Non-Interventional Study (NIS) Report	
NIS Name/Code	NIS-CGR-DUM-2009/1
Edition Number	FINAL
Date	17 FEBRUARY 2011

An Epidemiological Study of Acute Coronary Syndromes in The Greek Population. The 'TARGET' Study [Baseline Resuls]

Study dates:	**First Subject In:** 25 January 2010 **Last Subject Last Visit:** 29 June 2010

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1. STUDY SITES

Overall, 17 hospitals have participated in the present study covering the major prefectures of Greece. More than half of the participating hospitals (58.8%) are located outside Attica, whereas the rest of them (41.2%) are operating within the periphery of Attica. The majority of hospitals (64.7%) belong to the public sector and the rest of them (35.3%) are equally distributed (17.6%) between academic institutions and private sector hospitals. Moreover, slightly more than half of the hospitals (52.9%) have a catheterization laboratory (cath lab) available; it is noteworthy to mention that 55.5% of the hospitals with cath lab are located inside Attica. Detailed information on the participating sites and principal investigators is provided in Appendix B.

2. PUBLICATIONS

There are no publications at the moment.

3. STUDY DATES

First Subject In (obtainment of informed consent)**:** 25 January 2010

Last Subject Last Visit: 29 June 2010

The final study protocol, including the final version of the Patient's Informed Consent Form, have been approved by the competent IRBs (Scientific Committee/Administrative Council) of the participating Hospital Sites and the National Organization for Medicines (EOF) before the enrolment of any patient into the study and the performance of any study related procedure. No study amendments or administrative changes pertaining to the approved study documents have been applied until the completion of the cross-sectional phase of the present study.

4. BACKGROUND AND RATIONALE

ACS constitutes a major cause of morbidity and mortality worldwide. NSTEMI and UA account for about 2.5 million hospital admissions annually worldwide while STEMI account for another 1 million [1]. The incidence of ACS highly varies among different European countries mainly due to disparities in dietary habits and prevalence of CV risk factors [2]. This discordance has also been reflected in the significant differences presented when assessing the CV risk models among different European populations [3,4]. Furthermore, the management and outcome of ACS patients is highly dependent on the implementation rate of mortality-reducing therapies as well as the organization of health-care infrastructure to enable early patient management and timely reperfusion of the myocardium at risk.

It is generally accepted that national surveys are highly needed in order to shed light on the epidemiology, treatment and prognosis of everyday patient population. This type of epidemiological studies overcomes the main limitation of randomized clinical trials related to their highly controlled clinical setting that impairs the pragmatic assessment of the characteristics, management and outcome

of real-world patients. Furthermore, the value of properly designed observational studies lies within the provision of information on the prevalence of risk factors, the incidence of ACS, the level of use of various therapies (invasive and pharmaceutical) and the outcome of patients in relation to baseline characteristics and implemented therapies. Additionally, they may allow comparisons between practices in different hospitals around the country and the participation of a large number of hospitals and researchers, therefore improving the control and promotion of clinical responsibility [5-7].

In this perspective, TARGET, a multicenter, 2-phase observational study, aimed to further enrich the existing data by providing a depiction of the risk factors, current management and outcomes of ACS in Greece. In order to depict the current clinical practice at a realistic and broad basis, this study focused on two different time-points; primarily on the index event (from pain to hospitalization and patients' final discharge) and secondarily on 6 months after the index event, thus covering the important first 6-month follow-up period. Moreover, this study aimed to reveal any potential relationships between index event data, such as CV risk, lipid levels, ACS risk classification, standard and novel biomarker values as well as therapeutic strategy and 6-month outcomes.

5. OBJECTIVES

Primary objective of Cross-sectional phase ("TARGET Baseline")

- To evaluate the proportion of patients who were on target for LDL-C according to the 2004-updated NCEP ATPIII guidelines (per risk stratification), as estimated within the first 24-hours of hospital admission for an ACS.

Secondary objectives of Cross-sectional phase ("TARGET Baseline")

- To estimate the proportion of patients admitted to the hospital with STEMI, NSTEMI and unstable angina.
- To describe the transportation patterns from patients' call place to the hospital where the ACS event was eventually managed.
- To estimate the "pain-to-door-time" throughout different regions in Greece.
- To evaluate the levels of LDL-C as well as the proportion of patients with LDL-C levels below 160, 130, 100 and 70 mg/dl within 24 hours upon admission to the hospital for the index event.
- To evaluate the levels of the other lipid parameters such as TC, HDL-C, TG, ApoB, ApoAI and ApoB/ApoAI upon admission.
- To estimate the 10-year CV risk according to the Framingham point score (as per NCEP ATP III guidelines) for the study subjects upon admission.
- To estimate the 10-year CV risk according to SCORE (as per FJETF guidelines) for the study subjects upon admission.
- To estimate the percentage of sites measuring novel biomarkers such as hsCRP, BNP/NT-proBNP, sICAM-1, IL-6, PAI-1 in their clinical routine and the respective values of those biomarkers.
- To evaluate the GRACE risk score upon admission to the hospital for the index event.
- To describe the medication classes the patients receive upon admission for the index event.
- To describe the in-hospital management of ACS in terms of medicinal treatment and reperfusion/revascularization procedures.
- To describe the medication classes the patients receive upon discharge from the hospital after the index event.

- To describe the instructions provided to the patients upon discharge from the hospital after the index event.
- To estimate the in-hospital clinical event and mortality rate.

