Beta-Blockers in Stabilized MI Patients Without Heart Failure

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Disclosure

- Nothing Declared

Beta-Blocker Use in AMI Patients

2023 ESC Guideline for ACS

Beta-blockers		
Beta-blockers are recommended in ACS patients with LVEF ≤40% regardless of HF symptoms.[801,870–872]	I	A
Routine beta-blockers for all ACS patients regardless of LVEF should be considered.[798,873–878]	IIa	B

801: CARPRICORN Trial (Carvedilol) → AMI with LV Dysfunction

870: CIBIS-II Trial (Bisoprolol) → HF with LV Dysfunction
871: US Carvedilol → HF with LV Dysfunction
872: MERIT-HF Trial (Metoprolol) → HF with LV Dysfunction

798: Beta-blocker in AMI → Meta analysis
873: COMMIT Trial → IV Metoprolol in AMI
874: Beta-blocker in AMI → Meta analysis
875: Oral Beta-blocker in AMI with PCI→ Meta analysis
876: Effects of Beta-blocker Dose → Registry Data
877: BB Use in CAD (ACS + CCS) → Registry Data
878: BB Use in ASCVD → REACH Registry

Beta-Blocker in AMI without LV Dysfunction

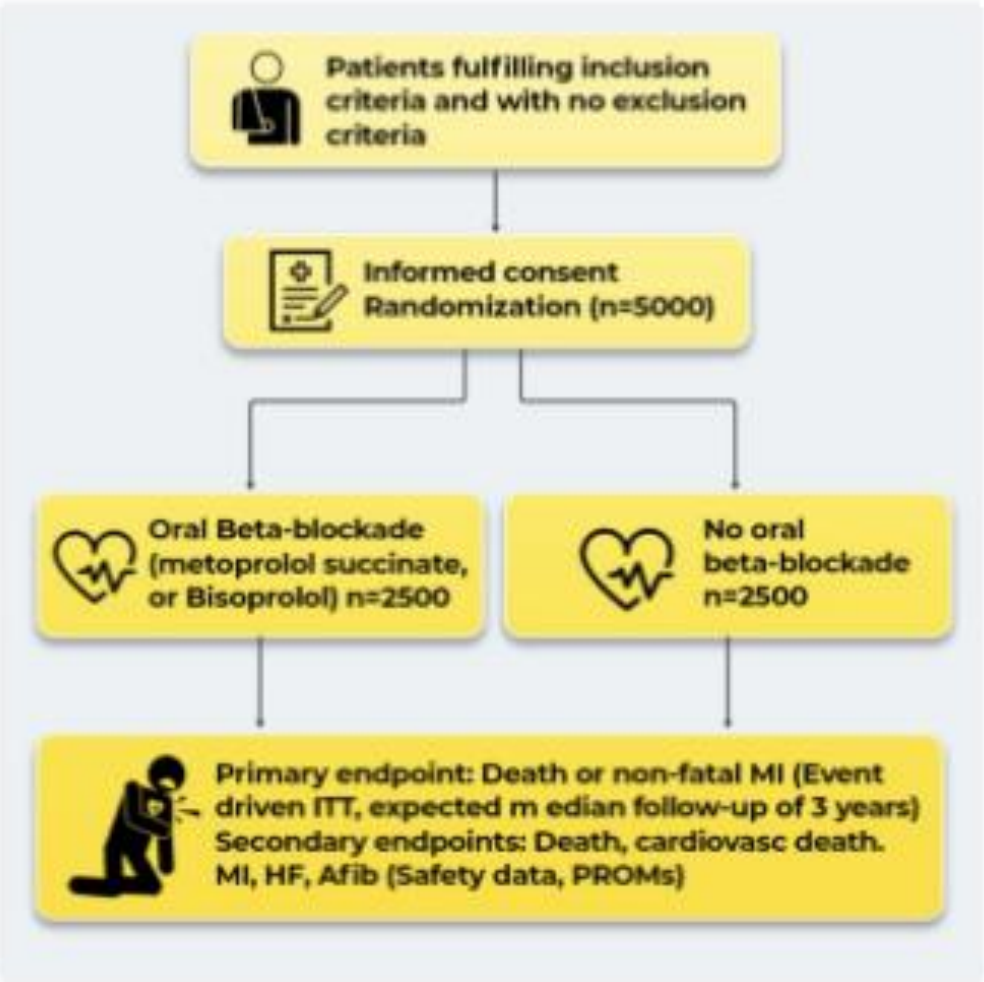
REDUCE-AMI Trial (September 2017 to the end of enrollment in May 2023)

Trial overview

Registry-based, prospective, randomized, open-label, parallel group clinical trial conducted in Sweden (38 centers), Estonia (1 center) and New Zealand (6 centers)

Power: 25% relative risk reduction (0.9% absolute risk reduction with 80% power at a two-sided 5% significance level, 379 events were required, which was planned to be obtained with about 5000 patients

