SASSICAIA-TRIAL

STRATEGIES OF LOADING WITH PRASUGREL VERSUS CLOPIDOGREL IN PCI-TREATED BIOMARKER NEGATIVE ANGINA

Multi-center, Randomized, Open-label, Assessor blinded, Single-dose trial
with a 30 days Follow-up period

This trial was conducted in compliance with Good Clinical Practice (GCP), the Declaration of Helsinki, and other regulatory requirements, the Clinical Investigation Plan and any conditions of approval imposed by the EC or regulatory authorities.

PROTOCOL CODE:	GE IDE MucT001-14
EUDRACT NUMBER:	2014-002171-29
TITLE OF THE TRIAL:	Intensified Loading with Prasugrel versus Standard Loading with Clopidogrel in PCI-treated Patients with Biomarker-Negative Angina pectoris
DEVELOPMENT PHASE:	Phase IV
INVESTIGATIONAL DRUG:	Prasugrel (Efient, Daiichi Sankyo Europe GmbH) Clopidogrel (Plavix, Sanofi-Aventis)
FIRST PATIENT IN:	17 September 2015
EARLY STUDY TERMINATION:	09 August 2018
LAST PATIENT COMPLETED:	30 November 2018
SPONSOR/ SPONSOR DELEGATED PERSON:	Klinikum der Universität München, represented by Prof. Dr. med. Julinda Mehilli Klinikum der Universität München Medizinische Klinik und Poliklinik I Marchioninistr. 15; 81377 München Tel.: +49 (0)89 4400 73093 Fax: +49 (0)89 4400 73842
DATE:	15 April 2020
VERSION:	V2.0
PREPERATED BY:	Prof. Dr. med. Julinda Mehilli

SIGNATURE PAGE

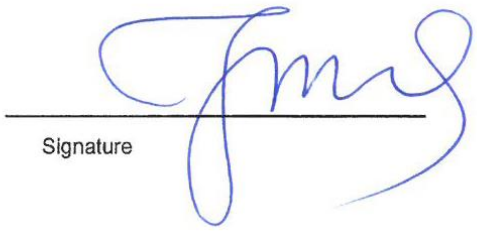
We have read this report and confirm that it accurately describes the conduct and results of the study. We further confirm that this clinical investigation was performed in accordance with the current versions of ICH-GCP, the Declaration of Helsinki and local legal requirements.

Sponsor/Sponsor Delegated Person (SDP):

Prof. Dr. med. Julinda Mehilli

(SDP)

27.04.2020 — Date

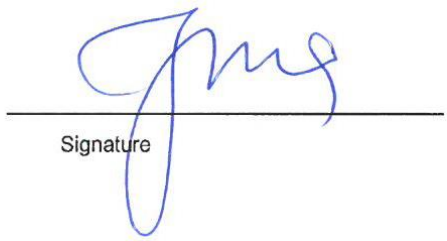
 — Signature

Coordinating Investigator (in accordance with German Drug Law)

Prof. Dr. med. Julinda Mehilli

(PI/LKP)

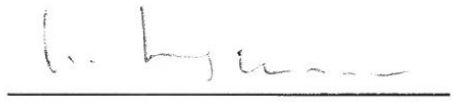
27.04.2020 — Date

 — Signature

Responsible Biometrician

Prof. Dr. rer. nat. Ulrich Mansmann

27.4.2020 — Date

 — Signature

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1 Name of Sponsor Company

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Represented by (Sponsor delegated Person):
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2 Name of Finished Product	3 Name of Active Substance
Effient (Daiichi Sankyo Germany GmbH)	Prasugrel
Plavix (Sanofi-Aventis Germany GmbH)	Clopidogrel

4 Individual Study Table Referring to Part of the Dossier

not applicable

5 Title of Study

Intensified Loading with Prasugrel versus Standard Loading with Clopidogrel in PCI-treated Patients with Biomarker-Negative Angina pectoris

Acronym:

Strategies of Lo**A**ding with Pra**S**ugrel Ver**S**us Clop**I**dogrel in P**C**I-Treated Biom**A**rker negat**I**ve **A**ngina (SASSICAIA) Trial

Latest Protocol Version: Version V6.0, September 21, 2017
(Amendment 21 September 2017 included)

Protocol Amendments:

Protocol Version 1.0, 20 March 2015

- not approved by Ethics Committee and Central Authority

Protocol Version 2.0, 07 Mai 2015

- not approved by Central Authority

Protocol Version 3.0, 03 June 2015

- first approved Protocol Version

Protocol Amendment 29 September 2015, Protocol Version 4.0

- Change from monocenter to multicenter (about 3 centers in Europe)
- More detailed instructions for inclusion of patients before randomization: range of high-sensitive troponin T 0.014 ng/ml - 0,05 ng/ml
- Definition of baseline procedures which are not considered as study specific
- More detailed instructions for treatment of patients after randomization:
    - PCI will be performed according to conventional and local standards as well as the use and type of stents
- Heparin administration, prasugrel and clopidogrel maintenance dose can be adopted in case of reasonable medical indication to the needs of the patient Harmonization of wording within the protocol:
    - Additional Time point "Time point 1 – Clinical evaluation" added
    - Only Adverse Events of Special Interest/AESI (any AEs with a causal relation to the study drugs according to the judgment of the local PI) and SAE's will be reported
    - Definition of events which are not defined as SAE´s
- Harmonization of data: the calculation sample size in each group is 1063

