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A randomised trial of unruptured brain arteriovenous malformations

Submission date
25/06/2006

Recruitment status
No longer recruiting

Registration date
11/09/2006

Overall study status
Completed

Last Edited
22/06/2020

Condition category
Circulatory System

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims:
Normally, blood from the heart moves from arteries to veins through a fine network of small blood vessels called a capillary bed. Here the nutrients from the blood are released into the brain tissue and the pressure of the blood flow reduces before it enters the veins on its journey back to the heart. Arteriovenous malformations or AVMs of the brain are abnormal tangles of arteries and veins which usually date back to birth but can also result from head injury. In an AVM the arteries and veins are connected directly without a capillary bed, exposing the thin walled veins to high pressures which puts them at risk for rupturing and bleeding into the brain. The aim of this study is to find better ways of caring for people who have been discovered to have an AVM in the brain that has never bled (unruptured). We want to find out whether it is better to leave the AVM alone and simply treat the symptoms (medical management), as it has never bled, or to eliminate the AVM using one of several available techniques, including surgery, catheter embolization or radiation treatment. Although both medical management and interventional treatment have been used before to treat AVMs, they never have been compared to see which works best. The risk of having an AVM of the brain is that it could rupture and bleed, possibly injuring the brain and causing symptoms of stroke. Removing or closing up an AVM by means of surgery, radiation treatment or interventional treatment can also injure brain tissue and cause a stroke. Currently whether do not know whether there is less chance of brain injury when an unbled AVM is eliminated or is left alone.

Who can participate?
Adults aged 18 and over with an unruptured AVM

What does the study involve?
Patients are randomly allocated into two groups: one group undergoes AVM elimination and the other group does not. Patients in the AVM elimination group receive interventional treatment, either surgery, radiation treatment, or some combination of treatments, chosen by their doctor. Patients in both groups are followed up for between 5 and 7.5 years depending on how long it takes to enroll the 800 patients needed for the study. Patients are seen every 6 months for the first two years, and at least every year after that until the end of the study.

What are the possible benefits and risks of participating?
The treatment risks are the same as they would be if you received any of the approved treatments outside of the study.

Where is the study run from?
100 different institutions in North America, Europe, Australia and South America

When is the study starting and how long is it expected to run for?
August 2006 to March 2014

Who is funding the study?
The National Institute of Health and the National Institute of Neurological Disorders and Stroke (USA)

Who is the main contact?
Prof. Jay Preston Mohr
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Study website
http://www.arubastudy.org

Contact information

Type(s)
Scientific

Contact name
Prof J. P. Mohr

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT00389181

Secondary identifying numbers
1 U01 NS051483-01A1

Study information

Scientific Title
A Randomised trial of Unruptured Brain Arteriovenous malformations

Acronym
ARUBA

Study objectives
The primary hypothesis of this trial is that medical management improves long-term outcomes of patients with unruptured Brain ArterioVenous Malformations (BAVM) compared to invasive therapy (with endovascular procedures, neurosurgery, or radiotherapy, alone or in combination).

Review of literature at http://www.ncbi.nlm.nih.gov/pubmed/16415679

Ethics approval required
Old ethics approval format

Ethics approval(s)
Columbia University Medical Center Institutional Review Board, 02/11/2005, IRB# AAAB6286

Study design
Randomised open parallel-group international multicenter trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Unruptured brain arteriovenous malformation

Interventions
All patients participating in the trial will receive the best medical management possible for the disorder being tested in the trial and for any general medical illnesses they are demonstrated to have. Those allocated to the invasive treatment arm will also receive endovascular attempts at occlusion of the nidus and feeding vessels, compiling or microsurgery for feeding artery aneurysms, microsurgery for BAVM itself, and
radiosurgery, these alone or in various combinations and timings.

