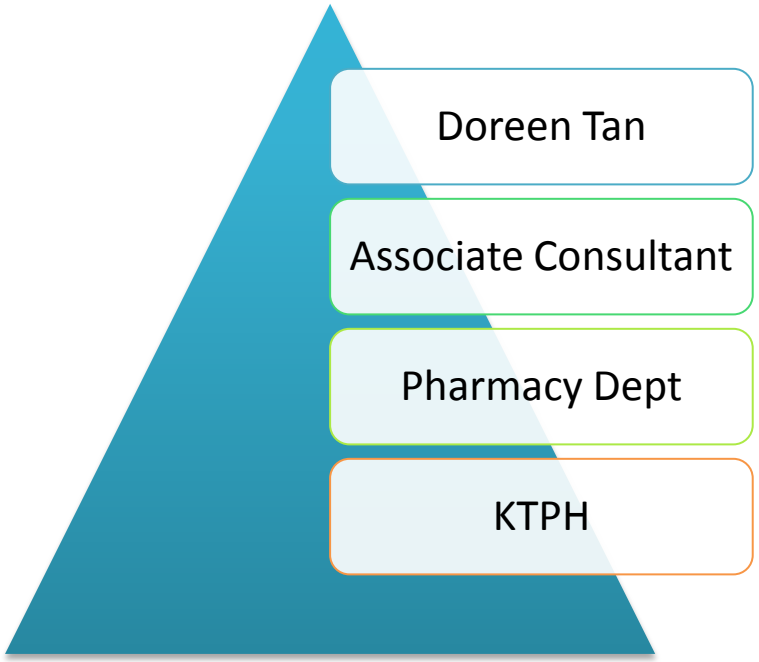
Prasugrel Use in an Underweight Dialysis Patient



SKH 53yo chinese female

CC:

- Presents to emergency department for acute pulmonary edema

PMH:

- Diabetes Mellitus (Type II), Endstage Kidney Disease on intermittent haemodialysis 3 days a week, Hypertension, Hyperlipidaemia.

PE:

- BP 110/78mmHg, HR 78, actual body weight 54kg

Medications prior to admission:

- Acarbose 50mg TDS, Calcitriol 1mg 2x/week, Ca Acetate 667mg BD, Amlodipine 5mg 4x/week, Lanthanum 500mg ON, Renalmin 1 tab OM, Tolbutamide 500mg TDS, Erythropoeitin beta 4000 units once a week on friday

57yo Malay Male

ECG:

- Evolved anterior Myocardial Infarction, underwent percutaneous coronary intervention with drug eluting stents inserted to proximal Left Anterior Descending Artery (Promus premier) & mid circumflex artery (Promus element)

Other issues:

