ESC 2021
TRIALS

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THE DIGITAL EXPERIENCE
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Cardio_Cast

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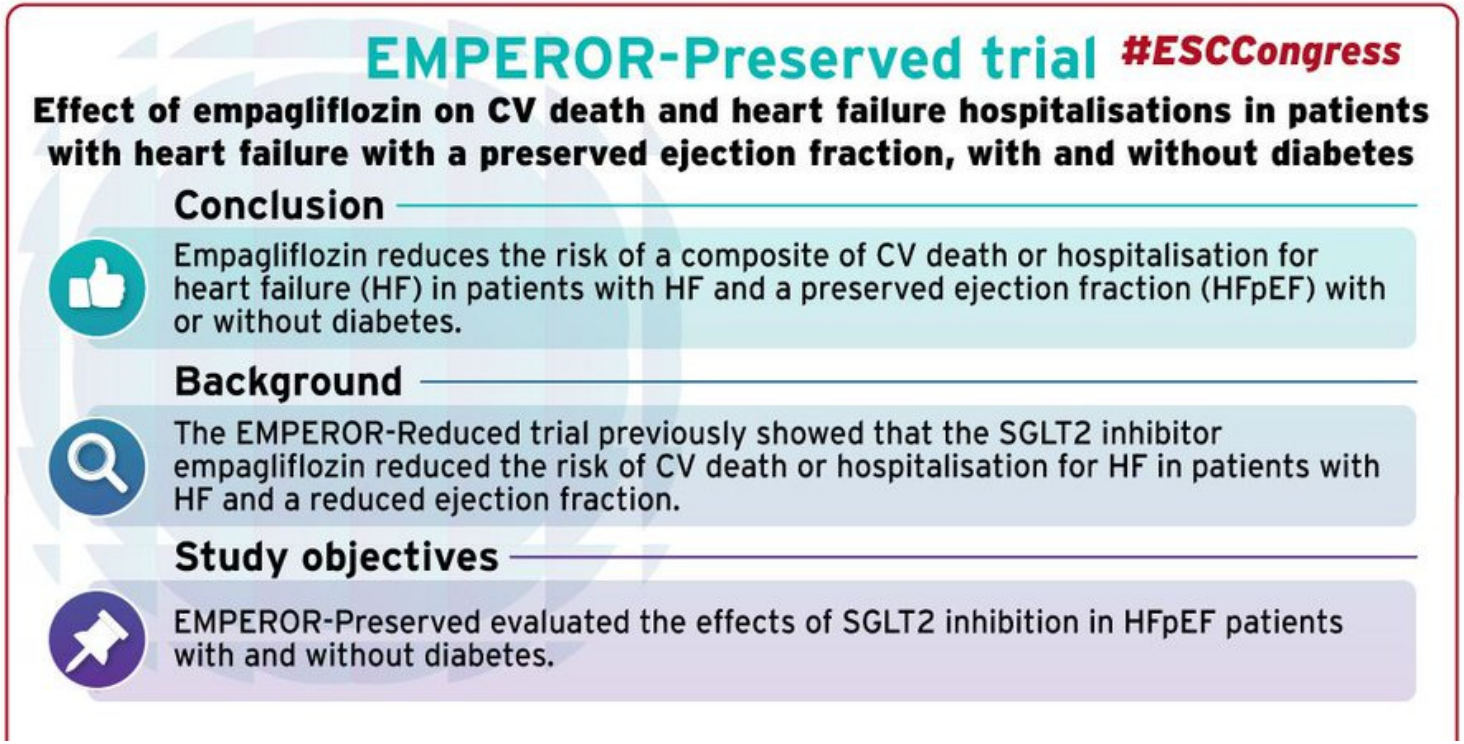
EMPAGLIFLOZIN IN HEART FAILURE WITH A PRESERVED EJECTION FRACTION

EMPEROR-Preserved



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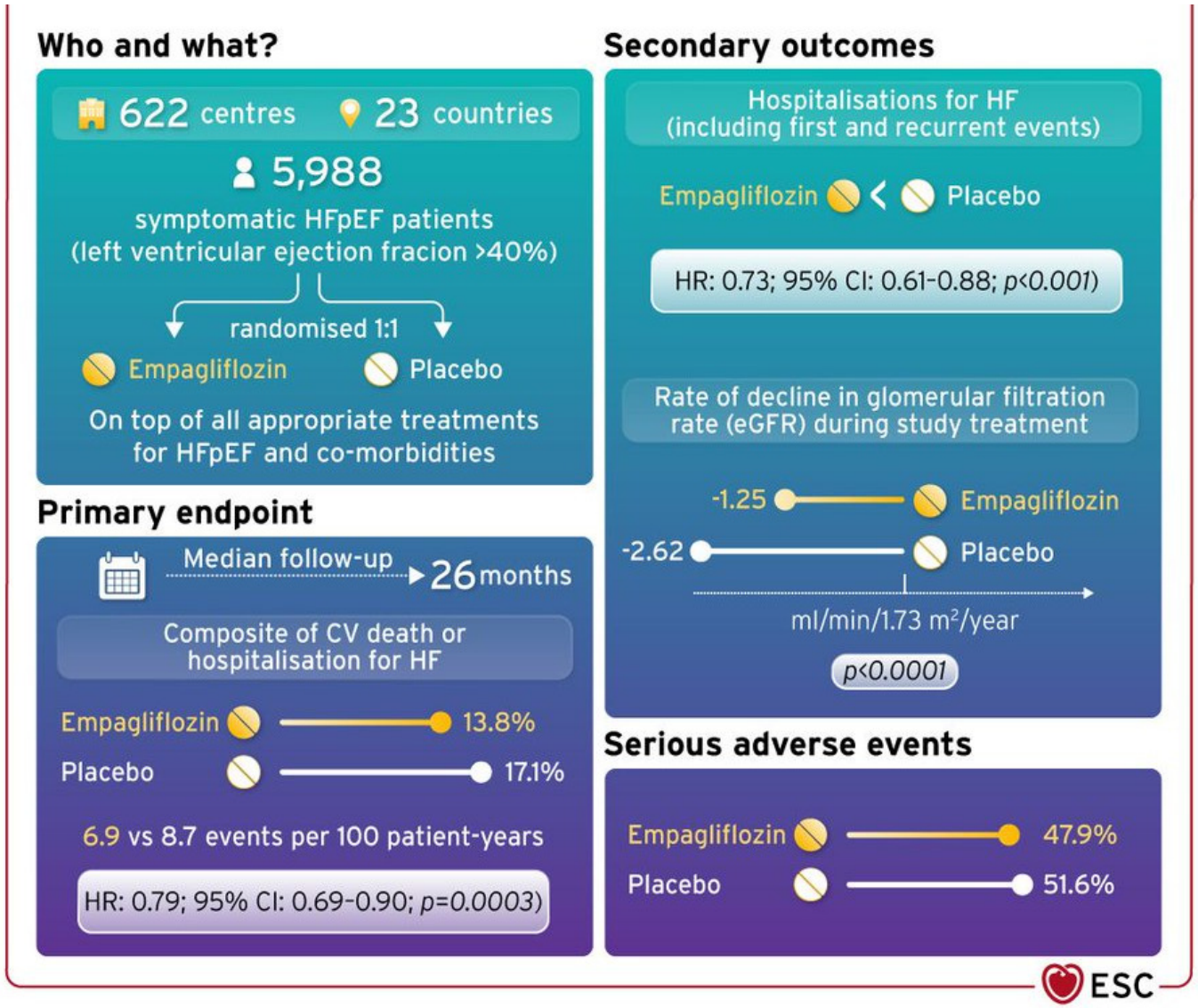

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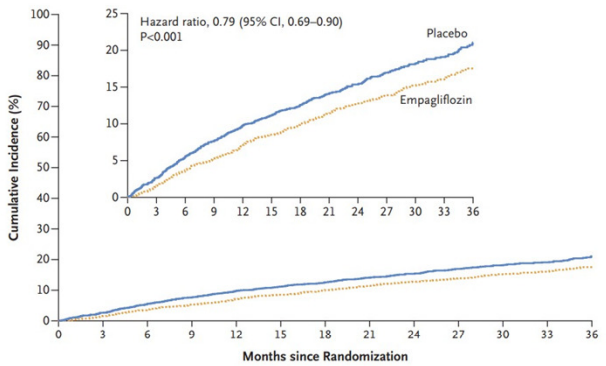

Figure 1. Primary Outcome, a Composite of Cardiovascular Death or Hospitalization for Heart Failure.
The estimated cumulative incidence of the primary outcome in the two groups is shown. The inset shows the same data on an expanded y axis.

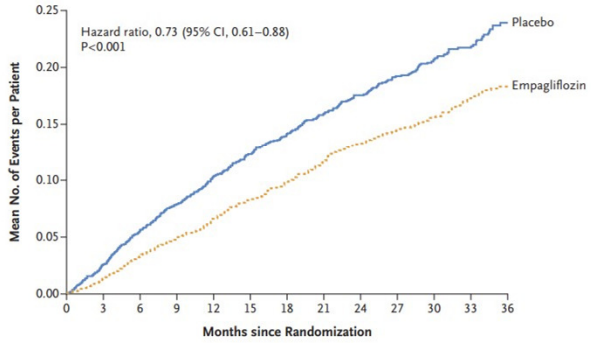

Figure 3. Hospitalizations for Heart Failure.
The mean number of events per patient for the first secondary outcome (total [first and recurrent] hospitalizations for heart failure) in the two groups is shown.

Table 2. Primary and Secondary Cardiovascular Outcomes.*

Variable	Empagliflozin (N=2997)		Placebo (N=2991)		Hazard Ratio or Difference (95% CI)	P Value
		events per 100 patient-yr		*events per 100 patient-yr*		
Primary composite outcome — no. (%)	415 (13.8)	6.9	511 (17.1)	8.7	0.79 (0.69–0.90)	<0.001
Hospitalization for heart failure	259 (8.6)	4.3	352 (11.8)	6.0	0.71 (0.60–0.83)	
Cardiovascular death	219 (7.3)	3.4	244 (8.2)	3.8	0.91 (0.76–1.09)	
Secondary outcomes specified in hierarchical testing procedure						
Total no. of hospitalizations for heart failure	407	—	541	—	0.73 (0.61–0.88)	<0.001
eGFR (CKD-EPI) mean slope change per year — ml/min/1.73 m^2†	−1.25±0.11	—	−2.62±0.11	—	1.36 (1.06–1.66)	<0.001
Other prespecified analyses						
Change in KCCQ clinical summary score at 52 wk‡	4.51±0.31	—	3.18±0.31	—	1.32 (0.45–2.19)	
Total no. of hospitalizations for any cause	2566	—	2769	—	0.93 (0.85–1.01)	
Composite renal outcome — no. (%)	108 (3.6)	2.1	112 (3.7)	2.2	0.95 (0.73–1.24)	
Onset of new diabetes in patients with prediabetes — no. (%)	120 (12.0)	6.1	137 (14.0)	7.4	0.84 (0.65–1.07)	
Death from any cause — no. (%)	422 (14.1)	6.6	427 (14.3)	6.7	1.00 (0.87–1.15)	

* All treatment effects are shown as hazard ratios, except for the slope of the change in the eGFR and the Kansas City Cardiomyopathy Questionnaire (KCCQ) clinical summary score. For all hazard ratios or treatment differences without P values, no adjustment has been made for multiple comparisons, so the intervals should not be used to infer definitive treatment effects.
† The eGFR (Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] formula) slope is analyzed on the basis of on-treatment data, using a random intercept–random slope model including age, baseline eGFR, and baseline left ventricular ejection fraction as linear covariates and sex, geographic region, baseline diabetes status, and baseline-by-time and treatment-by-time interactions as fixed effects; the model allows for randomly varying slope and intercept between patients.
‡ Change from baseline in KCCQ clinical summary score (scores range from 0 to 100, with higher scores indicating fewer or less severe symptoms or physical limitations) was analyzed with a mixed model for repeated measures, including age, baseline eGFR (CKD-EPI formula based on creatinine), and baseline left ventricular ejection fraction as linear covariates and baseline score-by-visit, visit-by-treatment, sex, geographic region, last projected visit based on dates of randomization and trial closure, and baseline diabetes status as fixed effects. The analysis is based on on-treatment data. The number of patients with available measurements for the KCCQ at week 52 in the empagliflozin and placebo groups are 2333 and 2335, respectively.