The primary endpoint was the composite of death of any cause or new MI



Beta-Blocker in AMI without LV Dysfunction

REDUCE-AMI Trial (September 2017 to the end of enrollment in May 2023)

Inclusion Criteria

1. Men or women age ≥18 at the time of signing the informed consent
2. Day 1-7 after MI, either ST elevation MI or non-ST-elevation MI, according to the fourth universal definition of MI type 1.
3. Coronary angiography performed during hospitalization.
4. Obstructive coronary artery disease documented by coronary angiography, i.e. stenosis ≥ 50 %, FFR ≤ 0.80 or iFR ≤ 0.89 in any segment at any time point before randomization.
5. Echocardiography performed after the MI showing a normal ejection fraction defined as EF≥50%.

Exclusion Criteria

1. Any condition that may influence the patient's ability to comply with study protocol.
2. Contraindications for beta-blockade (e.g. bradyarrhythmia)
3. Indication for beta-blockade other than as secondary prevention according to the treating physician (e.g. tachyarrhythmia)

Beta-Blocker in AMI without LV Dysfunction

REDUCE-AMI Trial (September 2017 to the end of enrollment in May 2023)

Characteristics	Beta-Blockers (N = 2508)	No Beta-Blockers (N = 2512)
Age — yr	65 (57–73)	65 (57–73)
Female — n (%)	563 (22.4)	568 (22.6)
Hypertension	1155/2507 (46.1)	1163/2509 (46.4)
Diabetes mellitus	346/2506 (13.8)	354/2509 (14.1)
Pulmonary rales	29/2445 (1.2)	42/2462 (1.7)
Median heart rate	74 (65–85)	73 (64–84)
Median systolic blood pressure (IQR)	150 (135–170)	151 (136–170)
ST-segment elevation myocardial infarction	877/2507 (35.0)	892/2512 (35.5)
PCI	2387/2491 (95.8)	2376/2496 (95.2)
CABG	92/2491 (3.7)	103/2496 (4.1)
Beta-blocker	2399/2505 (95.8)	247/2512 (9.8)

Beta-Blocker in AMI without LV Dysfunction

REDUCE-AMI Trial (September 2017 to the end of enrollment in May 2023)

1. Initial Sample Size
   → Assumed primary endpoint 7.2% / year in no BB group

   → 16.7% Reduction in BB group

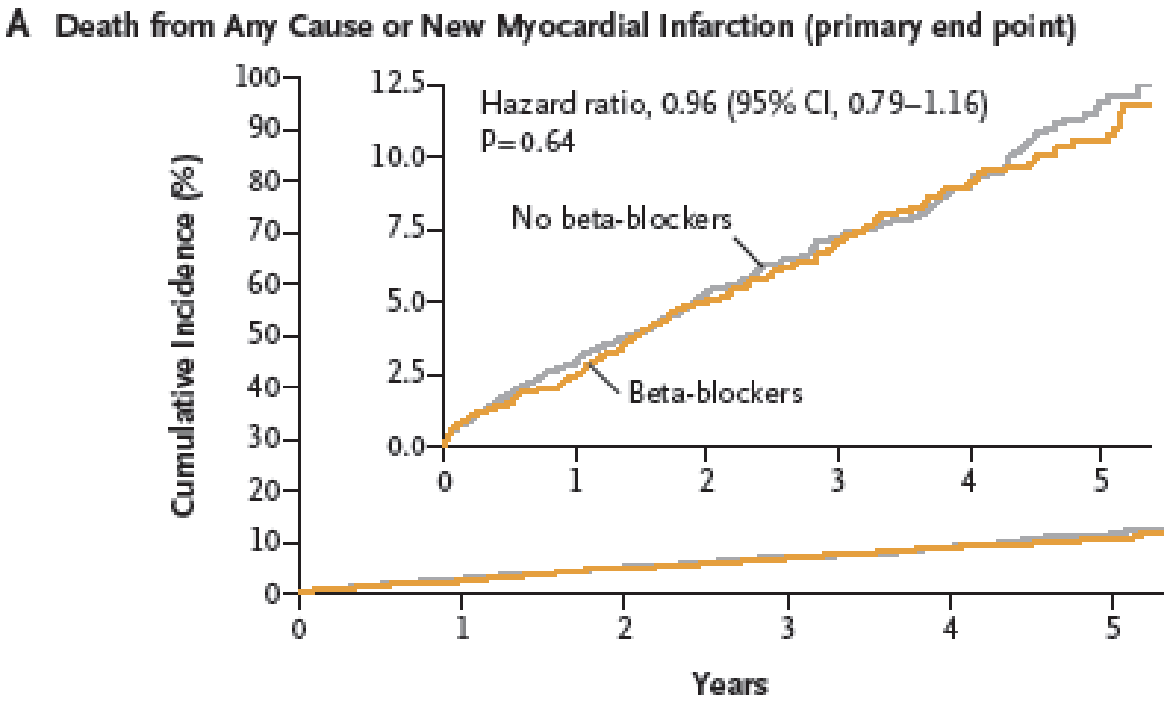
   (Absolute 1.2% lower risk per year)

