



ESTRATEGIAS CONTEMPORANEAS PARA LA PREVENCION Y MANEJO DE LA TROMBOSIS DEL STENT



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ESTRATEGIAS CONTEMPORANEAS PARA LA PREVENCIÓN Y MANEJO DE LA TROMBOSIS DEL STENT

Academic Research Consortium (ARC) *Standardized Definitions for ST*

- **Definite/Confirmed**
 - Acute coronary syndrome AND
 - Angiographic confirmation of thrombus or occlusion OR
 - Pathologic confirmation of acute thrombosis
- **Probable**
 - Unexplained death within 30 days
 - Target vessel MI without angiographic confirmation of thrombosis or other identified culprit lesion
- **Possible**
 - Unexplained death after 30 days

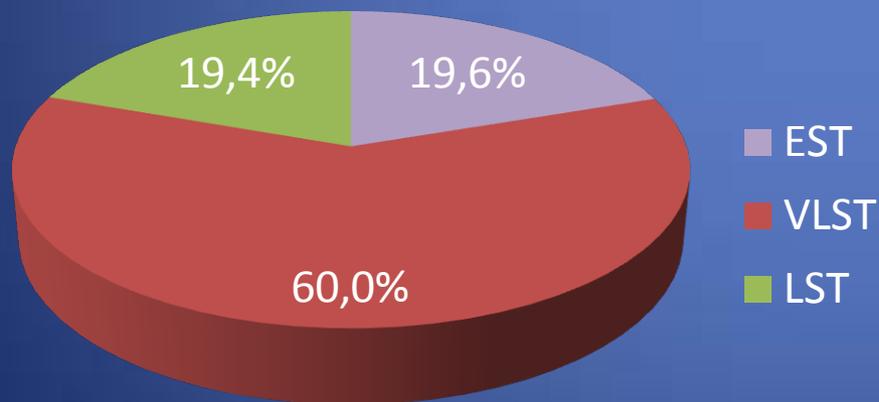


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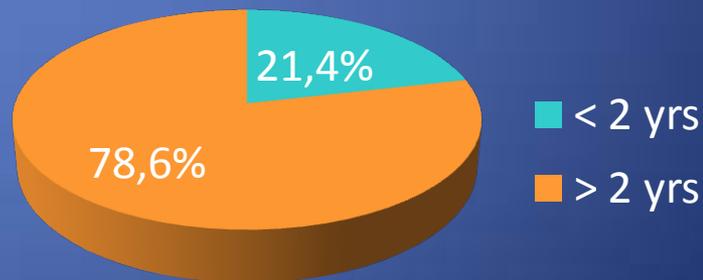
CathPCI Registry

- 1000 centers across the USA
- Feb 2009 to June 2010
- 7,315 from 585,123(1.8%)

STENT THROMBOSIS



VLST



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Eventos adversos secundarios a la ST

Table 3. In-Hospital Outcomes of Patients With ST

| | Early ST | Late ST | Very Late ST | p Value |
|----------------------------|-----------|----------|--------------|---------|
| Death | 110 (7.9) | 52 (3.8) | 155 (3.6) | <0.001 |
| Stroke | 14 (1.0) | 3 (0.2) | 11 (0.3) | <0.001 |
| Bleeding event within 72 h | 74 (5.4) | 43 (3.2) | 154 (3.6) | 0.003 |

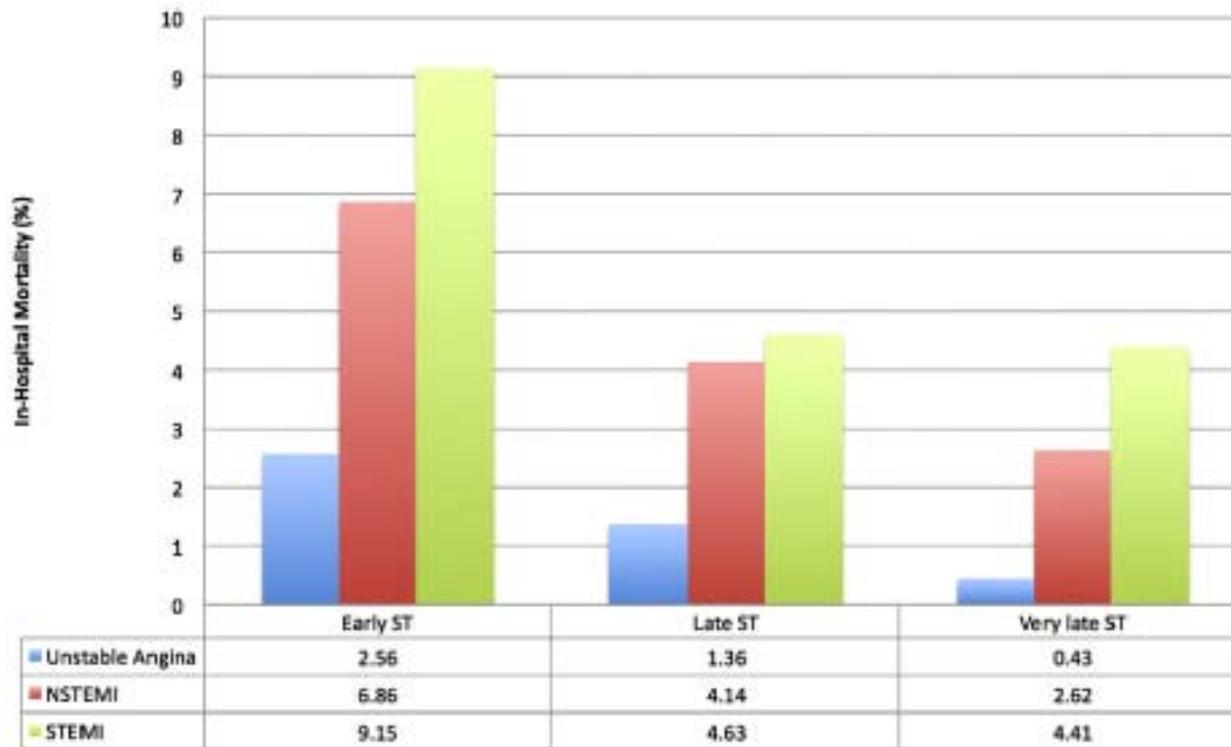
Values are n (%).

ST = stent thrombosis.



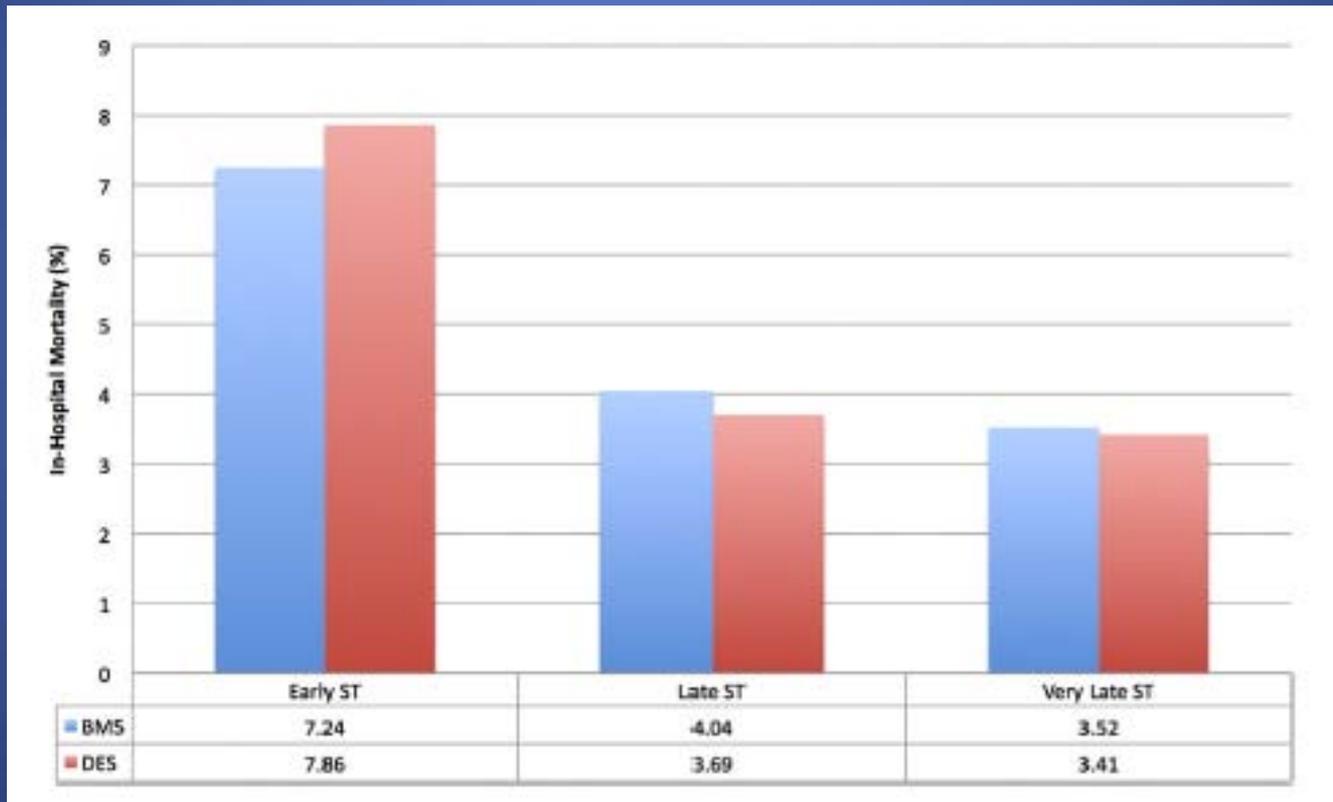
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Mortality according to presentation



