31 GIORNATE CARDIOLOGICHE TORINESI

TURIN
October
24th-26th
2019

Top five CAD trials of the last 12 months

Malcolm R. Bell, MBBS, FRACP
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Conflicts and disclosures – none

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Antithrombotic Therapy after Acute Coronary Syndrome or PCI in Atrial Fibrillation

Renato D. Lopes, M.D., Ph.D., Gretchen Heizer, M.S., Ronald Aronson, M.D., Amit N. Vora, M.D., M.P.H., Tyler Massaro, Ph.D., Roxana Mehran, M.D., Shaun G. Goodman, M.D., Stephan Windecker, M.D., Harald Darius, M.D., Jia Li, Ph.D., Oleg Averkov, M.D., Ph.D., M. Cecilia Bahit, M.D., Otavio Berwanger, M.D., Ph.D., Andrzej Budaj, M.D., Ph.D., Ziad Hijazi, M.D., Ph.D., Alexander Parkhomenko, M.D., Ph.D., Peter Sinnaeve, M.D., Ph.D., Robert F. Storey, M.D., Holger Thiele, M.D., Dragos Vinereanu, M.D., Ph.D., Christopher B. Granger, M.D., and John H. Alexander, M.D., M.H.S., for the AUGUSTUS Investigators*

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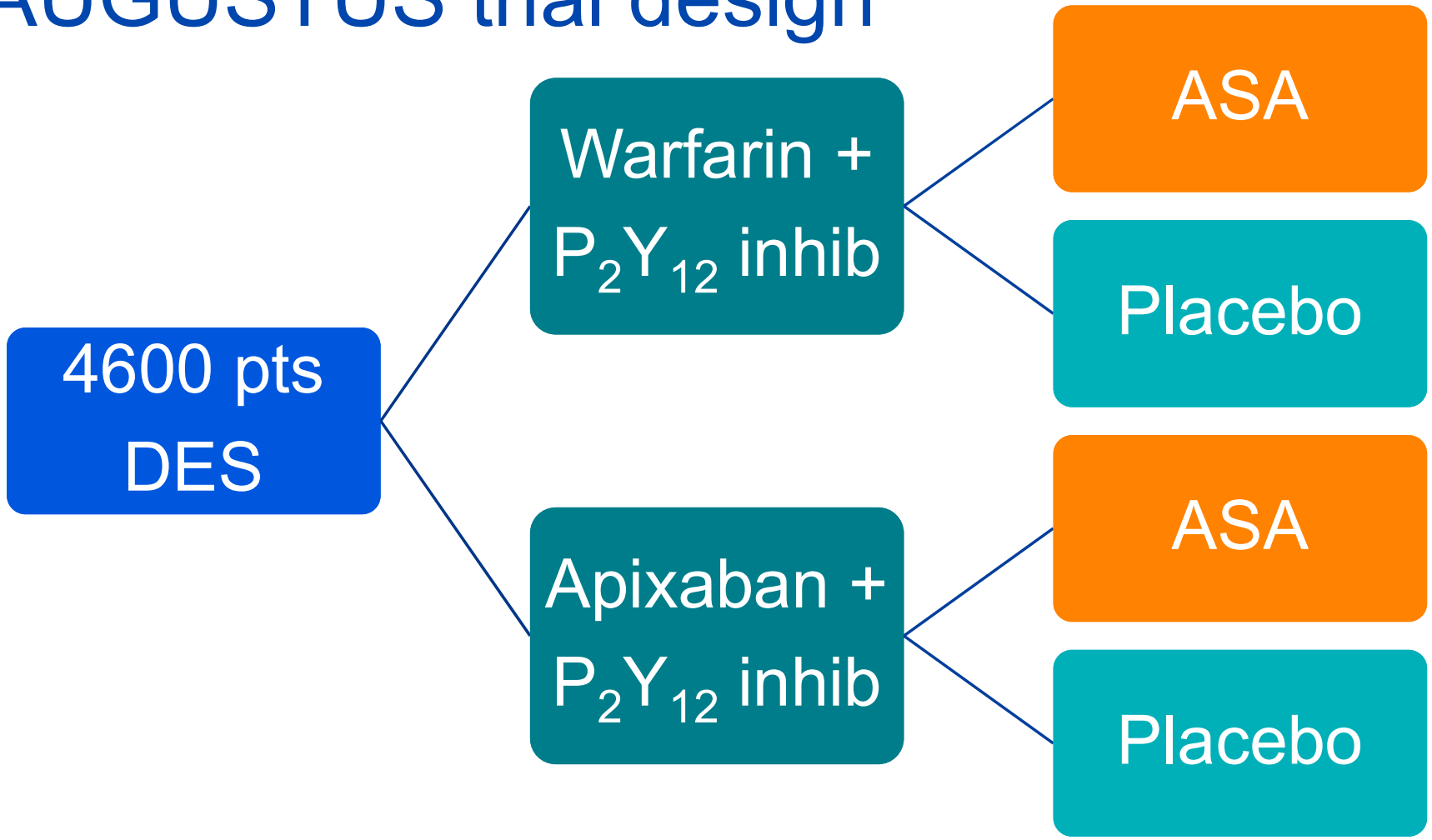
AUGUSTUS trial design



