Non-Interventional Study (NIS) Report Synopsis	
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A non-inTeRventional prospEctive observationAl Study to Understand the usage pattern of Ticagrelor in Indian patients with acute coronaRy syndromE (TREASURE)

Study dates:	**First Subject In:** 27 Aril 2017 **Last Subject Last Visit:** 20 June 2017
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Study dates:	**First Subject In:** 27 Aril 2017 **Last Subject Last Visit:** 20 June 2017

NIS REPORT SYNOPSIS

TREASURE NIS Study

Background/Rationale:

The choice of newer anti-platelet therapies and strategies is continuously evolving as well as the International guidelines for their use. The available data concerning the usage pattern of newer anti-platelet therapies in acute coronary syndrome (ACS) patients is largely derived, essentially from clinical trials.
Ticagrelor has been used in India since 2012however, retrospective analysis of available data is not possible due to poor infrastructure and lack of electronic case recording formats in the hospitals in India.

The TREASURE observational study was designed to address the need to understand the usage pattern of ticagrelor in real life scenario in a large number of ACS patients in India. This national study aimed to understand the usage pattern (including the duration of treatment) of ticagrelor in various ACS patient population undergoing percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG) or medical management (MM) in a real-life setting in India. The multicentre national participation allowed generating real life evidence by involving patients from different geographies and healthcare systems in India.

Objectives and Hypotheses:

Primary Objective:

To describe the usage pattern of ticagrelor in various ACS patient population (ST segment Elevation Myocardial Infarction [STEMI], non ST segment Elevation Myocardial Infarction [NSTEMI] and unstable angina [UA]) who undergo either PCI, CABG or MM in a real-life setting in India.

Secondary Objectives:

(1) To record various risk factors [i.e. elderly patients, diabetes, renal impairment, smoking, risk score (Global Registry of Acute Coronary Events {GRACE} score) and their association with ACS and usage of Ticagrelor.

(2) To observe the usage of ticagrelor in patients pre-loaded with Clopidogrel.

(3) To observe the duration of treatment with Ticagrelor.

(4) To describe the switching or discontinuation (< 12 months) of ticagrelor therapy and reasons for the same.

(5) To record clinical events (bleeding, dyspnoea, CV events) reported by the investigator during the follow-up period.

(6) To observe the usage of ticagrelor in patients who received fibrinolytic therapy for current ACS event.

Methods:

The study was planned to enroll a total of 3000 ACS patients. The duration of participation was 12 months with visits at 1, 3, 6 and 12 months, if subjects were not able to come to the site, telephonic visit were conducted. Once the subjects signed the informed consent and met eligibility criteria they were enrolled in the study. The data was collected on a case report form. Subject data pertaining to demographic characteristics, disease characteristics, medical history, vital signs, physical examination, laboratory investigations, angiography findings, management of ACS were recorded at baseline. Data regarding clinical events (bleeding, dyspnea, and CV events), ticagrelor discontinuation and ongoing current treatment were captured at all follow-up visits.

Inclusion Criteria:

Patients hospitalized with the diagnosis of UA, STEMI or NSTEMI were eligible to participate if all the following criteria met:

1. Written informed consent was provided.
2. Contact order form* was provided.
3. Aged 18 years or older.
4. Male/female with ACS on ticagrelor on discharge or ≤ one month.
5. The patient underwent PCI, CABG or MM for ACS.
6. Diagnosis of STEMI, NSTEMI or UA using the following definitions:

Criteria for STEMI diagnosis:

(a) History of chest pain/discomfort and

(b) Persistent ST-segment elevation (> 30 min) of ≥ 0.1 mV in 2 or more contiguous electrocardiogram (ECG) leads or presumed new left bundle branch block (LBBB) on admission and

(c) Elevation of cardiac biomarkers (creatinine kinase MBCK-MB, troponins): at least one value above the 99th percentile of the upper reference limit.

Criteria for NSTEMI diagnosis:

(a) History of chest pain/discomfort and

(b) Lack of persistent ST-segment elevation, LBBB or intraventricular conduction disturbances and

(c) Elevation of cardiac biomarkers (CK-MB, troponins): at least one value above the 99th percentile of the upper reference limit.

Criteria for Unstable Angina diagnosis:

(a) Symptoms of angina at rest or on minimal exercise and

(b) Transient ST-T changes and

(c) No significant increase in biomarkers of necrosis but objective evidence of ischaemia by non-invasive imaging or significant coronary stenosis (at angiography).

Exclusion Criteria:

The patient was excluded from the study if they fulfilled any of the following criteria:
1. Presence of any condition/circumstance which in the opinion of the treating physician significantly limited the complete follow up of the patient (e.g. tourist, non-native speaker or does not understand the local language, psychiatric disturbances).

2. Presence of serious/severe co-morbidities in the opinion of the investigator which limited short term (i.e. six months) life expectancy.

3. Current participation in a clinical trial with a non-licensed investigational medicinal product

4. Pregnancy or lactation

5. Patients with medical history of intracranial haemorrhage

6. All those patients who were not fit to receive ticagrelor as per the latest prescribing information.

Results:

The study recruited 2997 subjects from 49 sites in India. Approximately half ACS subjects had STEMI (48.9%), and PCI was used as management in 92.4% subjects. The mean (SD) duration of use of ticagrelor was 314 (110.2) days over a period of 12 months. Of 136 subjects (4.5%) who experienced any clinical events, CV deaths were reported in 20 (0.7%), MI and IS in five (0.2%) subjects each, and severe dyspnea was reported in 71 (2.4%) subjects. Out of 33 bleeding cases, 25 (0.8%) patients had TIMI minimal, seven (0.2%) had TIMI minor, and one TIMI major. PLATO major was reported in two subjects and CABG bleed in one subject.

Conclusion:

This real world study, observed use of ticagrelor across ACS types and in different management strategies in real world settings in India. Majority of the subjects who had STEMI and underwent PCI were prescribed ticagrelor. Moreover, the most commonly used stent was a drug eluting stent. In subjects who have an acute coronary syndrome with or without ST-segment elevation, treatment with ticagrelor reported the overall low incidence of CV events. The study observed the very low incidence of adverse effects with minor bleeding or dyspnea as the only non serious adverse effects. The major reason for discontinuation of the drug was non-affordability of treatment

Statistical Analysis

Statistical analysis wherever specified was performed using SAS version 9.4 (SAS Institute, Cary, NC, USA). This paper summarizes findings of an observational study and presents primary & secondary endpoint data from the analysis. Categorical variables were summarized with the frequency and percentage of patients in each category. Continuous variables were summarized descriptively with the number of patients, mean, standard deviation, minimum, median and maximum values.