Protocol Amendment 31 March 2017, Protocol Version 5.0

- More detailed instructions for inclusion of patients before randomization: high-sensitive troponin T values below 0,05 ng/ml
- Harmonization of wording within the protocol More detailed instructions for documentation of adverse events, Serious Adverse Events and reportable events

Protocol Amendment 21 September 2017, Protocol Version 6.0

- Corrected recruitment period in the time schedule: recruiting period 48 months, Planned end October 2019

6 PRINCIPAL INVESTIGATOR(S)	7 STUDY CENTRE(S)
Prof. Dr. med. Julinda Mehilli *(National Lead Investigator)*	Klinikum der Universität München Medizinische Klinik und Poliklinik I Campus Großhadern Marchioninistr. 15 81377 München Germany
Prof. Dr. med. Julinda Mehilli *(National Lead Investigator)*	Klinikum der Universität München Medizinische Klinik und Poliklinik I Campus Innenstadt Ziemssenstr. 1 80336 München Germany
Prof. Dr. med. Willibald Hochholzer	Universitäts-Herzzentrum Freiburg – Bad Krozingen Südring 15 79189 Bad Krozingen Germany
Dr. med. Markus Deichstetter *(since 12.04.2018)* PD Dr. med. Johannes Rieber *(till 12.04.2018)*	Städtisches Klinikum Bogenhausen Englschalkinger Str. 77 81925 München Germany
Prof. Dr. med. Adnan Kastrati	Deutsches Herzzentrum München Klinik für Herz- und Kreislauferkrankungen Lazarettstraße 36 80636 München Germany
Dr. Daniel Aradi *(National Lead Investigator)*	Heart Center Balatonfüred and Heart and Vascular Center Balatonfüred Gyógy tér 2 8230 Balatonfüred Hungary

8 PUBLICATION(S)

The paper "Randomized Comparison of Intensified and Standard P2Y12-Receptor-Inhibition Before Elective Percutaneous Coronary Intervention: the Strategies of LoAding with PraSugrel VerSus ClopIdogrel in PCI-treated biomArker negatIve Angina (SASSICAIA) trial" is accepted for publication at the Circulation: Cardiovascular Interventions Journal on March 31, 2020.

9 STUDIED PERIOD

Time Course	
Activities	**Date**
First patient enrolled	17 September 2015
Interim analysis	07 August 2018
Premature study termination /Recruitment stop	09 August 2018
Last patient last visit	30 November 2018
Database lock	24 April 2019

After obtaining approval of Ethics Committee and authority, the SASSICAIA study was started in September 2015. Initially it was planned to enroll 2240 subjects over a recruiting period of 24 months at two study sites of the Klinikum der Universität München (protocol V 3.0 / 03.06.2015).

Even if many efforts were done to increase the rate and number of patients including recruitment prolongation and initiation of new sites, a premature interim analysis was performed in August 2018 due to low recruitment status. Based on the results of the interim analysis the Sponsor Delegated Person decided in accordance with the Steering Committee to follow the recommendation of the Data Safety Monitoring Board and premature terminate the study.

Therefore the total duration of the study was 38 months. Of them, 35 months were needed for enrollment of patients and 3 months to complete the entire follow up period (30 days -2/+7 days for each patient) of all patients enrolled into the SASSICAIA trial.

10 PHASE OF DEVELOPMENT:

Phase IV in Germany

Phase III in Hungary

11 OBJECTIVES

The SASSICAIA trial compared the impact of only intensified loading vs. standard therapy in patients undergoing PCI on clinical outcomes. The trial hypothesis was, that a strategy of antiplatelet therapy based on intensified loading with 60mg of prasugrel just prior to PCI – when the coronary anatomy is known – and clopidogrel 75mg/d as a maintenance treatment is superior for prevention of the primary endpoint as compared to a standard antiplatelet therapy regimen based on 600mg clopidogrel loading plus clopidogrel 75mg/d regarding clinical outcomes at 30 days after PCI.

Primary Objectives:

The primary objective was to evaluate the incidence of the primary endpoint, defined as a combined outcome of all-cause death, any myocardial infarction, stent thrombosis, urgent revascularization and stroke up to 30 days after randomization. Any myocardial infarction was defined as post-interventional increase of high-sensitivity cardiac troponin > 3 times UNL or spontaneous MI (angina pectoris with either a rise of cardiac biomarker values with at least one value above the 99thpercentile UNL or new or presumably new ECG changes (ST-segment elevation or LBBB or pathological Q-wave) or imaging evidence of new loss of viable myocardium or new regional wall abnormality).

