DISEASE REGISTRY REPORT

Compound(s): Not applicable

Hypercholesterolemia Diagnosis, Treatment Patterns and Target Achievement in Clinical Practice in Germany in Patients with Acute Coronary Syndrome

Registry number: DIREGL07801

Registry name: HYDRA-ACS

Registry initiation date [date first patient in (FPI)]: 27-FEB-2017

Registry completion date [last patient completed/last patient out (LPO)]: 28-SEP-2020

Registry design: National, multicenter, non-interventional study with focus on therapeutic approaches; prospective longitudinal study: disease registry with follow-ups at 12 and 24 months**.**

Report date: 23-JUL-2021

This registry was performed in compliance with the guidelines for Good Epidemiology Practice. This report has been prepared based on the publication 'Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) – Guidelines for reporting observational studies – Ann Intern Med. 2007'.

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SYNOPSIS

Title of the registry:	Hypercholesterolemia Diagnosis, Treatment Patterns and Target Achievement in Clinical Practice in Germany in Patients with Acute Coronary Syndrome: HYDRA-ACS DIREGL07801
Design:	National, multicenter, non-interventional Prospective longitudinal study: disease registry with follow-ups at 12 and 24 months
Objectives:	**Primary objective**: Documentation of lipid target values in patients with acute coronary syndrome (ACS) in clinical practice in Germany. **Secondary objectives:** 1. The documentation of lipid profiles and lipid-lowering therapy in clinical practice in Germany 2. The validation of the applicability of the current guidelines for the treatment of dyslipidemia in secondary prevention in clinical practice in Germany. 3. The documentation of drug utilization pattern in secondary prevention in clinical practice in Germany. 4. The documentation of cardiovascular and cerebrovascular events over a follow-up period of 2 years.
Participants as of 30-	**Countries:** Germany **Number of planned sites**: 100 **Number of planned patients**: 3,000 **Site Settings:** Sites (hospitals) that routinely treat inpatients with ACS in Germany in order to represent the clinical care routine of this patient group as realistically as possible. A list of participating sites is provided in section 1.8. **Patient eligibility criteria:** - ≥ 18 years of age and capable of giving informed consent - Hospitalization due to ACS (STEMI, NSTEMI, unstable angina) - Patients with LDL cholesterol > 155 mg/dl AND a relative in the first degree with premature myocardial infarction (men <55 years, women <60 years) OR patients with LDL cholesterol >155 mg/dl AND premature myocardial infarction - Patients with LDL cholesterol >190 mg/dl without premature myocardial infarction or without premature myocardial infarction in relative in the first degree - Written informed consent - No concurrent participation in a clinical trial Apart from concurrent participation in a clinical trial, no explicit exclusion criteria were provided to avoid systematic bias in the inclusion of suitable patients and to present the clinical treatment routine without restrictions.
Scientific committee	Dr Anselm Gitt, Ludwigshafen (Chair) Prof Dr Klaus Parhofer, München Prof Dr Ulrich Laufs, Homburg Prof Dr Winfried März, Mannheim Prof Dr Nikolaus Marx, Aachen
Publications	To date, publications and abstracts resulting from the registry were not prepared.

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(reference):	Statement about initiatives for any local communication in participating countries/regions: Not applicable.
Introduction - Background/rationale:	Cardiovascular disease is the leading cause of death worldwide. Worldwide, about 17.3 million people died from cardiovascular disease in 2008, accounting for about one-third of all deaths that year. Of these, about 7.3 million people died from coronary heart disease (CHD), and another 6.2 million died from cerebral infarction [1]. In 2030, the number of deaths from cardiovascular disease is estimated to increase to approximately 23.3 million, with ischemic heart disease likely to remain the leading cause of death [2]. In clinical practice, acute coronary syndrome (ACS) is usually the first manifestation of subsequent manifest cardiovascular disease. However, successful treatment of ACS has progressed rapidly in recent decades. The introduction of interventional reperfusion and increasing drug treatment with anticoagulants and antiplatelet therapies have had a very positive impact on the course of the disease in ACS patients. Nevertheless, ACS remains a significant risk factor for subsequent disease in these patients [3]. Long-term therapy of cardiovascular risk factors, such as hyperlipidemia, hypertension, or diabetes mellitus, is critical to prevent progression of CHD and its complications. Large population-based studies as well as subgroup analyses of randomized clinical trials could show that patients with diabetes mellitus have a similar risk profile as patients with known manifest CHD and benefit decisively from lipid-lowering therapy. Furthermore, patients with chronic kidney disease could be identified as particularly at risk for cardiovascular disease. The SHARP study [4] demonstrated that patients with already advanced chronic kidney disease also benefited from LDL lowering by daily administration of 20mg simvastatin and 10mg ezetimibe, as it resulted in a significant reduction in the incidence of serious atherosclerotic events. The EuroAspire Registry, as part of the Euro-Heart Survey program, was one of the first registries to provide treatment data for secondary prevention in clinical practice; these data showed that although guideline-adherent treatment was increasingly common over time, there was certainly further potential for improvement. The 2L registry conducted in Germany documented widespread deficits in lipid-lowering therapy in the area of hospital-based and outpatient secondary prevention [5] [6]. The recent cross-sectional Dyslipidemia International Survey (DYSIS) in secondary prevention collected lipid target attainment data from 22,063 statin-treated patients and showed that despite chronic lipid-lowering therapy, 46.8% of high-risk patients did not reach recommended target levels for LDL cholesterol (< 100 mg/dl) and a high proportion of these patients also had elevated triglyceride levels and low HDL cholesterol levels [7]. The guidelines for the management of dyslipidemia issued in 2011 by the European Society of Cardiology (ESC) and the European Artherosclerosis Society (EAS) [8], which incorporated data from recent randomized clinical trials, established even more stringent targets for lipid control in secondary prevention for patients at very high cardiovascular risk, including patients with manifest cardiovascular disease, patients with type 2 diabetes mellitus, patients with type 1 diabetes mellitus and organ damage, and patients with moderate to severe chronic kidney disease. The most recent version of the 2016 guidelines also confirms these stricter target values for lipid control [9]. All analyses are based on the guidelines that were effective when the study was designed and initiated. More recent guidelines revised in the meantime (2019) with stricter target value attainment were, thus, not taken into account. To obtain an insight into the current treatment situation of patients with ACS, the multicenter HYDRA-ACS registry study was initiated to document the clinical characteristics of patients with acute coronary syndrome in everyday clinical practice in Germany. In addition, the lipid profiles, lipid-lowering therapy, and lipid target achievement in the course of treatment were documented over a period of 2 years.
Methodology:	**(a) Site and patient selection:** Site selection: Sites (hospitals) that routinely treat inpatients with ACS in Germany in order to represent the clinical care routine of this patient group as realistically as possible. Patient selection: The inclusion criteria were limited to the presence of acute coronary syndrome (hospital stay) in adult patients (≥ 18 years) and the written informed consent of the patient with the following criteria: - Patients with LDL cholesterol > 155 mg/dl AND a relative in the first degree with premature myocardial infarction (men <55 years, women <60 years) OR patients with LDL cholesterol >155 mg/dl AND premature myocardial infarction - Patients with LDL cholesterol >190 mg/dl without premature myocardial infarction or without

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premature myocardial infarction in relative in the first degree

Apart from concurrent participation in a clinical trial, no explicit exclusion criteria were provided to avoid systematic bias in the inclusion of suitable patients and to present the clinical treatment routine without restrictions.

To avoid systematic bias, suitable patients were included consecutively in the study sites. The study design should reflect the treatment situation of these patients under real conditions as closely as possible. Within the framework of this non-interventional observational study, all therapies that were approved for the treatment of this patient group could be applied. Treatment was solely at the discretion of the treating physician; the study did not provide explicit treatment guidelines.

(b) Data collection:

Data was collected electronically via eCRF.

(c) Safety data collection:

Since the study was designed as a disease registry, treatment with individual drugs was not investigated. Only adverse drug reactions (ADRs) were therefore collected. Adverse drug reactions were documented by the site investigator on an adverse drug reaction form (=ISI form) and then sent to the external service provider (IHF GmbH) within one working day. IHF GmbH transferred the contents of the adverse drug reaction form (ISI form/source document) in English within one working day to a separate ISI form, which was then sent within one working day together with any source document to the pharmacovigilance department at Sanofi. This procedure also applied to ADRs discovered at the time of an audit by IHF GmbH or during a telephone call to the site.

All ADRs that were presumed to be related to drugs from Sanofi-Aventis Deutschland GmbH, Winthrop Arzneimittel GmbH, Zentiva Pharma GmbH or Genzyme GmbH were forwarded to Sanofi and entered into the Sanofi pharmacovigilance database. Cases subject to reporting were reported to the authorities by Sanofi (see Appendix II).

(d) Data management, review, validation:

All data management processes are described in detail in the Data Management Plan (see Appendix III, section 3.5).

(e) Statistical considerations:

Due to the observational design of the registry, all collected parameters were evaluated descriptively.

Analysis sets: The statistical analyses include the data of all patients included in the study (i.e. all patients who have met the inclusion criteria and have given written consent to participate). If a patient cancels the study participation prematurely, their data are included in the analyses documented before the discontinuation of participation.

The **Baseline Analysis Set (BAS**) consists of all patients who meet all inclusion criteria according to the observation plan, have at least one further documented entry in the first documentation section of the eCRF and whose Baseline CRF is signed. The BAS is used to analyse the data collected in the context of the initial documentation (interim analysis of baseline data). The BAS was used to evaluate the baseline data.

The **Full-Analysis Set (FAS**) consists of all patients of the BAS with documented lipid parameter LDL-C and lipid-lowering therapy at the time of the index event, 12 month follow-up and 24 month follow-up and both follow-up CRFs signed. The FAS was used to evaluate the longitudinal data.

The above described analysis sets were extended post-hoc (based on the data obtained in the study; goal: to include a larger proportion of patients in the final analyses):

The **Extended Baseline Analysis Set (EBAS)** consists of all patients who meet all inclusion criteria according to the observation plan. The EBAS was used to evaluate the baseline data.

The **Extended Analysis Set (EAS)** consists of all patients of the EBAS with documented LDL-C values at the time of the index event and at 12-months follow-up. The acceptable time window for follow-ups was extended to ± 4 months (in contrast to ± 3 months in the FAS). The EAS was used to evaluate the longitudinal data.

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	Variables and evaluation criteria: All variables documented in the eCRF were evaluated in a descriptive report. Key variables were - Lipid target achievement as measured by the reduction of LDL cholesterol over time (baseline to 12-M FU to 24-M-FU); absolute and relative reduction of LDL cholesterol at 12 and 24 months following baseline (defined as (i) LDL < 70mg/dl and (ii) LDL < 70mg/dl or 50% reduction in LDL according to baseline LDL value). - Changes in other relevant lipid values over time; absolute and relative change of total cholesterol, HDL cholesterol, and triglycerides at 12 and 24 months following baseline. - Non-drug lipid lowering therapy in clinical routine (life style and nutrition); percentage of patients with non-drug lipid-lowering therapy over time (baseline, 12-M-FU, 24-M-FU) - Lipid-lowering pharmacotherapy in clinical routine; percentage of patients with lipid-lowering pharmacotherapy over time (baseline, 12-M-FU, 24-M-FU) - Drug utilization patterns in secondary prevention; percentage of patients with pharmacotherapy over time (baseline, 12-M-FU, 24-M-FU) - Cardiovascular and cerebrovascular events over time; percentage of patients with complications at baseline; percentage of patients with non-fatal events since baseline (12-M-FU, 24-M-FU) The following groupings were chosen: - Sex (male, female) - Age (18-65 years, >65 years) Data analyses: Categorical variables were presented as absolute and relative frequencies. Continuous variables were presented as absolute number n, mean, standard deviation, median, 1st and 3rd quartile, 1st and 99th percentile. No formal statistical tests were performed. The following graphical analyses were provided: - Distributions of lipid values are analyzed via histograms and kernel density curves (pre-post comparison, if necessary group comparisons) - Lipid lowering medication (single and combination therapies) are analyzed over time. graphically analyzed using bar charts (stacked) All statistical analyses as well as data handling processes (i.e. categorizations, calculation of derived variables, laboratory parameters, or pre-post differences etc.) are described in detail in the Statistical Analysis Plan (see Appendix III, section 3.2). No imputations were made to replace missing data. All available data was displayed. For time-to-event analyses, the patient data was censored on the basis of their last known follow-up on the right (i.e. in the case of premature drop-out, the last existing value was used).
Registry period:	This report includes patient data reported to the HYDRA-ACS Registry as of cutoff 30-NOV-2020.
RESULTS – Part I	The following result are based on the analysis sets BAS and FAS (as defined in section Methodology).

