SCA sin EST: Nuevas Estrategias Antitrombóticas, ¿Incrementan los Beneficios?

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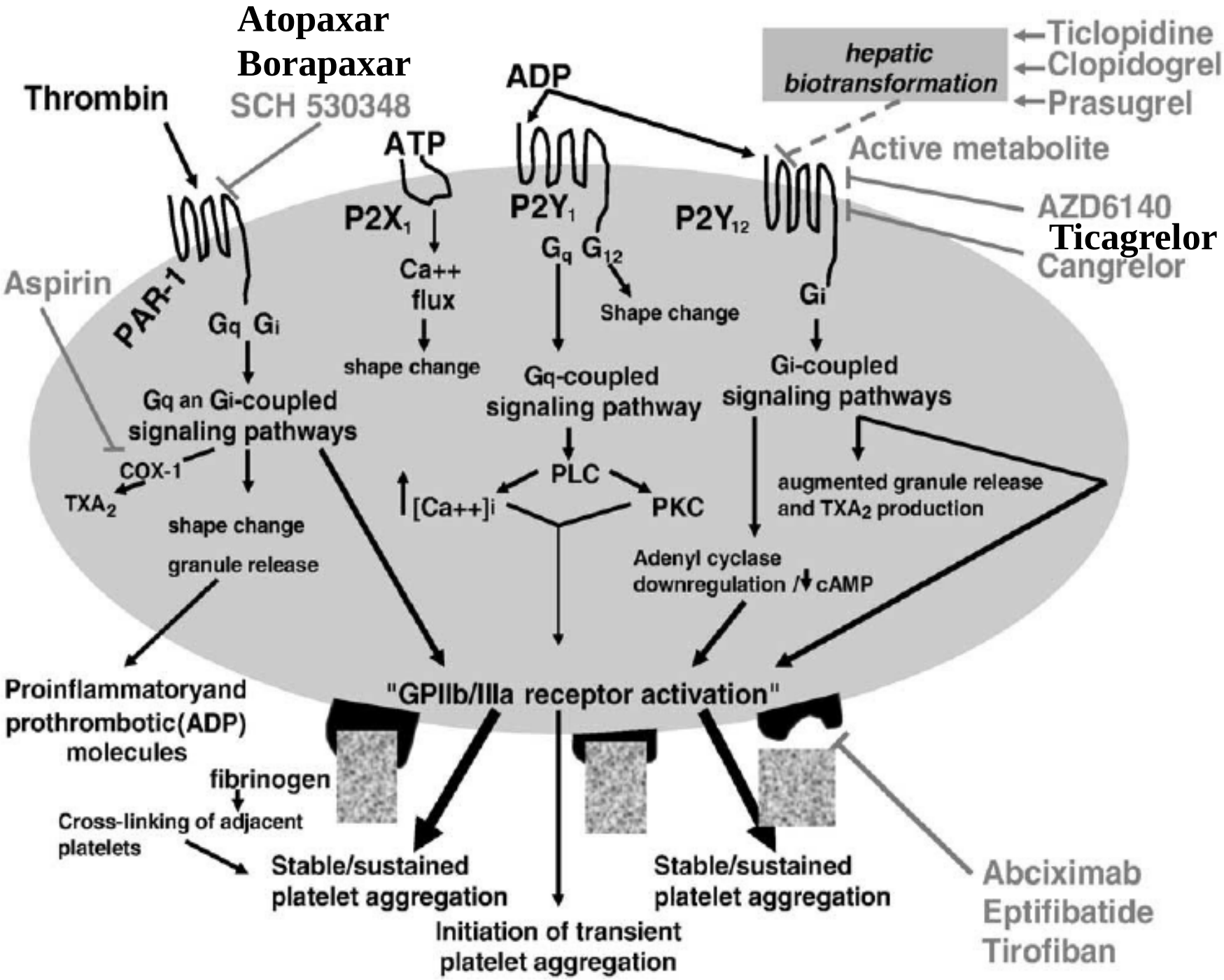
Antiplaquetarios

- Clopidogrel
- Prasugrel
- Ticagrelor
- Antagonistas PAR-1, Atopaxar, Borapaxar
- Antagonistas IIbIIIa.


Atopaxar
Borapaxar
Thrombin
SCH 530348
ADP
hepatic biotransformation
Ticlopidine
Clopidogrel
Prasugrel
ATP
Active metabolite
AZD6140
Ticagrelor
Cangrelor
P2X1
P2Y1
P2Y12
Aspirin
PAR-1
Gq Gi
Ca++ flux
Gq G12
Shape change
Gi
shape change
Gq-coupled signaling pathway
Gi-coupled signaling pathways
Gq an Gi-coupled signaling pathways
COX-1
TXA2
PLC
[Ca++]i
PKC
augmented granule release and TXA2 production
shape change
granule release
Adenyl cyclase downregulation /↓cAMP
Proinflammatoryand prothrombotic(ADP) molecules
"GPIIb/IIIa receptor activation"
fibrinogen
Cross-linking of adjacent platelets
Stable/sustained platelet aggregation
Initiation of transient platelet aggregation
Stable/sustained platelet aggregation
Abciximab
Eptifibatide
Tirofiban

Estudio CURRENT/OASIS-7

- > 14,000 pacientes con SCA sin EST + PCI.
- Clopidogrel 600 mg carga, 150 mg/d dia 2-7, 75 mg/d días 8-30.
- Vs. Clopidogrel 300 mg carga, 75 mg/d días 2-30.
- ASA > 300 mg carga y mantención de 75-100 mg/d vs. 300-325 mg/d.