Secondary Objectives:

Secondary endpoints included bleeding complications defined according to Bleeding Academic Research Consortium (BARC) criteria ≥2 and non-CABG TIMI major and minor bleeding. Further secondary endpoints were ischemic components (combined and singular) of the primary endpoint (incidence of peri-PCI myocardial infarction type 4a according to Third Universal Definition of Myocardial Infarction, any myocardial infarction, cardiovascular death, stroke) all-cause death, stent thrombosis according to Academic Research Consortium (ARC) criteria and urgent vessel revascularization.

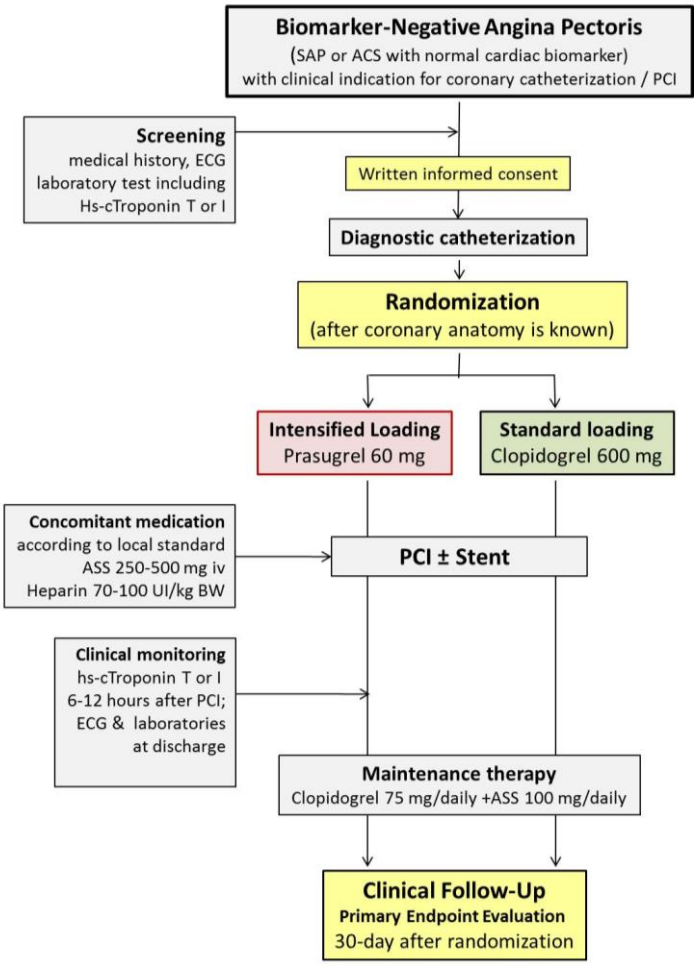
12 METHODOLOGY

The SASSICAIA study was a multicenter, randomized, parallel-group, open-label assessor-blinded clinical trial. Patients with stable or clinically unstable (biomarker-negative) angina pectoris who were in need of coronary intervention and met all eligibility criteria for study participation according to screening procedures were

randomly assigned in one of the treatment strategies just prior to percutaneous coronary intervention (PCI). The experimental arm consisted of an intensified single oral loading with 60mg of prasugrel along with the PCI procedure, which was followed by a 75mg/d clopidogrel maintenance treatment. The control arm of the study consisted of a standard single oral loading dose with 600mg of clopidogrel plus 75mg/d clopidogrel as maintenance therapy.

The patients were clinical monitored during hospital stay and a phone call was performed in a 30-day time frame (-2 / +7 days) post PCI to record all clinical events. Figure 1 summarizes the two different treatment arms and the study flow of patients within the trial.

Figure 1. SASSICAIA trial flow chart



Randomization was performed between intensified loading (prasugrel) and standard loading (clopidogrel) with a randomization sequence of 1:1. Allocation to treatment was made by means of a web-based computer-generated sequence using dedicated program software (MIC-Research Group, based at the Cardiology Department,

Klinikum der Universität München, Germany). Randomization was stratified by clopidogrel chronic therapy status. Randomly permuted block lengths of 30 were used. The two treatment groups were studied concurrently. Time zero was defined as the time of randomization. Patients were considered enrolled in the study and eligible for the final intention to treat analysis after he/she had provided signed informed consent and was randomized to study treatment.

The study was conducted in 6 European centers, which met required technical, professional and personnel requirements to conduct the trial and ensure high data quality. Site Monitoring was done by independent service providers according to a predefined monitoring manual. Endpoints of the trial and events relevant for drug safety were assessed by the site principal investigator and were confirmed by two independent members of the Event Adjudication Committee (EAC) blinded to the patient's allocation in accordance with the predefined EAC Charter. The CSC^{LMU} was contracted by the SDP to perform drug safety related activities. Therefore, an SAE had to be reported immediately (i. e. within 24 hours after becoming aware of the event) to the CSC^{LMU} except those SAEs the protocol identified as not requiring immediate reporting.

A steering committee was established with the responsibility of overseeing the good execution and administrative progress of the protocol. Furthermore a Data Safety Monitoring Board was responsible for making risk-benefit assessment and recommendations regarding interim and endpoint data analysis and any potential problems. It was also responsible for reviewing the final results of the clinical study regarding the analysis of major adverse cardiac events.

