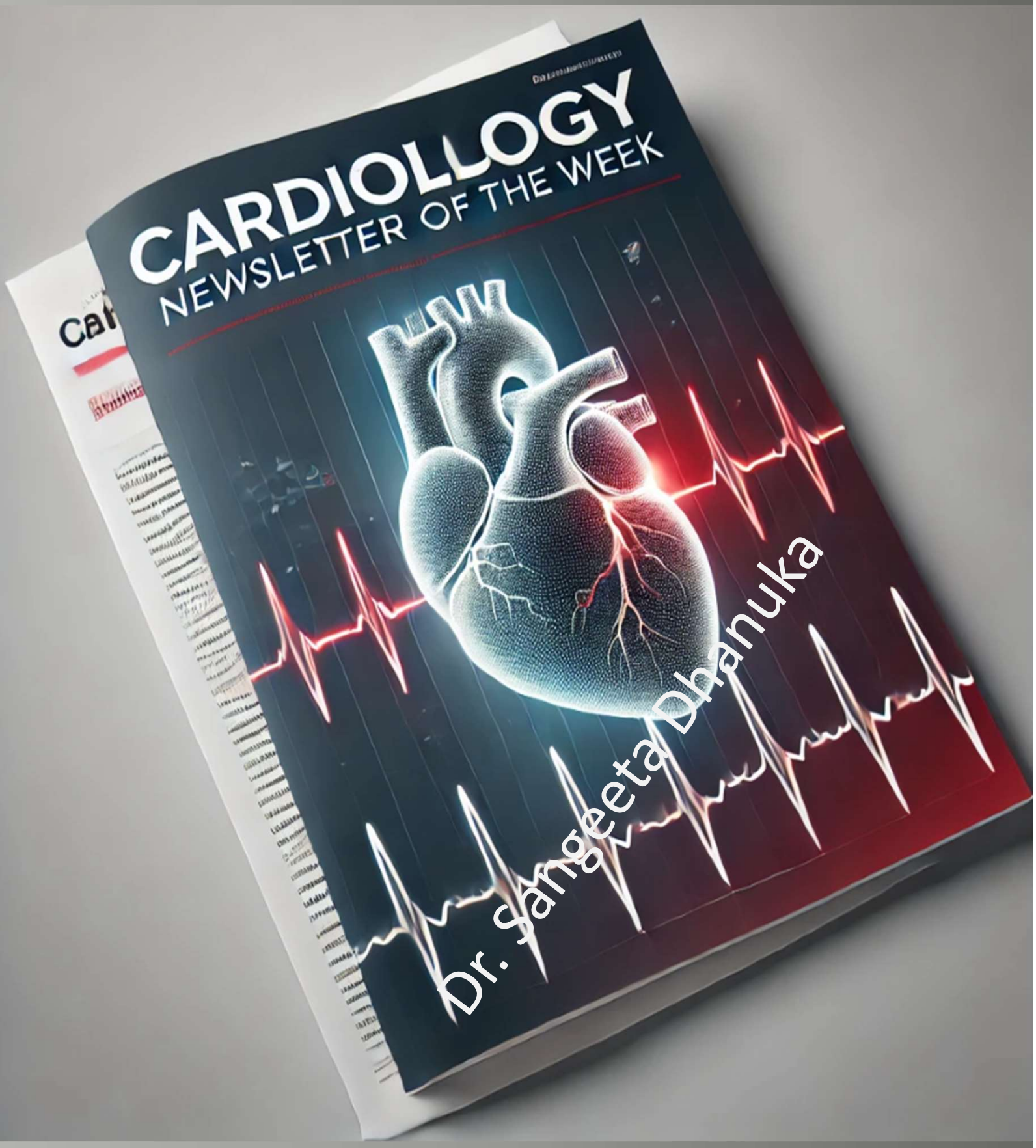

CARDIOLLOGY
NEWSLETTER OF THE WEEK
Dr. Sangeeta Dhanuka

Finerenone With and Without Concomitant SGLT2 Inhibitor in Heart Failure

DOI: 10.1161/CIRCULATIONAHA.124.072055

Why was the study conducted?

Data examining the clinical effects of finerenone and SGLT2 inhibitors in heart failure are lacking

What was studied?

