Bleeding rates on Ticagrelor versus Clopidogrel in Patients with Acute Cornary Syndrome

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3/2012

BACKGROUND

In patients who have acute coronary syndromes with or without ST-segment elevation, guidelines recommended dual antiplatelet therapy with aspirin and clopidogrel. The efficacy of clopidogrel is limited by slow and variable transformation of the prodrug to the active metabolite, modest and variable platelet inhibition and an increased risk of stent thrombosis and myocardial infarction in patients with poor physiologic response.

TIcagrelor is reversible and direct-acting oral antagonist of the P2Y12 receptor which provides a faster, greater, and more consistent P2Y12 inhibition than clopidogrel. The Study of Platelet Inhibition and Patient Outcomes (PLATO) was conducted to determine whether ticagrelor was superior to clopidogrel for the prevention of vascular events and death in patients with ACS.

Ticagrelor was shown to be superior to clopidogrel with decreased mortality rates. The two groups did not differ significantly with regard to the rates of major bleeding, However, the ticagrelor group had a higher rate of fatal intra-cranial bleeding (11 events in ticagrelor group vs 1 event in the clopidogrel group).

Despite this ticagrelor was approved by the FDA and the ACS protocol at CPMC was changed to include TIcagrelor as the preferred agent for platelet inhibition for NSTEMI or STEMI.

STUDY PURPOSE

The purpose of the proposed study is to further investigate the bleeding events at Columbia-Presbyterian Medical Center (CPMC) with ticagrelor compared to clopidogrel. The hope is that there will not be bleeding rates above that in the PLATO study and perhaps even a lower bleeding rate in-house.

STUDY DESIGN AND STATISTICAL ANALYSIS

A. The proposed study as an observational one.

B. Study Arms

    1. Using the CPMC EMR system, all patients who are prescribed loading doses of ticagrelor will be captured and their course will be tracked throughout their hospital stay

2. Similarly as the above, all patients who are prescribed loading doses of clopidogrel will be captured and their course will be tracked throughout the hospital stay

C. Primary Outcome: Any event of bleeding while in-house

D. Statistical Analysis

1. Sample size: Using the Chi-square test for proportions and using the PLATO statistic that overall ticagrelor bleeding rate is 4.5% and clopidogrel bleeding rate is 3.8% an effect size of 0.7% gives a sample size of 13, 030 with an alpha of 0.05 and 80% power

E. Study Procedure

1. Patients will be recruited as stated above by capturing the orders placed for the study medications. These patients will be followed during their hospital stay and bleeding events of any kind related to the study medication will be recorded and entered into the database

F. Study Drugs (as per established ACS protocol)

1. Ticagrelor: 180 mg loading dose x1 followed by 90 mg bId
2. Clopidogrel: 600 mg loading dose x 1 followed by 75 mg daily

G. Medical Device: n/a

H. Study Questionnaires: n/a

I. Study Subjects

I. Inclusion Criteria

I. All Patients with diagnosed with Acute Coronoary Syndrome whether STEMI or NSTEMI and prescribed clopidogrel or ticagrelor

II. Exclusion Criteria

I. previous history of stroke

II. previously on clopidogrel or ticagrelor

J. Recruitment of Subjects: as above

K. Confidentiality of Study Data

1. All study data will be coded and data will be stored in a secure location only accessible to study investigators

L. Potential conflict of interest: none to disclose

M. Location of the Study: CPMC

N. Potential Risks: bleeding, fatal or otherwise

O. Potential Benefits: decreased mortality and decreased risk of stent thrombosis

P. Alternative Therapies: N/A

Q. No Costs to subjects or Minors as research subjects

R. Radiation: patients will be exposed to radiation in the cardiac catheterization lab and the exposure will depend on procedure and operator

Solution

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