2. During the trial,
   Actual event rate of 3% / year

   → 25% Reduction in BB (absolute 0.9%)

   → 5000 patients will provide 80% of power at a two-sided significance level of 5%

The median follow-up was 3.5 years



Beta-Blocker in AMI without LV Dysfunction

REDUCE-AMI Trial (September 2017 to the end of enrollment in May 2023)

	Beta-Blockers (N = 2508)	No Beta-Blockers (N = 2512)	Hazard Ratio (95% CI)
Hospitalization for atrial fibrillation	27 (1.1)	34 (1.4)	0.79 (0.48 to 1.31)
Hospitalization for heart failure	20 (0.8)	22 (0.9)	0.91 (0.50 to 1.66)
Hospitalization for bradycardia, second- or third-degree AV block, hypotension, syncope, or implantation of a pacemaker	86 (3.4)	80 (3.2)	1.08 (0.79 to 1.46)
Hospitalization for asthma or COPD	15 (0.6)	16 (0.6)	0.94 (0.46 to 1.89)
Hospitalization for stroke	36 (1.4)	46 (1.8)	6.80 (−7.11 to 20.72) (restricted mean survival time)

Beta-Blocker in AMI without LV Dysfunction

REDUCE-AMI Trial (September 2017 to the end of enrollment in May 2023)

ACC.24 REDUCE-AMI

Beta-Blockers after Myocardial Infarction and Preserved Ejection Fraction

T. Yndigegn et al. NEJM

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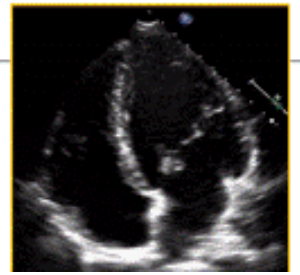
Population	Intervention	Control	Outcome	Time
5020 post-MI patients **LVEF EF ≥ 50%** CAG with obstructive CAD Median age: 65 yr Women: 22.5 % STEMI (35%)	Oral beta-blockade (n=2508) **Metoprolol 100 mg (62.2%) or Bisoprolol 5 mg (37.8%) daily** PCI = 95.8 %	No oral beta-blockade (n=2512) PCI = 95.2 %	Death from any cause or New myocardial infarction 7.9% vs 8.3% HR 0.96 95% CI 0.76-1.16 p=0.64	3.5 years

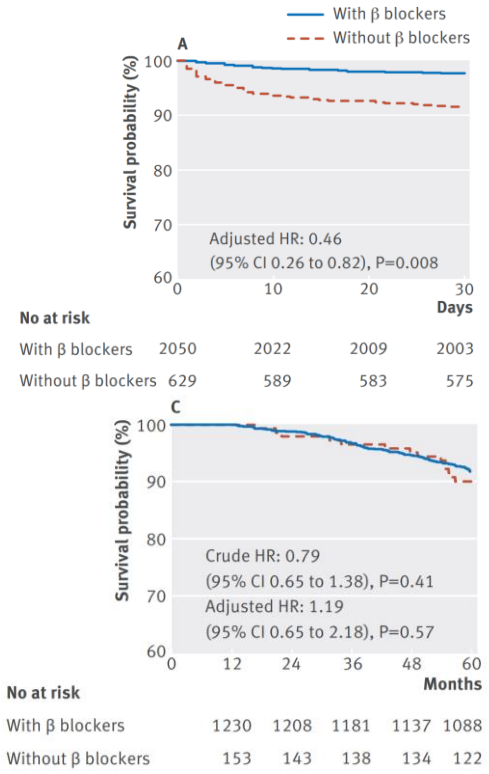


- ✓ **In patients with acute MI and preserved left ventricular EF (≥50%), long-term treatment with beta-blockers did not reduce the risk of the primary endpoint of death or MI.**
- ✓ **Secondary and safety outcomes were similar between groups.**

Upcoming Issues for Beta-Blocker in AMI

Beta-Blocker Discontinuation

Puymirat E et al.