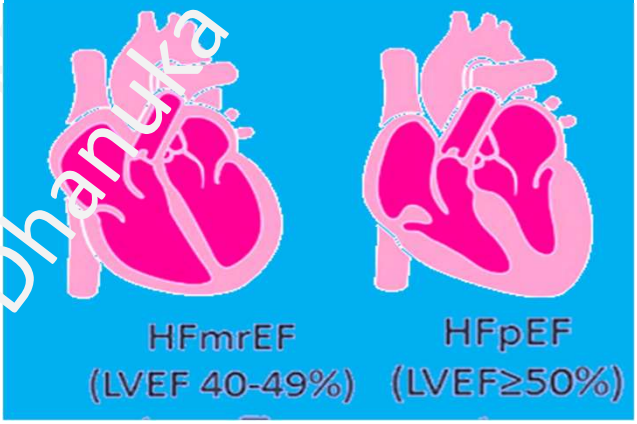
Treatment benefits of finerenone were observed irrespective of concomitant use of an SGLT2i in patients with HF

Study design and patient allocation

Randomized, double-blind; 37 countries
1:1 to finerenone vs placebo
Target dosing: 20 mg if baseline eGFR ≤60 mL·min·1.73 m² or 40 mg once daily if baseline eGFR >60 mL·min·1.73 m²

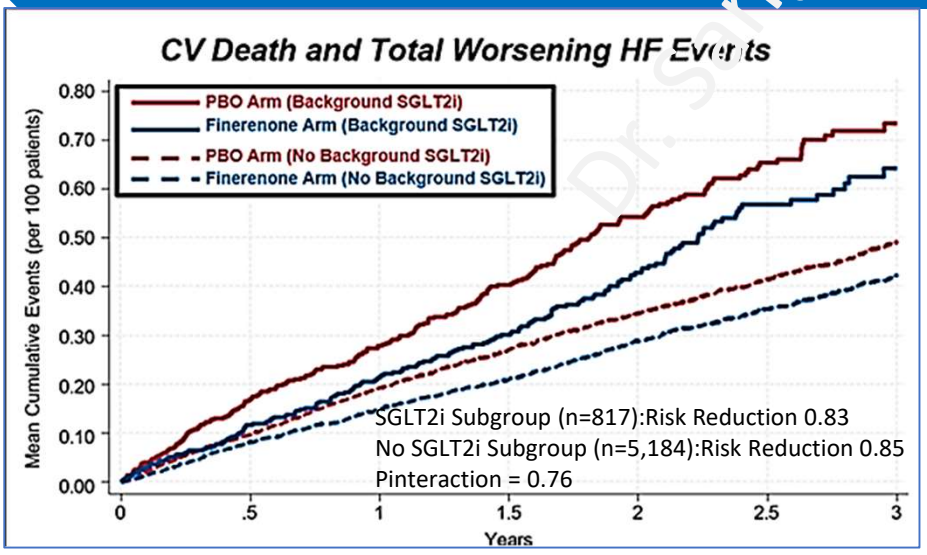
Patients

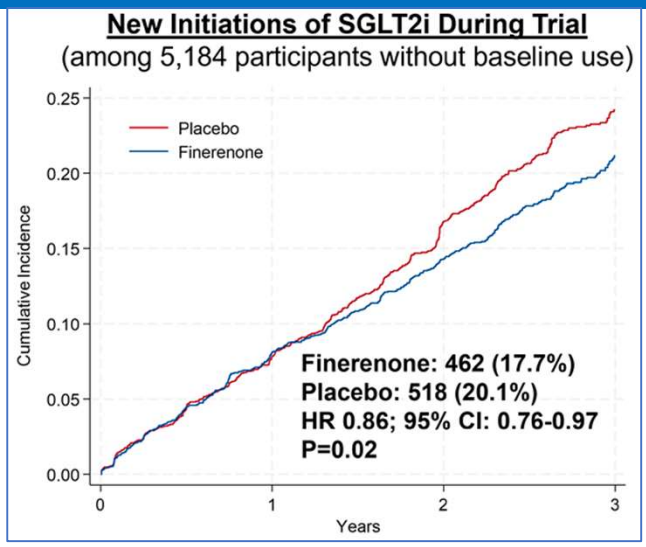
- 6001 patients; aged ≥40 yrs
- Symptomatic HFmrEF or HFpEF; 69% in NYHA class II
- LVEF ≥40%
- High natriuretic peptides
- Structural heart disease +
- Diuretic use for last 30 days
- Mean age 72.0±9.6 years