CURRENT

Clopidogrel: Double vs Standard Dose Primary Outcome

	Clop Standard	Clop Double	HR	P	P Int^n
ASA 300-325 mg	4.6	3.8	0.83	0.036	0.043
ASA 75-100 mg	4.2	4.5	1.07	0.43	

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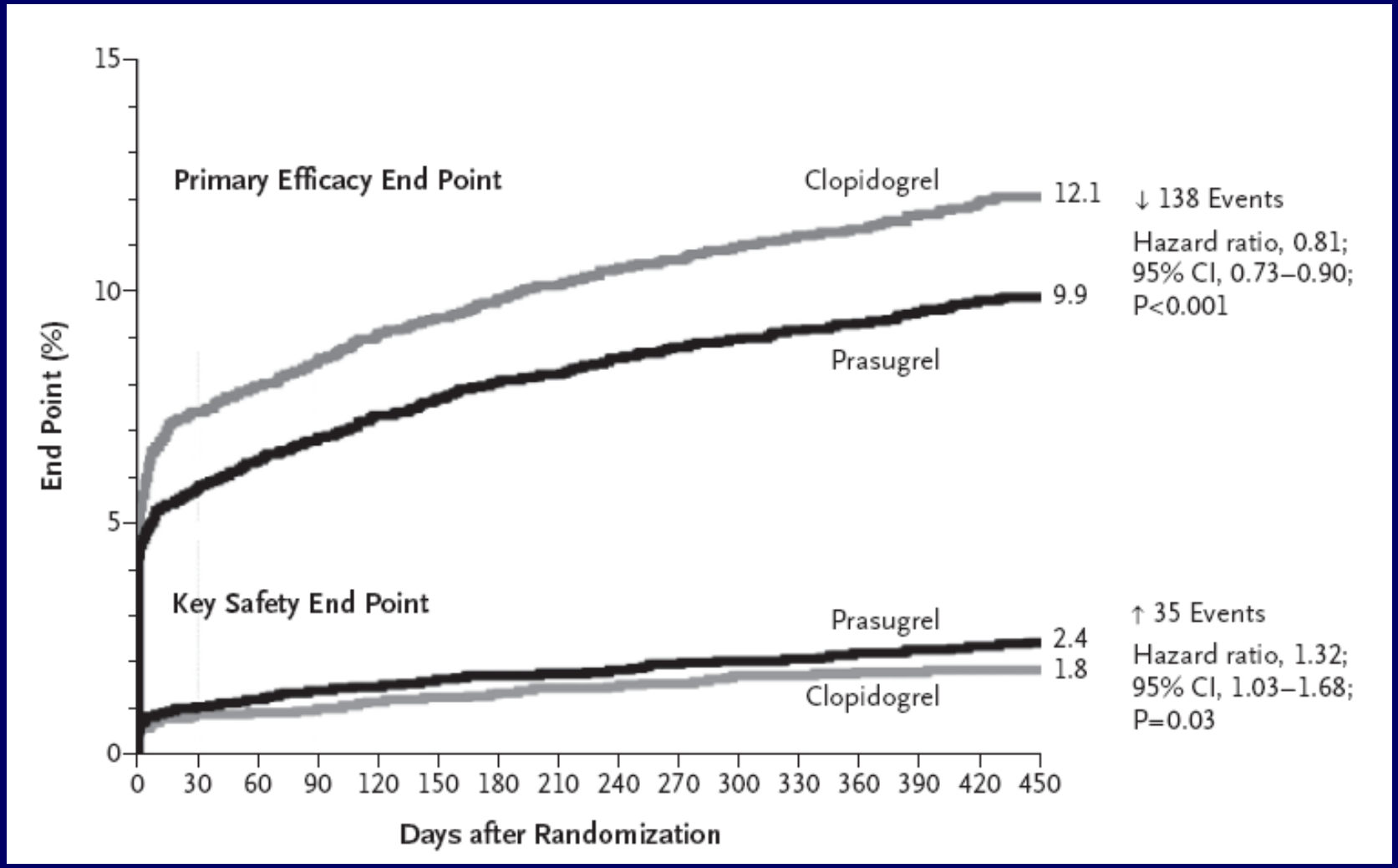
Prasugrel versus Clopidogrel in Patients with Acute Coronary Syndromes

Stephen D. Wiviott, M.D., Eugene Braunwald, M.D., Carolyn H. McCabe, B.S., Gilles Montalescot, M.D., Ph.D., Witold Ruzyllo, M.D., Shmuel Gottlieb, M.D., Franz-Joseph Neumann, M.D., Diego Ardissino, M.D., Stefano De Servi, M.D., Sabina A. Murphy, M.P.H., Jeffrey Riesmeyer, M.D., Govinda Weerakkody, Ph.D., C. Michael Gibson, M.D., and Elliott M. Antman, M.D., for the TRITON–TIMI 38 Investigators*