6. STUDY DESIGN AND SELECTION CRITERIA

6.1 Study Design

Overall, 17 hospital-based investigators participated in the study and were requested to enroll consecutive patients admitted with ACS (STEMI, NSTEMI or UA) referred to as index event. Participating sites encompassed public and private, academic and non-academic, as well as rural and urban hospitals, in order to represent all the potential sites where an ACS patient is referred to and treated.

Before the commencement of any study related procedure, the patients were informed about the nature of the study and signed accordingly the informed consent form. As soon as the informed consent form was signed, data on demographics, medical history, vital signs, medications used at admission, CV risk factors, lipid levels, time of symptoms onset, pain-to-door time, transportation details, ECG findings, myocardial necrosis markers and other biomarkers have been collected on a paper Case Report Form (pCRF). Moreover, data on patient final diagnosis, in-hospital management and outcome, discharge therapeutic strategy and instructions given to the patients have also been recorded.

All of the aforementioned have comprised the cross-sectional (baseline) data of the study, which lie within the scope of the present CSR.

For the needs of the prospective cohort phase of the study, participating hospitals have been requested to collect 6-month information of the enrolled subjects. The statistical analysis of these data will be performed after the completion of the cohort phase of the study and the relevant results will be incorporated into the final clinical study report.

The study flow chart is illustrated in Table 1.

Table 1 Study Flow Chart

Evaluation	Index Event	6-month follow-up
Hospital information[1]	X	
Informed consent[2]	X	
Sociodemographic and anthropometric characteristics	X	
Vital signs	X	
Medical history[3]	X	
CV risk factors	X	
GRACE score	X	
Lipidemic profile	X	X
Glucose level	X	
Medications	X	X
Index event information	X	
Biomarkers (if applicable)	X	X[4]
Index event management information[5]	X	
Framingham point score	X	
SCORE	X	
Discharge information	X	
NYHA classification	X	X
Changes in treatment from discharge		X
Treatment and instructions adherence		X
Major Adverse Cardiovascular Events	X	X
Mortality	X	X
Use of health care resources		X

1. *Before any patient enrolment*
2. *Before any study- related activity*
3. *CV and relevant medical history*
4. *hsCRP only (if applicable)*
5. *Including management during ambulance transportation where applicable*

6.2 Selection Criteria

Inclusion criteria

For inclusion in the study subjects had to fulfil all of the following criteria:

1. Provision of informed consent.
2. Females or males aged ≥18 years.
3. Diagnosis of an ACS (STEMI, NSTEMI, UA) at the time of hospital admission.

Exclusion criteria

Any of the following was regarded as a criterion for exclusion from the study:

1. Involvement in the planning and conduct of the study (applies to both AstraZeneca staff and staff at the study sites).
2. Participation in other clinical study in period between the index event and 6-month follow-up assessment with the exception of registering in registries or surveys not influencing the management of the ACS.

7. TARGET PATIENT POPULATION, STUDY DISEASE AND SAMPLE SIZE

Overall 418 patients with ACS were enrolled and completed the TARGET cross-sectional part of the study and were almost equally distributed on the basis of hospitals' location (49.3% were admitted to hospitals inside Attica; 50.7 to hospital outside Attica) and hospitals' cath lab availability (49.5% were admitted to cath lab hospitals & 50.5% to non cath lab hospitals, respectively).

The primary variable of the study was the proportion of patients who were on target for LDL-C according to the 2004-updated NCEP ATPIII guidelines (per risk stratification), as calculated within the first 24-hours of hospital admission for an ACS.

Sample size calculation was based on the need to ensure that the proportion of subjects referred to the primary and secondary endpoints could be estimated with sufficient precision to represent the heterogeneity of this population.

Hence, sample size determination was based on confidence limit approach rather than test power considerations aiming at ensuring adequate precision estimates. Based on this rationale, 385 patients were required to achieve a ± 5% precision of estimates, given that the expected percentage was 50%. Assuming a percentage of 8% of non-evaluable subjects, 418 patients should be enrolled, and were finally included in the current study.

8. CRITERIA FOR EVALUATION (MAIN VARIABLES)

Primary Variable

Proportion of patients (n,%) who are on target for LDL-C (according to the 2004-updated NCEP ATPIII guidelines) as calculated within 24 hours of hospital admission.