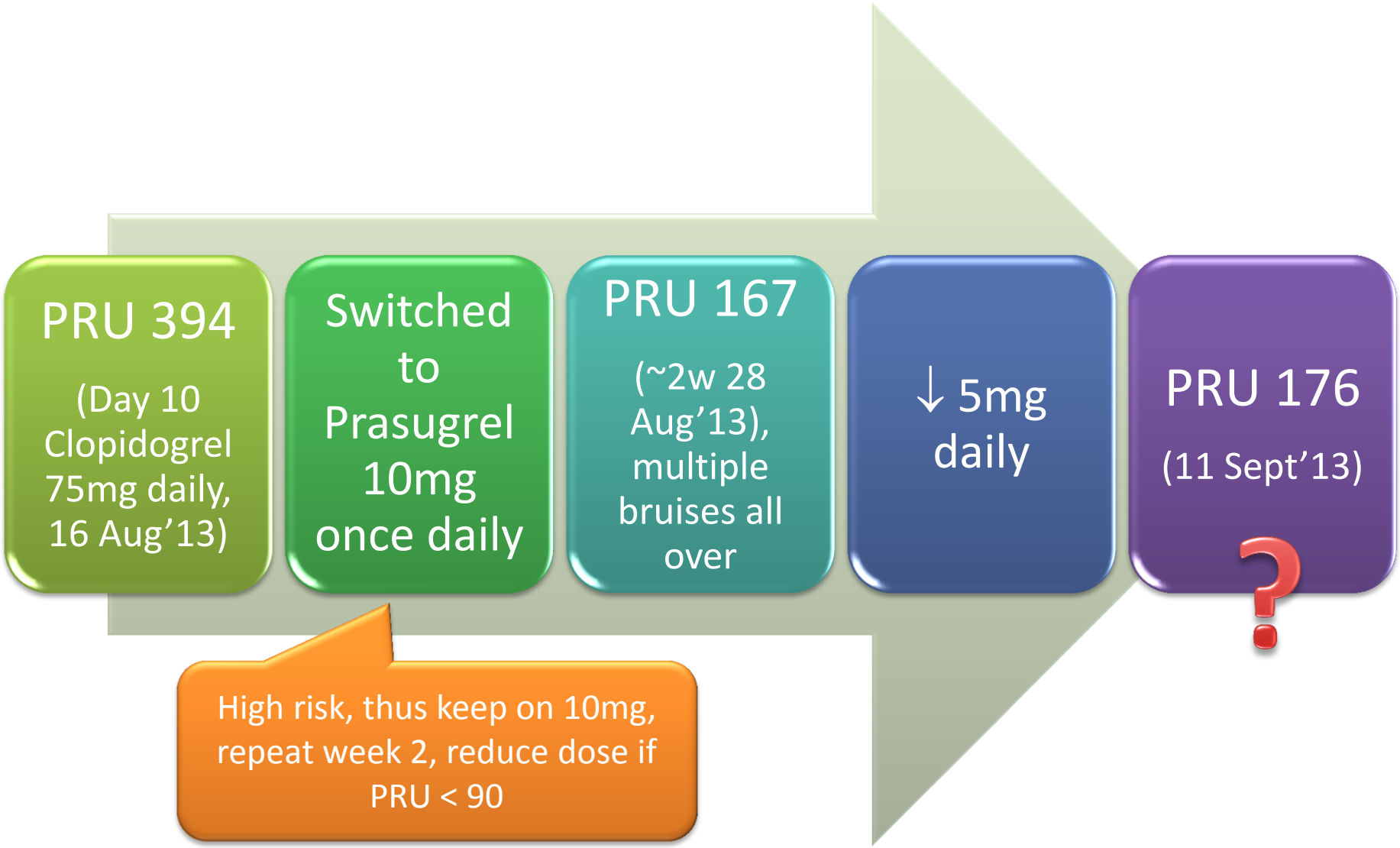
- Developed sepsis, likely pneumonia, put on continuous renal replacement therapy while in ICU

PRU 394 (Day 10)