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CARDIOVASCULAR EVENTS WITH FINERENONE IN KIDNEY DISEASE AND TYPE 2 DIABETES

FIGARO-DKD

FIGARO-DKD trial #ESCCongress

Finerenone in patients with chronic kidney disease and type 2 diabetes

Conclusion

Finerenone reduces the risk of CV morbidity and mortality in patients with mild-to-moderate kidney disease and type 2 diabetes (T2D).

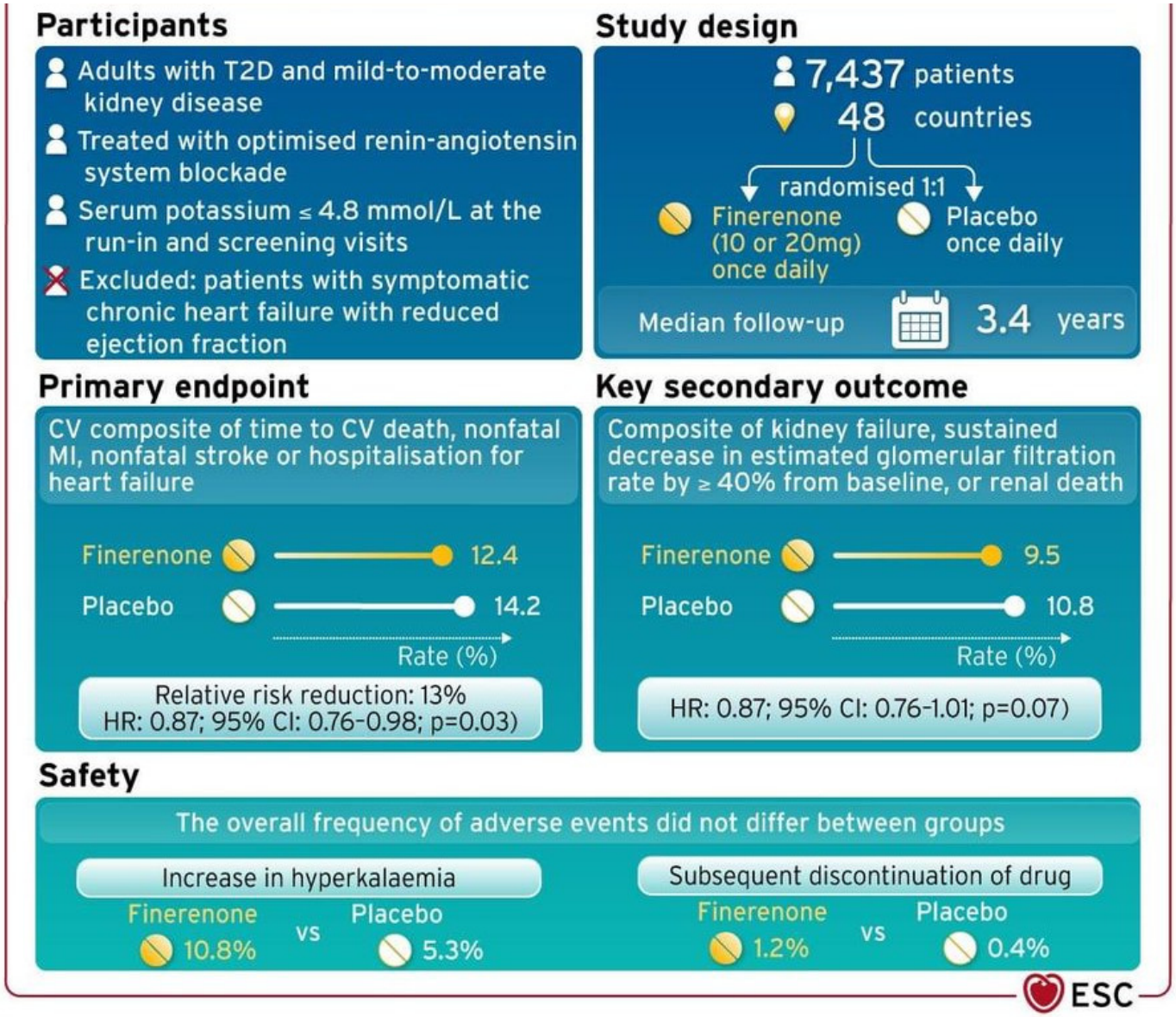
Impact on clinical practice

The FIDELIO-DKD trial previously reported that finerenone, a nonsteroidal mineralocorticoid receptor antagonist, slowed progression of kidney disease and improved CV outcomes in patients with predominantly advanced kidney disease and T2D.

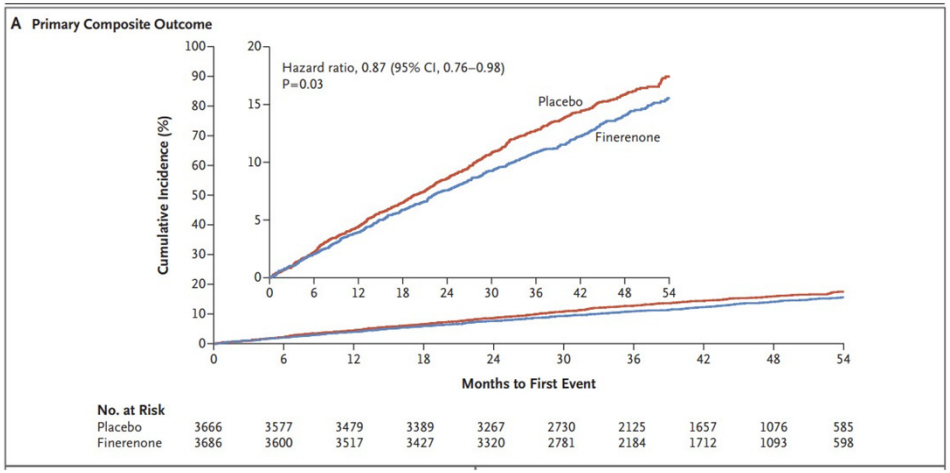
Study objectives

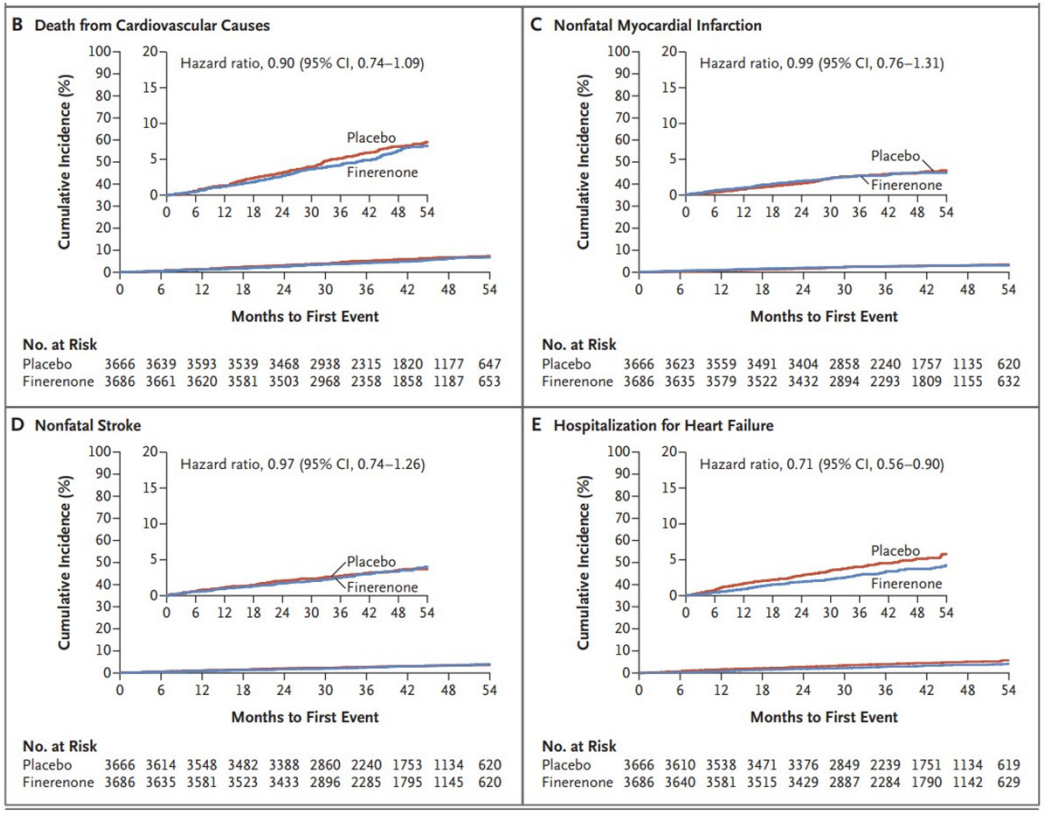
FIGARO-DKD investigated CV and renal outcomes with finerenone treatment in patients with mild-to-moderate kidney disease and type 2 diabetes.

FIGARO-DKD



FIGARO-DKD





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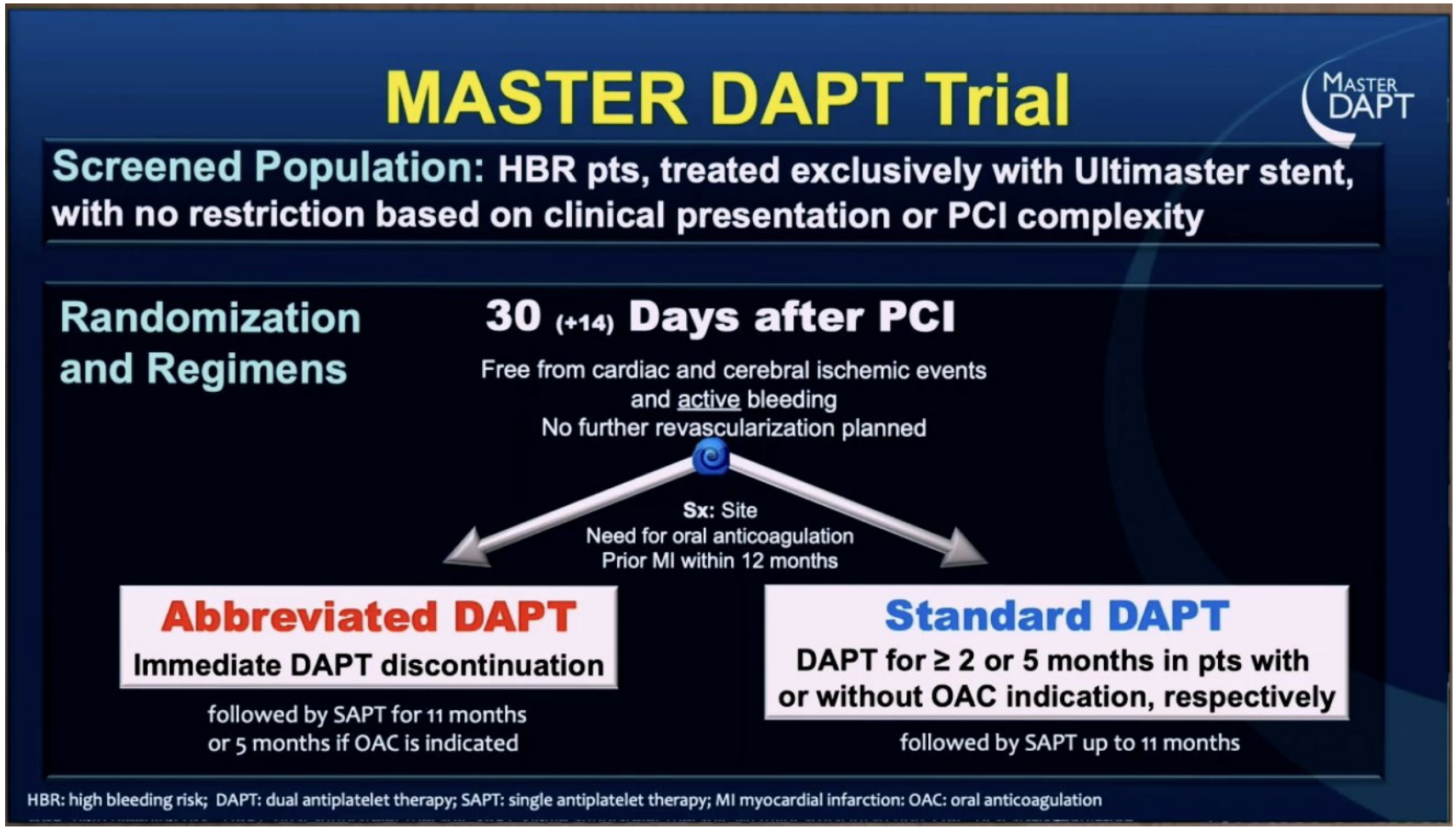
MASTER DAPT Trial
MASTER DAPT
Screened Population: HBR pts, treated exclusively with Ultimaster stent, with no restriction based on clinical presentation or PCI complexity
Randomization and Regimens
30 (+14) Days after PCI
Free from cardiac and cerebral ischemic events
and active bleeding
No further revascularization planned
Sx: Site
Need for oral anticoagulation
Prior MI within 12 months
Abbreviated DAPT
Immediate DAPT discontinuation
followed by SAPT for 11 months
or 5 months if OAC is indicated
Standard DAPT
DAPT for ≥ 2 or 5 months in pts with
or without OAC indication, respectively
followed by SAPT up to 11 months
HBR: high bleeding risk; DAPT: dual antiplatelet therapy; SAPT: single antiplatelet therapy; MI myocardial infarction: OAC: oral anticoagulation