Main Secondary Outcome Variables

- Patient baseline sociodemographic and anthropometric characteristics
  - Gender: male (n,%), female (n,%), male-to-female ratio (male:female)
  - Age [mean (+/-SD) yrs]
  - Race: white/caucasian (n,%), asian (n,%), black (n,%)
  - Education: no education (n,%), primary education (n,%), secondary education (n,%), trietary education (n,%)
  - Marital status: single (n,%), married (n,%), divorced (n,%), widowed (n,%)
  - Employment status: unemployed (n,%), employed in private sector (n,%), employed in public sector (n,%)
  - Height (mean (+/-SD) cm)
  - Weight (mean (+/-SD) kg)
  - Waist circumference [mean (+/-SD) cm]
  - Dietary patterns: mediterrenean dietary pattern (n,%), fast food/low-nutrition (n,%), other (n,%)
  - Physical activity (i.e. walking exercise): none (n,%), 1-2 times/week (n,%), more frequent (n,%)
- Cardiovascular risk factors and medical history
  - Diabetes mellitus (n,%)
  - Smoking status: no smoker (n,%), occasional smoker (n,%), previous smoker (n,%), current smoker (n,%), if current smoker: pack-years
  - Hypertension (n,%)
  - Dyslipidemia (n,%)
  - Family history of premature CHD (n,%)
  - History of documented CHD (n,%), cerebrovascular atherosclerotic disease including transient ischemic attack or/and stroke (n,%), PAD (n,%)
  - Previous PCI (n,%) or CABG (n,%)
  - Heart failure (n,%)
  - Arrhythmias (plus permanent pacemaker) (n,%)
- Medications used at the time of hospital admission
  - Cardiovascular medications
  - Other relevant medications (anti-diabetic & anti-obesity drugs)
- Laboratory parameters upon admission (lipids and biomarkers)
- Index event information
  - Transportation means: ambulance (n,%), self-transport (n,%), other (n,%)
  - Time from symptom onset to admission: mean (+/-SD) min
  - Diagnosis: STEMI (n,%), NSTEMI (n,%), UA (n,%)
  - Clinical events (death, MI, stroke/TIA, angina, etc.)
  - GRACE risk score (median) and risk categories
- Information pertaining to in-hospital management of the index event
  - Invasive cardiac procedures: coronary angiography (n,%), PCI (n,%), CABG (n,%)
  - Fibrinolysis (n,%)
  - In-hospital medication administered
  - Other procedures (n,%)
- Framingham point score (median) and four risk categories <10% (n,%), 10% to <20% (n,%), 20% to <30% (n,%), and ≥30% (n,%)
- SCORE (median) and four risk categories <5% (n,%), 5% to <10% (n,%), 10% to <15% (n,%), and ≥15% (n,%)

- Discharge information
  - Length of hospitalization: mean (+/-SD) days
  - Medication classes prescribed at discharge
  - Instructions on lifestyle changes at discharge: specific diet (n,%), specific LDL-C goal (n,%), quit smoking (n,%), physical activity (n,%), other (n,%).

9. STATISTICAL METHODS

Descriptive statistical analysis has been applied to all study cross-sectional data. All categorical variables are expressed in counts (N) and percentages (%). Continuous variables are summarized with the use of descriptive statistical measures [mean value, standard deviation (SD), median, and extreme values]. When necessary, the median and the 25th and 75th percentiles (first and third quartiles) are displayed as measures of centrality and variation respectively.
The normality of distribution of continuous variables has been examined using the Kolmogorov Smirnov test (K-S test) in order to determine whether or not to use parametric methods for the analysis of the sample data.
All the aforementioned statistical tests were two-sided and performed at a 0.05 significance level.
Missing data have not been replaced. No inferential statistics were used as all study objectives pertained to quantitative descriptions
Data processing and analysis were performed using the statistical package SPSS v. 17.0.

9.1 Population Analysis Sets

9.1.1 Definition of the target population

Statistical analysis was performed for the total of 418 subjects who participated in the study and completed its cross-sectional part, as predicted by the protocol. The analysis of TARGET cohort data is outside the scope of this report and is planned to be presented within the framework of the final CSR, as per predefined study milestones.

9.2 Statistical Analysis Result

9.2.1 Descriptive Analysis

9.2.1.1 Subject Demographic and Baseline Characteristics

There is a clear preponderance of males over females in the present study with a male-to-female ratio of 3.5 (males/females: 78.0%/22.0%). Almost all patients (99.5%) were Caucasians except from 2 subjects that were of Asian origin. Moreover 80% of patients were married, 74.6% were primary or secondary education graduates, and more than half of them (53.1%) were retired [Table 2].

Table 2 Subjects' socio-demographic characteristics

Socio-demographic Characteristics	n	%
Gender		
Male	326	78.0%
Female	92	22.0%
Race		
White/Caucasian	416	99.5%
Black	0	0.0%
Asian	2	0.5%
Other	0	0.0%
Marital status		
Single	20	4.8%
Married	334	79.9%
Divorced	14	3.3%
Widowed	50	12.0%
Education		
No education	38	9.1%
Primary education	177	42.3%
Secondary education	135	32.3%
Trietary education	68	16.3%
Employment status		
Employed in private sector	74	17.7%
Employed in public sector	34	8.1%
Freelancer	66	15.8%
Retired	222	53.1%
Unemployed	22	5.3%

The mean age of the study population was 63.9±12.9 years, whereas the mean BMI was 28.8±4.8 kg/m^2. Interestingly, 38.6% of male patients (126/326) and 60.9% (56/92) of females had a waist circumference greater than 102 cm and 88 cm respectively [Table 3].

Table 3 Subjects' anthropometric characteristics

Anthropometric Characteristics	Mean	Std Dev	Median	Minimum	Maximum	N
Age (years)	63.9	12.9	64.3	29.1	93.3	418
Height (cm)	169.3	8.4	170.0	142.0	195.0	417
Weight (kg)	82.6	16.5	80.0	48.0	155.0	418
BMI (kg/m^2)	28.8	4.8	28.1	19.4	49.6	417
Waist circumference (cm)	100.7	13.2	100.0	72.0	176.0	363

9.2.1.2 Subjects' dietary patterns and physical activity

Regarding subjects' physical activity and dietary patterns, 61.2% of the study participants were following a poor dietary pattern (characterized by the intake of foods of low nutritional value), and more than half of them (55.7%) had adopted a sedentary lifestyle with lack of physical activity.

9.2.1.3 Subjects' CV risk factors and medical history

51.4% (215/418) of the patients had a history of CAD (30.9%, 129 patients) or CAD risk equivalents (20.6%, 86 patients). Almost half of the subjects (46.7%) were current smokers while approximately one third of the study population had a family history of premature CHD. Hypertension and dyslipidemia were among the most frequent CV risk factors observed by 67.9% and 57.4% of the patients, respectively [Table 4].