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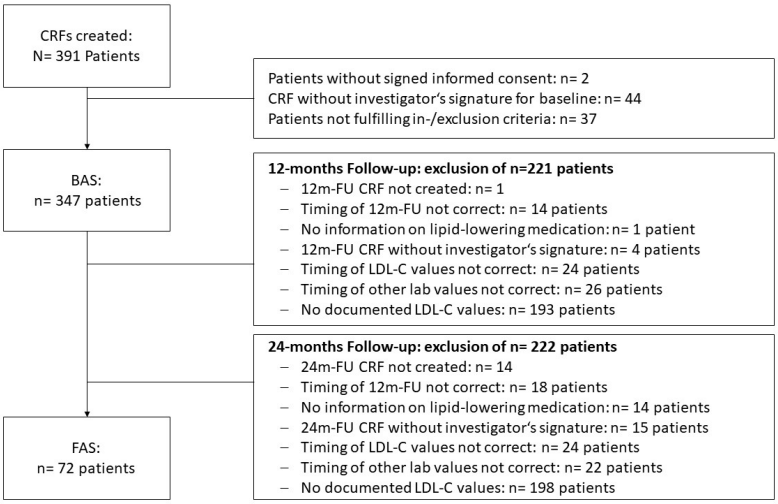
Participants (actual):	**(a) Overall participation status:** The registry was conducted in Germany. 24 sites participated in the registry. 347 patients were included in the baseline analyses. 72 patients were included in the full analysis set (FAS) to evaluate the longitudinal data. **(b) Participation per period of the registry:** The following flow chart illustrates the number of patients at each stage of the registry, including the number of patients lost to follow-up and the amount of missing data for the variables of interest (i.e. lipid profiles):  Of 347 patients in baseline, complete follow-up data (for both 12- and 24-months follow-up concurrently) were available in 72 patients. Overall, 275 patients were excluded from the longitudinal analyses: - 52 patients with incomplete data for 12-months follow-up - 53 patients with incomplete data for 24-months follow-up - 170 patients with incomplete data for both 12- and 24-months follow-up
Participant characteristics and primary analyses:	**(a) Descriptive data** Characteristics of registry physicians**:** Type of sites were as follows (see BAS tables CTR-1 to -5 in Appendix II): - Hospital, n= 19; - No information provided, n= 6 Characteristics of registry patients**:** The Baseline Analysis Set (BAS) consisted of 347 documented patients. Duration of enrolment was on average 231.9 days (SD: 149.6 days). On average, 13.9 patients (SD: 16.0; MD: 10) were enrolled per study site. The following table shows the demographic and clinical characteristics of the registry patients at baseline (BAS): **Characteristics** **N= 347**

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Sex – *no. of participants (%)*	
Male	257 (74.1)
Female	90 (25.9)
Mean age *(SD) - yr*	57.2 (11.3)
Cardiovascular History – *no. of participants (%)*	
Coronary heart disease,	114 (32.8)
PCI	88 (25.4)
Acute coronary syndrome	79 (22.8)
Aortocoronary bypass	19 (5.5)
Stroke	7 (2.0)
TIA	6 (1.7)
Comorbidities and Risk Factors – *no. of participants (%)*	
Arterial hypertension	237 (68.3)
Diabetes mellitus	60 (17.3)
Heart failure	59 (17.0)
Stable angina pectoris	55 (15.9)
Heart valve disease	27 (7.8)
Depression	27 (7.8)
Renal insufficiency	27 (7.8))
Atrial fibrillation	21 (6.1)
Peripheral arterial occlusive disease	17 (4.9)
Carcinoma	17 (4.9)
COPD	13 (3.8)
Device implantation	7 (2.0)
Deep vein thrombosis	6 (1.7)
Pulmonary embolism	1 (0.3)
Phenotypic Findings – *no. of participants (%)*	
Xanthomas	9 (2.6)
Xanthelasma	5 (1.4)
Arcus cornealis	7 (2.0)
Family History – *no. of participants (%)*	
Family history of MI	184 (53.0)
Family history of CHD	114 (32.8)
Family history of cerebral/vascular disease	67 (19.3)
Family history of elevated cholesterol levels	41 (11.8)
Family history of arcus cornealis	3 (0.9)
Family history of tendon xanthomas	0
Lipid Apheresis Therapy – *no. of participants (%)*	0
Body-mass Index, *mean (SD)*	28.5 (5.0)

More details on patient characteristics at baseline (incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (BAS; tables E1, E2, B1 – B18).

Follow-up duration (i.e. time from baseline to follow-up in days):
With regard to the Baseline Analysis Set (taking into account all patients regardless of completeness of follow-up data; n= 347 patients) time to follow-up was on average 384.0 days (SD: 28.1) for the 12-months follow-up and 758.5 days (SD: 34.4) for the 24-months follow-up.

A complete descriptive report of follow-up data for this population is given in Appendix II (12-months follow-up: tables 1FU1 – 1FU9, BAS; 24-months follow-up: tables 2FU1 – 2FU9, BAS).

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(b) Primary analyses: Lipid Target Achievement
The Full Analysis Set (FAS) consisted of 72 patients with complete (LDL) data on both 12-months and 24-months follow-up.

Follow-up duration (i.e. time from baseline to follow-up in days):
With regard to the Full Analysis Set (taking into account all patients with complete data on LDL cholesterol and correct timing for both follow-ups; n= 72) time to follow-up was on average 385.2 days (SD: 22.2) for the 12-months follow-up and 750.6 days (SD: 19.0) for the 24-months follow-up.

A complete descriptive report of follow-up data for this population is given in Appendix II (12-months follow-up: tables 1FU1 – 1FU9, FAS; 24-months follow-up: tables 2FU1 – 2FU9, FAS).

Distribution of LDL cholesterol values (mg(dl)**:**
The following table shows mean LDL cholesterol values at baseline, 12-months follow-up and 24-months follow-up (FAS):

	Mean	Standard deviation	Median	1st Quartile	3rd Quartile	N
LDL-Cholesterol [mg/dl] at admission	174.8	44.9	177	147	206	72
LDL-Cholesterol at 12MFU	92.9	33.9	89	69	106	72
LDL-Cholesterol at 24MFU	95.3	38.6	85	72	109	72

More details on LDL cholesterol values (incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (FAS; tables CHOL-7 – CHOL-9).

The following figure illustrates the distribution of LDL cholesterol values (mg/dl) at baseline, 12-months and 24-months follow-up (FAS):

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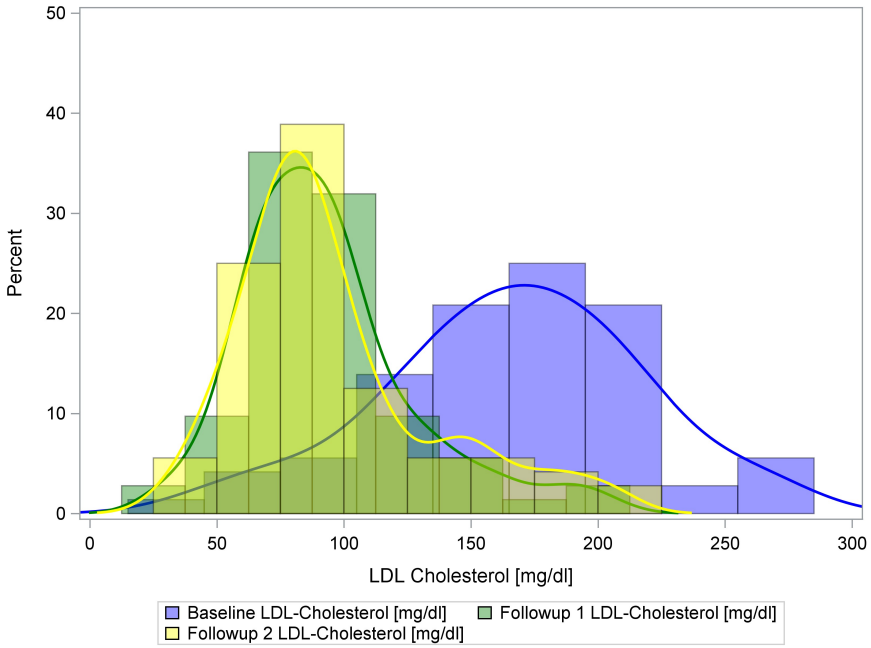

Target achievement of LDL cholesterol values (mg/dl):
Data were analysed according to lipid target achievement as measured by the reduction of LDL cholesterol over time (baseline to 12-M FU to 24-M-FU); absolute and relative reduction of LDL cholesterol at 12 and 24 months following baseline (FAS).

Target ranges were set as follows (see also SAP, section 7.2; Appendix III, section 3.2):

- Within target range: < 70mg/dl
- Above target range: ≥ 70 mg/dl

Within target range (LDL <70 mg/dl) were

- At baseline: n= 4 patients (5.6%)
- At 12-months follow-up: n= 19 patients (26.4%)
- At 24-months follow-up: n= 15 patients (20.8%)

Above target range (LDL ≥ 70 mg/dl) were

- At baseline: n= 68 patients (94.4%)
- At 12-months follow-up: n= 53 patients (73.6%)
- At 24-months follow-up: n= 57 patients (79.2%)

According to guidelines applicable at the time of data collection (see References [1]), target achievement was defined as LDL< 70mg/dl or 50% of reduction in LDL (see also SAP, section 6.1.1; Appendix III, section 3.2).

Within this target range (LDL< 70mg/dl or 50% of reduction in LDL) were:

- At 12-months follow-up: n= 37 patients (51.4%; 95% CI: 0.40, 0.63)
- At 24-months follow-up: n= 35 patients (48.6%; 95% CI: 0.40, 0.63)

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Above this target range (LDL< 70mg/dl or 50% of reduction in LDL) were:

- At 12-months follow-up: n= 37 patients (51.4%)
- At 24-months follow-up: n= 35 patients (48.6%)

More details on LDL-C target achievement (target ranges of LDL cholesterol at baseline and follow-up; incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (FAS; tables PZ-1 to PZ-18).

The following table shows lipid target achievement (LDL cholesterol; absolute and relative difference from baseline) in registry patients with complete data (FAS):

	Mean	Standard deviation	Median	1st Quartile	3rd Quartile	N
Absolute difference (Baseline -> FU 12-15 Month) LDL-C [mg/dl]	-73.8	56.6	-76	-120	-40	72
Relative difference (Baseline -> FU 12-15 Month) LDL-C [%]	-38.2	30.6	-46	-59	-26	72
Absolute difference (Baseline -> FU 24-27 Month) LDL-C [mg/dl]	-71.4	59.2	-86	-121	-31	72
Relative difference (Baseline -> FU 24-27 Month) LDL-C [%]	-36.2	36.7	-48	-60	-20	72

The 95% confidence interval for the mean relative difference from baseline to 12-months follow-up was -45.4, -31.1 (p< 0.00001).
The 95% confidence interval for the mean relative difference from baseline to 24-months follow-up was -44.9, -27.6 (p< 0.00001).

The following figure illustrates the distribution of LDL cholesterol values (mg/dl; absolute and relative difference from baseline) 12-months and 24-months follow-up; in registry patients with complete data (FAS):

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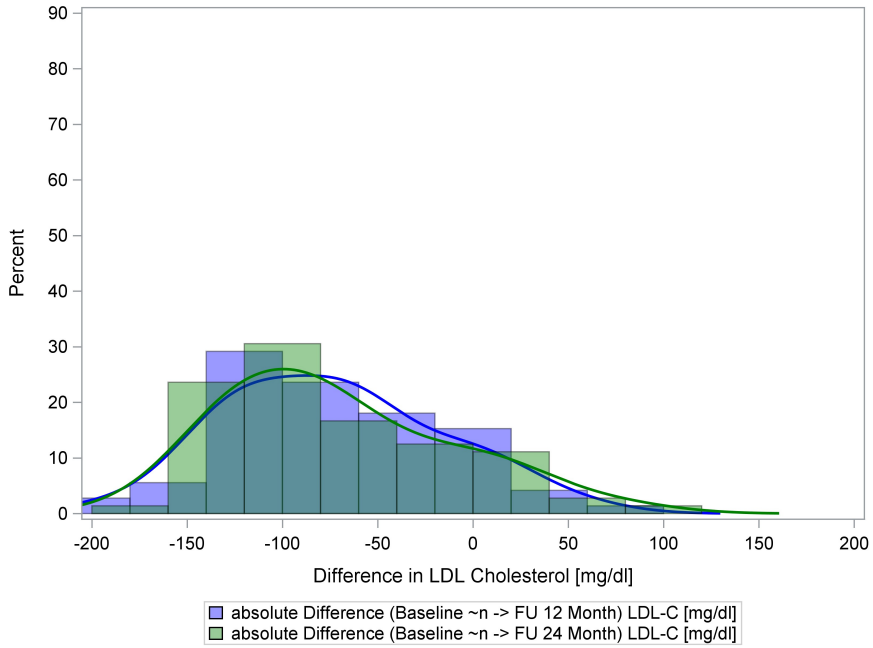

More details on LDL-C target achievement (LDL cholesterol; absolute and relative difference from baseline; incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (FAS; tables PZ1 – PZ18).

More details on LDL-cholesterol values (latest data available) at baseline and follow-up (incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (baseline: FAS; tables B13-5 – B13-10; 12-months follow-up: FAS; tables 1FU7-13 – 1FU13-16; 24-months follow-up: FAS, tables 2FU7-15 – 2FU7-18).

