DIABETES Y ENFERMEDAD CORONARIA EN 2011

Como mejorar el manejo médico de los diabéticos con SCA

Antonio Fernández-Ortiz

Jueves, 20 Octubre 2011

Instituto CardioVascular
Hospital Clínico San Carlos
Madrid

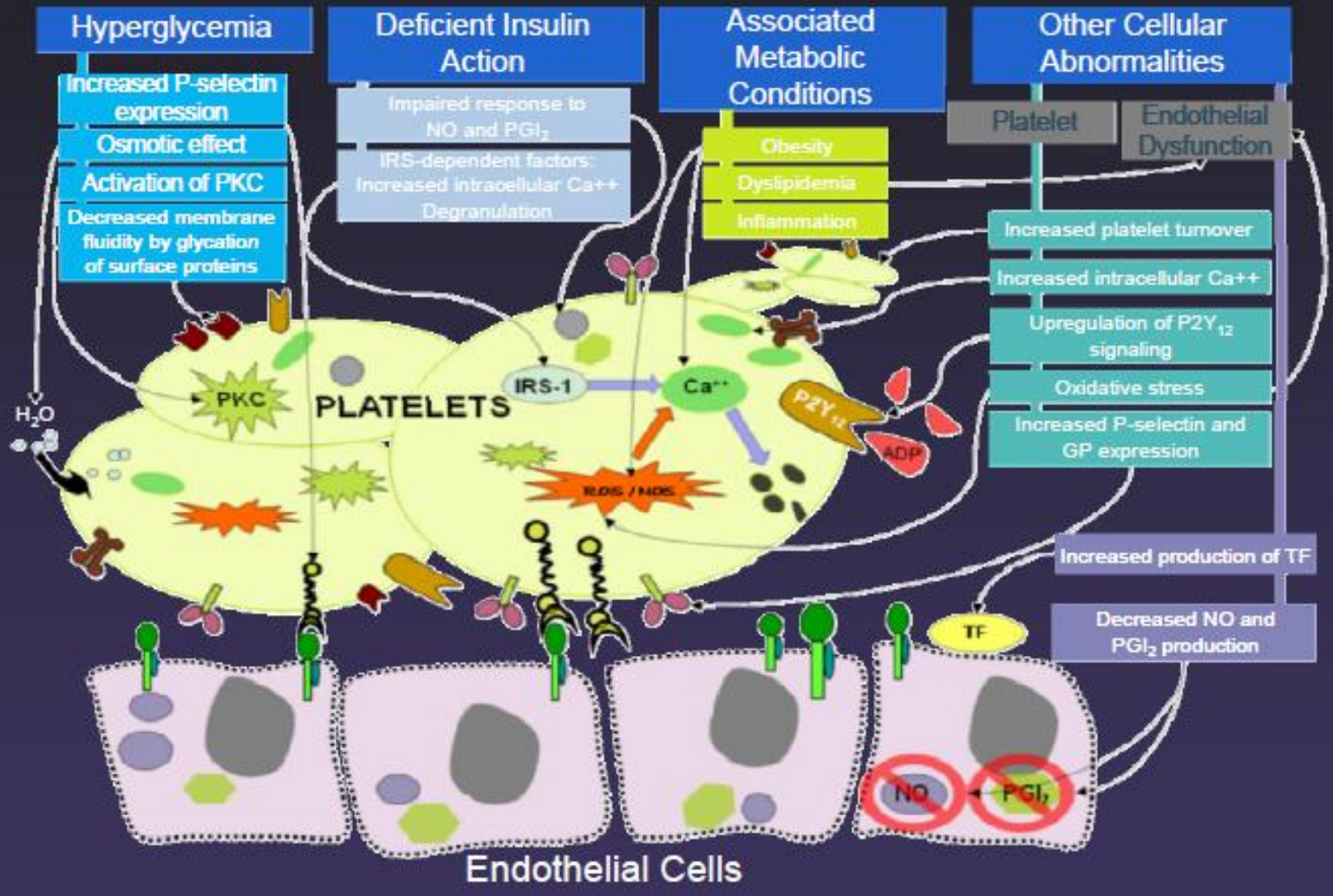
Conflicto de interés:

Antonio Fernández-Ortiz
ha recibido honorarios por charlas y/o consultoria de Eli Lilly, Daichii, Roche, Sanofi Aventis, Bayer, Chiesi, GSK, Astra-Zeneca, Abbott, MSD, The Medicines Company.

Diabetes Mellitus - IHD

- Individuals with type II diabetes have 2-4 fold increased risk of CAD
- Patients with DM without previous MI carry the same level of risk for subsequent ACS as non-diabetic patients with previous MI

Mechanisms Involved in Platelet Dysfunction in Diabetes Mellitus



ACP=adenosine disphosphate; GP=glycoprotein; IRS-1=insulin receptor substrate-1; NO=nitric oxide; PGI_2=prostacyclin; PKC= protein kinase C; TF=tissue factor.

Reprinted with permission from Ferreiro JL, Angiolillo DJ. *Circulation*. In press

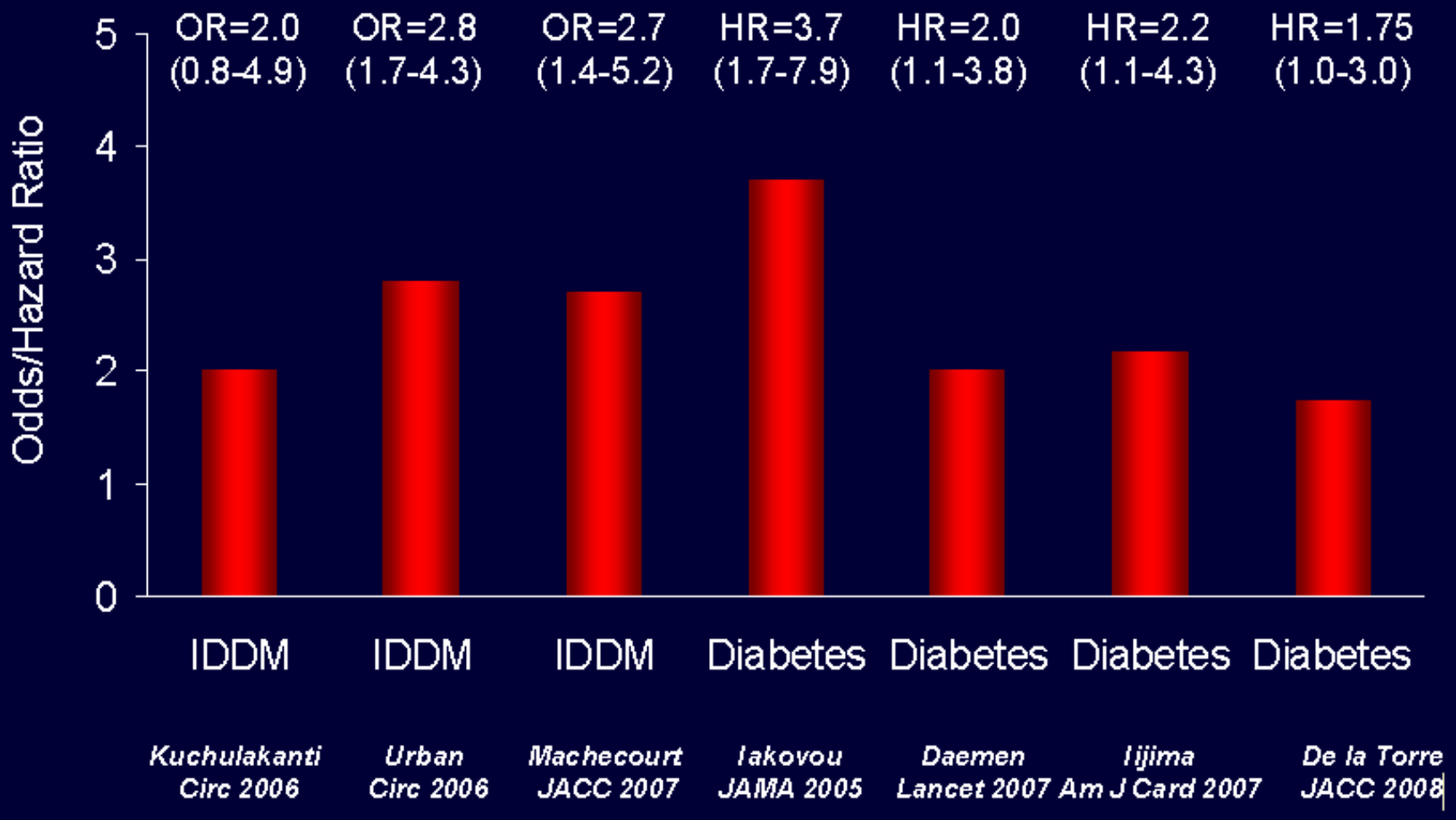
Diabetes Mellitus
- impact of platelet reactivity on cardiovascular outcomes -

	Total Population (n=173)	Q1 <44% (n=41)	Q2 (44-52%) (n=46)	Q3 (52-62%) (n=41)	Q4 >62% (n=45)	P value
Cardiovascular events, n (%)	34 (19.7)	7 (15.2)	5 (12.2)	5 (12.2)	17 (37.8)	0.005
CV death	2 (1.2)	1 (2.4)	1 (2.2)	0	0	0.57
STEMI	1 (0.6)	0	0	0	1 (2.2)	0.41
UA/non-STEMI	29 (16.8)	4 (9.8)	5 (10.9)	5 (12.2%)	15 (33.3)	0.007
ICTUS	2 (1.2)	0	1 (2.2)	0	1 (2.2)	0.61

Threshold of post-treatment platelet reactivity?