Table 4 Subjects' CV risk factors

Cardiovascular Risk Factors	n	%
Smoking status		
No smoker	109	26.1%
Previous smoker	111	26.6%
Occasional smoker	3	0.7%
Current smoker	195	46.7%
if current smoker: pack-years	*mean±SD* *median (min-max)*	*50.6±33.3* *45.0 (3.0-200.0)*
Hypertension	**284**	**67.9%**
Dyslipidemia	**240**	**57.4%**
Family history of premature CHD	**124**	**29.7%**
Coronary artery disease	**129**	**30.9%**
Stable angina	18	4.3%
Unstable angina	15	3.6%
AMI	71	17.0%
PCI	58	13.9%
CABG	26	6.2%
Cerebrovascular disease	**44**	**10.5%**
Stroke	29	6.9%
ischemic	*24*	*5.7%*
hemorrhagic	*2*	*0.5%*
unspecified	*3*	*0.7%*
Transient ischemic attack	23	5.5%
> 50% carotid artery obstruction	14	3.3%
Diabetes mellitus	**115**	**27.5%**
Type I	8	1.9%
Type II	107	25.6%
Peripheral arterial disease	**33**	**7.9%**
Abdominal aortic aneurysm	**7**	**1.7%**

Regarding subjects' relevant medical history as reported at baseline, 17.0% of the patients had heart failure (81.7% NYHA class I or II). Furthermore, 6.2% of the study population suffered from atrial fibrillation, and 20.9% from COPD, chronic kidney or liver disease, inflammatory disease or other relevant disease.

9.2.2 Primary Objective

9.2.2.1 Proportion of patients on target for LDL-C (2004-updated NCEP ATPIII guidelines)

Table 5 depicts the distribution of study population according to the LDL-C target category as per the 2004-updated NCEP ATPIII guidelines.

Table 5 Distribution of study population according to LDL-C target category (2004-updated NCEP ATPIII guidelines)

2004-updated NCEP ATPIII	LDL-C Target Category	N	%
Established CVD plus diabetes, smoker, low HDL-C and high TG, metabolic syndrome, or multiple risk factors	<70 mg/dL (1.81 mmol/L)	144	35.3%
CHD, or CHD Risk equivalents, or Framingham 10 year risk >20%	<100 mg/dL (2.59 mmol/L)	131	32.1%
2+ Risk Factors with Framingham 10 year risk between 10% and 20%	<100 mg/dL (2.59 mmol/L)	23	5.6%
2+ Risk Factors with Framingham 10 year risk <10%	<130 mg/dL (3.36 mmol/L)	99	24.3%
0-1 Risk Factor	<160 mg/dL (4.14 mmol/L)	11	2.7%
TOTAL		***408****	***100.0%***

**data were missing in 10 patients*

Overall, the majority of the patients with available LDL-C data (72.5%) were not on LDL-C target, and only 27.5% of the participants were at the recommended goal according to 2004-updated NCEP ATPIII guidelines [Table 6].

Table 6 Percentage of patients on LDL-C target (2004-updated NCEP ATPIII guidelines)

LDL-C Target Category	Study Population on LDL-C Target Upon Hospital Admission				P-value
	Yes (n=107)		No (n=282)		
	N	%	N	%	
<70 (n=136/144*)	22	16.2%	114	83.8%	<0.0001***
<100 (n=143/154**)	34	23.8%	109	76.2%	
<130 (n=99/99)	42	42.4%	57	57.6%	
<160 (n=11/11)	9	81.8%	2	18.2%	
Total	**107**	**27.5%**	**282**	**72.5%**	

** In 8 patients LDL-C value was missing*
*** In 11 patients LDL-C value was missing*
**** statistically significant as assessed by chi-square test (χ2)*

There was a statistically significant relationship between the LDL-C target category and the patients who were on LDL-C target ($p<0.0001$). In particular, as depicted in Table 6 the higher the LDL-C target, the greater the number of patients being on LDL-C target.

9.2.3 Secondary Objectives

9.2.3.1 Proportion of patients with STEMI, NSTEMI and UA

44.7% of the participating patients were diagnosed with STEMI, 34.2% with NSTEMI, and 21.1% with UA.

9.2.3.2 Transportation patterns from patients' call place to the hospital where the ACS event was eventually managed

More than half of the subjects (61.7%) were self transported to the hospital and 33.5% were admitted by ambulance [Table 7].

Table 7 Transportation patterns from patients' call place to the hospital

Transportation means		
Self-transport	258	61.7%
Ambulance	140	33.5%
Other	23	5.5%
By relative/friend/physician	*15*	*3.6%*
Transfer from another department (the patient was already hospitalized)	*6*	*1.4%*
By airplain	*2*	*0.5%*

9.2.3.3 "Pain-to-door-time"

Overall, the median "pain-to-door-time" time (from symptom onset to admission to the hospital) was 3 hrs (range 0.0 - 693 hrs) [Table 8].