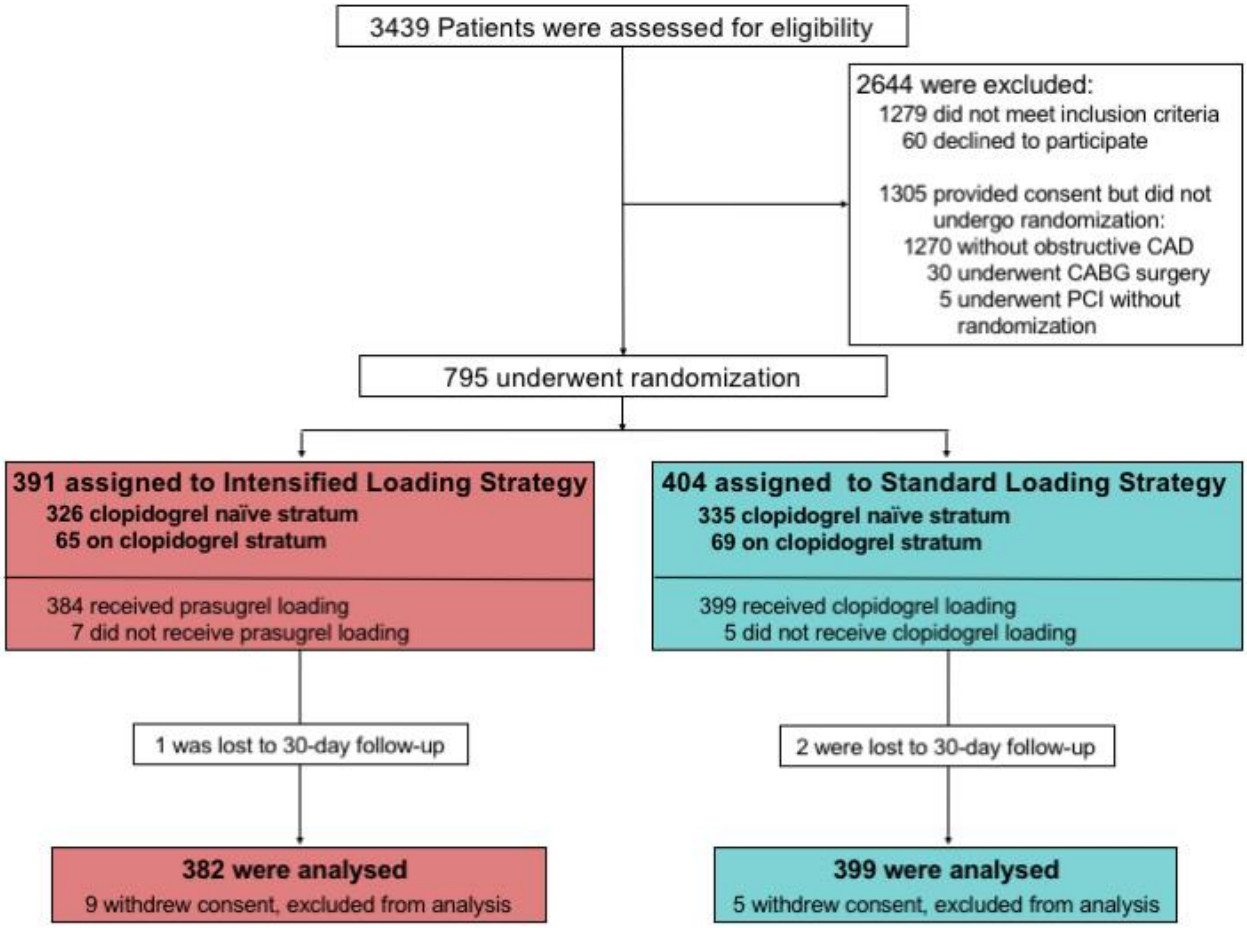
The study was performed in accordance with the current versions of Good Clinical Practice (GCP), the Declaration of Helsinki, and other local or national regulations. For detailed contact information of involved parties see appendix I.

13 NUMBER OF PATIENTS (PLANNED AND ANALYZED)

The study was designed to demonstrate the superiority of intensified loading vs. to standard loading regarding the incidence of the primary endpoint at 30 days after randomization. A primary endpoint rate in the clopidogrel arm of 26.0% and a reduction of primary endpoint of 19.78% in the prasugrel arm was assumed based on former study or registry results. Using of a continuity corrected chi-square test

(Casagrande, Pike, and Smith, 1978, Biometrics, pp. 483-486), a two-side 0.05 significance level, and a power of 80%, the calculation sample size in each group was 1063. The sample size calculation was performed with the software ADDPLAN Version 4. Considering patients drop-out it was planned to allocate 2240 patients (1120 patients per group) to the trial. Due to low recruitment status a premature interim analysis was performed and the study was premature terminated in August 2018 after 795 patients were enrolled.

