasugrel or ticagrelor will be given immediately after randomisation to those patients who previously received clopidogrel. ACS: acute coronary syndrome; DES: drug-eluting stent; PCI: percutaneous coronary intervention*

ANALYSIS FOR THE CO-PRIMARY ENDPOINTS

All patients will be analysed following the intention-to-treat principle and reported according to their randomised arm, irrespective of the treatment they receive. Cumulative incidences of the co-primary and secondary endpoints within 365 days of randomisation will be estimated using the Kaplan-Meier method. A sensitivity analysis will be performed in the per-protocol population, excluding participants with violations of the inclusion/exclusion criteria at the time of randomisation and/or who did not receive the assigned treatment at the time of randomisation. Follow-up will be

censored at the last date of known outcome status or at 12 months from randomisation, whichever comes first.

All adjudicated events occurring from randomisation to 365 days post-randomisation will be considered. A hazard ratio (HR) and 95% confidence interval (CI) for the primary endpoint will be generated using the Cox proportional hazards model that will include the treatment group (SAPT vs DAPT) as a covariate. For the ischaemic endpoint, a 1-sided non-inferiority test with a type 1 error of 0.025 will be performed. The null hypothesis will be rejected if the upper limit of the 95% CI for the absolute

difference in risk in 12-month event rates is less than 2.5%. In case non-inferiority for the ischaemic endpoint is demonstrated, the SAPT scheme will be tested for its superiority in reducing the bleeding co-primary endpoint in comparison with DAPT, using a 2-sided alpha level of 0.025. Analyses for the secondary endpoints and for subgroups are presented in **Supplementary Appendix 3**.

SAFETY MONITORING

An independent data and safety monitoring board (DSMB) is reviewing unblinded patient-level data for safety on an ongoing basis during the trial. A preliminary safety analysis occurred on 20 December 2021 after 400 subjects were enrolled and followed for at least 30 days. The first interim analysis was performed on 30 June 2022 after inclusion and 30-day follow-up of one-third (n=1,133) of the trial population, and the second interim analysis occurred on 19 December 2022 after inclusion and 30-day follow-up of half (n=1,700) of the trial population. The DSMB recommended that the trial continue as planned after these 3 analyses. One more interim analysis will occur after three-fifths (n=2,040) of the sample size have been enrolled and followed for at least 30 days. Additional interim analyses can be convened at the discretion of the DSMB chairperson, especially if new scientific data or concerns are raised during the conduct of the study that justify such a decision. The DSMB members do not have a primary affiliation with the study sponsor or the Steering Committee of the trial. For each interim analysis, the DSMB reviews data regarding the primary and secondary endpoints, as well as adverse events in the 2 study arms. Based on the data, the DSMB may recommend modifications to the protocol, suspension, or termination of the trial to the Steering Committee. All final decisions regarding trial modifications rest with the Steering Committee.

Discussion

The primary hypothesis of the NEOMINDSET Trial is that SAPT with a potent P2Y$_{12}$ inhibitor (ticagrelor or prasugrel without aspirin) started shortly after successful PCI with DES in ACS patients will provide adequate ischaemic protection while mitigating bleeding risk when compared to traditional DAPT (aspirin plus prasugrel or ticagrelor). This trial differs from other trials investigating antithrombotic strategies in ACS since ASA will be withdrawn in the first 96 hours of hospital admission in the SAPT arm, thus challenging the concept that classic DAPT with ASA is necessary for a minimum of 1-3 months post-PCI for the prevention of recurrent thrombotic events in the very early phase of ACS.

DAPT is commonly indicated for 12 months following hospital admission for ACS. However, current guidelines suggest that patient profiles and procedural features should be used to guide antithrombotic treatment choice and duration[2]. Indeed, the use of latest-generation DES is associated with lower risks of thrombotic and restenotic complications compared with bare metal stents, which, theoretically, would decrease the need for prolonged treatment with antiplatelet agents[15,16]. Additionally, patients at high

bleeding risk are often encountered in daily practice and are a subset for whom the benefits of prolonged DAPT are not well known, due to the fact that these patients are commonly excluded from clinical trials. Thus, it is possible that DAPT may be used for a shorter duration, or even substituted by SAPT, in a substantial number of ACS patients treated with potent P2Y$_{12}$ inhibitors.