MASTER DAPT trial #ESCCongress

Dual antiplatelet therapy after coronary stenting in high bleeding risk patients

Conclusion

1 month of dual antiplatelet therapy (DAPT) following stent implantation in high bleeding risk patients preserves ischaemic benefits and reduces bleeding risk.

Impact on clinical practice

The duration of DAPT in patients at high risk of bleeding is unclear. Guidelines recommend shortening DAPT duration in these patients to 6 months or less, or even 1 month only. The recommendation is level of evidence C, indicating that it reflects the expert opinion of the task force members.

Study objectives

To assess whether 1 month of DAPT preserved the benefit in relation to CV events, while mitigating bleeding outcomes, compared with longer treatment durations. This was a noninferiority study with sequential superiority testing.

MASTER DAPT

- Acute or chronic coronary syndrome
- At high risk for bleeding
- Underwent percutaneous coronary intervention (PCI) of all coronary artery stenoses with biodegradable polymer sirolimus-eluting stents.

Patients free from ischaemic and bleeding events and who adhered to a DAPT regimen were screened for inclusion 30 to 44 days after PCI

What?

Patients in 30 countries

4,579

randomised 1:1

A median of 34 days after PCI

Abbreviated DAPT

Immediately discontinued DAPT and continued single antiplatelet therapy until study completion – except for those receiving clinically indicated oral anticoagulation, who continued single antiplatelet therapy up to 6 months after PCI

Standard DAPT

Continued DAPT for at least 5 additional months (6 months after PCI) – or, for those receiving clinically indicated oral anticoagulation, for at least 2 additional months (3 months after PCI) and continued thereafter on single antiplatelet therapy

Complete follow-up data at 335 days were available for 4,547 (99.3%) patients

1 Net adverse clinical events

composite of all-cause death, MI, stroke, and major or clinically relevant nonmajor bleeding

abbreviated DAPT was noninferior to standard DAPT

7.5% vs 7.7%

HR: 0.97
95% CI: 0.78-1.20

difference in risk: –0.23 percentage points
(95% CI –1.80 to 1.33; p<0.001 for noninferiority)

2 Major adverse cardiac and cerebral events

composite of all-cause death, MI, and stroke

abbreviated DAPT was noninferior to standard DAPT

6.1% vs 5.9%

HR: 1.02
95% CI: 0.80-1.30

difference in risk: 0.11 percentage points
(95% CI –1.29 to 1.51; p=0.0014 for noninferiority)

3 Major or clinically relevant nonmajor bleeding

occurring between randomisation and 335 days defined as Bleeding Academic Research Consortium type 2, 3 or 5 bleeding

abbreviated DAPT was superior to standard DAPT

6.5% vs 9.4%

HR: 0.68
95% CI: 0.55-0.84
p<0.001 for superiority

difference in risk: –2.82 percentage points
(95% CI –4.40 to –1.24)

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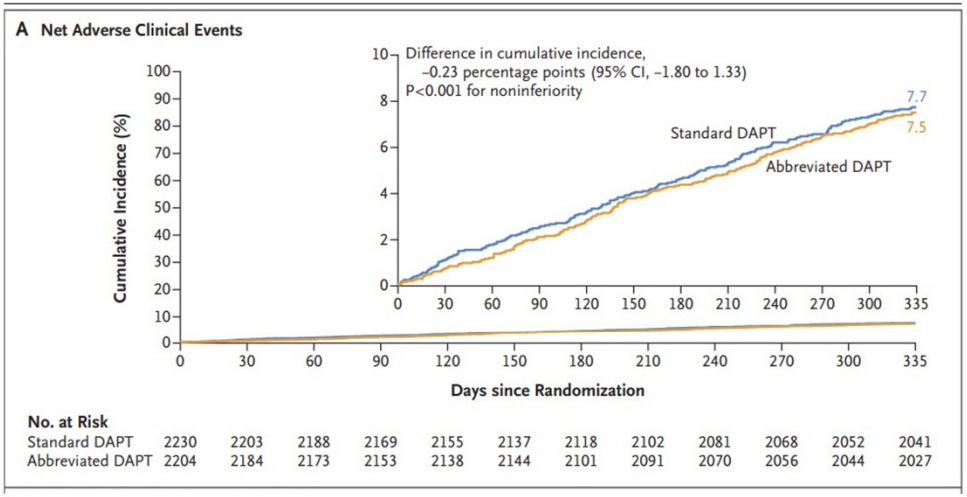
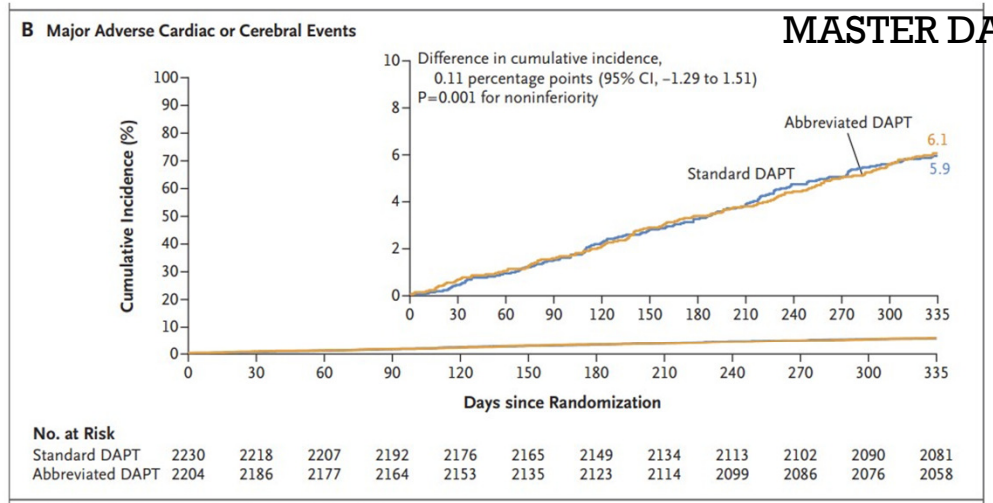
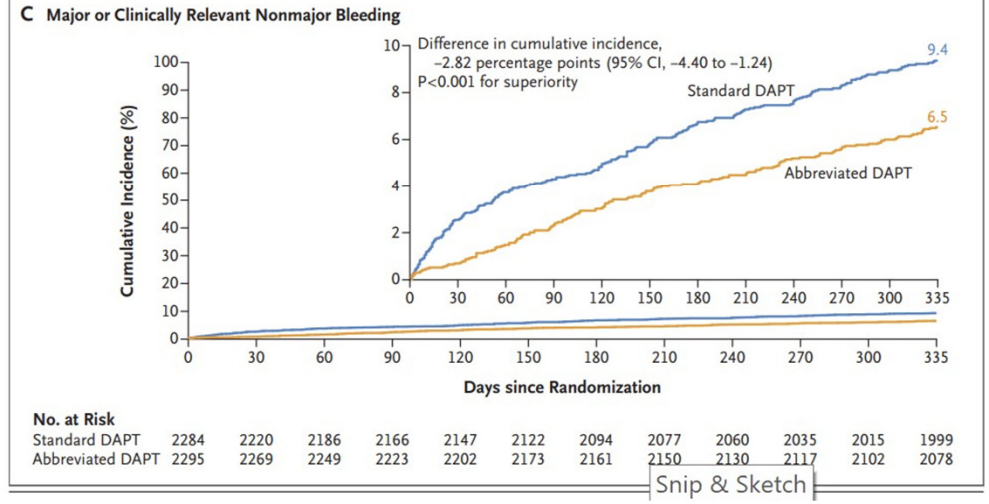
MASTER DAPT







Snip & Sketch

Figure 2 (facing page). Cumulative Incidence of Three Primary Composite Outcomes at 335 Days.

The three ranked primary outcomes were a composite of death from any cause, myocardial infarction, stroke, or major bleeding (net adverse clinical events), which was assessed in the per-protocol population (Panel A); a composite of death from any cause, myocardial infarction, or stroke (major adverse cardiac or cerebral events), which was assessed in the per-protocol population (Panel B); and major or clinically relevant nonmajor bleeding, which was assessed in the intention-to-treat population (Panel C). The per-protocol population excluded patients who did not fulfill the selection criteria or did not implement protocol-mandated therapy within 14 days after randomization. The intention-to-treat population included all the patients who underwent randomization. Insets show the same data on enlarged y axes.

DOI: 10.1056/NEJMoa2108749

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SMART-MI trial

#ESCCongress

Implantable cardiac monitors in high-risk post-infarction patients with cardiac autonomic dysfunction and moderately reduced left ventricular ejection fraction - A randomised trial

Conclusion

Remote monitoring of implantable cardiac monitors (ICMs) is highly effective for early detection of serious arrhythmias in high-risk post-infarction patients with cardiac autonomic dysfunction and moderately reduced ejection fraction.

