XLIV Jornadas SOLACI
15° Región Cono Sur
30 de junio / 01 de julio

Mesa Redonda: SOLACI y SPCyCC
Módulo: Cardiopatía Isquémica Crónica (SCC)

08:45 – 09:00 h Aspirina vs Clopidogrel para el mantenimiento crónico tras una intervención coronaria percutánea HOST-EXAM

Dr. Oscar L Paredes G, PhD, FACC
Cardiólogo Intervencionista

Conflicto de intereses

- **Investigación**
  - TERUMO (TERUMO Medical Planex - Japan)
  - NIMEDICAL (NICaS – Israel)
  - Scios Inc. - (J&J – USA)
- **Educación Médica**
  - Pharma Internacional SA
  - Comfar SAECA
- **Advisory Board**
  - Abbott Vascular
  - Boston Sci
  - Novo Nordisk

Delineamiento de la charla

- **Background del Tema**
- **Resultados y legado del HOST Exam**
- **Perspectivas y Conclusiones sobre el tema principal.**

Cuál es el trasfondo de esto?

Circulation
Volume 123, Issue 7, 22 February 2011; Pages 768-778
https://doi.org/10.1161/CIRCULATIONAHA.110.963843

CONTEMPORARY REVIEWS IN CARDIOVASCULAR MEDICINE

Aspirin

A Historical and Contemporary Therapeutic Overview

Valentin Fuster, MD, PhD and Joseph M. Sweeny, MD

Among the many useful discoveries which this age has made, there are very few which better deserve the attention of the public that what I am going to lay before your Lordship.
—Reverend Edward Stone
–Chipping-Norton, Oxfordshire
–April 25, 1763

Lifelong Aspirin for All in the Secondary Prevention of Chronic Coronary Syndrome

Still Sacrosanct or Is Reappraisal Warranted?

Alan P. Jacobsen, Inbar Raber, Cian P. McCarthy, Roger S. Blumenthal, Deepak L. Bhatt, Ronan W. Cusack, Patrick W.J.C. Serruys, William Wijns and John W. McEvoy

Originally published 4 Sep 2020 |
https://doi.org/10.1161/CIRCULATIONAHA.120.045695 |
Circulation. 2020;142:1579–1590

Cuál es el trasfondo de esto?

Table 1. Historical Trials of Aspirin After Myocardial Infarction

Trial (year)	Mean age of participants, y	Participants, n (% women)	Daily aspirin dose, mg	Time from index MI event to enrollment*	Average follow-up, mo	Lipid-lowering medicine/β-blocker use, %	Aspirin: control ratio of annual serious vascular events (95% CI)	Aspirin: control ratio of annual CHD death events (95% CI)
Cardiff I (1974)[26]	55	1239 (0)	300	3 months	12	—	0.72 (0.46–1.13)	0.74 (0.45–1.23)
Cardiff II (1979)[27]	56	1682 (15)	900	34% within 3 days; 66% >7 days	12	—	0.70 (0.52–0.93)	0.77 (0.54–1.11)
CDPA (1976)[28]	56†	1529 (0)	972	75% >5 years	22	—	0.74 (0.50–1.09)	0.77 (0.44–1.35)
PARIS (1980)[29]	56‡	2026 (13)	972	20% 2 to 6 months; 80% 6 to 60 months	41	<20	0.76 (0.52–1.10)	0.77 (0.46–1.29)

Clin Med Res. 2014 Dec; 12(3-4): 147–154.

Cuál es el trasfondo de esto?

S 0)[30]	55	4524 (11)	1000	25 months	36	<15	0.89 (0.74–1.06)	1.06 (0.82–1.3
MIS 0)[31]	59§	946 (22)	1500	30 to 42 days	24	—	0.68 (0.37–1.27)	0.56 (0.23–1.3

MIS indicates Aspirin Myocardial Infarction Study; ATT, Anti-Thrombotic Trialists; CDPA, Coronary Drug Project Aspirin Study; CHD, coronary hea disease; GAMIS, German–Austrian Aspirin Trial; MI, myocardial infarction; and PARIS, Persantine–Aspirin Reinfarction Study.

The average time from index MI to enrollment in these trials was not consistently reported in the published articles and, if a time was reported, th uthors did not indicate whether it was the mean or median. Therefore, the times listed here are provided in an effort to summarize these data to th extent possible.

† The mean age was not reported in the original report of this study but was in ATT reports; 61.4% of participants were ≥55 years old.

‡ The mean age was not reported in the original report of this study but was in ATT reports; 57.7% of participants were ≥55 years old.

The mean age was not reported in the original report of this study but was in ATT reports; 30% of participants were 45 to 55 years old and 70% participants were 55 to 70 years old.

Clin Med Res. 2014 Dec; 12(3-4): 147–154.

Que sabemos en la actualidad?

