

Sitagliptin for implantation

Submission date 19/12/2016	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
Registration date 19/12/2016	Overall study status Completed	<input type="checkbox"/> Protocol
Last Edited 17/06/2020	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

Background and study aims

Miscarriage is defined as the loss of pregnancy before 24 weeks of pregnancy and is the most common complication of pregnancy. 15-25% of pregnancies end in miscarriage, and between 25 and 50% of women will experience at least one miscarriage. Around 1% of all women experience recurrent miscarriage, where they experience several miscarriages in a row. Currently, the only effective treatment to prevent miscarriage is heparin and aspirin for those women with antiphospholipid syndrome (APLS). APLS is a disorder of the immune system that causes an increased risk of blood clots, and occurs in around 15% of women who experience recurrent miscarriage. However, there is no effective treatment for the 85% of recurrent miscarriage patients who do not also suffer from APLS. This study is based on new evidence that has shown that there is a strong association between recurrent miscarriage and a deficiency in stem cells at the endometrium (lining of the womb). The aim of this study is to find out if taking a medication called Sitagliptin, which has been shown in animal studies to increase the number of stem cells in other areas of the body in response to injury, can help increase the number of stem cells in the endometrium.

Who can participate?

Women who have experienced recurrent miscarriage

What does the study involve?

Participants are randomly allocated to one of two groups. Those in the first group receive 100mg Sitagliptin and those in the second group receive a placebo (dummy pill). At the start of the study and then after three months, the stem cell count in the endometrium is measured and the lining of the womb is assessed to see if it has become more favourable for successful implantation.

What are the possible benefits and risks of participating?

Not provided at time of registration

Where is the study run from?

East Surrey Hospital (UK)

When is the study starting and how long is it expected to run for?

June 2016 to August 2017

Who is funding the study?
National Institute of Academic Anaesthesia (UK)

Who is the main contact?
Professor Siobhan Quenby
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Contact information

Type(s)
Scientific

Contact name
Prof Siobhan Quenby

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Additional identifiers

Clinical Trials Information System (CTIS)
2016-001120-54

Protocol serial number
31796

Study information

Scientific Title
Does the DPP4 Inhibitor (Sitagliptin) Increase Endometrial Mesenchymal Stem Cells in Women with Recurrent Miscarriage?

Acronym
SIMPLANT

Study objectives
The aim of this study is to assess whether Sitagliptin increases endometrial mesenchymal stem cells in women with repeated miscarriage compared to placebo.

Ethics approval required
Old ethics approval format

Ethics approval(s)

South Central - Hampshire B Research Ethics Committee, 14/06/2016, ref: 16/SC/0229

Study design

Randomised; Interventional; Design type: Prevention, Drug, Cellular

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Specialty: Reproductive health and childbirth, Primary sub-specialty: Maternal/ Fetal medicine; UKCRC code/ Disease: Reproductive Health and Childbirth/ Other disorders originating in the perinatal period, Reproductive Health and Childbirth/ Fetus and newborn affected by maternal factors and by complications of pregnancy, labour and deliver

Interventions

Participants are randomised to receive 100mg sitagliptin or placebo. Participants are followed up after three months.

Intervention Type

Drug

Phase

Phase II

Drug/device/biological/vaccine name(s)

Sitagliptin

Primary outcome(s)

The number of colonies per thousand endometrial stromal cells after three months of the IMP determined by a clonogenic assay.

Key secondary outcome(s)

1. Change in the expression of DPP4 at the endometrium determined by immunohistochemistry
2. RNA sequencing
3. Methylation status of implantation related genes
4. Adverse events/serious adverse events
5. Acceptability of study determined by questionnaire
6. Follow up pregnancy rates and outcomes

Completion date

31/08/2017

Eligibility

Key inclusion criteria

1. Provision of informed written consent
2. History of recurrent miscarriage - 3 or more miscarriages (three or more spontaneous pregnancy losses prior to 24 weeks gestation)
3. Age 18-42 years at consent
4. Any BMI – no dose adjustment needed for BMI. BMI has no clinically meaningful effect on the pharmacokinetics of Sitagliptin.
5. Willing and able to give consent for the study and endometrial biopsy.
6. Ability to fully understand the requirements of the protocol
7. Adequate renal function , defined as Urea 2.5 – 7.8mmol/L, Creatinine 50 -90umol/L, potassium 3.5 – 5.3mmol/L, Sodium 133 -146mmol/L
8. Adequate hepatic function, defined as total protein 60 – 80g/L, Albumin 35-50g/L, Bilirubin 4-20umol/L, Alkaline Phosphatase (ALP) 35-105U/L, Alanine Transferase (ALT) 5-38 U/L
9. Negative pregnancy test on the day of randomisation

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Upper age limit

42 years

Sex

Female

Total final enrolment

38

Key exclusion criteria

1. Under 18 years of age – the safety and effectiveness of Sitagliptin in paediatric patients under 18 has not yet been established
2. Type I Diabetes – Sitagliptin should not be used in type 1 diabetes
3. Type II Diabetes – based on medical history
4. Pregnancy (tested at multiple points in trial)
5. Breast feeding – Caution is advised when prescribing Sitagliptin to breastfeeding mothers as it is not known if it is secreted in breast milk.
6. Known hypersensitivity to Sitagliptin
7. Not taking any medications with potential to react with interventional product:
 - 7.1. Digoxin –plasma monitoring is needed if Sitagliptin used concomitantly in those at risk of digoxin toxicity
 - 7.2. Enalapril – Sitagliptin appears to alter the hypotensive effects of enalapril
8. Previous diagnosis of pancreatitis
9. Renal impairment with eGFR<50 mL/min

10. Liver impairment, defined as any value out of normal range (total protein 60 – 80g/L, Albumin 35-50g/L, Bilirubin 4-20umol/L, Alkaline Phosphatase (ALP) 35-105U/L, Alanine Transferase (ALT) 5-38 U/L)
11. Inclusion in another intervention trial
12. Unwilling to use effective contraception for the duration of the trial (from consent)
13. Allergy/sensitivity to excipients of the IMP/placebo

Date of first enrolment

14/09/2016

Date of final enrolment

01/06/2017

Locations

Countries of recruitment

United Kingdom

England

Study participating centre

University Hospitals Coventry and Warwickshire NHS Trust

Clifford Bridge Road

Walsgrave

Coventry

United Kingdom

CV2 2DX

Sponsor information

Organisation

University Hospitals Coventry and Warwickshire NHS Trust

ROR

<https://ror.org/025n38288>

Funder(s)

Funder type

Charity

Funder Name

Tommy's Baby Charity

Alternative Name(s)

Funding Body Type

Private sector organisation

Funding Body Subtype

Other non-profit organizations

Location

United Kingdom

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?
Basic results			17/06/2020	No	No
HRA research summary			28/06/2023	No	No