Lopes RD: NEJM 2019

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Major bleeding:

Apixaban superior to VKA NNT=24

Death or hospitalization:

Apixaban superior to VKA NNT=25

Ischemic events:

No difference

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Major bleeding:

More with ASA than placebo NNH=13

Death or hospitalization:

No difference ASA and placebo

Ischemic events:

No difference ASA and placebo

JAMA Cardiology | Original Investigation

Safety and Efficacy of Antithrombotic Strategies in Patients With Atrial Fibrillation Undergoing Percutaneous Coronary Intervention

A Network Meta-analysis of Randomized Controlled Trials

Renato D. Lopes, MD, PhD; Hwanhee Hong, PhD; Ralf E. Harskamp, MD, PhD; Deepak L. Bhatt, MD, MPH; Roxana Mehran, MD; Christopher P. Cannon, MD; Christopher B. Granger, MD; Freek W. A. Verheugt, MD, PhD; Jianghao Li, MS; Jurriën M. ten Berg, MD, PhD; Nikolaus Sarafoff, MD; C. Michael Gibson, MD; John H. Alexander, MD, MHS

Supplemental content

IMPORTANCE The antithrombotic treatment of patients with atrial fibrillation (AF) and coronary artery disease, in particular with acute coronary syndrome (ACS) and/or percutaneous coronary intervention (PCI), poses a significant treatment dilemma in clinical practice.

OBJECTIVE To study the safety and efficacy of different antithrombotic regimens using a network meta-analysis of randomized controlled trials in this population.

DATA SOURCES PubMed, EMBASE, EBSCO, and Cochrane databases were searched to identify randomized controlled trials comparing antithrombotic regimens.

STUDY SELECTION Four randomized studies were included (n = 10 026; WOEST, PIONEER AF-PCI, RE-DUAL PCI, and AUGUSTUS).

JAMA Cardiology | Original Investigation

Safety and Efficacy of Antithrombotic Strategies in Patients With Atrial Fibrillation Undergoing

STUDY SELECTION Four randomized studies were included (n = 10 026; WOEST, PIONEER AF-PCI, RE-DUAL PCI, and AUGUSTUS).

- Support use of dual therapy, avoiding ASA
- DOAC the preferred anticoagulant
- VKA and DAPT should be avoided

Lopes RD: JAMA Cardiology 2019

JAMA | Original Investigation

Effect of P2Y12 Inhibitor Monotherapy vs Dual Antiplatelet Therapy on Cardiovascular Events in Patients Undergoing Percutaneous Coronary Intervention
The SMART-CHOICE Randomized Clinical Trial

Joo-Yong Hahn, MD; Young Bin Song, MD; Ju-Hyeon Oh, MD; Woo Jung Chun, MD; Yong Hawn Park, MD; Woo Jin Jang, MD; Eul-Soon Im, MD; Jin-Ok Jeong, MD; Byung Ryul Cho, MD; Seok Kyu Oh, MD; Kyeong Ho Yun, MD; Deok-Kyu Cho, MD; Jong-Young Lee, MD; Young-Youp Koh, MD; Jang-Whan Bae, MD; Jae Woong Choi, MD; Wang Soo Lee, MD; Hyuck Jun Yoon, MD; Seung Uk Lee, MD; Jang Hyun Cho, MD; Woong Gil Choi, MD; Seung-Woon Rha, MD; Joo Myung Lee, MD; Taek Kyu Park, MD; Jeong Hoon Yang, MD; Jin-Ho Choi, MD; Seung-Hyuck Choi, MD; Sang Hoon Lee, MD; Hyeon-Cheol Gwon, MD; for the SMART-CHOICE Investigators

IMPORTANCE Data on P2Y12 inhibitor monotherapy after short-duration dual antiplatelet therapy (DAPT) in patients undergoing percutaneous coronary intervention are limited.