Early scientific evidence for the safety of SAPT was published by Colombo et al[17]. In their study, using Palmaz-Schatz stent implantation guided by intracoronary ultrasound, 321 patients treated with ticlopidine or aspirin showed optimal final intracoronary ultrasound outcomes. Stent thrombosis rates were 0.8% (2 events) among 252 patients treated with ticlopidine alone and 1.4% (1 event) among 69 patients treated with aspirin alone after stenting. With the technological development of stents with thinner mesh, bioabsorbable polymers and a better balance between antistenotic effects and mesh coverage, it can be hypothesised that stent thrombosis rates would be even lower than those seen with Palmaz-Schatz, making SAPT a safe and attractive option. The findings of the ASET Pilot Study, which showed no acute thrombotic complications in 201 patients treated with SAPT − only prasugrel − after successful PCI with everolimus-eluting stent implantation for stable coronary disease, support this concept[18]. Additionally, the OPTICA Study tested SAPT with ticagrelor or prasugrel following PCI in 75 patients with non-ST-segment elevation MI, and no stent thrombosis occurred in 6 months[19].

Several contemporary trials have tested different antithrombotic strategies following PCI in acute and stable settings[20,21]. NEOMINDSET differs from prior studies in the following aspects: a) this trial is fully dedicated to ACS patients undergoing successful PCI with DES, including both ST-segment elevation and non-ST-segment elevation ACS; b) ASA is dropped in the SAPT group within the first 96 hours of hospital admission; c) all participants are treated with potent P2Y$_{12}$ inhibitors and the choice between prasugrel or ticagrelor is made at the investigator's discretion in a pragmatic manner; d) there are no restrictions on stent type, as long as latest-generation DES are used. We believe our results will be applicable to a broad population of ACS patients as it reflects real-world clinical practice. In conclusion, NEOMINDSET will provide important insights on the efficacy and safety of an early aspirin-free strategy − immediately following PCI − in ACS patients treated with potent P2Y$_{12}$ inhibitors and will help to inform international guidelines and guide clinical practice.

Limitations

The COVID-19 pandemic delayed site activation and participant recruitment in the trial. The first patient was enrolled in NEOMINDSET in October 2020, and enrolment is expected to continue until October 2023. At present, 51 sites have been activated with a total enrolment of 2,900 patients.

Conclusions

The NEOMINDSET Trial is a multicentre, randomised, open-label trial with a blinded outcome assessment designed to compare SAPT

versus DAPT in 3,400 ACS patients undergoing PCI with latest-generation DES. This study will provide important insights on the efficacy and safety of withdrawing aspirin in the early phase of ACS.

Appendix. Authors' affiliations

1. Hospital Israelita Albert Einstein, São Paulo, Brazil; 2. Instituto do Coracao (InCor), Hospital das Clinicas HCFMUSP, Faculdade de Medicina, São Paulo, Brazil and Universidade de São Paulo, São Paulo, Brazil; 3. Research Center, Clínica do Coração, Aracaju, Brazil; 4. Hospital Universitário São Francisco de Assis na Providência de Deus, Bragança Paulista, Brazil; 5. Hospital Santa Lucia, Poços de Caldas, Brazil; 6. Instituto de Cardiologia de Santa Catarina, São José, Brazil; 7. Irmandade da Santa Casa de Misericórdia de Marilia, Marilia, Brazil; 8. Hospital Universitário Ciências Médicas, Belo Horizonte, Brazil; 9. Instituto Cardiovascular de Linhares, Linhares, Brazil; 10. Hospital Santa Casa de Misericórdia de Vitória, Vitória, Brazil; 11. Instituto Nacional de Cardiologia, Rio de Janeiro, Brazil; 12. Dante Pazzanese Institute of Cardiology, São Paulo, Brazil; 13. Beneficência Portuguesa de São Paulo, São Paulo, Brazil; 14. Instituto de Cardiologia do Rio Grande do Sul/Fundação Universitária de Cardiologia, Porto Alegre, Brazil; 15. Department of Internal Medicine, School of Medical Sciences, State University of Campinas, Campinas, Brazil; 16. Duke Clinical Research Institute, Duke University, Durham, NC, USA; 17. Department of Cardiology, University of Galway, Galway, Ireland; 18. Cardiocentro Ticino Institute, Ente Ospedaliero Cantonale, Lugano, Switzerland 19. Università della Svizzera Italiana, Lugano, Switzerland; 20. Division of Cardiology, University of Florida College of Medicine, Jacksonville, FL, USA

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Conflict of interest statement

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Supplementary data

Supplementary Appendix 1. Study treatment administration.

