AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA

FINISHED PRODUCT: None
ACTIVE INGREDIENT: None

Study No: NIS-CBG-XXX-2013/1; NCT02001545
RE-ACT - REAL WORLD INFORMATION ON CARDIOVASCULAR DRUG MANAGEMENT PATTERNS IN ACUTE CORONARY SYNDROME PATIENTS

Developmental Phase: Non-Interventional Study
Study Completion Date: 30/09/2014
Date of Report: 20/08/2015

Study type

RE-ACT is a national, multi-centre, observational, prospective, longitudinal cohort study which will include patients hospitalized for ACS within 24 hours of symptom onset and who have a final diagnosis of ST-segment elevation myocardial infarction (STEMI) or non-ST-segment elevation myocardial infarction (NSTEMI).

OBJECTIVES:

(a) Primary objective

To describe the short-term (at the end of the first month after index event) antithrombotic management patterns (AMPs) in a "real-life" setting for patients hospitalized with an acute coronary syndrome (i.e. STEMI and NSTEMI).

(b) Main secondary objectives

1. To describe the variations in the acute clinical management strategies and AMPs
2. To evaluate the determinants of AMP choices (i.e. patient's characteristics, hospital characteristics, coronary intervention strategies and type of coronary stents used)
3. To evaluate the impact of the different AMPs on quality of life at discharge from hospital
4. To describe the variations in AMPs for STEMI and NSTEMI
5. To evaluate the impact of the different AMPs on quality of life at the end of the first month after discharge from the hospital

6. To document compliance with the national and/or international guidelines for AMP use.

METHODS:

Patients underwent clinical assessments and received the standard medical care as determined by the treating cardiologist. Patients who received experimental intervention or experimental treatment were not eligible for participation in the RE-ACT observational study. In addition, it was the intention of this study to collect data on patients diagnosed with STEMI or NSTEMI under conditions of routine clinical care.

In order to obtain a true real-life overview of the medical management of ACS patients in Bulgaria, the different treatment patterns were reflected in the selected sites and within the proportion as they are provided to ACS patients in a real-life setting. Therefore a strict site selection process was followed.

The study subjects were enrolled in the NIS at the moment of discharge from the hospital following hospitalization for ACS (STEMI, NSTEMI). A second NIS visit took place at the end of the first month after discharge from the hospital, in line with local clinical practice.

The study was completed between February, 2014 (First Patient First Visit was on 2014-02-10) and September, 2014 (Last Patient Last Visit was on 2014-09-30).

Target subject population

Patients aged 18 years or older, hospitalized and diagnosed with STEMI (ST-segment elevation myocardial infarction) or NSTEMI (non-ST-segment elevation myocardial infarction) within 24 hours of symptom onset.

Diagnosis and Main Criteria for Inclusion:

Inclusion Criteria

- Provision of subject informed consent
- Female and male aged 18 years and over
- Patients hospitalized and diagnosed with STEMI or NSTEMI
- Hospitalized within 24 hours of onset of symptoms or transferred from another hospital within 24 hours of the onset of symptoms

Exclusion criteria:

- STEMI and NSTEMI precipitated by or as a complication of surgery, trauma, or GI bleeding or post-PCI.
- STEMI and NSTEMI occurring in patients already hospitalized for other reasons.

- Presence of any condition/circumstance which in the opinion of the investigator could significantly limit the complete follow up of the patient (e.g. tourist, non-native speaker or does not understand the local language, psychiatric disturbances).

- Already included in the RE-ACT study.

- Presence of serious/severe co-morbidities in the opinion of the investigator which may limit short term (i.e.1-3) life expectancy.

Evaluations:

Primary endpoint

Primary endpoint was calculated on the Full Analysis Set.

Secondary endpoints

Secondary endpoints were calculated on the Full Analysis Set, except the EUROQoL questionnaire outcomes which were calculated on Per Protocol Population.

Statistical Methods:
Primary variable
- Number of patients on different antiplatelet therapies were characterise by descriptive statistical tools.