OBJECTIVE To determine whether P2Y12 inhibitor monotherapy after 3 months of DAPT is noninferior to 12 months of DAPT in patients undergoing PCI.

DESIGN, SETTING, AND PARTICIPANTS The SMART-CHOICE trial was an open-label, noninferiority, randomized study that was conducted in 33 hospitals in Korea and included 2993 patients undergoing PCI with drug-eluting stents. Enrollment began March 18, 2014, and follow-up was completed July 19, 2018.

INTERVENTIONS Patients were randomly assigned to receive aspirin plus a P2Y12 inhibitor for 3 months and thereafter P2Y12 inhibitor alone (n = 1495) or DAPT for 12 months (n = 1498).

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Related article page 2414
Audio and Supplemental content

JAMA | Original Investigation

Effect of P2Y12 Inhibitor Monotherapy vs Dual Antiplatelet Therapy on Cardiovascular Events in Patients Undergoing Percutaneous Coronary Intervention

Monotherapy after 3 months noninferior to DAPT for 12 months

2993 patients undergoing PCI with drug-eluting stents. Enrollment began March 18, 2014, and follow-up was completed July 19, 2018.

INTERVENTIONS Patients were randomly assigned to receive aspirin plus a P2Y12 inhibitor for 3 months and thereafter P2Y12 inhibitor alone (n = 1495) or DAPT for 12 months (n = 1498).

Hahn JY: JAMA 2019

Research

JAMA | Original Investigation

Effect of 1-Month Dual Antiplatelet Therapy Followed by Clopidogrel vs 12-Month Dual Antiplatelet Therapy on Cardiovascular and Bleeding Events in Patients Receiving PCI
The STOPDAPT-2 Randomized Clinical Trial

Hirotoshi Watanabe, MD; Takenori Domei, MD; Takeshi Morimoto, MD; Masahiro Natsuaki, MD; Hiroki Shiomi, MD; Toshiaki Toyota, MD; Masanobu Ohya, MD; Satoru Suwa, MD; Kensuke Takagi, MD; Mamoru Nanasato, MD; Yoshiki Hata, MD; Masahiro Yagi, MD; Nobuhiro Suematsu, MD; Takafumi Yokomatsu, MD; Itaru Takamisawa, MD; Masayuki Doi, MD; Toshiyuki Noda, MD; Hideki Okayama, MD; Yoshitane Seino, MD; Tomohisa Tada, MD; Hiroki Sakamoto, MD; Kiyoshi Hibi, MD; Mitsuru Abe, MD; Kazuya Kawai, MD; Koichi Nakao, MD; Kenji Ando, MD; Kengo Tanabe, MD; Yuji Ikari, MD; Keiichi Igarashi Hanaoka, MD; Yoshihiro Morino, MD; Ken Kozuma, MD; Kazushige Kadota, MD; Yutaka Furukawa, MD; Yoshihisa Nakagawa, MD; Takeshi Kimura, MD; for the STOPDAPT-2 Investigators

IMPORTANCE Very short mandatory dual antiplatelet therapy (DAPT) after percutaneous coronary intervention (PCI) with a drug-eluting stent may be an attractive option.

Editorial page 2409
Related article page 2428
Audio and Supplemental content

Tomohisa Tada, MD; Hiroki Sakamoto, MD; Kiyoshi Hibi, MD; Mitsuru Abe, MD; Kazuya Kawai, MD; Koichi Nakao, MD; Kenji Ando, MD; Kengo Tanabe, MD; Yuji Ikari, MD; Keiichi Igarashi Hanaoka, MD; Yoshihiro Morino, MD; Ken Kozuma, MD; Kazushige Kadota, MD; Yutaka Furukawa, MD; Yoshihisa Nakagawa, MD; Takeshi Kimura, MD; for the STOPDAPT-2 Investigators

Monotherapy after 1 month
noninferior and superior to DAPT for 12 months

INTERVENTIONS Patients were randomized either to 1 month of DAPT followed by clopidogrel monotherapy (n=1523) or to 12 months of DAPT with aspirin and clopidogrel (n=1522).