Figure 2. CONSORT diagram of SASSICAIA trial flow



14 DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION

Patients with stable or unstable biomarker-negative angina and planned PCI were considered candidates for participation in this study. Based on protocol V6.0, the manufacturer-provided cut-off values for the high-sensitive troponin T (hsTnT) and the former recommendations for the evaluation of the hsTnTn, the patients presenting hsTnT values below 0.05 ng/ml (non-specific for coronary heart disease) were considered to be biomarker-negative. After diagnostic catheterization – when the coronary anatomy is known – the final decision for study inclusion was made.

Inclusion criteria:

- Patients with biomarker negative stable or unstable angina pectoris undergoing PCI
- Written informed consent
- In women with childbearing potential a pregnancy test was obligatory.

15 TEST PRODUCT, DOSE AND MODE OF ADMINISTRATION

Test product: Prasugrel

Dose: 60mg loading. Patients with 75-80 years of age and those with a body weight <60 kg received 30mg orally. Further, a loading dose of 60mg was given to patients on chronic clopidogrel therapy.

Administration: oral, open-label at the catheterization laboratory after decision for PCI is taken, but before start of PCI.

Preparation: Prasugrel and clopidogrel are part of the routine pre-treatment of patients undergoing PCI in study sites. No special preparation of packaging was done for the study at German sites. Required by Hungarian authorities, prasugrel was labelled in the pharmacy of the Klinikum der Universität München and shipped to the study site at Balatonfüred (Batch Number: 20180228A).

16 DURATION OF TREATMENT

Administration of prasugrel and clopidogrel (as per study protocol) was single-loading-dose just before start of PCI. As per standard clinical routine after PCI all patients received 75mg clopidogrel daily orally as maintenance therapy. In case of reasonable medical indication the maintenance therapy could be adapted to the

clinical needs of the patient. Decision of standard treatment duration was at the discretion of the treating physician and depended on the type of lesion and the implanted stent.

17 REFERENCE THERAPY, DOSE AND MODE OF ADMINISTRATION

Reference product: Clopidogrel

Dose: 600mg loading according to the hospital standards. The same loading dose was given to patients on chronic clopidogrel therapy.

Administration: oral, open-label at the catheterization laboratory after decision for PCI is taken, but before start of PCI.

Preparation: Clopidogrel is part of the routine pre-treatment of patients undergoing PCI in all study sites. No special preparation of packaging was done for the study.

18 CRITERIA FOR EVALUATION

Efficacy:

To assess the comparative performance of peri-interventional antithrombotic therapy a combined outcome of all-cause death, any myocardial infarction, stent thrombosis, urgent vessel revascularization and stroke within 30 days after randomization was selected which characterizes the drug efficacy as primary endpoint.

There is still no data regarding the value of the new definition of peri-PCI myocardial infarction type 4a according to the Third Universal Myocardial Infarction Definitions on long-term outcomes. For this reason it was one of the secondary endpoints of the trial.

Safety:

Safety endpoints were the incidence of bleeding complications at 30 days post PCI according to BARC (class ≥2 bleeding) and TIMI (Non-CABG related TIMI major and minor bleeding) definitions which better predicts outcomes after PCI.

19 STATISTICAL METHODS

Analysis of the primary and secondary endpoints were performed according to age, gender, complexity of PCI, presence of diabetes and chronic clopidogrel treatment at the time of the index PCI procedure. All efficacy analyses were performed primarily

on an intention-to-treat basis and in a blinded manner regarding the randomly assigned treatment in both study groups. Tests were two-sided and an alpha level of 0.05 was considered statistically significant. The details of the analyses were determined before breaking the random code in the Statistical Analysis Plan.

Primary Statistical Analysis

The primary analysis was performed by testing superiority in terms of the incidence of the primary endpoint at 30 days after randomization. More particularly we were interested in the comparison of the proportions of patients experiencing any of the composite primary endpoint components in the control vs. experimental arm of the study within 30 days after randomization and the index PCI procedure. The analysis of the primary endpoint was performed by a logistic regression which also allowed incorporating the stratification factor. Two models were compared by a likelihood ratio test to reject the Null hypothesis of equal rates between the two treatment groups: Modell 1 was a main effect model which contained the treatment group variable and the stratification factor; Modell 2 was a main effect model which only contained the stratification factor used for adjustment but no treatment group information. Furthermore, analysis was based on a Wang and Tsiatis group sequential design. At the time of interim analysis the primary analysis null hypothesis was rejected if the two sided p-value was below 2.36%. For the remaining cases it was possible to adjust the design sample size according to the principle developed by Müller & Schäfer. For the final analysis the nominal two-sided type I error level was 3.76%.

Secondary Statistical Analyses of the Primary Endpoint - Sensitive Analyses

The influence of some prognostic factors was investigated by their incorporation as explanatory variables in the logistic regression analysis of the primary endpoint. The time of the first occurrence of any of the composite endpoint components defining the primary endpoint was recorded and used for different survival analyses (Patients suffering a primary endpoint event were followed for other possible adverse events throughout the entire study timeframe). Time-to-event outcomes estimated with Kaplan–Meier methods, were compared by means of the log-rank test or proportional hazards regression (Cox) if adjustment factors had to be included in order to test the null hypothesis of equal cumulative incidence between the two treatment groups.

