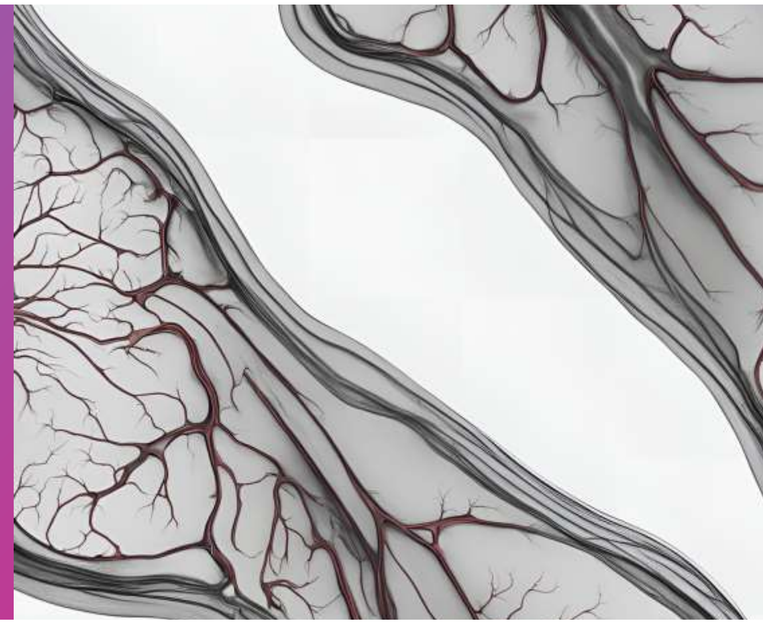
Coronary artery disease and Percutaneous Interventions at the ACC 2024



Ph.Gabriel Steg

Hôpital Bichat, Assistance Publique – Hôpitaux de Paris,
Université Paris-Cité, INSERM U-1148-LVTS, Paris, France,
FACT: French Alliance for Cardiovascular clinical Trials
Innovation Chair- Institut Universitaire de France

@gabrielsteg

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- Senior Associate Editor at ***Circulation***
- CMO **Bioquantis**

CAD and Percutaneous Interventions at ACC 2024

- Impella in Cardiogenic Shock: **the DAN-GER trial**
- Preventive stenting of vulnerable lesions: **PREVENT**
- Coronary sinus reducer in refractory angina: **ORBITA COSMIC**
- Ticagrelor monotherapy 1-month post PCI in ACS : **ULTIMATE DAPT**
- Routine Beta blockers after MI without HF or LV dysfunction: **REDUCE AMI**

ACC.24

One-month Ticagrelor Monotherapy After PCI in Acute Coronary Syndromes: **Principal Results From the Double-blind, Placebo-controlled ULTIMATE-DAPT Trial**

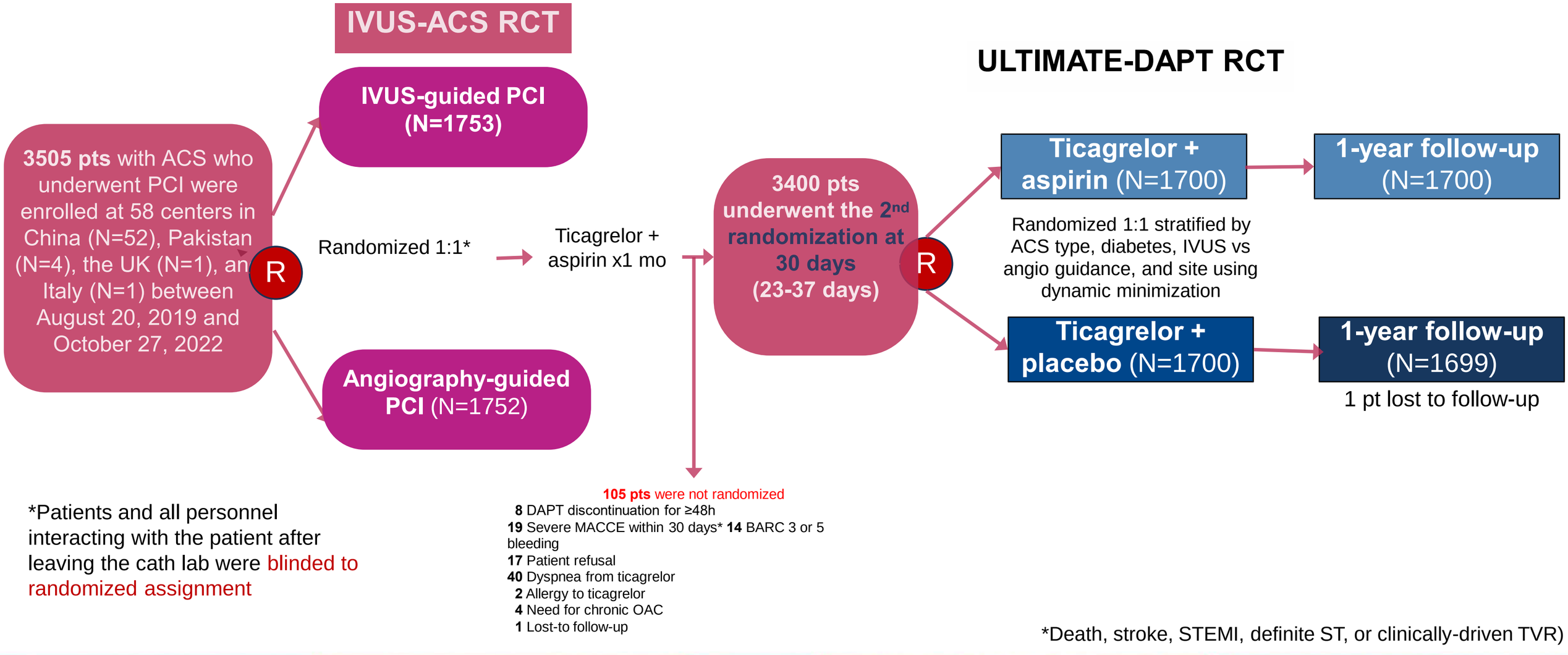
Gregg W Stone MD
Icahn School of Medicine at Mount Sinai
on behalf of Shao-Liang Chen and the ULTIMATE-DAPT Investigators
@GreggWStone