DJ, Angiolillo, A Fernández-Ortiz, et a. J Am Coll Cardiol 2007: 50 (16): 1541-1547

Diabetes Mellitus
- as a predictor of stent thrombosis -

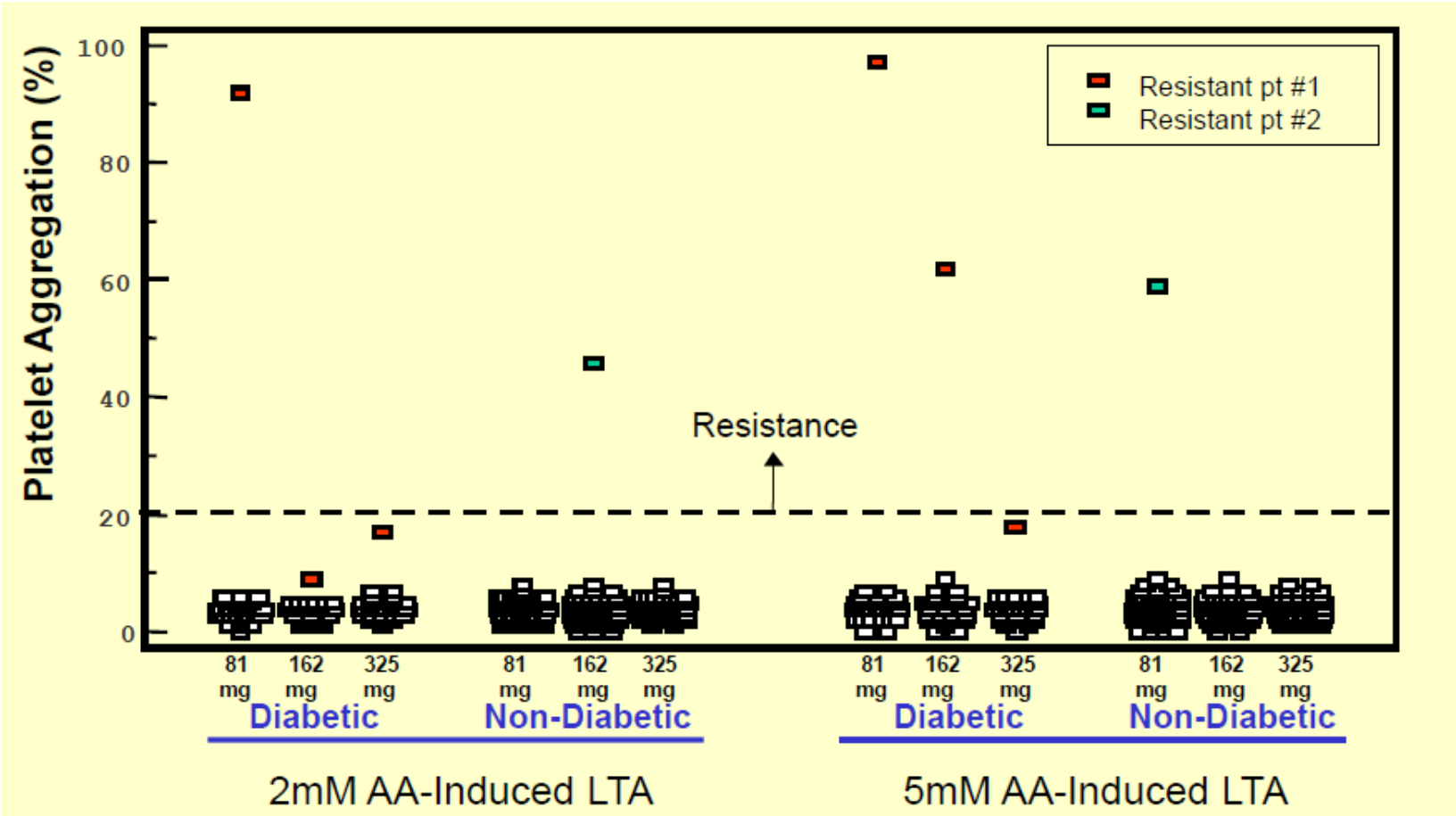


Particularidades de los antiagregantes en diabeticos:

- Aspirina
- Clopidogrel
- Prasugrel
- Ticagrelor
- Inh. GPIIb/IIIa

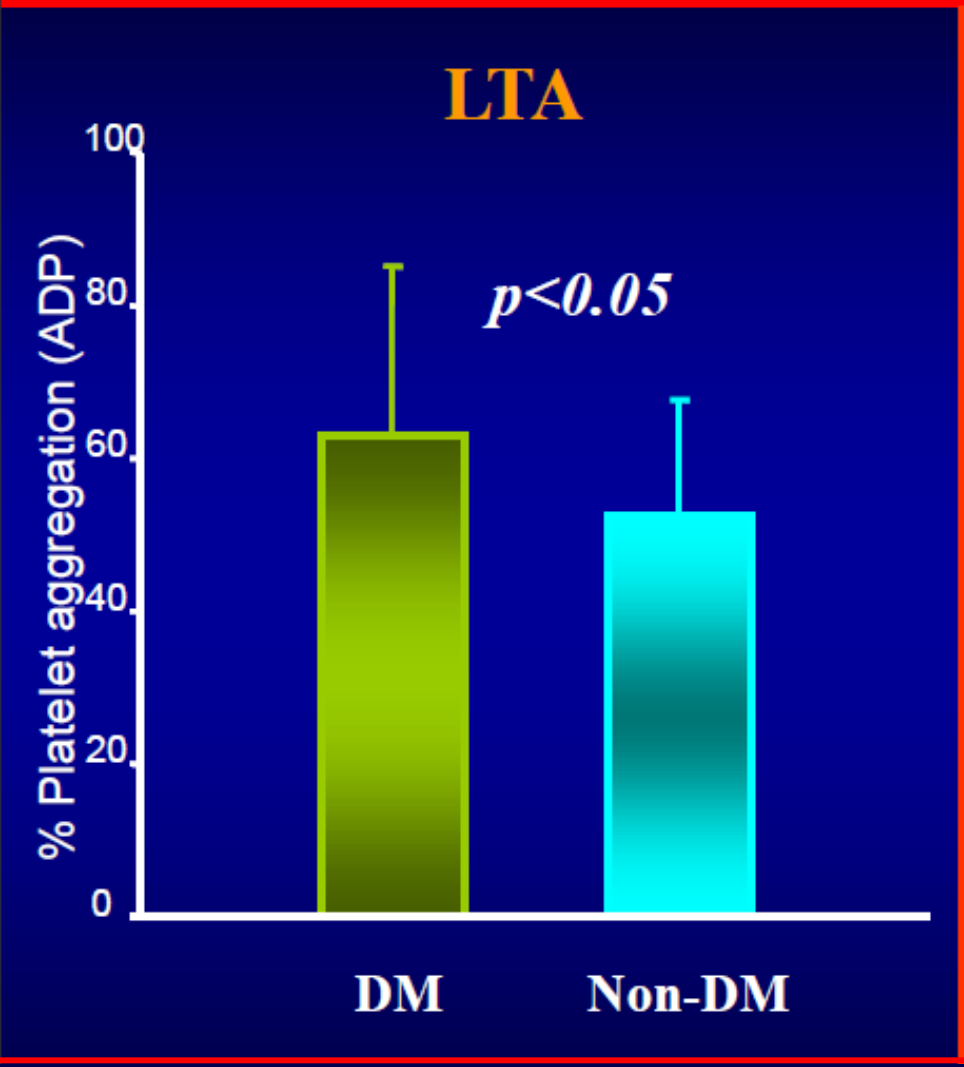
ASPIRINA - DIABETES

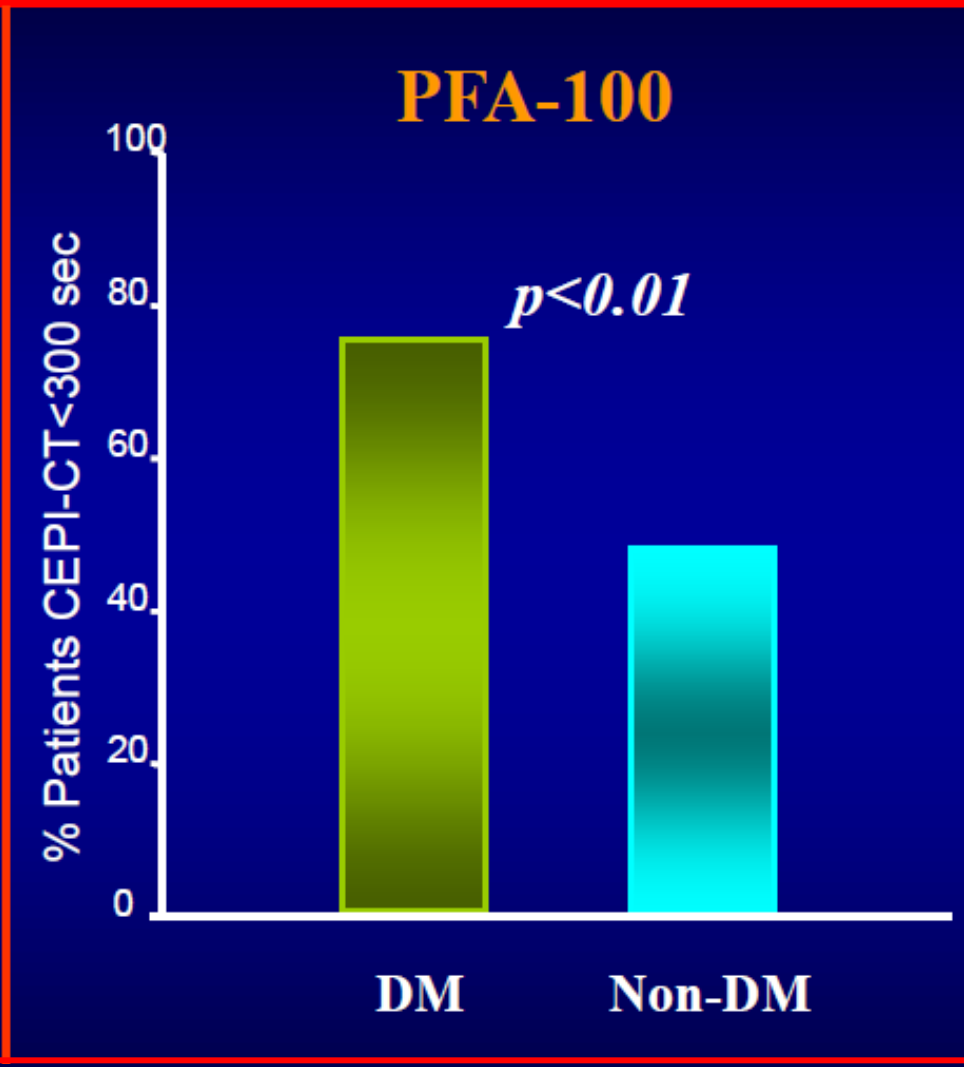
Prevalence "ASA resistance" using COX-1 specific assays



DiChiara J, et al. Diabetes 2007;56:3014-9.