Secondary variables
- Number of patients on different antiplatelet and anticoagulant treatment patterns classified by hospital characteristics, haemoglobin level, vascular access, culprit lesion territory, type of stent used, diagnosis, presence of diabetes mellitus, age group, gender, history of myocardial infarction, history of prior PCI and history of atrial fibrillation.
- Number of patients on ticagrelor and clopidogrel, application of multiple binary logistic regression model for identification significant determinants in choice of antiplatelet therapy.
- EuroQoL Total Score at follow-up with antiplatelet therapy.

RESULTS:

Primary endpoint:

The patterns of the antiplatelet therapy were as follows:

- ASA + ticagrelor with 226 subjects (27.8%), ASA + ticagrelor + GPIIb/IIIa with 184 subjects (22.6%), ASA + clopidogrel with 196 subjects (24.1%), ASA + clopidogrel + GPIIb/IIIa with 94 subjects (11.5%) and other therapy pattern with 110 subjects (13.5%). The pattern is unknown for 4 subjects (0.5%).

- The patterns of the anticoagulant therapy were as follows – considering the availability of hospital characteristics: “Unfractionated heparin” with 390 subjects (47.9%), “UFH + LMW heparin” with 276 subjects (33.9%) and “Other therapy pattern” with 132 subjects (16.2%). The pattern was unknown for 16 subjects (2.0%).

Secondary endpoints:

Significant differences were identified according the following characteristics:

- Hospital characteristics, antiplatelet therapy ($p < 0.0001$)
- Hospital characteristics, anticoagulant therapy ($p < 0.001$)
- Hemoglobin level, anticoagulant therapy ($p = 0.0002$)
- Vascular access, antiplatelet therapy
- Vascular access, anticoagulant therapy ($p = 0.0103$)
- Type of stent used, antiplatelet therapy ($p = 0.0027$)
- Diagnosis, antiplatelet therapy ($p < 0.0001$)
- Age group, antiaplatelet therapy ($p < 0.0001$)
- History of prior PCI, antiplatelet therapy ($p = 0.0009$)
- History of atrial fibrillation, antiplatelet therapy ($p = 0.0095$)
- History of atrial fibrillation, anticoagulant therapy ($p < 0.0001$).

Significant determinant for ticagrelor and clopidogrel choice:

- Significant determinants for ticagrelor choice are: *75years and above* as significant negative determinant and *Prior PCI* as significant negative determinant.
- Significant determinant for ticagrelor choice in STEMI patients is *75 years and above* as significant negative determinant.
- Significant determinant for ticagrelor choice in NSTEMI patients is *75 years and above* as significant negative determinant.
- Significant determinants for clopidogrel choice are *75 years and above* as significant positive determinant, *High creatinine* as significant positive determinant, *Oral anticoagulants* as significant positive determinant and *Prior PCI* as significant positive determinant.
- Significant determinant for clopidogrel choice in STEMI patients is *75 years and above* as significant positive determinant.

EUROQoL-5D results

- Mobility: The mean score was higher (representing a better condition) at follow-up (0.89 vs. 0.84).

- Self-care: The mean score was higher at follow-up (0.96 vs. 0.92).
- Usual activities: The mean score was higher at follow-up (0.92 vs. 0.84).
- Pain/Discomfort: The mean score was higher at follow-up (0.92 vs. 0.86).
- Anxiety / Depression: The mean score was higher at follow-up (0.87 vs. 0.78).
- Total score: The mean score was higher at follow-up (0.91 vs. 0.85).
- Visual analog score: The mean score was higher at follow-up (79.34 vs. 68.83).