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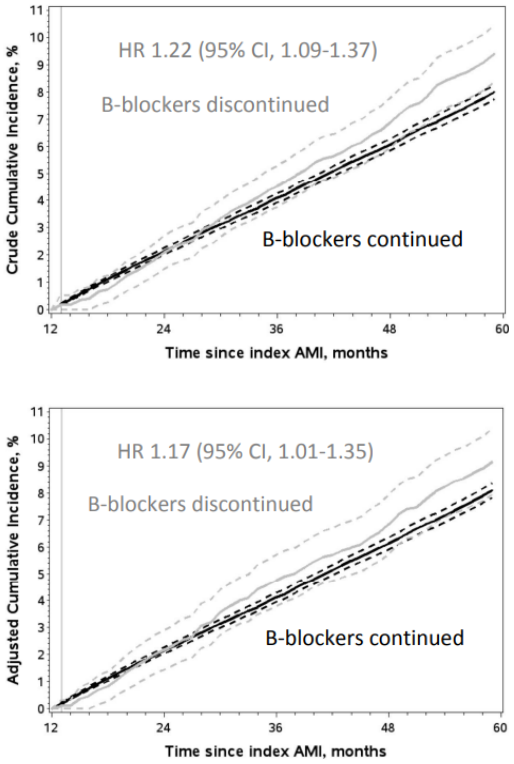
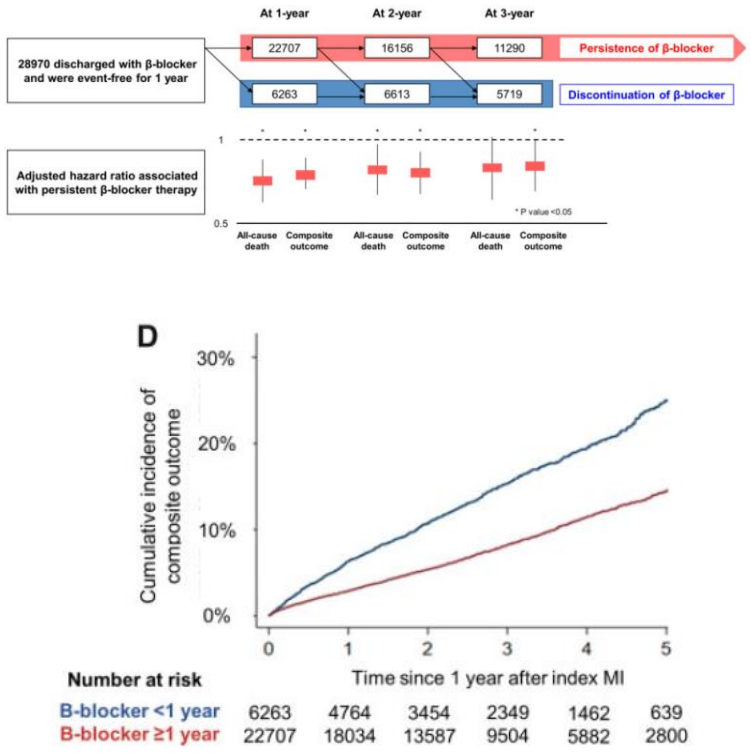
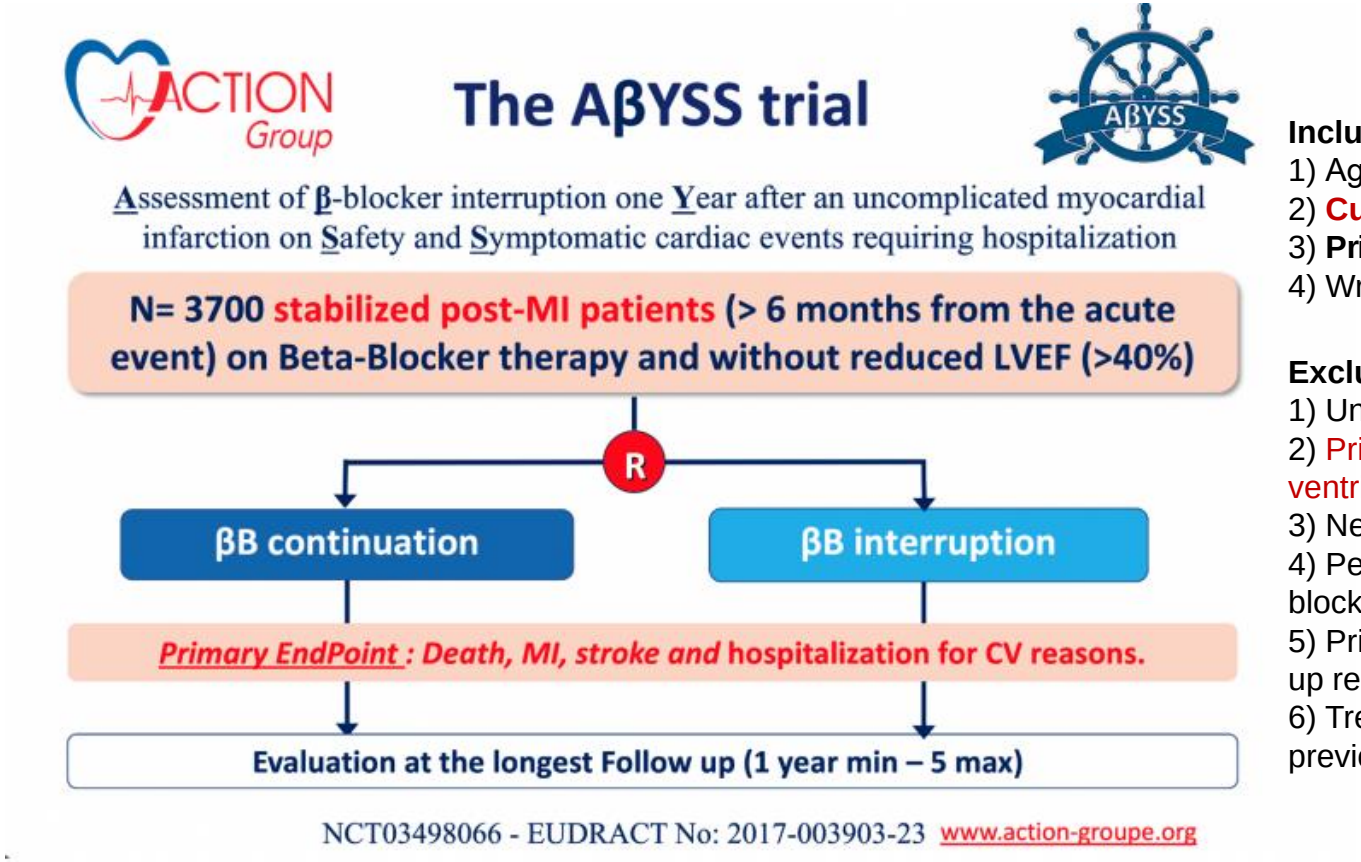