TRITON -TIMI 38

Muerte CV + Infarto + ACV
Hemorragia TIMI Mayor



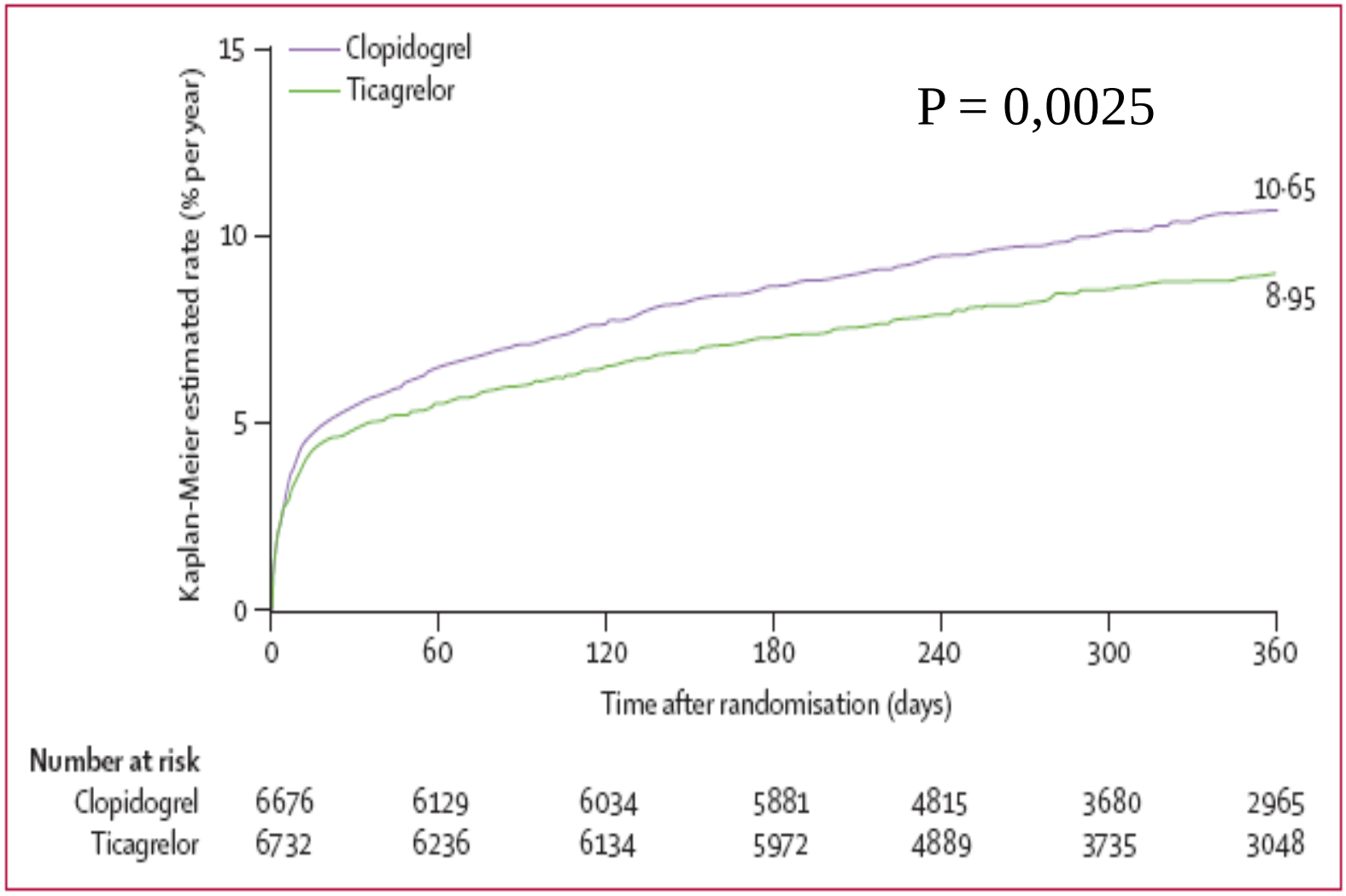
Prasugrel

- Mayor riesgo de sangramiento en:
  - > 75 años.
  - < 60 kgs.
  - Historia de ACV o CIT.
- Actualmente aprobado por la FDA y en uso en varios países.
- Advertencia de la FDA para no usar en grupos de riesgo.

