**STUDY REPORT SYNOPSIS**

# RuSsian RegisTry of Acute CoronaRy SyndromE TreAtMent and Approach in Dual Antiplatelet Therapy (STREAM)

## Study Sites, number of subjects

**It is confirmed that 4442 patients with acute coronary syndrom have been included to the Registry from January, 01 2012 till March, 01 2015 in the cross-sectional part of the study and 1013 patients have been enrolled in the single-arm cohort part of the project. 20 clinical sites have participated in this study from different Russian regions.**

**Milestones:**

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| Date of first subject in | 13 Apr 2015 |
| Date of last subject in | 30 Jun 2016 |
| Date of last subject last visit | 27 Jul 2018 |
| Date of Data Base lock | 28 Sep 2018 |

**Phase of development:** Non-interventional study (NIS)

**Sponsor:** AstraZeneca

This study was performed in compliance with Good Clinical Practice (GCP) and Good Pharmacoepidemiology Practice (GPP), including the archiving of essential documents.



**Background/rationale:**

Acute Coronary Syndrome (ACS) is one of the principal causes that contribute to the high mortality rate in the Russian Federation (RF) due to cardiovascular disease. During last years the quality of medical management has increased greatly at the pre-hospital, in-hospital stage due to implementation of advanced medical techniques and improvement of drug supply and overall quality of public medical services in the Russia. Nowadays standardised approaches in the treatment of ACS, including pre-hospital and in-hospital thrombolysis, percutaneous coronary intervention (PCI), necessary drug therapy (incl. anticoagulants and antiplatelets) can significantly contribute to the reduction of the short-term and long-term CV mortality. Internet-based Russian ACS Registry started in 2008, and since that time more than 140 000 ACS patients in 167 hospitals from 46 different Russian regions have been enrolled in this registry. This Registry is carried out in cooperation with the Russian Ministry of Health. However, the Russian ACS Registry includes information on organization of medical care for ACS patients in hospital setting only, without collecting any follow up data. Therefore, no data is available on long-term perspective for ACS patients and no possibility to trace the dual antiplatelet therapy (DAT) duration for ACS patients and understand reasons of DAT discontinuation in Russia.

Ticagrelor is not included in the essential drug list, so there is no State support and reimbursement for patients and they buy ticagrelor by themselves for their money, which is not refunded by the State, for this reason, the average real life duration of ticagrelor usage in Russia is 3 months in case of conservative treatment of ACS and 6 months for invasive strategy according to market research data. Moreover, in Russia there is no information what happens with patients after 12 months after the ACS. What antiplatelet therapy they take, what doctor (cardiologist or GP) they visit, how often they visit the doctor, what are the reasons of the visit to a doctor after 12 months.

Acute coronary syndrome (ACS) encompasses a spectrum of adverse coronary events, including unstable angina (UA), ST-elevation myocardial infarction (STEMI), and non-STEMI (NSTEMI). Acute coronary syndrome is one of the principal causes that contribute to the high mortality rate in the Russian Federation due to cardiovascular disease. In average, every year approximately 520 000 ACS cases are registered in the RF (36.4% o of cases are MI, 63.6% - UA). ACS in the RF is connected with significant social and economic damage

due to premature mortality of working-age population, temporary disability, payment of disability benefits and direct costs of expensive medical services (including costs related to the drug therapy, emergency hospitalizations and vascular surgery interventions).

Antiplatelet therapy is the cornerstone of acute and long-term therapy in patients with ACS, reducing the rates of CV-death and other cardiovascular events. According to current guidelines, dual antiplatelet therapy (DAT), consisting of acetylsalicylic acid (ASA) and P2Y12 inhibitors (clopidogrel, ticagrelor, prasugrel), is recommended for all patients with ACS (regardless of the initial revascularisation strategy) for up to 12 months. Treatment with new antiplatelet agents along with enhancement of adherence to current guidelines has the potential for improvement of short- and long-term outcomes in patients with ACSA.

**Objectives:** The main aims of the stufy are to understand the short-term antithrombotic management approach in a real-life setting for patients hospitalized with an acute coronary syndrome (Part A - cross sectional study) and to describe long-term perspective for patients with an acute coronary syndrome taking ticagrelor as a part of complex antiplatelet therapy after discharge from hospital during 2 years of prospective follow up period in real-life setting (Part B – single cohort study).

This study also aims to understand the approaches in the acute clinical management of patients hospitalized with ACS depends on type of ACS (Part A), to study factors determining the choice of anti-platelet therapy in the acute phase of ACS (Parts A and B), to understand the impact of specific clinical and non-clinical events during the follow-up on antithrombotic treatment interruptions (Part B), and on the occurrence of subsequent thrombo-embolic events (Part B), to document adherence of patients to ticagrelor treatment and duration of dual antiplatelet therapy in real-life setting (Part B). The other secondary objectives are to determine reasons for discontinuation of dual antiplatelet therapy in real-life setting (Part B), to describe cardiovascular complications developed over the long term (second year) after the event used as a reason for inclusion in the study in real clinical practice (Part B), to understand the antithrombotic therapy in long-term perspective (second year) after index event and to investigate the proportion of patients who managed by cardiologists, therapeutists and other physicians after ACS patients discharge from the hospital (Part B).

**Study design:** A multi-centre, observational, descriptive, cross-sectional study.

**Data source:** The extraction of data from the Russian ACS Registy for the purpose of analyzing the data according to the study objectives was conducted (applicable for Part A). In the part B collection of data received during the phone calls was performed.