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Other analyses:

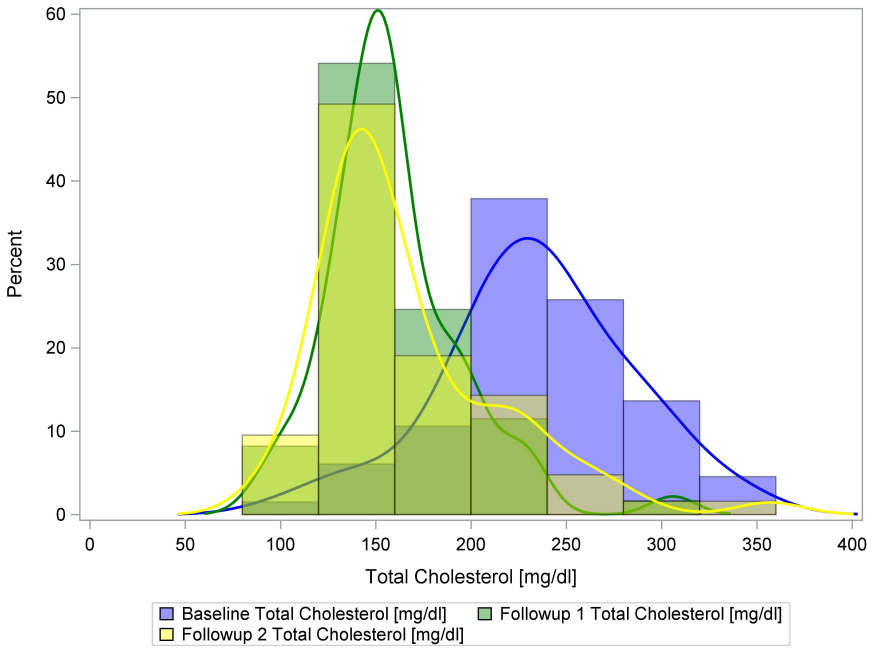
(1) Progression of other relevant lipid parameters

The Full Analysis Set (FAS) consisted of 72 patients with complete data (regarding LDL data) on both 12-months and 24-months follow-up.

Data were analysed according to changes in other relevant lipid values over time; absolute and relative change of total cholesterol, HDL cholesterol, and triglycerides at 12 and 24 months following baseline.

Total cholesterol

The following figure illustrates the distribution of total cholesterol values (mg/dl) at baseline, 12-months and 24-months follow-up (FAS):



The following table shows lipid target achievement (total cholesterol; absolute and relative difference from baseline) in registry patients with complete data (FAS):

	Mean	Standard deviation	Median	1st Quartile	3rd Quartile	N
Absolute difference (Baseline -> FU 12-15 Month) total cholesterol [mg/dl]	-76.2	55.8	-77	-122	-45	56
Relative difference (Baseline -> FU 12-15 Month) total cholesterol [%]	-29.2	22.6	-34	-44	-22	56
Absolute difference (Baseline -> FU 24-27 Month) total cholesterol [mg/dl]	-68.3	65.1	-81	-115	-29	59
Relative difference (Baseline -> FU 24-27 Month) total cholesterol [%]	-25.6	28.2	-35	-45	-13	59

More details on total cholesterol target achievement (total cholesterol; absolute and relative difference from baseline; incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (FAS; tables SZ2 – SZ5).

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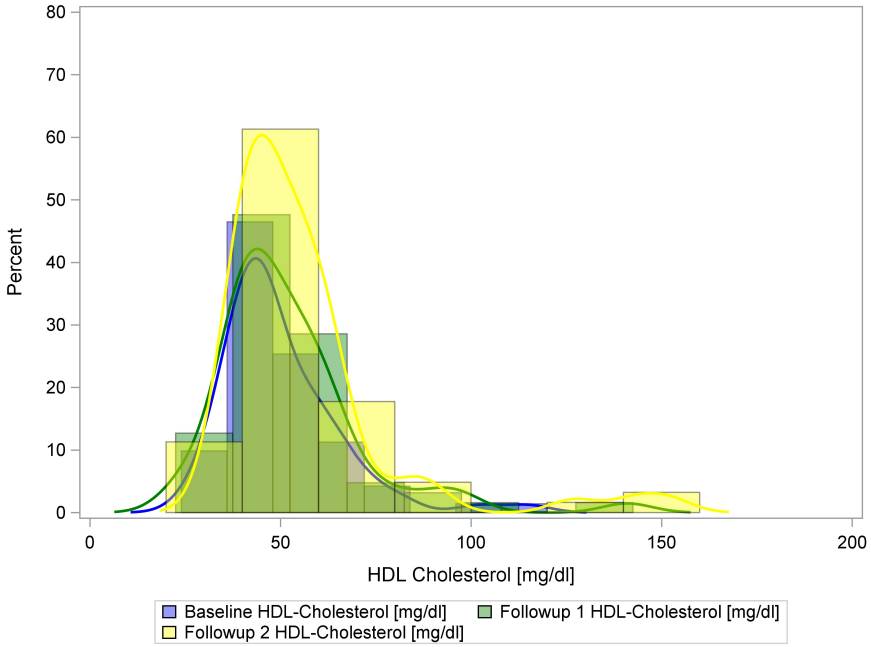
More details on total cholesterol values (latest data available) at baseline and follow-up (incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (baseline: FAS; tables B13-1 – B13-4; 12-months follow-up: FAS; tables 1FU7-1 – 1FU7-4; 24-months follow-up: FAS, tables 2FU7-3 – 2FU7-6).

HDL cholesterol

The following figure illustrates the distribution of HDL cholesterol values (mg/dl) at baseline, 12-months and 24-months follow-up (FAS):



The following table shows lipid target achievement (HDL cholesterol; absolute and relative difference from baseline) in registry patients with complete data (FAS):

	Mean	Standard deviation	Median	1st Quartile	3rd Quartile	N
Absolute difference (Baseline -> FU 12-15 Month) HDL-C [mg/dl]	3.3	17.2	2	-5	8	62
Relative difference (Baseline -> FU 12-15 Month) HDL-C [%]	8.4	35.2	5	-9	17	62
Absolute difference (Baseline -> FU 24-27 Month) HDL-C [mg/dl]	6.6	19.9	3	-2	12	61
Relative difference (Baseline -> FU 24-27 Month) HDL-C [%]	14.7	34.3	7	-4	23	61

More details on HDL cholesterol target achievement (HDL cholesterol; absolute and relative difference from baseline; incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (FAS; tables SZ6 – SZ9).

More details on HDL cholesterol values (latest data available) at baseline and follow-up (incl.

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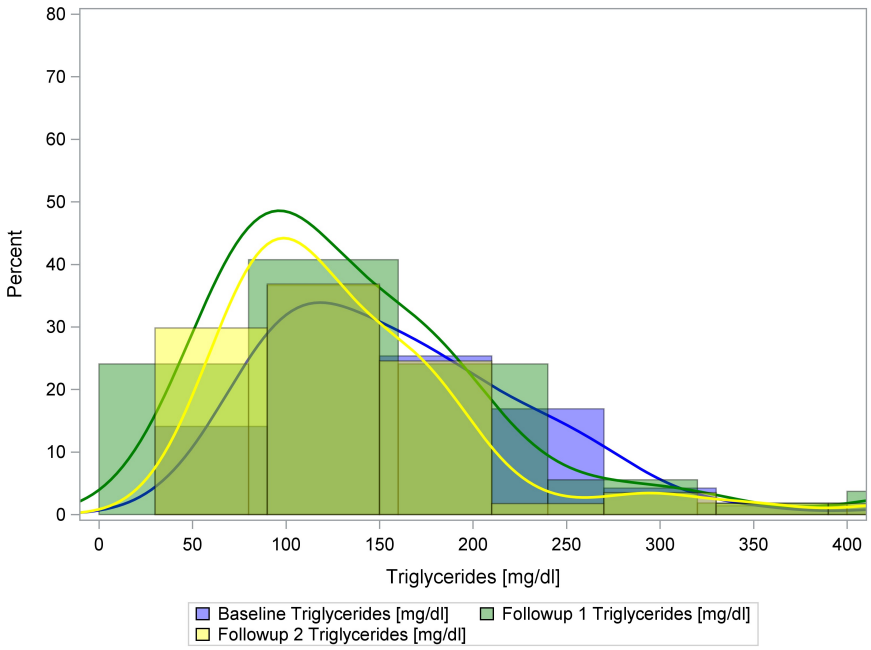
stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (baseline: FAS; tables B13-11 – B13-14; 12-months follow-up: FAS; tables 1FU7-9 – 1FU7-12; 24-months follow-up: FAS, tables 2FU7-11 – 2FU7-14).

Triglycerides

The following figure illustrates the distribution of triglycerides values (mg/dl) at baseline, 12-months and 24-months follow-up (FAS):



The following table shows lipid value changes (triglycerides; absolute and relative difference from baseline) in registry patients with complete data (FAS):

	Mean	Standard deviation	Median	1st Quartile	3rd Quartile	N
Absolute difference (Baseline -> FU 12-15 Month) Triglycerides [mg/dl]	-28.6	87.7	-37	-69	0	53
Relative difference (Baseline -> FU 12-15 Month) Triglycerides [%]	-11.3	45.4	-24	-42	0	53
Absolute difference (Baseline -> FU 24-27 Month) Triglycerides [mg/dl]	-32.3	80.5	-26	-81	8	57
Relative difference (Baseline -> FU 24-27 Month) Triglycerides [%]	-12.2	45.1	-23	-39	5	57

More details on triclycerides value changes (triglycerides; absolute and relative difference from baseline; incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (FAS; tables SZ10 – SZ13).

More details on triclycerides values (latest data available) at baseline and follow-up (incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (baseline: FAS; tables

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B13-19 – B13-22; 12-months follow-up: FAS; tables 1FU7-25 – 1FU7-28; 24-months follow-up: FAS, tables 2FU7-27 – 2FU7-30).

(2) Evaluation of lipid-lowering therapy in clinical routine
The Full Analysis Set (FAS) consisted of 72 patients with complete data on both 12-months and 24-months follow-up.

(2a) Pharmacotherapy
The following table shows the proportions of patients with lipid-lowering pharmacotherapy over time: baseline (at inclusion / at discharge) to 12-months follow-up to 24-months follow-up (FAS).

Pharmacotherapy (type)	Baseline (at inclusion; before index event)		Baseline (at discharge)		12-months Follow-up		24-months Follow-up	
	N	%	N	%	N	%	N	%
P2Y12 antagonist								
No	64	88.89%	18	25.00%	45	62.50%	62	86.11%
Yes	8	11.11%	54	75.00%	27	37.50%	10	13.89%
Other platelet aggregation inhibitor								
No	49	68.06%	8	11.11%	15	20.83%	19	26.39%
Yes	23	31.94%	64	88.89%	57	79.17%	53	73.61%
Vitamin-K antagonist								
No	72	100.00%	71	98.61%	72	100.00%	72	100.00%
Yes	0		1	1.39%	0		0	
Direct Oral Anticoagulant (DOA)								
No	68	94.44%	61	84.72%	64	88.89%	61	84.72%
Yes	4	5.56%	11	15.28%	8	11.11%	11	15.28%
Beta blocker								
No	52	72.22%	15	20.83%	22	30.56%	25	34.72%
Yes	20	27.78%	57	79.17%	50	69.44%	47	65.28%
Angiotensin II receptor blocker								
No	60	83.33%	54	75.00%	54	75.00%	50	69.44%
Yes	12	16.67%	18	25.00%	18	25.00%	22	30.56%
ACE inhibitor								
No	51	70.83%	29	40.28%	41	56.94%	49	68.06%
Yes	21	29.17%	43	59.72%	31	43.06%	23	31.94%
Diuretic								
No	54	75.00%	38	52.78%	44	61.11%	48	66.67%
Yes	18	25.00%	34	47.22%	28	38.89%	24	33.33%
If channel inhibitor								
No	71	98.61%	69	95.83%	68	94.44%	70	97.22%
Yes	1	1.39%	3	4.17%	4	5.56%	2	2.78%
Calcium channel blocker								
No	53	73.61%	56	77.78%	57	79.17%	56	77.78%
Yes	53	73.61%	16	22.22%	15	20.83%	16	22.22%
Oral Antidiabetic								
No	68	94.44%	66	91.67%	67	93.06%	67	93.06%
Yes	4	5.56%	6	8.33%	5	6.94%	5	6.94%
GLP-1 receptor agonist								
No	72	100.00%	72	100.00%	72	100.00%	72	100.00%
Insulin								