Dr. Sangeeta Dhanuka

Results





Clinical implication

Finerenone reduces cardiovascular death and total HF events irrespective of baseline or subsequent SGLT2i use and supports the complementary roles of finerenone and SGLT2i in the management of patients with HFmrEF or HFpEF

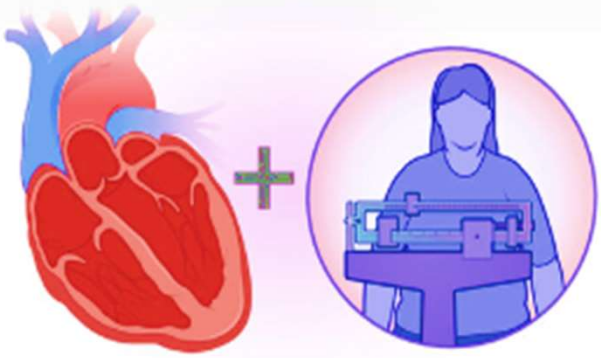
Tirzepatide leads to a lower risk of a composite of death from cardiovascular causes or worsening heart failure and improves health status in patients with heart failure with preserved ejection fraction and obesity

In this trial, researchers examined cardiovascular outcomes of treatment with tirzepatide in patients with heart failure with preserved ejection fraction and obesity.

Most patients with **heart failure and a preserved ejection fraction** also have obesity, and visceral adiposity contributes to the evolution and progression of heart failure.

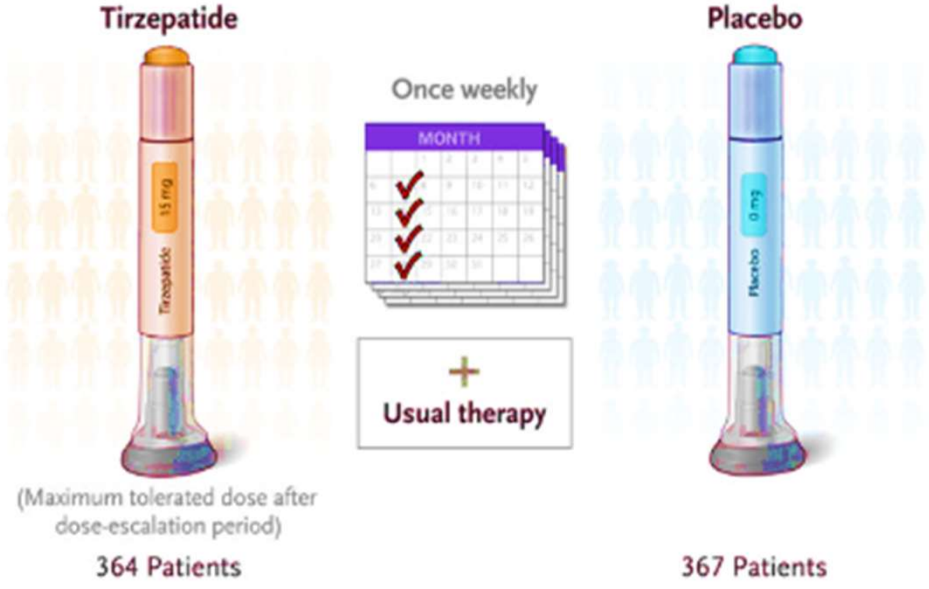
WHY WAS THE TRIAL DONE?

Tirzepatide, a long-acting agonist of glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 receptors, causes considerable weight loss, but data on its effects on cardiovascular outcomes are lacking.



HOW WAS THE TRIAL CONDUCTED?

Adults with chronic heart failure, an ejection fraction of at least 50%, and a body-mass index (BMI) of at least 30 were assigned to receive subcutaneous tirzepatide (up to 15 mg per week) or placebo, in addition to usual therapy. The two primary end points were a composite of adjudicated death from cardiovascular causes or a worsening heart-failure event resulting in hospitalization, intravenous therapy in an urgent care setting, or intensification of oral diuretic therapy, and the change in the Kansas City Cardiomyopathy Questionnaire clinical summary score (KCCQ-CSS; range, 0 to 100, with higher scores indicating better quality of life) at 52 weeks.