ClinicalTrials.gov number:
NCT03971500

Background

- International guidelines currently recommend **DAPT** with aspirin plus a potent **$P2Y_{12}$ receptor inhibitor** for **12** months in most patients presenting with an **ACS** treated with **PCI** to prevent **MI** and **stent thrombosis**
- Limited data exist regarding the use of **single antiplatelet therapy** with a potent **$P2Y_{12}$** inhibitor starting **1 month** after **PCI** in **ACS**, and no such trials have been **placebo-controlled**

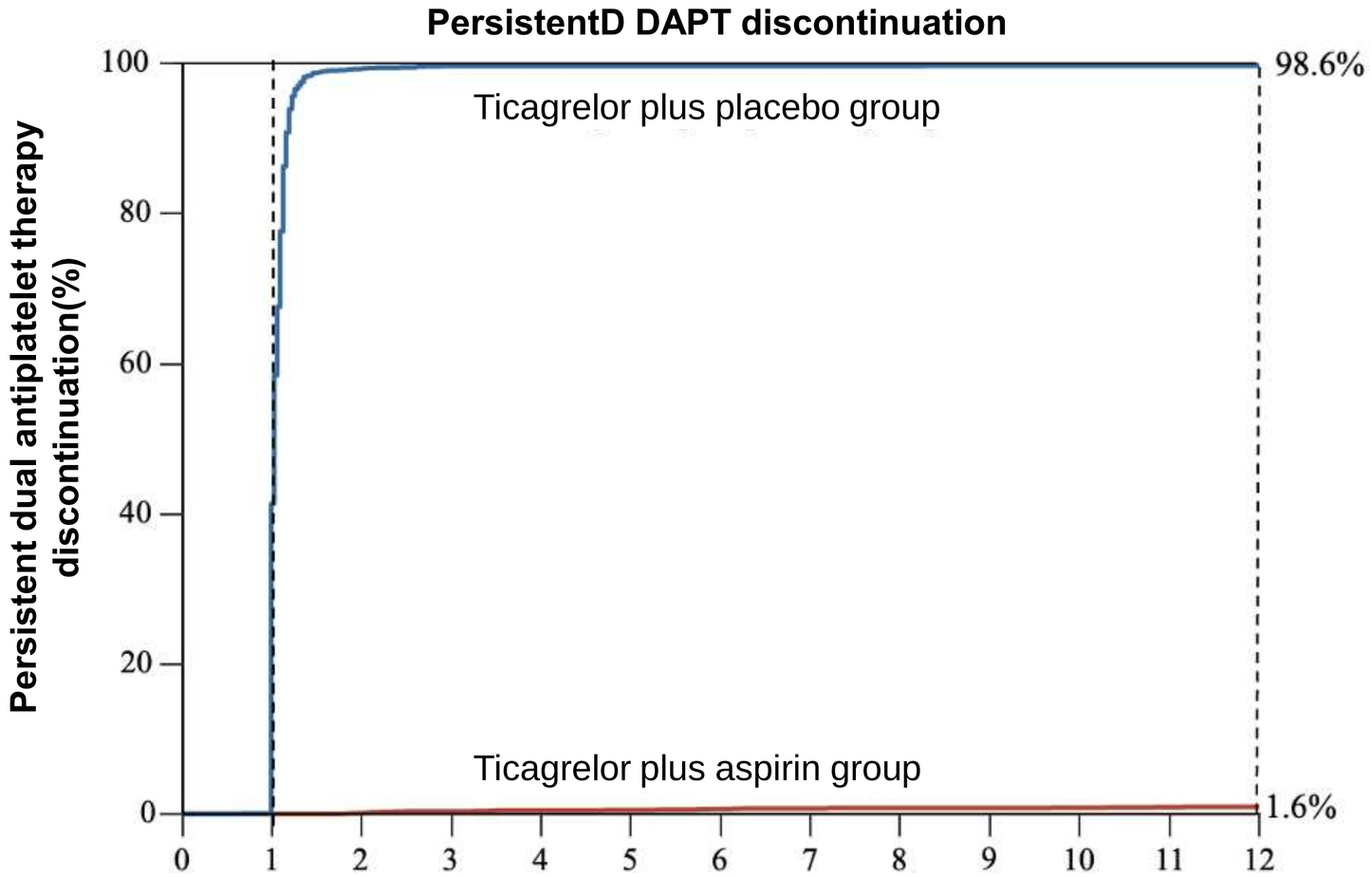
2x2 Randomization and Study Flowchart



*Patients and all personnel interacting with the patient after leaving the cath lab were blinded to randomized assignment

*Death, stroke, STEMI, definite ST, or clinically-driven TVR)

DAPT Adherence During Follow-up



No. at risk													
Ticagrelor plus placebo	1700	1002	13	6	6	6	6	6	6	6	6	6	6
Ticagrelor plus aspirin	1700	1700	1697	1692	1688	1686	1683	1679	1676	1676	1673	1672	1672

- Persistent DAPT discontinuation was defined as permanent discontinuation of either aspirin as dictated by the study protocol or non-directed discontinuation of either aspirin or ticagrelor for >60 days.