Other Secondary Analyses

Statistical analyses of the secondary endpoints were similar to those performed for the primary endpoints. They involve the use of a logistic regression to test the null hypothesis of equal rates between the two treatment groups. Time-to-event analyses in order to test the null hypothesis of equal cumulative incidence between the two treatment groups with the creation of Kaplan-Meier plots, the performance of log-rank tests or proportional hazards regression (Cox) if adjustment factors had to be included. Categorical variables such as demographics and medical history data were summarized using frequencies and proportions and were compared using the chi-square test. Continuous data was summarized using mean ± standard deviation or median [25th, 75th percentiles] and was compared using Student t test or nonparametric Wilcoxon rank-sum test.

20 SUMMARY – CONCLUSION

Efficacy results

No differences were observed among randomized groups (intensified oral loading strategy (ILS), standard loading strategy (SLS)) regarding baseline and demographic characteristics. Compared to SLS, significantly less patients assigned to ILS underwent PCI for chronic totally occluded arteries, 6.6% vs. 10.7%, p = 0.01. Crossover rate was low, 1.8% from SLS to ILS and 0.8% from ILS to SLS. At discharge, significant more patients assigned to ILS patients received prasugrel (7.3%) compared to SLS patients (3.3%), p = 0.02 (treating physicians' decision). At 30 days, 3 patients (2 in ILS and 1 patient in SLS group) were lost to follow-up. None of them experienced any adverse event until the last contact. The primary endpoint occurred in 66 patients (17.3%) assigned to ILS and 74 patients (18.5%) assigned to SLS, (OR 0.92, 95% CI 0.64 – 1.32, P = 0.64), on the basis of the prespecified logistic-regression analysis, which adjusted for randomization strata. The sensitivity analysis for the primary endpoint done to adjust for differences in baseline angiographic characteristics, yielded an OR of 0.95, 95% CI 0.66 – 1.38, P=0.80. Only one patient (ILS group) died 9 days after randomization due to cardiovascular causes.

Peri-PCI type 4a MI according to 3rd Universal Definition occurred in 11 patients (2.9%) assigned to ILS and 6 patients (1.5%) assigned to SLS group, OR 1.94, 95% CI 0.71 – 5.30, P = 0.19. The most frequently observed evidence for prolonged

ischemia was prolonged chest pain (11 cases, 64.7%), followed by side branch occlusion (5 cases, 29.4%), slow-flow or thrombus (4 cases, 23.5%) and ECG changes (4 cases, 23.5%). According to 4th Universal Definition, peri-PCI type 4a MI was observed among 10 patients (2.6%) of ILS group and 3 patients (0.8%) of SLS group, OR 3.55, 95% CI 0.97 – 13.0, P = 0.08.
Regarding primary endpoint, our trial showed no strong evidence of differential results by prespecified subgroups of interest according to age, gender, presence or absence of diabetes and multilesion PCI.

Safety results

BARC 2 bleeding events were observed in 16 patients (4.2%) assigned to ILS and 19 patients (4.8%) assigned to SLS, P=0.70. There were 6 patients experiencing TIMI major bleeding complications, 1 assigned to ILS (pericardial effusion due to vessel perforation) and 5 assigned to SLS (2 gastrointestinal bleeds due to anal fissure and gastric ulcer, 2 pericardial effusions and 1 subarachnoid haemorrhage while on triple therapy), respectively 0.3% vs. 1.3%, P = 0.22. There were no concerns regarding the safety of study drugs during the whole trial duration. In total 40 SAE´s were recorded (for SAE listing see appendix II). There was no need for administration of other drugs or for changing the study drug dose at any time during the trial. Based on the accumulated data and the safety monitoring provisions foreseen in the study protocol, it can be concluded that the administration of prasugrel and clopidogrel as defined in the respective study protocol was safe and well tolerated.

Conclusion

In summary, in patients with biomarker-negative stable and unstable AP undergoing elective PCI, no conclusive differences were observed among intensified prasugrel-based and standard clopidogrel-based loading strategies regarding efficacy and safety. Therefore, both loading strategies might be safely applied among these patients.

APPENDIX I

Contact details of participating parties

Steering Committee

Function	Name	Contact
Chair	Prof. Steffen Massberg	Klinikum der Universität München Medizinische Klinik und Poliklinik I Marchioninistr. 15 81377 München
Principal Investigator	Prof. Julinda Mehilli	Klinikum der Universität München Medizinische Klinik und Poliklinik I Marchioninistr. 15 81377 München
Co-Principal Investigator	Prof. Dirk Sibbing	Klinikum der Universität München Medizinische Klinik und Poliklinik I Marchioninistr. 15 81377 München
Member	Prof. Franz-Josef Neumann	Universitäts-Herzzentrum Freiburg Bad Krozingen Südring 15 79189 Bad Krozingen
Principle Investigator	Prof. Wilibald Hochholzer	Universitäts-Herzzentrum Freiburg Bad Krozingen Südring 15 79189 Bad Krozingen

Data and Safety Monitoring Board (DSMB)

