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ANTIPLATELET THERAPY

CRT-100.12

Risk of Bleeding Among Cangrelor-Treated Patients Administered Upstream P2Y12 Inhibitor Therapy

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INTRODUCTION Little is known about the use of cangrelor in patients with MI who are treated with an oral P2Y12 inhibitor upstream prior to cardiac catheterization.

METHODS CAMEO (Cangrelor in Acute MI: Effectiveness and Outcomes) is a 12-hospital observational registry studying platelet inhibition for MI patients undergoing cardiac cath. Upstream oral P2Y12 inhibition was defined as receipt of an oral P2Y12 inhibitor within 24 hours prior to hospitalization or in-hospital prior to cath. Among cangrelor-treated patients, we compared bleeding after cangrelor use through 7 days post-discharge between patients with and w/o upstream oral P2Y12 inhibitor exposure using logistic regression. We examined rates of bleeding among patients with a shorter (<1 hour) vs. longer (1-3 hours or >3 hours) duration between the last oral dose and cangrelor start.

RESULTS Among 1,775 cangrelor-treated MI patients, 433 (24.4%) had upstream oral P2Y12 inhibitor treatment prior to cath. Of these, 165 patients (38%) started cangrelor within 1 hour, 109 (25%) between 1-3 hours, and 134 (31%) > 3 hours after the in-hospital oral P2Y12 inhibitor dose. Cangrelor-treated patients who received upstream treatment were more likely to have a history of prior PCI, MI, PAD, and diabetes and to be clopidogrel-treated (all p<0.01) compared w/o upstream treatment. There was no significant difference in risk of bleeding among cangrelor-treated patients with and w/o upstream oral P2Y12 inhibitor exposure (**Table**). While bleeding events were higher in patients with longer delays to cangrelor initiation, bleeding risk was not significant after adjustment (**Table**).

CONCLUSIONS Bleeding risk was not observed to be higher in cangrelor-treated patients after upstream oral P2Y12 inhibitor exposure compared with patients treated with cangrelor w/o upstream oral P2Y12 inhibitor exposure.

Table. Observed Rates of Bleeding among Cangrelor-Treated Patients who were treated with an upstream oral P2Y12 inhibitor vs. those without upstream treatment

Comparison	Observed Bleeding Rates	Adjusted OR (95% CI)	Adjusted p-value
Upstream (N=34) vs. no upstream (N=114) (ref)*	7.9% vs. 8.5%	0.65 (0.41-1.04)	0.07
**adjusted for: age, sex, race, diabetes, MI type, prior percutaneous coronary intervention (PCI), prior MI, prior CABG, prior peripheral arterial disease (PAD), left ventricular ejection fraction < 40%, and mechanical circulatory support use			
Among in-hospital upstream, when cangrelor was started after last oral P2Y12 inhibitor dose (adjusting for age, sex, race, and CRUSADE bleeding risk)			
1-3 hours (N =11) vs. <1 hour (ref) (N=5)	10.6% vs. 5.0%	2.63 (0.85-8.19)	0.10
>3 hours (N=12) vs. <1 hour (ref)	10.4% vs. 5.0%	1.70 (0.58-5.62)	0.31

CRT-100.25

MicroRNAs as Novel Biomarkers to Guide DAPT After PCI – Preliminary Assessment

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BACKGROUND Although both genetic testing and platelet reactivity measurements are implemented, there is an unmet need for newer biomarkers developed for a simple, quick, reliable and comprehensive prediction of insufficient response to clopidogrel. MicroRNAs are described in the literature as such potential biomarkers. These microRNAs are small non-coding sequences of nucleotides which bind to mRNA sites and block transcription. This causes a decrease in the production of protein. The microRNAs may regulate ADME genes and affect the effective drug concentration in blood. MicroRNAs can be biomarkers for clopidogrel resistance through the ADME genes involved in the metabolism of clopidogrel. In this study we tested six prospective microRNAs as potential biomarkers for guiding antiplatelet therapy among patients with ACS who have undergone PCI.

METHODS 80 patients with an acute coronary syndrome undergoing percutaneous coronary intervention treated in a multidisciplinary hospital in Moscow were consecutively enrolled. As part of dual antiplatelet therapy (DAPT), the patients took aspirin 100 mg daily and either clopidogrel 75mg SID (n=35) or ticagrelor 90 mg BID (n=45). The carriership of 6 clinically relevant polymorphisms for ticagrelor and 17 for clopidogrel was detected. Expression levels of six prospective miRNAs were measured. VerifyNow ("Instrumentation laboratory", MA, US) platelet reactivity was assessed.

RESULTS MiRNAs expression levels showed connection with the results of the platelet reactivity assessment by utilizing VerifyNow assay. MiR-126 (β coefficient=-0.076, SE=0.032, p= 0.021), miR-223 (β coefficient=-0.089, SE=0.041, p= 0.032), miR-29 (β coefficient=-0.042, SE=0.018, p= 0.026), miR-142 (β coefficient=-0.072, SE=0.026, p= 0.008) have the potential to be used as biomarkers and may substitute platelet reactivity testing. ADME genes that demonstrated statistically significant connection with miRNA expression levels showed connection to the following ADME genes: *P2Y12R (A>G, rs3732759)* and miR-29 (p=0.017), miR-34 (p=0.003); *CYP2C19*17 (C-806T, rs1224856)* and miR-142 (p=0.012); *PON1 (Q192R, rs662)* and miR-29 (p=0.004), *ABCG2 (G>T, rs2231142)* and miR-34 (p=0.007).

CONCLUSION This study has revealed new biomarkers for P2Y12-inhibitors resistance testing: miR-29, miR-34, miR-126, miR-142, miR-223.

CRT-100.33

A 30-Day Pooled Analysis of Acetyl Salicylic Elimination Trials (ASET) in Brazil and Japan: Synergy Stent with Prasugrel Monotherapy Without Aspirin

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