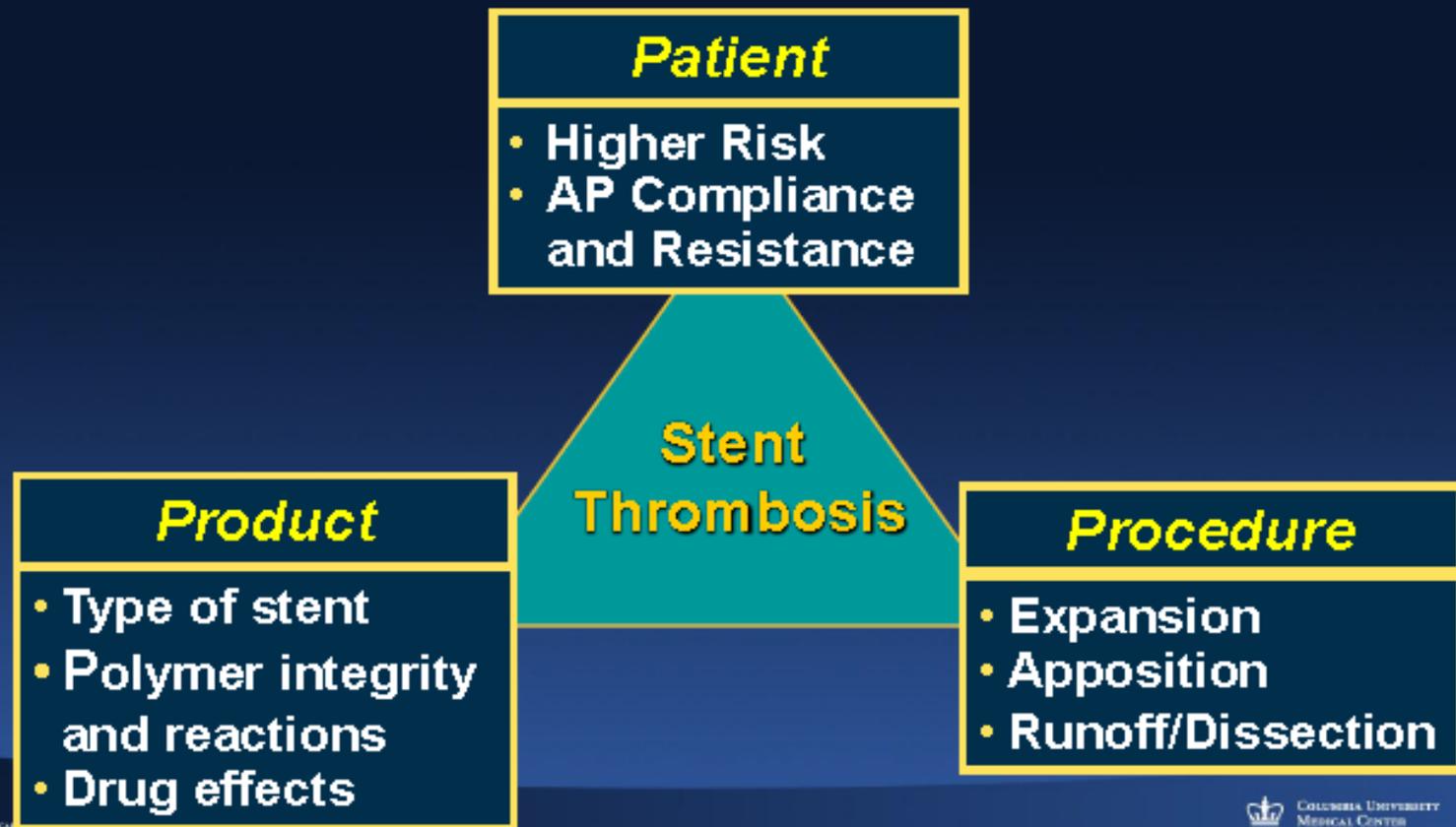
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Mortality according to Stent type



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Stent Thrombosis *Patient, Product, Procedure*



ESTRATEGIAS CONTEMPORANEAS PARA LA PREVENCION Y MANEJO DE LA TROMBOSIS DEL STENT

Características Patológicas Asociadas a la TS

| CARACTERISTICA |
|--|
| Cicatrización retardada |
| - Deposición persistente de fibrina |
| - Pobre endotelización |
| Reacción local de hipersensibilidad |
| Stent en bifurcación u ostial |
| Falta de adhesión a la pared (malapposition) |
| Reestenosis |
| Penetración de celdillas al núcleo necrótico |



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Características Patológicas Asociadas a la TS

Cypher

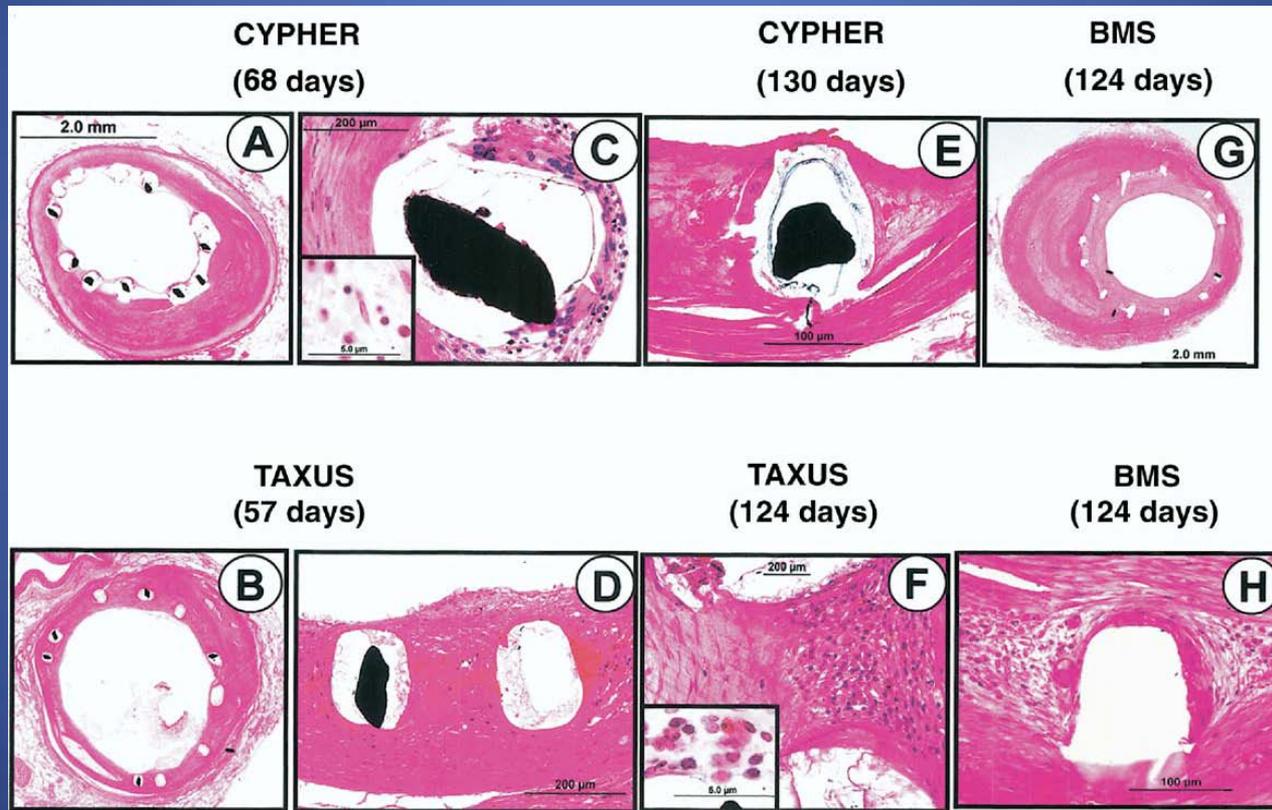


BxVelocity



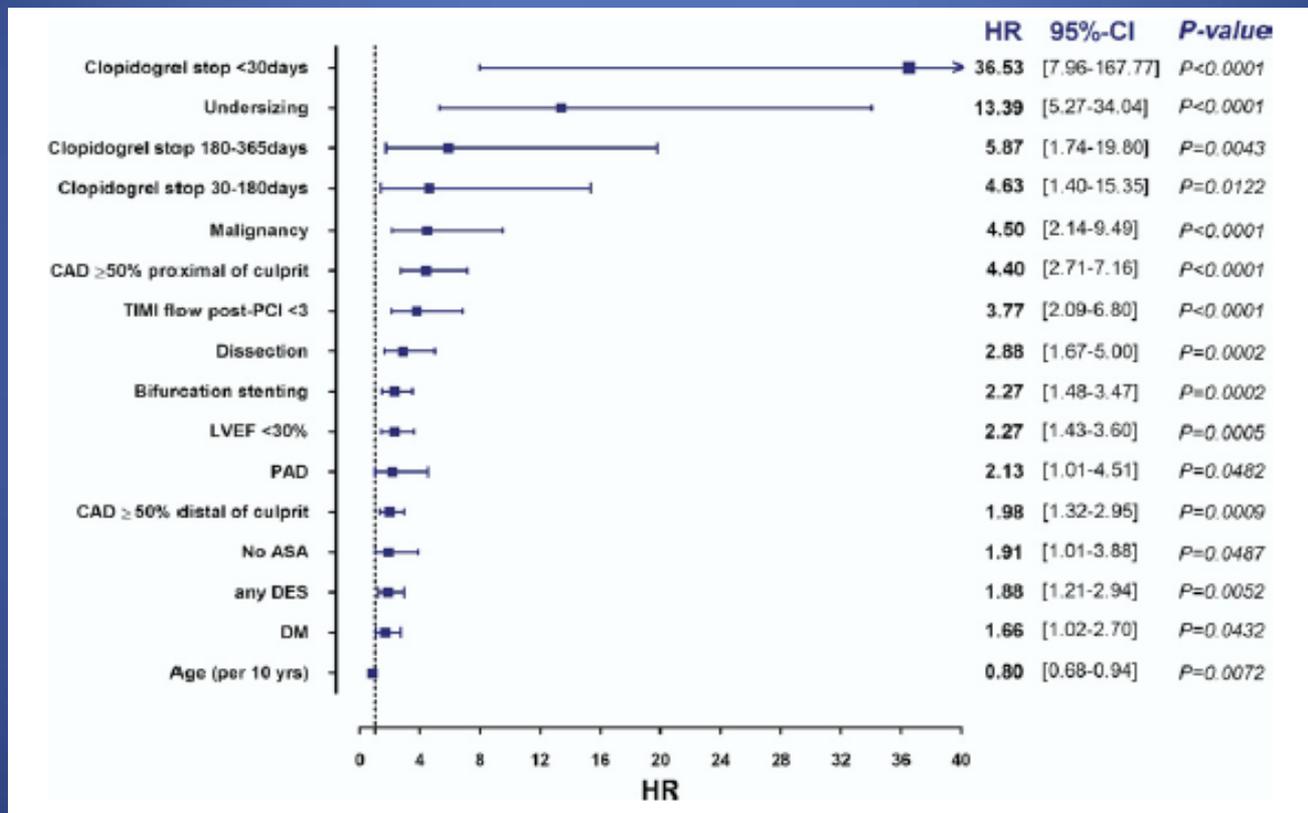
ESTRATEGIAS CONTEMPORANEAS PARA LA PREVENCION Y MANEJO DE LA TROMBOSIS DEL STENT

Características Patológicas Asociadas a la TS



ESTRATEGIAS CONTEMPORANEAS PARA LA PREVENCIÓN Y MANEJO DE LA TROMBOSIS DEL STENT

Predictores Clínicos de Trombosis del Stent



ESTRATEGIAS CONTEMPORANEAS PARA LA PREVENCIÓN Y MANEJO DE LA TROMBOSIS DEL STENT

Hallazgos de IVUS en TS

| | ST (n = 18) | Control Subjects (n = 36) | p Value |
|---------------------------------------|------------------|------------------------------|---------|
| Reference segment | | | |
| Mean EEM CSA, mm ² | 13.6 ± 3.9 | 13.7 ± 3.5 | 0.50 |
| Mean lumen CSA, mm ² | 6.9 ± 1.7 | 6.9 ± 1.8 | 0.96 |
| Stent segment | | | |
| Mean EEM, mm ² | 19.4 ± 5.8 | 15.1 ± 4.6 | 0.003 |
| Remodeling index | 1.24 (1.06–1.43) | 0.99 (0.90–1.11) | <0.001 |
| Mean stent CSA, mm ² | 7.8 ± 1.6 | 7.6 ± 1.4 | 0.42 |
| Minimal stent CSA, mm ² | 5.7 ± 1.4 | 5.9 ± 1.4 | 0.99 |
| Minimal stent CSA < 4 mm ² | 3 (16.7) | 3 (8.3) | 0.38 |
| Stent expansion index | 0.87 ± 0.3 | 0.91 ± 0.3 | 0.69 |
| ISA | 14 (77.8) | 15 (41.7) | 0.01 |
| Maximal ISA CSA, mm ² | 4.11 ± 2.3 | 1.16 ± 1.5 | 0.001 |