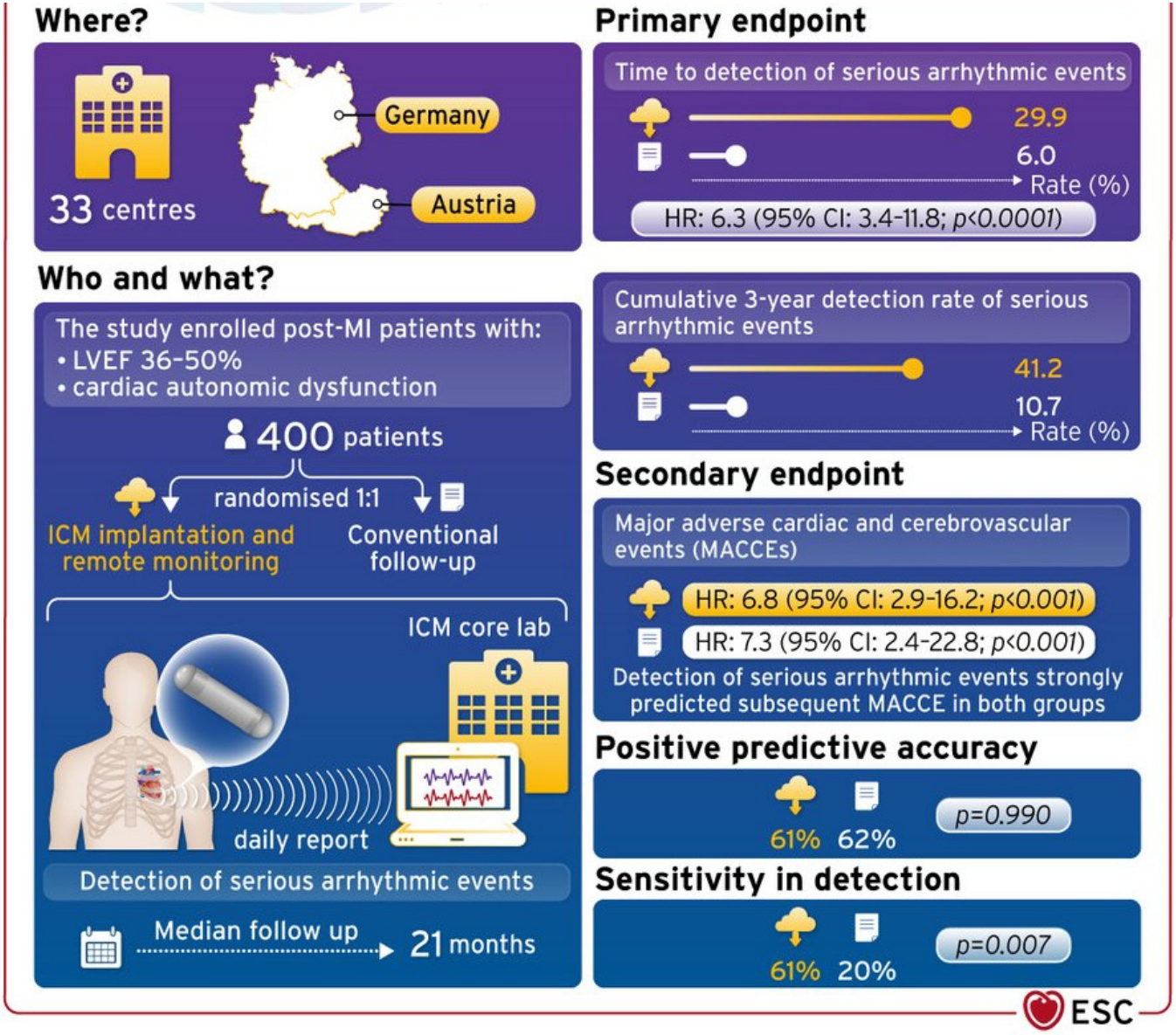
Background

Patients with severely reduced left ventricular ejection fraction (LVEF≤ 35%) after MI are candidates for prophylactic implantation of a cardioverter defibrillator. However, the vast majority of fatal and non-fatal complications after MI occur in patients with LVEF above 35%, for whom no specific preventive measures exist.

Study objectives

Previous studies in post-MI patients with reduced LVEF suggested that CV complications are preceded by arrhythmic events. However, as most of these arrhythmias are asymptomatic or subclinical, their detection escapes conventional follow-up. The SMART-MI trial examined whether ICMs could provide early detection of such arrhythmias.

SMART-MI



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- Overall results showed the primary endpoint occurred in 29.9% (n=60) of patients in the ICM group and 6% (n=12) in the control group. Researchers observed an improved detection for all types of serious arrhythmic events in the ICM group, including atrial fibrillation, higher degree atrioventricular block, fast non-sustained ventricular tachycardia and sustained ventricular tachycardia/ventricular fibrillation. Additionally, ICM-based detection of serious arrhythmic events was associated with a 6.82-fold increased risk for subsequent major adverse cardiac and cerebrovascular events, the researchers said.
- "The study found that post-infarction patients with cardiac autonomic dysfunction and only moderately reduced LVEF developed a high number of serious subclinical arrhythmic events that could be detected early and effectively with ICMs," said **Axel Bauer, MD**, principal investigator of the study. "The spectrum and frequency of arrhythmias in these patients was comparable to that of post-infarction patients with reduced LVEF, who are currently candidates for prophylactic ICD therapy. Our study supports the use of ICMs in high-risk post-MI patients with moderately reduced LVEF and cardiac autonomic dysfunction as a sensitive tool for continuous risk assessment."

TOMAHAWK trial #ESCCongress

Immediate angiography after out-of-hospital cardiac arrest

Conclusion

Early coronary angiography in out-of-hospital cardiac arrest (OHCA) patients without ST-segment elevation is not superior to a delayed/selective approach.

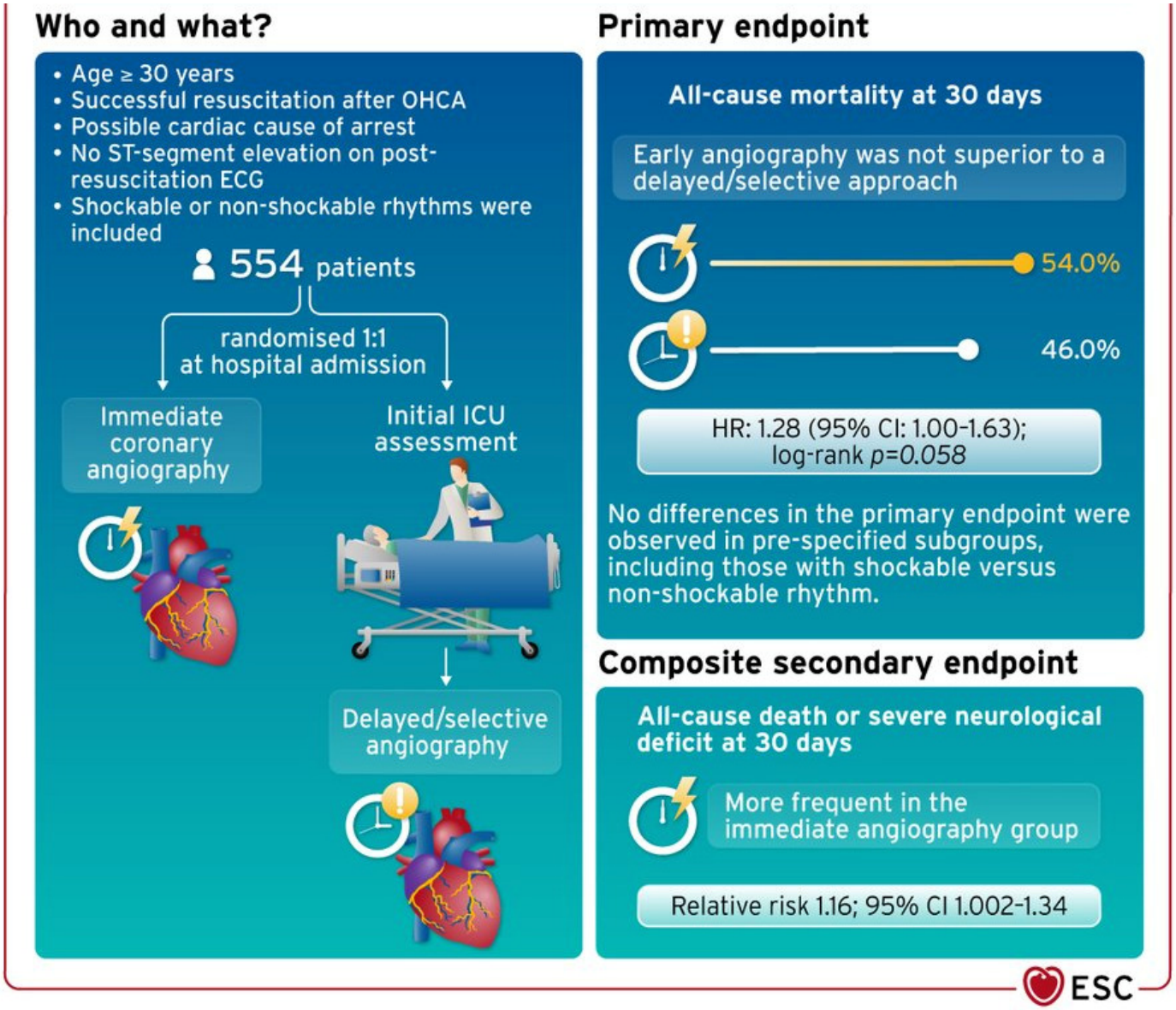
Impact on clinical practice

The usefulness and timing of coronary angiography in OHCA survivors without ST-segment elevation are uncertain. In up to one-third of these patients, acute MI is the cause of cardiac arrest, suggesting that diagnostic coronary angiography and potential percutaneous coronary intervention could be beneficial.

Study objectives

The TOMAHAWK trial examined whether immediate coronary angiography for treating or ruling out acute coronary events in OHCA survivors without ST-segment elevation is beneficial for all-cause mortality at 30 days compared with initial intensive care unit (ICU) assessment and delayed/selective angiography.

TOMAHAWK



TOMAHAWK

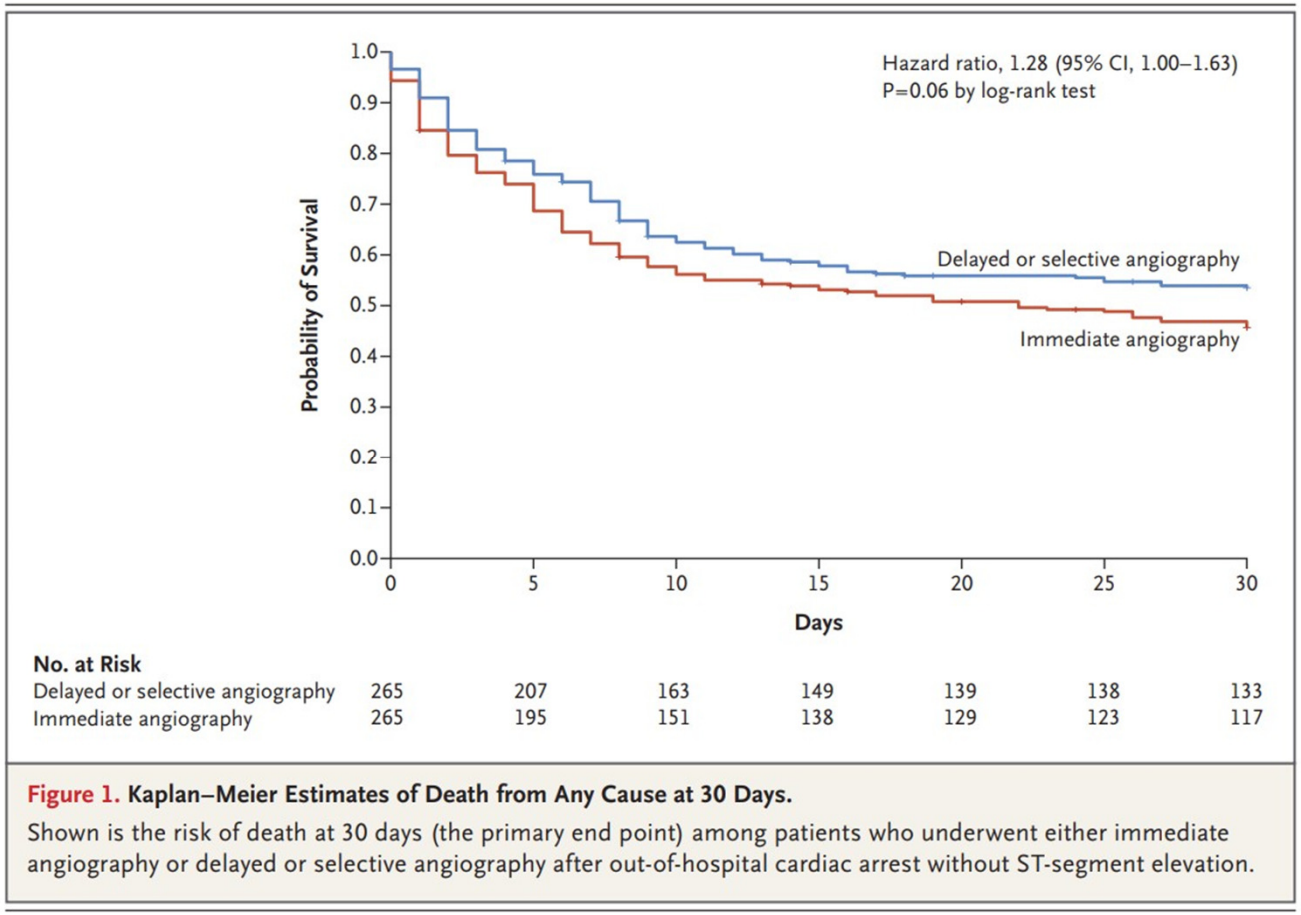


Figure 1. Kaplan–Meier Estimates of Death from Any Cause at 30 Days.