PATIENTS

WHO

- 731 adults
- Age: at least 40 years (mean, 65 years)
- Women: 54%; Men: 46%

CLINICAL STATUS

- Chronic heart failure (NYHA class II to IV)
- Left ventricular ejection fraction: at least 50%
- BMI: at least 30
- 6-minute walk distance: 100 to 425 m
- KCCQ-CSS: 80 or lower
- One of the following: an elevated NT-proBNP level, left atrial enlargement, or elevated filling pressures
- Heart-failure decompensation within 12 months before baseline or an eGFR of less than 70 ml per minute per 1.73 m^2 at baseline

TRIAL DESIGN

- DOUBLE-BLIND
- RANDOMIZED
- PLACEBO-CONTROLLED
- LOCATION: 129 CENTERS IN 9 COUNTRIES

DOI: 10.1056/NEJMoa2410027

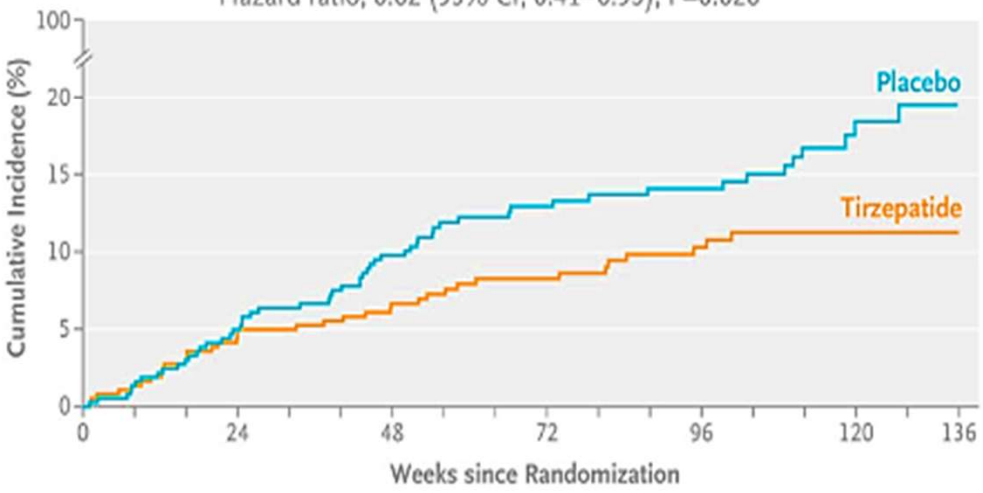
Tirzepatide leads to a lower risk of a composite of death from cardiovascular causes or worsening heart failure and improves health status in patients with heart failure with preserved ejection fraction and obesity

RESULTS

During a median follow-up of 2 years, death from cardiovascular causes or a worsening heart-failure event occurred significantly less often in the tirzepatide group than in the placebo group. At 52 weeks, improvement in the KCCQ-CSS was significantly greater in the tirzepatide group.

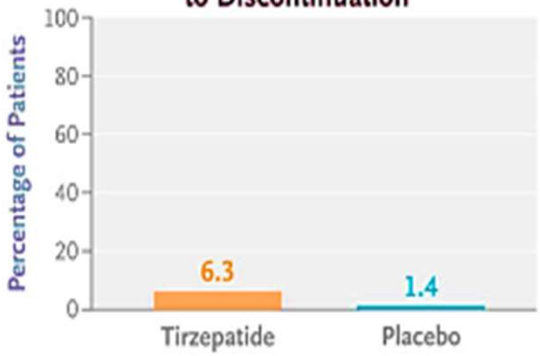
Death from Cardiovascular Causes or a Worsening Heart-Failure Event

Hazard ratio, 0.62 (95% CI, 0.41–0.95); P=0.026

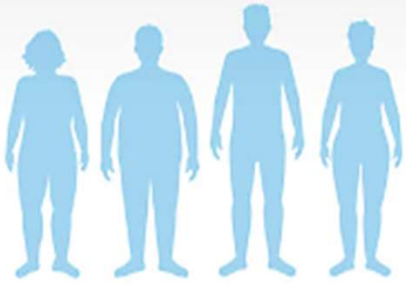


Nonfatal adverse events leading to discontinuation of the regimen — mainly gastrointestinal events — were more common in the tirzepatide group.