Supplementary Appendix 2. Definitions of trial endpoints.

Supplementary Appendix 3. Analyses for the secondary endpoints and subgroup analysis.

Supplementary Table 1. Study endpoints.

Supplementary Figure 1. Study treatments after randomisation.

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Supplementary data

Supplementary Appendix 1. Study treatment administration.

For those with prior stroke or transient ischemic attack, ticagrelor 90 mg twice daily is recommended. For those with body weight of less than 60 kilograms or aged older than 75 years, prasugrel 5 mg daily or ticagrelor 90 mg twice daily may be used. For all other patients, prasugrel 10 mg daily or ticagrelor 90 mg twice daily may be chosen at the discretion of the treating physician. Those with no prior use of the respective agent should receive a loading dose of the potent P2Y12 inhibitor (60 mg of prasugrel or 180 mg of ticagrelor) right after randomization, following by initiation of maintenance dose the day after. In case a patient receives prasugrel or ticagrelor prior to randomization and the investigator decides to switch to one another, a loading dose of the chosen agent is given 24 hours after the last dose of the prior agent[1].

Switching between prasugrel and ticagrelor is allowed during follow-up. Switching from a potent P2Y12 inhibitor to clopidogrel after randomization is allowed only when the investigator decides it is the best choice for the patient, usually following adverse events or study endpoints.

Supplementary Appendix 2. Definitions of trial endpoints.

All deaths are categorized into cardiovascular or non-cardiovascular, according to predefined criteria. Cardiovascular deaths are defined as death due to coronary heart disease, acute myocardial infarction, sudden cardiac death, heart failure, cerebrovascular event, cardiovascular procedure, cardiovascular hemorrhage (i.e., aortic dissection), or other cardiovascular events (i.e, pulmonary embolism). Myocardial infarction (MI) is classified according to the fourth universal definition[2]. Type 4a MI during hospitalization is identified when troponin levels rise above 5 times the 99th percentile of the upper limit of normal (ULN) if baseline values are normal or the elevation is greater than 20% compared with the prior pre-procedure value and is above 5 times the 99th percentile of the ULN. This criterion should be added to electrocardiogram (ECG) alterations, imaging or angiographic findings consistent with ischemia. Type 4b MI during hospitalization is defined as MI associated with stent thrombosis confirmed by coronary

angiography (with symptoms, ECG alterations, or troponin elevation) or autopsy. MI after discharge is defined as rise and/or fall of troponin levels greater than the 99th percentile of the ULN associated with symptoms of myocardial ischemia, ECG alterations, imaging findings consistent with ischemia, or evidence of coronary thrombus by angiography or autopsy. Target-vessel revascularization/stent thrombosis is classified according to the Academic Research Consortium criteria.

Supplementary Appendix 3. Analyses for the secondary endpoints and subgroup analysis.

Cumulative incidence of the secondary endpoints will be estimated using the Kaplan-Meier method, from the time of randomization to the first occurrence of the individual components of the key secondary endpoint by treatment groups. A HR and 95% CI for the key secondary endpoint will be generated using the Cox proportional hazards model that includes treatment group (SAPT versus DAPT) as a covariate. A superiority test at a two-sided 0.05 level will be performed.

One-year event rates for the two co-primary endpoints will be calculated in the following clinically relevant subgroups: age $\geq$ 75 years vs. < 75 years; female vs. male sex, diabetes mellitus, prior stroke, prior known peripheral artery disease, high bleeding risk vs. non-high bleeding risk, type of ACS (ST-elevation MI vs. non-ST-elevation MI vs. unstable angina), body mass index below median vs. above median, history of prior MI, history of prior coronary artery bypass graft surgery, presence of multivessel coronary disease, left main PCI, multivessel PCI, SYNTAX score (< 22 vs. 22-32 vs. $\geq$ 33), femoral vs. radial access, staged vs. single index procedure, and type of P2Y12 inhibitor use after randomization (ticagrelor vs. prasugrel), days from ACS presentation to randomization (1 vs. 2 vs. 3 vs. 4 days). Stratum-specific HRs and corresponding 95% CI will be calculated for each subgroup using a Cox proportional hazards model. Formal interaction testing will be performed using the subgroup by treatment allocation as an additional term in the Cox model.