Table 8 "Pain-to-door-time" time for the total study population and by prefecture

Time from Symptom Onset to Hospital Admission (hours)	Mean	Std	Min	1st Quartile	Median	3rd Quartile	Max	N
TOTAL	17.5	53.6	0.0	1.5	3.0	9.2	693.0	411
ATTICA	23.3	63.9	0.0	1.5	3.0	14.2	693.0*	205
HERAKLION	37.8	107.7	0.5	3.0	5.0	10.0	487.0*	21
RHODOPE	5.2	5.1	0.6	1.8	3.6	6.0	17.5	18
IOANNINA	3.5	3.5	0.6	1.2	2.6	4.3	11.3	8
CHIOS	3.0	2.9	0.5	1.0	2.0	3.2	12.5	29
KOZANI	16.3	29.5	0.5	0.7	2.1	22.0	91.5	14
EVIA	4.6	5.7	0.5	1.5	2.5	4.5	26.2	36
PELLA	7.4	13.1	0.5	1.5	2.8	5.4	50.0	15
CHANIA	32.1	50.0	0.8	1.5	3.8	55.2	171.8	18
LARISSA	2.8	3.2	0.3	1.0	1.8	3.0	12.0	18
MAGNISIA	10.1	18.5	0.5	1.5	5.0	9.2	98.5	29

** Extreme values (693 & 487 hrs, i.e., approximately 30 days & 20 days respectively) refer to 2 patients diagnosed with UA*

9.2.3.4 Levels of LDL-C as well as of the proportion of patients with LDL-C levels below 160, 130, 100 and 70 mg/dl

Table 9 LDL-C levels upon hospital admission

LDL-C (mg/dL)	mean±SD	123.2±41.6
	median (min-max)	120 (36-263)
	n	389

Table 10 presents the distribution of patients according to LDL-C level as measured upon hospital admission.

Table 10 Distribution of study population according to LDL-C level upon hospital admission

LDL-C Value	N	%
<70 mg/dL	31	8.0%
70 - 99 mg/dL	91	23.4%
100 - 129 mg/dL	107	27.5%
130 - 159 mg/dL	81	20.8%
≥ 160 mg/dL	79	20.3%
Total	***389***	***100.0%***

9.2.3.5 Levels of other lipid parameters (TC, HDL-C, TG, ApoB, ApoAI and ApoB/ApoAI) upon admission

Table 11 shows the descriptive statistics of the other lipid parameters upon hospital admission.

Table 11 Other lipid parameters upon hospital admission

Lipidemic Profile		
TC (mg/dL)	mean±SD	194.7±47.2
	median (min-max)	191 (85-386)
	n	399
HDL-C (mg/dL)	mean±SD	42.3±11.8
	median (min-max)	40 (22-116)
	n	387
TG (mg/dL)	mean±SD	156.8±104.2
	median (min-max)	129.5 (45-821)
	n	398
ApoB (mg/dL)	mean±SD	80.3±21.3
	median (min-max)	82 (42-121)
	n	35
ApoAI (mg/dL)	mean±SD	111.2±42.6
	median (min-max)	115 (37-239)
	n	35
ApoB/ApoAI	mean±SD	0.9±0.5
	median (min-max)	0.73 (0.3-2.5)
	n	35

9.2.3.6 10-year CV risk according to Framingham point score and SCORE upon admission

Risk stratification according to Framingham and SCORE was performed for patients with no CAD or its risk equivalents (N=203; 48.6% of total study population) in order to estimate the 10-year risk of CHD event and CV death respectively. For the purposes of this study, the SCORE model version for Greece was used.

The median Framingham point score in the study population was 14.0 (min-max: 1.0-30.0). With regard to patients' distribution in Framingham risk categories, 41.3% of the evaluable patients were ranked in the intermediate risk range, 31.8% of the patients were at high or very high risk and 27.0% of the patients were belonging in the low risk category [Table 12].

Regarding the HeartScore risk classification system, the median score of the patients was 6.0 (min-max: 1.0-27.0). In particular 38.9% of the patients were categorized as low risk, 33.7% as intermediate risk and 27.4% as high or very high risk [Table 12].

Table 12 Risk Stratification according to Framingham and HEART SCORE

Risk Stratification According to Framingham and SCORE (n=203)		
Framingham Point Score		
mean±SD median (min-max) n	14.7±7.9 14.0 (1.0-30.0) 181	
Risk categories	***N***	***%***
<10%	51	27.0%
10%-20%	78	41.3%
20%-30%	47	24.9%
≥30%	13	6.9%
Total*	189	100.0%
SCORE		
mean±SD median (min-max) n	7.0±5.1 6.0 (1.0-27.0) 193	
Risk categories	***N***	***%***
<5%	75	38.9%
5%-10%	65	33.7%
10%-15%	35	18.1%
≥15%	18	9.3%
Total**	193	100.0%

* Scores for 14 patients are missing
** Scores for 10 patients are missing

9.2.3.7 Percentage of sites measuring novel in their clinical routine and the respective values of those biomarkers

Except from CK-MB that was assessed by 82% (14 sites) of the participating sites, cTnT & cTnI that were measured by 58.8% (10 sites) and 64.7% (11 sites) of sites respectively, and fibrinogen that was measured by 47.1% (8 sites), the rest of the potential novel biomarkers were not assessed by the majority of the investigational sites as per their usual clinical practice [Table 13].