Kim J et al.



Beta-blocker Interruption during Follow-Up

The ABYSS Trial



Inclusion criteria

1) Age ≥ 18 years.
2) **Current treatment with beta-blocker, whatever the drug or the dose used**
3) **Prior documented acute myocardial infarction 6 months or more before**
4) Written informed consent was provided.

Exclusion criteria

1) Uncontrolled arterial hypertension according to the investigator's decision.
2) Prior episode of heart failure in the past two years of follow-up and/or low left ventricular ejection fraction <40% requiring the use of beta-blocker.
3) New ACS (in the past 6 months).
4) Persistent angina or ischemia (>10% viable myocardium) requiring the use of beta-blocker
5) Prior episode of ventricular or supraventricular arrhythmia in the past year of follow-up requiring the use of the beta-blocker
6) Treatment with other investigational agents or devices within the previous 30 days, or previous enrolment in this trial.

Beta-blocker Interruption during Follow-Up

The ABYSS Trial

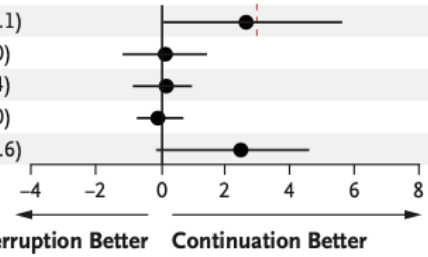
	Beta-Blocker Interruption (n = 1846)	Beta-Blocker Continuation (n = 1852)
Mean age, yr	63.5±11.2	63.5±10.9
Male sex	530 (82.9	1531 (82.7)
Hypertension	786 (42.6)	805 (43.5)
Diabetes mellitus	372 (20.2)	375 (20.2)
Dyslipidemia	948 (51.4)	994 (53.7)
Median time from index MI, yr	2.9 (1.2–6.2)	2.8 (1.1–6.6)
STEMI	1168 (63.3)	1162 (62.7)
NSTEMI	678 (36.7)	690 (37.3)
Multivessel disease	955 (51.7)	979 (52.9)

	Beta-Blocker Interruption (n = 1846)	Beta-Blocker Continuation (n = 1852)
Revascularization for MI	1755/1846 (95.1)	1757/1852 (94.9)
Completeness	601/1753 (91.2)	1619/1755 (92.1)
PCI	709/1755 (97.4)	1693/1757 (96.4)
LVEF, %		
Median (IQR)	60 (52–60)	60 (52–60)
40-50%	430 (23.3)	435 (23.5)
Residual angina	21 (1.1)	30 (1.6)

