

from ongoing All-patient Investigation in patients with pulmonary arterial hypertension (PAH).

METHODS 818 case report forms from patients receiving tadalafil were collected from December 2009 (the drug launch time) to October 2013. The observation period was up to 2 years. 815 eligible patients data was analyzed for safety and 765 PAH patients data was analyzed for effectiveness. WHO functional classification of PAH and 6-minute walking test were used to evaluate effectiveness. The study was conducted in accordance with the Good Post-marketing Study Practice (GPSP) Ministerial Ordinance.

RESULTS The major patient characteristics were: median age (45.4 years), female (67.7%), and patient receiving tadalafil for PAH treatment (93.9%). 37.7% patients were with idiopathic PAH (IPAH), 2.0% were familial PAH (FPAH), and 53.5% were associated with other diseases (APAH) such as collagen vascular diseases (28.0%) and congenital systemic-to-pulmonary shunts (23.9%). 31.17% of the patients developed drug-related treatment-emergent adverse events (TEAEs) such as headache (8.83%), epistaxis (2.33%) and diarrhea (2.21%), which is consistent with the existing safety profile. As for effectiveness, patients who improved more than 1 class of WHO functional classification (e.g. from Class II to Class I) were: 16.1% (120/744) after 3 months treatment, 25.6% (73/285) after 12 months, and 32.4% (34/105) after 24 months. While patients who worsened over 1 class (e.g. from Class I to II) were: 1.5% (11/744) after 3 months, 1.4% (4/285) after 12 month, and 4.8% (5/105) after 24 months. At the end of observation (24 months since the administration), 6-minute walking distance (6MWD) of 52 cases was increased by 51.7 m (mean distance change, 95% CI, 23.0 - 80.4 m).

CONCLUSIONS The interim analysis of the All-Patient Investigation suggests that no new safety concerns were identified in patients receiving long-term tadalafil treatment in daily clinical practice. Based on the results of effectiveness analysis, in spite of limited numbers of cases evaluated, improvement in effectiveness was noted in the course of tadalafil treatment.

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Evaluation of thienopyridine-resistance in Indian patients by measuring platelet aggregation in post-PCI patients receiving antiplatelet medication: Outcomes with 'AggreGuide A-100' platelet aggregometer

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OBJECTIVES In the current era of interventions, monitoring the effectiveness of antiplatelet medications is vital. Considering the emergence of antiplatelet resistance, reduced response to antiplatelet therapy may leads to the stent thrombosis which is associated with high morbidity and mortality. In the present study we evaluated the effectiveness of thienopyridine-based antiplatelet regimens in post-PCI patients using AggreGuide A-100 platelet aggregometer (Aggre-dyne Inc., USA), a new, FDA-approved, easy-to-use, point-of-care device developed to monitor platelet aggregation in whole blood using laser-light scattering technique.

METHODS In this prospective, single-center study, patients who received antiplatelet therapy after undergoing coronary stent implantation at an Indian tertiary care center during May-October, 2014 were enrolled. Platelet aggregation was evaluated from the blood sample of each study participant after 2-3 days of antiplatelet therapy using the AggreGuideA-100. Test results were obtained as platelet activity index (PAI), on a scale ranging from 0 to 10. Since the PAI value <2 is obtained as no detectable aggregation during the test, such observations were assigned the PAI value of 2. Test findings were interpreted as (a) therapy working if the PAI value is 2-5 and (b) therapy not working if the PAI value is above 5.

RESULTS A total of 220 patients (mean age: 55.35±9.51 years; 74.5% males) were enrolled in the study. Among the study group, 79 (35.9%), 100 (45.5%), and 41 (18.6%) patients received Clopidogrel-, Prasugrel-, and Ticagrelor based antiplatelet therapy respectively, at the discretion of the treating physician. The AggreGuide A-100 testing indicated that the effectiveness of antiplatelet therapy was inadequate in 43 (19.5%) patients. In particular, 30 (38.0%) patients receiving Clopidogrel-, 11 (11.0%) patients receiving Prasugrel-, and 2 (4.9%) patients receiving Ticagrelor- based antiplatelet therapy displayed inadequate platelet response. Antiplatelet therapy was optimized accordingly for these patients.