Table 13 Proportion of investigational sites measuring novel biomarkers

Novel Biomarkers	Number of sites (n=17)	%
NT-proBNP	**6**	**35.3%**
Inside Attica	*1*	*16.7%*
Outside Attica	*5*	*83.3%*
BNP	**5**	**29.4%**
Inside Attica	*2*	*40.0%*
Outside Attica	*3*	*60.0%*
hsCRP	**3**	**17.6%**
Inside Attica	*2*	*66.7%*
Outside Attica	*1*	*33.3%*
IL-6	**0**	**0.0%**
sICAM-1	**0**	**0.0%**
PAI-1	**0**	**0.0%**

Table 14 Biomarker levels upon hospital admission

Biomarkers		
CK-MB (IU/L)	mean±SD	66.8±119.7
	median (min-max)	23.9 (0-1369)
	n	311
hsCRP (mg/L)	mean±SD	11.7±27.8
	median (min-max)	3.2 (0.05-142)
	n	65
IL-6		NA
sICAM-1		NA
PAI-1		NA
cTnT (ng/mL)	mean±SD	1.4±2.7
	median (min-max)	0.6 (0-24.4)
	n	136
cTnI (ng/mL)	mean±SD	12.6±37.6
	median (min-max)	2.4 (0-370.2)
	n	192
BNP (pg/mL)	mean±SD	269±331.3
	median (min-max)	162 (6.9-1299.4)
	n	27
NT-proBNP (pg/mL)	mean±SD	1867.7±3029.6
	median (min-max)	768.3 (24.1-15472)
	n	62

9.2.3.8 GRACE risk score upon admission to the hospital

GRACE 'At Admission' Risk Model was used for predicting 'in-hospital' and 'from hospital admission to 6 months' mortality for all patients participating in the study. Tables 15 and 16 depict the descriptive statistics for GRACE risk score pertaining to both the absolute scores and the percent predicted mortality.

Table 15 GRACE absolute risk score

GRACE Risk Absolute Score At Admission (In Hospital/From Admission to 6 Months)		Mean	Std	Median	Min	Max	N
In Hospital	Probability of in-hospital death absolute score	129.4	43.5	123.0	40.0	297.0	391
	Probability of in-hospital death/MI absolute score	162.4	62.8	149.0	36.0	404.0	391
To 6 months	Probability of death (to 6 months) absolute score	107.1	35.6	103.0	30.0	230.0	391
	Probability of death/MI (to 6 months) absolute score	144.2	50.3	137.0	37.0	321.0	391

Table 16 GRACE percentage risk score

GRACE Risk Percentage Score At Admission (In Hospital/From Admission to 6 Months)		Mean	Std	Median	Min	Max	N
In Hospital	Probability of in-hospital death percentage score (%)	4.2	7.4	1.0	0.0	70.0	391
	Probability of in-hospital death/MI percentage score (%)	13.0	8.6	10.0	3.0	>70.0	391
To 6 months	Probability of death (to 6 months) percentage score (%)	9.2	12.3	4.0	0.4	90.0	391
	Probability of death/MI (to 6 months) percentage score (%)	23.9	13.3	20.0	6.0	>90	391

Table 17 presents the distribution of patients according to GRACE risk categories.

Table 17 Risk Stratification according to GRACE ACS Risk Model

In Hospital Mortality					
Non STE - ACS			STE - ACS		
Distribution of Patients by GRACE Risk Category			Distribution of Patients by GRACE Risk Category		
Probability of in hospital death	n	%	Probability of in hospital death	n	%
Low (<1%)	58	26.5%	Low (<2%)	107	62.2%
Intermediate (1-3%)	89	40.6%	Intermediate (2-5%)	41	23.8%
High (>3%)	72	32.9%	High (>5%)	24	14.0%
Total*	***219***	***100.0%***	***Total*****	***172***	***100.0%***

* Data of 12 patients are missing

** Data of 15 patients are missing

9.2.3.9 Medication classes upon admission

69.1% of the patients were receiving antihypertensive/anti-ischemic medications, 45.9% were treated with antiplatelets/anticoagulants and 41.4% were on lipid-lowering therapy. [Table 18]. Furthermore, 23.2% of the patients were receiving anti-diabetic agents and none of them was on anti-obesity medication.

Table 18 CV medications used at the time of admission

Antihypertensives/Anti-ischemics (n=289; 69.1%)			Antiplatelets/Anticoagulants (n=192; 45.9%)		
Medication class	**N**	**%**	**Medication class**	**N**	**%**
Beta-blockers	148	35.4%	Vitamin K antagonist	15	3.6%
Calcium channel blockers	90	21.5%	Heparin	18	4.3%
Diuretics	102	24.4%	ADP receptor antagonist	102	24.4%
Aldosterone receptor antagonists	11	2.6%	Aspirin	157	37.6%
ACE inhibitors	104	24.9%	**Lipid-lowering drugs (n=173; 41.4%)**		
Angiotensin II receptor antagonists	112	26.8%	Statins	167	40.0%
Nitrates	65	15.6%	Ezetimibe	11	2.6%
Other	12	2.9%	Fibrates	4	1.0%
Other CV drugs (n=19; 4.5%)			Niacin	0	0.0%
Antiarrhythmics	7	1.7%	Bile acid sequestrants	0	0.0%
Digoxin	9	2.2%	Omega-3 fatty acids	15	3.6%
Other	5	1.2%	Other	0	0.0%

9.2.3.10 In-hospital management of ACS

Table 19 presents the in-hospital non pharmaceutical management of the index event.

It is noteworthy to mention that almost all patients (98.2%; 166/169) who underwent invasive cardiac procedures were initially admitted to hospitals with cath lab, since for hospitals without cath labs no information is available at the time of writing this report regarding the referral of patients to hospitals with cath lab for potential invasive management of the index event; such information will be captured at the second prospective part of the study.

Taking into account only the patients treated by hospitals with cath labs, 54.1% (112/207) underwent PCI and 1.9% (4/207) CABG [Table 20].