Beta-blocker Interruption during Follow-Up

The ABYSS Trial

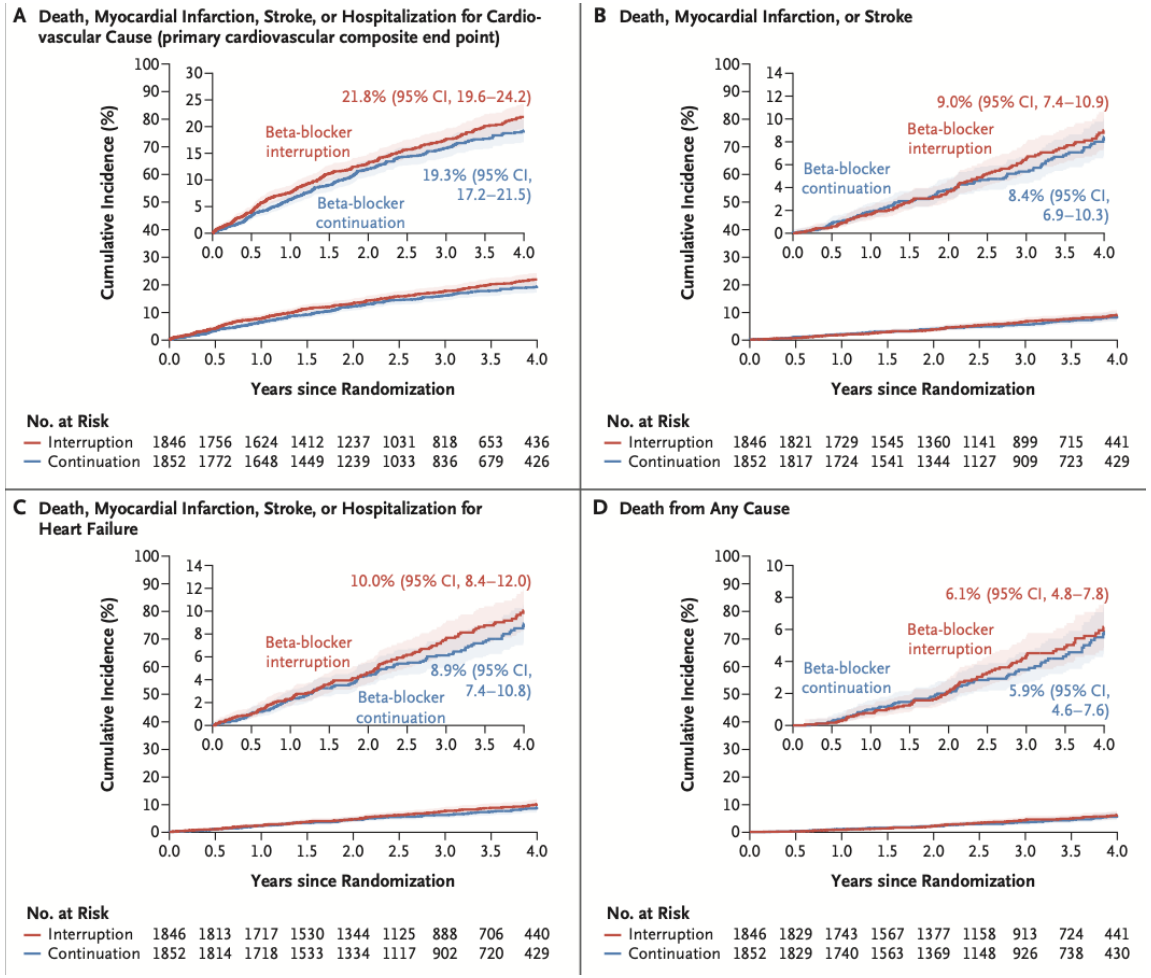
End Point	Beta-Blocker Interruption (N=1846)	Beta-Blocker Continuation (N=1852)	Risk Difference (95% CI) (percentage points)
	no. of patients with event (%)		Prespecified margin of noninferiority
Primary end point	432 (23.8)	384 (21.1)	2.8 (<0.1 to 5.5)
Death	76 (4.1)	74 (4.0)	0.1 (−1.2 to 1.4)
Myocardial infarction	46 (2.5)	44 (2.4)	0.1 (−0.9 to 1.1)
Stroke	18 (1.0)	19 (1.0)	−0.1 (−0.7 to 0.6)
Hospitalization for cardiovascular reason	349 (18.9)	307 (16.6)	2.3 (−0.1 to 4.8)



Pre-specified margin of noninferiority → 3.0%

Beta-blocker interruption was not non-inferior to beta-blocker continuation for the primary endpoint (P = 0.44 for noninferiority).

Rather, the risk of the primary endpoint was higher in the beta-blocker interruption group (HR 1.16, 95% CI 1.01-1.33).