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No	69	95.83%	70	97.22%	68	94.44%	67	93.06%
Yes	3	4.17%	2	2.78%	4	5.56%	5	6.94%
Renin inhibitor								
No	72	100.00%	72	100.00%	72	100.00%	72	100.00%
Muscarinic receptor blocker								
No	72	100.00%	72	100.00%	71	98.61%	72	100.00%
Yes	0		0		1	1.39%	0	
Antianginous Drug								
No	70	97.22%	66	91.67%	69	95.83%	68	94.44%
Yes	2	2.78%	6	8.33%	3	4.17%	4	5.56%
Fibrates								
No	72	100.00%	72	100.00%	72	100.00%	72	100.00%
Cholesterol resorption inhibitor								
No	68	94.44%	64	88.89%	48	66.67%	45	62.50%
Yes	4	5.56%	8	11.11%	24	33.33%	27	37.50%
PCSK-9 inhibitor								
No	72	100.00%	71	98.61%	71	98.61%	70	97.22%
Yes	0		1	1.39%	1	1.39%	2	2.78%
Statin								
No	41	56.94%	3	4.17%	9	12.50%	13	18.06%
Yes	22	30.56%	69	95.83%	63	87.50%	59	81.94%
Other lipid-lowering therapy								
No	59	81.94%	66	91.67%	70	97.22%	71	98.61%
Yes	13	18.06%	6	8.33%	2	2.78%	1	1.39%
None								
No	48	66.67%	72	100.00%	72	100.00%	72	100.00%
Yes	24	33.33%	0		0		0	

The following figure illustrates the distribution of lipid lowering medication at inclusion, baseline, 12-months and 24-months follow-up (FAS):

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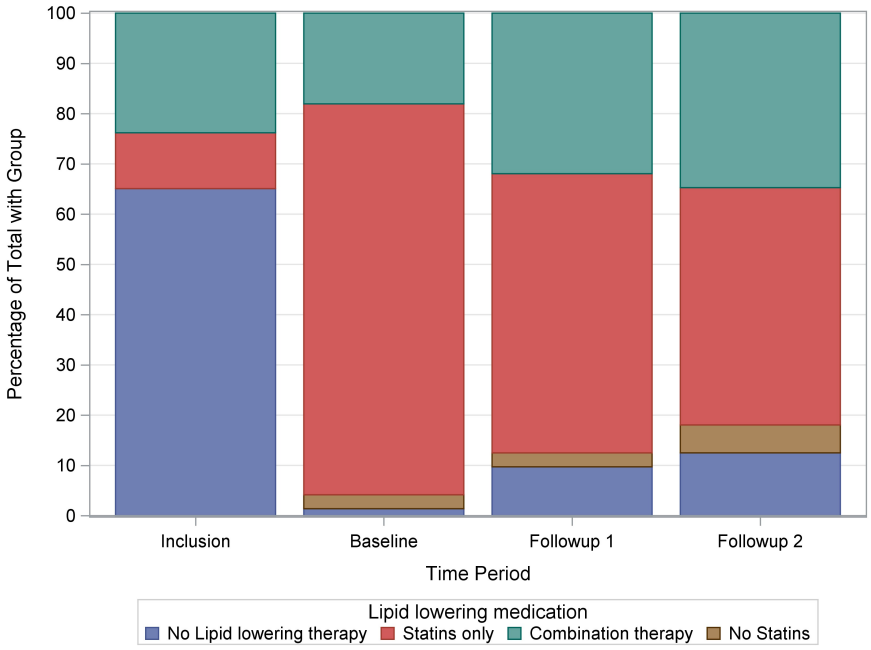

Combination therapy: statins and other lipid-lowering therapy (fibrates, cholesterol resorption inhibitors, PCSK-9 inhibitors)
No Statins: other lipid-lowering therapy (fibrates, cholesterol resorption inhibitors, PCSK-9 inhibitors)

More details on lipid-lowering pharmacotherapy (incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (FAS, tables B10-1 – B10-14 and tables B19-1 – B19-16; FAS, tables 1FU9-1 – 1FU9-14 and 2FU9-1 – 2FU9-14).

(2b) Non-drug lipid lowering therapy
The following table shows the proportions of patients with non-drug lipid-lowering pharmacotherapy (lifestyle and diet) over time: baseline (at inclusion) to 12-months follow-up to 24-months follow-up (FAS).

	Baseline		12-months Follow-up		24-months Follow-up	
	N	%	N	%	N	%
Physical exercise						
None	22	30.56%	11	15.28%	17	23.61%
1x per week	7	9.72%	19	26.39%	14	19.44%
2-3x per week	26	36.11%	18	25.00%	21	29.17%
>3x per week	17	23.61%	17	23.61%	10	13.89%
Unable	0		4	5.56%	5	6.94%
Fruit and vegetable consumption						
≥3x per week	66	91.67%	65	90.28%	58	80.56%
<3x per week	4	5.56%	4	5.56%	9	12.50%
None	2	2.78%	0		0	
Fish consumption						
≥2x per week	18	25.00%	22	30.56%	16	22.22%

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<2x per week	50	69.44%	43	59.72%	46	63.89%
None	4	5.56%	4	5.56%	5	6.94%
Alcohol consumption (amount of alcoholic beverages)						
≥2x per day	7	9.72%	2	2.78%	2	2.78%
<2x per day	32	44.44%	32	44.44%	37	51.39%
None	33	45.83%	35	48.61%	28	38.89%
Smoking status						
Non-smoker	29	40.28%	34	47.22%	26	36.11%
Current smoker	19	26.39%	6	8.33%	8	11.11%
Ex-smoker	24	33.33%	29	40.28%	33	45.83%

More details on non-drug lipid-lowering therapy (incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (FAS, tables B9-1 – B9-28; FAS, tables 1FU8-1 – 1FU8-18 and 2FU8-1 – 2FU8-18).

(3) Drug utilization pattern in secondary prevention
The Full Analysis Set (FAS) consisted of 72 patients with complete data on both 12-monts and 24-months follow-up.

The following table shows the proportions of patients with (any) pharmacotherapy over time (baseline visit [first digit], 12-months follow-up [second digit], 24-months follow-up [third digit]; 0= no medication; 1= medication intake; FAS).

Pharmacotherapy (type)	N	%
None		
0 0 0	72	100.00%
Beta blocker		
0 0 0	8	11.11%
0 0 1	2	2.78%
0 1 0	3	4.17%
0 1 1	2	2.78%
1 0 0	8	11.11%
1 0 1	4	5.56%
1 1 0	6	8.33%
1 1 1	39	54.17%
Other platelet aggregation inhibitor		
0 0 0	4	5.56%
0 1 0	1	1.39%
0 1 1	3	4.17%
1 0 0	6	8.33%
1 0 1	5	6.94%
1 1 0	8	11.11%
1 1 1	45	62.50%
Oral Antidiabetic		
0 0 0	66	91.67%
1 0 0	1	1.39%
1 1 1	5	6.94%
Insulin		
0 0 0	67	93.06%
0 0 1	1	1.39%

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0 1 1	2	2.78%
1 1 1	2	2.78%
Renin inhibitor		
0 0 0	72	100.00%
Muscarinic receptor blocker		
0 0 0	71	98.61%
0 1 0	1	1.39%
Angiotensin II receptor blocker		
0 0 0	64	88.89%
0 0 1	1	1.39%
0 1 1	1	1.39%
1 0 0	3	4.17%
1 0 1	1	1.39%
1 1 0	1	1.39%
1 1 1	1	1.39%
Fibrates		
0 0 0	72	100.00%
Cholesterol resorption inhibitor		
0 0 0	39	54.17%
0 0 1	4	5.56%
0 1 0	3	4.17%
0 1 1	18	25.00%
1 0 0	2	2.78%
1 0 1	3	4.17%
1 1 0	1	1.39%
1 1 1	2	2.78%
PCSK-9-Inhibitor		
0 0 0	69	95.83%
0 0 1	1	1.39%
0 1 0	1	1.39%
1 0 1	1	1.39%
Statins		
0 0 0	2	2.78%
0 1 1	1	1.39%
1 0 0	2	2.78%
1 0 1	5	6.94%
1 1 0	9	12.50%
1 1 1	53	73.61%
GLP-1 receptor agonist		
0 0 0	72	100.00%
P2Y12 antagonist		
0 0 0	11	15.28%
0 0 1	1	1.39%
0 1 0	4	5.56%
0 1 1	2	2.78%
1 0 0	30	41.67%
1 0 1	3	4.17%
1 1 0	17	23.61%
1 1 1	4	5.56%
Vitamin-K antagonist		
0 0 0	71	98.61%

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1 0 0	1	1.39%
Direct Oral Anticoagulant (DOA)		
0 0 0	55	76.39%
0 0 1	4	5.56%
0 1 1	2	2.78%
1 0 0	5	6.94%
1 1 0	1	1.39%
1 1 1	5	6.94%
Angiotensin II receptor blocker		
0 0 0	44	61.11%
0 0 1	5	6.94%
0 1 0	2	2.78%
0 1 1	3	4.17%
1 0 0	3	4.17%
1 0 1	2	2.78%
1 1 0	1	1.39%
1 1 1	12	16.67%
ACE inhibitor		
0 0 0	23	31.94%
0 0 1	1	1.39%
0 1 0	2	2.78%
0 1 1	3	4.17%
1 0 0	15	20.83%
1 0 1	2	2.78%
1 1 0	9	12.50%
1 1 1	17	23.61%
Diuretic		
0 0 0	33	45.83%
0 0 1	1	1.39%
0 1 0	1	1.39%
0 1 1	3	4.17%
1 0 0	7	9.72%
1 0 1	3	4.17%
1 1 0	7	9.72%
1 1 1	17	23.61%
If channel inhibitor		
0 0 0	68	94.44%
0 1 1	1	1.39%
1 1 0	2	2.78%
1 1 1	1	1.39%
Other lipid-lowering therapy		
0 0 0	64	88.89%
0 0 1	1	1.39%
0 1 0	1	1.39%
1 0 0	5	6.94%
1 1 0	1	1.39%
Calcium channel blocker		
0 0 0	49	68.06%
0 0 1	1	1.39%
0 1 0	2	2.78%
0 1 1	4	5.56%

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1 0 0	4	5.56%
1 0 1	3	4.17%
1 1 0	1	1.39%
1 1 1	8	11.11%

(4) Cardiovascular and cerebrovascular events within the follow-up period of two years
With regard to the Baseline Analysis Set (taking into account all patients regardless of completeness of follow-up data; n= 347 patients) the following non-fatal events since baseline were documented:

Intrahospital complications; n (%)	
STEMI	5 (1.44)
NSTEMI	1 (0.29)
Stroke	2 (0.58)
TIA	0

More details on intrahospital complications (incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (BAS, B16-1 – B16-8).

Non-fatal events since baseline were documented in 169 patients (48.70%) at 12-months follow-up since baseline and in 197 patients (56.77%) at 24-months follow-up since baseline.

Event type, n (%)	**12-months follow-up (since baseline) n= 347**	**24-months follow-up (since baseline) n=347**
Myocardial infarction	3 (0.9) 95% CI: -0.00, 0.02	6 (1.7) 95% CI: 0.00, 0.03
Cardiac Catheter Examination without PCI	24 (6.9) 95% CI: 0.04, 0.10	32 (9.2) 95% CI: 0.06, 0.12
Balloon dilatation (PCI)	36 (10.4) 95% CI: 0.07, 0.14	46 (13.3) 95% CI: 0.10, 0.17
Bypass surgery	4 (1.2) 95% CI: 0.00, 0.02	5 (1.4) 95% CI: 0.00, 0.03
Stroke	1 (0.3) 95% CI: -0.00, 0.01	2 (0.6) 95% CI: -0.00, 0.01
TIA	0	1 (0.3) 95% CI: -0.00, 0.01
Hospitalisation due to event	63 (18.2)	80 (23.1)
Hospitalisation due to event; *mean duration*	4.1 days (SD: 3.3)	5.5 days (SD: 5.7)
Rehabilitation	102 (29.4) 95% CI: 0.25, 0.34	113 (32.6) 95% CI: 0.28, 0.38
Other inpatient stay	55 (15.9) 95% CI: 0.12, 0.20	88 (25.4) 95% CI: 0.21, 0.30
Other inpatient stay, *mean duration*	9.3 days (SD: 9.2)	13.3 days (SD: 18.5)

More details on non-fatal events since baseline (incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (BAS, 12-months follow-up: tables 1FU2-1 – 1FU2-14; 24-months follow-up: tables 2FU2-1 – 2FU2-14).

With regard to the Full Analysis Set (taking into account all patients with complete data on LDL cholesterol and correct timing for both follow-ups; n= 72) the following non-fatal events were documented:

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Intrahospital complications: no events documented in this population.

Non-fatal events since baseline were documented in 50 patients (69.44%) at 12-months follow-up since baseline and in 57 patients (79.17) at 24-months follow-up since baseline.