Shown is the risk of death at 30 days (the primary end point) among patients who underwent either immediate angiography or delayed or selective angiography after out-of-hospital cardiac arrest without ST-segment elevation.

DOI: 10.1056/NEJMoa2101909

Cardio_Cast

TOMAHAWK

Table 3. Clinical Outcomes at 30 Days.*

End Point	Immediate Angiography (N=265)	Delayed or Selective Angiography (N=265)	Effect Size (95% CI)†
Primary end point			
Death from any cause — no. (%)	143 (54.0)	122 (46.0)	Hazard ratio, 1.28 (1.00 to 1.63)
Secondary efficacy end points‡			
Myocardial infarction — no./total no. (%)	0/248	2/250 (0.8)	Relative risk, 0 (0 to 1.93)
Severe neurologic deficit — no./total no. (%)§	21/112 (18.8)	16/126 (12.7)	Relative risk, 1.48 (0.82 to 2.67)
Death from any cause or severe neurologic deficit — no./total no. (%)	164/255 (64.3)	138/248 (55.6)	Relative risk, 1.16 (1.00 to 1.34)
Median length of ICU stay (IQR) — days	7 (3–11)	8 (4–13)	HLE, −1 (−2 to 0)
Median peak SAPS II (IQR)¶	70 (55–83)	69 (54–82)	HLE, 0 (−4 to 4)
Rehospitalization for congestive heart failure — no./total no. (%)	1/246 (0.4)	1/249 (0.4)	Relative risk, 1.00 (0.19 to 1.85)
Median peak release of myocardial enzymes (IQR)			
Troponin T — μg/liter	0.39 (0.14–1.26)	0.34 (0.12–1.07)	HLE, 0.04 (−0.03 to 0.11)
Troponin I — μg/liter	1.46 (0.42–5.69)	1.10 (0.40–5.75)	HLE, 0.06 (−0.37 to 0.49)
Median peak creatinine (IQR) — μmol/liter	133 (101–193)	133 (98–199)	HLE, 2.08 (−8.06 to 12.22)
Secondary safety end points — no./total no. (%)‡			
Moderate or severe bleeding‖	12/260 (4.6)	8/232 (3.4)	Relative risk, 1.34 (0.57 to 3.14)
Stroke	4/258 (1.6)	5/242 (2.1)	Relative risk, 1.13 (0.33 to 3.84)
Acute kidney failure leading to renal-replacement therapy	49/259 (18.9)	38/241 (15.8)	Relative risk, 1.14 (0.78 to 1.68)

DOI: 10.1056/NEJMoa2101909

SECOND ASYMPTOMATIC CAROTID SURGERY TRIAL (ACST-2)

- The goal of the trial was to evaluate carotid artery stenting compared with carotid endarterectomy among patients with asymptomatic carotid artery stenosis.
- Study Design
  - Randomization
  - Parallel
- Participants with asymptomatic carotid stenosis were randomized to carotid artery stenting (n = 1,811) versus carotid endarterectomy (n = 1,814).
  - Total number of enrollees: 3,625
  - Duration of follow-up: mean 5 years
  - Percentage female: 30%
- Inclusion criteria:
  - Unilateral or bilateral carotid artery stenosis ≥60% as assessed by ultrasound
  - Patients eligible by ultrasound then had computed tomography or magnetic resonance imaging to confirm that carotid artery stenting and carotid endarterectomy were both practical

Halliday A, Bulbulia R, Bonati LH, et al. Second asymptomatic carotid surgery trial (ACST-2): a randomized comparison of carotid artery stenting versus carotid endarterectomy. *Lancet* 2021;Aug 29:[Epub ahead of print].

- Exclusion criteria:
  - Previous stroke or transient ischemic attack within the previous 6 months
  - Unsuitability for carotid stenting (for example, due to calcium or tortuosity) or carotid endarterectomy
  - High procedural risk (for example, due to recent acute myocardial infarction)
  - High risk of cardiac emboli
  - Major life-threatening condition
- Principal Findings:
  - Procedural death or disabling stroke at 30 days: 1.0% in the carotid stent group compared with 0.9% in the carotid endarterectomy group
  - Procedural death or disabling stroke at 5 years: 3.4% in the carotid stent group compared with 3.5% in the carotid endarterectomy group (p = 0.86)
  - Procedural death or any stroke at 5 years: 8.6% in the carotid stent group compared with 7.1% in the carotid endarterectomy group (p = 0.09)
  - Nonprocedural fatal or disabling stroke at 5 years: (relative risk [RR] 0.98, p = 0.91)
  - Nonprocedural stroke at 5 years: (RR = 1.16, p = 0.33)
- Interpretation:
  - Among patients with asymptomatic carotid stenosis, carotid artery stenting was safe. Carotid artery stenting was associated with a low incidence of procedural death or disabling stroke within 30 days. The incidence of procedural death or disabling stroke within 30 days was similar to the incidence from carotid endarterectomy. Procedural death or disabling stroke within 5 years was also similar between treatment groups.

Halliday A, Bulbulia R, Bonati LH, et al. Second asymptomatic carotid surgery trial (ACST-2): a randomized comparison of carotid artery stenting versus carotid endarterectomy. *Lancet* 2021;Aug 29:[Epub ahead of print].

	Allocated CAS (n=1811)	Allocated CEA (n=1814)
Procedural stroke or death	63	47
No procedural stroke or death*	1748	1767
Worst non-procedural stroke, by mRS score†		
6 (fatal)	16 (0·9%)	20 (1·1%)
3–5 (disabling)	28 (1·6%)	25 (1·4%)
2	9	5
1	23	17
0	15	12
0–2 (non-disabling)	47 (2·7%)	34 (1·9%)
Total: any non-procedural stroke	91 (5·2%)	79 (4·5%)

CAS=carotid artery surgery. CEA=carotid endarterectomy. mRS=modified Rankin Scale. *Denominator for percentages; this includes patients with no procedure. †Corresponding numbers of first non-procedural strokes (CAS *vs* CEA): 12 versus 17 fatal, 23 versus 22 disabling, 56 versus 40 non-disabling, and totals 91 versus 79; these totals include 15 strokes (seven CAS and eight CEA) with neither procedure beforehand, of which five were in the first month (ie, shortly after randomisation, while awaiting treatment) and ten were later (at mean 25 months after entry).

***Table 3:* Non-procedural strokes during follow-up**

	Allocated CAS (n=1811)	Allocated CEA (n=1814)	p value	Had CAS first	Had CEA first
Had no carotid procedure	106	78	..	..	..
Had a carotid procedure†	1705	1736	..	1653	1788
Worst procedural stroke, mRS score					
6 (fatal)	7	5	0·77	6	6
3–5 (disabling)	6	7	1·00	8	5
2	9	9	1·00	9	9
1	23	15	0·25	21	17
0	16	5	0·03	15	6
0–2 (non-disabling)	48 (2·7%)	29 (1·6%)	0·03	45 (2·7%)	32 (1·8%)
Subtotal: any stroke	61 (3·6%)	41 (2·4%)	0·06	59 (3·6%)	43 (2·4%)
MI					
Fatal	0	4	0·13	0	4
Non-fatal	5	8	0·58	4	9
Subtotal: any MI	5 (0·3%)	12 (0·7%)	0·15	4 (0·2%)	13 (0·7%)
Other death‡	2	2	1·00	3	1
Death, MI, or any stroke	67 (3·9%)	55 (3·2%)	0·26	65 (3·9%)	57 (3·2%)
Death or any stroke	63 (3·7%)	47 (2·7%)	0·12	62 (3·8%)	48 (2·7%)
Death or disabling stroke	15 (0·9%)	18 (1·0%)	0·77	17 (1·0%)	16 (0·9%)

Data are n or n (%), unless otherwise specified. CAS=carotid artery surgery. CEA=carotid endarterectomy. MI=myocardial infarction. mRS=modified Rankin Scale. *First carotid procedure undergone after randomisation. †Denominator for percentages. ‡One groin haemorrhage after CAS, one unrelated trauma death after CAS, one cervical haemorrhage after CEA, and one generalised sepsis (allocated CEA but got CAS).

Table 2:* Death, stroke, or MI within 30 days of first carotid procedure

Halliday A, Bulbulia R, Bonati LH, et al. Second asymptomatic carotid surgery trial (ACST-2): a randomized comparison of carotid artery stenting versus carotid endarterectomy. *Lancet* 2021;Aug 29:[Epub ahead of print].

ACST-2

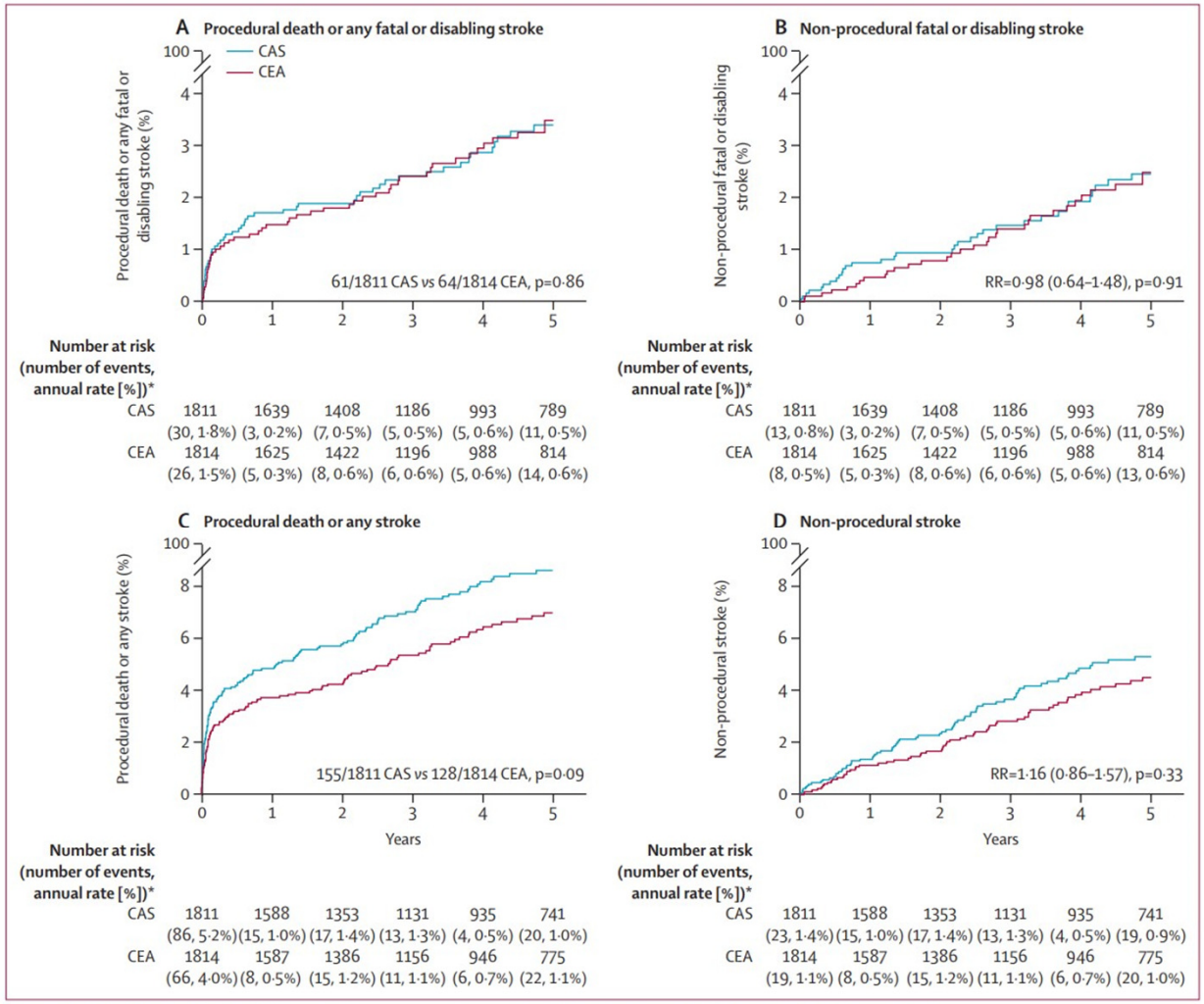


Figure 2: **Kaplan-Meier estimates of 5-year outcomes among asymptomatic patients randomly allocated to CAS versus CEA**
CAS=carotid artery stenting. CEA=carotid endarterectomy. *Last rate is after year 5 (and all three procedural strokes due to a second carotid procedure were after year 5).

