

## **Correlation Between Response to Prasugrel and Levels of Reticulated Platelets in Patients with ST-Elevation Myocardial Infarction**

**Leor Perl**<sup>1,2</sup>, Eldad Rechavia<sup>1</sup>, Tamir Bental<sup>1</sup>, Dorit Leshem-Lev<sup>1,2</sup>, Pablo Codner<sup>1</sup>, Alon Eisen<sup>1</sup>, Katia Orvin<sup>1</sup>, Oshrat Dadush<sup>1,2</sup>, Hila Lerman<sup>2</sup>, Alex Battler<sup>1,2</sup>, Ran Kornowski<sup>1</sup>, Eli Lev<sup>1,2</sup>

<sup>1</sup>*Cardiology, Rabin Medical Center, Israel*

<sup>2</sup>*Laboratory of Cardiovascular Biology, Felsenstein Medical Research Institute, Israel*

### **Background:**

Prasugrel is a 3<sup>rd</sup> generation thienopyridine, with significant pharmacodynamic and clinical advantages over clopidogrel. However, despite a lower rate of high on treatment platelet reactivity with prasugrel, there appears to be certain variability in response to this drug as well. The underlying mechanism of this phenomenon is unclear, and may be related to the levels of reticulated platelets (RP) in the circulation. RP are large, young, hyper-reactive platelets, which increase in situations of enhanced platelet turnover. We aimed to determine whether response to prasugrel is associated with the proportion of RP in the circulation, in patients with ST-elevation myocardial infarction (STEMI).

### **Methods:**

Patients with STEMI treated with primary percutaneous intervention (PCI) and prasugrel were tested for platelet reactivity using the VerifyNow P2Y12 assay and the Multiplate analyzer, and for the levels of RP using a flow cytometry assay with Thiazole Orange staining. Tests were performed at two time points: early-at 3-4 days after the PCI, and at follow up: 30 days after the STEMI.

### **Results:**

Thirty two patients with STEMI were included (mean age = 57±9.56, 15.6±0.37% were women, and 26.7±0.45% had diabetes). The levels of RP were strongly correlated with platelet reactivity when evaluated by the VerifyNow assay (Pearson's  $r=0.57$  for PRU) and the Multiplate analyzer results (Pearson's  $r=0.45$ ). When the levels of RP were stratified into tertiles, and the corresponding platelet reactivity was compared, the upper tertile of RP displayed higher platelet reactivity when compared to the lower tertile, according to VerifyNow assay (102.4±62.3 vs. 52.4±38.4 PRU,  $p=0.02$ ) and Multiplate analyzer (21.0±20.5 vs. 7.8±4.2 units,  $p=0.03$ ).

### **Conclusions:**

The proportion of circulating RP strongly correlates with the response to prasugrel in patients with STEMI treated with PCI. Increased levels of RPs are associated with increased platelet reactivity despite prasugrel treatment.