Event type, n (%)	12-months follow-up (since baseline) n=72	24-months follow-up (since baseline) n=72
Myocardial infarction	1 (1.4) 95% CI: -0.01, 0.04	2 (2.8) 95% CI: -0.01, 0.07
Cardiac Catheter Examination without PCI	3 (4.2) 95%CI: -0.01, 0.09	7 (9.7) 95% CI: 0.03, 0.17
Balloon dilatation (PCI)	15 (20.8) 95% CI: 0.11, 0.30	18 (25.0) 95% CI: 0.15, 0.35
Bypass surgery	0	1 (1.4) 95% CI: -0.01, 0.04
Stroke	0	0
TIA	0	0
Hospitalisation due to event	18 (25.0)	24 (33.3)
Hospitalisation due to event; *mean duration*	4.1 days (SD: 2.8)	6.9 days (SD: 8.1)
Rehabilitation	35 (48.6) 95% CI: 0.37, 0.60	39 (54.2) 95% CI: 0.42, 0.66
Other inpatient stay	13 (18.1) 95% CI: 0.09, 0.27	23 (31.9) 95% CI: 0.21, 0.43
Other inpatient stay, mean duration	7.9 days (SD: 5.2)	13.7 days (SD: 22.7)

More details on non-fatal events since baseline (incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (FAS, 12-months follow-up: tables 1FU2-1 – 1FU2-14; 24-months follow-up: tables 2FU2-1 – 2FU2-14).

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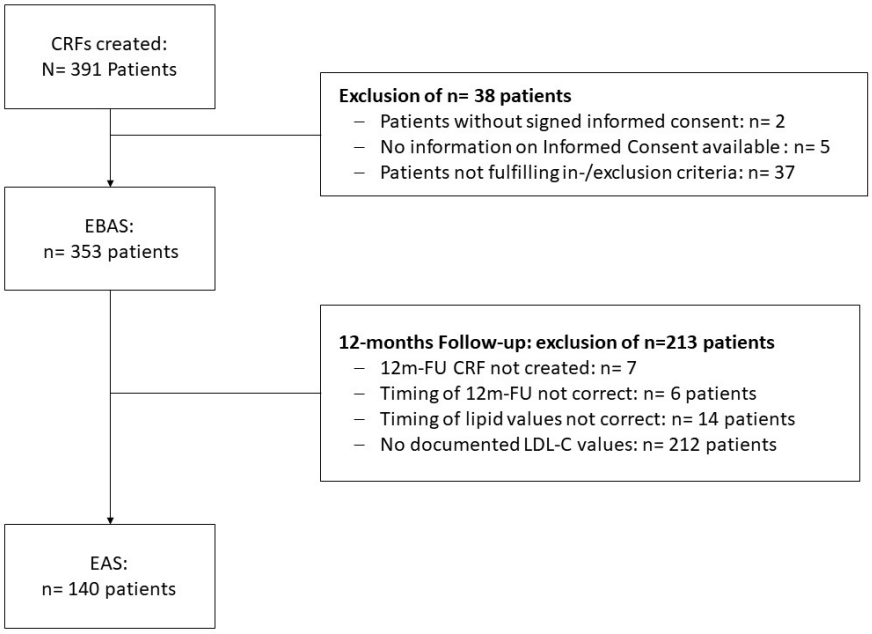
RESULTS – Part II	**The following result are based on the analysis sets EBAS and EAS (as defined in section Methodology).**
Participants (actual):	**(a) Overall participation status:** The registry was conducted in Germany. 24 sites participated in the registry. 353 patients were included in the baseline analyses. 140 patients were included in the extended analysis set (EAS) to evaluate the longitudinal data. **(b) Participation per period of the registry:** The following flow chart illustrates the number of patients at each stage of the registry, including the number of patients lost to follow-up and the amount of missing data for the variables of interest (i.e. lipid profiles):  Of 347 patients in baseline, complete follow-up data (for both 12- and 24-months follow-up concurrently) were available in 72 patients. Overall, 213 patients were excluded from the longitudinal analyses.
Participant characteristics and primary analyses:	**(a) Descriptive data** <u>Characteristics of registry physicians</u>**:** Type of sites were as follows (see EBAS tables CTR-1 to -5 in Appendix II): - Hospital, n= 19; - No information provided, n= 6 <u>Characteristics of registry patients</u>**:** The Extended Baseline Analysis Set (EBAS) consisted of 353 documented patients. Duration of enrolment was on average 231.9 days (SD: 149.6 days). On average, 14.1 patients (SD: 16.2; MD: 10) were enrolled per study site. The following table shows the demographic and clinical characteristics of the registry patients at

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baseline (EBAS):

Characteristics	N= 353
Sex – *no. of participants (%)*	
Male	259 (73.4)
Female	94 (26.6)
Mean age *(SD) - yr*	57.3 (11.4)
Cardiovascular History – *no. of participants (%)*	
Coronary heart disease,	116 (32.9)
PCI	90 (25.5)
Acute coronary syndrome	81 (22.9)
Aortocoronary bypass	20 (5.7)
Stroke	8 (2.3)
TIA	6 (1.7)
Comorbidities and Risk Factors – *no. of participants (%)*	
Arterial hypertension	242 (68.6)
Diabetes mellitus	61 (17.3)
Heart failure	59 (17.0)
Stable angina pectoris	56 (15.9)
Heart valve disease	27 (7.7)
Depression	28 (7.9)
Renal insufficiency	27 (7.7)
Atrial fibrillation	21 (5.9)
Peripheral arterial occlusive disease	17 (4.8)
Carcinoma	17 (4.8)
COPD	13 (3.7)
Device implantation	7 (2.0)
Deep vein thrombosis	6 (1.7)
Pulmonary embolism	1 (0.3)
Phenotypic Findings – *no. of participants (%)*	
Xanthomas	9 (2.6)
Xanthelasma	6 (1.7)
Arcus cornealis	7 (2.0)
Family History – *no. of participants (%)*	
Family history of MI	185 (52.4)
Family history of CHD	115 (32.6)
Family history of cerebral/vascular disease	68 (19.3)
Family history of elevated cholesterol levels	41 (11.6)
Family history of arcus cornealis	3 (0.9)
Family history of tendon xanthomas	0
Lipid Apheresis Therapy – *no. of participants (%)*	0
Body-mass Index, *mean (SD)*	28.6 (5.0)

More details on patient characteristics at baseline (incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (EBAS; tables E1, E2, B1 – B18).

Follow-up duration (i.e. time from baseline to follow-up in days):
With regard to the Extended Baseline Analysis Set (taking into account all patients regardless of completeness of follow-up data; n= 353 patients) time to follow-up was on average 384.0 days (SD: 28.1) for the 12-months follow-up and 758.5 days (SD: 34.4) for the 24-months follow-up.

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A complete descriptive report of follow-up data for this population is given in Appendix II (12-months follow-up: tables 1FU1 – 1FU9, EBAS; 24-months follow-up: tables 2FU1 – 2FU9, EBAS).

(b) Primary analyses: Lipid Target Achievement
The Extended Analysis Set (EAS) consisted of 140 patients with complete (LDL) data at 12-months follow-up.

Follow-up duration (i.e. time from baseline to follow-up in days):
With regard to the Extended Analysis Set (taking into account all patients with complete data on LDL cholesterol and correct timing for the 12-months follow-up; n= 140) time to follow-up was on average 382.1 days (SD: 20.1) for the 12-months follow-up and 749.6 days (SD: 34.3) for the 24-months follow-up.

A complete descriptive report of follow-up data for this population is given in Appendix II (12-months follow-up: tables 1FU1 – 1FU9, EAS; 24-months follow-up: tables 2FU1 – 2FU9, EAS).

Distribution of LDL cholesterol values (mg(dl)**:**
The following table shows mean LDL cholesterol values at baseline, 12-months follow-up and 24-months follow-up (EAS):

	Mean	Standard deviation	Median	1st Quartile	3rd Quartile	N
LDL-Cholesterol [mg/dl] at admission	170.7	46.6	169	144	199	140
LDL-Cholesterol at 12MFU	92.0	31.5	87	70	106	140
LDL-Cholesterol at 24MFU	93.0	38.6	83	70	106	140

More details on LDL cholesterol values (incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (EAS; tables CHOL-7 – CHOL-9).

The following figure illustrates the distribution of LDL cholesterol values (mg/dl) at baseline, 12-months and 24-months follow-up (EAS):

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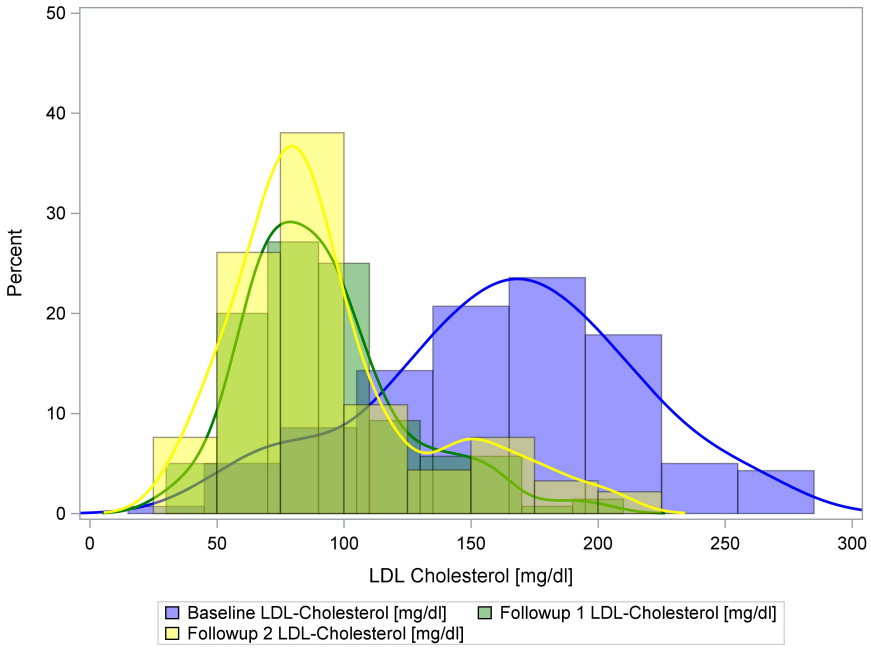

Target achievement of LDL cholesterol values (mg/dl):
Data were analysed according to lipid target achievement as measured by the reduction of LDL cholesterol over time (baseline to 12-M FU to 24-M-FU); absolute and relative reduction of LDL cholesterol at 12 and 24 months following baseline (EAS).

Target ranges were set as follows (see also SAP, section 7.2; Appendix III, section 3.2):

- Within target range: < 70mg/dl
- Above target range: ≥ 70 mg/dl

Within target range (LDL <70 mg/dl) were

- At baseline: n= 8 patients (5.7%)
- At 12-months follow-up: n= 35 patients (25.0%)
- At 24-months follow-up: n= 23 patients (16.4%; n= 48 (34.3%) missing values)

Above target range (LDL ≥ 70 mg/dl) were

- At baseline: n= 132 patients (94.3%)
- At 12-months follow-up: n= 105 patients (75.0%)
- At 24-months follow-up: n= 69 patients (49.3%; n= 48 (34.3%) missing values)

According to guidelines applicable at the time of data collection (see References [1]), target achievement was defined as LDL< 70mg/dl or 50% of reduction in LDL (see also SAP, section 6.1.1; Appendix III, section 3.2).

Within this target range (LDL< 70mg/dl or 50% of reduction in LDL) were:

- At 12-months follow-up: n= 70 patients (50.0%, [70/140]; 95% CI: 0.42, 0.58)
- At 24-months follow-up: n= 46 patients (50.0% [46/92]; 95% CI: 0.40, 0.60)

Above this target range (LDL< 70mg/dl or 50% of reduction in LDL) were:

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- At 12-months follow-up: n= 70 patients (50.0%)
- At 24-months follow-up: n= 46 patients (50.0%; n= 48 missing values)

More details on LDL-C target achievement (target ranges of LDL cholesterol at baseline and follow-up; incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (EAS; tables PZ-1 to PZ-18).

The following table shows lipid target achievement (LDL cholesterol; absolute and relative difference from baseline) in registry patients with complete data (EAS):

	Mean	Standard deviation	Median	1st Quartile	3rd Quartile	N
Absolute difference (Baseline -> FU 12-15 Month) LDL-C [mg/dl]	-70.5	53.1	-74	-112	-30	140
Relative difference (Baseline -> FU 12-15 Month) LDL-C [%]	-37.5	28.8	-44	-57	-23	140
Absolute difference (Baseline -> FU 24-27 Month) LDL-C [mg/dl]	-71.5	58.8	-84	-122	-34	92
Relative difference (Baseline -> FU 24-27 Month) LDL-C [%]	-36.5	36.1	-47	-61	-24	92

The 95% confidence interval for the mean relative difference from baseline to 12-months follow-up was -42.3, -32.7 (p< 0.00001).
The 95% confidence interval for the mean relative difference from baseline to 24-months follow-up was -44.0, -29.0 (p< 0.00001).