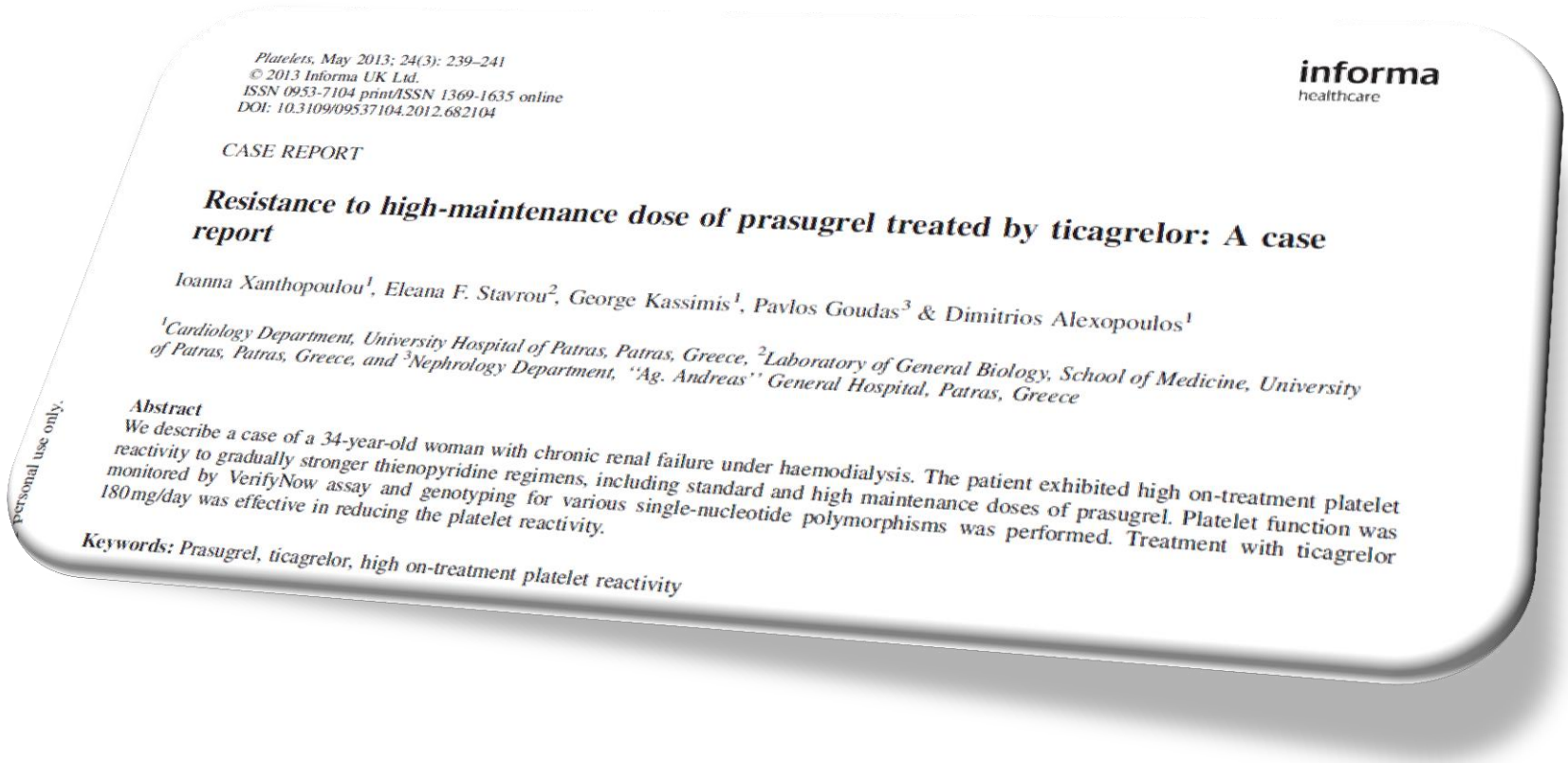
What will you do?

A. Do nothing
B. Double dose of clopidogrel
C. Switch to Ticagrelor in view of BW < 60kg
D. Switch to Prasugrel 5mg daily

Timecourse of platelet reactivity assays (SKH)



PRASUGREL IN RENAL FAILURE



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CASE REPORT

Resistance to high-maintenance dose of prasugrel treated by ticagrelor: A case report

Ioanna Xanthopoulou[1], Eleana F. Stavrou[2], George Kassimis[1], Pavlos Goudas[3] & Dimitrios Alexopoulos[1]

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Abstract

We describe a case of a 34-year-old woman with chronic renal failure under haemodialysis. The patient exhibited high on-treatment platelet reactivity to gradually stronger thienopyridine regimens, including standard and high maintenance doses of prasugrel. Platelet function was monitored by VerifyNow assay and genotyping for various single-nucleotide polymorphisms was performed. Treatment with ticagrelor 180 mg/day was effective in reducing the platelet reactivity.

Keywords: Prasugrel, ticagrelor, high on-treatment platelet reactivity

Personal use only.