ESTRATEGIAS CONTEMPORANEAS PARA LA PREVENCION Y MANEJO DE LA TROMBOSIS DEL STENT

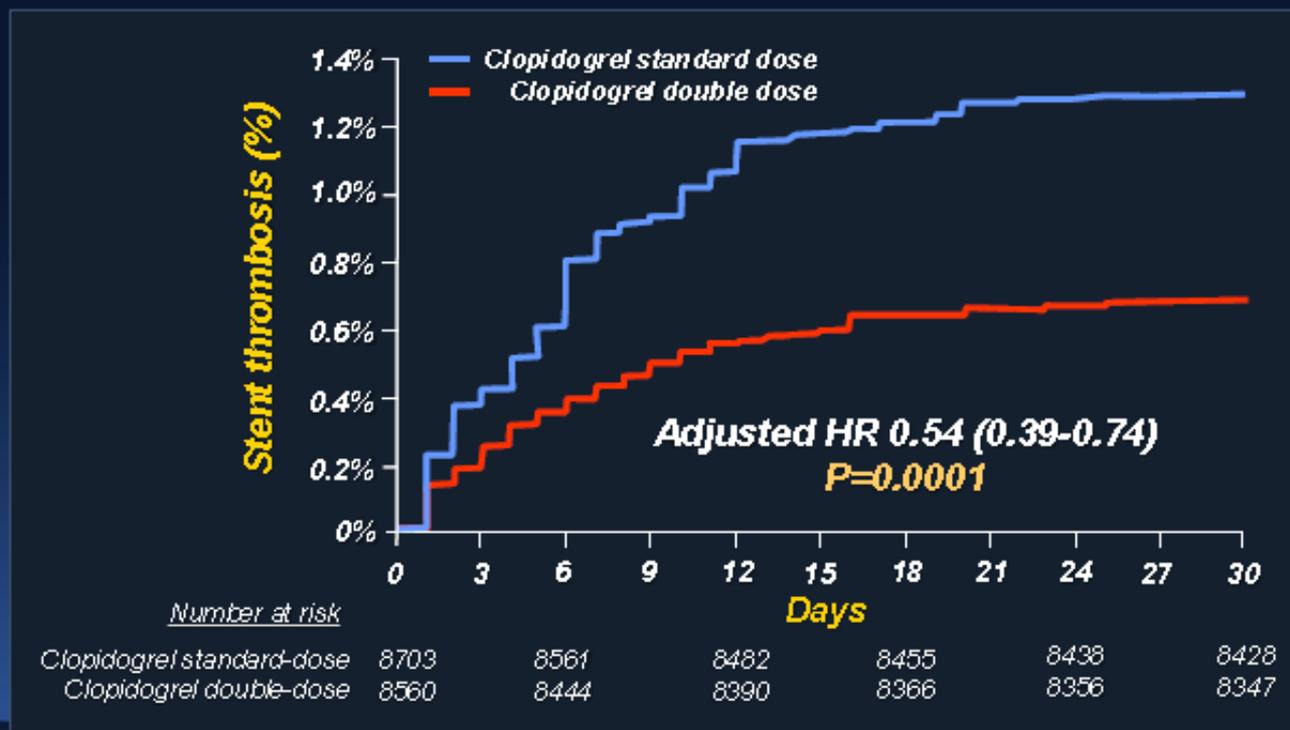
Hallazgos de TCO en TS

| | ST (n = 18 Lesions; 4,407 Struts) | Control Subjects (n = 36 Lesions; 9,064 Struts) | p Value |
|--|---|---|---------|
| Cross-section level analysis | | | |
| Minimum stent area, mm ² | 5.04 ± 1.23 | 5.50 ± 1.27 | 0.26 |
| Mean stent area, mm ² | 7.24 ± 0.97 | 7.69 ± 1.61 | 0.20 |
| Mean neointimal area, mm ² | 1.57 ± 0.68 | 1.68 ± 0.71 | 0.41 |
| Strut-level analysis | | | |
| Number of struts analyzed/patient | 244 ± 131 | 251 ± 86 | 0.81 |
| Number of uncovered struts/patient | 25.00 (8.25–52.25) | 9.00 (4.25–14.00) | 0.006 |
| Frequency of uncovered struts/patient, % | 12.27 (5.50–23.33) | 4.14 (3.00–6.22) | 0.001 |
| Number of malapposed struts/patient | 10.00 (2.25–21.75) | 4.00 (0.00–7.00) | 0.02 |
| Frequency of malapposed struts/patient, % | 4.60 (1.85–7.19) | 1.81 (0.00–2.99) | 0.001 |
| Neointimal thickness of covered struts, mm | 0.23 ± 0.15 | 0.17 ± 0.09 | 0.28 |



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CURRENT Clopidogrel Double vs Standard Dose: Definite Stent Thrombosis (angio confirmed)

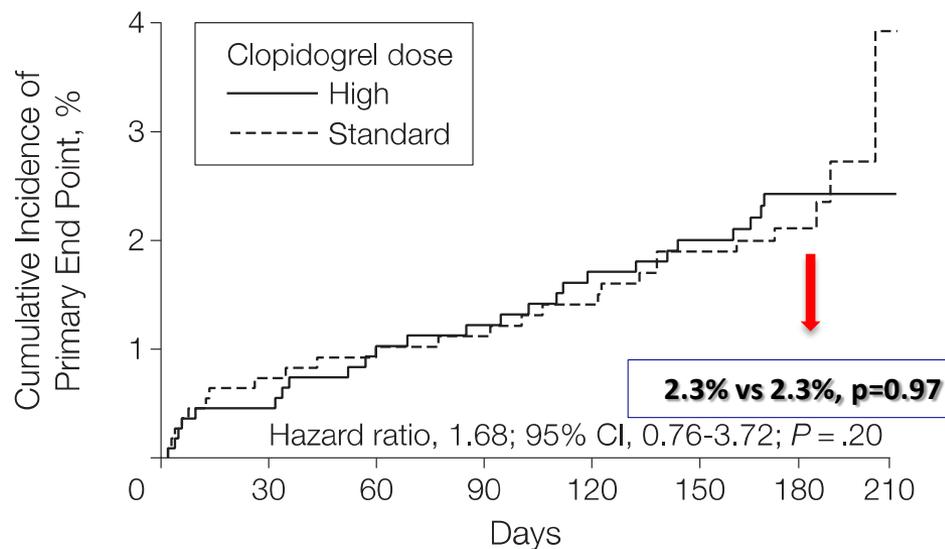


ESTRATEGIAS CONTEMPORANEAS PARA LA PREVENCIÓN Y MANEJO DE LA TROMBOSIS DEL STENT

GRAVITAS

High vs Standard Clopidogrel Maintenance Dose in High On-treatment Platelet Reactivity

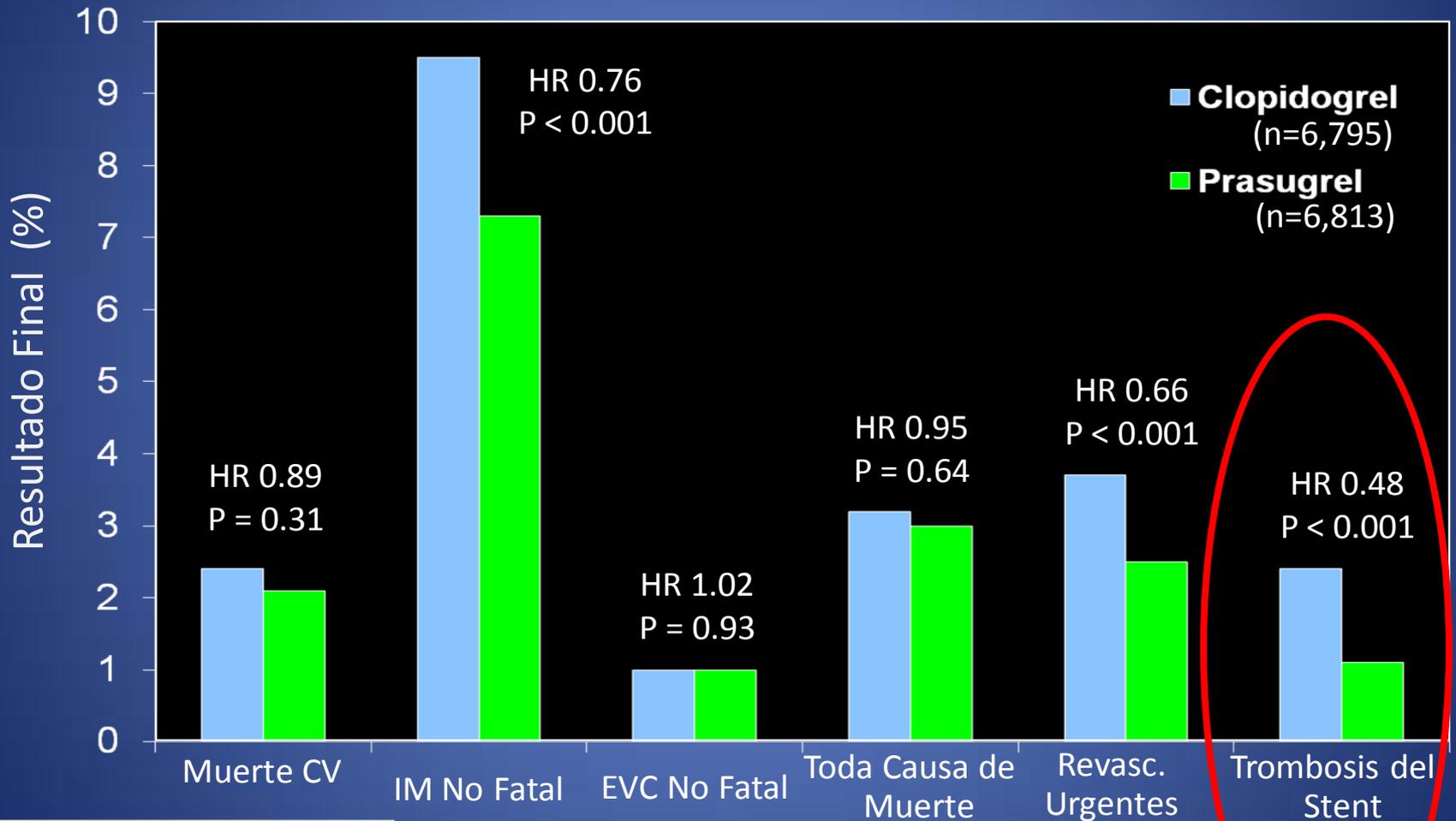
Patients with high on-treatment platelet reactivity receiving high- or standard-dose clopidogrel