MAYO CLINIC

Watanabe H: JAMA 2019

Implications and caveats

Confidence that DAPT can be stopped earlier if needed

Most were getting clopidogrel as monotherapy

Question any added value of ASA

Open label design

Stable angina (lower risk)

- 62% in STOPDAPT-2
- 42% in SMART-CHOICE

Underpowered for stent thrombosis, but rare event

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Complete Revascularization with Multivessel PCI for Myocardial Infarction

Shamir R. Mehta, M.D., David A. Wood, M.D., Robert F. Storey, M.D., Roxana Mehran, M.D., Kevin R. Bainey, M.D., Helen Nguyen, B.Sc., Brandi Meeks, M.Sc., Giuseppe Di Pasquale, M.D., Jose López-Sendón, M.D., David P. Faxon, M.D., Laura Mauri, M.D., Sunil V. Rao, M.D., Laurent Feldman, M.D., P. Gabriel Steg, M.D., Álvaro Avezum, M.D., Tej Sheth, M.D., Natalia Pinilla-Echeverri, M.D., Raul Moreno, M.D., Gianluca Campo, M.D., Benjamin Wrigley, M.D., Sasko Kedev, M.D., Andrew Sutton, M.D., Richard Oliver, M.D., Josep Rodés-Cabau, M.D., Goran Stanković, M.D., Robert Welsh, M.D., Shahar Lavi, M.D., Warren J. Cantor, M.D., Jia Wang, M.Sc., Juliet Nakamya, Ph.D., Shrikant I. Bangdiwala, Ph.D., and John A. Cairns, M.D., for the COMPLETE Trial Steering Committee and Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Complete revascularization superior to culprit only for the primary endpoint of CV death and MI

Richard Oliver, M.D., Josep Rodés-Cabau, M.D., Goran Stanković, M.D., Robert Welsh, M.D., Shahar Lavi, M.D., Warren J. Cantor, M.D., Jia Wang, M.Sc., Juliet Nakamya, Ph.D., Shrikant I. Bangdiwala, Ph.D., and John A. Cairns, M.D., for the COMPLETE Trial Steering Committee and Investigators*

PPCI in STEMI with multivessel disease

Primary PCI (PPCI) of culprit lesion

Dilemma….staged revascularization of remaining disease?

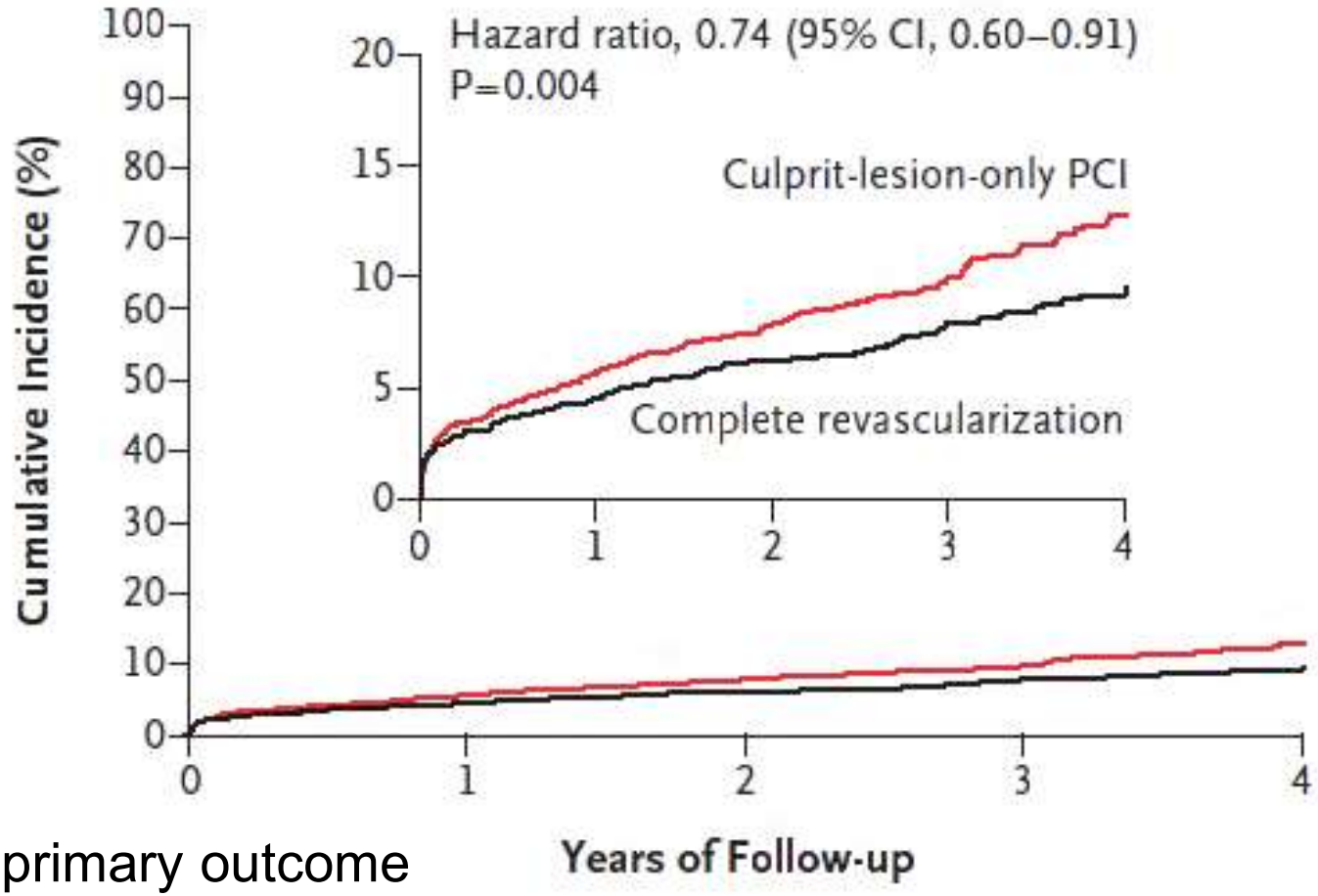
Clinical benefit in observational studies - but selection bias?