Supplementary Table 1. Study endpoints.

Primary Endpoint

Co-primary Efficacy Endpoint (non-inferiority hypothesis)
Composite of all-cause death, stroke, myocardial infarction or urgent target vessel revascularization at 12 months.

Co-primary Safety Endpoint (superiority hypothesis)
BARC 2, 3, or 5 bleeding events at 12 months

Secondary Endpoints

- **All-cause deaths, deaths due to cardiac and non-cardiac causes**
- **Sudden death within 30 days**
- **Stroke**
- **Myocardial Infarction**
- **Stent thrombosis**
- **Unscheduled invasive coronary intervention**
- **Bleeding type BARC 1-5[14]**
- **Net composite endpoint (occurrence of the co-primary efficacy endpoint or the co-primary safety endpoint)**
- **Cost-effectiveness profiles**
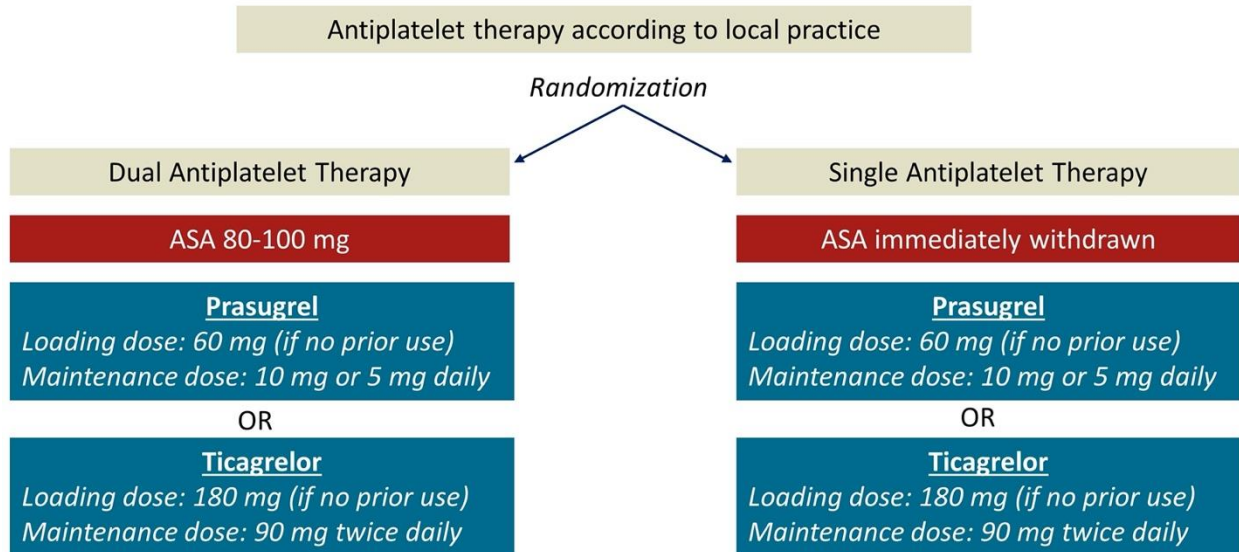
Supplementary Figure 1. Study treatments after randomisation.

Up to randomization, antiplatelet treatments will be administered according to local practice. Protocol-mandated therapy starts right after randomization. In the dual antiplatelet therapy group, aspirin will be given at an 80-100 mg daily dose. In the single antiplatelet group, aspirin will be discontinued immediately after randomization. The choice between ticagrelor and prasugrel will be made at investigator's discretion following drug label. A loading dose of the potent P2Y12 inhibitor (60 mg of prasugrel or 180 mg of ticagrelor) will be given for those with no prior use of the respective agent. In case the patient receives prasugrel or ticagrelor prior to randomization and the investigator decides to switch to one another, a loading dose of the chosen agent will be given 24 hours after the last dose of the prior agent. ASA denotes acetyl salicylic acid.