Nonfatal Adverse Events Leading to Discontinuation



BODY-MASS INDEX



The risk of heart failure (especially in patients with preserved ejection fraction) increases as BMI increases. The mean BMI of patients in this trial was 38.3 at baseline.

LIMITATIONS AND REMAINING QUESTIONS

- This study included only patients with a BMI of 30 or greater; however, many patients with heart failure with preserved ejection fraction have a BMI of less than 30 but an abnormal waist-to-height ratio, which is a more reliable indicator of excess visceral adiposity. More study is needed in these patients.

CONCLUSIONS

Treatment with tirzepatide led to a lower risk of a composite of death from cardiovascular causes or worsening heart failure than placebo and improved health status in patients with heart failure with preserved ejection fraction and obesity.

DOI: 10.1056/NEJMoa2410027

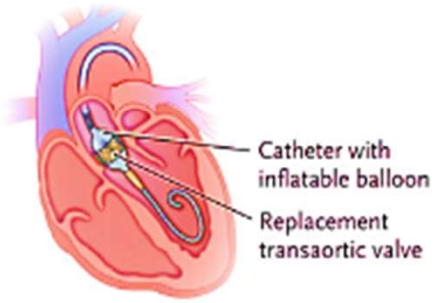
In patients undergoing TAVI and receiving oral anticoagulants for a concomitant disease, continuing anticoagulation during TAVI was not noninferior to interrupting anticoagulation with respect to adverse outcomes

In this trial, researchers assessed the efficacy and safety of continuing oral anticoagulation, as compared with interrupting it, during transcatheter aortic-valve implantation (TAVI).

Approximately one third of patients undergoing TAVI have an indication for oral anticoagulation owing to concomitant diseases, mainly atrial fibrillation.

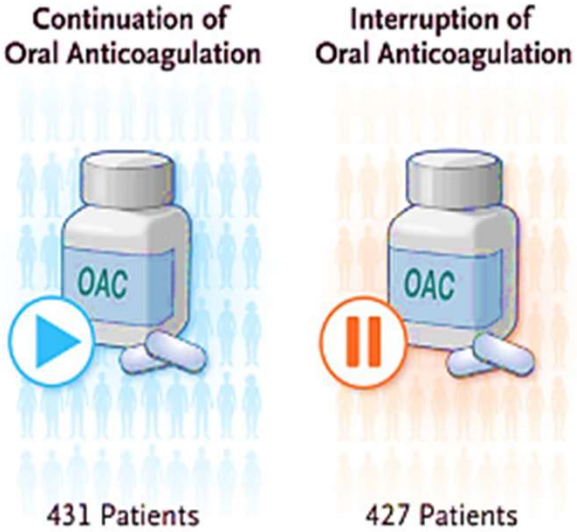
WHY WAS THE TRIAL DONE?

International guidelines advise interrupting oral anticoagulation in patients undergoing interventions with a high risk of bleeding, but the appropriate strategy for managing anticoagulation in patients undergoing TAVI has not been well studied.

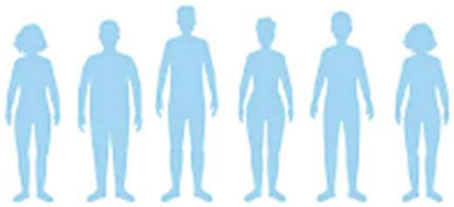


HOW WAS THE TRIAL CONDUCTED?

Patients who were planning to undergo TAVI and who were receiving long-term oral anticoagulants were assigned either to continue oral anticoagulation or to interrupt it before the procedure. The primary outcome was a composite of death from cardiovascular causes, stroke from any cause, myocardial infarction, major vascular complications, or major bleeding within 30 days after TAVI.