Post-interventional and maintenance treatment		
Life-long single antiplatelet therapy, usually aspirin, is recommended.[681,683]	I	A
Instruction of patients about the importance of complying with antiplatelet therapy is recommended.	I	C

Tratamiento posoperatorio y de mantenimiento		
Se recomienda el tratamiento por tiempo indefinido con un antiagregante, normalmente AAS[681,683]	I	A
Se recomienda instruir a los pacientes sobre la importancia de cumplir el tratamiento antiagregante	I	C
Para pacientes con EC estable tratados con implante de *stents* coronarios, se recomienda el TAPD con clopidogrel y AAS generalmente durante 6 meses, independientemente del tipo de *stent* implantado[c,690-694]	I	A
Para pacientes con EC estable tratados con *stent* reabsorbible, debe considerarse el TAPD durante al menos 12 meses o hasta que se estime la reabsorción completa del *stent*, con base en la evaluación individualizada de los riesgos isquémico y hemorrágico	IIa	C
Para pacientes con EC estable tratados con balón recubierto de fármaco, debe considerarse el TAPD durante 6 meses[369,371]	IIa	B
Para pacientes con EC estable y riesgo hemorrágico estimado alto (p. ej., una puntuación PRECISE-DAPT ≥ 25), debe considerarse el TAPD durante 3 meses[d,695,696]	IIa	A
Para pacientes con EC estable que han tolerado el TAPD sin complicaciones de sangrado y bajo riesgo hemorrágico pero alto riesgo trombótico, puede considerarse la ampliación del TAPD con clopidogrel durante más de 6 meses y hasta 30 meses[697-700]	IIb	A
Para pacientes con EC estable para quienes el TAPD de 3 meses pueda suponer algún peligro, puede considerarse el TAPD durante 1 mes	IIb	C

©ESC 2018

AAS: ácido acetilsalicílico; EC: enfermedad coronaria; ICP: intervención coronaria percutánea; i.v.: intravenoso; TAPD: tratamiento antiagregante plaquetario doble.
[a]Clase de recomendación.
[b]Nivel de evidencia.
[c]Estas recomendaciones se refieren a *stents* probados en estudios aleatorizados a gran escala, con evaluación de variables clínicas por las que obtuvieron la marca CE.
[d]La evidencia que respalda esta recomendación procede de 2 estudios sobre el *stent* modelo Endeavour (liberador de zotarolimus) combinado con un régimen de TAPD de 3 meses.

*F.-J. Neumann et al. / Rev Esp Cardiol. 2019;**72(1)**:73.e1-e102* 43

Cuál es el trasfondo de esto?

Recommendations for event prevention I

Recommendations	Class[a]	Level[b]
Antithrombotic therapy in patients with CCS and in sinus rhythm		
Aspirin 75–100 mg daily is recommended in patients with a previous MI or revascularization.[270]	I	A
Clopidogrel 75 mg daily is recommended as an alternative to aspirin in patients with aspirin intolerance.[273]	I	B
Clopidogrel 75 mg daily may be considered in preference to aspirin in symptomatic or asymptomatic patients, with either PAD or a history of ischaemic stroke or transient ischaemic attack.[273]	IIb	B
Aspirin 75–100 mg daily may be considered in patients without a history of MI or revascularization, but with definitive evidence of CAD on imaging.	IIb	C
Adding a second antithrombotic drug to aspirin for long-term secondary prevention should be considered in patients with a **high risk** of ischaemic events[c] and without high bleeding risk[d] (see *Table 9* for options).[289,296,297,307]	IIa	A
Adding a second antithrombotic drug to aspirin for long-term secondary prevention may be considered in patients with at least a **moderately increased risk** of ischaemic events[e] and without high bleeding risk[d] (see *Table 9* for options).[289,296,297,307]	IIb	A

Que sabemos en la actualidad?

(19) An assessment of coronary vasomotor function should be considered in patients with non-significant epicardial CAD and objective evidence of ischaemia.

10 Gaps in the evidence

10.1 Diagnosis and assessment

More information on the effects of various risk factors, biomarkers, and comorbidities on the PTP of obstructive CAD is needed. Adequately powered RCTs are needed to compare the effectiveness of different diagnostic strategies, and to evaluate how to best integrate diagnostic tests in patient care in terms of clinical outcomes and the use of healthcare resources.

10.2 Assessment of risk

Studies should address whether an initial invasive strategy, in addition

of aspirin + $P2Y_{12}$ inhibitor with aspirin + factor Xa inhibitor are warranted to determine which subgroups may be preferentially treated with one or other strategy. The potential clinical benefit of ticagrelor monotherapy, while stopping aspirin, remains unproved at present.

The role of biomarkers in stratifying patients' risk of ischaemic events and bleeding requires clarification, including the role of growth differentiation factor-15 in guiding the risk of bleeding with DAPT. It is uncertain what effect novel lipid-lowering strategies will have on the net clinical benefit of DAPT, with similar implications of other strategies such as intensive BP lowering and, potentially in the future, selective anti-inflammatory therapies.

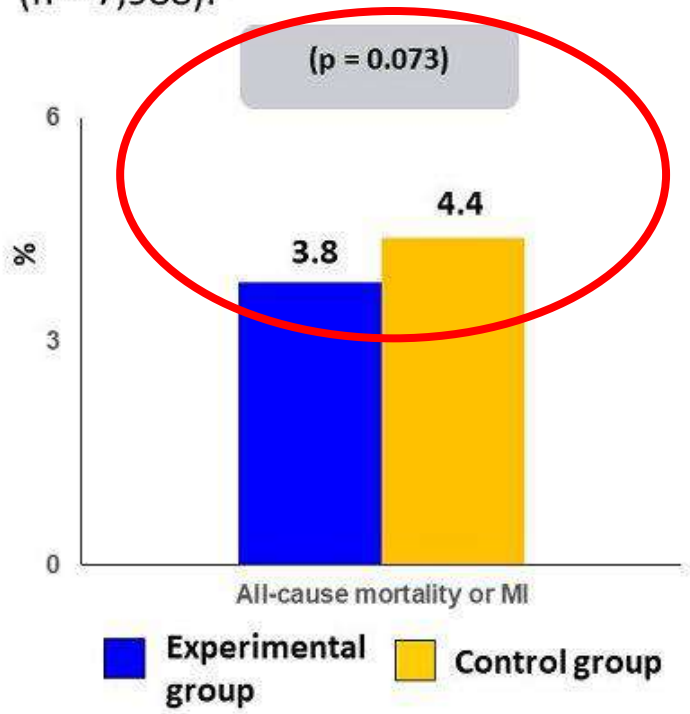
10.5 Revascularization

Further studies, including RCTs, are needed to assess the value of functional vs. anatomical guidance for CABG. The concept of com-

Que sabemos en la actualidad?

