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

Submission date	Recruitment status	[_] Prospectively registered
20/12/2005	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
20/12/2005	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
09/04/2014	Pregnancy and Childbirth	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
NTR206

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

Primary study design
Interventional

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

Study type(s)
Treatment

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(s)
Live birth rate

Key secondary outcome(s)
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 haemorragic complications
7. Thrombocytopaenia
8. Allergic reactions

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

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

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)

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
Viatris BV (The Netherlands) - manufacturer of carbasalate calcium

Results and Publications

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