Platelet function (COX-1 non-specific) in DM vs non-DM on aspirin



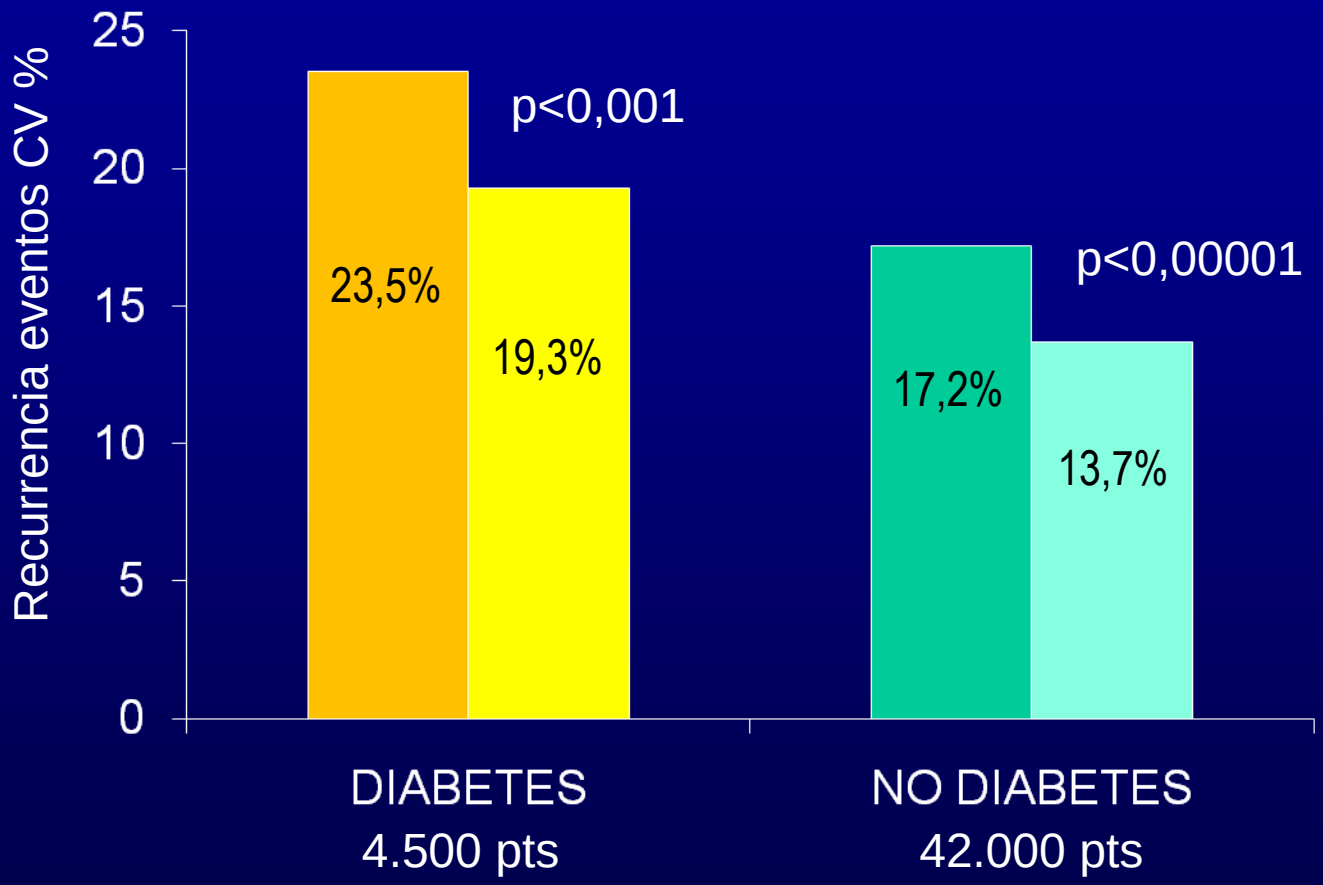


Angiolillo DJ, Fernández-Ortiz A, et al. Diabetes 2005;54:2430-5

Angiolillo DJ, Fernández-Ortiz A, et al. Am J Cardiol 2006;97:38-43.

ASPIRINA – DIABETES en PREVENCION SECUNDARIA:

Antithrombotic Trialists' Collaboration (ATC)



Recomendación : ASPIRINA 75-150 mg diarios de por vida

CLOPIDOGREL - DIABETES

CURE

Beneficial Outcomes with Clopidogrel in Various Subgroups

Characteristic	No. of Patients	Percentage of Patients with Event: Clopidogrel + ASA*	Percentage of Patients with Event: Placebo + ASA*
Overall	12562	9.3	11.4
Associated MI	3283	11.3	13.7
No associated MI	9279	8.6	10.6
Male sex	7726	9.1	11.9
Female sex	4836	9.5	10.7
≤65 yr old	6354	5.4	7.6
> 65 yr old	6208	13.3	15.3
ST-segment deviation	6275	11.5	14.3
No ST-segment deviation	6287	7.0	8.6
Enzymes elevated at entry	3176	10.7	13.0
Enzymes not elevated at entry	9386	8.8	10.9
Diabetes	2840	14.2	16.7
No diabetes	9722	7.9	9.9
Low risk	4187	5.1	6.7
Intermediate risk	4185	6.5	9.4
High risk	4184	16.3	18.0
History of revascularization	2246	8.4	14.4
No history of revascularization	10316	9.5	10.7
Revascularization after randomization	4577	11.5	13.9
No revascularization after randomization	7985	8.1	10.0

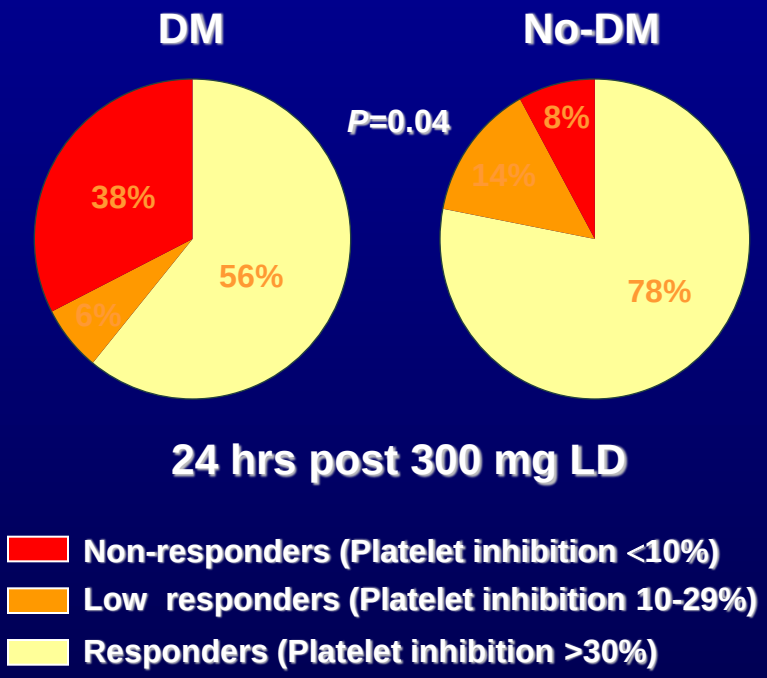
* In combination with standard therapy

The CURE Trial Investigators. *N Engl J Med.* 2001;345:494-502.

CLOPIDOGREL - DIABETES

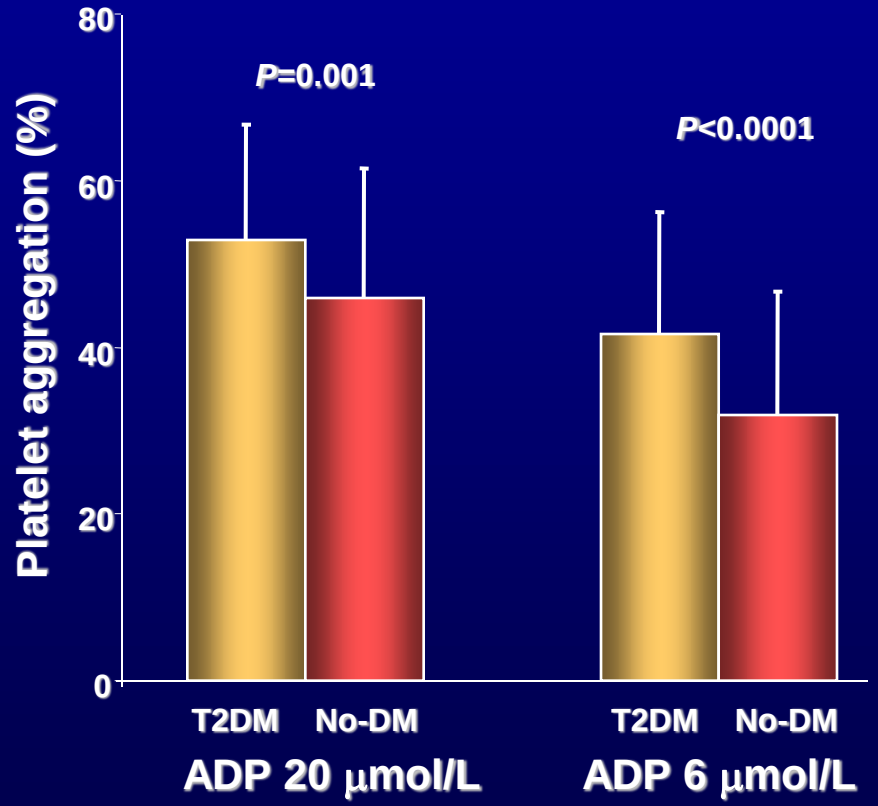
- reduced responsiveness to clopidogrel -

Acute phase of treatment



Angiolillo DJ , Fernández-Ortiz A, et al.
Diabetes. 2005;54:2430-5.