- During FU a reduction in ticagrelor from 90 mg to 60 mg bid was required in 12 pts (0.7%) treated with ticagrelor plus placebo and 16 pts (0.9%) treated with ticagrelor plus aspirin. Conversion from ticagrelor to clopidogrel was required in 22 (1.3%) and 19 (1.1%) pts respectively. Unblinding was required during follow-up in 39 pts (1.1%) who had a BARC 3 or 5 bleed (11 in the ticagrelor alone group and 28 in the ticagrelor plus aspirin group) and in 8 pts (0.2%) who had a stent thrombosis (3 in the ticagrelor alone group and 5 in the ticagrelor plus aspirin group).

Bleeding Endpoints

Between 1- and 12-months post-PCI	Ticagrelor plus placebo (N = 1700)	Ticagrelor plus aspirin (N = 1700)	**Hazard ratio (95% CI)**	**P-value**
Primary endpoint: Clinically-relevant bleeding (BARC types 2, 3, or 5)	35 (2.1%)	78 (4.6%)	0.45 (0.30 – 0.66)	**<0.0001**
Major bleeding				
BARC types 3 or 5	11 (0.7%)	28 (1.7%)	0.39 (0.19 – 0.79)	**0.009**
TIMI major or minor	11 (0.7%)	27 (1.6%)	0.41 (0.20 – 0.82)	**0.01**
Major	8 (0.5%)	19 (1.1%)	0.42 (0.18 – 0.96)	**0.04**
Minor	3 (0.2%)	8 (0.5%)	0.39 (0.10 – 1.46)	0.16
GUSTO moderate, severe or life-threatening	8 (0.5%)	19 (1.1%)	0.42 (0.18 – 0.96)	**0.04**
Moderate	3 (0.2%)	10 (0.6%)	0.30 (0.08 – 1.10)	0.07
Severe or life-threatening	5 (0.3%)	9 (0.5%)	0.56 (0.19 – 1.66)	0.29
ISTH major bleeding	8 (0.5%)	21 (1.2%)	0.38 (0.17 – 0.86)	**0.02**
BARC types 1-5				
1	8 (0.5%)	12 (0.7%)	0.67 (0.27 – 1.63)	0.37
2	24 (1.4%)	50 (2.9%)	0.48 (0.29 – 0.78)	**0.003**
3	10 (0.6%)	24 (1.4%)	0.42 (0.20 – 0.88)	**0.02**
5	1 (0.1%)	4 (0.2%)	0.25 (0.03 – 1.98)	0.20