Prior RCTs:

- Decrease need for subsequent revascularization
- Under powered for hard endpoints

Current trial powered for death and MI as primary endpoint

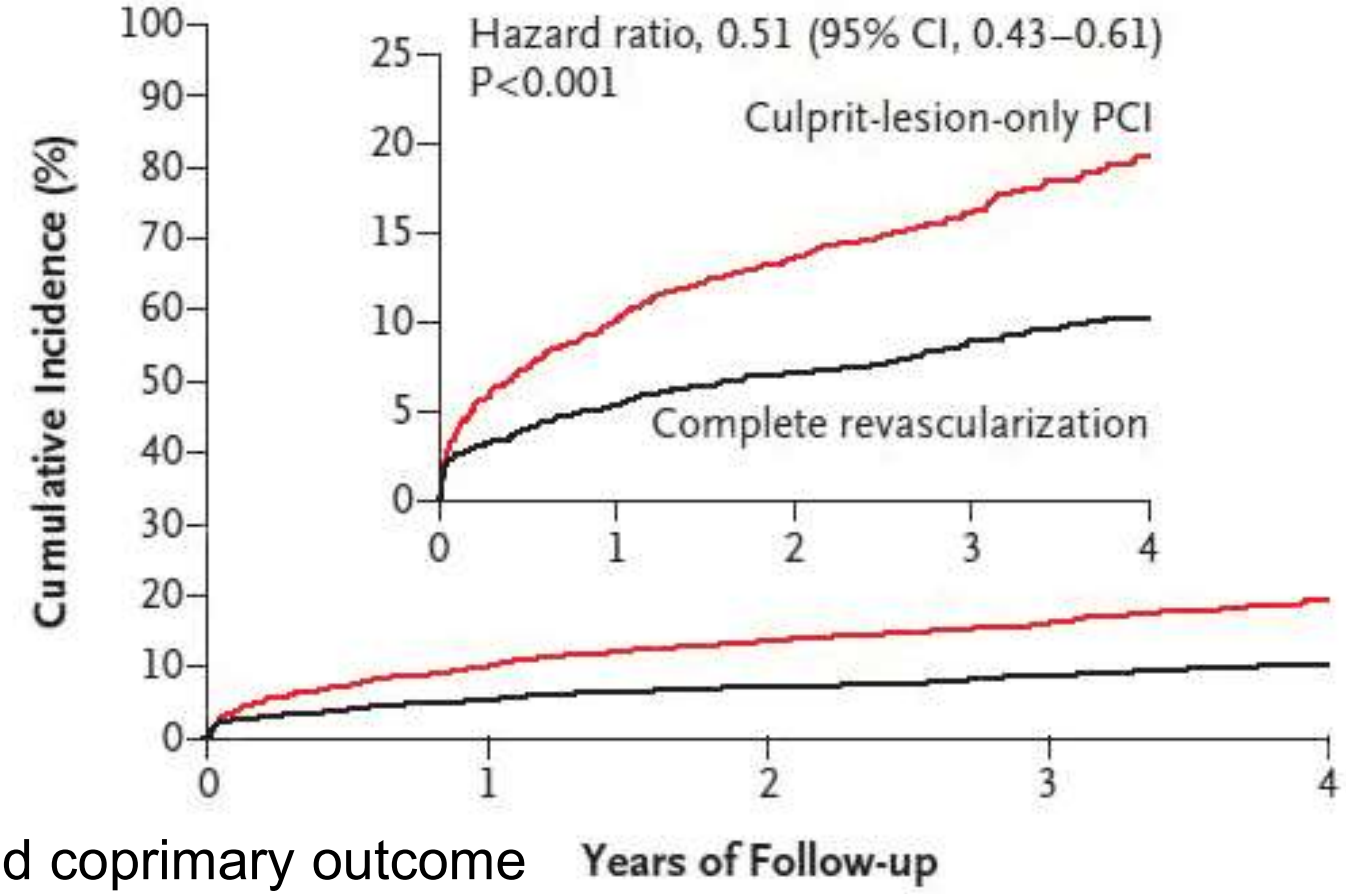
CV death or new MI*



*First coprimary outcome

Mehta SR: NEJM 2019

CV death, new MI, ischemia-driven revascularization*



*Second coprimary outcome

Mehta SR: NEJM 2019

Commentary

First trial powered to look at death/MI as endpoint
    >4x larger than the largest of the prior trials

Lesion complexity low - selection bias?