PATIENTS



WHO

858 patients

Mean age, 81 years

Men: 66%; Women: 34%

CLINICAL STATUS

Plan to undergo transfemoral or transsubclavian TAVI

Long-term receipt of oral anticoagulation (owing to atrial fibrillation in 95%)

No mechanical heart valve prosthesis, intracardiac thrombus, venous thromboembolism within 3 months before TAVI, or TIA or stroke in patients with atrial fibrillation within 6 months before TAVI

TRIAL DESIGN

- OPEN-LABEL
- RANDOMIZED
- NONINFERIORITY
- LOCATION: 22 EUROPEAN SITES

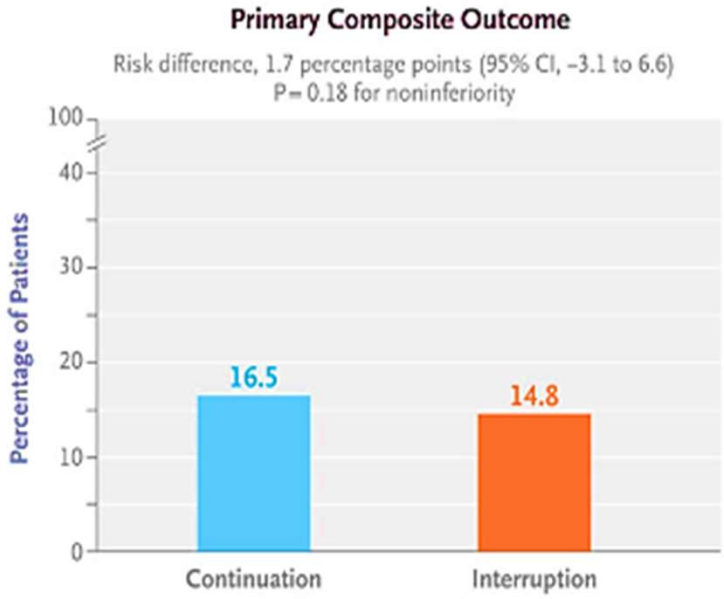
DOI: 10.1056/NEJMoa2407794

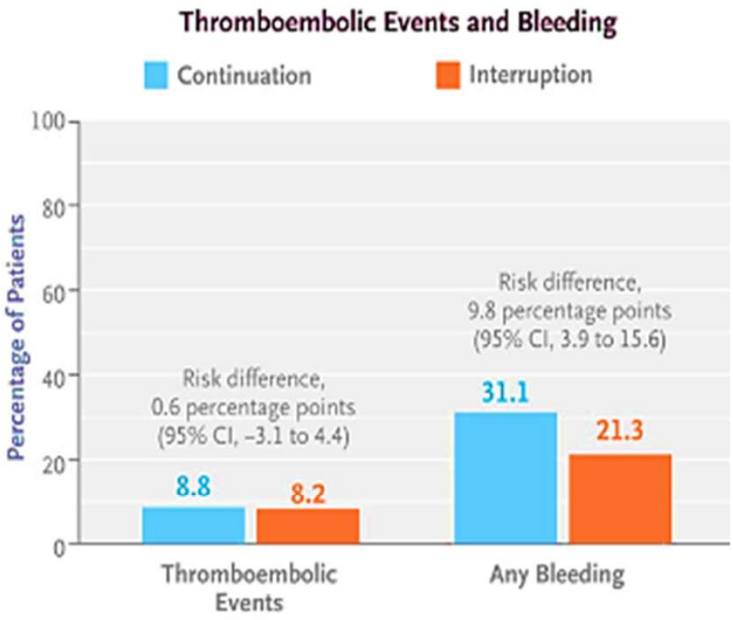
In patients undergoing TAVI and receiving oral anticoagulants for a concomitant disease, continuing anticoagulation during TAVI was not noninferior to interrupting anticoagulation with respect to adverse outcomes

RESULTS

Continuation of oral anticoagulation was not found to be noninferior to interruption of anticoagulation with respect to the primary composite outcome.

There were no apparent differences in thromboembolic events (a secondary outcome) between the groups, whereas bleeding complications (another secondary outcome) were more common with continued than with interrupted anticoagulation.





LIMITATIONS AND REMAINING QUESTIONS

- The trial was open-label and therefore potentially subject to reporting and ascertainment biases.
- Not all patients underwent a neurologic examination or neuroimaging; the trial relied on clinical events reported by health care professionals.
- The trial was powered to show noninferiority with respect to the primary composite outcome alone. No clinical inferences should be drawn about the separate components of the primary outcome or about the secondary outcomes.

CONCLUSIONS

In patients undergoing TAVI and receiving oral anticoagulants for a concomitant disease, continuing anticoagulation during TAVI was not noninferior to interrupting anticoagulation with respect to a composite of death from cardiovascular causes, stroke from any cause, myocardial infarction, major vascular complications, or major bleeding within 30 days.

DOI: 10.1056/NEJMoa2407794