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 |



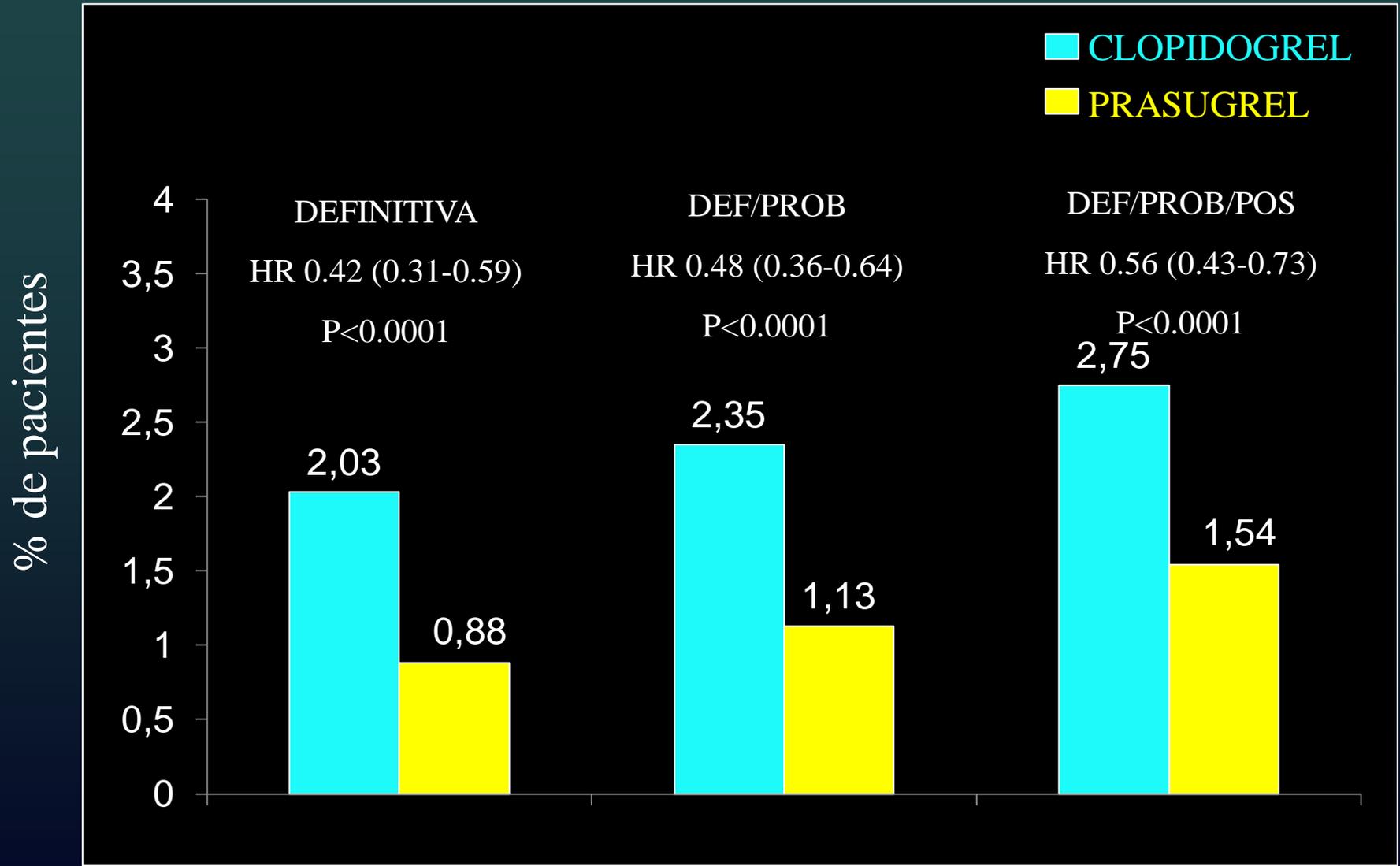


HR basados en estimados de Kaplan-Meier a 15 meses

Wiviott SD, et al. NEJM 2007;357:2001-2015



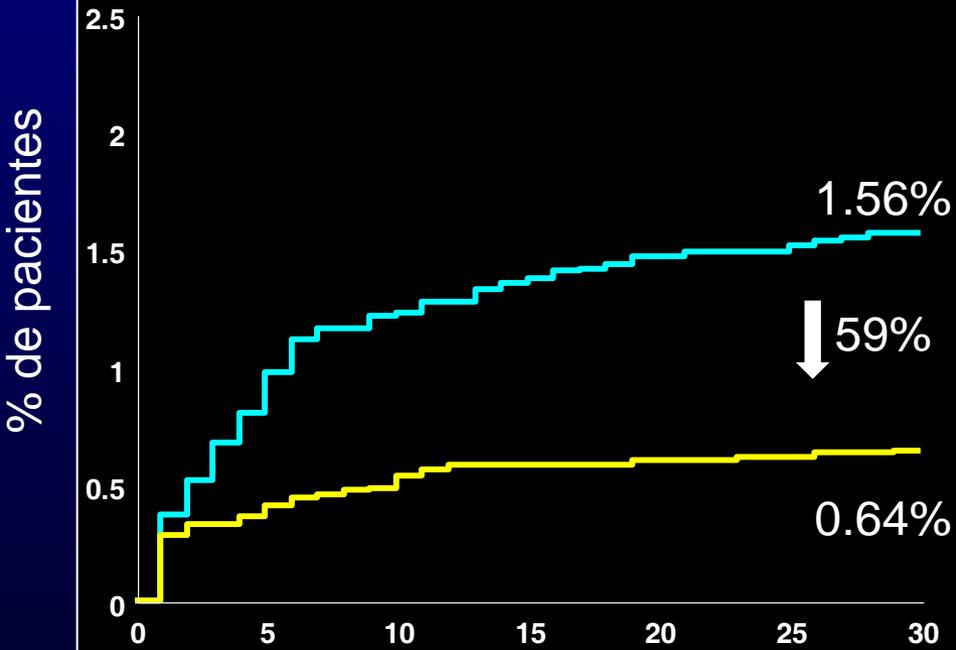
Trombosis con stent por categoría de ARC (N=12,844)



Trombosis de stent definitiva/probable: cualquier stent (N=12,844)

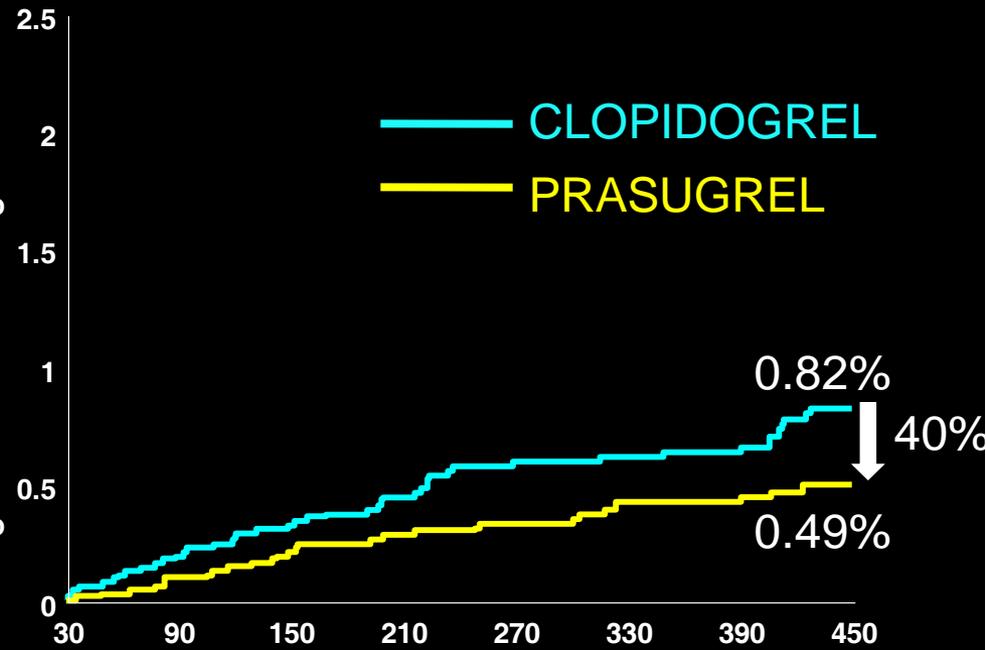
Trombosis de stent TEMPRANA

HR 0.41 [0.29-0.59]
P<0.0001



Trombosis de stent TARDÍA

HR 0.60 [0.37-0.97]
P=0.03

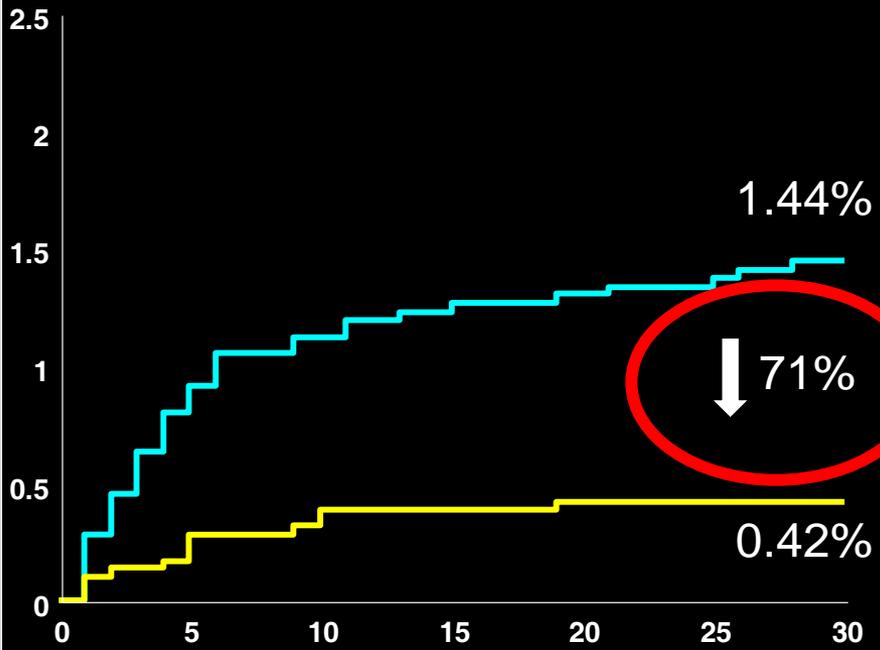


DÍAS

Trombosis de stent Definitiva/Probable: Únicamente DES (N=5743)