Seems safe

Optimal timing of staged procedure unclear

Complete revascularization not performed at index PPCI

The NEW ENGLAND JOURNAL of MEDICINE

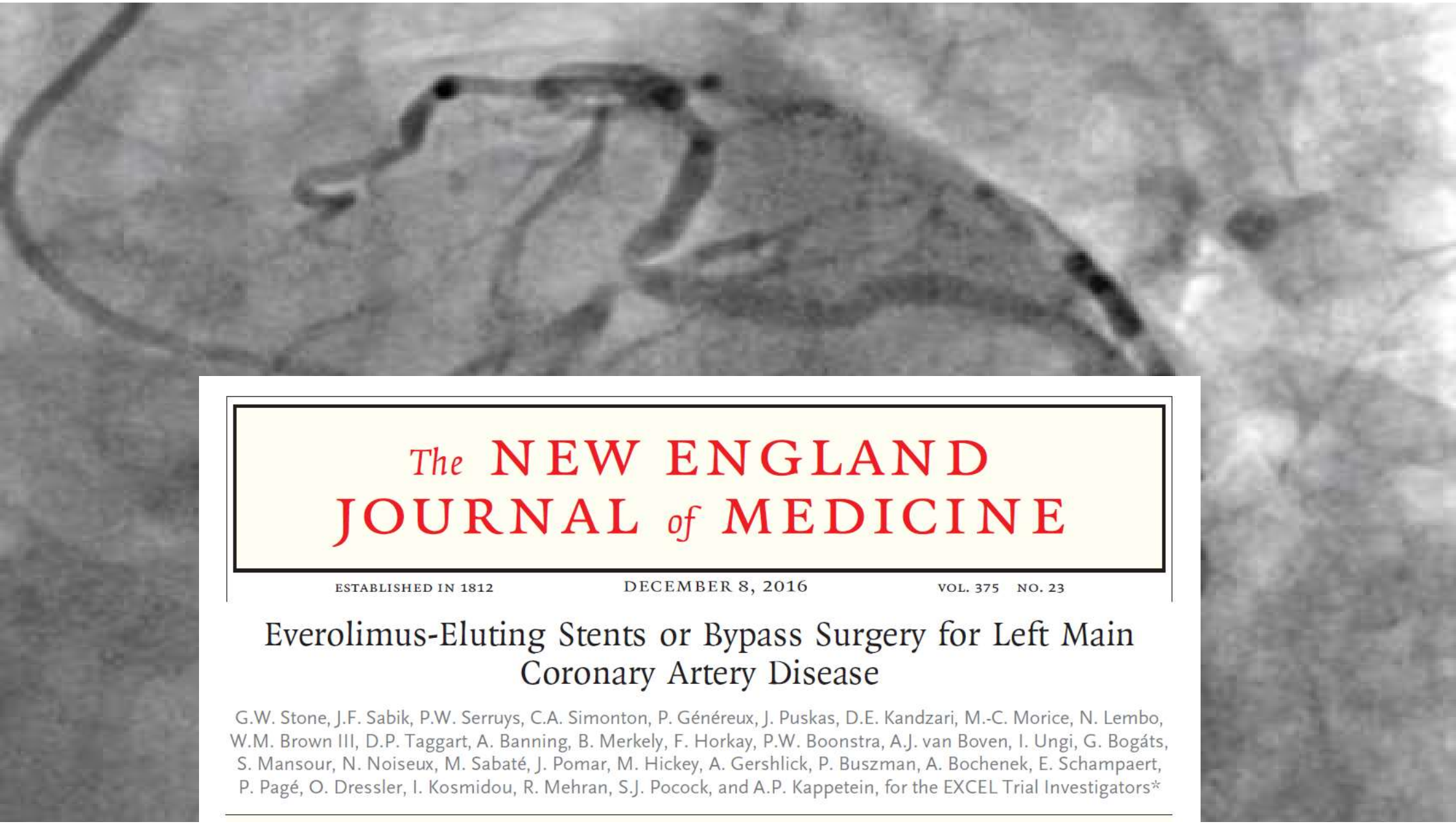
ORIGINAL ARTICLE

Five-Year Outcomes after PCI or CABG for Left Main Coronary Disease

G.W. Stone, A.P. Kappetein, J.E. Sabik, S.J. Pocock, M.-C. Morice, J. Puskas
and P.W. Serruys, for the EXCEL Trial Investigators*

EXCEL at 5 years
"….no difference in death, MI and CVA between PCI and CABG"

Stone GW: NEJM 2019



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ESTABLISHED IN 1812 DECEMBER 8, 2016 VOL. 375 NO. 23

Everolimus-Eluting Stents or Bypass Surgery for Left Main Coronary Artery Disease

G.W. Stone, J.F. Sabik, P.W. Serruys, C.A. Simonton, P. Généreux, J. Puskas, D.E. Kandzari, M.-C. Morice, N. Lembo, W.M. Brown III, D.P. Taggart, A. Banning, B. Merkely, F. Horkay, P.W. Boonstra, A.J. van Boven, I. Ungi, G. Bogáts, S. Mansour, N. Noiseux, M. Sabaté, J. Pomar, M. Hickey, A. Gershlick, P. Buszman, A. Bochenek, E. Schampaert, P. Pagé, O. Dressler, I. Kosmidou, R. Mehran, S.J. Pocock, and A.P. Kappetein, for the EXCEL Trial Investigators*

EXCEL results in 2016

