

Aspirin and/or low-molecular weight heparin for women with unexplained recurrent miscarriages and/or intra-uterine foetal death

Submission date 20/12/2005	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
Registration date 20/12/2005	Overall study status Completed	<input type="checkbox"/> Protocol
Last Edited 09/04/2014	Condition category Pregnancy and Childbirth	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

Study information

Scientific Title

Acronym

ALIFE - Anticoagulants for Living Foetuses

Study objectives

There is reasonable evidence to suggest that some cases of recurrent pregnancy loss (RPL), including recurrent miscarriage (RM) and/or later intra-uterine foetal death, are associated with placental thrombosis and infarction. Approximately 5% of women experience two or more consecutive pregnancy losses. Recurrent miscarriage, defined as two or more spontaneous first trimester pregnancy losses, may affect as many as 1% to 2% of women of reproductive age. The prognosis in subsequent pregnancies of women with RM or late foetal death is a rate of live birth of approximately 65% and 50%, respectively, without any therapeutic intervention. Some haematologic conditions, such as the antiphospholipid syndrome (APLS) are associated with RPL. Compared to controls, women with familial thrombophilia, especially those with combined defects or antithrombin deficiency, have an increased risk of RM (odds ratio: 1.35) and late foetal death (odds ratio: 3.6).

Heparin and low-dose aspirin have been shown to be effective and safe in reducing the pregnancy loss rate in patients with APLS, with significantly better pregnancy outcome than low dose aspirin alone. While several non-randomised studies have suggested that anticoagulant therapy in women with RPL with or without thrombophilia may be of benefit resulting in an increased live birth rate, strong evidence based on randomised controlled trials is still lacking. The aim of the present trial is to evaluate the efficacy of different anticoagulant therapies in women with RPL with or without thrombophilia.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Ethics approval received from the local medical ethics committee

Study design

Randomised, double-blind, placebo controlled, parallel group trial

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Health condition(s) or problem(s) studied

Unexplained recurrent miscarriages, intra-uterine foetal death

Interventions

After inclusion in the study, patients will be randomised to the following groups:

1. Placebo
2. Aspirin (carbasalate calcium) 100 mg/day
3. Aspirin (carbasalate calcium) 100 mg/day plus low dose LMWH subcutaneously (s.c.)

Placebo or low-dose aspirin is given from inclusion until 36 weeks of gestation. LMWH is given from 7 weeks gestation confirmed by foetal heartbeat throughout gestation.

Intervention Type

Drug

Phase

Not Specified

Drug/device/biological/vaccine name(s)

Aspirin, low-molecular-weight heparin

Primary outcome measure

Live birth rate

Secondary outcome measures

Prevalence of adverse pregnancy outcomes:

1. Pre-eclampsia
2. Haemolysis, elevated liver enzymes, low blood levels of platelets (HELLP) syndrome
3. Intra-uterine growth retardation
4. Premature delivery
5. Congenital malformations
6. Prevalence of thromboembolic and haemorrhagic complications
7. Thrombocytopaenia
8. Allergic reactions

Overall study start date

01/02/2004

Completion date

01/09/2008

Eligibility

Key inclusion criteria

Women with at least two unexplained miscarriages and/or intra-uterine foetal deaths

Participant type(s)

Patient

Age group

Adult

Sex

Female

Target number of participants

300

Key exclusion criteria

1. Previous thromboembolism
2. Antiphospholipid syndrome (APLS)
3. Uterine abnormalities
4. Patients or their partners abnormal karyotype
5. Indication for anticoagulant treatment during pregnancy (for instance prosthetic heart valves)
6. Metabolic and toxic factors (diabetes mellitus, radiation exposure)
7. Known erythrocyte antibody anti-P syndrome
8. Pregnancy losses due to documented foetal malformation or the result of an infectious complication
9. Known allergy to at least three different low-molecular-weight heparin (LMWH) preparations
10. Previous inclusion in the ALIFE trial (for another pregnancy)

Date of first enrolment

01/02/2004

Date of final enrolment

01/09/2008

Locations**Countries of recruitment**

Netherlands

Study participating centre

Academic Medical Centre

Amsterdam

Netherlands

1105 AZ

Sponsor information**Organisation**

Academic Medical Centre (AMC) (Netherlands)

Sponsor details

Department of Obstetrics and Gynaecology
Meibergdreef 9
Amsterdam
Netherlands
1105 AZ

Sponsor type

Hospital/treatment centre

Website

<http://www.amc.uva.nl/>

ROR

<https://ror.org/03t4gr691>

Funder(s)

Funder type

Hospital/treatment centre

Funder Name

Sanofi-Aventis (The Netherlands)

Funder Name

Academic Medical Centre (AMC) (The Netherlands) - Department of Vascular Medicine and
Department of Obstetrics and Gynaecology

Funder Name

Viatrix BV (The Netherlands) - manufacturer of carbasalate calcium

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?
Results article	results	29/04/2010		Yes	No
Results article	results	01/06/2014		Yes	No