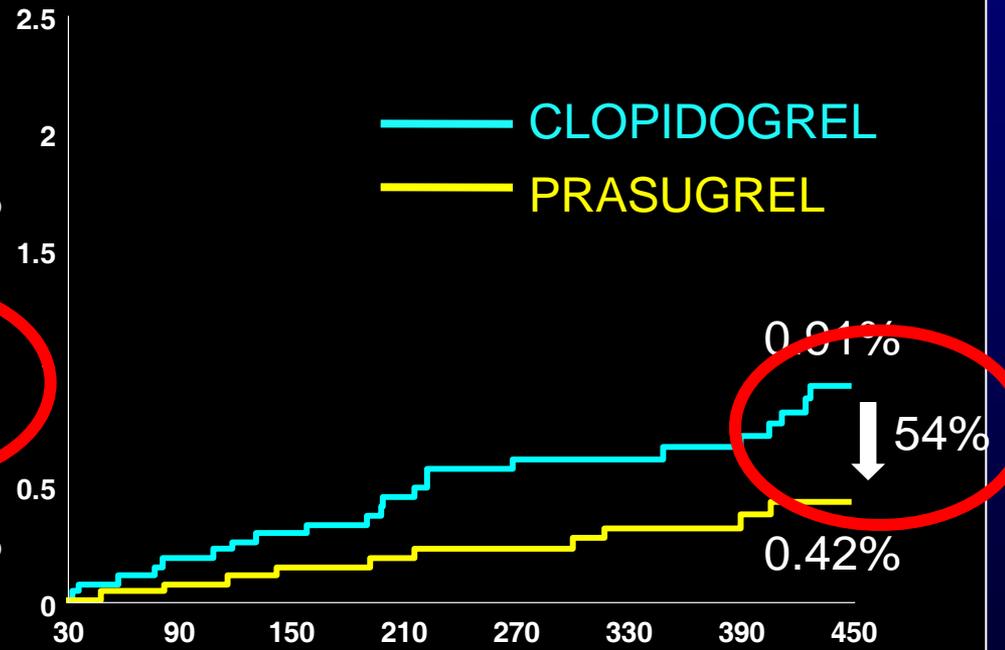
Trombosis Temprana

HR 0.29 [0.15-0.56]
P=0.0001



Trombosis Tardía

HR 0.46 [0.22-0.97]
P=0.04



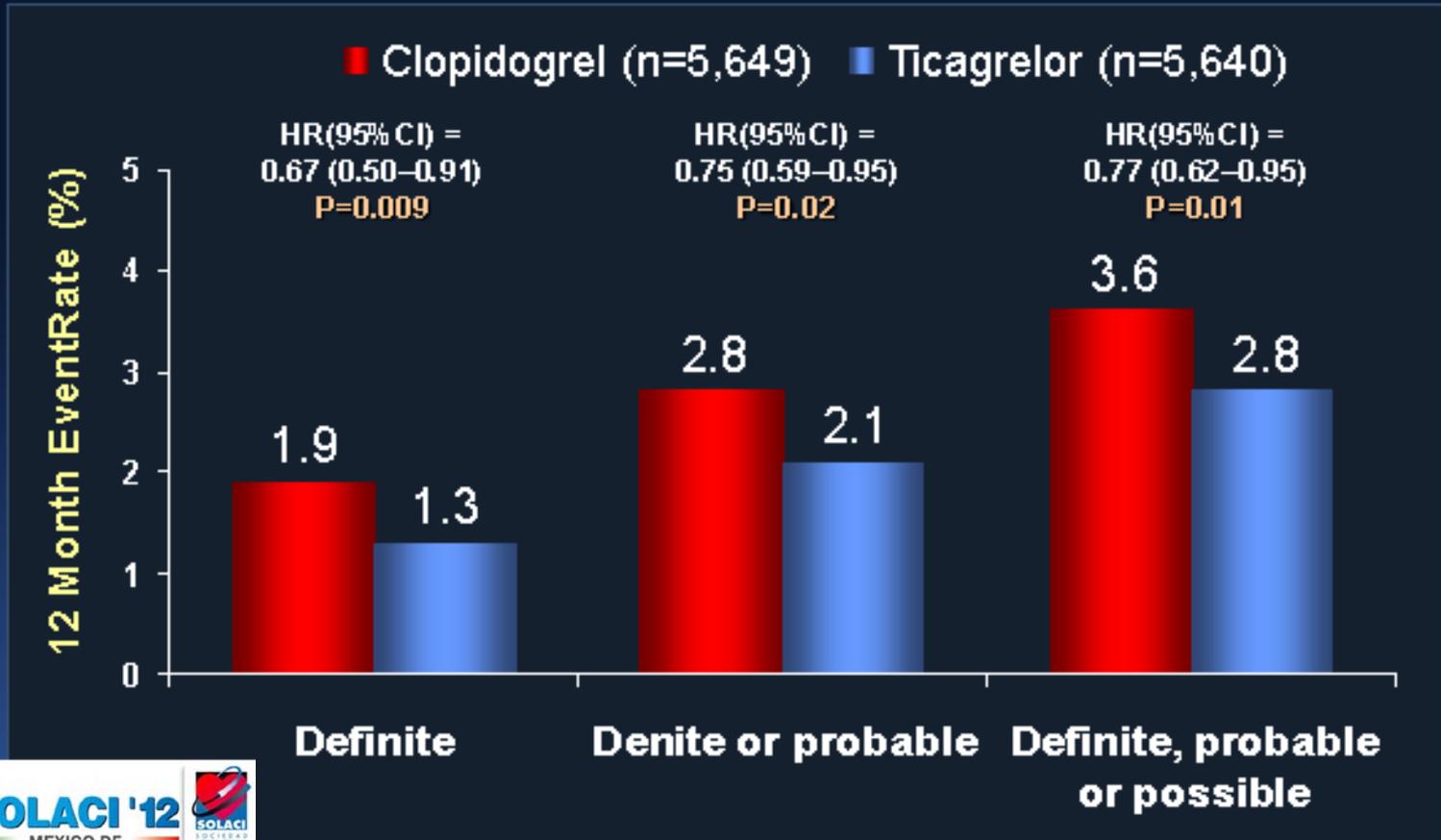
DIAS

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PLATO

PLATO

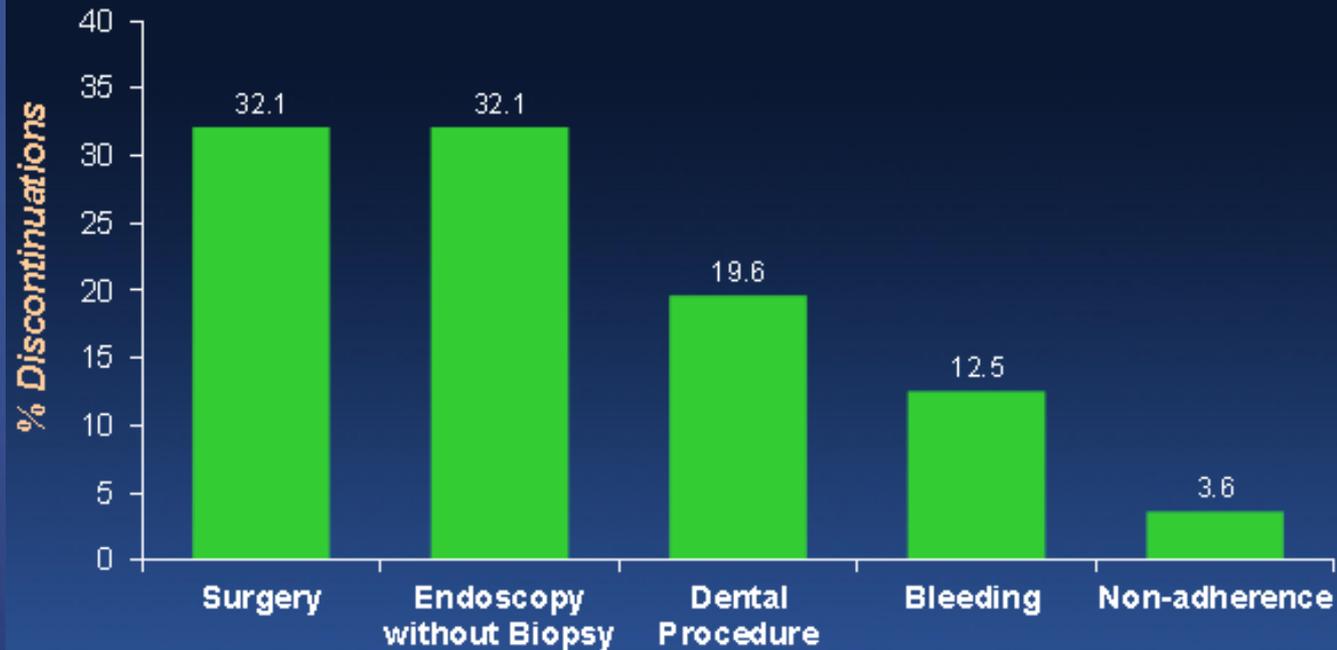
Stent Thrombosis



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Specific Reasons for Discontinuation of Antiplatelet Treatment

Reasons for 56 d/c episodes (46 pts; 18%); mean 11 mo



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Bridging Strategies

- Stop aspirin and continue P2Y12 inhibitor
- If bleeding risk is too high and necessitates discontinuation of DAPT, continue ASA and minimize time off the P2Y12 inhibitor
 - Use a shorter-acting P2Y12 inhibitor
 - Use platelet reactivity testing to measure platelet inhibition?
- If no AP therapy can be used at all perioperatively, consider IIb/IIIa bridge



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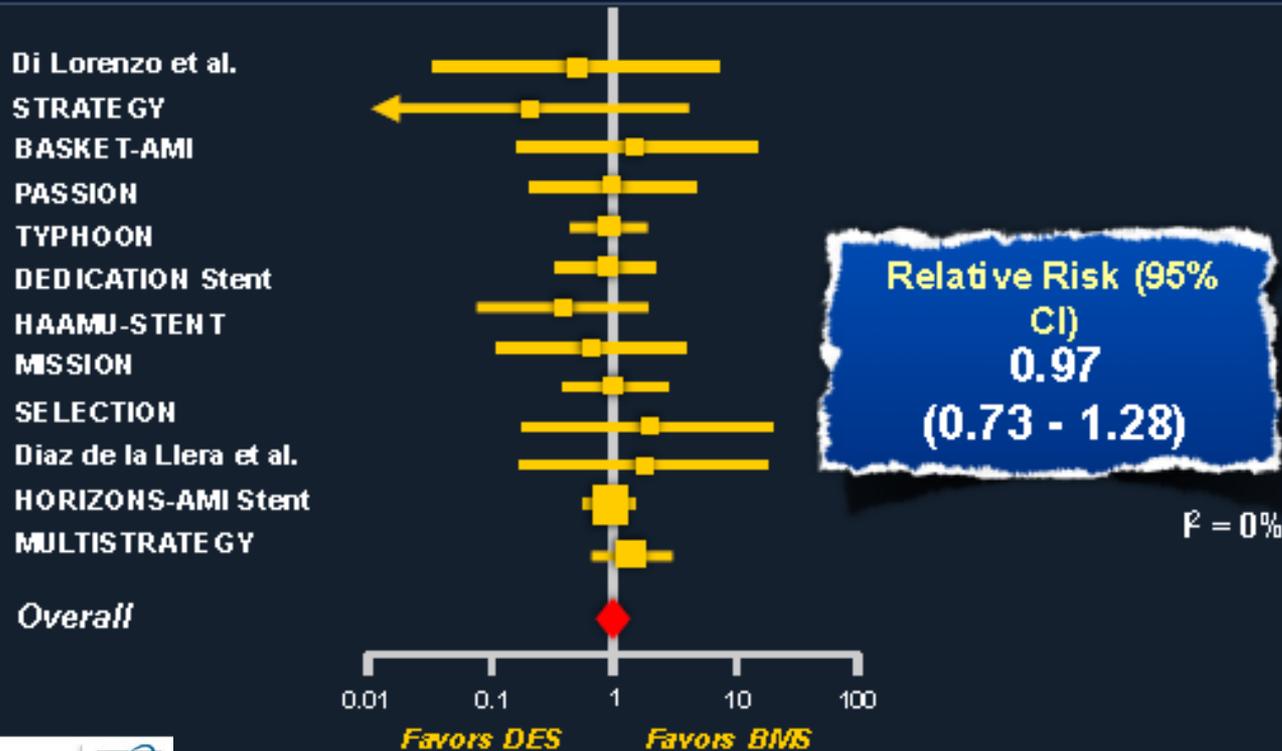
HORIZONS - AMI