GLOBAL LEADERS #ESCCongress

Trial design: Patients undergoing PCI were randomized to dual antiplatelet therapy (DAPT) aspirin/ticagrelor for 1 month, followed by ticagrelor for 23 months (n = 7,980) vs. DAPT for 12 months, followed by aspirin for 12 months (n = 7,988).



RESULTS

- All-cause mortality or MI: 3.8% of the experimental group vs. 4.4% of the control group (p = 0.073)
- All-cause mortality: 2.8% of the experimental group vs. 3.2% of the control group (p = 0.18)
- MI: 1.0% of the experimental group vs. 1.3% of the control group (p = 0.14)

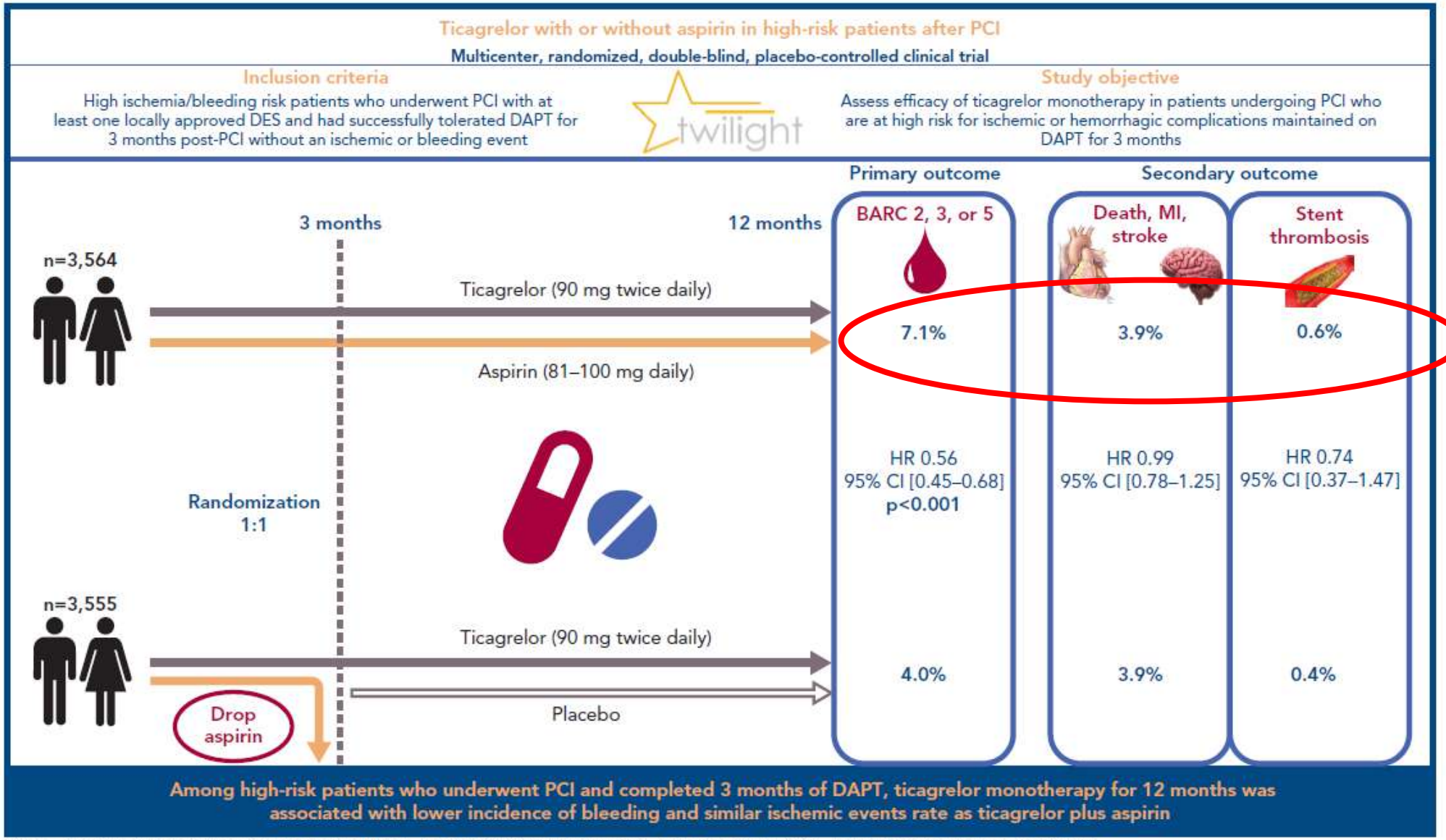
CONCLUSIONS

- Among patients who underwent PCI with a biolimus-eluting stent, ticagrelor monotherapy for 23 months after 1 month of DAPT was not superior to aspirin monotherapy for 12 months after 12 months of DAPT