Halliday A, Bulbulia R, Bonati LH, et al. Second asymptomatic carotid surgery trial (ACST-2): a randomized comparison of carotid artery stenting versus carotid endarterectomy. *Lancet* 2021;Aug 29:[Epub ahead of print].

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ACST-2

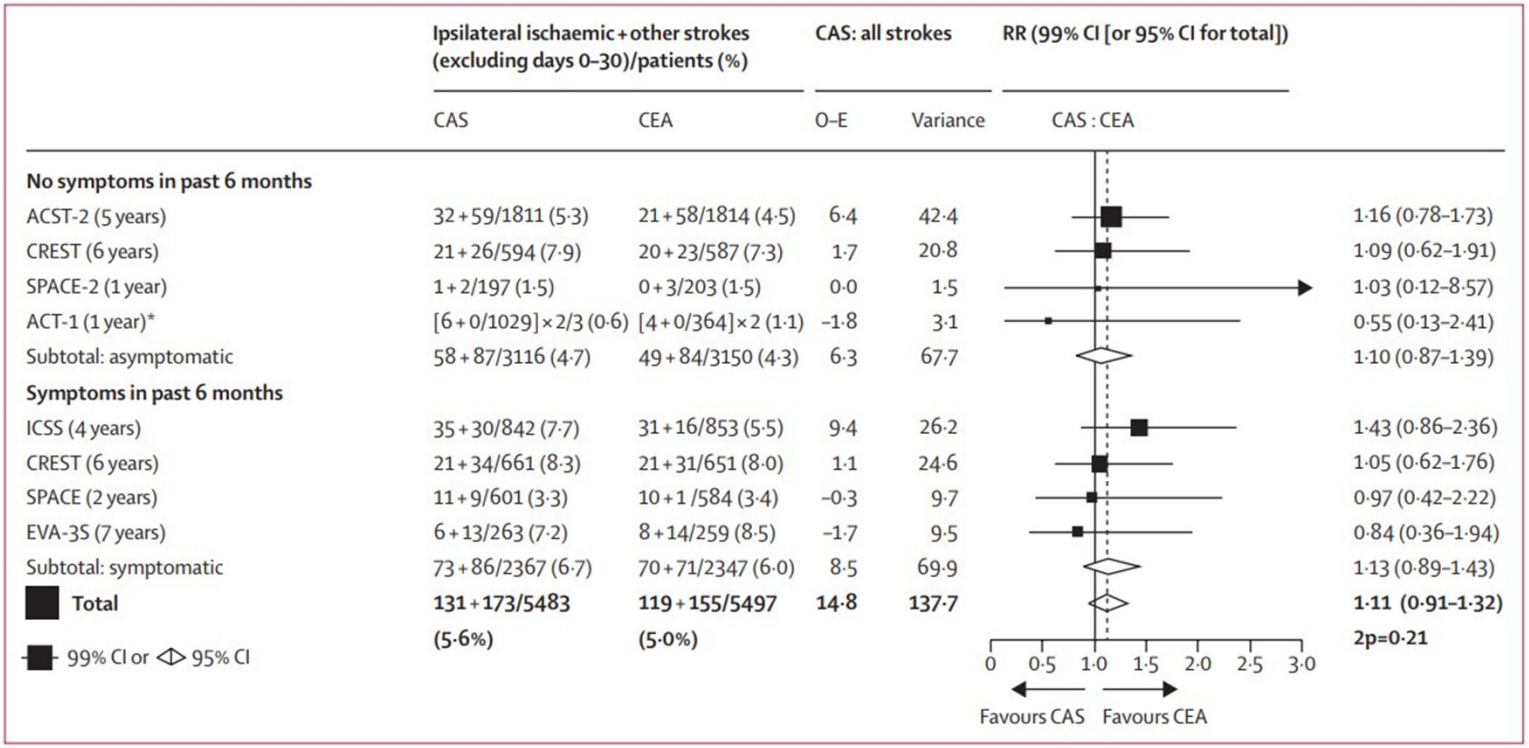

Figure 4: **Trials of CAS versus CEA for asymptomatic or symptomatic carotid stenosis—ITT analyses of non-procedural strokes (ipsilateral ischaemic stroke plus other strokes)**

The figure excludes the 13 smaller trials (all evenly randomised) identified by the 2020 Cochrane review, which reported that they had, in total, 30 non-procedural strokes in 692 patients with CAS versus 24 non-procedural strokes in 715 patients with CEA. A repeat search on July 31, 2021, re-using the Cochrane search criteria identified no more trials of CAS versus CEA. 2p=two-sided p value. CAS=carotid artery stenting. CEA=carotid endarterectomy. ITT=intention-to-treat. O–E=log-rank observed minus expected. Var (O–E)=variance of (O–E). *ACT-1 allocated patients in a 3:1 ratio; for balance, therefore, it contributes two thirds of its CAS cases and double its CEA cases to the subtotal and the total case numbers; its main report provides exact numbers only for ischaemic strokes within 1 year.

Halliday A, Bulbulia R, Bonati LH, et al. Second asymptomatic carotid surgery trial (ACST-2): a randomized comparison of carotid artery stenting versus carotid endarterectomy. *Lancet* 2021;Aug 29:[Epub ahead of print].

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THE APAF-CRT MORTALITY TRIAL

AV junction ablation and cardiac resynchronization for patients with permanent atrial fibrillation and narrow QRS: The APAF-CRT Mortality Trial. ***Brignole M et al.***

Trial population	Randomization	Optimization	Death from any cause (ITT analysis)
133 pts with: • Permanent AF • Narrow QRS • ≥1 HF hospitalization • Severe symptoms	**63** Rate control **ABL+CRT**	HR = **70** bpm	**11%** (7 pts)
	70 Rate control **DRUGS**	HR = **82** bpm	**29%** (20 pts)

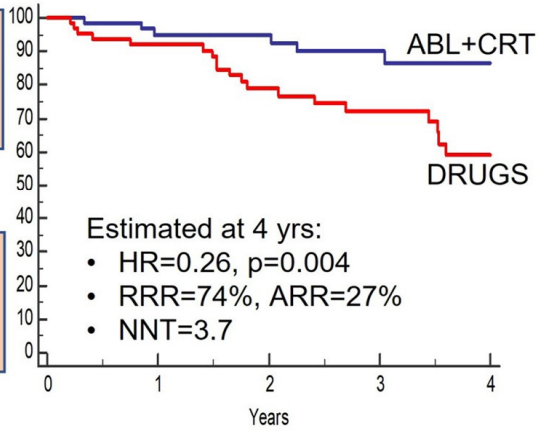

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Table 2 **Efficacy outcomes**[a]

Outcomes	Ablation + CRT ($n = 63$)	Drug ($n = 70$)	Hazard ratio[b] (95% CI)	*P*-value
Death from any cause (patients)	7 (11%)	20 (29%)	0.26 (0.10–0.65)	0.004
Cardiovascular cause	5 (8%)	12 (17%)	0.35 (0.12–1.02)	0.05
Non-cardiovascular cause	2 (3%)	8 (11%)	0.25 (0.05–1.16)	0.08
Combined endpoint of death from any cause or hospitalization for HF, patients (%)	18 (29%)	36 (51%)	0.40 (0.22–0.73)	0.002
Death from any cause and EF ≤35% (patients)	3/27 (11%)	8/28 (29%)	0.34 (0.06–1.92)	0.22
Death from any cause and EF >35% (patients)	4/36 (11%)	12/42 (29%)	0.27 (0.08–0.84)	0.02

CI, confidence interval; CRT, cardiac resynchronization therapy; EF, ejection fraction; HF, heart failure.
[a]The primary and secondary clinical outcomes were analysed according to the intention-to-treat principle.
[b]Hazard ratios were calculated by means of the Cox proportional hazard model.

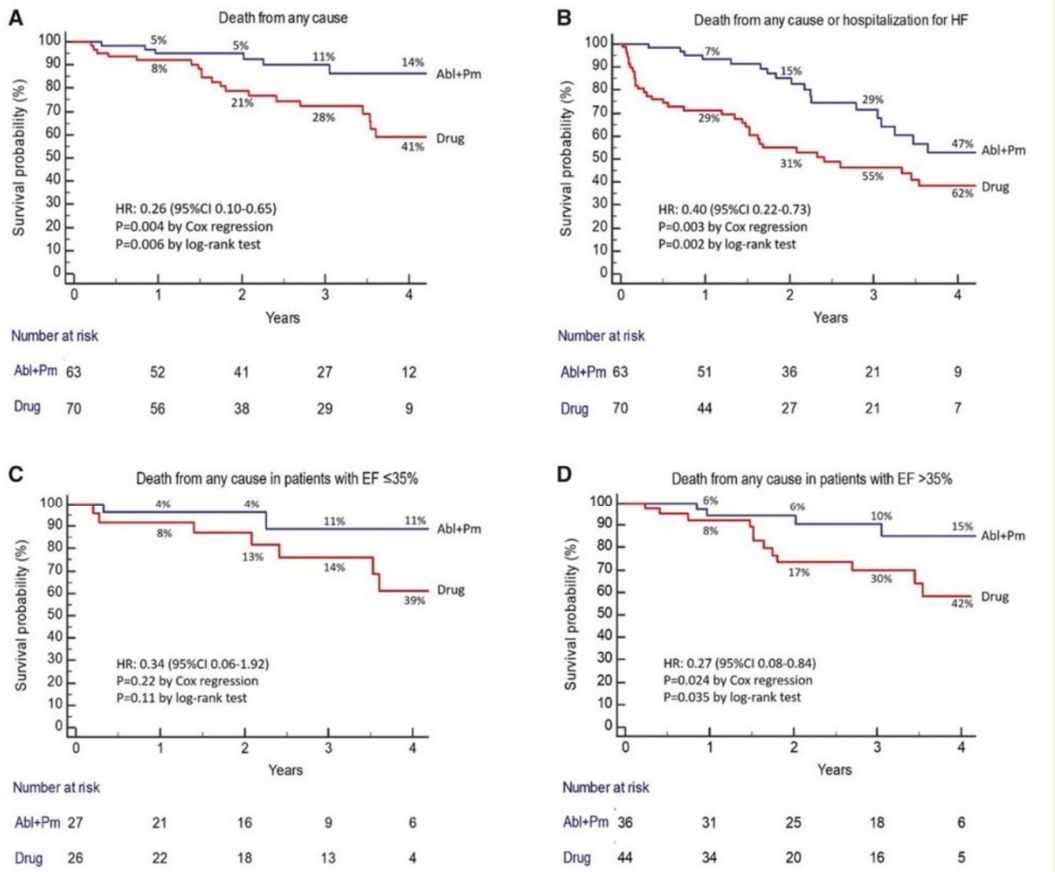

Figure 2 Kaplan–Meier curves comparing primary and secondary outcomes between Ablation + Cardiac Resynchronization Therapy arm and Drug arm. Event-free probability and yearly cumulative incidence are shown. (*A*) The incidence of the primary outcome of death from any cause. (*B*) The incidence of combined endpoint of death from any cause or hospitalization for heart failure. (*C*) The incidence of death from any cause in patients with ejection fraction ≤35%. (*D*) The incidence of death from any cause in patients with ejection fraction >35%. CI, confidence interval; EF, ejection fraction; HF, heart failure; HR, hazard ratio.