2 Años



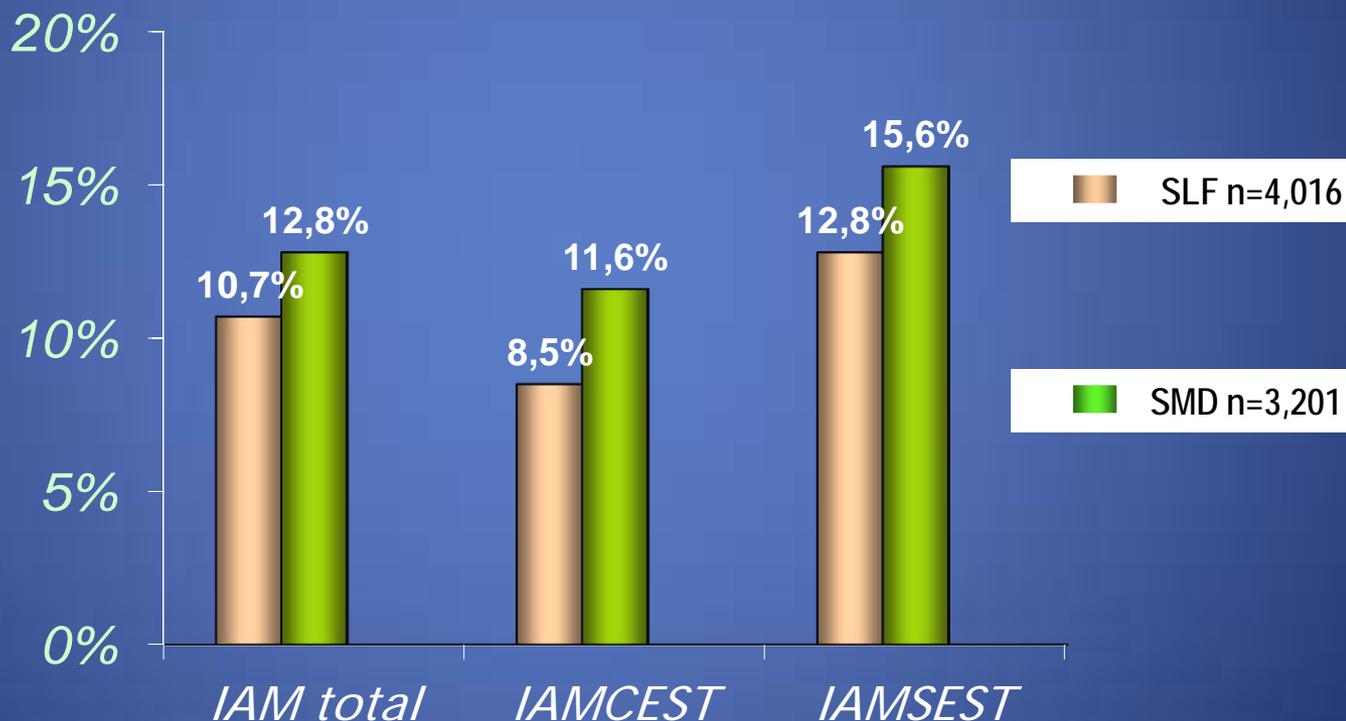
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DES in AMI Meta-Analysis Stent Thrombosis (RCTs)



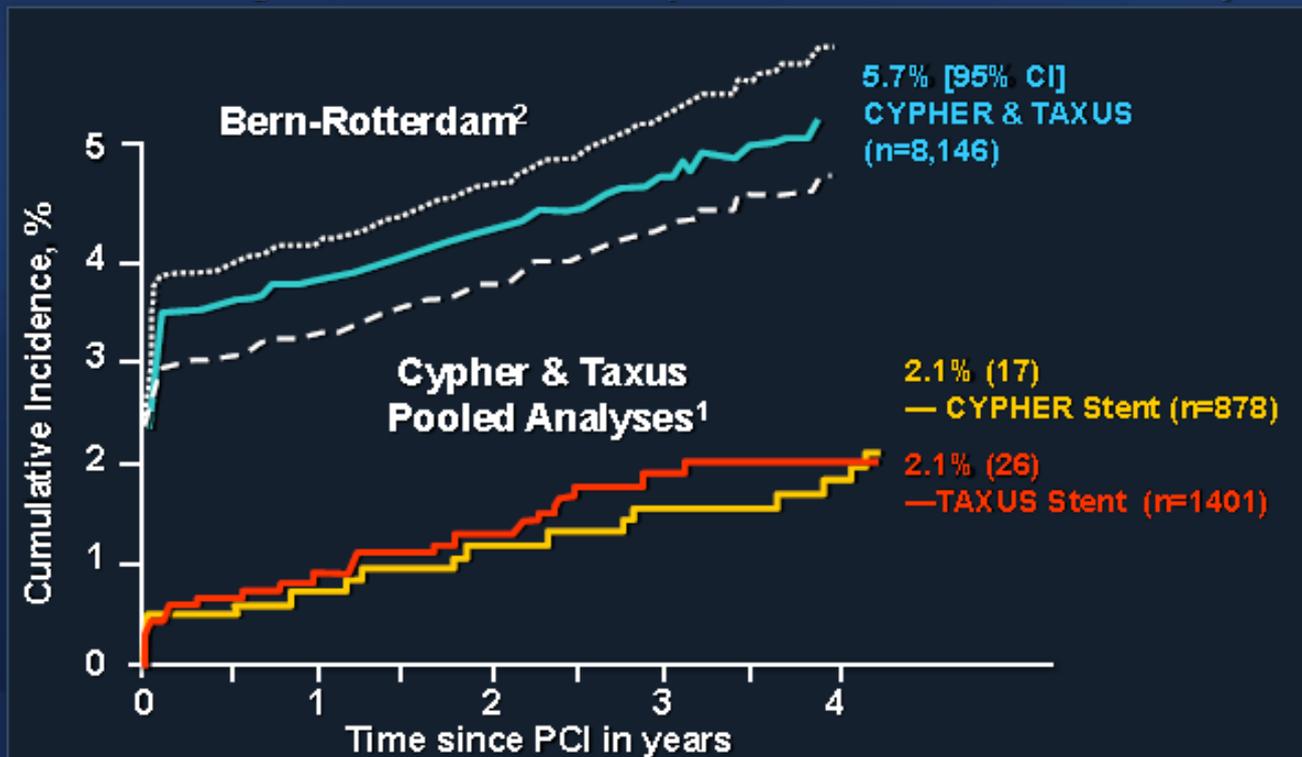
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REGISTRO ESTATAL DE ICP EN MASSACHUSETTS: MORTALIDAD A 2 AÑOS



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Cumulative Incidence of ARC Def/Prob ST over 4 yrs after DES (CYPHER & TAXUS)



¹ Mauri et al; N Engl J Med 2007;356:1020-9

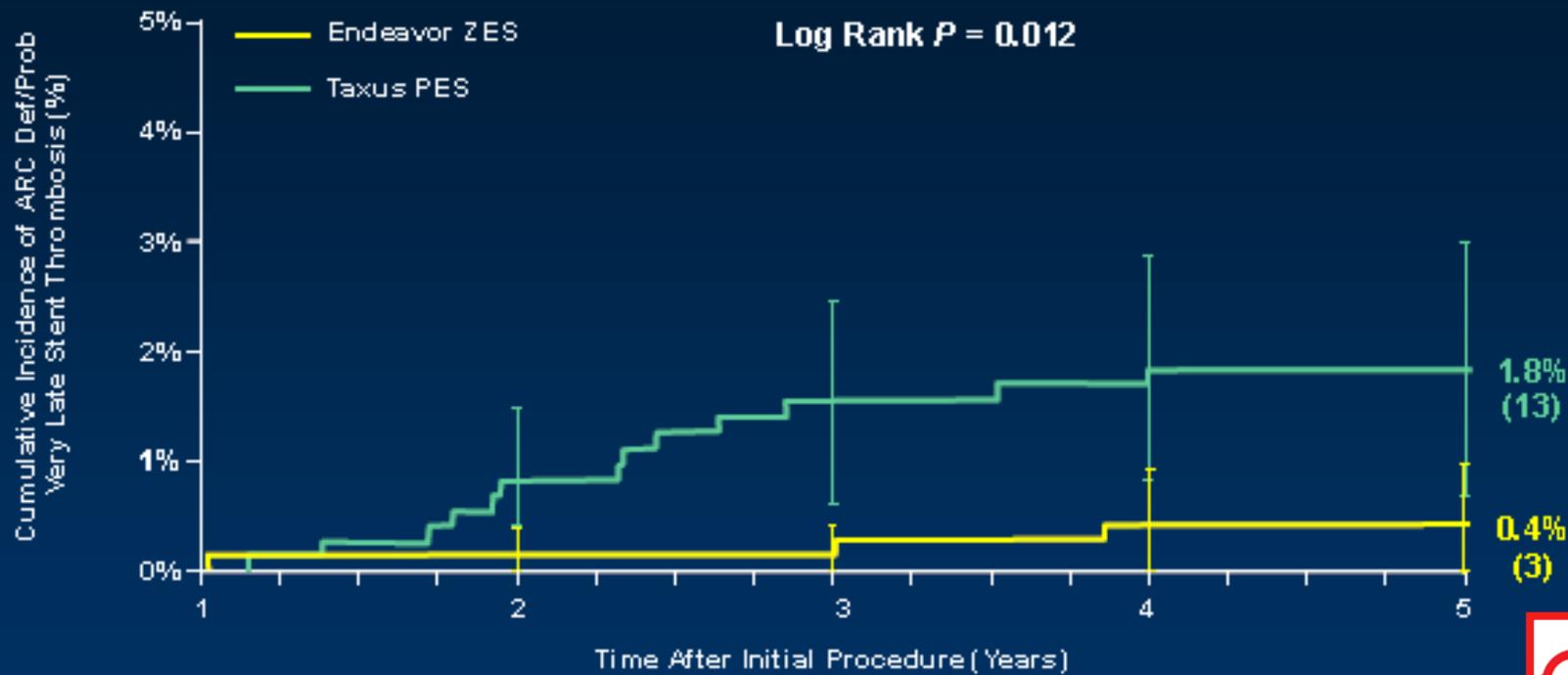
² Wenaweser et al; J Am Coll Cardiol 2008;52:1134-40



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ENDEAVOR IV

Cumulative Incidence of Very Late ST to 5 Years



ESTRATEGIAS CONTEMPORANEAS PARA LA PREVENCIÓN Y MANEJO DE LA TROMBOSIS DEL STENT

Individual component of primary endpoint (ITT)

| Variables | E-ZES+3-month DAPT (n=1,059) | Standard therapy (n=1,058) | Difference (95% CI) | P |
|--------------------------------|------------------------------|----------------------------|---------------------------|-------------|
| Death, n (%) | | | | |
| From any cause | 5 (0.5) | 8 (1.0) | -0.5% (-1.4 - 0.4) | 0.39 |
| From cardiovascular cause | 2 (0.2) | 4 (0.4) | -0.2% (-0.6 - 0.3) | 0.41 |
| MI, n (%) | 2 (0.2) | 4 (0.4) | -0.2% (-0.7 - 0.3) | 0.41 |
| TVR, n (%) | 31 (3.9) | 27 (3.7) | 0.2% (-2.3 - 2.6) | 0.70 |
| Non-TVR, n (%) | 15 (1.5) | 11 (1.5) | 0.0% (-1.3 - 1.4) | 0.52 |
| Stent thrombosis, n (%) | 2 (0.2) | 3 (0.3) | -0.1% (-0.5 - 0.3) | 0.65 |
| < 1 months | 2 | 0 | | |
| 1-3 months | 0 | 0 | | |
| 3-12 months | 0 | 3 | | |
| Bleeding, n (%) | | | | |
| Major or minor | 5 (0.5) | 10 (1.0) | -0.5% (-1.2 - 0.2) | 0.20 |
| Major | 2 (0.2) | 6 (0.6) | -0.4% (-0.9 - 0.1) | 0.16 |
| CVA, n (%) | 6 (0.6) | 6 (0.7) | 0.1% (-0.1 - 1.0) | 0.96 |