Long-term phase of treatment

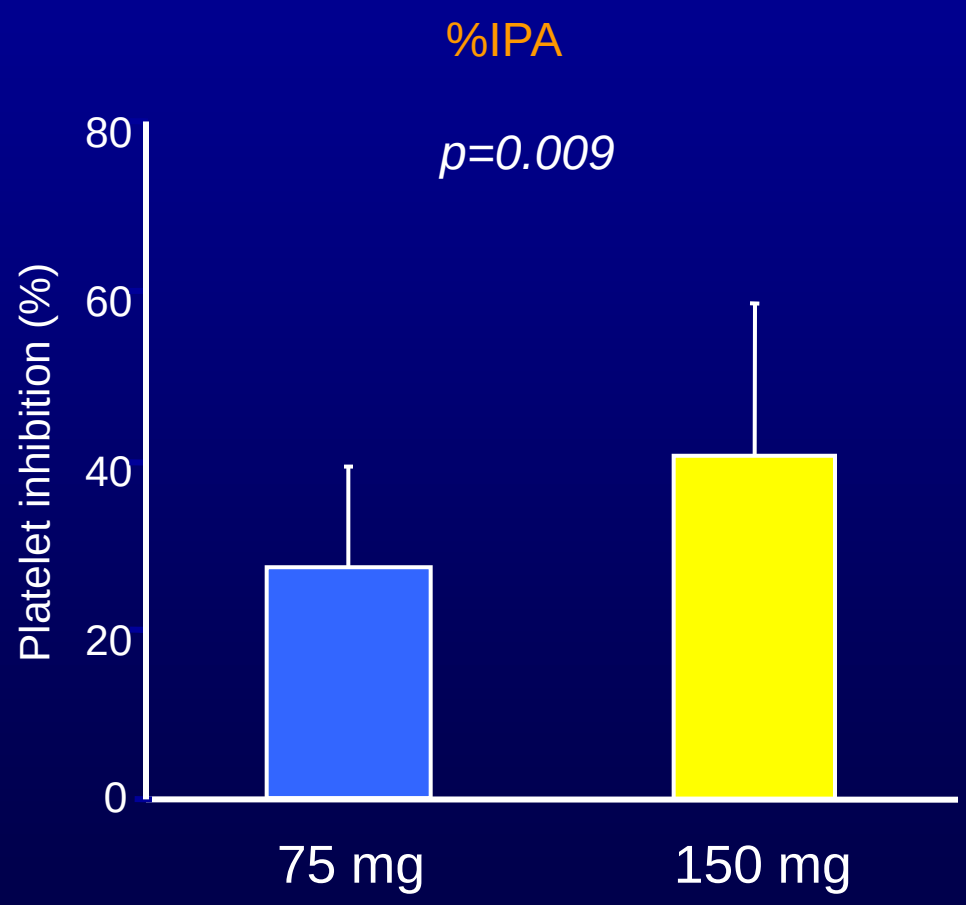


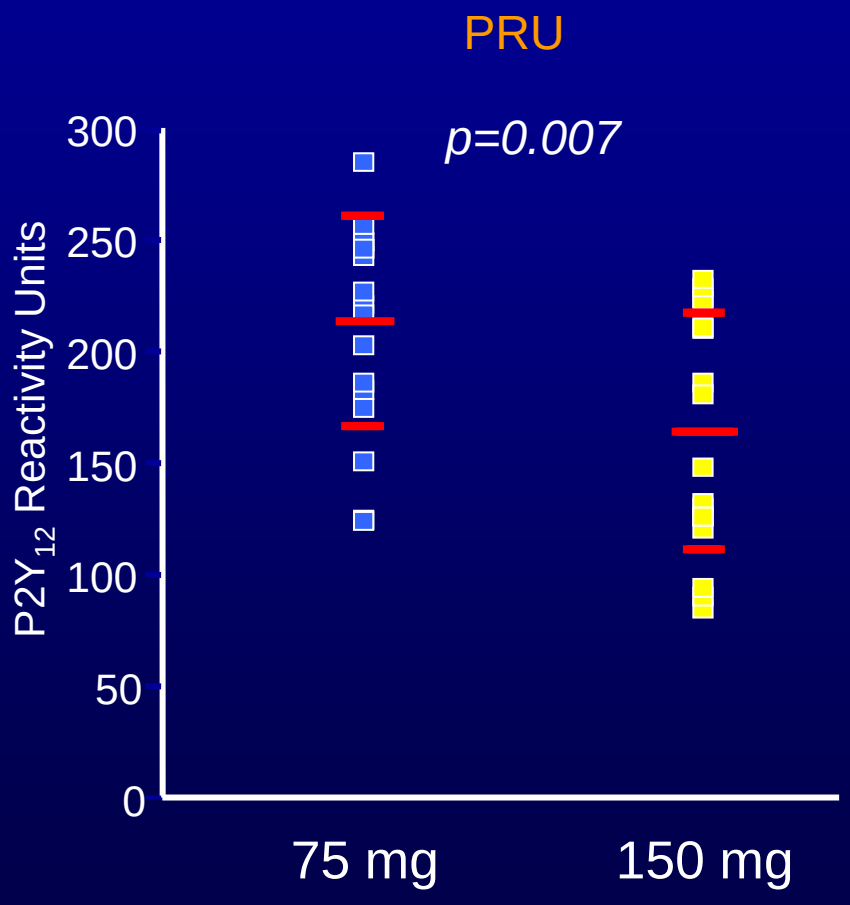
Angiolillo DJ , Fernández-Ortiz A, et al.
J Am Coll Cardiol 2006;48 298-304.

OPTIMUS (Optimizing Antiplatelet Therapy in Diabetes Mellitus)

Impact of high clopidogrel maintenance dosing on platelet function in DM patients with suboptimal clopidogrel response

VerifyNow $P2Y_{12}$ substudy

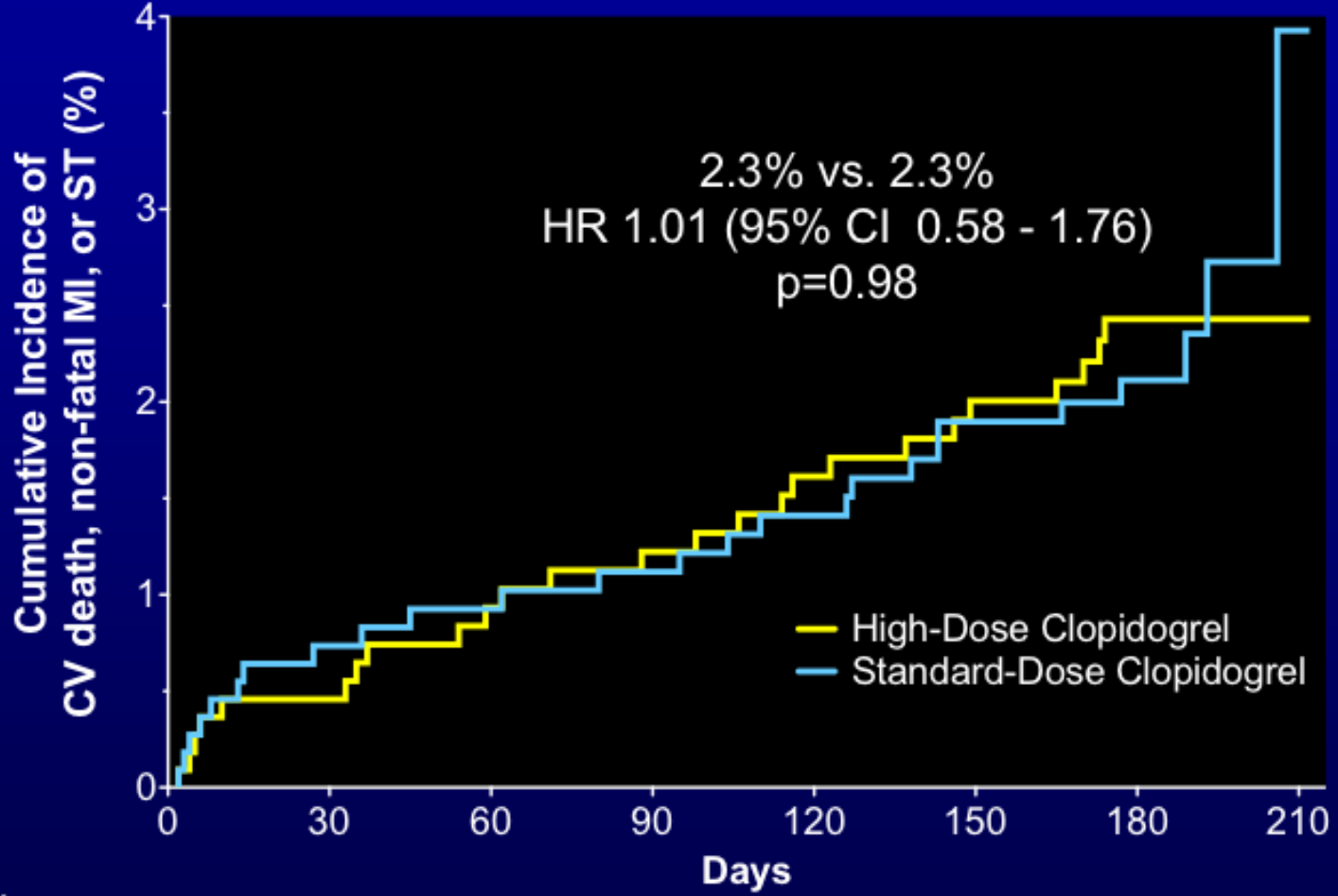




Angiolillo DJ et al. *Circulation.* 2007;115:708-16.

GRAVITAS results

Primary Endpoint: CV Death, MI, Stent Thrombosis



No. at Risk								
High Dose Clopidogrel	1109	1056	1029	1017	1007	998	747	54
Standard Dose Clopidogrel	1105	1057	1028	1020	1015	1005	773	53

Observed event rates are listed; P value by log rank test.

