Fluvastatin and bisoprolol for the reduction of perioperative cardiac mortality and morbidity in high-risk patients undergoing non-cardiac surgery.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON21523

Source
Nationaal Trial Register

Brief title
DECREASE IV

Health condition

non-cardiac surgery; beta-blocker; statin; perioperative cardiac complications

Sponsors and support

Primary sponsor: Department of Anesthesiology, Erasmus MC Rotterdam, the Netherlands
Source(s) of monetary or material Support: fund = initiator = sponsor

Intervention

Outcome measures

Primary outcome

The primary efficacy objective is to determine the impact of perioperative administration of

bisoprolol, fluvastatin and their combination on the incidence of 30-day cardiovascular events, i.e. the composite of cardiac death, and non fatal MI, in moderate and high risk patients undergoing noncardiac surgery.

Secondary outcome

Secondary efficacy objectives of the DECREASE-IV study are
1. To determine the impact of perioperative administration of bisoprolol and/or fluvastatin on:
a.The incidence of total mortality, cardiovascular death, and nonfatal myocardial infarction during 1 year follow-up;
b. The length of hospital stay, and length of ICU/CCU stay;
c. The 30-day incidence of clinically significant cardiac arrhythmias and heartfailure and the need for coronary revascularisation procedures.
2. The DECREASE-IV trial has five safety objectives, namely:
a. To determine the impact of the different treatments on: (1) the 30-day congestive heart failure;
b. The 30-day incidence of clinically significant bradycardia;
c. The 30-day incidence of clinically significant hypotension;
d. The 30-day incidence of clinically significant liver dysfunction;
e. The occurence of myopathy.

Study description

Background summary

This is an open-label randomised controlled clinical trial of bisoprolol (n=1500), fluvastatin (n=1500), both (n=1500), or neither (n=1500) in patients undergoing noncardiac surgery. The aim of the study is to determine the impact of perioperative administration of bisoprolol, fluvastatin, and their combination on the incidence of 30-day cardiovascular events (defined as cardiovascular death, nonfatal myocardial infarction, cardiac arrest) in moderate and high risk patients undergoing noncardiac surgery.
Patients planned for elective surgery will be screened at the preoperative screening visit according to a newly developed cardiovascular risk-evaluation scheme. A computerised version of this scheme will be applied, which enables an automated check on all in- and exclusion criteria. According to the outcome of the risk-evaluation scheme, patients with a chance of more than 2% on perioperative cardiovascular death will undergo further cardiac evaluation. Participants will then be randomised according to an open-label, factorial design between (1) beta-blocker therapy (bisoprolol), (2) statin (fluvastatin), (3) combination of beta-blockers and statins (bisoporolol and fluvastatin) and (4) neither beta-blockers nor statins (control group). Study medication is started within 0-30 days prior to surgery and will be continued until 30 days after surgery. The starting dose of bisoprolol is 2.5 mg orally per day, irrespective of the resting heart rate (note that patients with a resting heart rate <50 bpm are excluded). During hospital admission, the resting heart rate will be evaluated on a daily basis, and the bisoprolol regimen might be modified with +/- 2.5 mg daily (up to a maximum

dose of 12.5 mg daily), in order to obtain the target resting heart rate of 50-70 bpm. If the resting heart rate is consistently below 50 bpm the bisoprolol dose will be held and the subsequent dosages will be halved (i.e. bisoprolol 1.25, 2.5, 3.75, 5.0, 6.25 mg). To assess perioperative cardiac events, an ECG will be made at days 1, 3 and 7 postoperatively. On these same days bloodsamples will be taken to assess heart- and liverenzymes. Patients will be evaluated at follow-up visits 30 days and 1 year after surgery. Time-to-the first ocurence of one of the components of the primary efficacy endpoint will be presented using the Kaplan-Meier estimator. The rate of occurence of the primary endpoint between the randomised groups will be compared using the log-rank statistics. Employing the Cox proportional hazards model, the hazard ratio and its associated 95% confidence interval, will derive treatment effect. Univariable and multivariable analysis will be c onducted.

Study objective

The general objective of the DECREASE-IV trial is to assess the clinical efficacy of beta-blocker therapy, statin therapy and combination therapy with beta-blockers and statins in patients undergoing major noncardiac surgery.

Intervention

A computerised version of this scheme will be applied, which enables an automated check on all in- and exclusion criteria. According to the outcome of the risk-evaluation scheme, patients with a chance of more than 2% on perioperative cardiovascular death will undergo further cardiac evaluation, including ECG and/or stress myocardial testing. Patients with extensive myocardial ischemia are exluded. Participants will then be randomised according to an open-label, factorial design between (1) beta-blocker therapy (bisoprolol), (2) statin (fluvastatin), (3) combination of beta-blockers and statins (bisoporolol and fluvastatin) and (4) neither beta-blockers nor statins (control group). Study medication is started within 0-30 days prior to surgery and will be continued until 30 days after surgery.

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Eligibility criteria

Inclusion criteria

Patients who are (1) aged 40 years or older, (2) scheduled for elective noncardiac surgery and (3) have an estimated risk for cardiovascular death of more than 1%, will be enrolled in the DECREASE-IV trial.

Exclusion criteria

Exclusion criteria for this trial are: the use of beta-blockers; a contraindication for beta-blocker use; the use of statins prior to randomisation; a contraindication for statin use; unstable coronary heart disease, evidence of 3-vessel disease or left main disease; elevated cholesterol according to the national cholesterol consensus; emergency surgery; unability or unwillingness to provide written informed consent; and previous participation in this same trial.

Study design

Design

Study type:	Interventional
Intervention model:	Factorial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-07-2004
Enrollment:	6000

Type:	Anticipated

Ethics review

Positive opinion Date:	12-02-2007
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL885
NTR-old	NTR900
Other	: N/A
ISRCTN	ISRCTN47637497

Study results

Summary results
Fluvastatin and bisoprolol for the reduction of perioperative cardiac mortality and morbidity in high-risk patients undergoing non-cardiac surgery: rationale and design of the DECREASE-IV study.
Am Heart J. 2004 Dec;148(6):1047-52.