The following figure illustrates the distribution of LDL cholesterol values (mg/dl; absolute and relative difference from baseline) 12-months and 24-months follow-up; in registry patients with complete data (EAS):

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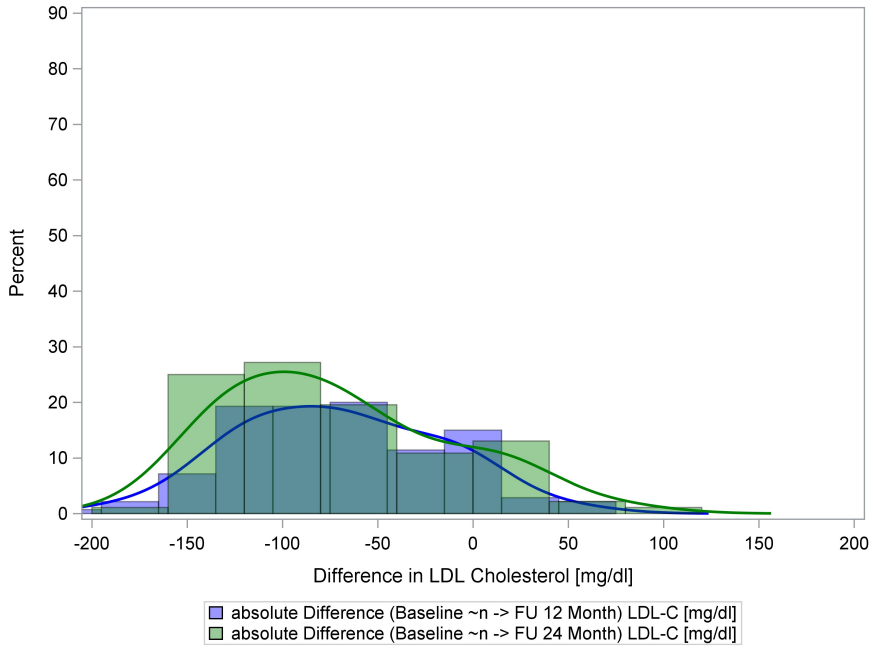

More details on LDL-C target achievement (LDL cholesterol; absolute and relative difference from baseline; incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (EAS; tables PZ1 – PZ18).

More details on LDL-cholesterol values (latest data available) at baseline and follow-up (incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (baseline: EAS; tables B13-5 – B13-10; 12-months follow-up: EAS; tables 1FU7-13 – 1FU13-16; 24-months follow-up: EAS, tables 2FU7-15 – 2FU7-18).

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Other analyses:

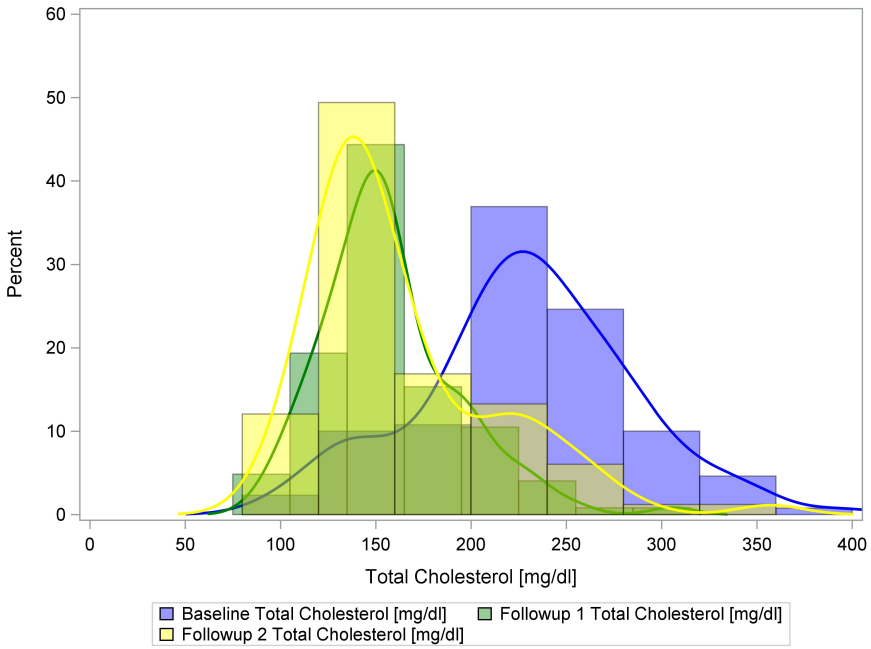
(1) Progression of other relevant lipid parameters

The Extended Analysis Set (EAS) consisted of 140 patients with complete data (regarding LDL data) at 12-months follow-up.

Data were analysed according to changes in other relevant lipid values over time; absolute and relative change of total cholesterol, HDL cholesterol, and triglycerides at 12 and 24 months following baseline.

Total cholesterol

The following figure illustrates the distribution of total cholesterol values (mg/dl) at baseline, 12-months and 24-months follow-up (EAS):



The following table shows lipid target achievement (total cholesterol; absolute and relative difference from baseline) in registry patients with complete data (EAS):

	Mean	Standard deviation	Median	1st Quartile	3rd Quartile	N
Absolute difference (Baseline -> FU 12-15 Month) total cholesterol [mg/dl]	-71.0	56.3	-74	-110	-33	115
Relative difference (Baseline -> FU 12-15 Month) total cholesterol [%]	-27.5	21.4	-33	-42	-18	115
Absolute difference (Baseline -> FU 24-27 Month) total cholesterol [mg/dl]	-71.1	68.1	-76	-16	-29	78
Relative difference (Baseline -> FU 24-27 Month) total cholesterol [%]	-26.3	27.6	-35	-45	-17	78

More details on total cholesterol target achievement (total cholesterol; absolute and relative difference from baseline; incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (EAS; tables SZ2 – SZ5).

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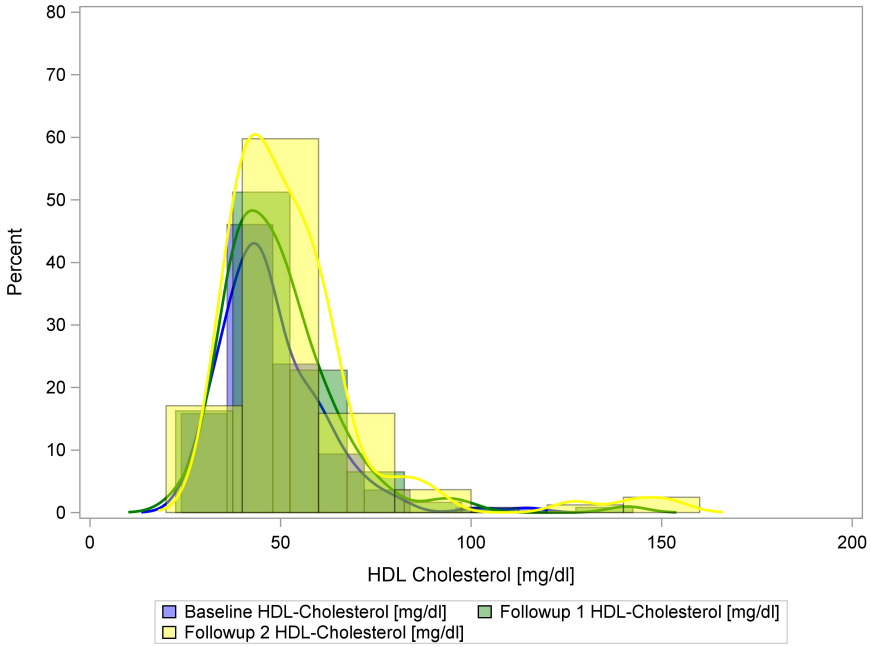
More details on total cholesterol values (latest data available) at baseline and follow-up (incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (baseline: EAS; tables B13-1 – B13-4; 12-months follow-up: EAS; tables 1FU7-1 – 1FU7-4; 24-months follow-up: EAS, tables 2FU7-3 – 2FU7-6).

HDL cholesterol

The following figure illustrates the distribution of HDL cholesterol values (mg/dl) at baseline, 12-months and 24-months follow-up (EAS):



The following table shows lipid target achievement (HDL cholesterol; absolute and relative difference from baseline) in registry patients with complete data (EAS):

	Mean	Standard deviation	Median	1st Quartile	3rd Quartile	N
Absolute difference (Baseline -> FU 12-15 Month) HDL-C [mg/dl]	2.9	14.0	2	-4	8	122
Relative difference (Baseline -> FU 12-15 Month) HDL-C [%]	8.4	29.6	5	-7	19	122
Absolute difference (Baseline -> FU 24-27 Month) HDL-C [mg/dl]	5.2	18.1	3	-2	9	81
Relative difference (Baseline -> FU 24-27 Month) HDL-C [%]	12.1	31.7	7	-4	22	81

More details on HDL cholesterol target achievement (HDL cholesterol; absolute and relative difference from baseline; incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (EAS; tables SZ6 – SZ9).

More details on HDL cholesterol values (latest data available) at baseline and follow-up (incl.

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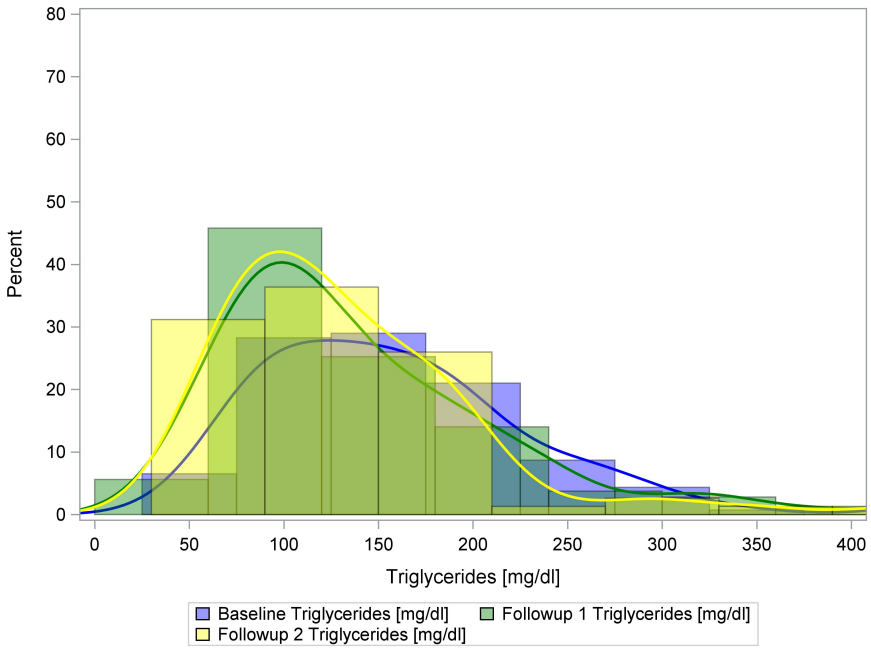
stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (baseline: EAS; tables B13-11 – B13-14; 12-months follow-up: EAS; tables 1FU7-9 – 1FU7-12; 24-months follow-up: EAS, tables 2FU7-11 – 2FU7-14).

Triglycerides

The following figure illustrates the distribution of triglycerides values (mg/dl) at baseline, 12-months and 24-months follow-up (EAS):



The following table shows lipid value changes (triglycerides; absolute and relative difference from baseline) in registry patients with complete data (EAS):

	Mean	Standard deviation	Median	1st Quartile	3rd Quartile	N
Absolute difference (Baseline -> FU 12-15 Month) Triglycerides [mg/dl]	-23.1	86.7	-29	-65	12	105
Relative difference (Baseline -> FU 12-15 Month) Triglycerides [%]	-4.4	57.9	-22	-39	12	105
Absolute difference (Baseline -> FU 24-27 Month) Triglycerides [mg/dl]	-37.1	78.3	-29	-83	0	77
Relative difference (Baseline -> FU 24-27 Month) Triglycerides [%]	-13.9	45.2	-25	-46	0	77

More details on triclycerides value changes (triglycerides; absolute and relative difference from baseline; incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (EAS; tables SZ10 – SZ13).

More details on triclycerides values (latest data available) at baseline and follow-up (incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (baseline: EAS; tables

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B13-19 – B13-22; 12-months follow-up: EAS; tables 1FU7-25 – 1FU7-28; 24-months follow-up: EAS, tables 2FU7-27 – 2FU7-30).

(2) Evaluation of lipid-lowering therapy in clinical routine
The Extended Analysis Set (EAS) consisted of 140 patients with complete data at 12-months follow-up.

(2a) Pharmacotherapy
The following table shows the proportions of patients with lipid-lowering pharmacotherapy over time: baseline (at inclusion / at discharge) to 12-months follow-up to 24-months follow-up (EAS).