Presented at AHA Chicago 2010

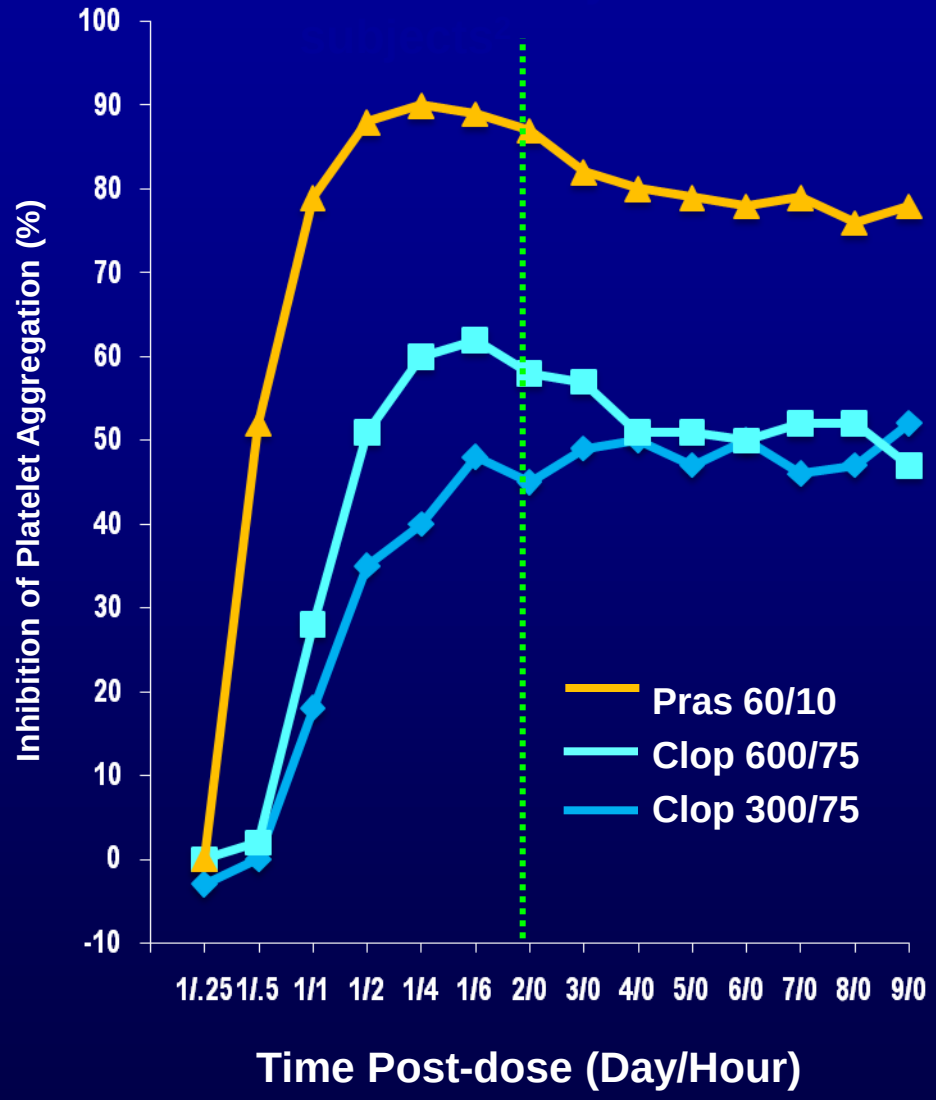
Particularidades de los antiagregantes en diabeticos:

- Aspirina
- Clopidogrel
- Prasugrel
- Ticagrelor
- Inh. GPIIb/IIIa

Platelet Inhibition With Antiplatelet Therapies

Prasugrel vs Clopidogrel[1]

- Greater potency
- More rapid in onset
- More consistent inhibition of platelet aggregation (IPA)
- Less frequent poor IPA response
- More efficient generation of its active metabolite