SEVERANCE CARDIOVASCULAR HOSPITAL

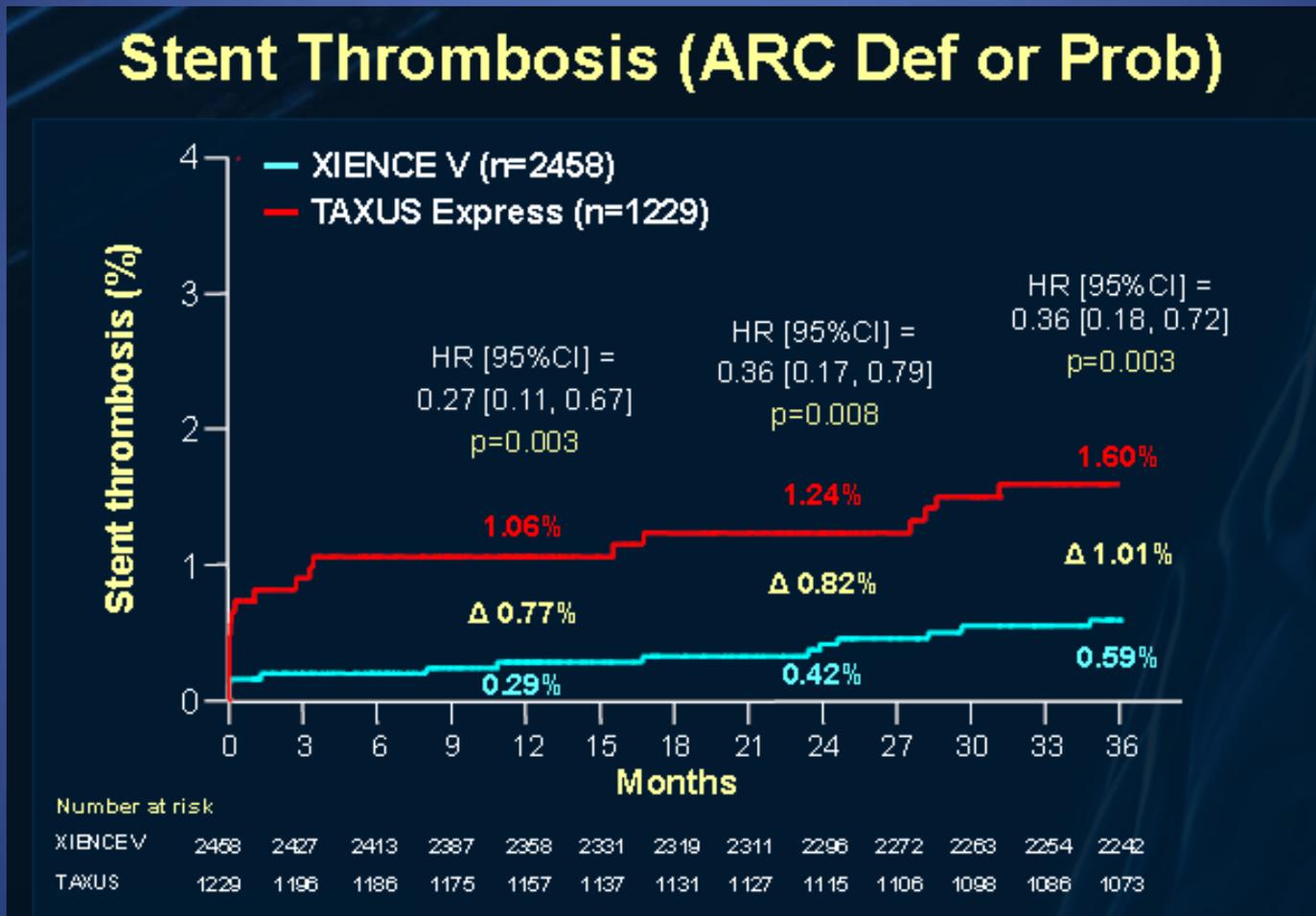


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RESET



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G. Stone, TCT 2011

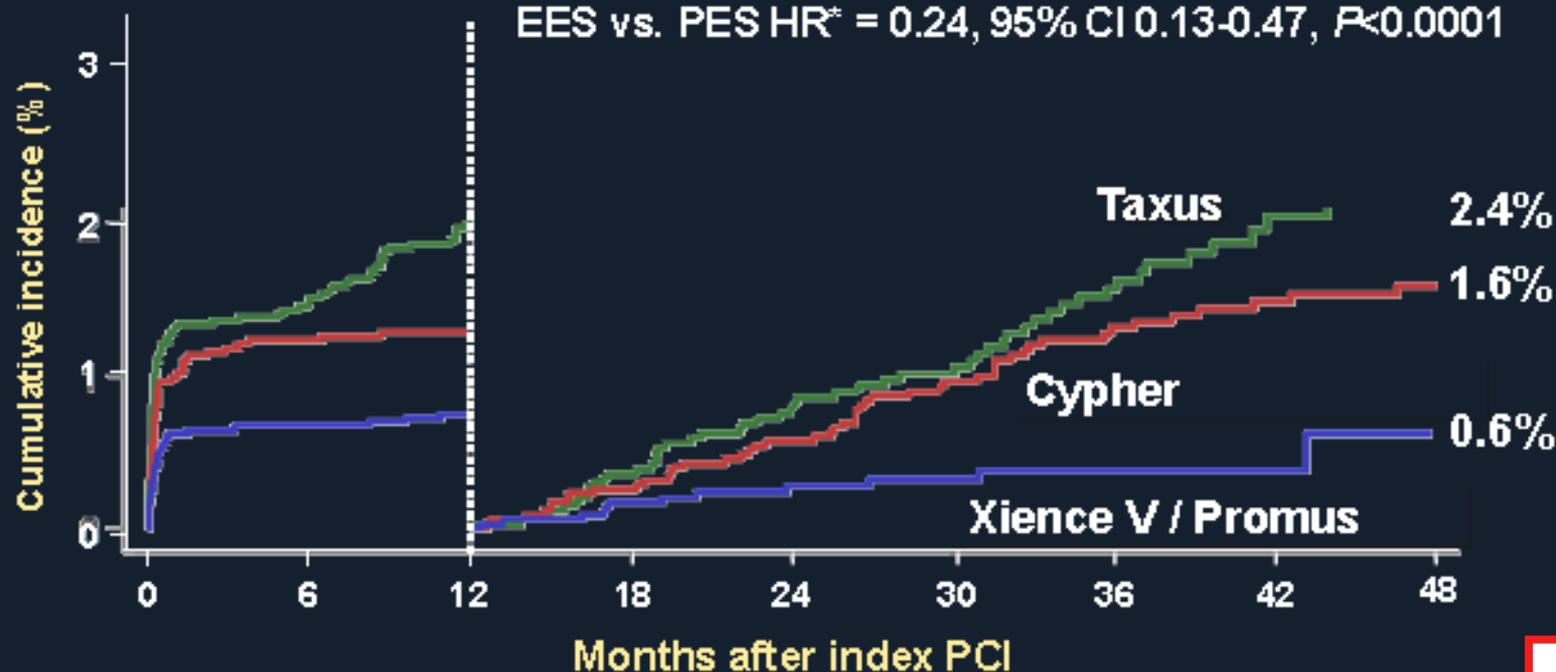
Spirit IV



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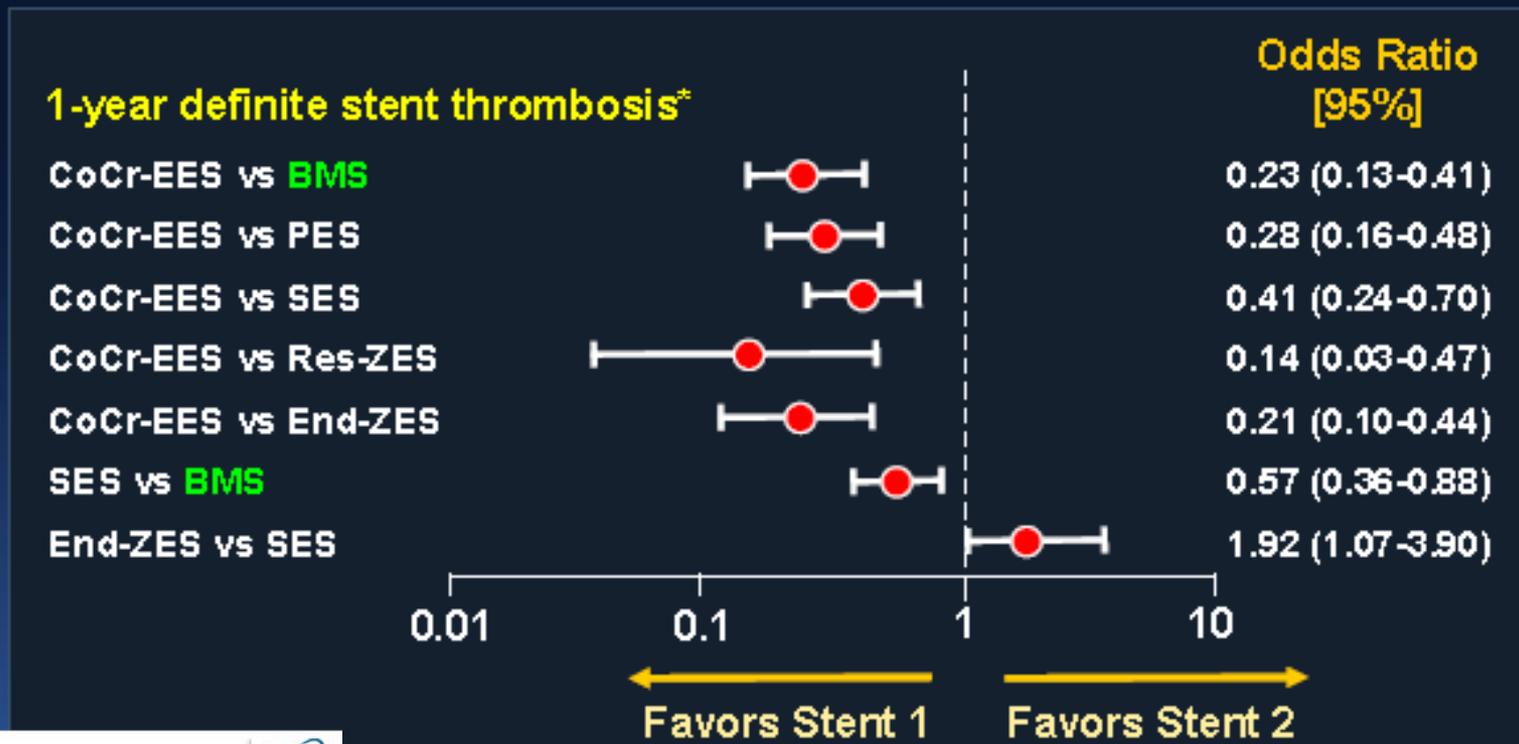
Bern Rotterdam (n=12,339 pts) ARC Definite ST: Landmark analysis