CONCLUSIONS Monitoring individual's platelet activity should become a new standard-of-care for patients on antiplatelet therapy.

Using AggreGuide A-100, nearly 20% of patients were identified to have inadequate response to thienopyridine-based antiplatelet therapy in our study. Antiplatelet therapy was optimized accordingly for these patients with inadequate response.

GW26-e0691

Variability of ticagrelor antiplatelet responsiveness in Chinese ACS patients

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OBJECTIVES Ticagrelor provides more consistent, rapid, and potent platelet inhibition than clopidogrel, however, the interindividual variability in response to ticagrelor was not absent. This study sought to display the various distribution of ticagrelor antiplatelet responsiveness in Chinese acute coronary syndrome (ACS) patients.

METHODS Consecutive Chinese-Han patients with ACS who received maintenance dose of ticagrelor (90 mg, bid) and aspirin (100 mg, qd) were recruited from General Hospital of Chinese People's Liberation Army. After 5 days ticagrelor maintenance treatment, 5μmol/L ADP induced residue platelet aggregation (RPA) by light transmittance aggregometry (LTA), and platelet inhibition (PI_{ADP}) measured by thrombelastography (TEG) were measured.

RESULTS Overall, 532 ACS patients (Male: 72.56%, Age: 60±11 years) under ticagrelor maintenance treatment were recruited. Antiplatelet responsiveness measured by LTA was available in 146 patients, and by TEG in 176 patients. After 5 days' ticagrelor maintenance dose therapy, the value of RPA measured by LTA was (13.87±9.41)% on average (range from 1.80% to 51%). With the pre-specific cutoffs for HTPR (5μmol/L ADP induced RPA >40%), 4 patients (2.74%) were identified as HTPR. The value of PRA <10% could be seen in fifty-six patients (38.36%). The value of PI_{ADP} measured by TEG was (85.92±17.79)% on average (ranged from 4.80% to 100%). The distribution curve of both RPA and PI_{ADP} values moved to the direction of strong antiplatelet responsiveness with the possibility of increased risk for bleeding.

CONCLUSIONS The variability of ticagrelor antiplatelet responsiveness could be detected in Chinese ACS patients. Association of the ticagrelor antiplatelet responsiveness variability to clinical efficacy and safety outcomes should be evaluated in the future.

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Ticagrelor overcomes high on-clopidogrel treatment platelet reactivity in patients with acute myocardial infarction or coronary artery in-stent restenosis: a randomized controlled trial

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OBJECTIVES High on-treatment platelet reactivity (HTPR) after clopidogrel therapy is accompanied by an increased risk of adverse outcomes. Direct comparison between ticagrelor and high-dose clopidogrel has not yet been reported in patients with acute myocardial infarction (AMI) or coronary artery in-stent restenosis (ISR).

METHODS In a prospective, single-center, single-blind, randomized trial, consecutive patients with AMI or coronary artery ISR treated with standard-dose clopidogrel (75 mg/day) were screened with the VerifyNow assay, defining HTPR as P2Y₁₂ reaction units (PRUs) >208. Of the 102 screened patients, 48 (47.06%) patients with HTPR were randomly assigned to either ticagrelor (180 mg/90 mg twice daily) or high-dose clopidogrel (150 mg/day) for 24 hours.

RESULTS Baseline characteristics and mean PRUs were similar in both groups. After 24 hours, ticagrelor was associated with a significantly lower platelet reactivity than high-dose clopidogrel (44.38 ± 40.26 vs. 212.58 ± 52.34 PRU, *P*<0.05). No patient receiving ticagrelor exhibited HTPR, whereas 15 (62.50%) patients after treatment with high-dose clopidogrel remained HTPR (*P*<0.05). During the follow-up (mean, 138.42 ± 53.59 days), no patient exhibited a major bleeding event in either treatment group.

CONCLUSIONS The prevalence of HTPR is high in patients with AMI or coronary artery ISR after standard clopidogrel treatment. Ticagrelor is significantly more effective compared with high-dose clopidogrel in overcoming HTPR.

Clinical Trial Registration—URL: <http://www.Chictr.org>. Unique identifier: RCS14004303