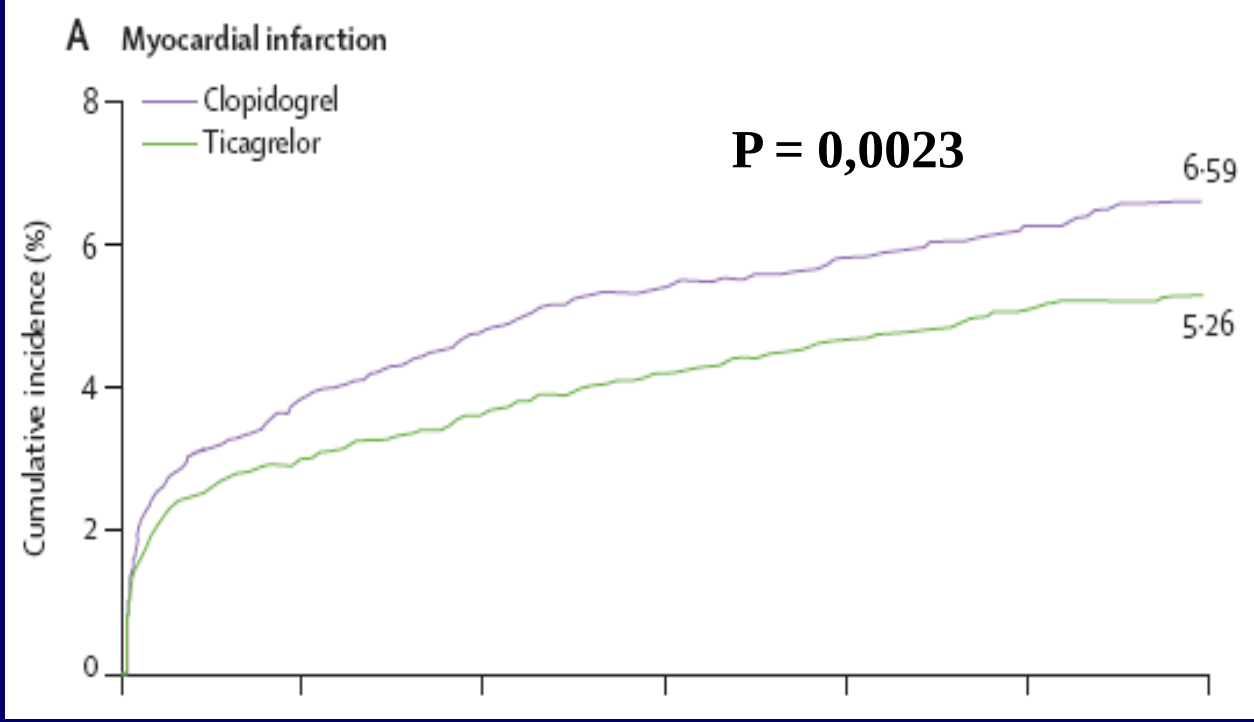
Ticagrelor

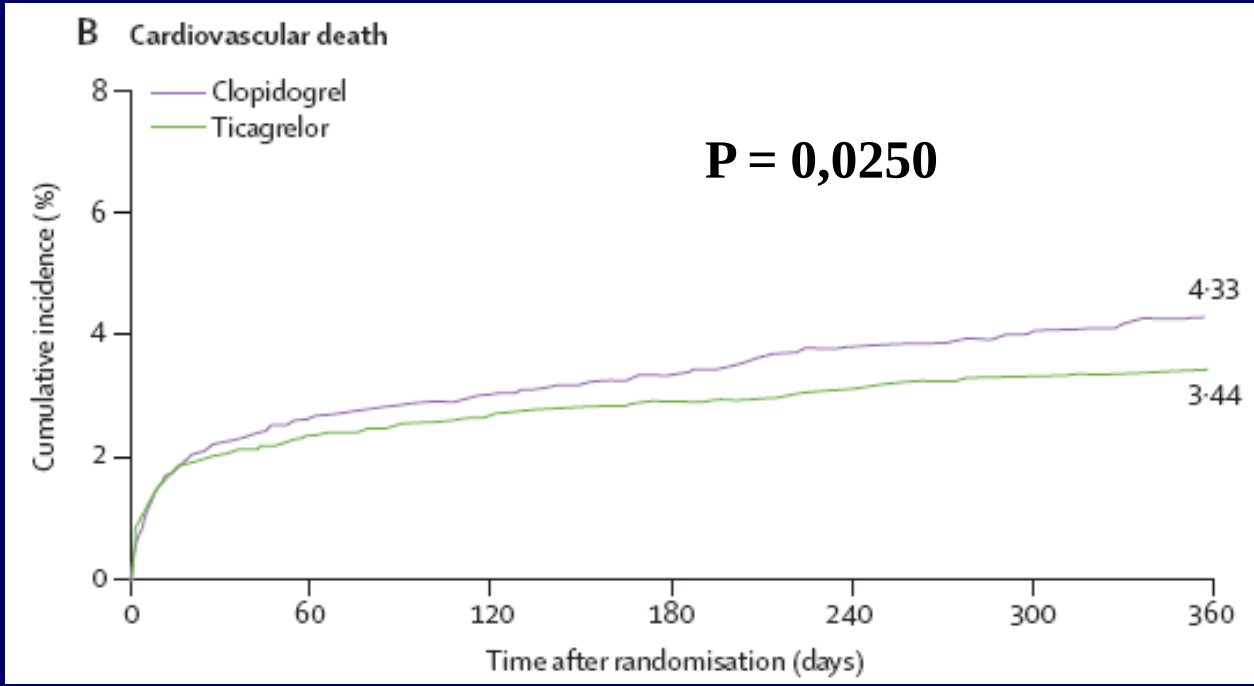
- Uso oral, 2 veces al día.
- Antagonista competitivo del receptor del PY_{12} del ADP.
- Rápido inicio de acción.
- Rápidamente reversible (tto. Quirúrgico)
- Más potente que clopidogrel

PLATO: Punto Final Primario Muerte + Infarto + ACV

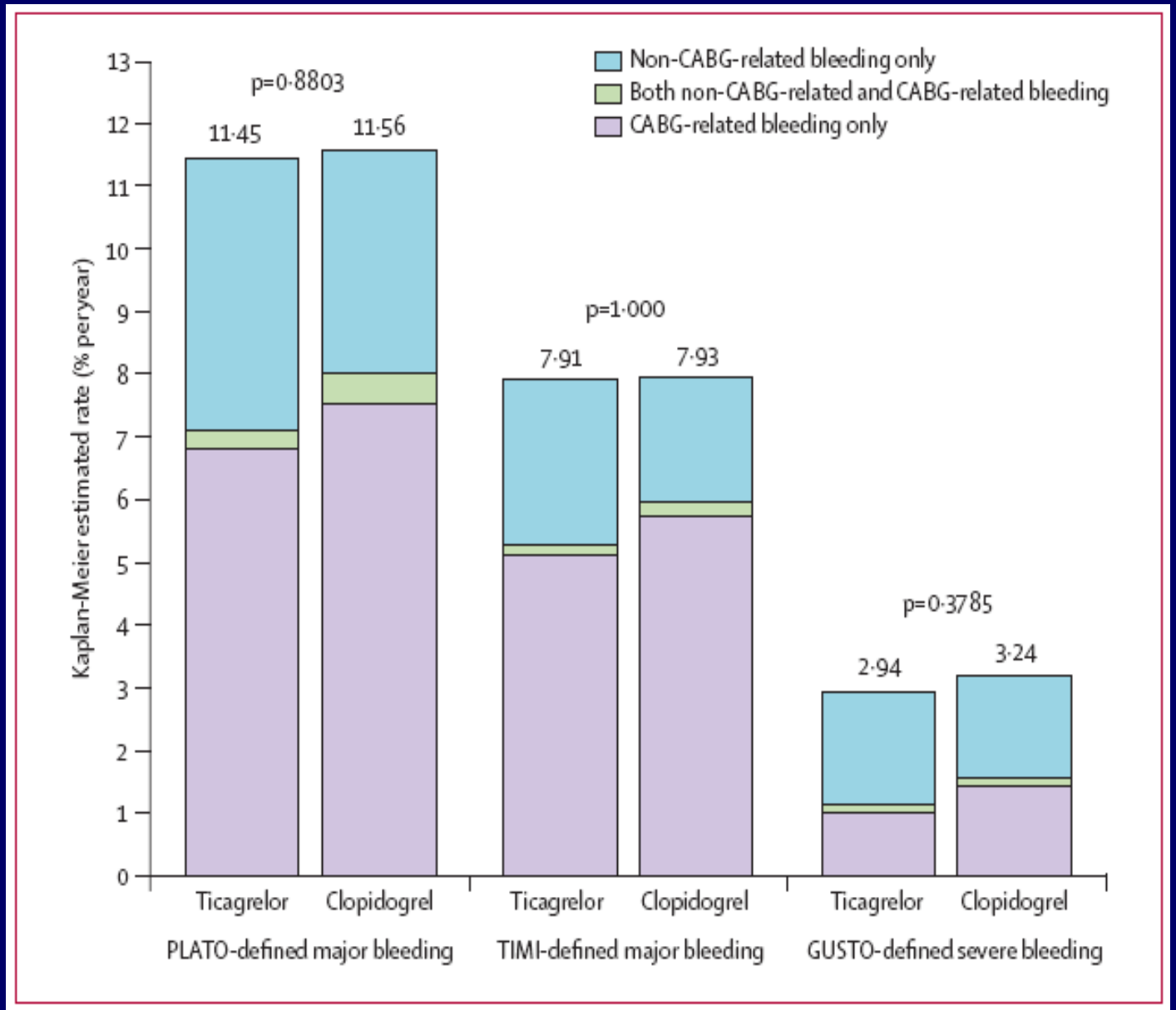


PLATO


A Myocardial infarction
Clopidogrel
Ticagrelor
P = 0,0023
6·59
5·26
Cumulative incidence (%)
0
2
4
6
8