Classificiation	Treatment	Findings	Significance
Hospital characteristics	Antiplatelet	• ASA + TICA+ GPIIb/IIIa - more frequently applied in regional hospitals (33.1% vs. 13-18%), • ASA + CLO was the most frequent treatment at university hospitals (28.8%) and general hospitals (31.5%)	p < 0.0001
	Anticoagulant	• UFH was the most frequent treatment in all types of hospitals but with a big variation (40.1% - 72.6%), • UFH + fondaparinux was applied for 41 subjects in regional hospitals, while it was applied only for 7 subjects in the remaining types of hospitals, • LMWH was applied for 22 subjects in university hospitals, while it was applied only for 6 subjects in the remaining types of hospitals, • UFW + LMWH was applied in 35-39% in regional and university hospitals but only in 17% in general hospitals.	p < 0.0001
Hemoglobin level	Antiplatelet		NS
	Anticoagulant	• UFH was the most frequent treatment in both categories but with big big variation (43.7% and 57.4%) • UFH + fondaparinux was 4 times and UFW + LMWH - 2 times more frequently applied for patients without anemia (7.6% vs. 2%) and (5.2% vs. 2.8%) resp.	p = 0.0002
Vascular access	Antiplatelet	• ASA + CLO is the most frequent treatment for femoral vascular access (28.4%), • ASA + TICA is the most frequent treatment for radial vascular access (29.3%), 2 times more frequent than ASA + CLO •	p=0.0378
	Anticoagulant	• UFW + LMWH was the most frequently applied treatment for femoral vascular access (52.7%), • UFH was the most frequently applied treatment for radial vascular access (49.2%), •	p = 0.0103
Type of stent used DES: Yes/no	Antiplatelet	• ASA + TICA is the most frequent treatment in both groups (yes: 37.6%; no: 25.8%), • frequency of ASA + CLO is practically identical with that of ASA + TICA in stent without drug subgroup, •	p = 0.0027
	Anticoagulant		NS
Diagnosis	Antiplatelet	• ASA + TICA is the most frequently applied treatment for patients with STEMI (28.8%), • ASA + CLO is the most frequently applied treatment for patient with NSTEMI (40.6%), • frequency of application of ASA + TICA + GPIIb/IIIa is comparable to that of ASA + TICA in STEMI group (26.3% vs. 28.8%), but remarkably different in NSTEMI group 23.2% vs. 40.6%), • ASA + CLO was applied with two times higher frequency in NSTEMI group than in STEMI group (40.6% vs. 20.2%).	p < 0.0001
	Anticoagulant		NS
Age group	Antiplatelet	• ASA + TICA is the most frequently applied treatment for patients below 75 years (29.7%), • ASA + CLO is the most frequently applied treatment for patient 75 years and above (40.4%), • ASA + CLO was applied with two times higher frequency in patients with 64 years and above (40.4% vs. 20.4%), • application of ASA + TICA + GPIIb/IIIa is 5% less frequent in 75 years and above group (13.9% vs.	p < 0.0001

Classificiation	Treatment	Findings	Significance
		24.6%), • application of ASA + CLO + GPIIb/IIIa is 5% less frequent in below 75 years group (10.7% vs. 15.2%).	
History of prior PCI	Antiplatelet	• ASA + TICA is the most frequently applied treatment for patients with no history of prior PCI (28.5%), • ASA + CLO is the most frequently applied treatment for patient with history of prior PCI (34.3%), • application of ASA + TICA + GPIIb/IIIa is 10% less frequent for patients with history of prior PCI (13.3% vs. 24%),	p = 0.0009
	Anticoagulant		NS
History of atrial fibrillation	Antiplatelet	• ASA + TICA is the most frequently applied treatment for patients with no history of atrial fibrillation (28.7%), • ASA + CLO is the most frequently applied treatment for patient with history of atrial fibrillation (38.3%), • application of ASA + TICA + GPIIb/IIIa is more than two times frequent for patients with no history of atrial fibrillation (23.2% vs. 10.6%), • application of ASA + CLO is 15% less frequent for patients with no history of atrial fibrillation (23.2% vs. 38.3%), • application of ASA + TICA is more than two times more frequent for patients with no history of atrial fibrillation (28.7% vs. 12.8%).	p = 0.0095
	Anticoagulant	• UFH is the most frequently applied treatment for patients with no history of atrial fibrillation (49%), • UFH + LMWH and UFH fondaparinux are equally frequently applied treatments for patient with history of atrial fibrillation (29.8% each), • application of UFH is 20% less frequent in patient with history of atrial fibrillation (29.8% vs. 49%).	p < 0.0001

Subanalysis by gender, culprit lesion territory, presence or not of diabetes (all patients as well as by subdiagnosis STEMI and NSTEMI), history of MI, TIA/stroke did not reveal significant difference in antiplatelet and anticoagulant treatment pattern.