Pharmacotherapy (type)	Baseline (at inclusion; before index event)		Baseline (at discharge)		12-months Follow-up		24-months Follow-up	
	N	%	N	%	N	%	N	%
P2Y12 antagonist								
No	127	90.71%	32	22.86%	90	64.29%	125	89.93%
Yes	13	9.29%	108	77.14%	50	35.71%	14	10.07%
Other platelet aggregation inhibitor								
No	103	73.57%	21	15.00%	31	22.14%	43	30.94%
Yes	37	26.43%	119	85.00%	109	77.86%	96	69.06%
Vitamin-K antagonist								
No	139	99.29%	137	97.86%	139	99.29%	138	99.28%
Yes	1	0.71%	3	2.14%	1	0.71%	1	0.72%
Direct Oral Anticoagulant (DOA)								
No	134	95.71%	120	85.71%	128	91.43%	123	88.49%
Yes	6	4.29%	20	14.29%	12	8.57%	16	11.51%
Beta blocker								
No	107	76.43%	43	30.71%	50	35.71%	63	45.32%
Yes	33	23.57%	97	69.29%	90	64.29%	76	54.68%
Angiotensin II receptor blocker								
No	117	83.57%	104	74.29%	98	70.00%	101	72.66%
Yes	23	16.43%	36	25.71%	42	30.00%	38	27.34%
ACE inhibitor								
No	99	70.71%	52	37.14%	81	57.86%	95	68.35%
Yes	41	29.29%	88	62.86%	59	42.14%	44	31.65%
Diuretic								
No	115	82.14%	96	68.57%	100	71.43%	104	74.82%
Yes	25	17.86%	44	31.43%	40	28.57%	35	25.18%
If channel inhibitor								
No	137	97.86%	134	95.71%	135	96.43%	136	97.84%
Yes	3	2.14%	6	4.29%	5	3.57%	3	2.16%
Calcium channel blocker								
No	109	77.86%	106	75.71%	109	77.86%	111	79.86%
Yes	31	22.14%	34	24.29%	31	22.14%	28	20.14%
Oral Antidiabetic								
No	132	94.29%	129	92.14%	132	94.29%	131	94.24%
Yes	8	5.71%	11	7.86%	8	5.71%	8	5.76%
GLP-1 receptor agonist								
No	139	99.29%	140	100.00%	140	100.00%	138	99.28%
Yes	1	0.71%	0		0		1	0.72%
Insulin								

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No	137	97.86%	136	97.14%	136	97.14%	134	96.40%
Yes	3	2.14%	4	2.86%	4	2.86%	5	3.60%
Renin inhibitor								
No	140	100.00%	140	100.00%	140	100.00%	139	100.00%
Muscarinic receptor blocker								
No	140	100.00%	140	100.00%	139	99.29%	138	99.28%
Yes	0		0		1	0.71%	1	0.72%
Antianginous Drug								
No	135	96.43%	129	92.14%	133	95.00%	131	94.24%
Yes	5	3.57%	11	7.86%	7	5.00%	8	5.76%
Fibrates								
No	139	99.29%	140	100.00%	140	100.00%	139	100.00%
No	1	0.71%	0		0		0	
Cholesterol resorption inhibitor								
No	128	91.43%	118	84.29%	94	67.14%	92	66.19%
Yes	12	8.57%	22	15.71%	46	32.86%	47	33.81%
PCSK-9 inhibitor								
No	140	100.00%	139	99.29%	139	99.29%	137	98.56%
Yes	0		1	0.71%	1	0.71%	2	1.44%
Statin								
No	73	52.14%	4	2.86%	21	15.00%	36	25.90%
Yes	42	30.00%	136	97.14%	119	85.00%	103	74.10%
Other lipid-lowering therapy								
No	116	82.86%	127	90.71%	137	97.86%	138	99.28%
Yes	24	17.14%	13	9.29%	3	2.14%	1	0.72%
None								
No	92	65.71%	140	100.00%	140	100.00%	139	100.00%
Yes	48	34.29%	0		0		0	

The following figure illustrates the distribution of lipid lowering medication at inclusion, baseline, 12-months and 24-months follow-up (EAS):

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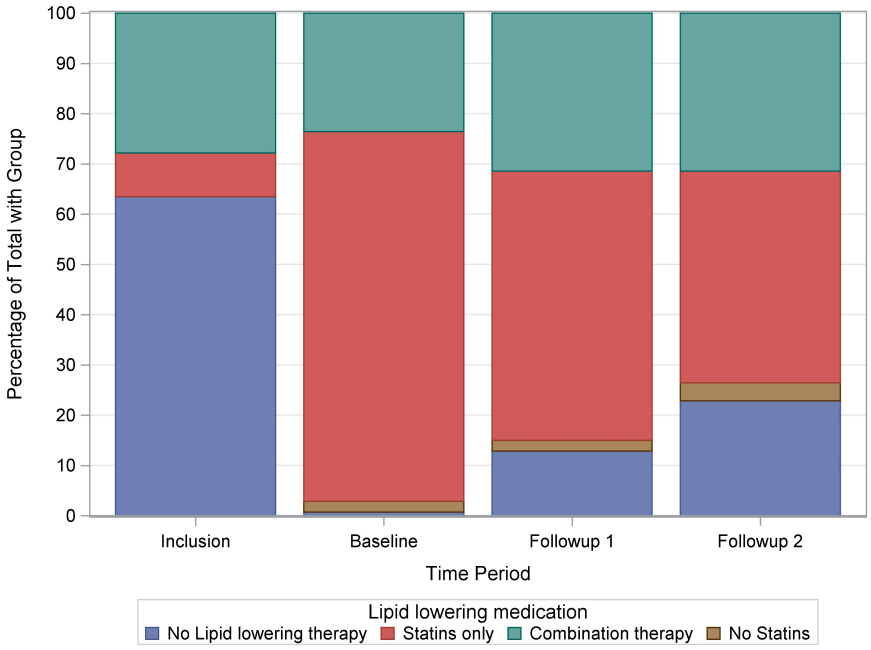

Combination therapy: statins and other lipid-lowering therapy (fibrates, cholesterol resorption inhibitors, PCSK-9 inhibitors)
No Statins: other lipid-lowering therapy (fibrates, cholesterol resorption inhibitors, PCSK-9 inhibitors)

More details on lipid-lowering pharmacotherapy (incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (EAS, tables B10-1 – B10-14 and tables B19-1 – B19-16; EAS, tables 1FU9-1 – 1FU9-14 and 2FU9-1 – 2FU9-14).

(2b) Non-drug lipid lowering therapy
The following table shows the proportions of patients with non-drug lipid-lowering pharmacotherapy (lifestyle and diet) over time: baseline (at inclusion) to 12-months follow-up to 24-months follow-up (EAS).

	Baseline		12-months Follow-up		24-months Follow-up	
	N	%	N	%	N	%
Physical exercise						
None	56	40.0	31	22.1	33	23.7
1x per week	25	17.9	26	18.5	18	12.9
2-3x per week	34	24.3	35	25.0	36	25.9
>3x per week	25	17.9	29	20.7	21	15.1
Unable	0		8	5.7	8	5.8
Fruit and vegetable consumption						
≥3x per week	115	82.1	117	83.6	100	71.9
<3x per week	17	12.1	11	7.9	16	11.5
None	8	5.7	1	0.7	0	
Fish consumption						
≥2x per week	31	22.1	46	32.9	26	18.7

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<2x per week	98	70.0	74	52.9	79	56.8
None	11	7.9	9	6.4	11	7.9
Alcohol consumption (amount of alcoholic beverages)						
≥2x per day	13	9.3	3	2.7	3	2.2
<2x per day	74	52.9	64	45.7	62	44.6
None	53	37.9	62	44.3	51	36.7
Smoking status						
Non-smoker	48	34.3	63	45.0	43	30.9
Current smoker	48	34.3	17	12.1	15	10.8
Ex-smoker	44	31.4	49	35.0	58	41.7

More details on non-drug lipid-lowering therapy (incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (EAS, tables B9-1 – B9-28; EAS, tables 1FU8-1 – 1FU8-18 and 2FU8-1 – 2FU8-18).

(3) Drug utilization pattern in secondary prevention
The Extended Analysis Set (EAS) consisted of 140 patients with complete data at 12-monts follow-up.

The following table shows the proportions of patients with (any) pharmacotherapy over time (baseline visit [first digit], 12-months follow-up [second digit], 24-months follow-up [third digit]; 0= no medication; 1= medication intake; EAS).

Pharmacotherapy (type)	N	%
None		
0 0 0	140	100.00%
Beta blocker		
0 0 0	23	16.43%
0 0 1	4	2.86%
0 1 0	10	7.14%
0 1 1	6	4.29%
1 0 0	18	12.86%
1 0 1	5	3.57%
1 1 0	13	9.29%
1 1 1	61	43.57%
Other platelet aggregation inhibitor		
0 0 0	8	5.71%
0 0 1	2	1.43%
0 1 0	2	1.43%
0 1 1	9	6.43%
1 0 0	12	8.57%
1 0 1	9	6.43%
1 1 0	22	15.71%
1 1 1	76	54.29%
Oral Antidiabetic		
0 0 0	129	92.14%
1 0 0	2	1.43%
1 0 1	1	0.71%
1 1 0	1	0.71%
1 1 1	7	5.00%
Insulin		

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0 0 0	133	95.00%
0 0 1	1	0.71%
0 1 1	2	1.43%
1 0 0	2	1.43%
1 1 1	2	1.43%
Renin inhibitor		
0 0 0	140	100.00%
Muscarinic receptor blocker		
0 0 0	138	98.57%
0 0 1	1	0.71%
0 1 0	1	0.71%
Angiotensin II receptor blocker		
0 0 0	126	90.00%
0 0 1	1	0.71%
0 1 1	2	1.43%
1 0 0	4	2.86%
1 0 1	2	1.43%
1 1 0	2	1.43%
1 1 1	3	2.14%
Fibrates		
0 0 0	140	100.00%
Cholesterol resorption inhibitor		
0 0 0	76	54.29%
0 0 1	8	5.71%
0 1 0	7	5.00%
0 1 1	27	19.29%
1 0 0	7	5.00%
1 0 1	3	2.14%
1 1 0	3	2.14%
1 1 1	9	6.43%
PCSK-9-Inhibitor		
0 0 0	137	97.86%
0 0 1	1	0.71%
0 1 0	1	0.71%
1 0 1	1	0.71%
Statins		
0 0 0	2	1.43%
0 1 0	1	0.71%
0 1 1	1	0.71%
1 0 0	10	7.14%
1 0 1	9	6.43%
1 1 0	24	17.14%
1 1 1	93	66.43%
GLP-1 receptor agonist		
0 0 0	139	99.29%
0 0 1	1	0.71%
P2Y12 antagonist		
0 0 0	20	14.29%
0 0 1	1	0.71%
0 1 0	9	6.43%
0 1 1	2	1.43%

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1 0 0	65	46.43%
1 0 1	4	2.86%
1 1 0	32	22.86%
1 1 1	7	5.00%
Vitamin-K antagonist		
0 0 0	137	97.86%
1 0 0	1	0.71%
1 0 1	1	0.71%
1 1 0	1	0.71%
Direct Oral Anticoagulant (DOA)		
0 0 0	113	80.71%
0 0 1	5	3.57%
0 1 1	2	1.43%
1 0 0	10	7.14%
1 1 0	1	0.71%
1 1 1	9	6.43%
Angiotensin II receptor blocker		
0 0 0	85	60.71%
0 0 1	5	3.57%
0 1 0	6	4.29%
0 1 1	8	5.71%
1 0 0	6	4.29%
1 0 1	2	1.43%
1 1 0	5	3.57%
1 1 1	23	16.43%
ACE inhibitor		
0 0 0	44	31.43%
0 0 1	2	1.43%
0 1 0	3	2.14%
0 1 1	3	2.14%
1 0 0	31	22.14%
1 0 1	4	2.86%
1 1 0	18	12.86%
1 1 1	35	25.00%
Diuretic		
0 0 0	83	59.29%
0 0 1	3	2.14%
0 1 0	3	2.14%
0 1 1	7	5.00%
1 0 0	10	7.14%
1 0 1	4	2.86%
1 1 0	9	6.43%
1 1 1	21	15.00%
If channel inhibitor		
0 0 0	133	95.00%
0 1 1	1	0.71%
1 0 0	2	1.43%
1 1 0	2	1.43%
1 1 1	2	1.43%
Other lipid-lowering therapy		
0 0 0	124	88.57%

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0 0 1	1	0.71%
0 1 0	2	1.43%
1 0 0	12	8.57%
1 1 0	1	0.71%
Calcium channel blocker		
0 0 0	96	68.57%
0 0 1	1	0.71%
0 1 0	2	1.43%
0 1 1	7	5.00%
1 0 0	8	5.71%
1 0 1	4	2.86%
1 1 0	6	4.29%
1 1 1	16	11.43%

(4) Cardiovascular and cerebrovascular events within the follow-up period of two years
With regard to the Extended Baseline Analysis Set (taking into account all patients regardless of completeness of follow-up data; n= 353 patients) the following non-fatal events since baseline were documented:

Intrahospital complications; n (%)	
STEMI	5 (1.42)
NSTEMI	1 (0.28)
Stroke	2 (0.57)
TIA	0

More details on intrahospital complications (incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (EBAS, B16-1 – B16-8).

Non-fatal events since baseline were documented in 169 patients (48.88%) at 12-months follow-up since baseline and in 197 patients (55.81%) at 24-months follow-up since baseline.