**Study population:** Subjects whose data have been entered in the Russian ACS Registry and who were discharged from hospital after MI with ST-segment elevation (STEMI), MI NST

segment elevation (NSTEMI) or Unstable angina were included in part A. The single-cohort study (Part B) was focused on patients discharged from hospital from hospital after MI with ST-segment elevation (STEMI), MI NST segment elevation (NSTEMI) or Unstable angina who were on ticagrelor at the time of discharge.

**Inclusion criteria:** For Part A: 1. Subjects whose data have been entered in the Russian ACS Registry; 2. Discharged from hospital after MI with ST-segment elevation (STEMI), MI NST segment elevation (NSTEMI) or Unstable angina; 3. Hospitalized during 24 hours of ACS symptoms onset; 4. Age 18 years or older;

For Part B: 1. Discharged fromhospital after MI with ST-segment elevation (STEMI), MI NST segment elevation (NSTEMI) or Unstable angina; 2. Patients on ticagrelor at the time of discharge from hospital. 3. Written informed consent provided by patients enrolled into prospective part of the study prior its start. 4. Age 18 years or older.

**Exclusion criteria:** 1. The existence of serious / severe concomitant diseases which can in the short term (i.e. within 6 months) limit the duration of life; 2. Current participation in a clinical trial with a non-licensed investigational medicinal product.

**Statistical methods:** All statistical analysis was performed by means of the SAS® statistical software system. A comprehensive Statistical Analysis Plan was prepared before database lock. For statistical analysis of results of this non-interventional study descriptive statistics methods was used. No hypothesis was verified or refuted at that. Continuous variables were added up using descriptive statistics techniques (sample number, mean value, standard deviation, median, the 25th and 75th percentile, minimum and maximum). Categorical variables were added up using one-way tables (N, %). For primary endpoints the 95% confidence interval was calculated.

**Results:** Most of the STEMI patients underwent an invasive treatment (1546/1982, 78,00%). Almost half of them (n = 835; 54,01%) were administered with aspirin + clopidogrel combination. Ticagrelor was prescribed in combinations with aspirin (n = 257/1546); 16,62%), aspirin + clopidogrel (n = 189/1546; 12,23%), aspirin + GP IIb/IIIa inhibitors (n = 37/1546; 2,39%) or aspirin + clopidogrel + GP IIb/IIIa inhibitors (n = 6/1546; 0,39%). Patients from the STEMI group who were treated conservatively (n = 435) were mainly prescribed with aspirin + clopidogrel (n = 410/435; 94,25%).

Among NST ACS patients the vast majority received a conservative treatment (1423/2462). Almost all of these patients (n = 1197/1423; 84,12%) were administered with aspirin + clopidogrel combination. Ticagrelor was prescribed in combinations with aspirin (n = 47/1423; 3,30%) or aspirin + clopidogrel (n = 66/1423; 4,64%). Patients from the NST ACS group who received invasive treatment (n = 1039) were mainly prescribed with aspirin +

clopidogrel (n = 669/1039; 64,39%), aspirin + ticagrelor (n = 206/1039; 19,83%) or aspirin + clopidogrel + ticagrelor (n = 97/1039; 9,34%).

Another important finding was that STEMI patients very rarely (n = 7) were prescribed with one antiplatelet drug while 105 NST ACS patients received oral antiaggregant monotherapy (95 patients used aspirine, 10 patients used clopidogrel).

The single-cohort study was focused on patients discharged from hospital after MI with ST-segment elevation (STEMI), MI NST segment elevation (NSTEMI) or Unstable angina who were on ticagrelor at the time of discharge. Only 3 patients (0,30%) were receiving it as monotherapy. The majority of these patients (n = 658, 64,96%) were receiving ticagrelor in combination with aspirin. Nearly 1/4 of patients (199/961; 20,71%) discontinued ticagrelor treatment within 3 months after prescriprion. Almost half of the patients (417/961; 43,39%) stopped taking ticagrelor after using it for 12–15 months. Only 2,91% of patients have been using it for more than 2 years. During the first 9 months the most common reasons for ceasing ticagrelor treatment were financial reasons and switch to another medication. Later (12 months onwards) patients stopped taking the medicine mostly because of the end of the recommended therapy course, less frequent but important reasons included financial ones and switch to another medication. Regarding cardiovascular complications, which occurred to these patients after hospital discharge the most common ones were repeated hospitalization due to cardiovascular disease (n = 70; 7,28%), urgent repeated myocardial revascularization (n = 14; 1,46%) and miocardial infaction (n = 11; 1,14%). Thus, overall 11,12% patients experienced cardiovascular complications after hospital discharge which is consistent with litarature data.

Analysis of baseline demographics revealed that the majority of patients were males (66,71% in Part A and 75,22% in Part B). The average age was 62,76 ± 11,76 for patients enrolled in Part A study and 58,88 ± 11,00 was patients enrolled in Part B.

**Conclusion:** This study was set out to gain a better understanding of ACS management in hospitals and assess the frequency of cardiovascular complications, which occurred after hospital discharge, to patients who had been recommended treatment with ticagrelor upon discharge. The investigation of different types of short-term antithrombotic treatment has shown that aspirin + clopidogrel combination was the most widespread regardless of ACS type (with or without ST-elevation) and general treatment approach (invasive or non-invasive).

When frequency of cardiovascular complications, which occurred after hospital discharge to patients with unstable angina and STEMI and NSTEMI patients, was evaluated this study has identified that the most common complications were repeated hospitalization due to cardiovascular disease (n = 70; 7,28%), urgent repeated myocardial revascularization (n = 14;

1,46%) and miocardial infaction (n = 11; 1,14%). Thus, overall 11,12% patients experienced cardiovascular complications after hospital discharge with is in allignment with the literature data.