PROTOCOL AND STATISTICAL ANALYSIS PLAN

Study Title: Cangrelor in ST-Elevation Myocardial Infarction to Decrease Infarct Size

Institution/Site:	University of Kentucky-Gill Heart Institute
Document (Approval/Update) Date:	12/13/2017
NCT Number:	NCT03043274
IRB Number	16-0990-F6A
Coversheet created:	05/22/2020

Methods:

Patients presenting with STEMI from February 2017 to February 2019 at the University of Kentucky hospitals were randomized to receive either cangrelor and ticagrelor or ticagrelor alone (standard group) before PPCI. All patients provided written informed consent approved by the institutional review board. Patients who were hemodynamically unstable with evidence of cardiogenic shock, mechanically intubated, already on dual antiplatelet therapy, or received thrombolytics were excluded. Patients received cangrelor with a dose of 30 mcg/kg bolus followed by a 4 mcg/kg/min intravenous infusion, started prior to PPCI and continued for 2 hours or for the duration of the procedure, whichever is longer. The detailed study protocol was previously reported (NCT03043274). The study was terminated because of slow recruitment. Peripheral blood (PB) samples were collected at the beginning of the PPCI procedure and before intervention (baseline), at 10-minute after starting study drug and at the end of the procedure to assess platelet aggregation in response to adenosine diphosphate (ADP) and thrombin receptor activating peptide (TRAP) using Multiplate system. Additionally, we examined circulating pro-inflammatory cells, cytokine levels, and surrogate markers for neutrophil extracellular traps (NETs), such as plasma elastase and myeloperoxidase (MPO) in the PB before PPCI, then at 6 and 12 hours after randomization using Milliplex human cytokine magnetic kit (MILLIPLEX MAP for Luminex xMap Technology, Millipore, USA) or standard ELISA kits (BD biosciences, USA) according to the manufacturer's protocol. Myocardial damage/edema (defined as myocardial tissue enhancement greater than 5 SD) were assessed using late gadolinium enhancement (LGE) on cardiac magnetic resonance at 48 hours (before hospital discharge) and at 3 months after randomization (6). Troponin I was measured during the first 12 hours after iniating the study drug.

For baseline characteristics, categorical variables were presented as frequencies and proportions and were compared using chi-square test. Continuous variables were summarized as mean with standard deviations or median with interquartile ranges as appropriate, and were compared using student T-test or Mann Whitney U test. ADP-and-TRAP-induced platelet aggregations, inflammatory cells, pro-

inflammatory cytokines, total elastase and elastase-myeloperoxidase, left ventricular ejection fraction (LVEF), and LGE-5SD were compared between both groups. All statistical analyses were performed using SPSS software (IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp Released 2016) and GraphPad Prism 8 (San Diego, USA).