Vranckx P, et al. Lancet 2018;Aug 27:[Epub]

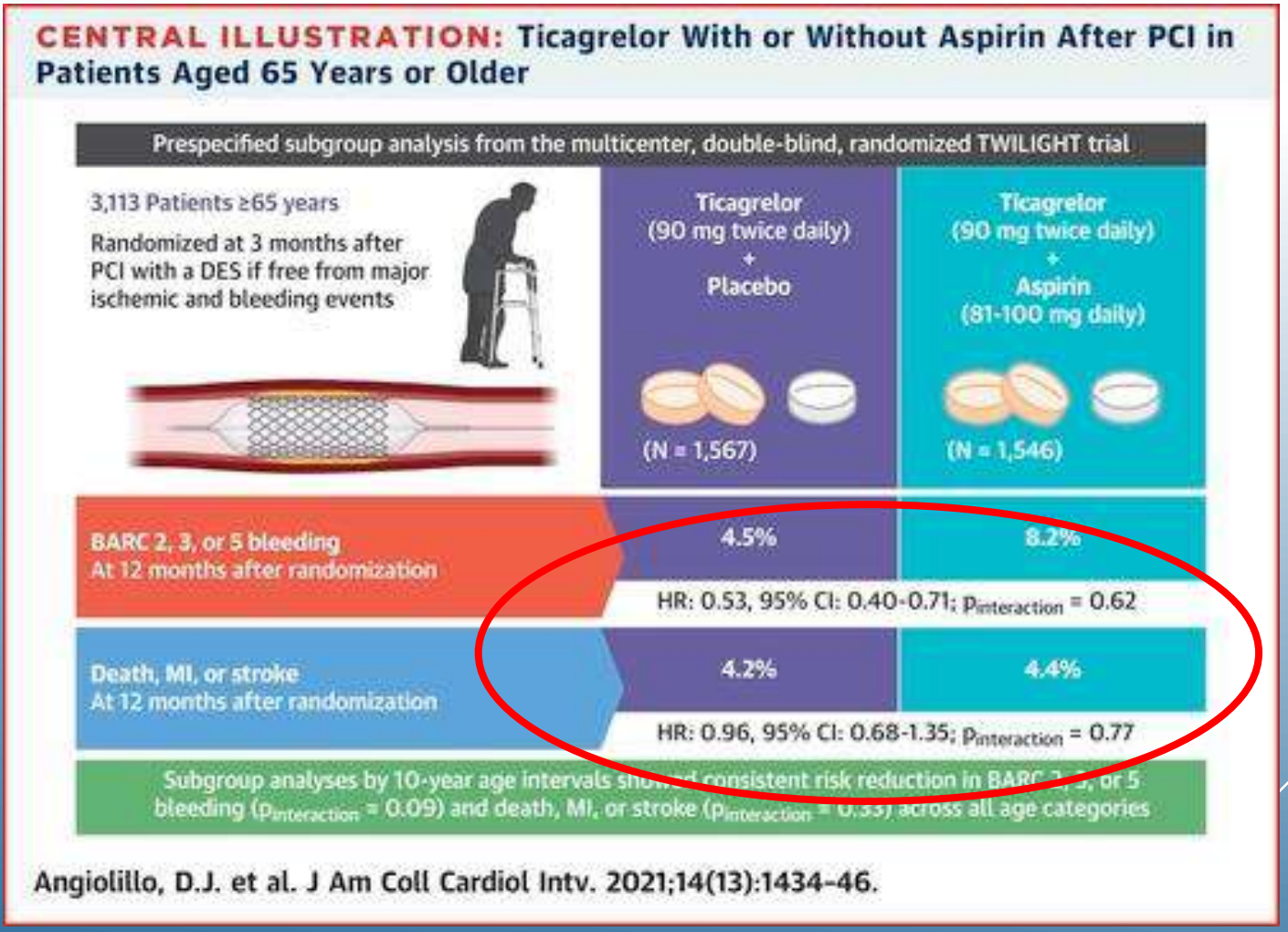
AMERICAN COLLEGE of CARDIOLOGY

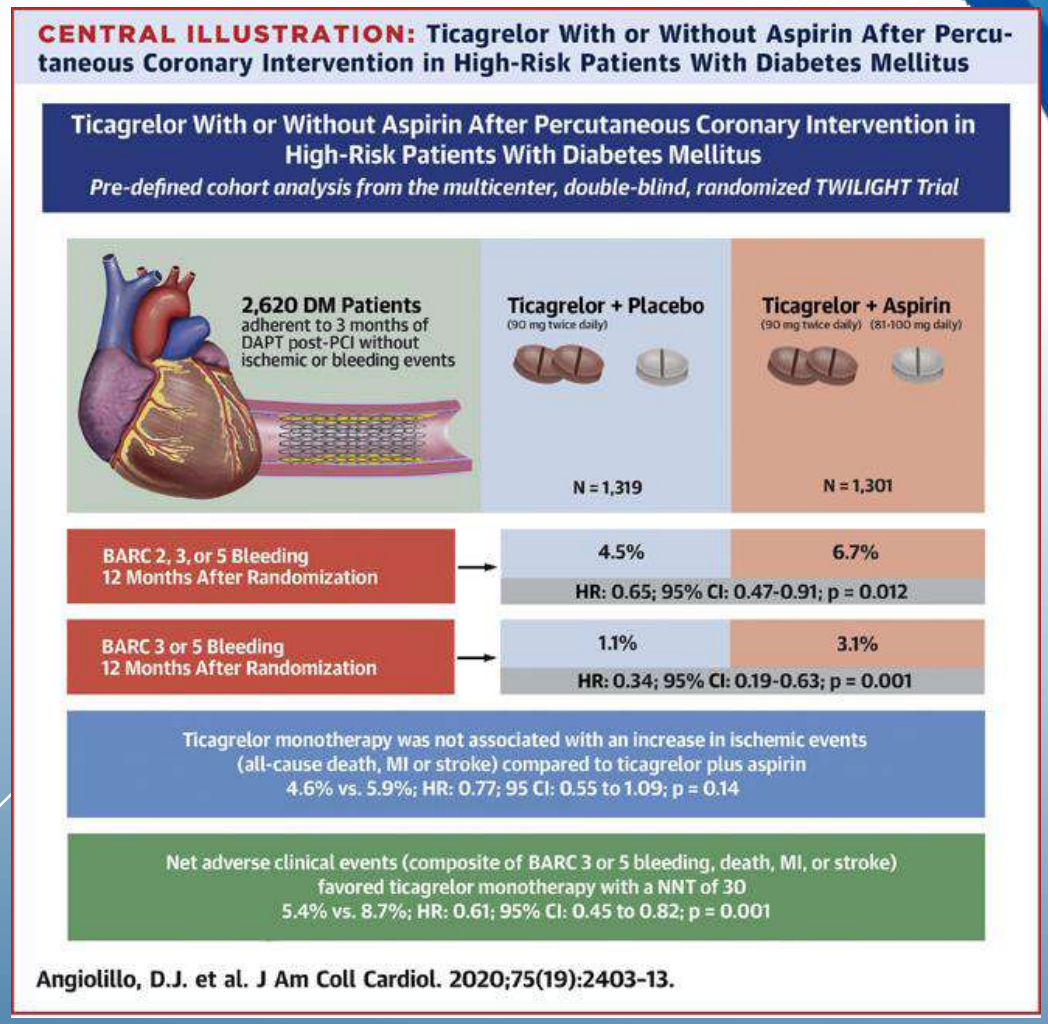
Figure 2: TWILIGHT Trial



BARC = Bleeding Academic Research Consortium; DAPT = dual antiplatelet therapy; DES = drug-eluting stent; PCI = percutaneous coronary intervention.

Que sabemos en la actualidad?

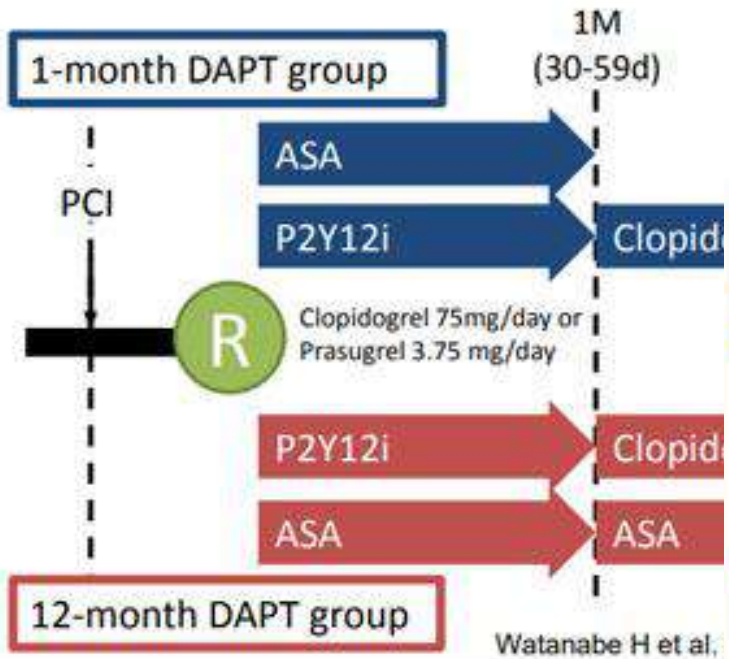




Que sabemos en la actualidad?

STOPDAPT-2

Prospective multicenter open-label randomized trial
comparing 1-month versus 12-month DAPT after CoCr-EES implantation
with limited exclusion criteria



STOPDAPT-2 ACS: one-month dual antiplatelet therapy followed by clopidogrel monotherapy in ACS

Population	Intervention	Control	Outcomes	Time
4136 pts. with ACS	1-month DAPT	12-month DAPT	Bleeding	1 year
• Mean age 67 • 79% male • 30% diabetes • 56% STEMI • 85% radial approach • 97% IVUS or OCT	 1-month DAPT  11 months Clopidogrel alone	 12-month DAPT 	HR 0.46, CI95% 0.23-0.94  1 1-month DAPT better Myocardial infarction HR 1.91, CI95% 1.06-3.44  1 1-month DAPT worse	Primary analysis at 1 year post ACS 5-year follow-up planned

HOST EXAM

EXtended Antiplatelet Monotherapy

Aspirin vs. Clopidogrel for Chronic Maintenance Monotherapy after Percutaneous Coronary Intervention

The HOST-EXAM trial

Session of Late Breaking Clinical Trials Session III

ACC.21 Congress

Hyo-Soo Kim, MD/PhD
Cardiovascular Center,
Seoul National University Hospital, Korea