Intervention Type
Mixed

Primary outcome measure
1. To determine whether medical management is superior to invasive therapy for preventing the composite outcome of death from any cause or stroke (hemorrhage or infarction confirmed by imaging) in the treatment of unruptured BAVMs
2. If medical management is not superior to invasive therapy, to determine whether medical management is not inferior to invasive therapy for preventing the composite outcome of death from any cause or stroke (hemorrhage or infarction confirmed by imaging) in the treatment of unruptured BAVMs

Secondary outcome measures
To determine whether treatment of unruptured BAVMs by medical management decreases the risk of death or clinical impairment (Rankin Score more than or equal to two) at five years post-randomization compared to invasive therapy.

Overall study start date
01/08/2006

Completion date
01/03/2014

Eligibility

Key inclusion criteria
1. Patient must have unruptured BAVM diagnosed by Magnetic Resonance Imaging (MRI), Magnetic Resonance Angiography (MRA) and/or angiogram
2. Patient must be 18 years of age or older
3. Patient must have signed informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
800

Total final enrolment
226

Key exclusion criteria
1. Patient has BAVM presenting with evidence of recent or prior hemorrhage
2. Patient has received prior BAVM therapy (endovascular, surgical, radiotherapy)
3. Patient has BAVM deemed untreatable by local team, or has concomitant vascular or brain disease that interferes with/or contraindicts any invasive therapy type (stenosis/occlusion of neck artery, prior brain surgery/radiation for other reasons)
4. Patient has baseline Rankin more than or equal to two
5. Patient has concomitant disease reducing life expectancy to less than ten years
6. Patient has thrombocytopenia (less than 100,000/nl)
7. Patient has coagulopathy (spontaneous or iatrogenic Inernational Normalised Ratio(INR) more than 1.5, Prothrombin Time (PT) more than 30)
8. Patient is pregnant, lactating, or plans to become pregnant
9. Patient has known allergy against iodine contrast agents
10. Patient has multiple-foci BAVMs
11. Patient has any form of arteriovenous or spinal fistulas
12. Patient has a diagnosed Vein of Galen type malformation
13. Patient has a diagnosed cavernous malformation
14. Patient has a diagnosed dural arteriovenous fistula
15. Patient has a diagnosed venous malformation
16. Patient has a diagnosed neurocutaneous syndrome such as cerebro-retinal angiomatosis (von Hippel-Lindau), encephalo-trigeminal syndrome (Sturge-Weber), or Wyburn-Mason syndrome
17. Patient has diagnosed BAVMs in context of moya-moya-type changes
18. Patient has diagnosed hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber)

Date of first enrolment
01/08/2006

Date of final enrolment
01/03/2014

Locations

Countries of recruitment
Australia

Brazil

Canada

Czech Republic

Finland

France

Germany

Italy

Lithuania

Netherlands

Portugal

Spain

Sweden

Switzerland

United Kingdom

United States of America

Study participating centre
Columbia University
New York
United States of America
10032

Sponsor information

Organisation
NIH - National Institute of Neurological Disorders and Stroke (USA)

Sponsor details
c/o Claudia S. Moy
Neuroscience Center, Room 2214
6001 Executive Blvd., MSC9520
Bethesda MD
United States of America
20892-9520

Sponsor type
Government

Website
http://www.nih.gov/

ROR
https://ror.org/01s5ya894

Funder(s)

Funder type
Government

Funder Name
National Institutes of Health

Alternative Name(s)
Institutos Nacionales de la Salud, US National Institutes of Health, NIH

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United States of America

Funder Name
National Institute of Neurological Disorders and Stroke: 1 U01 NS051483-01A1

Alternative Name(s)
National Institute of Neurological Disorders & Stroke, NIH/National Institute of Neurological Disorders and Stroke, NIH National Institute of Neurological Disorders and Stroke, Instituto Nacional de Trastornos Neurológicos y Accidentes Cerebrovasculares, The National Institute of Neurological Disorders and Stroke, National Institute of Neurological Disorders and Blindness, National Institute of Neurological and Communicative Disorders and Stroke, NINDS, NINDB, NINCDS

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United States of America

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	01/01/2010		Yes	No
Results article	results	15/02/2014		Yes	No
Results article	5-year follow-up results	01/07/2020	22/06/2020	Yes	No