APAF-CRT

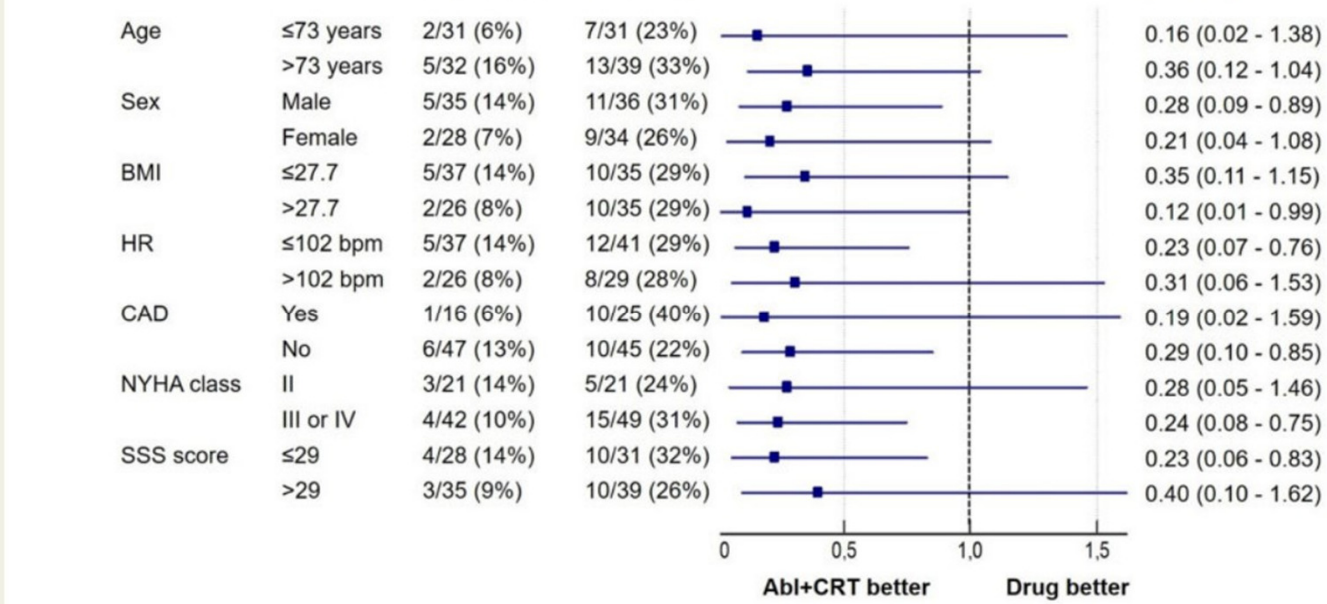

Figure 3 Subgroup analyses of the primary endpoint. A subgroup analysis of the primary outcome did not evidence interactions between subgroups. BMI, body mass index; CAD, coronary artery disease; CI, confidence interval; CRT, cardiac resynchronization therapy; HR, heart rate; NYHA, New York heart Association class; SSS, Specific Symptoms Scale score.

Conclusions

Ablation þ CRT was superior to pharmacological therapy in reducing mortality in patients with permanent AF and narrow QRS who were hospitalized for HF, irrespective of their baseline EF.

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DECAAF II trial

#ESCCongress

Efficacy of DE-MRI-guided fibrosis ablation vs. conventional catheter ablation of persistent atrial fibrillation

Conclusion

Image-guided fibrosis ablation in addition to pulmonary vein isolation (PVI) does not improve ablation success rates compared to PVI alone in patients with persistent atrial fibrillation (AF), according to an intention-to-treat analysis. In as-treated analyses, covering low grade atrial fibrosis with ablation lesions led to a significant reduction in atrial arrhythmia recurrence.

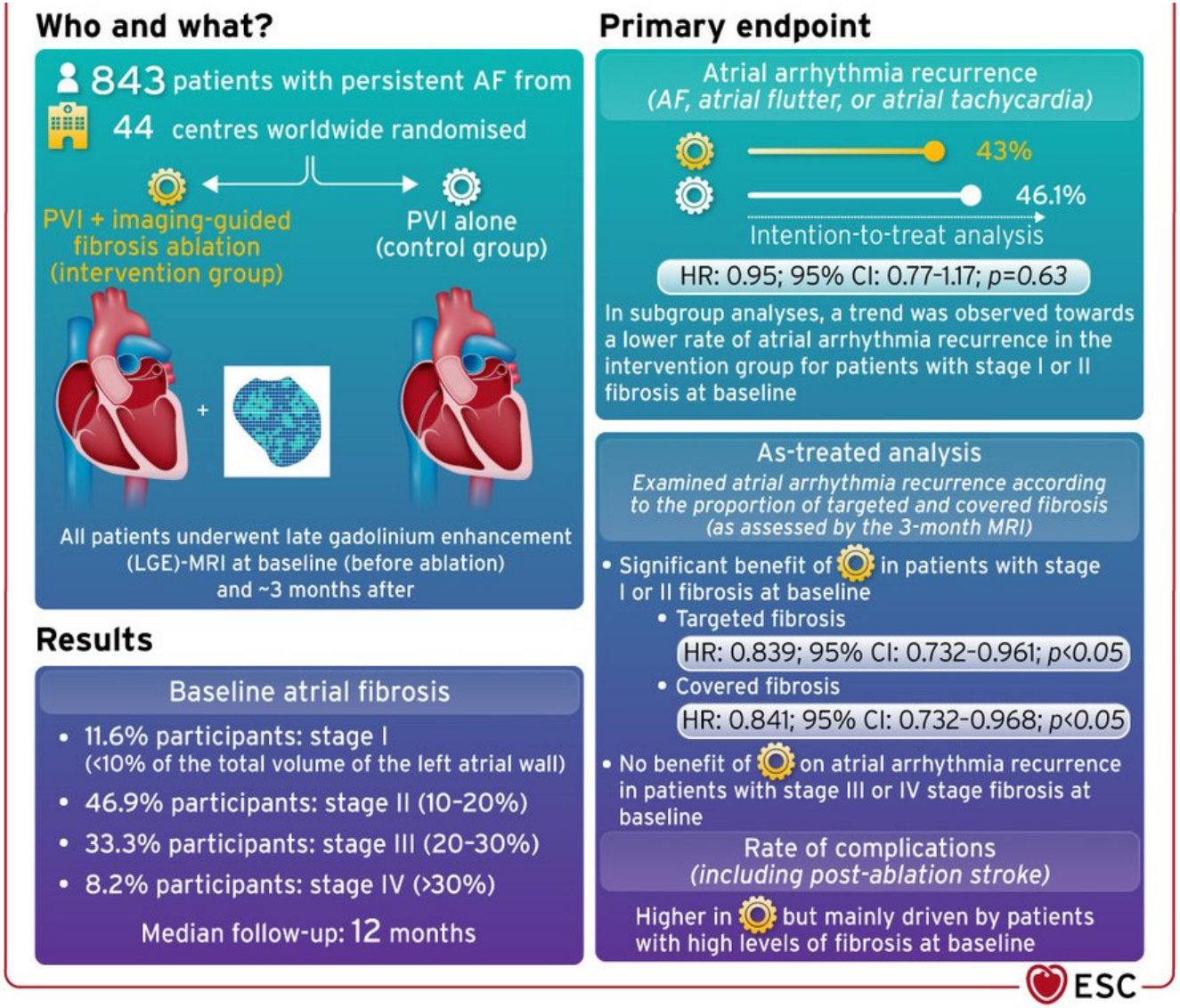
Background

The multicentre DECAAF study previously reported that among AF patients undergoing catheter ablation, atrial tissue fibrosis estimated by delayed enhancement magnetic resonance imaging (MRI) was independently associated with the likelihood of recurrent arrhythmia.

Study objectives

The DECAAF II trial tested the hypothesis that imaging-guided fibrosis ablation in addition to conventional PVI is superior to PVI alone in improving ablation success rates in patients with persistent AF.

DECAAF II



DECAAF II

- The trial enrolled 843 patients (median age 62 years, 78.8% men) with persistent AFib from 44 centers around the world. Participants were randomized to receive either PVI plus imaging-guided fibrosis ablation (intervention group) or PVI alone. All patients underwent late gadolinium enhancement (LGE)-MRI at baseline prior to ablation and then approximately three months after. The baseline images were used during the procedure in the intervention group to guide ablation of fibrotic tissue. Operators were instructed to either cover or encircle the green areas on the images (i.e., the fibrotic tissue), in addition to PVI. Operators in the control group were instructed to only encircle the pulmonary veins, without adding additional lesions. The three-month MRI evaluated the formation of lesions secondary to ablation. The primary endpoint was atrial arrhythmia recurrence for 12 to 18 months.

- Overall results found baseline fibrosis was predictive of AFib ablation outcomes, especially at higher fibrosis levels – findings that confirmed the results of the initial DECAAF study. In the intention-to-treat analysis, no statistically significant difference was observed in the primary endpoint between groups in the total study population. Atrial arrhythmia recurrence occurred in 43% of patients (n=175) in the intervention group and 46.1% of patients (n=188) in the PVI-only group.

- Subgroup analyses suggested a trend towards a lower rate of atrial arrhythmia recurrence in the intervention group for patients with stage I or II fibrosis at baseline. As-treated analyses examining atrial arrhythmia recurrence according to the proportion of targeted and covered fibrosis (as assessed by the three-month MRI) found a significant benefit of substrate ablation in patients with stage I or II fibrosis at baseline. However, researchers observed no benefit of image-guided fibrosis ablation on atrial arrhythmia recurrence in patients with stage III or IV stage fibrosis at baseline. They also noted that the rate of complications, including post-ablation stroke, was higher in the image-guided ablation group but was mainly driven by patients with high levels of fibrosis at baseline.
- "The results suggest that targeting atrial fibrosis in AFib patients with low levels of fibrotic disease (less than 20%) may help improve ablation outcomes," said principal investigator **Nassir Marrouche, MD**. "In addition, the findings indicate that PVI should remain the mainstream ablation strategy in AFib patients with high levels of fibrosis (more than 20%)."