B Cardiovascular death
Clopidogrel
Ticagrelor
P = 0,0250
4·33
3·44
Cumulative incidence (%)
0
2
4
6
8
0
60
120
180
240
300
360
Time after randomisation (days)

PLATO: Sangramiento Mayor



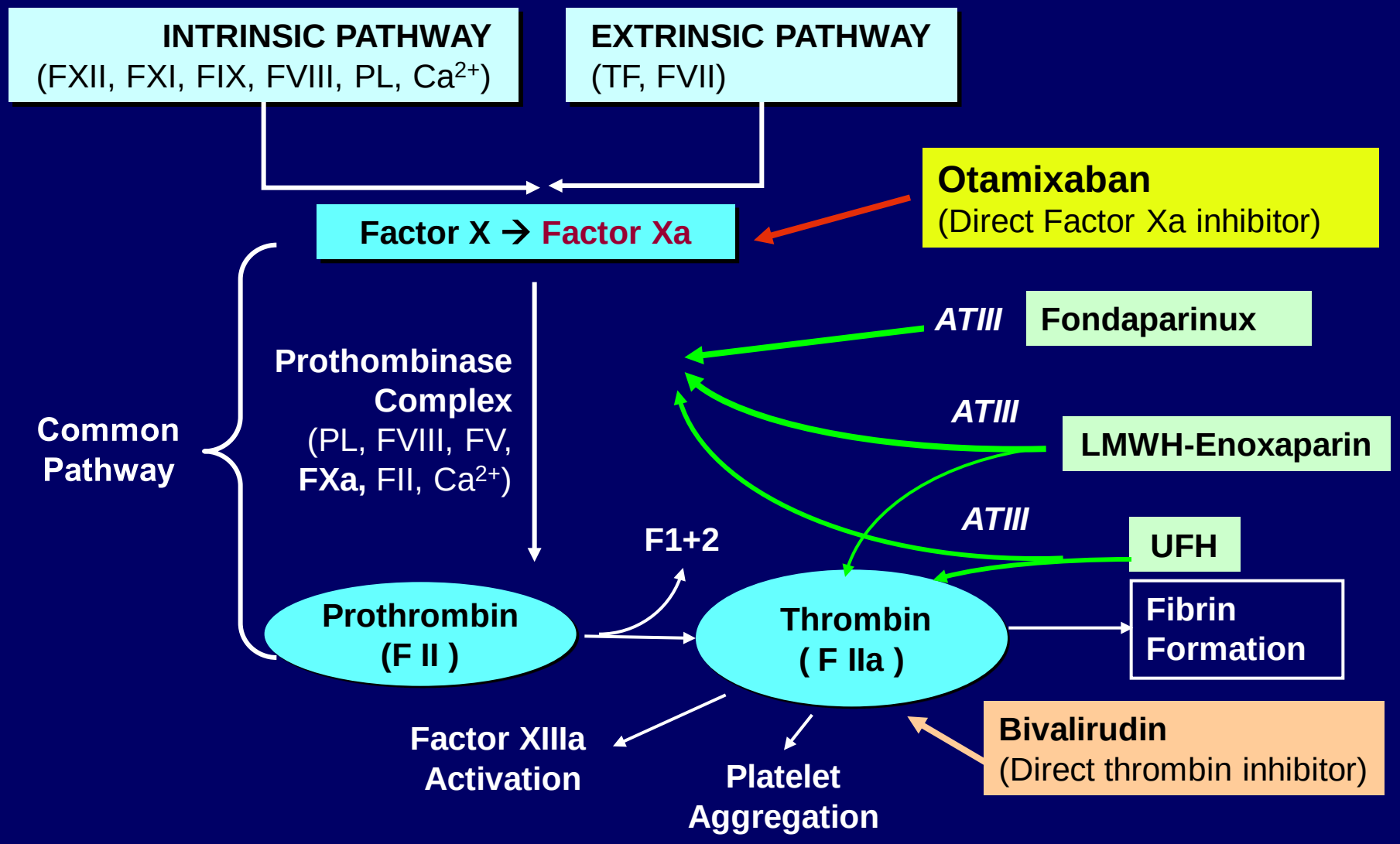
Antiplaquetarios IV en SCA sin EST

- El uso rutinario de entrada de IIbIIIa tendría un rol limitado en presencia de ASA + Clopidogrel en particular si la dosis de carga se recibió antes de 2-6 horas de la PCI electiva.
- Uso selectivo en pacientes de alto riesgo.
- Evitar el uso en pacientes en riesgo de sangramiento.