Event type, n (%)	**12-months follow-up (since baseline) n= 353**	**24-months follow-up (since baseline) n=353**
Myocardial infarction	3 (0.8) 95% CI: -0.00, 0.02	6 (1.7) 95% CI: 0.00, 0.03
Cardiac Catheter Examination without PCI	24 (6.8) 95% CI: 0.04, 0.09	32 (9.1) 95% CI: 0.06, 0.12
Balloon dilatation (PCI)	36 (10.2) 95% CI: 0.07, 0.13	46 (13.0) 95% CI: 0.10, 0.17
Bypass surgery	4 (1.1) 95% CI: 0.00, 0.02	5 (1.4) 95% CI: 0.00, 0.03
Stroke	1 (0.3) 95% CI: -0.00, 0.01	2 (0.6) 95% CI: -0.00, 0.01
TIA	0	1 (0.3) 95% CI: -0.00, 0.01
Hospitalisation due to event	63 (17.6)	80 (22.7)
Hospitalisation due to event; *mean duration*	4.1 days (SD: 3.3)	5.5 days (SD: 5.7)
Rehabilitation	102 (28.9) 95% CI: 0.24, 0.34	113 (32.0) 95% CI: 0.27, 0.37
Other inpatient stay	55 (15.6) 95% CI: 0.12, 0.19	88 (24.9) 95% CI: 0.20, 0.29

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Other inpatient stay, *mean duration*	9.3 days (SD: 9.2)	13.4 days (SD: 18.5)

More details on non-fatal events since baseline (incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (EBAS, 12-months follow-up: tables 1FU2-1 – 1FU2-14; 24-months follow-up: tables 2FU2-1 – 2FU2-14).

With regard to the Extended Analysis Set (taking into account all patients with complete data on LDL cholesterol and correct timing at 12-months follow-up; n= 140) the following non-fatal events were documented:

Intrahospital complications; n (%)	
STEMI	3 (2.14)
NSTEMI	1 (0.71)
Stroke	2 (1.43)
TIA	0

Non-fatal events since baseline were documented in 85 patients (60.71%) at 12-months follow-up since baseline and in 97 patients (69.29) at 24-months follow-up since baseline.

Event type, n (%)	**12-months follow-up (since baseline) n=140**	**24-months follow-up (since baseline) n=140**
Myocardial infarction	2 (1.4) 95% CI: -0.01, 0.03	4 (2.9) 95% CI: 0.00, 0.06
Cardiac Catheter Examination without PCI	11 (7.9) 95%CI: 0.03, 0.12	17 (12.1) 95% CI: 0.07, 0.18
Balloon dilatation (PCI)	22 (15.7) 95% CI: 0.10, 0.22	27 (19.3.0) 95% CI: 0.13, 0.26
Bypass surgery	0	1 (0.7) 95% CI: -0.01, 0.02
Stroke	0	0
TIA	0	0
Hospitalisation due to event	33 (23.6)	42 (30.0)
Hospitalisation due to event; *mean duration*	3.8 days (SD: 2.9)	5.6 days (SD: 6.5)
Rehabilitation	58 (41.4) 95% CI: 0.33, 0.50	65 (46.4) 95% CI: 0.38, 0.55
Other inpatient stay	21 (15.0) 95% CI: 0.09, 0.21	383 (27.1) 95% CI: 0.20, 0.35
Other inpatient stay, mean duration	9.8 days (SD: 8.2)	12.4 days (SD: 18.6)

More details on non-fatal events since baseline (incl. stratification by sex [male, female] and age [18-65 years, >65 years] are given in Appendix II (EAS, 12-months follow-up: tables 1FU2-1 – 1FU2-14; 24-months follow-up: tables 2FU2-1 – 2FU2-14).

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Discussions:	**(a) Key results – Part I (Analysis sets BAS / FAS)** In general: The HYDRA-ACS registry was conducted in 24 participating sites in Germany. 347 patients were included in the baseline analyses and 72 patients were included in the full analysis set (FAS) to evaluate the longitudinal data. Of 347 patients in baseline, complete follow-up data (for both 12- and 24-months follow-up concurrently; regarding complete information on LDL values at follow-up and correct timing) were available in 140 patients. Overall, 275 patients were excluded from the longitudinal analyses (n= 52 patients with incomplete data for 12-months follow-up; 53 patients with incomplete data for 24-months follow-up; 170 patients with incomplete data for both 12- and 24-months follow-up). The main reasons for exclusion from longitudinal analyses were incorrect timing of LDL value assessment at follow-up and the lack of documented LDL values at follow-up. Duration of enrolment was on average 231.9 days (SD: 149.6 days). On average, 13.9 patients (SD: 16.0; MD: 10) were enrolled per study site. Baseline characteristics: 257 patients (74.1%) were male. The mean age of the patients was 57.2 years. The most common diseases and conditions in cardiovascular history were coronary heart disease (32.8%), PCI (25.4%) and acute coronary syndrome (22.8%). The most common comorbidities in this population were arterial hypertension (68.3%), diabetes mellitus (17.3%), heart failure (17.0%), and stable angina pectoris (15.9%). Phenotypic findings in this population were quite rare: xanthelasma (1.4%), xanthomas (2.6%), and arcus cornealis (2.0%). With regard to the family history, the most frequent diseases and conditions were myocardial infarction (53.0%), coronary heart disease (32.8%), cerebral/vascular disease (19.3%), and elevated cholesterol levels (11.8%). LDL target achievement: Among the 72 patients with valid follow-up data, around half achieved the therapeutic target of LDL < 70 mg/dl or a reduction of at least 50% from baseline (37 patients (51.4%) at 12-months follow-up and 35 patients (48.6%) at 24-months follow-up). In addition, a considerable decrease in LDL-C could be observed over time (i.e. average reduction in LDL-C over time: -38.2% (SD: 30.6) from baseline to 12-months follow-up and -36.2% (SD: 36.7) from baseline to 24-months follow-up). Non-fatal events since baseline: In the overall population (n= 347), only few intrahospital complications were observed at baseline (type of events: STEMI, 5 patients; NSTEMI, 1 patient; stroke, 2 patients). Since baseline, a considerable amount of non-fatal events were observed (at 12-months follow-up: non-fatal events in 169 patients [48.7%; type of events: myocardial infarction, 3 (0.9%); cardiac catheterization without PCI, 24 (6.9%); balloon dilatation/PCI, 36 (10.4%); CABG, 4 (1.2 %); Stroke, 1 (0.3%); other hospitalization, 55 (15.9%)]; at 24-months follow-up: non-fatal events in 197 patients [56.8%; type of events: myocardial infarction, 6 (1.7%); cardiac catheterization without PCI, 32 (9.2%); balloon dilatation/PCI, 46 (13.3%); CABG, 5 (1.4%); stroke, 2 (0.6%); TIA, 1 (0.3%); other hospitalization, 88 (6.4%)]). Hospitalization due to a non-fatal event was observed in 63 patients (18.2%) with a mean duration of 4.1 days (12-months follow-up) and in 80 patients (23.1%) with a mean duration of 5.5 days (24-months follow-up). **(b) Key Results – Part II (Analysis sets EBAS / EAS)** In general: Taking into account less stringent criteria for the analysis sets (see Methodology) the analyzable population could be enlarged considerably: 353 patients were included in the baseline analyses (EBAS) and 140 patients were included in the extended analysis set (EAS) to evaluate the longitudinal data. Of 353 patients in baseline, complete follow-up data (for the 12- follow-up; regarding complete information on LDL values at follow-up and

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	correct timing) were available in 140 patients. Overall, 213 patients were excluded from the longitudinal analyses. The main reasons for exclusion from longitudinal analyses were the lack of documented LDL values at follow-up (n= 212 patients). Duration of enrolment was on average 231.9 days (SD: 149.6 days). On average14.1 patients (SD: 16.2; MD: 10) were enrolled per study site. Baseline characteristics: 259 patients (73.4%) were male. The mean age of the patients was 57.3 years. The most common diseases and conditions in cardiovascular history were coronary heart disease (32.9%), PCI (25.5%), acute coronary syndrome (22.9%) and aortocoronary bypass (5.7%). The most common comorbidities in this population were arterial hypertension (68.6%), diabetes mellitus (17.3%), heart failure (17.0%), and stable angina pectoris (15.9%). Phenotypic findings in this population were quite rare: xanthelasma (1.7%), xanthomas (2.6%), and arcus cornealis (2.0%). With regard to the family history, the most frequent diseases and conditions were myocardial infarction (52.4%), coronary heart disease (32.6%), and cerebral/vascular disease (19.3%). Family history of elevated cholesterol levels could be observed in 11.8% of the patients. LDL target achievement: Among the 140 patients with valid follow-up data, 50% achieved the therapeutic target of LDL < 70 mg/dl or a reduction of at least 50% from baseline (70 patients (50.0%) at 12-months follow-up and 46 patients (50.0%; n= 48 missing) at 24-months follow-up). In addition, a considerable decrease in LDL-C could be observed over time (i.e. average reduction in LDL-C over time: -37.5% (SD: 28.8) from baseline to 12-months follow-up and -36.5% (SD: 36.1) from baseline to 24-months follow-up). Non-fatal events since baseline: In the overall population (n= 353), only few intrahospital complications were observed at baseline (type of events: STEMI, 5 patients; NSTEMI, 1 patient; stroke, 2 patients). Since baseline, a considerable amount of non-fatal events were observed (at 12-months follow-up: non-fatal events in 169 patients [48.9%; type of events: myocardial infarction, 3 (0.8%); cardiac catheterization without PCI, 24 (6.8%); balloon dilatation/PCI, 36 (10.2%); CABG, 4 (1.1 %); Stroke, 1 (0.3%); other hospitalization, 55 (15.6%)]; at 24-months follow-up: non-fatal events in 197 patients [55.8%; type of events: myocardial infarction, 6 (1.7%); cardiac catheterization without PCI, 32 (9.1%); balloon dilatation/PCI, 46 (13.0%); CABG, 5 (1.4%); stroke, 2 (0.6%); TIA, 1 (0.3%); other hospitalization, 88 (24.9%)]). Hospitalization due to a non-fatal event was observed in 63 patients (17.8%) with a mean duration of 4.1 days (12-months follow-up) and in 80 patients (22.7%) with a mean duration of 5.5 days (24-months follow-up). **(c) Interpretation and generalizability:** There are considerable limitations in the interpretation of the results regarding lipid target achievement due to the fact that only a small proportion of the initially enrolled patients could be included in the analysis of the follow-up data (BAS/FAS: 72 of 347 patients; EBAS/EAS: 140 of 353 patients). The main reasons for exclusion from the longitudinal analyses were the lack of documented LDL values at follow-up.

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Conclusions:	Overall, taking into account less stringent criteria for the analysis sets (e.g. expanding the acceptable time window for follow-ups from 3 to 4 months etc.; see section Methodology) the analyzable population could be enlarged considerably, but was still unsatisfactory with roughly 40% of the patients with analyzable follow-up data. The main reason (i.e. lack of documented LDL values or the incongruous timing of these) are largely owed to the non-interventional design of the study. This mainly affects the availability of the required lipid values (especially LDL as the primary endpoint): it is very likely that this non-interventional design of the study did not sufficiently reflect clinical routine regarding the assessment of lipid parameters. As opposed to an interventional clinical trial, study site visits of the patients to collect a satisfactory proportion of the endpoints could not be performed; thus, it was inevitable to cope with the amount of lipid parameters available within the limits of clinical routine. In particular, at the telephone follow-up calls patients were unable to provide the required current LDL levels. Lack of representativeness: In general, the study itself was subject to a considerable sample bias due to its observational design. In addition, it is doubtable, whether the observed sample was representative for the target population of patients with acute coronary syndrome (ACS), in particular since participation was strictly voluntary and it can, thus, be expected that not every eligible patient finally consented to participate. In this study, only few patients consented to participate (it was planned to include 3,000 patients, while eventually only n= 347 [BAS] and n= 353 [EBAS] were enrolled at baseline): (a) Site recruitment. Initially, more than 300 sites were contacted and invited to participate. It was planned to involve about 100 sites. Eventually, only 24 sites actively enrolled patients (in detail: 37 sites consented to participate, among those 35 signed a study contract and 24 actively participated by enrolling patients). (b) Patient enrolment. Initially, enrolment duration was planned for 12 months, and eventually, enrolment was extended by 6 months to reach the planned number of enrolled patients. The main reason for failing to reach the planned sample size was largely due to the fact that most eligible patients were already under lipid-lowering therapy and thus, LDL levels had to be extrapolated to an estimated value without lipid-lowering therapy. Initially, it was planned to enroll 3,000 patients, while eventually, only n= 347 [BAS] and n= 353 [EBAS] were enrolled by 24 sites at baseline. Moreover, longitudinal data were available for even fewer patients (FAS: n= 72; EAS: n= 140), due to largely unavailable current LDL levels at the time of the due telephone follow-ups. The lack of representativeness is particularly reflected in the collected data and their corresponding statistical characteristics (i.e. the considerable lengths of the 95% confidence intervals as well as the large standard deviations indicate rather low precision). In addition, mitigating these limitations with quality auditing measures was not entirely promising, since only a very small amount of auditing visits at sites were initially scheduled to be performed (i.e. in 5% of the sites, only) and LDL target achievement was assessed using follow-up telephone calls, where a large proportion of patients were unable to provide current LDL levels.
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