Analysis Population and Events	Rates in Propensity Matched Groups*		Hazard Ratio (95% Confidence Interval)*
Overall Analysis Population	**Bivalirudin**	**Heparin±GPI**	
30-day GUSTO bleeding	3.0%	4.1%	0.72 (0.57-0.90)
30-day MACE	7.6%	8.2%	0.91 (0.78-1.06)
Bivalirudin Group	**Prasugrel**	**Clopidogrel**	
30-day GUSTO bleeding	2.7%	2.5%	1.07 (0.64-1.77)
30-day MACE	7.5%	6.7%	1.09 (0.80-1.48)
Heparin±GPI Group	**Prasugrel**	**Clopidogrel**	
30-day GUSTO bleeding	4.0%	4.3%	0.90 (0.63-1.30)
30-day MACE	5.4%	6.8%	0.85 (0.63-1.15)

*Unadjusted event rates and hazard ratios compare each outcome between treatment groups after 1:1 propensity matching within the described analysis population.

TCT-495

VerifyNow in DIabetes high-on-treatment platelet reactivity: a pharmacodynamic study on switching from clopidogrel to prasugrel (VERDI study)

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Background: Diabetic patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI) frequently exhibit high platelet reactivity (HPR) while on clopidogrel. We aimed to test the hypothesis that in diabetic patients with ACS undergoing PCI exhibiting HPR after standard treatment with clopidogrel, a loading dose of 60 mg of prasugrel is superior to the standard treatment with clopidogrel for the achievement of optimal P2Y12 inhibition within the first 24-36 hours post-PCI.
Methods: The VERDI was a prospective, randomized, single-center, single-blind, parallel design study (NCT01684813). Consecutive diabetic patients with ACS undergoing PCI and loaded with clopidogrel were considered for platelet reactivity (PR) assessment immediately before PCI with the VerifyNow assay (Accumetrics Inc, San Diego, CA), measured in P2Y12 reaction units (PRU). Out of 63 screened patients, 50 (79.3%) patients were found with HPR (defined as PRU $\geq$208) and were randomized to receive a loading dose of 60 mg prasugrel vs the standard dose of clopidogrel. Platelet function was assessed again 24h post-PCI.
Results: Greater platelet inhibition was achieved by prasugrel compared with clopidogrel at 24h post-PCI [38 (9-72) vs 285 (240-337), respectively; median (interquartile range); $p < 0.001$]. The primary end point of non-HPR rate (PRU < 208) at 24h post-PCI was higher in the prasugrel group, twenty-five patients (100%) in the prasugrel group achieved optimal antiaggregation versus 4 patients (16%) in the clopidogrel group; $p < 0.001$. No significant acute bleeding was documented in either group.
Conclusions: Among type 2 diabetic patients with ACS and HPR undergoing PCI with stent, switching from clopidogrel to prasugrel was superior to standard treatment with clopidogrel for the achievement of optimal antiaggregation within the first 24h post-PCI.

TCT-496

Impact of platelet reactivity on clopidogrel after PCI with 2nd generation DES on late lumen loss