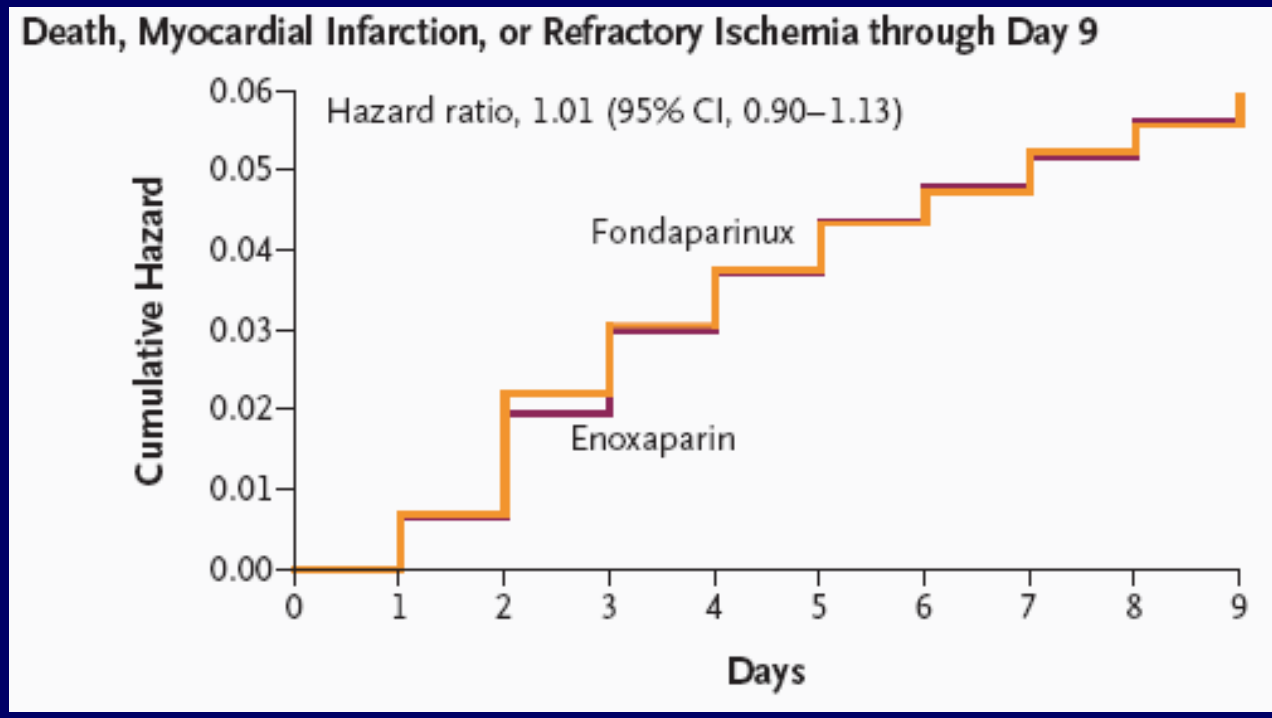
Antitrombóticos

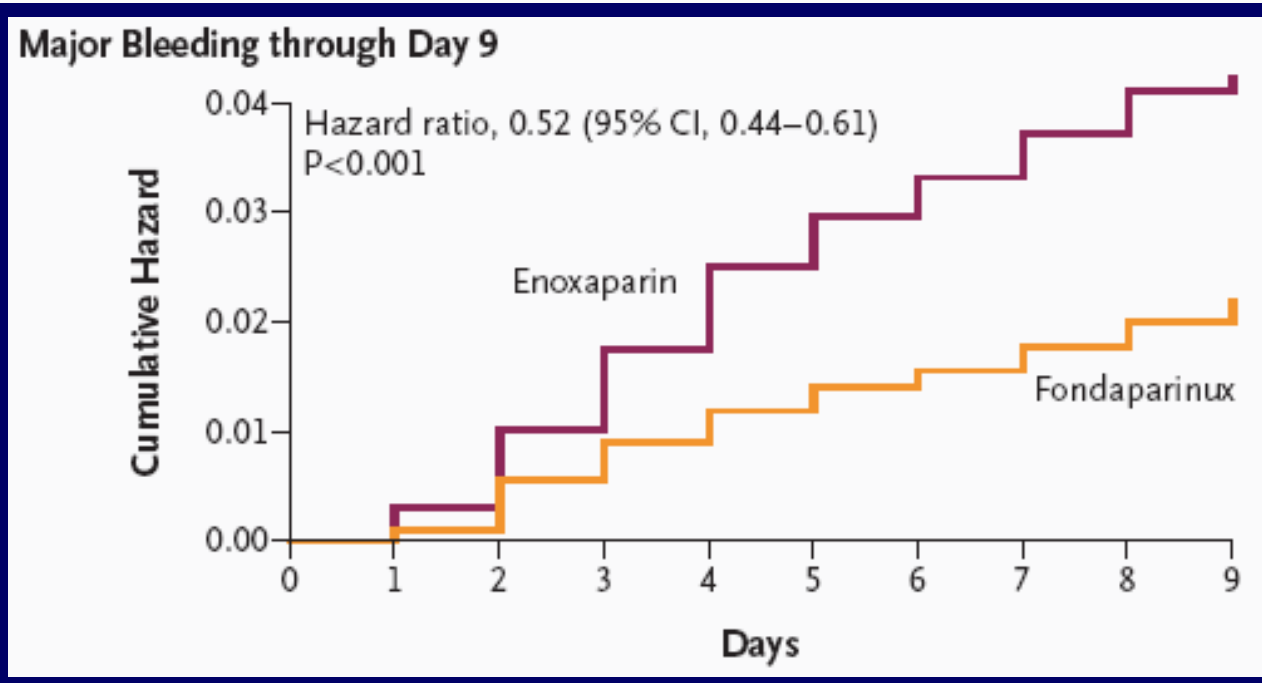
- Enoxaparina.
- Fondaparinux.
- Bivalirudina.
- Otamixaban.