CASE REPORT: PRASUGREL NON-RESPONSE

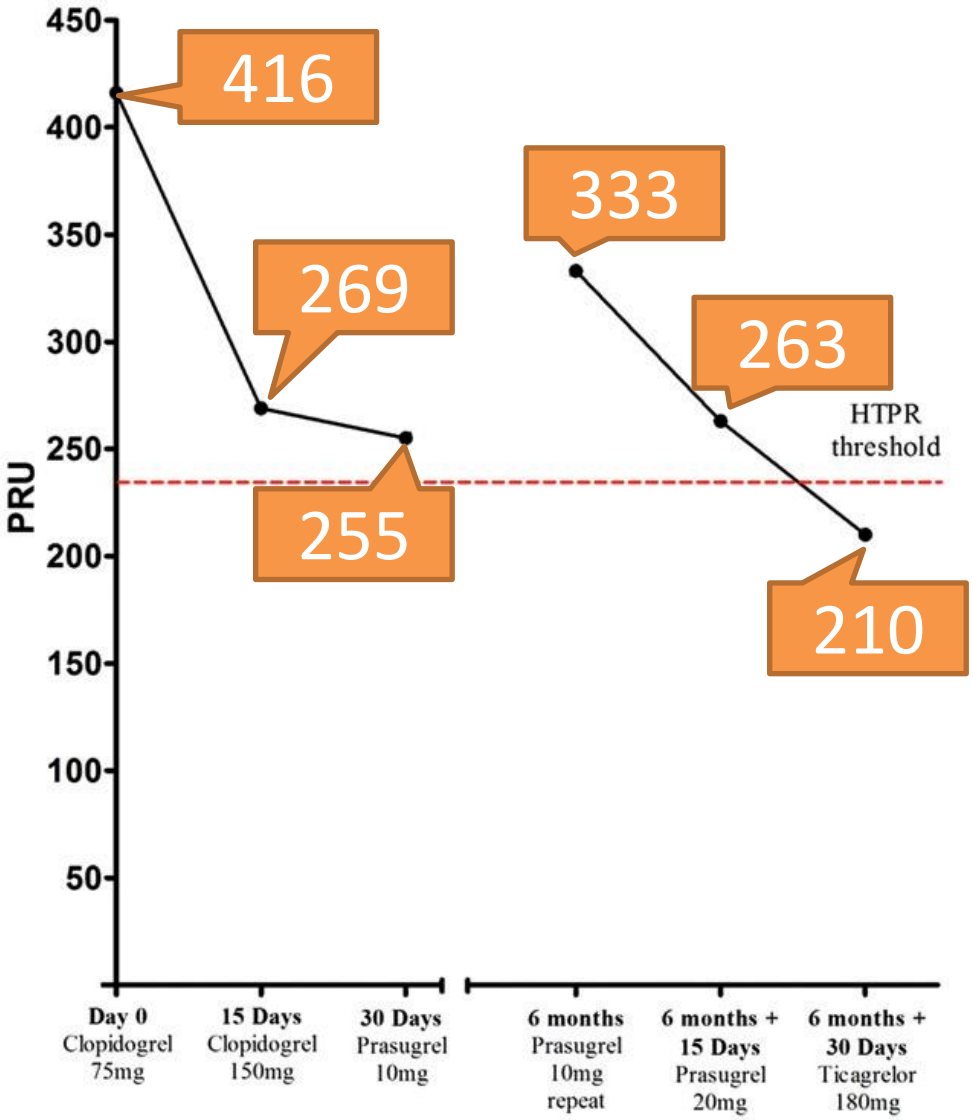
Platelets. 2013;24(3):239-41

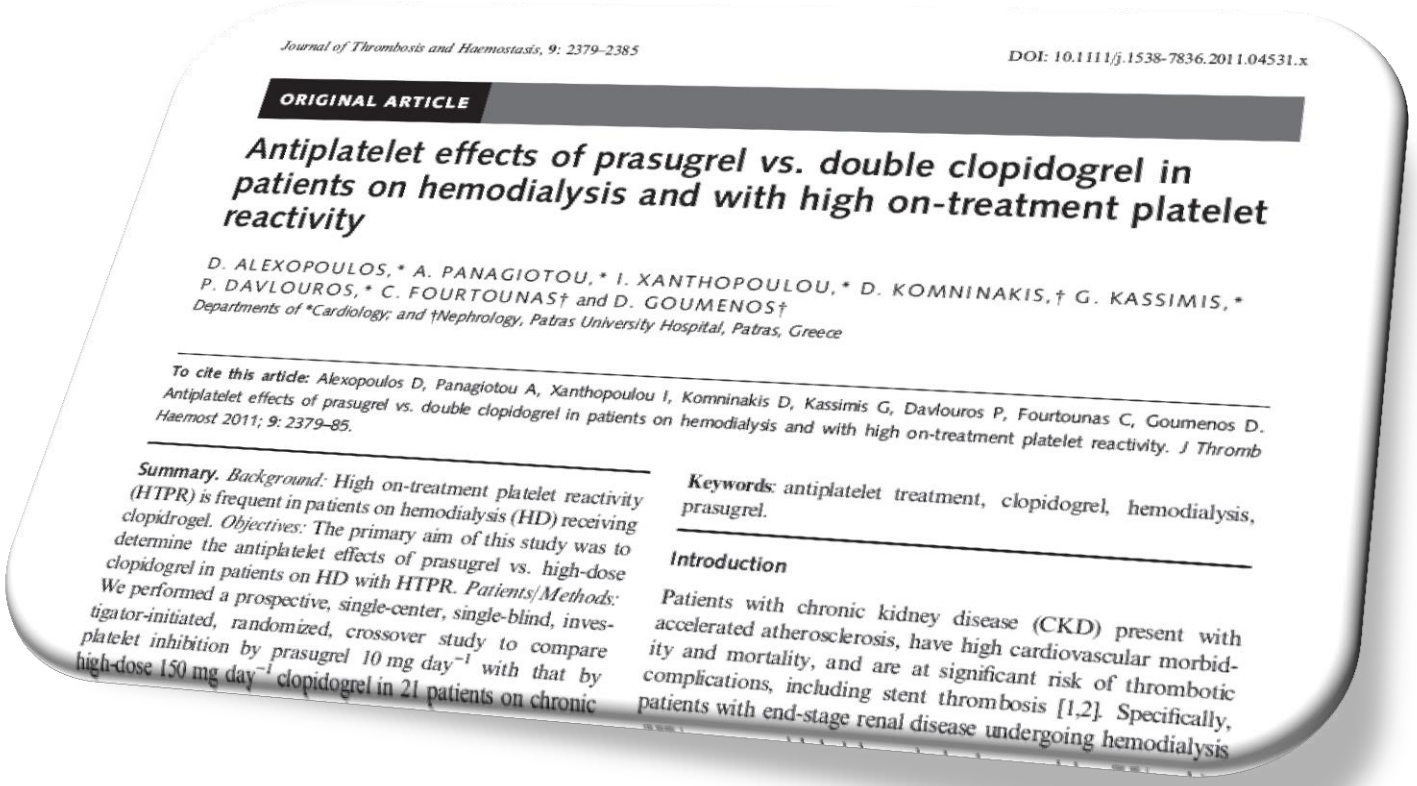
34 yo female

- BMI 28.7 kg/m2, on clopidogrel for thrombotic complications of the vascular access used on haemodialysis
- PMH: Type I Diabetes Mellitus, Chronic Renal Failure undergoing haemodialysis for the past 14 months, presented a persistent inadequate response to gradually stronger thienopyridine regimens.
- Current medication: omeprazole, calcium channel blocker, insulin, and erythropoietin
- Haemodialysis characteristics were kept constant during all PR assessments.

Platelet reactivity trend

- Mainly CYP3A4 and CYP2B6, CYP2C19 and CYP2C9, less significant contribution
- Genetic variation – 2B6, 2C9*3, P2Y12
- Omeprazole & calcium channel blocker





Journal of Thrombosis and Haemostasis, 9: 2379–2385 DOI: 10.1111/j.1538-7836.2011.04531.x

ORIGINAL ARTICLE

Antiplatelet effects of prasugrel vs. double clopidogrel in patients on hemodialysis and with high on-treatment platelet reactivity

D. ALEXOPOULOS,* A. PANAGIOTOU,* I. XANTHOPOULOU,* D. KOMNINAKIS,† G. KASSIMIS,* P. DAVLOUROS,* C. FOURTOUNAS† and D. GOUMENOS†
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Summary. Background: High on-treatment platelet reactivity (HTPR) is frequent in patients on hemodialysis (HD) receiving clopidrogel. Objectives: The primary aim of this study was to determine the antiplatelet effects of prasugrel vs. high-dose clopidogrel in patients on HD with HTPR. Patients/Methods: We performed a prospective, single-center, single-blind, investigator-initiated, randomized, crossover study to compare platelet inhibition by prasugrel 10 mg day^{-1} with that by high-dose 150 mg day^{-1} clopidogrel in 21 patients on chronic

Keywords: antiplatelet treatment, clopidogrel, hemodialysis, prasugrel.