Limitations

- The primary efficacy endpoint included minor bleeding (BARC type 2)

However, major bleeding was also significantly reduced with ticagrelor monotherapy (BARC types 3 or 5, TIMI major or minor, GUSTO and ISTH)

- Non-inferiority for MACCE was tested with an absolute margin of 2.5%. Given the lower observed ischemic event rate in the control group than anticipated (3.7% vs. 6.2%), this relative margin is wide

Given the 95% CI of the observed difference, it is likely that the absolute MACCE rate with ticagrelor monotherapy is <1.2% greater than with ticagrelor + aspirin

- ~40% of pts had biomarker-negative unstable angina

hs-troponin assays were not widely available in China and Pakistan during the enrollment period, and it is likely that many of these pts had NSTEMI

- 88.1% of pts were from China, possibly affecting the generalizability of the results

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4. 88.1% of pts were from China, possibly affecting the generalizability of the results

Conclusions and Clinical Implications

The present results demonstrate that in pts with ACS treated with PCI with contemporary DES who are free from major adverse ischemic and bleeding events after 1 month on DAPT, treatment with ticagrelor alone between 1 and 12 months will decrease clinically-relevant and major bleeding while providing similar protection from MACCE compared with ticagrelor plus aspirin

These results, in concert with prior trials, warrant updating the guidelines and change in practice to treat most pts with ACS after PCI with 1-month DAPT only followed by conversion to SAPT with a potent $P2Y_{12}$ inhibitor (with the strongest evidence to date supporting ticagrelor)

Acronym	Clinical Trials.gov No	No.of Patients	Trial Location	Patients'Condition	Question	Primary End Point	Expected Completion
REDUCE-AMI	NCT03278509	500	Sweden,Estonia, and NewZealand	Acute MI with LVEF>50% and receipt of angi ograph	Beta-blocker vs.no beta-blocker	Death from any cause or new MI	Completed
DANBLOCR	NCT03778554	2760	Denmark	s2 wk after Ml and LVEF >40%	Beta-blocker vs.no beta-blocker	Death from any cause,recurrent ML, revascularization with PClo CABG,ischemic stroke,incident heart failure,malignant ventricular arrhythmia,or resuscitated cardiac arrest	2024
BETAMI	NCT03646357	290	Noray	Type 1 MI treated with PCl or lysis	Beta-blocker vs.no beta-blocker	Death from any cause,recurrent ML heart failure,coronary revascular zation,ischemic stroke,malig- nant ventricular arrnythmia,or esuscitated cardiac arrest	2024
REBOOT	NCT03596385	8468	Spain and Italy	MI without heart failure and with LVEF>40%	Beta-blocker vs.no beta-blocker	MACE+	2024
SMART DECISION	NCT04769362	254	South Korea	MI without heart failure and with LVEF>40%	Continuation of beta- blocker vs.discon tinuation	MACE+	2025
AβYSS	NCT03498066	3700	France	STEMI or NSTEMI treated with beta-blocker, without heart failure or LVEF<40%	Continuation of beta- blockervs.discon- tinuation at>6 mo after MI	Death from any cause,MI,stroke,or hospitalization for cardiovascular causes	2024
ABBREVIATE	NCT05081999	8500	Canada	Stable ischemic heart disease,without left ventricular dysfunction or heart failure	Continuation of beta- blocker vs.discon- tinuation	Death from any cause,nonfatal MI hospitalization for resuscitated cardiac arrest,unstable angina eading to urgent revasculariza- tion,or heart failure	2026

CABG denotes coronary-artery bypass grafting,LVEF left ventricular ejection fraction, MACE major adverse cardiac events, Ml myocardial infarction, NSTEMI, non-ST-segment eleva- tion myocardial infarction,PCI percutaneous coronary intervention, and STEMI ST-seg gment elevation myocardial infarction.
ABBREVIATE denotes De-Adoption of Beta-Blockers in Patients with Stable Ischemic t Heart Disease,ABYSS Beta-Blocker Interruption after Uncomplicated Myocardial Infarction.
BETAMI Beta-Blocker Treatment after Acute Myocardial Infarction in Patients without Reduced Left Ventricular Systolic Function,DANBLOCK Danish Trial of Beta-Blocker Treatment after Myocardial Infarction without Reduced Ejection Fraction,REBOOT Treatment wi ith Beta-Blockers after Myocardial Infarction without Reduced Ejection Fraction,REDUCE-AMI Randomized Evaluation of Decreased Usage of Beta-Blockers after Acute Myocardial Infarction, and SMART DECISION Long-term Beta-Blocker Therapy after Acute Myocardial Infarction.
MACE was defined as death from any cause, Ml, or hospitalization for heart failure.

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