Function	Name	Contact
Chair	Prof. Albert Schömig	Praxis NY Höfe Praxis für Innere Medizin und Kardiologie Nymphenburger Straße 10d 80335 München, Germany
Member	Dritan Poci, MD, PhD	Örebro University Hospital Cardiology 701 85 Örebro, Schweden
Member	PD Dr. Martin Hadamitzky	Institut für Radiologie und Nuklearmedizin, Deutsches Herzzentrum München, Germany

Member	Dr. rer. biol. Hum. Siegfried Zedler	Clinical Study Center (CSC) Klinikum der Universität München Hermann-Schmid-Str. 10 80336 München, Germany

Event Adjudication Committee

Function	Name	Contact
Chair	Prof. Dr. Jürgen Pache	Benedictus Krankenhaus Tutzing Bahnhofstraße 5 82327 Tutzing
Member	Prof. Heidi Estner	Klinikum der Universität München Medizinische Klinik und Poliklinik I Marchioninistr. 15 81377 München
Member	Prof. Dr. med. Helmut Schühlen	Auguste-Viktoria-Klinikum Berlin Rubensstraße 125 12157 Berlin

Participating Academic Research Organisation

Function	Contact
Coordinating Research Center (Project Management)	CSC^{LMU}, Clinical Study Center Hermann-Schmid-Str. 10 80336 München
Drug Safety	CSC^{LMU}, Clinical Study Center Hermann-Schmid-Str. 10 80336 München
Biostatistics	Prof. Dr. rer. nat. Ulrich Mansmann Institut für medizinische Informationsverarbeitung, Biometrie und Epidemiologie (IBE) Marchioninistr. 15 81377 München

APPENDIX II

SAE-Overview

Interne Case-ID	Patient ID	Year of birth	Patient sex	IMP / Study Group	Prasugrel start date	Clopidogrel start date	SAE Verbatim Term	SAE start date	SAE end date	SAE outcome	Causality (investigator)	Causality (sponsor)	Expectedness
01	01-0257	1961	M	Clopidogrel	NA	2016-12-07	Angina Pectoris	2016-12-13	2016-12-16	Recoverd/Resolved	Not related	not related	unexpected
02	01-0142	1938	M	Prasugrel	NA	2016-04-06	Syncope	2016-04-08	2016-04-13	Recoverd/Resolved	Not related	not related	unexpected
03	01-0268	1962	M	Prasugrel	2017-01-03	NA	Planned PCI	2017-01-05	2017-01-10	Recoverd/Resolved	Not related	not related	unexpected
04	01-0268	1962	M	Prasugrel	2017-01-03	NA	pericardial effusion	2017-01-05	2017-01-05	Recoverd/Resolved	Not related	not related	unexpected
05	01-0365	1938	M	Clopidogrel	2017-06-20	NA	Exacerbation COPD	2017-07-11	2017-07-20	Recovering/Resolving	Not related	not related	unexpected
06	02-0229	1947	F	Prasugrel	2016-09-08	NA	cardiac arrest	2016-09-08	2016-09-08	Recovered/Resolved	Not related	not related	unexpected
07	03-0037	1949	M	Prasugrel	2017-08-18	NA	hypertensive crisis	2017-08-21	2017-08-22	Recovered/Resolved	Not related	not related	unexpected
08	03-0041	1948	M	Clopidogrel	NA	2017-09-05	INI: Chest Pain FU: atypical thoracic compliant	2017-09-25	2017-09-27	Recovered/Resolved	Not related	not related	unexpected
09	03-0036	1946	M	Prasugrel	2017-08-18	NA	atypical thoracic pain caused by spinal canal stenosis	2017-08-24	2017-08-30	Recovered/Resolved	Not related	not related	unexpected
10	01-0388	1938	F	Prasugrel	2017-07-14	NA	cardiac decompensation	2017-08-13	2017-08-17	Recovered/Resolved	Not related	not related	unexpected
11	03-0041	1948	M	Clopidogrel	NA	2017-09-05	hypertensive crisis	2017-10-05	2017-10-06	Recovered/Resolved	Not related	not related	unexpected
12	04-0052	1957	M	Clopidogrel	NA	2017-10-19	Angina Pectoris	2017-11-08	2017-11-11	Recovered/Resolved	Not related	not related	unexpected
13	04-0059	1949	M	Prasugrel	2017-11-15	NA	Urethra injury	2017-12-07	2017-12-11	Recovering/Resolving	Not related	not related	unexpected
14	01-0290	1932	M	Clopidogrel	NA	2017-03-21	rehospitalisation by dyspnea	2017-03-11	2017-03-17	Recovered/Resolved	Not related	not related	unexpected
15	01-0328	1946	M	Prasugrel	2017-05-04	NA	suspected oesophagus spasm	2017-05-16	2017-05-26	Recovered/Resolved	Not related	not related	unexpected
16	01-0471	1938	M	Prasugrel	2017-10-25	NA	rehospitalisation due to cystitis	2017-11-25	2017-11-30	Recovered/Resolved	Not related	not related	unexpected
17	01-0410	1941	M	Prasugrel	2017-08-09	NA	suspected radiation related colitis	2017-08-23	2017-08-30	Recovered/Resolved	Not related	not related	unexpected
18	01-0534	1938	F	Clopidogrel	NA	2018-02-08	traumatic brain injury grade I	2018-03-03	2018-03-07	Recovered/Resolved	Not related	not related	unexpected
19	01-0573	1946	M	Prasugrel	2018-04-04	NA	rehospitalizarion due to thoracal discomfort/ psychogenic	2018-04-10	2018-04-13	Recovered/Resolved	Not related	not related	unexpected
20	01-0410	1941	M	Prasugrel	2017-08-09	NA	infected hydronephrosis of kidney, prolongned hospitalization	2017-08-10	2017-08-17	Recovered/Resolved	Not related	not related	unexpected