Beta-blocker Interruption during Follow-Up

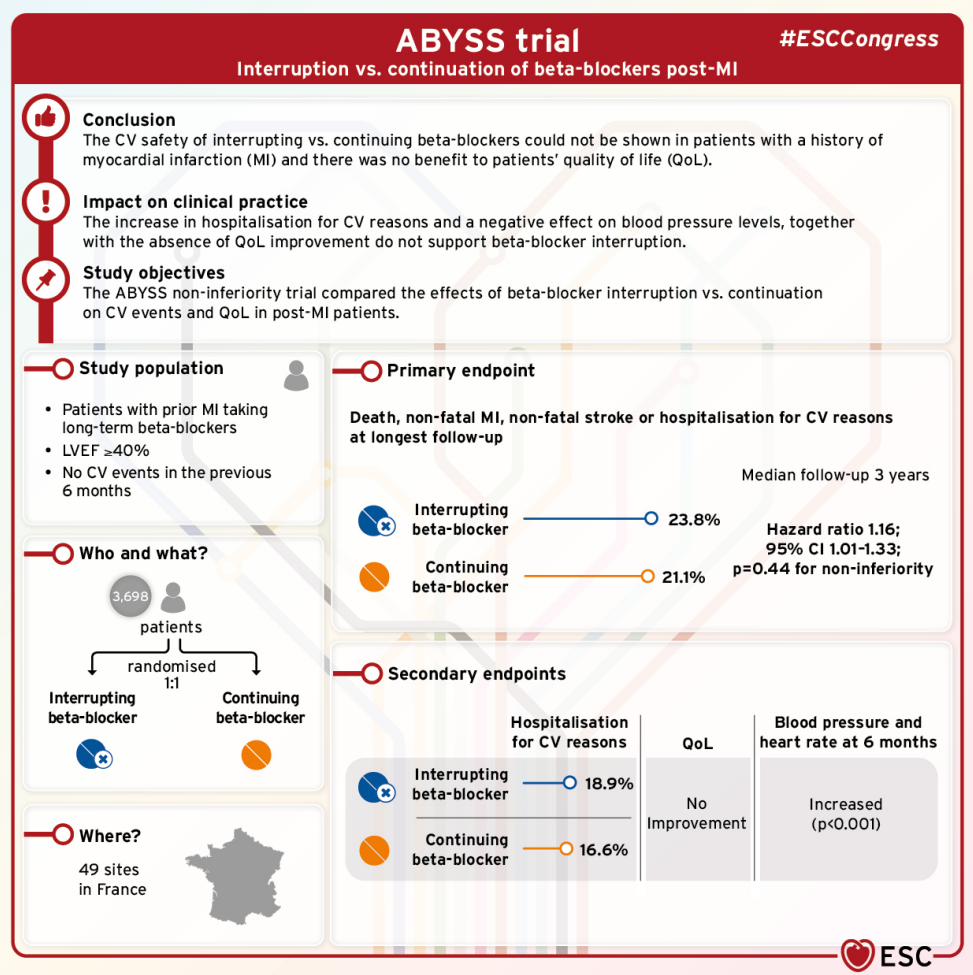
The ABYSS Trial

Hospitalization for cardiovascular reason — no. (%)	349 (18.9)	307 (16.6)
Coronary-related reason	263 (14.2)	221 (11.9)
Angina or ischemia	67 (3.6)	55 (3.0)
Angiography	146 (7.9)	117 (6.3)
Percutaneous coronary intervention	90 (4.9)	84 (4.5)
Coronary-artery bypass grafting	4 (0.2)	4 (0.2)
Heart failure	34 (1.8)	23 (1.2)
Tachycardia		
Supraventricular	28 (1.5)	28 (1.5)
Ventricular	6 (0.3)	7 (0.4)
Syncope or dizziness	28 (1.5)	25 (1.3)
Invasive procedure aside from pacemaker implantation	31 (1.7)	24 (1.3)
Pacemaker or equivalent implantation	11 (0.6)	11 (0.6)
Conduction disorder	2 (0.1)	2 (0.1)
High blood pressure	5 (0.3)	3 (0.2)
Peripheral artery disease or limb ischemia	34 (1.8)	23 (1.2)
Aortic dissection or aneurysm	4 (0.2)	8 (0.4)
Valvular reason	4 (0.2)	4 (0.2)
Bleeding event	18 (1.0)	15 (0.8)
Other cardiovascular event	18 (1.0)	11 (0.6)

Beta-blocker interruption was associated with a numerical increase in the risk of recurrent angina and other coronary-related conditions leading to hospitalization and coronary procedures.

Beta-blocker Interruption during Follow-Up

The ABYSS Trial



- **The non-inferiority of this strategy was not shown with respect to the risk of death, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for cardiovascular reasons (the composite primary outcome).**
- **Interruption of beta-blocker therapy did not result in an improvement in patient-reported quality of life.**
- **Considering the REDUCE-AMI trial, the main difference is an increase in hospitalization for cardiovascular reasons with beta-blocker interruption, an endpoint that was not evaluated in REDUCE-AMI.**

REDUCE-AMI and ABYSS trials

These recent trials evaluated different aspects of beta-blocker treatment after AMI.