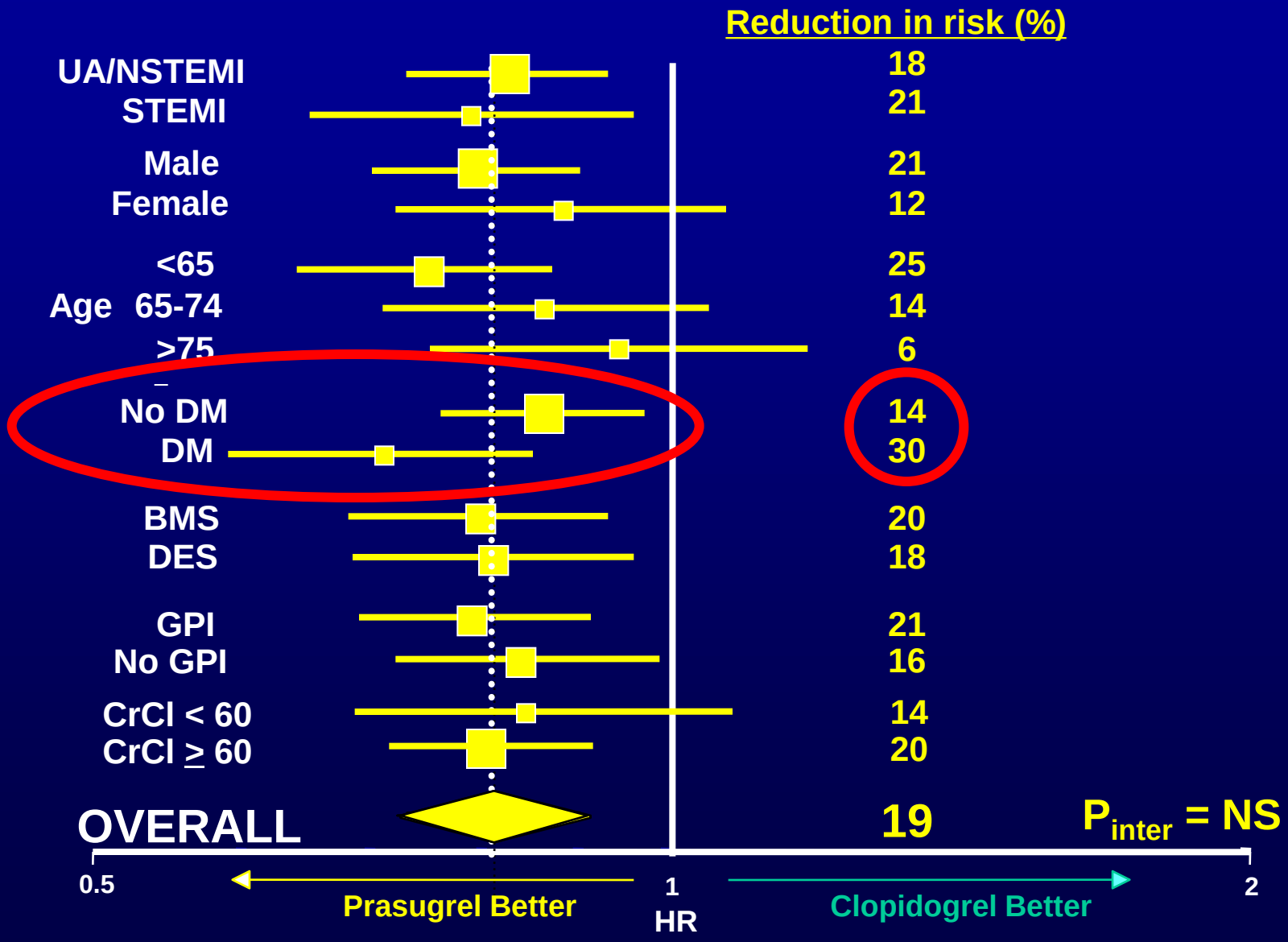


1. Wiviott SD et al. *Am Heart J.* 2006;152:627-635.
2. Payne CD et al. *Am J Cardiol.* 2006;98:S8.

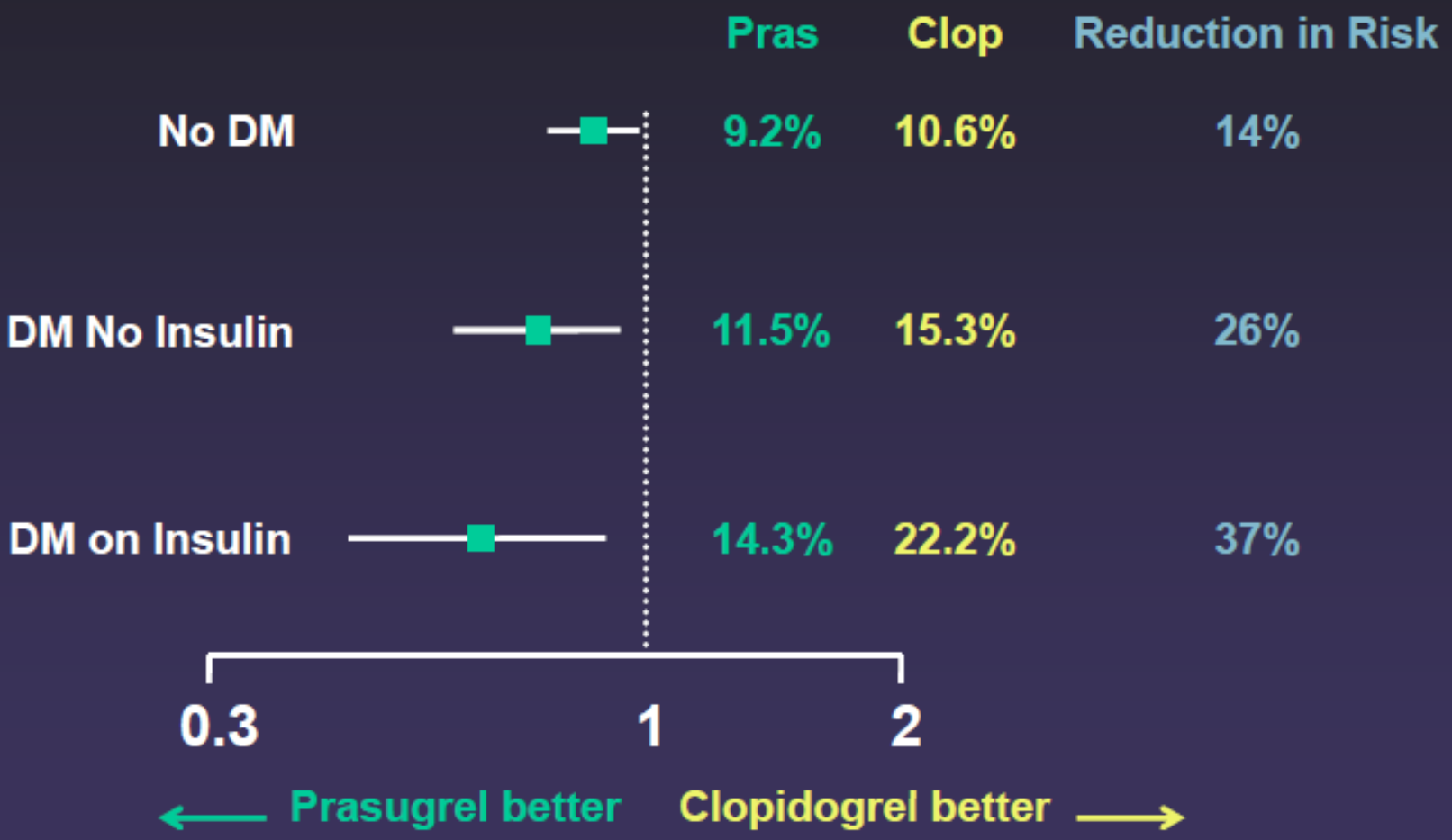
TRÎTON TIMI-38

PRASUGREL - DIABETES

CV Death, MI, Stroke *Major Subgroups*

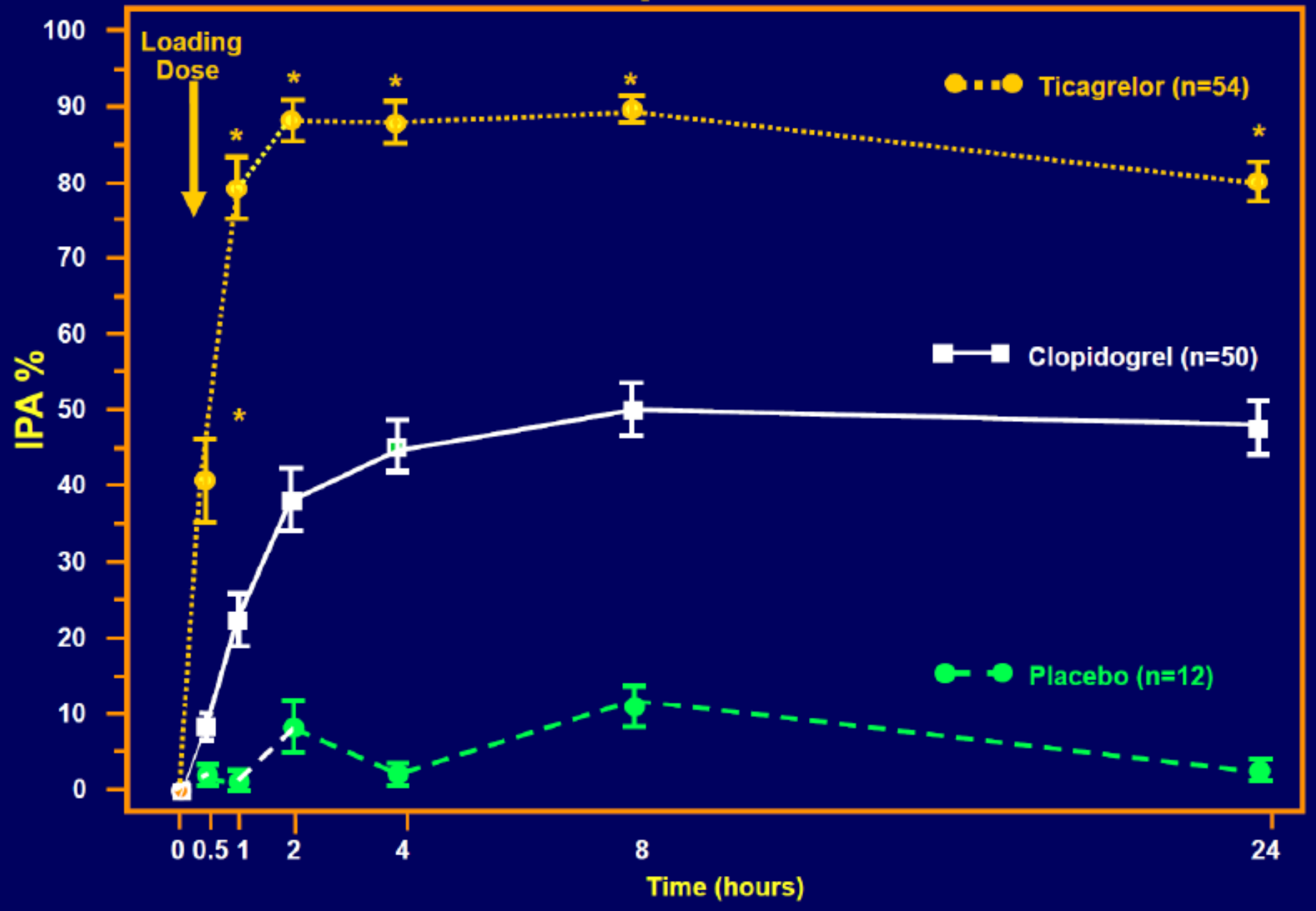


TRITON TIMI-38:
CV Death/MI/Stroke by Diabetic Status



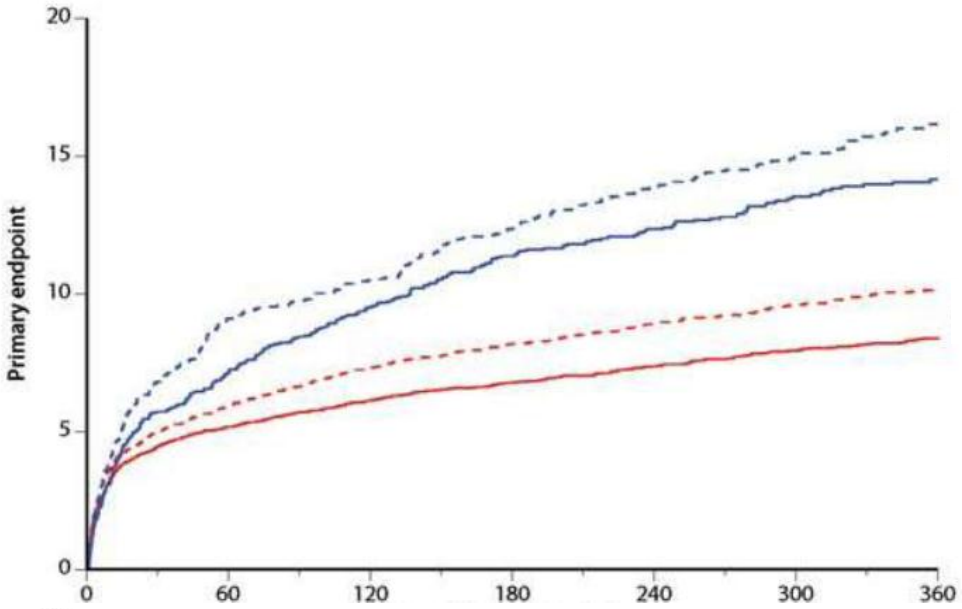
Wiviott SD, Braunwald E, Angiolillo DJ et al. *Circulation*. 2008;118:1626-36.

On-set of platelet inhibition



(Gurbel PA et al. *Circulation*, 2009)

TICAGRELOR - DIABETES



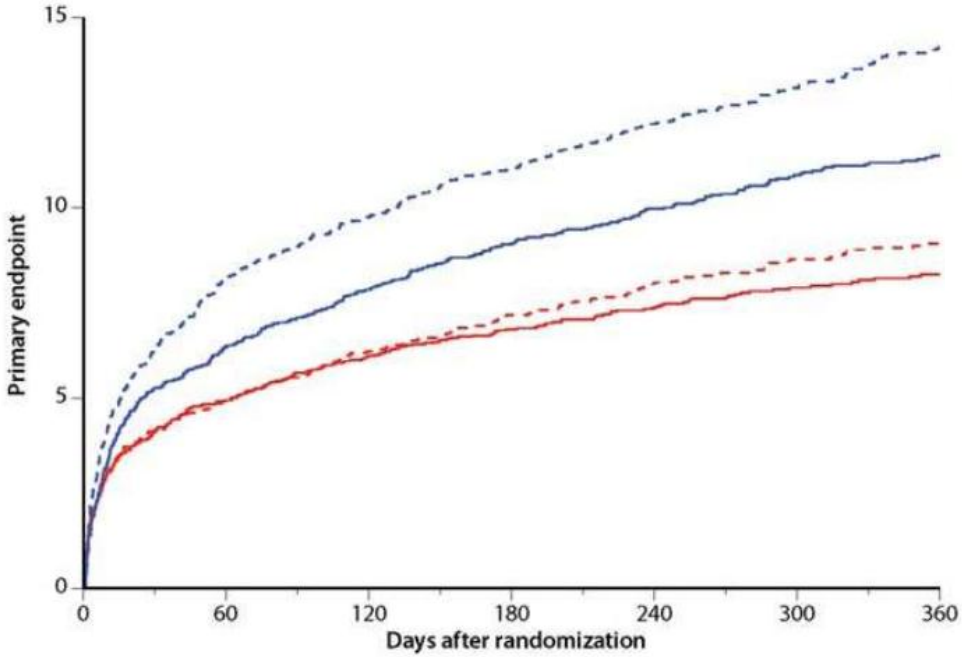
Diabetes 16,2% vs 14,1% (HR 0,88 0,76-1,03)