QUADRUPLE ULTRA-LOW-DOSE TREATMENT FOR HYPERTENSION - QUARTET

- The QUARTET trial showed that a strategy of quarter dosing of four antihypertensive medications into one polypill ("quadpill") is superior to full-dose monotherapy with irbesartan in improving BP control among patients with a diagnosis of HTN on no medications or therapy with only one medication at baseline.
- Description:
  - The goal of the trial was to assess the efficacy and safety of a polypill/quadpill containing quarter doses of four antihypertensive medications compared with monotherapy among patients with hypertension (HTN).
- Study Design
  - Eligible patients were randomized in a double-blind 1:1 fashion to either a quadpill (n = 300) or irbesartan 150 mg (n = 291). The quadpill contained bisoprolol 2.5 mg, irbesartan 37.5 mg, amlodipine 1.25 mg, and indapamide 0.625 mg.
- Total screened: 743
- Total number of enrollees: 591
- Duration of follow-up: 52 weeks
- Mean patient age: 59 years
- Percentage female: 40%

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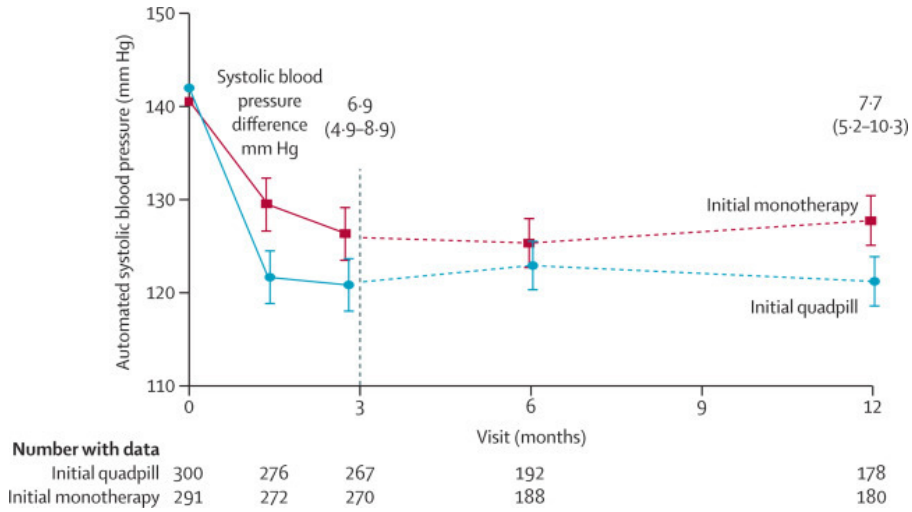
QUARTET

- Inclusion criteria:
  - Age ≥18 years
  - Diagnosis of HTN, and
  - Criteria A: Untreated HTN ≥4 weeks with clinic systolic blood pressure (SBP) ≥140/90 mm Hg or daytime 24-hour ambulatory BP (ABP) ≥135/85 mm Hg
  - Criteria B: Monotherapy for HTN with clinic SBP ≥130/85 mm Hg or daytime ABP ≥125/80 mm Hg
- Exclusion criteria:
  - Contraindication to study drugs
  - Secondary causes of HTN
  - Concomitant illness
  - Breastfeeding, women not on contraception
- Other salient features/characteristics:
  - White race: 82%
  - No BP medications at baseline: 54%
  - Mean office BP: 153/89 mm Hg
- Principal Findings:
  - The primary outcome, unattended office SBP for quadpill vs. monotherapy at week 12, was 121/71 mm Hg vs. 127/79 mm Hg; mean difference in SBP was -6.9 mm Hg ($p < 0.01$).
- Secondary outcomes for quadpill vs. monotherapy:
- Mean difference in diastolic BP (DBP) at week 12: -5.8 mm Hg ($p < 0.0001$)
- BP control <140/90 mm Hg at week 12: 76% vs. 58% ($p < 0.0001$)
- Mean difference in SBP/DBP at week 52: -7.8/-6 mm Hg ($p < 0.0001$)
- Dizziness at week 12: 31% vs. 25.4% ($p = 0.08$)
- Serum creatinine at week 12: 0.9 vs. 0.85 mg/dl ($p = 0.006$)

QUARTET

- Interpretation:
- The results of this trial indicate that a strategy of quarter dosing of four antihypertensive medications into one polypill (“quadpill”) is superior to full-dose monotherapy with irbesartan for improving BP control among patients with a diagnosis of HTN on no medications or therapy with only one medication at baseline. Due to COVID-19, the total enrollment target could not be achieved. Side effects were more or less similar, with a small (but likely clinically insignificant) increase in serum creatinine and potassium with the quadpill approach. The trial was not powered for clinical endpoints. It adds to the body of favorable literature on a polypill approach for the management of chronic cardiovascular conditions. This may be particularly useful among elderly patients where polypharmacy and HTN undertreatment both tend to be common.



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STOPDAPT-2 ACS trial #ESCCongress

One-month dual antiplatelet therapy (DAPT) followed by clopidogrel monotherapy in acute coronary syndrome (ACS)

Conclusion

One-month DAPT and subsequent clopidogrel monotherapy failed to achieve noninferiority for net clinical benefit compared with standard 12-month DAPT after ACS. There was a trend toward an increase in CV events despite a reduction in major bleeding events.

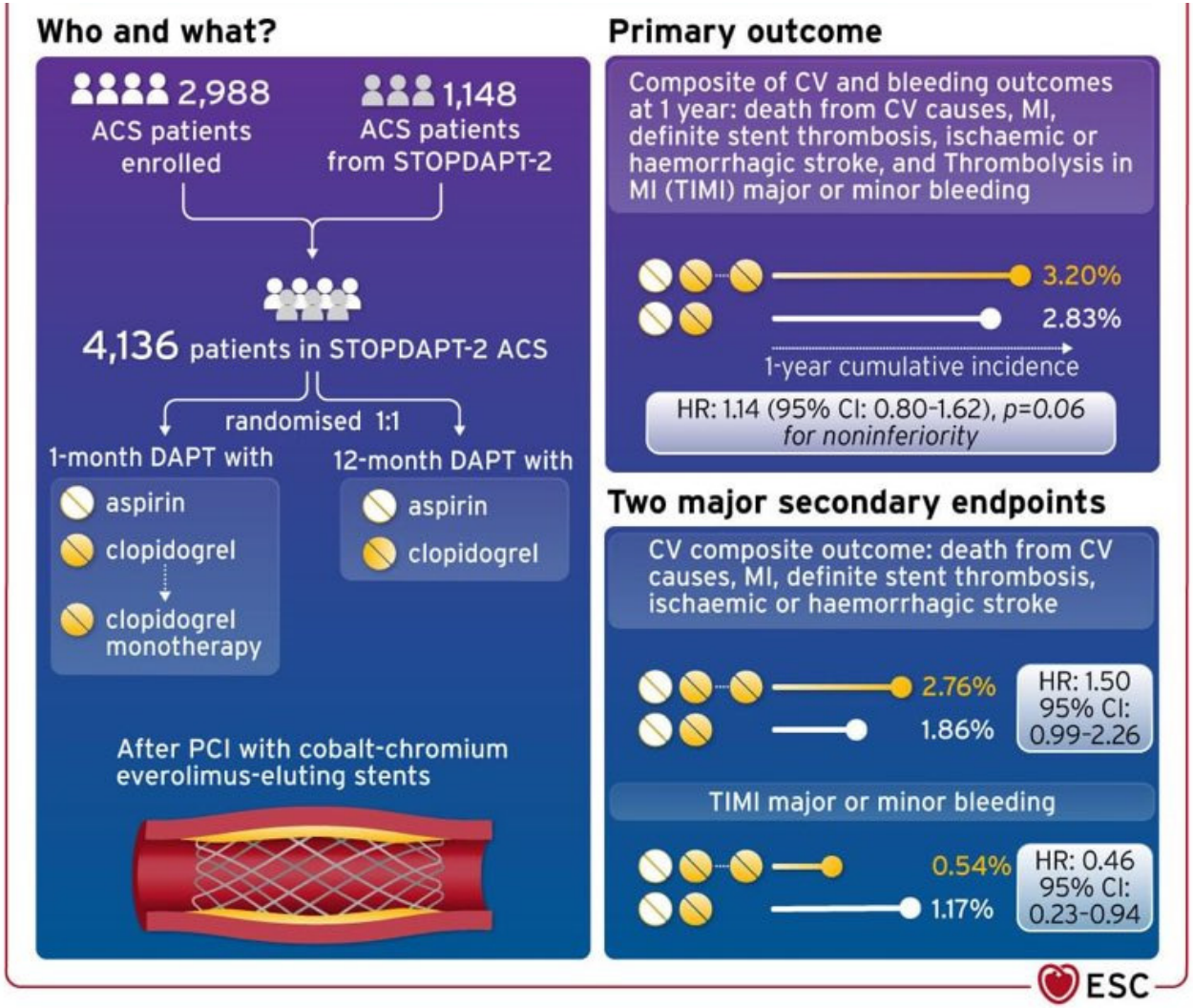
Background

The STOPDAPT-2 trial previously demonstrated that among patients undergoing percutaneous coronary intervention (PCI), one month of DAPT followed by clopidogrel monotherapy resulted in a significantly lower rate of a composite of CV and bleeding events, compared with 12 months of DAPT with aspirin and clopidogrel. In that trial, 62% of patients had stable coronary artery disease and 38% had ACS.

Study objectives

To generate sufficient statistical power to compare the effect of the two treatments in ACS patients alone, the STOPDAPT-2 ACS trial enrolled 2,988 ACS patients and pooled the results with the 1,148 ACS patients in STOPDAPT-2 - for a total of 4,136 patients. Both trials used the same protocol.

STOPDAPT-2 ACS



STOPDAPT-2 ACS

- Inclusion criteria:
  - PCI for ACS with cobalt-chromium everolimus-eluting stent (CoCr-EES)
- Exclusion criteria:
  - Oral anticoagulants
  - Prior intracranial hemorrhage
  - Contraindication to aspirin or clopidogrel
  - Serious in-hospital complication (reinfarction, stroke, bleeding)
- Other salient features/characteristics:
  - ST-segment elevation MI (STEMI): 56%, NSTEMI: 20%, unstable angina: 24%
  - Killip class IV: 3.2%, intra-aortic balloon pump: 4%
  - Prior myocardial infarction (MI): 6%, prior PCI: 11%
  - Target lesions: 1.3
- Principal Findings:
  - The primary outcome, cardiovascular death, MI, stroke, stent thrombosis, TIMI major or minor bleeding, for 1-month vs. 12-month DAPT, was 3.2% vs. 2.8% (hazard ratio [HR] 1.14, 95% confidence interval [CI] 0.80-1.62, p for noninferiority = 0.06).
- Secondary outcomes for 1-month vs. 12-month DAPT:
  - Cardiovascular death/MI/stroke/stent thrombosis: 2.8% vs. 1.9% (HR 1.50, 95% CI 0.99-2.26)
  - TIMI major/minor bleeding: 0.5% vs. 1.2% (HR 0.46, 95% CI 0.23-0.94)
  - All-cause mortality: 1.4% vs. 0.9%
  - MI: 1.6% vs. 0.9% (HR 1.91, 95% CI 1.06-3.44, $p < 0.05$)
  - Definite stent thrombosis: 0.45% vs. 0.2%
  - Bleeding academic research consortium (BARC) 3/5 bleeding: 0.5% vs. 1.3% (HR 0.41, 95% CI 0.20-0.83)

- Interpretation:
- The results of this trial indicate that 1-month DAPT followed by clopidogrel monotherapy for 11 months did not meet criteria for noninferiority compared with standard-duration 12-month DAPT for the composite ischemic/bleeding endpoint among patients undergoing ACS PCI with a CoCr DES. In fact, the composite ischemic endpoint trended towards harm in the 1-month DAPT arm, with a significant nearly 2-fold increase in the risk of MI. Both major and minor bleeding events were lower with 1-month DAPT. One caveat is that these were all East Asian patients, and clopidogrel resistance was not assessed.
- These are interesting findings, and add to the body of literature on the optimal duration and type of antiplatelet agent post-PCI. Contrary to the current trial, short-duration followed by clopidogrel monotherapy was noninferior to standard 12-month duration DAPT in the SMART-CHOICE (3 months) and STOPDAPT-2 (1 month) trials. These two trials included <50% of patients with ACS, and an even smaller number with STEMI. The current trial included all-comers with STEMI (including shock); these patients comprised 56% of all patients enrolled. Similar to the current trial, SMART-DATE included ACS patients undergoing PCI and found a higher risk of MI with 6 months of DAPT (clopidogrel being the P2Y12 inhibitor of choice in ~80%) compared with 12 months of DAPT. Other trials such as TWILIGHT and TICO demonstrated noninferiority for ticagrelor monotherapy after 3 months compared with standard 12-month duration, with a lower risk of bleeding. TWILIGHT trial did not include STEMI patients.

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