A randomised trial of unruptured brain arteriovenous malformations

Submission date 25/06/2006	Recruitment status No longer recruiting	Prospectively registered[X] Protocol	
Registration date 11/09/2006	Overall study status Completed	[_] Statistical analysis plan [X] Results	
Last Edited 22/06/2020	Condition category Circulatory System	[] 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 jpm10@mail.cumc.columbia.edu

Study website http://www.arubastudy.org

Contact information

Type(s) Scientific

Contact name Prof J. P. Mohr

Contact details

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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

IPD sharing plan summary Not provided at time of registration

Study outputs

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