Effect of Bivalirudin on Aortic Valve Intervention Outcomes.

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The hypothesis is that bivalirudin will lower bleeding rates as compared to UFH and will improve the overall clinical outcomes of transfemoral TAVR.

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON27624

Bron
Nationaal Trial Register

Verkorte titel
BRAVO 2/3

Aandoening

- patients undergoing TAVR via transfemoral access
- aortic valve replacement
- aortaklepvervanging

Ondersteuning

Primaire sponsor: The Medicines Company
8 Sylvan Way
Parsippany, NJ07054
Overige ondersteuning: The Medicines Company
8 Sylvan Way
Parsippany, NJ07054

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The primary end point will be major bleeding defined as Bleeding Academic Research Consortium (BARC) type ≥3 at 48 hours or hospital discharge whichever occurs first. BARC type 3 bleeding includes bleeds that are evident clinically, or by laboratory or imaging results, which result in treatment with blood transfusion, surgical intervention, or administration of intravenous vasoactive drugs; overt bleeds with a hemoglobin drop of at least 3g/dL; bleeding that causes cardiac tamponade; and intracranial or intraocular bleeds that compromise vision. BARC type 4, CABG related bleeding, is not applicable to this study. BARC type 5, fatal bleeding, describes bleeds that directly result in death with no other cause. The co-primary endpoint will be net adverse cardiac events (NACE) at 30 days that is the composite of major adverse cardiovascular events (MACE) + major bleeding (BARC type ≥3). The composite of major adverse cardiovascular events (MACE) is defined as all-cause mortality, myocardial infarction, and stroke. All events will be adjudicated using source documents by an independent clinical events committee blinded to the antithrombotic agents.
Each component of the co-primary endpoint will be tested in a hierarchical manner with a superiority test for bleeding followed by a non-inferiority and then superiority test for NACE.

Toelichting onderzoek

Achtergrond van het onderzoek

The objective of this study is to assess the safety and efficacy of using bivalirudin instead of unfractionated heparin (UFH) in transcatheter aortic valve replacements (TAVR). The hypothesis is that bivalirudin will reduce bleeding rates compared to UFH, and will improve the overall clinical outcomes of TAVR patients.

All patients undergoing transfemoral TAVR at the participating centers will be eligible. All sites will initiate enrolment with 2 feasibility roll-in bivalirudin treated patients and thereafter patients will be randomly assigned to either standard dosing of bivalirudin or UFH as control. The 2 roll-in cases per site will constitute the feasibility cohort that will be followed and analyzed separately. Patients will undergo TAVR according to current standard of care practices at the treating centers. Use of antiplatelet agents pre, during, and post procedure, and possibly oral anticoagulants post procedure, will be according to the sites’ standard practice.

Doel van het onderzoek

The hypothesis is that bivalirudin will lower bleeding rates as compared to UFH and will improve the overall clinical outcomes of transfemoral TAVR.

Onderzoeksopzet

For patients receiving bivalirudin, the initial bolus will be administered immediately following successful arterial access, and the infusion continued until successful valve treatment is achieved. The patient’s overall participation in this study is approximately 60 days from screening.

Onderzoeksproduct en/of interventie

Transcatheter aortic valve replacements.

Bivalirudin will be administered as a bolus and infusion. It is recommended that the bolus (0.75 mg/kg) be directly administered through the valve delivery sheath immediately following its successful delivery via percutaneous femoral access.

For patients receiving bivalirudin, the initial bolus will be administered immediately following successful arterial access, and the infusion continued until successful valve treatment is achieved.

The control group will receive UFH. The dose of UFH should adhere to the standard institutional practice.

Contactpersonen

Publiek

Innere Margarethenstrasse 5
Ilknur Lechthaler
Basel 4051
Germany
+41 79 829 56 97

Wetenschappelijk

Innere Margarethenstrasse 5
Ilknur Lechthaler
Basel 4051
Germany
+41 79 829 56 97

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. ≥ 18 years of age;

2. High risk (Euroscore ≥18, or considered inoperable) for surgical aortic valve replacement;

3. Undergoing TAVR via transfemoral arterial access;

4. Provide written informed consent before initiation of any study related procedures.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Contraindication to bivalirudin or UFH;

2. Refusal to receive blood transfusion;

3. Mechanical valve (any location) or mitral bioprosthetic valve;

4. Extensive calcification of the common femoral artery, or minimal luminal diameter< 6.5 mm;

5. Use of elective surgical cut-down for transfemoral access;

6. Concurrent performance of percutaneous coronary intervention with TAVR;

7. International normalized ratio (INR) ≥ 2 on the day of TAVR procedure, or known history of bleeding diathesis;

8. History of hemorrhagic stroke, intracranial hemorrhage, intracerebral mass or aneurysm, or arteriovenous malformation;

9. Severe left ventricular dysfunction (left ventricular ejection fraction<15%);

10. Severe aortic regurgitation or mitral regurgitation (4+);

11. Hemodynamic instability (e.g. requiring inotropic or IABP support) within 2 hours of the procedure;

12. Serum Creatinine >4.0 mg/dL or dialysis dependent;

13. Administration of thrombolytics, glycoprotein IIb/IIIa inhibitors, or warfarin in the 3 days prior to the procedure;

14. Acute myocardial infarction, major surgery or any therapeutic cardiac procedure (other than balloon aortic valvuloplasty) within 30 days;

15. Percutaneous coronary intervention with drug-eluting stent(s) within 30 days;

16. Upper gastrointestinal or genitourinary bleed within 30 days;

17. Stroke or transient ischemic attack within 30 days;

18. Any surgery or biopsy within 2 weeks;

19. Administration of:

A. UFH within 30 minutes of the procedure;

B. Enoxaparin within 8 hours of the procedure;

C. Fondaparinux or other LMWHs within 24 hours of the procedure;

D. Dabigatran, rivaroxaban or other oral anti-Xa or antithrombin agent within 48 hours of the procedure;

E. Thrombolytics, GPI, or warfarin within 72 hours of the procedure.

20. Absolute contraindications or allergy that cannot be pre-medicated to iodinated contrast;

21. Contraindications or allergy to aspirin or clopidogrel;

22. Known or suspected pregnant women, or nursing mothers. Women of child-bearing potential will be asked if they are pregnant and will be tested for pregnancy;

23. Previous enrolment in this study;

24. Treatment with other investigational drugs or devices within the 30 days preceding enrollment or planned use of other investigational drugs or devices before the primary endpoint of this study has been reached.

Patients excluded for any of the above reasons may be re-screened for participation at any time if the exclusion characteristic has changed.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	31-08-2012
Aantal proefpersonen:	620
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	13-07-2012
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL3391
NTR-old	NTR3533
Ander register	Protocol No / EudraCT : TMC-BIV-11-02 / 2012‐000632‐26;
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A