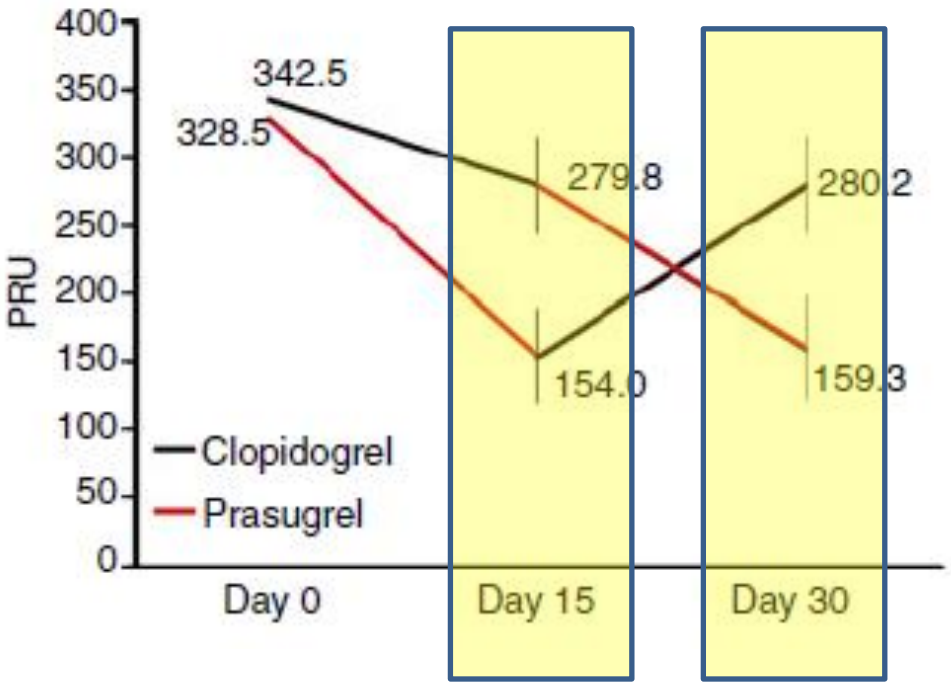
Introduction

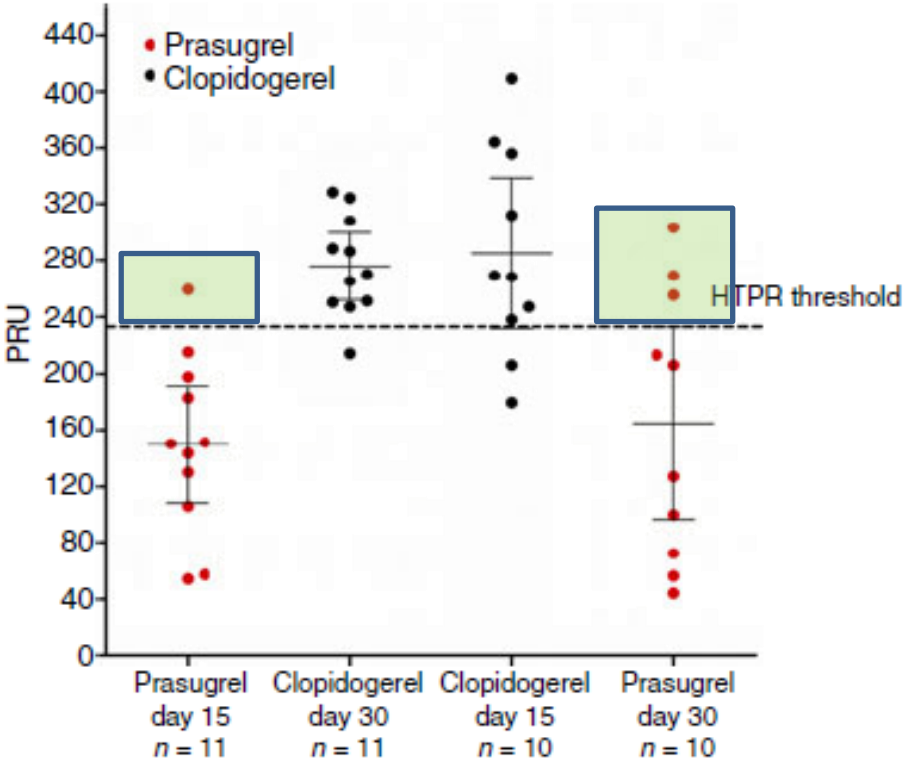
Patients with chronic kidney disease (CKD) present with accelerated atherosclerosis, have high cardiovascular morbidity and mortality, and are at significant risk of thrombotic complications, including stent thrombosis [1,2]. Specifically, patients with end-stage renal disease undergoing hemodialysis

PRASUGREL VS DOUBLE CLOPIDOGREL

J Thromb Haemost. 2011;9(12):2379-85.