ACC.21

THE LANCET
Volume 397, Issue 10293, 26 June–2 July 2021, Pages 2487-2496

Articles

Aspirin versus clopidogrel for chronic maintenance monotherapy after percutaneous coronary intervention (HOST-EXAM): an investigator-initiated, prospective, randomised, open-label, multicentre trial

Hyo-Soo Kim, on behalf of the HOST-EXAM investigators
Lancet **2021; 397: 2487–96**

Study Design and Patient Population

HOST EXAM
EXtended Antiplatelet Monotherapy

- ***5,530 eligible patients screened, from 37 centers in Korea***

✓ ***Key criterias***

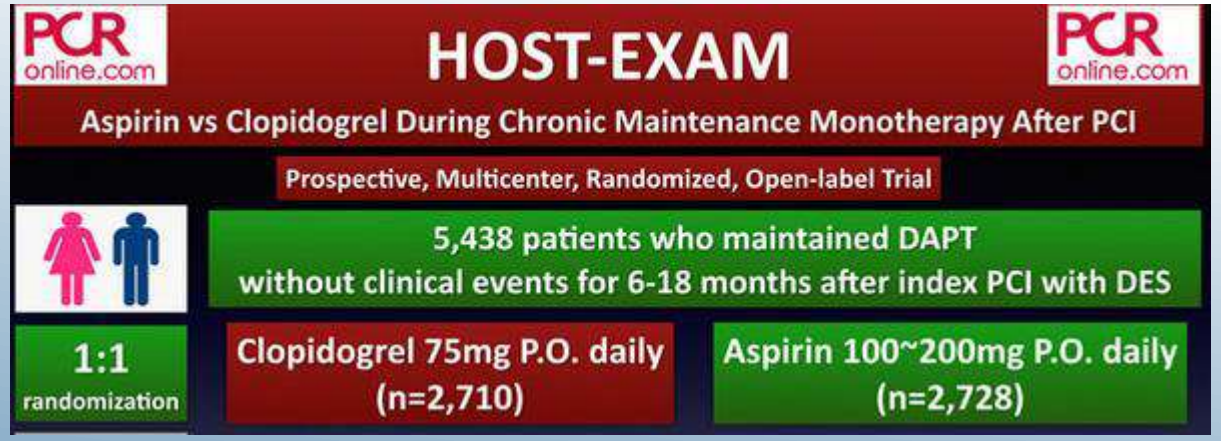
Patients who recieved PCI with a drug-eluting stent (DES) and maintained DAPT without any clinical events during 12 ± 6 months after PCI.

No exclusion criteria of the clinical risk factors / clinical diagnosis / complexity of the PCI

Inclusion Criteria
a) Subject must be ≥ 20 years
b) Maintenance of DAPT for at least 12 ± 6 months after PCI with DES
c) No history of clinical event after PCI with DES before enrollment
d) Agreement to give written informed consent
Exclusion Criteria
a) Known hypersensitivity or contraindication to key medications
b) Patients with active pathologic bleeding
c) Female of childbearing potential, unless a pregnancy test is negative
d) History of bleeding diathesis, known coagulopathy
e) Non-cardiac co-morbid conditions with life expectancy <1 year

ACC.21

Análisis del diseño



Centros de un (1) solo país

"open label"

Prospectivo

Multicéntrico

Randomizado

Sin criterios de exclusión por complejidad de las intervenciones, factores de riesgo o diagnostico clinico

Baseline Profiles

HOST EXAM
EXtended Antiplatelet Monotherapy

		Clopidogrel (N = 2710)	Aspirin (N = 2728)
Demographics	Age, years	63.5 ± 10.7	63.4 ± 10.7
	Men	74.4% (2015)	74.7% (2039)
Comorbidities	Diabetes mellitus	34.1% (925)	34.3% (935)
	Hypertension	61.4% (1664)	61.4% (1674)
	Dyslipidemia	69.5% (1884)	69.0% (1883)
	Current smoker	20.1% (545)	21.3% (581)
	Chronic renal failure	13.1% (356)	12.4% (337)
	Previous MI	16.1% (437)	15.9% (435)
	Previous CVA	4.4% (120)	4.9% (133)
Clinical indication of PCI *(performed 6-18 months before randomization)*	Silent ischemia	2.1% (58)	2.6% (70)
	Stable angina	25.4% (688)	25.7% (701)
	Unstable angina	36.0% (975)	35.2% (959)
	Non-ST elevation MI	19.4% (526)	19.4% (528)
	ST elevation	17.1% (463)	17.2% (470)