No diabetes

PLATO

18.624 pacientes

4.662 diabéticos

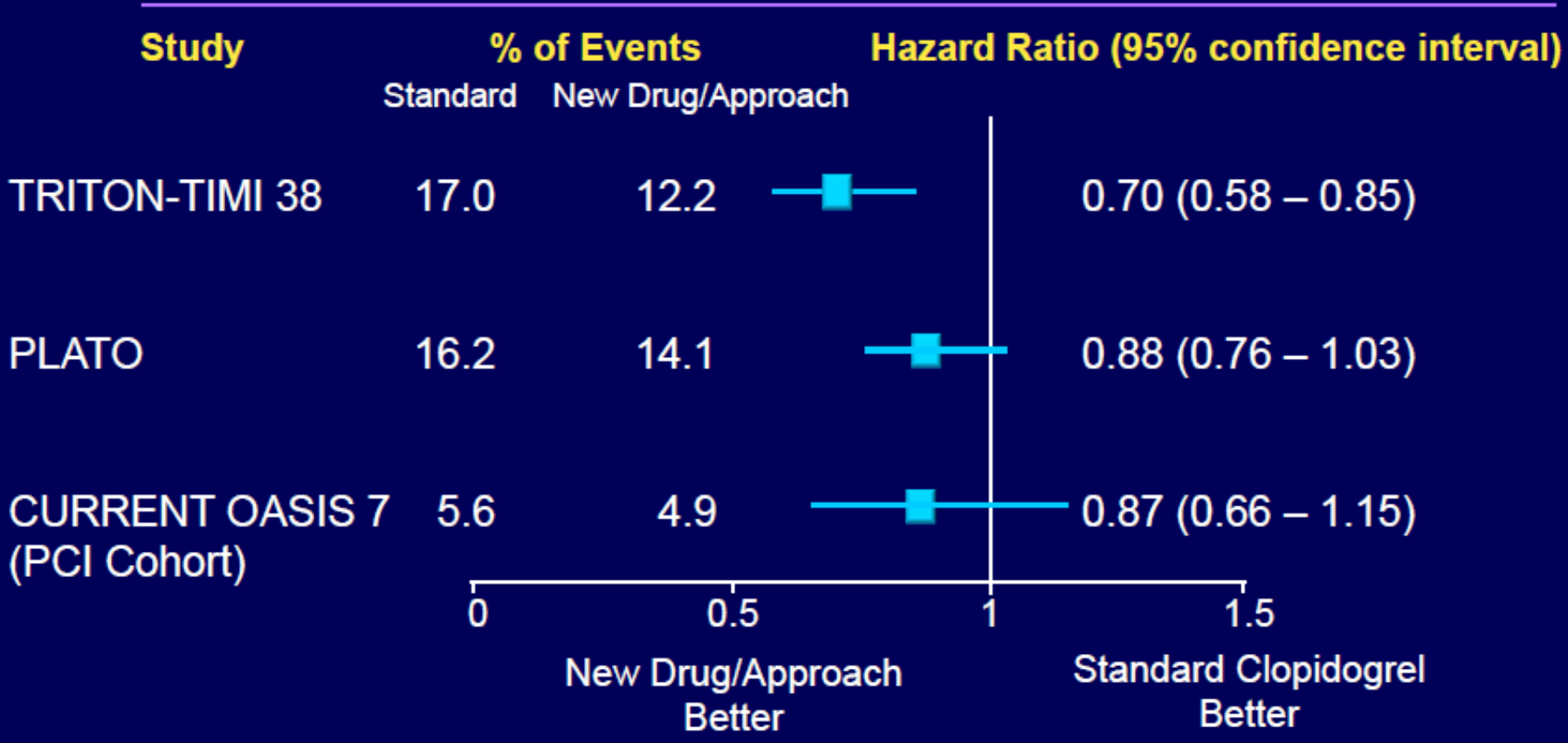


HbA1c ≥6 14,2% vs 11,4% (HR 0,80 0,70-0,91)

HbA1c <6

James S, et al
Eur Heart J 2010; Aug 29

Efficacy of New Drugs/Approaches in Reducing Adverse Outcomes in Diabetes Mellitus From Large-Scale Clinical Trials



CURRENT-OASIS= Clopidogrel Optimal Loading Dose Usage to Reduce Recurrent Events Optimal Antiplatelet Strategy for Interventions; PCI=percutaneous intervention; PLATO= A Study of Platelet Inhibition and Patient Outcomes; TRITON-TIMI= Trial To Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel Thrombolysis in Myocardial Infarction.

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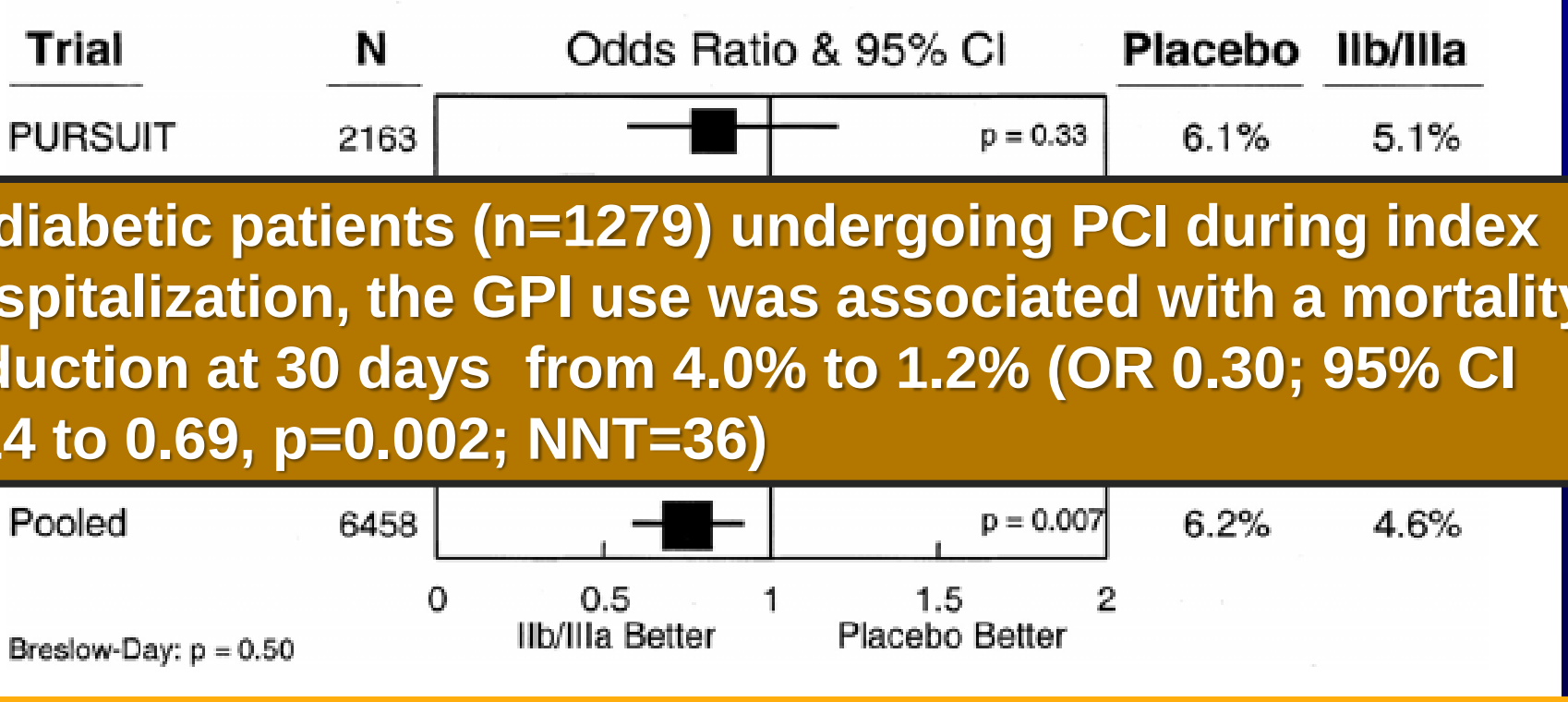
- Inh. GPIIb/IIIa

Diabetes Mellitus
- role of GP IIb/IIIa inhibitors -

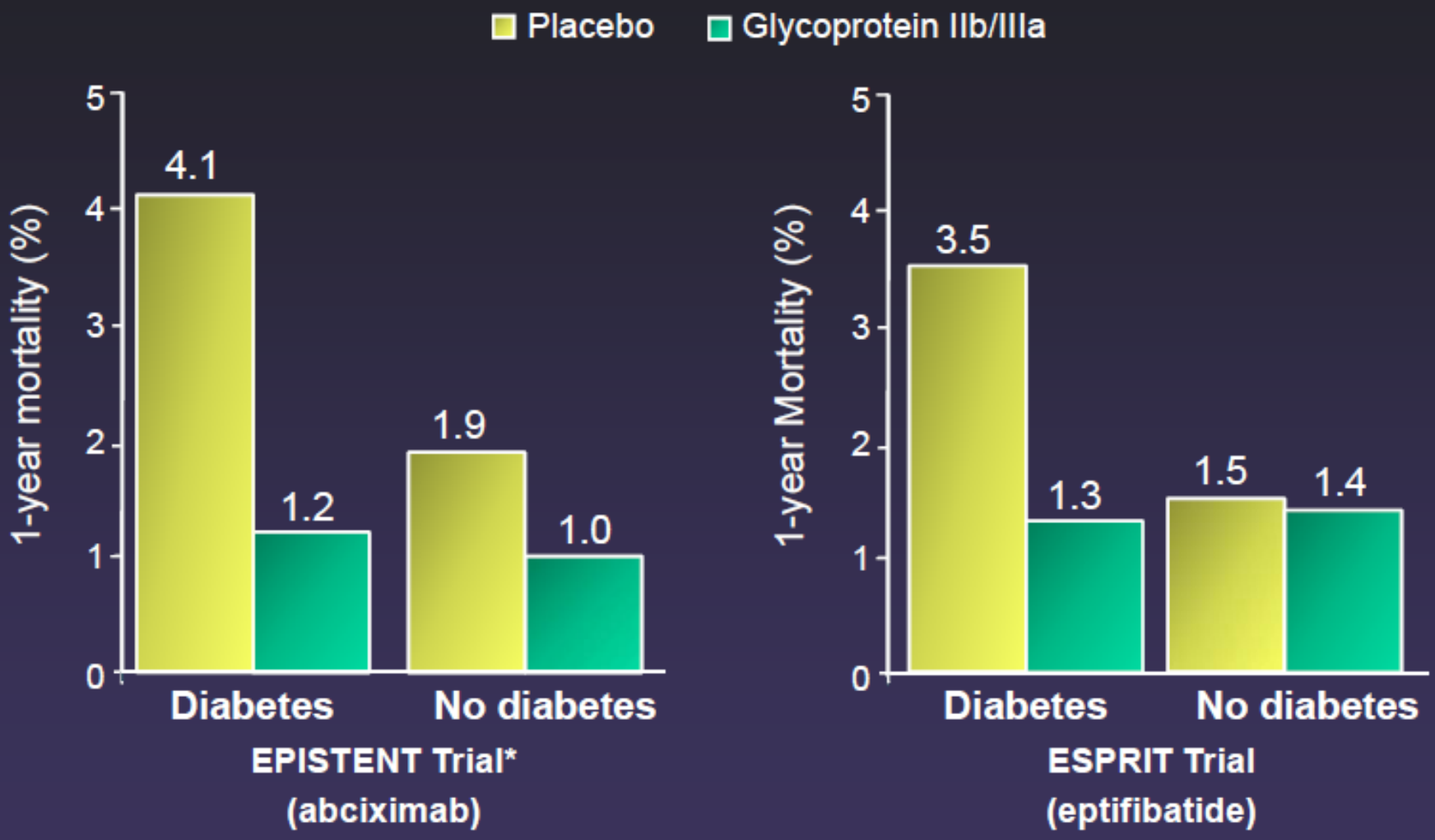
30-day mortality in diabetic NSTEACS patients from 6 randomized clinical trials