Endpoint	PCI	CABG	Non Inferior	Superior
Primary: Death, CVA or MI at 3 years	15.4%	14.7%	Yes	No
Secondary: Death, CVA or MI at 30 days	4.9%	7.9%	Yes	Yes
Death, CVA, MI, revascularization at 3 years	23.1%	19.1%	Yes	No

Stone GW: NEJM 2016

EXCEL results in 2019 – the 5 year results

Endpoint	PCI	CABG	% difference (CI)	P value
Primary: Death, CVA or MI	22.0%	19.2%	2.8% (-0.9-6.5)	0.13
Secondary: Death, CVA, MI, revascularization	31.3%	24.9%	6.5% (2.4-10.6)	0.002
All-cause death	13.0%	9.9%	3.1% (0.2-6.1)	--

MAYO CLINIC

Stone GW: NEJM 2019

EXCEL results in 2019 – the 5 year results

Endpoint	PCI	CABG	% difference (CI)	P value
Primary: Death, CVA or MI	22.0%	19.2%	2.8% (-0.9-6.5)	0.13
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All-cause death	13.0%	9.9%	3.1% (0.2-6.1)	--

Stone GW: NEJM 2019

Accusations and heated controversy!

Resignation of chair of EXCEL surgical committee - alleging:

- Changing definition of MI midway through trial
- Minimizing the difference between the 2 groups in death
- Involvement of industry and conflicts of interest

Strongly defended by PI

NEJM reviewer responsibility challenged

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AFIRE TRIAL