EES vs. SES HR* = 0.33, 95% CI 0.15 – 0.72, P=0.006
EES vs. PES HR* = 0.24, 95% CI 0.13-0.47, P<0.0001



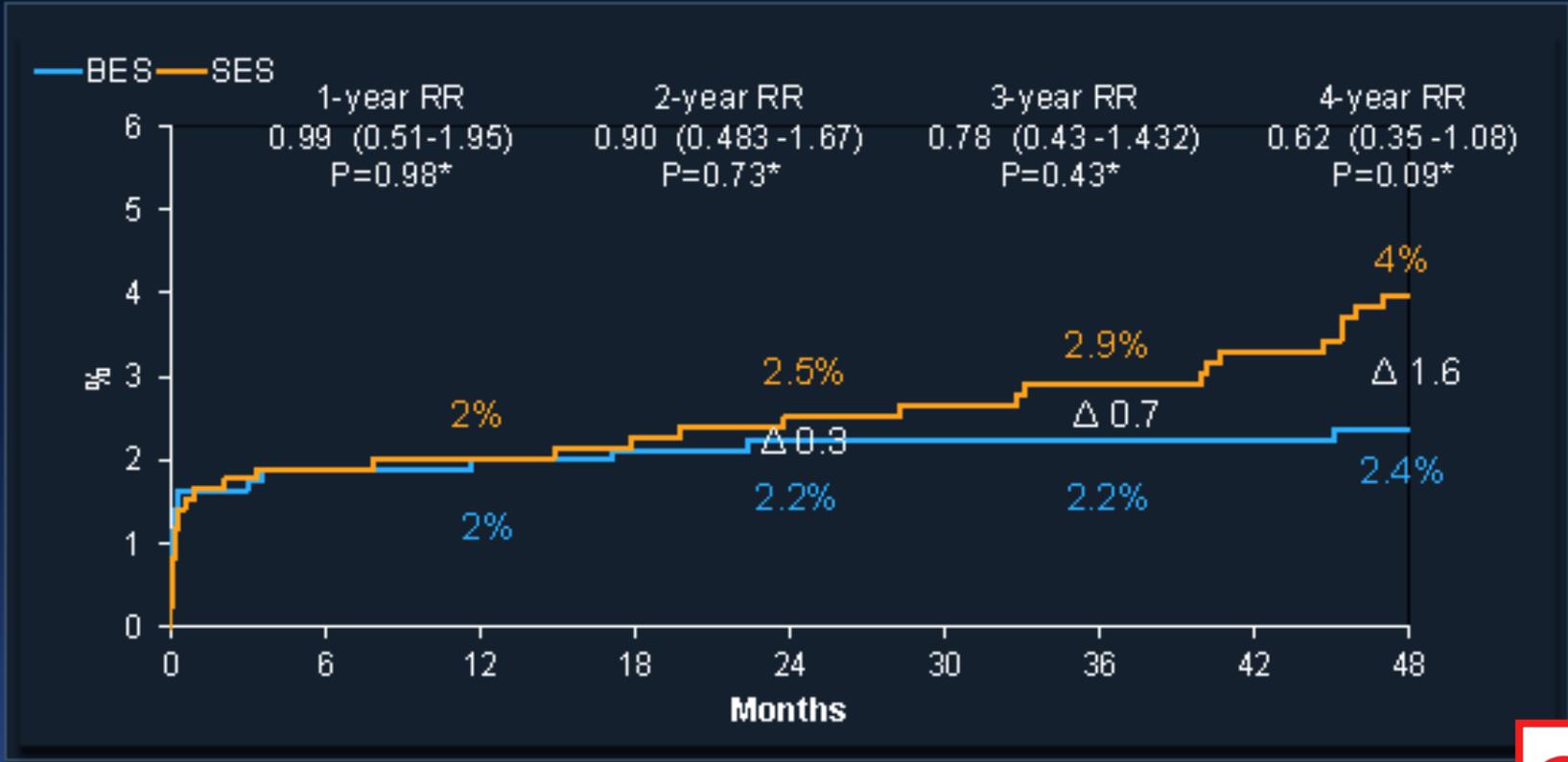
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Stent Thrombosis Network Meta-analysis Primary EP: ARC Definite ST (FU through 2 years) 49 RCTs, 50,844 pts



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LEADERS: Definite ST (ARC)



ESTRATEGIAS CONTEMPORANEAS PARA LA PREVENCIÓN Y MANEJO DE LA TROMBOSIS DEL STENT

Tx Modality in ST

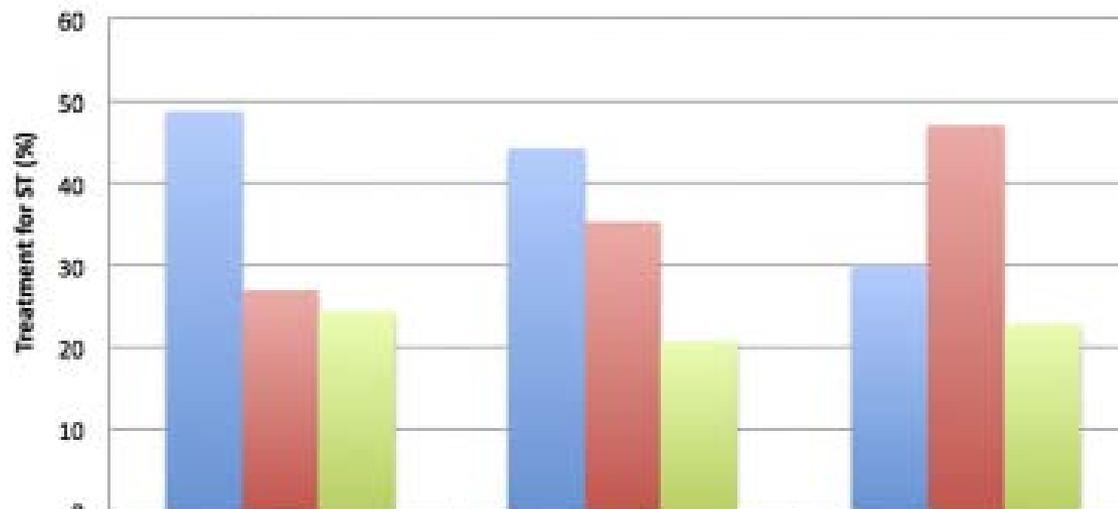
| | Early ST (n = 1,391) | Late ST (n = 1,370) | Very Late ST (n = 4,318) | p Value |
|--|-------------------------|------------------------|-----------------------------|---------|
| Procedural characteristics | | | | |
| Thrombectomy performed | 447 (32.1) | 401 (29.3) | 1,475 (34.2) | 0.003 |
| Additional stent placed | | | | <0.001 |
| DES | 374 (26.9) | 482 (35.2) | 2,031 (47.0) | |
| BMS | 338 (24.3) | 284 (20.7) | 968 (22.9) | |
| No stent placed | 679 (48.8) | 604 (44.1) | 1,299 (30.1) | |
| IABP or other mechanical support placed during procedure | 186 (13.4) | 119 (8.7) | 403 (9.3) | <0.001 |
| Dissection | 28 (2.0) | 22 (1.6) | 39 (0.9) | 0.002 |
| Coronary perforation | 6 (0.4) | 8 (0.6) | 11 (0.3) | 0.172 |
| Post-procedure TIMI flow grade | | | | 0.003 |
| 3 | 1,274 (91.6) | 1,286 (93.9) | 4,085 (94.6) | |
| 0-2 | 96 (6.9) | 71 (5.2) | 198 (4.6) | |



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Treatment Modality in ST

A Overall Group



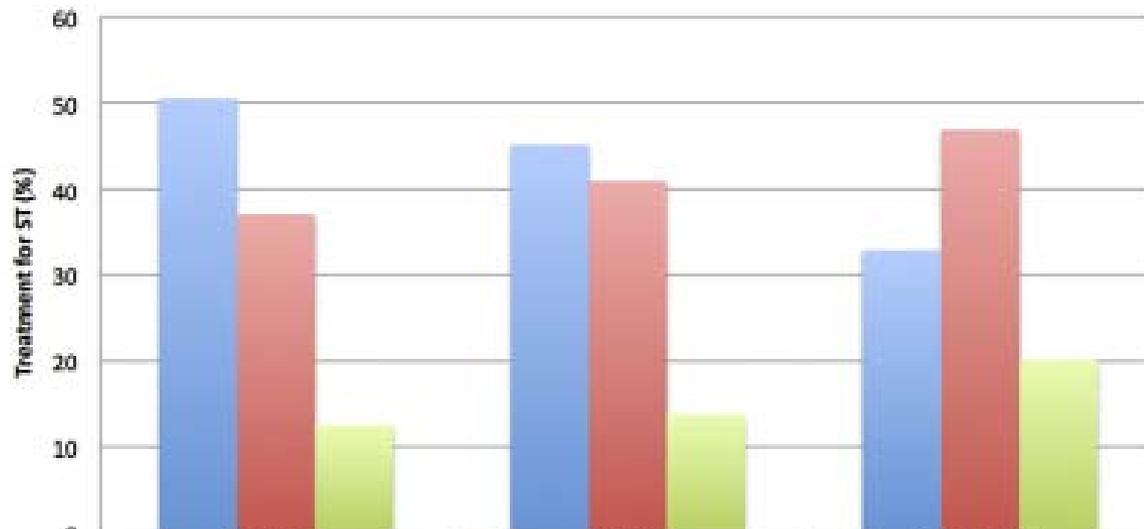
| | Early ST | Late ST | Very Late ST |
|----------------|----------|---------|--------------|
| POBA | 48.8 | 44.1 | 30.1 |
| New DES placed | 26.9 | 35.2 | 47 |
| New BMS placed | 24.3 | 20.7 | 22.9 |



ESTRATEGIAS CONTEMPORANEAS PARA LA PREVENCIÓN Y MANEJO DE LA TROMBOSIS DEL STENT

Treatment Modality in ST

B Stent Thrombosis of a DES



| | Early ST | Late ST | Very Late ST |
|----------------|----------|---------|--------------|
| POBA | 50.5 | 45.2 | 32.9 |
| New DES placed | 37 | 41 | 46.9 |
| New BMS placed | 12.5 | 13.8 | 20.2 |



ESTRATEGIAS CONTEMPORANEAS PARA LA PREVENCIÓN Y MANEJO DE LA TROMBOSIS DEL STENT

Tx Modalities in ST

| | Early ST (n = 1,391) | Late ST (n = 1,370) | Very Late ST (n = 4,318) | p Value |
|---------------------------------|-------------------------|------------------------|-----------------------------|---------|
| Intra-procedural medications | | | | |
| Anticoagulants | | | | |
| Unfractionated heparin | 989 (71.1) | 948 (69.0) | 3,180 (73.9) | 0.001 |
| Bivalirudin | 416 (29.9) | 493 (36.0) | 1,354 (31.4) | 0.001 |
| LMWH | 169 (12.2) | 154 (11.3) | 499 (11.6) | 0.736 |
| Fondaparinux | 15 (1.1) | 19 (1.4) | 57 (1.3) | 0.737 |
| Aspirin | 1,224 (90.1) | 1,219 (90.0) | 3,901 (90.9) | 0.536 |
| Glycoprotein IIb/IIIa inhibitor | 1,023 (73.9) | 876 (64.0) | 2,949 (68.7) | <0.001 |
| Thienopyridines | | | | |
| Clopidogrel | 1,102 (80.6) | 1,099 (81.4) | 3,355 (79.2) | 0.1609 |
| Prasugrel | 175 (12.6) | 127 (9.3) | 329 (7.6) | <0.001 |
| Ticlopidine | 11 (0.8) | 14 (1.0) | 24 (0.6) | 0.174 |



ESTRATEGIAS CONTEMPORANEAS PARA LA PREVENCIÓN Y MANEJO DE LA TROMBOSIS DEL STENT

Abordaje Integral para la Prevención de la TS

Cómo Minimizar la Trombosis del Stent

• Mejor Selección del Paciente

Escrutinio para probabilidad de adherencia y riesgo de sangrado/ posibilidad de tolerar la TAPD
Ausencia de procedimientos quirúrgicos

• Mejor Selección del Stent y de la Técnica

Considerar stents con menor riesgo de trombosis
Medición apropiada del diámetro del vaso, implante y post-dilatación a altas presiones
Asegurar ausencia de disecciones residuales o enfermedad no tratada proximal o distal
Evitar en la medida de lo posible el uso de dos stents en las bifurcaciones

• Mejor Cuidado peri y Post-procedimiento

Uso de antiplaquetarios más potentes en escenarios clínicos apropiados (síndromes coronarios agudos en ptes con bajo riesgo de sangrado)

La educación del paciente y un seguimiento clínico apropiado son esenciales

Uso de los antiagregantes plaquetarios sin interrupción durante un período de un año