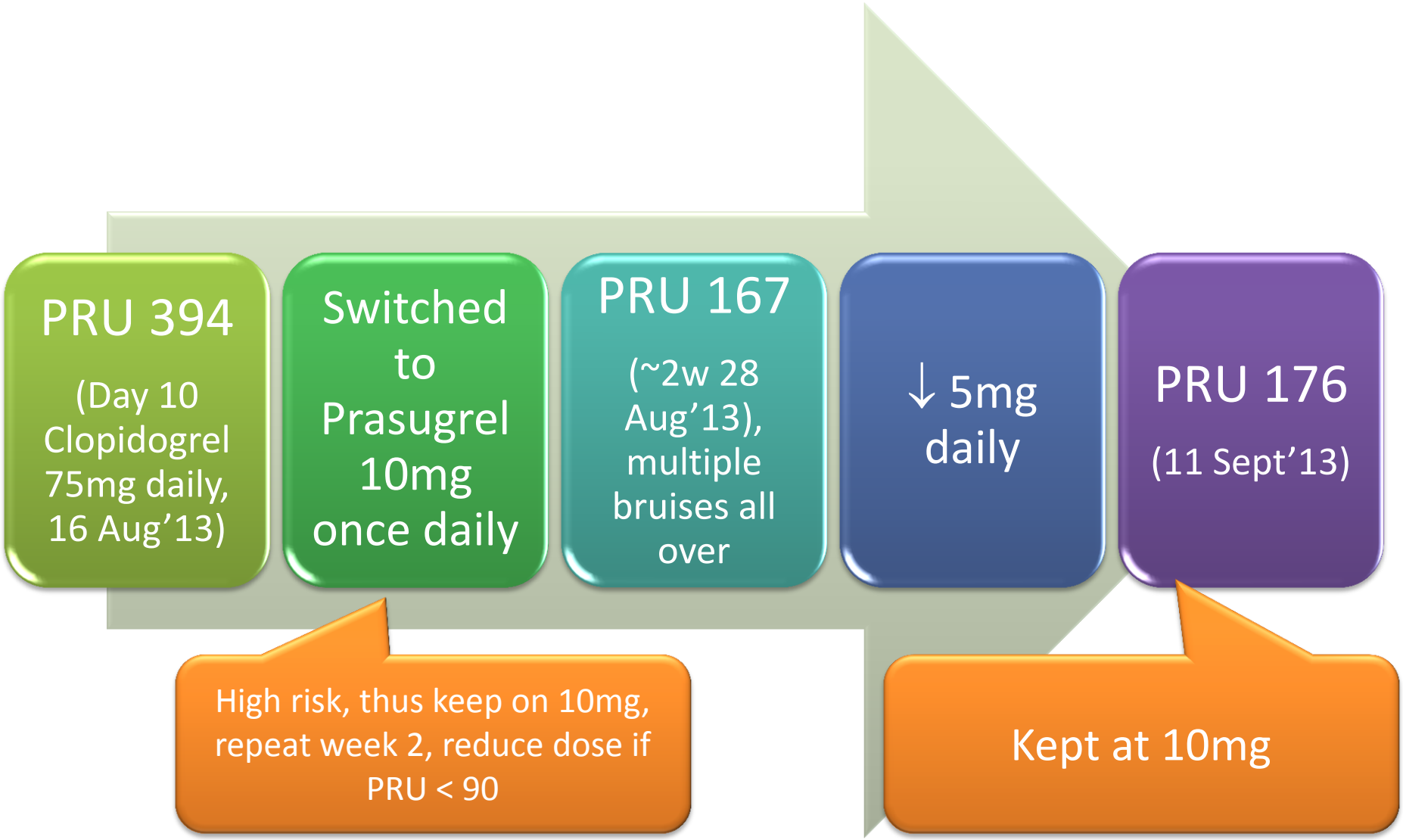
Findings





Prasugrel more effective in dialysis population
19% “resistant” to Prasugrel
Platelet reactivity higher in dialysis population?