Baseline Profiles

HOST EXAM
EXtended Antiplatelet Monotherapy

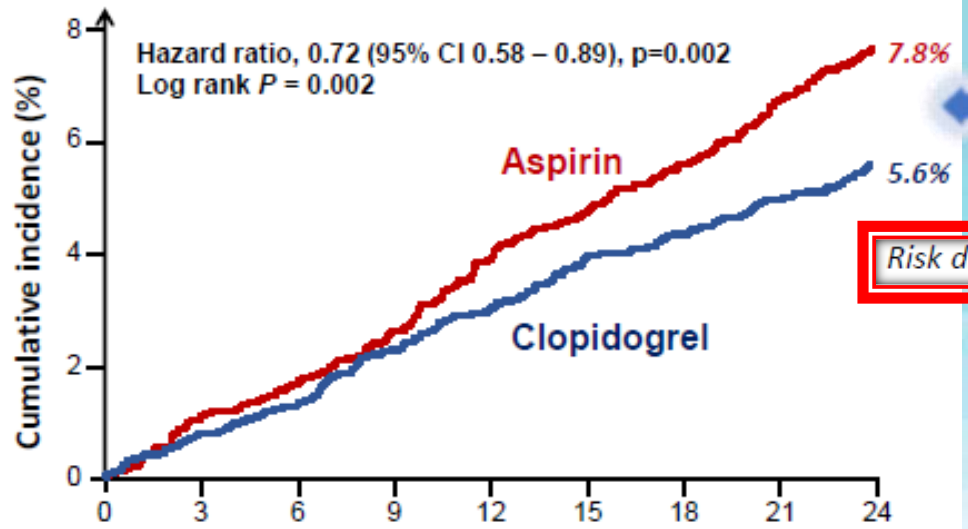
		Clopidogrel (N = 2710)	Aspirin (N = 2728)
Days from PCI to randomization		383.0 (357.0-424.0)	380.0 (358.0-421.0)
DAPT just before Randomization	Aspirin plus clopidogrel	81.8% (2218)	81.1% (2212)
	Aspirin plus ticagrelor	9.8% (266)	9.8% (268)
	Aspirin plus prasugrel	7.8% (212)	8.6% (235)
	Others	0.5% (14)	0.5% (13)
Angiographic data per patient	1-vessel disease	50.4% (1367)	50.4% (1376)
	2-vessel disease	31.5% (855)	30.9% (844)
	3-vessel disease	18.0% (488)	18.6% (507)
	Left main disease	5.2% (142)	4.8% (130)
	PCI for bifurcation lesion	10.5% (285)	10.8% (295)
	PCI for CTO lesion	9.5% (257)	9.3% (254)
	Total length of implanted stents	36.1 ± 24.2	35.7 ± 23.6
	Total number of implanted stents	1.5 ± 0.8	1.5 ± 0.8

Primary Outcome

HOST EXAM
EXtended Antiplatelet Monotherapy

Primary Outcome

All-cause death, nonfatal MI, stroke,
readmission due to ACS,
major bleeding (BARC type ≥3)



Number at risk					
Clopidogrel	2648	2614	2570	2532	2498
Aspirin	2655	2610	2551	2507	2448

NNT = 50.6 pacientes

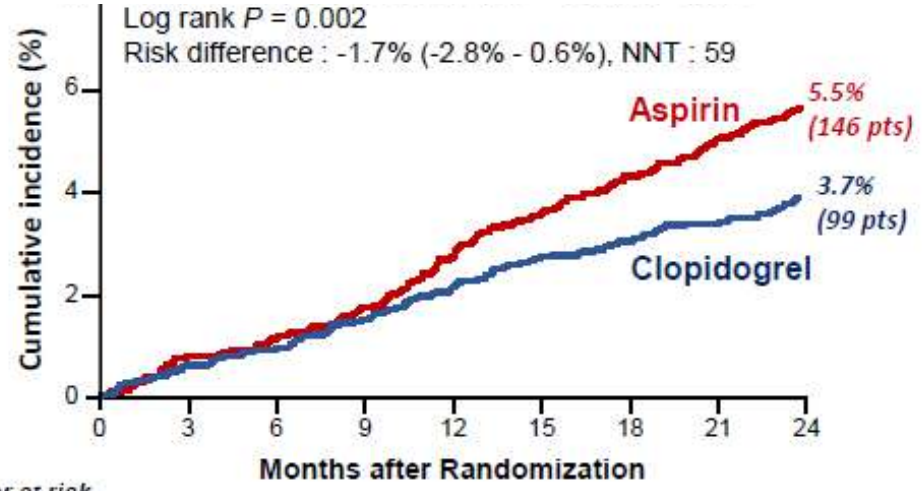
Risk difference : -2.0% (-3.3% - 0.6%)

Secondary Outcomes

HOST EXAM
EXtended Antiplatelet Monotherapy

Thrombotic composite outcome
(cardiac death, non-fatal MI, ischemic stroke, readmission due to ACS, and definite or probable stent thrombosis)

Any bleeding
(BARC type ≥2 bleeding)



Number at risk

Clopidogrel	2710	2661	2612	2569	2524	2710	2664	2621	2585	2542
Aspirin	2728	2670	2608	2557	2495	2728	2677	2626	2595	2547

Component of Outcomes for 2 years

HOST EXAM
EXtended Antiplatelet Monotherapy

	Clopidogrel (n=2710)	Aspirin (n=2728)	Hazard Ratio (95% CI)	P value
	No. of patients (%)			
All-cause death	1.9% (51)	1.3% (36)	1.43 (0.93-2.19)	0.101
Cardiac death	0.7% (19)	0.5% (14)	1.37 (0.69-2.73)	0.374
Non-cardiac death	1.2% (32)	0.8% (22)	1.47 (0.85-2.52)	0.167
Non-fatal myocardial infarction	0.7% (18)	1.0% (28)	0.65 (0.36-1.17)	0.150
Stroke	0.7% (18)	1.6% (43)	0.42 (0.24-0.73)	0.002
Ischemic stroke	0.5% (14)	1.0% (26)	0.54 (0.28-1.04)	0.064
Hemorrhagic stroke	0.2% (4)	0.6% (17)	0.24 (0.08-0.70)	0.010
Readmission due to ACS	2.5% (66)	4.1% (109)	0.61 (0.45-0.82)	0.001
Major bleeding (BARC type ≥3)	1.2% (33)	2.0% (53)	0.63 (0.41-0.97)	0.035
Any revascularization	2.1% (56)	2.6% (69)	0.82 (0.57-1.16)	0.261
Target lesion revascularization	0.9% (24)	1.4% (36)	0.67 (0.40-1.12)	0.130
Target vessel revascularization	1.4% (37)	1.8% (48)	0.78 (0.50-1.19)	0.245
Definite or probable stent thrombosis	0.4% (10)	0.6% (16)	0.63 (0.29-1.39)	0.251
Any minor GI complaints	10.2% (272)	11.9% (320)	0.85 (0.72-1.00)	0.048