In diabetic patients (n=1279) undergoing PCI during index hospitalization, the GPI use was associated with a mortality reduction at 30 days from 4.0% to 1.2% (OR 0.30; 95% CI 0.14 to 0.69, p=0.002; NNT=36)

Roffi M et al. Circulation 2001; 104:2767

GP IIb/IIIa Blockade and Diabetes



*Stent arms only

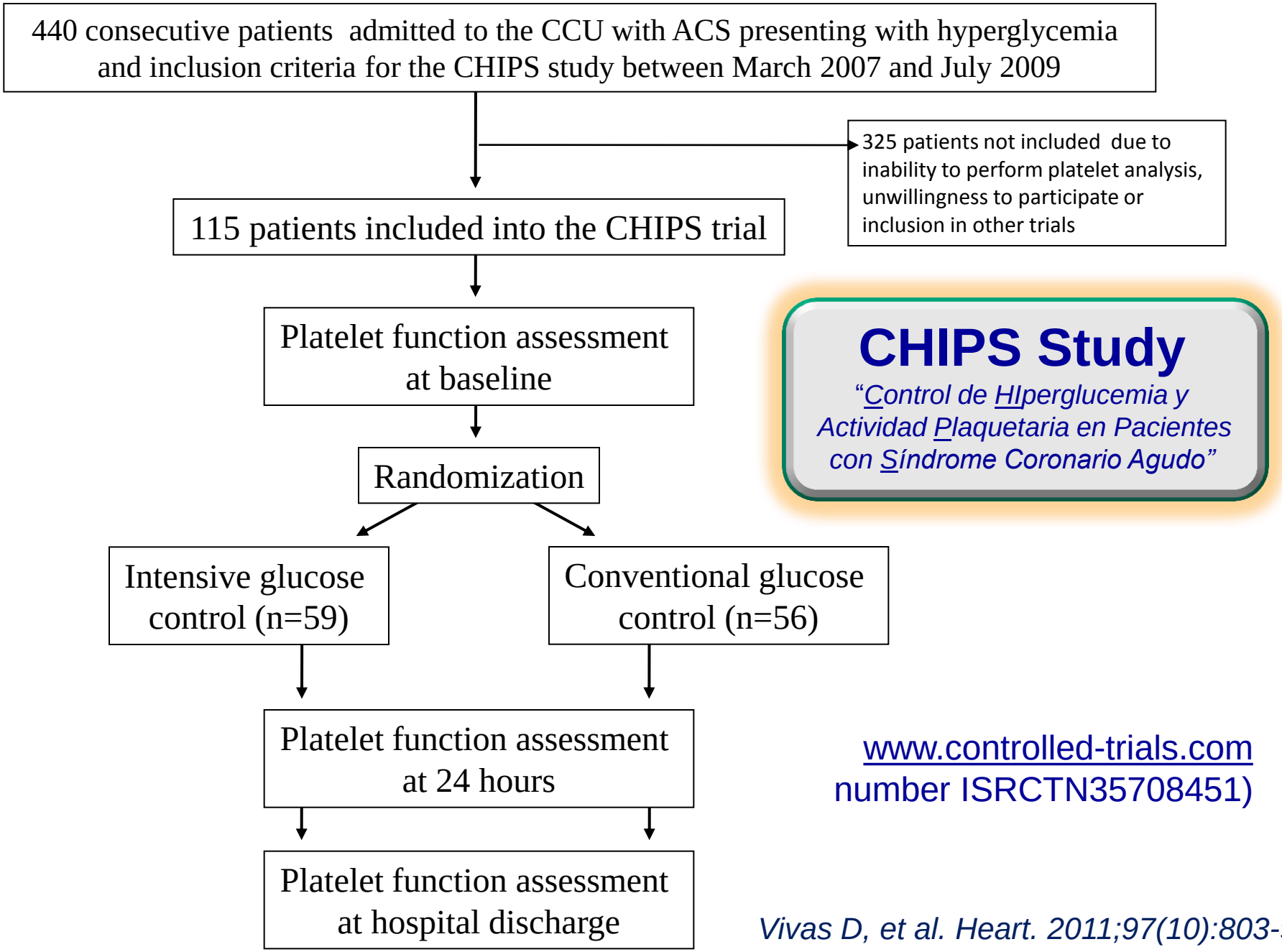
Lincoff AM. *Circulation*. 2003;107:1556-9.

ABCs of Treatment of Diabetic Patients and Impact on Thrombosis

A A1C (blood glucose): <7%

B Blood pressure: <130/80 mm Hg

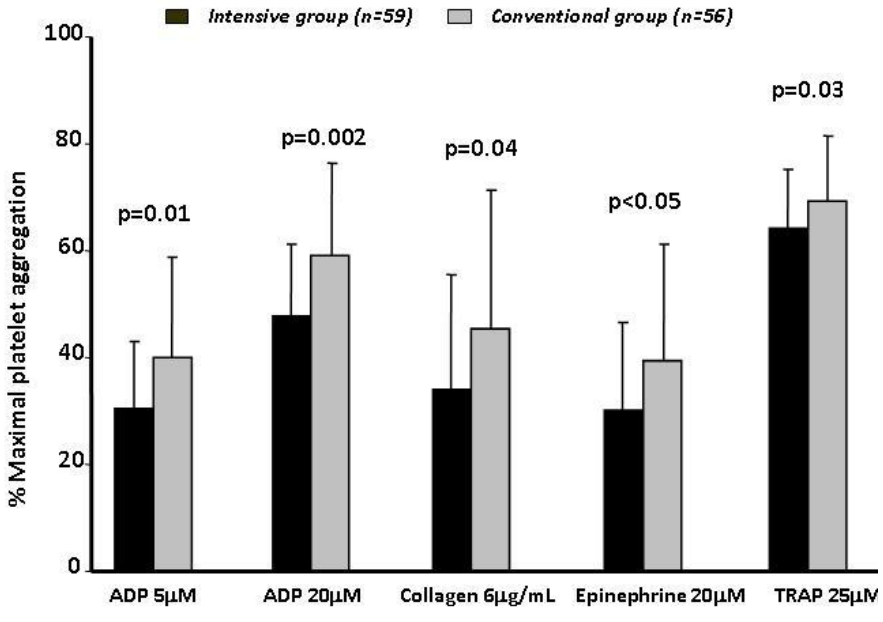
C Cholesterol-LDL: <70 mg/dl


440 consecutive patients admitted to the CCU with ACS presenting with hyperglycemia and inclusion criteria for the CHIPS study between March 2007 and July 2009
325 patients not included due to inability to perform platelet analysis, unwillingness to participate or inclusion in other trials
115 patients included into the CHIPS trial
Platelet function assessment at baseline
Randomization
Intensive glucose control (n=59)
Conventional glucose control (n=56)
Platelet function assessment at 24 hours
Platelet function assessment at hospital discharge
CHIPS Study
"Control de HIperglucemia y Actividad Plaquetaria en Pacientes con Síndrome Coronario Agudo"
www.controlled-trials.com
number ISRCTN35708451)
Vivas D, et al. Heart. 2011;97(10):803-9.

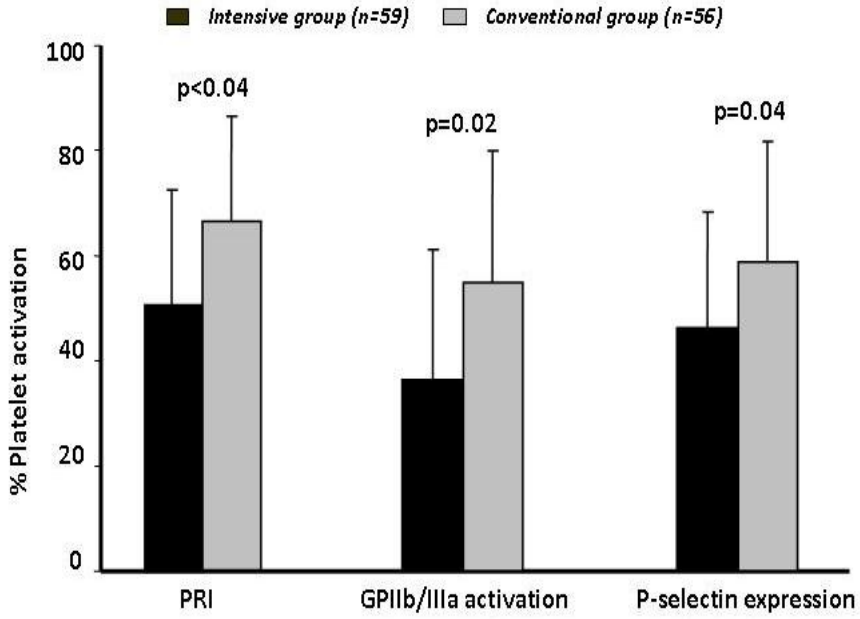
CHIPS study

Platelet reactivity at hospital discharge

Platelet aggregation



Platelet activation



Vivas D, et al. Heart. 2011;97(10):803-9.

Conclusions

Platelets from DM patients are dysfunctional:

- increased platelet reactivity
- reduced responsiveness to standard antiplatelet agents

Increased platelet reactivity and reduced responsiveness to aspirin plus clopidogrel are associated with atherothrombotic risk

The introduction of novel and more potent antiplatelet agents will enable more efficient blockade of the diabetic platelet