Anticoagulantes

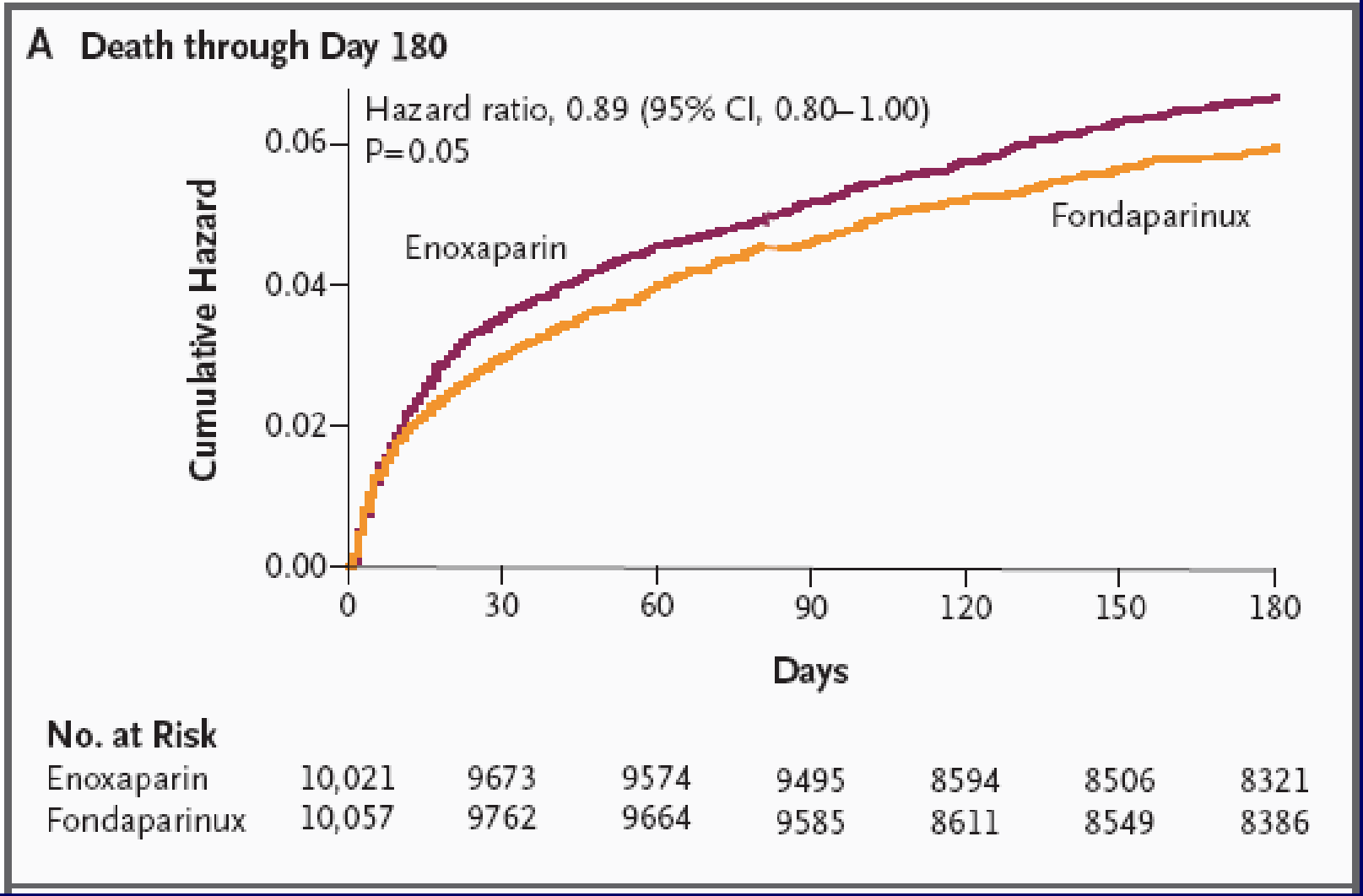


OASIS 5: Fondaparinux vs. Enoxaparina en SCA sin EST





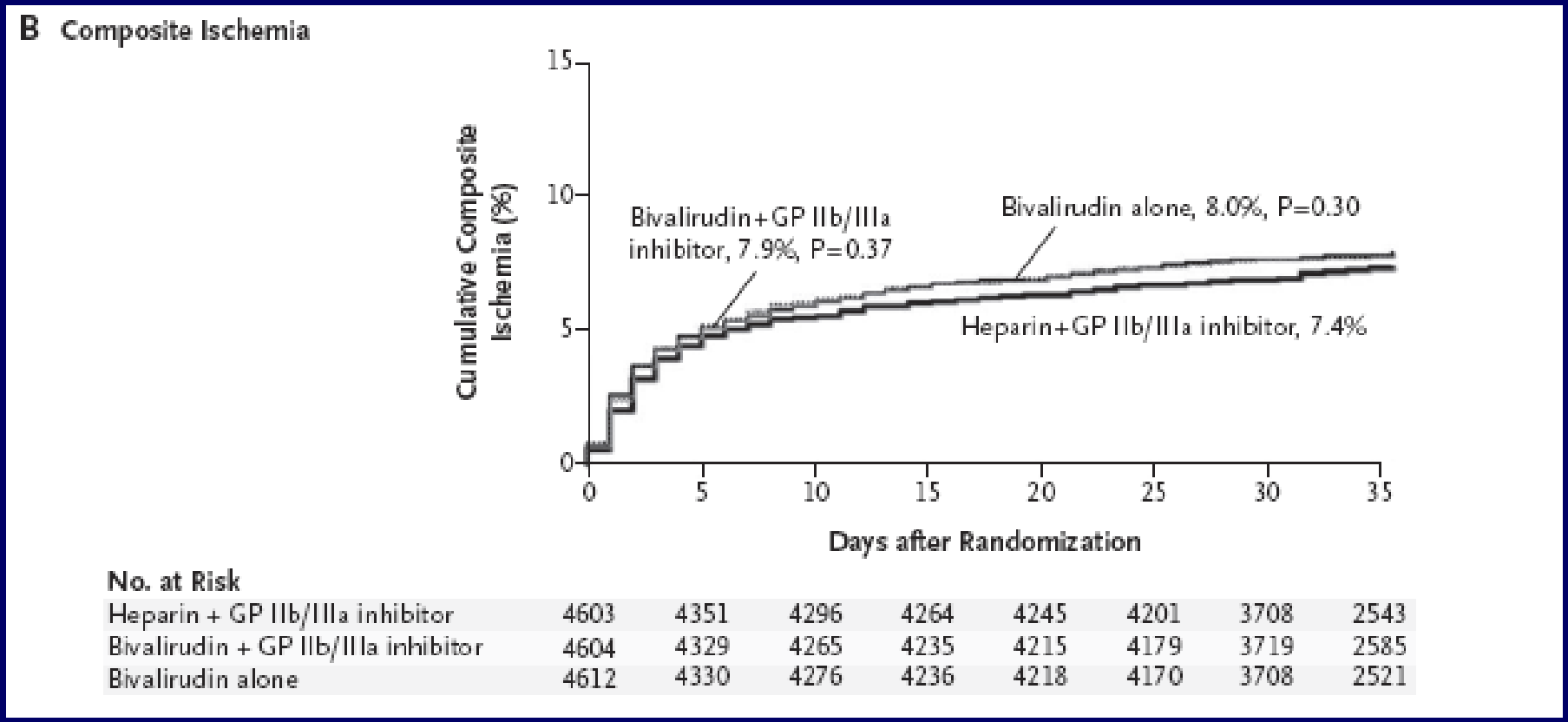
OASIS 5: Reducción de Mortalidad



ACUITY: Bivalirudina en SCA

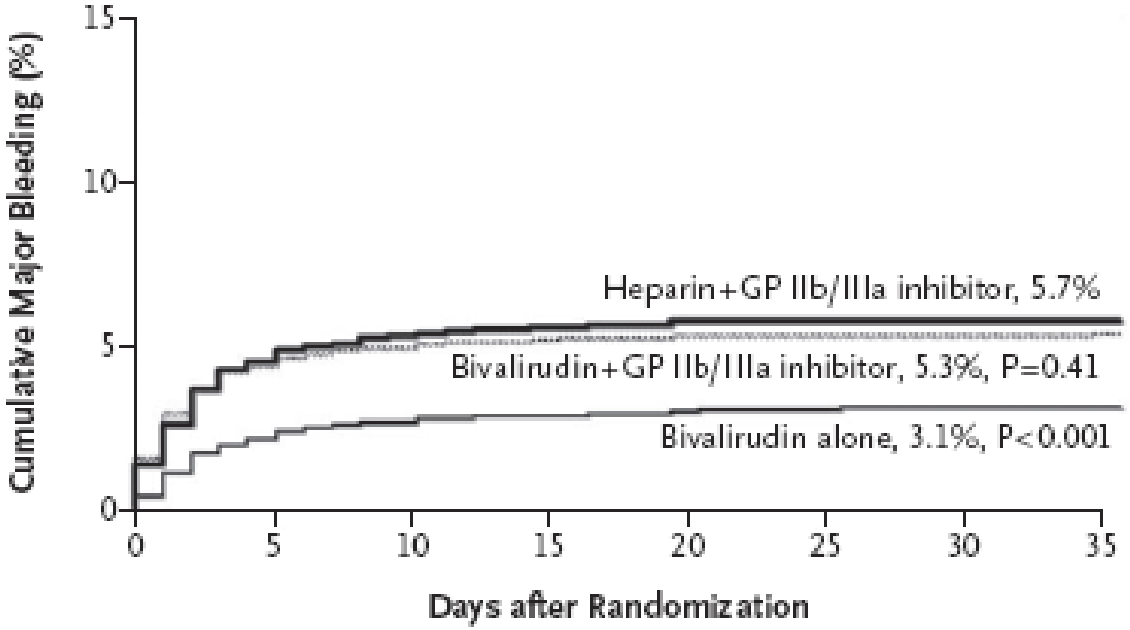
- 13.819 pacientes con SCA sin EST moderado y alto riesgo.
- Randomizados a:
  - HNF o Enoxaparina + IIbIIIa.
  - Bivalirudina + IIbIIIa.
  - Bivalirudina.

ACUITY:
Muerte, Infarto y Revascularización no planeada por isquemia



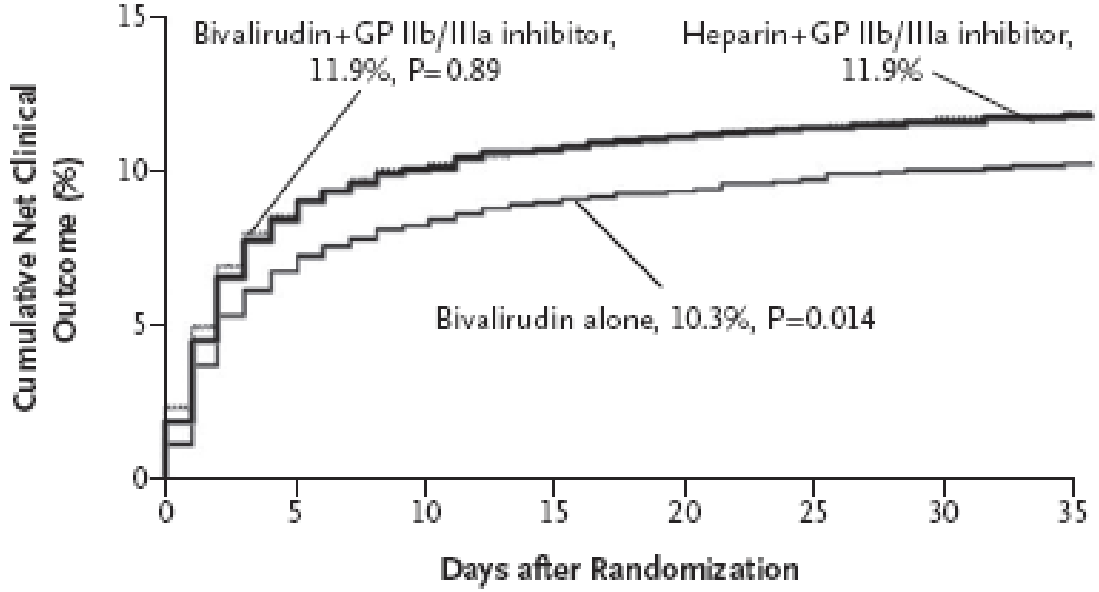
ACUITY: Sangramiento Mayor

C Major Bleeding



No. at Risk								
Heparin + GP IIb/IIIa inhibitor	4603	4336	4282	4258	4240	4208	3729	2575
Bivalirudin + GP IIb/IIIa inhibitor	4604	4329	4286	4266	4250	4222	3761	2625
Bivalirudin alone	4612	4423	4389	4366	4352	4312	3846	2633

ACUITY: Combinado de Isquemia + Sangramiento Mayor



No. at Risk								
Heparin + GP IIb/IIIa inhibitor	4603	4172	4091	4054	4030	3992	3529	2422
Bivalirudin + GP IIb/IIIa inhibitor	4604	4158	4084	4053	4030	3996	3550	2467
Bivalirudin alone	4612	4246	4173	4133	4112	4065	3614	2452

Gracias…

SOLACI '11

SANTIAGO DE CHILE

XVII SOLACI CONGRESS

August 3-5, 2011

CHILE