Cause of Mortality for 2 years

HOST EXAM
EXtended Antiplatelet Monotherapy

(No. of patients)	Total	Clopidogrel group	Aspirin group	P value
Cardiac cause	33	19	14	0.374
- Cardiac arrest	18	11	7	0.338
- Unknown origin of death	15	8	7	0.786
Non-cardiac cause	54	32	22	0.217
- Cerebrovascular accident	10	6	4	0.520
- Malignancy	29	18	11	0.186
Gastrointestinal origin	12	8	4	
Respiratory origin	8	4	4	
Endocrinology origin	2	1	1	
Genitourinary origin	4	2	2	
Other	3	3	0	
- Infectious disease	9	4	5	0.746
- Suicide or Trauma	3	2	1	0.560
- Others	3	2	1	0.560

Perspectivas y conclusiones

JACC Journals

Journals Topics Guidelines Author Center CME/MOC

Journal of the American College of Cardiology

JACC Journals › JACC › Archives › Vol. 75 No. 19

Twilight, the Dawn of a New Era of Aspirin-Free PCI?*

Editorial Comment

Patrick W. Serruys, Kuniaki Takahashi, Ply Chichareon, and Yoshinobu Onuma

J Am Coll Cardiol. 2020 May, 75 (19) 2425–2429

SEE PAGES 2403 AND 2414

THE U-TURN OF TRIALISTS: STOPPING THE ASPIRIN AND CONTINUING THE SPECIFIC AND POTENT ANTIPLATELET AGENT

Over the last decade, the thickness of the struts has decreased from 140 to 160 μm to 60 μm, reducing considerably the thrombogenic hemodynamic micro-environment related to thick struts (disturbed shear stress around the struts) and thereby the risk of stent

ASPIRIN AFTER PCI: PERMANENT DEMISE, RENAISSANCE WITH A NOVEL PHARMACOLOGICAL FORMULATION OR REPLACEMENT BY NOVEL ADJUNCTIVE ANTI-INFLAMMATORY DRUGS? Over the last few years, we have seen a succession of trials progressively reducing the duration of administration of aspirin from 12 months to 6 months, to 3 months, to 1 month, to 15 days, and, more recently in the ASET trial, to testing the total elimination of aspirin

Perspectivas y conclusiones

The impact of patients selection on clinical outcomes in RCT

All-comer Single-center registry nested in the STOPDAPT-2 trial (N=2190)

Enrolled in the STOPDAPT-2 trial N=582	**Not enrolled** in the STOPDAPT-2 trial N=1087	**Ineligible** for the STOPDAPT-2 trial N=521
	Physicians' judgement 	*Exclusion criteria*
	Patients' unwillingness 	*OAC* 
		Prior ICH 
		In-hospital events 
Primary outcome measure: cardiovascular death, MI, definite stent thrombosis, stroke, or TIMI major or minor		
4.5%	7.2%	21.2%
	All-cause death	
0.9%	4.1%	9.9%
	TIMI major or minor bleeding	
2.1%	4.3%	13.5%

Kanenawa et al. *Circ Cardiovasc Interv*. February 2021.

Circulation: Cardiovascular Interventions

Conclusiones

Medscape EDUCATION

the heart.org from WebMD

One Size May Not Fit All: A New Aspirin Option for the High-Risk Patient

Moderator
Seth J. Baum, MD
Chief Medical Officer
MB Clinical Research
President Elect
American Society of Preventive Cardiology

...because one size does **not** fit all...

Conclusiones

Diferentes escenarios y complejidad anatómica

- SCA vs SCC
- Multivasos
- TCI – Bifurcaciones
- Longitud de STENTs
- Calcificaciones

Diferentes perfiles de riesgo secundario

- Diabéticos
- Renales Crónicos
- Anticoagulados
- Edad de los pacientes
- Ateromatosis vascular difusa
- Eventos previos (ACV – VP)

Conclusiones

- A 24 meses de seguimiento, con un **NNT=50.6**, se observó una diferencia significativa a favor de la monoterapia con clopidogrel en términos del objetivo combinado primario (7.7% vs. 5.7%; p=0.005), en relación a la aspirina.

Published online 2021 Sep 24. doi: 10.14797/mdcvj.293 PMID: 34824680

Aspirin in the Modern Era of Cardiovascular Disease Prevention

Ella Murphy, MB BCh BAO, MSc,[1] James M. G. Curneen, MB BCh BAO,[1] and John W. McEvoy, MB BCh BAO, MEd, MHS[1]

"**In secondary prevention,** use of $P2Y_{12}$ inhibitors has modified the need for aspirin in patients with higher bleeding risks. Further trials with direct comparisons between the different $P2Y_{12}$ inhibitors and with longer follow-up periods are needed, as are trials truly testing whether PCI can be performed without administering aspirin"

Muchas Gracias !