Table 19 In-hospital non-pharmaceutical management of the index event

In-hospital Non Pharmaceutical Management of the Index Event*	n	%
Invasive cardiac procedures**	**169**	**40.4%**
Coronary angiography	**136**	**32.5%**
Percutaneous coronary intervention/PCI	**113**	**27.0%**
- primary PCI	*52*	*46.0%*
- rescue PCI	*9*	*8.0%*
- facilitated PCI	*5*	*4.4%*
- planned (not emergency) PCI	*47*	*41.6%*
Time from admission to the initiation of the PCI *mean +/-SD (hrs)* *median (min-max)* *n*	27.4±44.5 8.25 (0.25-260.0) 108	
Coronary artery bypass graft surgery (CABG)	**4**	**1.0%**
Other *(pacemaker placement)*	**1**	**0.2%**
Other procedures	**391**	**93.5%**
Cardiac ultrasound	**391**	**93.5%**
Scintigraphy	**16**	**3.8%**
Radionuclide ventriculography	**0**	**0.0%**
CT	**7**	**1.7%**
MRI	**2**	**0.5%**
Other***	**24**	**5.7%**

* *Without taking into consideration the potential referrals from non cath lab hospitals to cath lab hospitals*

** *51 patients were reported to have undergone coronary angiography only; 82 patients both coronary angiography & PCI; 31 patients PCI only; 3 patients coronary angiography & CABG; 1 patient CABG only; and 1 patient other (pacemaker).*

*** *Other procedures that were applied included stress test (8 patients), stress echo test (8 patients), modified Bruce protocol stress test (5 patients), upper abdominal ultrasound (1 patient), coronary CT angiograph (1 patient) and electrical cardioversion (1 patient).*

Table 20 In-hospital invasive cardiac procedures for the index event per type of hospital

In-hospital Invasive Cardiac Procedures for the Index Event*	N	%
Hospitals with Cath Lab	**Total number of patients: 207**	
Invasive cardiac procedures	**166**	**80.2%**
Coronary angiography	135	65.2%
Percutaneous coronary intervention/PCI	112	54.1%
Coronary artery bypass graft surgery (CABG)	4	1.9%
Hospitals without Cath Lab	**Total number of patients: 211**	
Invasive cardiac procedures	**3**	**1.4%**
Coronary angiography	1	0.5%
Percutaneous coronary intervention/PCI	1	0.5%
Coronary artery bypass graft surgery (CABG)	0	0.0%
Other (pacemaker placement)	1	0.5%

* *Without taking into consideration the potential referrals from non cath lab hospitals to cath lab hospitals*

Thrombolysis was applied to 22.7% of the study population (95/418) and in 90.5% of the cases (86/95) it was performed at the participating site.

During hospitalisation, almost all patients received antihypertensive/anti-ischemics (98.1%), antiplatelets/anticoagulants (100%) and lipid lowering medication (96.2%) [Table 21].

24.6% of the patients received anti-diabetic medications while hospitalized while none of them was administered anti-obesity drugs.

Table 21 In-hospital pharmaceutical management (CV drugs)

Antihypertensives/Anti-ischemics (n=410, 98.1%)			**Antiplatelets/Anticoagulants (n=418, 100%)**		
Beta-blockers	365	87.3%	Aspirin	405	96.9%
Calcium channel blockers	60	14.4%	ADP receptor antagonist	387	92.6%
Diuretics	111	26.6%	Low molecular weight heparin	224	53.6%
Aldosterone receptor antagonists	44	10.5%	Heparin	156	37.3%
ACE inhibitors	228	54.5%	Fondaparinux	85	20.3%
Angiotensin II receptor antagonists	99	23.7%	GP IIa/IIIb inhibitors	81	19.4%
Nitrates	264	63.2%	Vitamin K antagonist	10	2.4%
Other	6	1.4%	Bivalirudin	0	0.0%
Other CV drugs (n=64, 15.3%)			**Lipid-lowering drugs (n=402, 96.2%)**		
Antiarrhythmics	47	11.2%	Statins	401	95.9%
Digoxin	7	1.7%	Ezetimibe	14	3.3%
Other	20	4.8%	Fibrates	1	0.2%
Other Drugs			Niacin	0	0.0%
Fibrinolytics*	89	21.3%	Bile acid sequestrants	0	0.0%
Tenectaplase	*54*	*60.7%*	Omega-3 fatty acids	38	9.1%
Reteplase	*34*	*38.2%*	Other	0	0.0%
Alteplase	*1*	*1.1%*			
Other	6	1.4%			

** In 5 out of the 95 patients who underwent thrombolysis, fibrinolytic has not been checked since thrombolysis was not carried out at the participating hospital; In 1 patient who was treated with thrombolysis at the participating hospital information on fibrinolytic administered is missing*

9.2.3.11 Medication classes upon discharge from the hospital

Detailed information on the CV medication prescribed at discharge is presented in Table 22. Furthermore, antidiabetic treatment was prescribed in 21.2% of the patients, whereas no patient was advised to take any anti-obesity agents.