Interne Case-ID	Patient ID	Year of birth	Patient sex	IMP / Study Group	Prasugrel start date	Clopidogrel start date	SAE Verbatim Term	SAE start date	SAE end date	SAE outcome	Causality (investigator)	Causality (sponsor)	Expectedness
21	02-0528	1941	F	Prasugrel	2018-02-05	NA	hospitalization due to influenza A-infection/ bad general condition	2018-03-08	2018-03-16	Recovered/Resolved	Not related	not related	unexpected
22	04-0092	1946	M	Clopidogrel	NA	2018-05-17	air embolism into coronary artery due to ruptur of high pressure balloon	2018-05-17	2018-05-17	Recovered/Resolved	Not related	not related	unexpected
23	02-0395	1951	M	Prasugrel	2017-07-19	NA	rehospitalization due to vertigo, tinnitus and headache	2017-07-29	2017-08-01	Recovered/Resolved	Not related	not related	unexpected
24	01-0495		M	Prasugrel	2017-11-21	NA	prolonged hospitalization due to planned PCI	2017-11-23	2017-11-28	Recovered/Resolved	Not related	not related	unexpected
25	10-0011	1972	M	Prasugrel	2018-05-04	NA	rehospitalization due to increase of hypertension	2018-05-07	2018-05-07	Recovered/Resolved	Not related	not related	unexpected
26	10-0011	1972	M	Clopidogrel	2018-05-04	NA	rehospitalization due to syncope	2018-05-17	2018-06-01	Recovered/Resolved	Not related	not related	unexpected
27	10-0016	1947	M	Clopidogrel	NA	2018-05-10	rehosp due to iAP	2018-05-27	2018-05-29	Recovered/Resolved	Not related	not related	unexpected
28	01-0485	1943	M	Clopidogrel	NA	2017-11-08	prolonged hospitalization due to thromboendarterectomy	2017-12-13	2017-12-27	Recoverd/Resolved	Not related	not related	unexpected
29	02-0577	1964	M	Clopidogrel	NA	2018-04-06	embolism (DD spasm) during AFS-stenosis intervention	2018-04-17	2018-04-18	Recovered/Resolved	Not related	not related	unexpected
30	04-0098	1945	M	Prasugrel	2018-06-20	NA	aneurysma spuria at the right groin	2018-06-20	2018-06-20	Recovered/Resolved	Not related	not related	unexpected
31	01-0481	1937	M	Prasugrel	2017-11-06	NA	prolonged hospitalization due to recurrent ischemia	2017-11-08	2017-11-22	Recovered/Resolved	Not related	not related	unexpected
32	02-0135	1948	F	Prasugrel	2016-03-24	NA	prolonged hospitalization due to cardiogenic shock	2016-03-24	2016-04-06	Recovered/Resolved	Not related	not related	unexpected
33	01-0083	1971	M	Prasugrel	2016-01-25	Na	Hospital admission due to angina and dyspnoe	2016-01-29	2016-01-30	Recovered/Resolved	Not related	not related	unexpected
34	01-0130	1936	F	Prasugrel	2016-03-21	Na	Rehospitalization due to suspected ACS	2016-04-07	2016-04-09	Recovered/Resolved	Not related	not related	unexpected
35	01-0103	1939	M	Clopidogrel	Na	2016-02-18	prolonged hospitalization due to acute gout episode of righ	2016-02-20	2016-03-03	Recovered/Resolved	Not related	not related	unexpected
36	01-0037	1952	M	Prasugrel	2015-11-30	Na	Rehospitalization due to chest pain	2015-12-07	2015-12-08	Recovered/Resolved	Not related	not related	unexpected
37	01-0469	1968	M	Clopidogrel	NA	2017-10-24		2017-11-07	2017-11-09	Recovered/Resolved	Not related	not related	unexpected
38	01-0241	1950	M	Clopidogrel	NA	2016-10-07		2016-10-11	2016-10-13	Recovered/Resolved	Not related	not related	unexpected
39	01-0102	1936	M	Prasugrel	2016-02-18	NA	Prolonged hospitalization	2016-02-19	2016-02-24	Recovered/Resolved	Not related	not related	unexpected
40	01-0452	1967	F	Prasugrel	2017-10-04	NA	Rehospitalization due to hypertensive urgency and atypical	2017-10-29	2017-11-03	Recovered/Resolved	Not related	not related	unexpected