Timecourse of platelet reactivity assays (SKH)



Thank you

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10. Rasoulpour M, Banco L, Laut JM, Burke GS. Inability of community-based laboratories to identify pathological casts in urine samples. *Arch Pediatr Adolesc Med*. 1996;150(11):x1201-1204.

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Ticagrelor in Clopidogrel-Resistant Patients Undergoing Maintenance Hemodialysis

To the Editor:

Patients with chronic kidney disease (CKD) and particularly those receiving hemodialysis (HD) frequently are poor responders to clopidogrel (ie, have high on-treatment platelet reactivity).[1-3] Ticagrelor is a cyclopentyl-triazolo-pyrimidine that acts directly on the $P2Y_{12}$ receptor, reversibly antagonizing it. In 3,237 patients with non–dialysis-dependent CKD, ticagrelor reduced ischemic end points and mortality compared with clopidogrel, with no difference in bleeding.[4] To the best of our knowledge, there is no previous report of ticagrelor administration in maintenance HD patients who are clopidogrel poor responders.

This was a prospective 2-center study in which consecutive patients receiving regular maintenance (>6 months) HD and ongoing (≥2 months) treatment with clopidogrel, 75 mg/d, were approached for platelet reactivity assessment. Exclusion criteria and blood sampling details are provided in Item S1. Platelet function was tested with the VerifyNow (Accumetrics Inc, www.accumetrics.com) point-of-care $P2Y_{12}$ assay (results reported as $P2Y_{12}$ reaction units [PRU], with ≥235 PRU considered high on-treatment platelet reactivity) and the Multiplate Analyzer (Dynabyte Informationssysteme, www.multiplate.net; results given in arbitrary aggregation units [AU] per minute).[5,6] Patients with high on-treatment platelet reactivity were prescribed ticagrelor, 90 mg, twice daily for 15 days, when platelet reactivity was assessed. Drug identity was masked from physicians and those assaying platelet function; an independent physician monitored bleeding and other adverse events. Patient adherence to study medication was closely followed by repeated interviews and pill counting. All HD characteristics were kept constant during the study period, and all patients were receiving an appropriate HD dose (Kt/V_{urea} >1.4).

Table 1. Demographic and Clinical Characteristics

	Analyzed Patients (n = 20)	Excluded Patients[a] (n = 4)
Age (y)	67.1 ± 14.0	67.0 ± 5.6
Men	14 (70)	3 (75)
BMI (kg/m^2)	26.5 ± 3.1	26.9 ± 4.5
Time on HD (mo)	57 [268]	100 [127]
Last clopidogrel dose (h)	8 [20]	11 [9]
Last ticagrelor dose (h)	4 [6]	NA
Hyperlipidemia	4 (20.0)	2 (50.0)
Hypertension	16 (80.0)	3 (75)
Diabetes mellitus	11 (55.0)	2 (50.0)
Smoking	0 (0)	0 (0)
Indication for clopidogrel use		
Prior MI	2 (10.0)	0 (0)
Prior PCI	5 (25.0)	1 (25.0)
PAD	6 (30.0)	2 (50.0)
Prevention of thrombosis of HD vascular access	7 (35.0)	1 (25.0)
Laboratory evaluation		
Hematocrit (%)	36.6 ± 3.2	35.5 ± 2.6
Platelets (× 10^3/μL)	236.6 ± 174.7	215.3 ± 83.8
Medication		
Omega-3 fatty acids	9 (45.0)	1 (25.0)
Statins	5 (25.0)	2 (50.0)
Proton pump inhibitors	13 (65.0)	3 (75.0)
ACEi	3 (15.0)	0 (0)
ARB	3 (15.0)	0 (0)
CCB	8 (40.0)	0 (0)
Aspirin	6 (30.0)	1 (25.0)
Nitrates	6 (30.0)	0 (0)
Insulin	7 (35.0)	1 (25.0)
PR at baseline (PRU)	310.4 ± 52.9	288.3 ± 43.8
PR at baseline (AU/min)	485.3 ± 172.8	483.8 ± 148.6

Alexopoulos D, Ticagrelor in clopidogrel-resistant patients undergoing maintenance hemodialysis. Am J Kidney Dis. 2012;60(2):332-3.