	REDUCE-AMI	ABYSS
Study population	AMI patients with Preserved EF (≧50%)	OMI patients with Preserved EF (≧40%)
Study design	Superiority design	Non-inferiority design
Comparator	Beta-blocker	Beta-blocker interruption
Control	No beta-blocker	Beta-blocker continuation
Randomization	Within 1-7 days after AMI	6 months after AMI (Median 2.9 yeas)
Primary endpoint	Death or non-fatal MI	Death, non-fatal MI, non-fatal stroke, or hospitalization for CV reasons
Other endpoints	Safety endpoints	EQ-5D
FU duration	Median 3.5 years	Median 3 years
Outcome collection	Registry-based	Central adjudication
Conclusion	No definite benefit of beta-blocker	No benefit for beta-blocker interruption

Beta-blocker Interruption during Follow-Up

Beta-Blocker Discontinuation Trial (SMART-DECISION)

2540 Patients without HF or left ventricular systolic dysfunction and who have been continuing β-blocker therapy for at least 1 year after AMI

↓

Randomization (1:1)
Discontinuation of β-blocker therapy
stratified by participating center, clinical presentation ST-segment elevation MI or non-ST-segment elevation MI), type of β-blocker (carvedilol, bisoprolol, nebivolol, or others)

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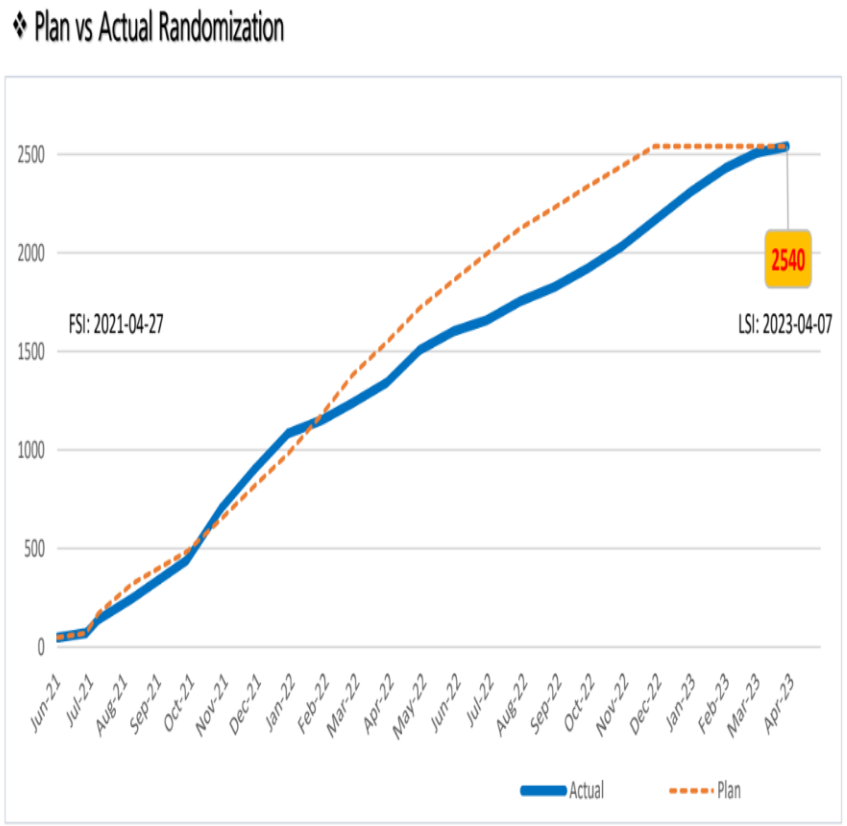
β-blocker discontinuation group N = 1270	**β-blocker maintenance group** N = 1270

Primary Endpoint	**Major adverse cardiac events (a composite of all-cause death, MI, hospitalization for HF)**



Beta-blocker Interruption during Follow-Up

Beta-Blocker Discontinuation Trial (SMART-DECISION)

Beta-blocker Therapy in Stabilized Patients After Acute Myocardial Infarction (SMART-DECISION, NCT04769362)

Primary Hypothesis:
Discontinuation of β-blocker after stabilization of AMI would be noninferior to continuation of β-blocker.

Primary Endpoint:
A composite of all-cause death, MI, or hospitalization for HF

Key Secondary Endpoints:
PROMIS-29, cost, atrial fibrillation

Study Population/Design:
2540 stabilized AMI patients without HF or LV systolic dysfunction 1:1 randomized to either β-blocker discontinuation or maintenance

Trial Status:
First patient in → April 2021
Last patient in→ April 2023
Expected end of follow-up → October 2025

Clinical Implications:
The SMART-DECISION trial will provide valuable insights into the optimal duration of β-blocker therapy in stabilized AMI patients without HF or LV systolic dysfunction.

Conclusion

- In patients presenting with an acute MI (STEMI or NSTEMI) with a preserved EF treated with modern pharmacotherapy and reperfusion strategies,
- Beta blockers do not lead to a reduced incidence of all-cause death or MI.
- There was a cross-over rate in both arms with 14% of the no-beta-blocker group taking beta-blockers at one year and 18% of the beta-blocker group not taking beta-blockers at one year which may influence the neutral outcome.
- Additionally, there is insufficient evidence regarding the discontinuation of beta-blockers in patients who have been taking them stably for a long period following myocardial infarction.
- The results of the SMART-DECISION trial will add important scientific evidence about the optimal duration of β-blocker therapy after stabilization of AMI without HF or LV systolic dysfunction.

Thank you for Your Attention!

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