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Background: Previous studies had reported that high platelet reactivity (HPR) is associated with recurrent ischemic events after PCI. However, 1st generation drug-eluting stents (DES) were mainly used in those studies. We measured platelet reactivity after clopidogrel loading, late lumen loss by quantitative coronary angiographic analysis (QCA) and assessed mid-term clinical outcomes in patients who underwent PCI with 2nd generation DES.
Methods: Platelet reactive units (PRU) was measured by VerifyNow P2Y12 assays in 396 patients underwent PCI with Everolimus- or Biolimus-eluting stents between August 2010 and May 2013. All patients received 300mg clopidogrel loading immediately after PCI, 368 patients were followed by a maintenance dose of clopidogrel (75-50mg/d) and aspirin (100mg/d). Blood samples were obtained 12 to 24 hours after PCI (initial phase) and 2-4 weeks later (chronic phase). HPR on clopidgrel was defined as 240 or more in PRU. We assessed major adverse cardiovascular event (MACE) including the composite of death, nonfatal MI, stent thrombosis, stroke, and target lesion revascularization (TLR), and bleeding events, QCA was evaluated at baseline and 1-year follow-up.
Results: The value of PRU and rate of HPR on the chronic phase were significantly lower than in the initial phase (249±81 vs. 214±83; p< 0.001, 58% vs. 42%; p< 0.001). In the chronic phase, HPR group had more female and older patients than non-HPR group. There were no significant differences in MACE and bleeding events between two groups (HPR 7.7% vs. non-HPR 7.5%; p=NS). According to QCA, late lumen loss was significantly larger in HPR group compared to non-HPR group (0.29±0.40mm vs. 0.17±0.37mm; p=0.01). Multiple logistic regression analysis indicated that HPR was the only independent predictor for late lumen loss of 0.3mm and over (p=0.015).
Conclusions: There was no significant impact of platelet reactivity on clopidogrel on clinical outcomes after PCI with 2nd generation DES. However, adequate inhibition of platelet reactivity reduced late lumen loss.

TCT-497

Antiplatelet Effects of Clopidogrel and Aspirin During 6 Months of Follow-up After Stent Implantation: An ADAPT-DES Substudy

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Background: Clinical studies have demonstrated an association between high on-treatment platelet reactivity and ischemic events after coronary stent placement, suggesting that platelet function testing may be used to guide antiplatelet therapy. However, periprocedural platelet activation may falsely increase the proportion of patients with high on-treatment platelet reactivity. We therefore investigated the temporal variability in response to clopidogrel and aspirin for up to 6 months after elective coronary placement of drug-eluting stents.
Methods: We determined platelet reactivity in whole blood (VerifyNow P2Y12 and Aspirin assays) and in platelet rich plasma (light transmission aggregometry - LTA) obtained from 121 unselected patients on day 1 after PCI following loading with aspirin ($\geq$300 mg), clopidogrel (600mg), and administration of the first maintenance dose of clopidogrel 75mg, followed by measurements on day 30 and day 180 after PCI on chronic treatment (clopidogrel 75mg qd, ASA 100mg qd). Residual platelet aggregation (RPA) was determined by LTA using adenosine diphosphate (ADP; 5 and 20μM) and arachidonic acid (AA; 500 mg/L). P2Y12 Reaction Units (PRU) and Aspirin Reaction Units (ARU) were assessed using VerifyNow assays.
Results: As seen in the Table, platelet inhibition in response to aspirin was consistent from day 1 to 180. The platelet response to clopidogrel decreased slightly over time. However, defining clopidogrel hyporesponsiveness as a PRU >208, the percentages of hyporesponsive patients were 36.4%, 40.9% and 42.2% on day 1, 30 and 180 respectively (p=0.40).

Antiplatelet Effects of Clopidogrel and Aspirin

		Day 1	Day 30	Day 180	p-value
Clopidogrel effect	VerifyNow PRU	169 (92, 240)	183 (122, 252)	194 (125, 245)	0.047
	- PRU >208	36.4%	40.9%	42.2%	0.40
	RPA ADP 5μM	11 (4, 22)	17 (8, 29)	15 (6, 31)	0.003
	RPA ADP 20μM	24 (10, 43)	36 (22, 49)	32 (17, 49)	0.007
Aspirin effect	VerifyNow ARU	393 (384, 408)	394 (384, 409)	395 (380, 411)	0.55
	RPA AA 500 mg/L	4 (2, 7)	6 (3, 8)	5 (4, 8)	0.18

Results shown as median (interquartile range); p-values by Friedman test.

Conclusions: Serial platelet function testing measured 1 day after aspirin and clopidogrel loading and PCI reliably reflects the response to antiplatelet treatment for at least 6 months.