Table 22 CV medications prescribed at discharge

Antihypertensives/Anti-ischemics (n=401/410, 97.8%)			Antiplatelets/Anticoagulants (n=406/410, 99.0%)		
Beta-blockers	353	86.1%	Vitamin K antagonist	16	3.9%
Calcium channel blockers	63	15.4%	Heparin	11	2.7%
Diuretics	94	22.9%	ADP receptor antagonist	344	83.9%
Aldosterone receptor antagonists	45	11.0%	Aspirin	387	94.4%
ACE inhibitors	214	52.2%	**Lipid-lowering drugs (n=385/410, 93.9%)**		
Angiotensin II receptor antagonists	101	24.6%	Statins	382	93.2%
Nitrates	180	43.9%	Ezetimibe	18	4.4%
Other	9	2.2%	Fibrates	0	0.0%
Other CV drugs (n=37/410, 9.0%)			Niacin	0	0.0%
Antiarrhythmics	22	5.4%	Bile acid sequestrants	0	0.0%
Digoxin	5	1.2%	Omega-3 fatty acids	39	9.5%
Other	12	2.9%	Other	0	0.0%

9.2.3.12 Instructions to the patients upon discharge

92.7% of the subjects were instructed to adopt lifestyle changes at discharge. In particular, 75.6% of the patients were advised to follow a specific diet, 67.8% were instructed to reach a specific LDL-C goal, 87.9% of those who were occasional or current smokers were advised to quit smoking and 14.6% were recommended to perform regular exercise [Table 23].

Table 23 Instructions on lifestyle changes at discharge

Instructions on Lifestyle Changes at Discharge	N*	%
Instructions on lifestyle changes provided at discharge (NO)	***30***	***7.3%***
Instructions on lifestyle changes provided at discharge (YES)	***380***	***92.7%***
i) Specific diet	310	75.6%
ii) Specific LDL-C goal	278	67.8%
iii) Quit smoking**	174	87.9%
iv) Regular physical activity	60	14.6%
v) Other	14	3.4%
- Rest	*6*	*1.5%*
- Weight loss-glycaemic control	*3*	*0.7%*
- Weight loss	*2*	*0.5%*
- Alcohol consumption cessation	*1*	*0.2%*
- Glycaemic control	*1*	*0.2%*
- Walking	*1*	*0.2%*

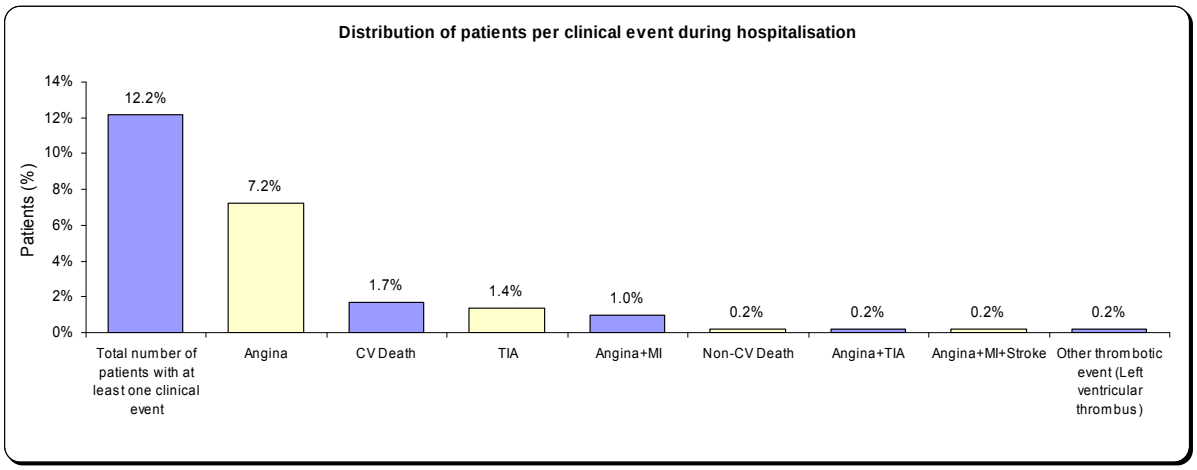
**missing values refer to patients who have died*

***relevant percentage pertains to subgroup of patients who were occasional or current smokers*

9.2.3.13 In-hospital clinical event and mortality rate

Overall 12.2% of the total study population (51/418) experienced at least one clinical event during hospitalisation [Figure 1], while the total number of events recorded was 58; 8 deaths and 50 other clinical events. 2.9% of the total study population (12/418) experienced major CV events (i.e., CV death/MI/Stroke) during hospitalisation.

Figure 1 Distribution of patients per clinical event occurred during hospitalisation



In-hospital all-cause mortality rate was 1.9% (8/418) whereas CV mortality rate was 1.7% (7/418). Reasons of CV death included: stroke (1 patient); MI (1 patient); pulmonary edema (1 patient); atrial fibrillation/acute pulmonary edema (1 patient); cardiogenic shock (2 patients); and heart failure (1 patient).

10. SAFETY

NA

11. ETHICS

11.1 Ethical conduct of the study

The study has been conducted after the obtainment of the required approvals by the competent IRBs (Scientific Committee/Administrative Council) of the participating Hospital Sites and the National Organization for Medicines (EOF), and in accordance with the ethical principles that have their origin in the Declaration of Helsinki (ICH-GCP guidelines), all applicable national and E.U. laws and regulations, and AstraZeneca policy on Bioethics.

11.2 Subject information and consent

Prior to the conduct of any study-related procedure, investigators ensured that each potential participating patient was provided accurate and adequate oral and written information about the nature, purpose, possible risks and benefits of the present study. Each patient's signed informed consent form

(ICF) was obtained in duplicate before his/her enrolment into the study. The original signed and dated ICF was maintained by the investigator at the study file while a copy of the signed ICF was given to the patient.

12. DATE OF THE REPORT

17 February 2011

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