ISRCTN15948785 https://doi.org/10.1186/ISRCTN15948785

Thyroid AntiBodies and LEvoThyroxine study (TABLET)

Submission date	Recruitment status	[X] Prospectively registered
31/10/2011	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
31/10/2011	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
28/05/2020	Pregnancy and Childbirth	

Plain English summary of protocol
Not provided at time of registration

Study website
http://www.birmingham.ac.uk/research/activity/mds/trials/bctu/trials/womens/tablet/index.aspx

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2011-000719-19

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
11051

Study information

Scientific Title
A randomised controlled trial of the efficacy and mechanism of levothyroxine treatment on pregnancy and neonatal outcomes in women with thyroid antibodies

Acronym
TABLET

Study objectives
Current study hypothesis as of 29/04/2013:
Levothyroxine will assist women aged 16-40 with a history of one or more miscarriage or who are being treated for infertility, who have been identified as having thyroid antibodies (TPO antibody positive) trying to conceive within 1 year of miscarriage.

Previous study hypothesis until 29/04/2013:
Levothyroxine will assist women aged 16-40 with a history of one or more miscarriage, who have been identified as having thyroid antibodies (TPO antibody positive) trying to conceive within 1 year of miscarriage.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South West C REC, 29/03/2011, ref: 11/SW/0036

Study design
Randomised interventional trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

http://www.birmingham.ac.uk/research/activity/mds/trials/bctu/trials/womens/tablet/investigators/documentation.aspx

Health condition(s) or problem(s) studied
Reproductive health, childbirth

Interventions
Current interventions as of 29/04/2013:
Women aged 16-40 with a history of one or more miscarriage or who are being treated for infertility, who have been identified as having thyroid antibodies (TPO antibody positive), and will be trying to conceive within 1 year.

Prevous interventions until 29/04/2013:
Women aged 16-40 with a history of one or more miscarriage, who have been identified as having thyroid antibodies (TPO antibody positive), and will be trying to conceive within 1 year of miscarriage.

Levothyroxine, 50mcg Levothyroxine, overencapsulated to be taken orally daily versus placebo, to match investigational medicinal products (IMP). Followed Up at 21 month(s)

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Levothyroxine

Primary outcome measure
Current primary outcome measures as of 14/09/2017:
Live birth at or beyond 34 weeks (greater than or equal to 34). The denominator of this proportion will be all women randomised, and the numerator will be those women who proceed to have a live birth at or beyond 34 weeks.

Previous primary outcome measures:
Live birth measured at beyond 34 weeks gestational age

Secondary outcome measures
Current secondary outcome measures as of 14/09/2017:
1. Clinical pregnancy assessed using urine test at 7 weeks
2. Ongoing pregnancy assessed using scan at 12 weeks
3. Miscarriage <24 weeks, clinical assessment
4. Stillbirth (inter-uterine death ≥24 weeks), clinical assessment
5. Ectopic pregnancy, clinical assessment
6. Termination (and reasons), clinical assessment
7. Live birth <34 weeks, clinical assessment
8. Time from conception to pregnancy end (any reason)
9. Mode of initiation of labour (spontaneous/induced)
10. Mode of delivery (vaginal/operative vaginal/caesarean)
11. Gestation at delivery, weeks (scan)

12. Time from conception to live birth
13. Gestation at delivery <28 weeks/<34 weeks/<37 weeks
14. Birth weight, grams
15. Birth weight adjusted for gestational age and sex, centiles
16. Birth weight adjusted for gestational age, sex, parity, maternal BMI and ethnicity, centiles
17. Small for gestational age and sex (birth weight proportion<10th centile)
18. Small for gestational age, sex, parity, maternal BMI and ethnicity (birth weight proportion<10th centile)
19. Large for gestational age and sex (birth weight proportion>=90th centile)
20. Large for gestational age, sex, parity, maternal BMI and ethnicity (birth weight proportion>=90th centile)
21. APGAR score, clinical assessment at 1 minute/5 minutes
22. Serum TSH concentration (mu/l; log transformed), assessed by blood test at each assessment time (3 months, 6 months, 9 months, 6-8 weeks pregnancy, 16-18 weeks pregnancy and 28 weeks pregnancy)
23. Serum free T4 level (pmol/L), assessed by blood test at each assessment time (3 months, 6 months, 9 months, 6-8 weeks pregnancy, 16-18 weeks pregnancy and 28 weeks pregnancy)
24. Maternal antenatal complications (hyperemesis gravidarum/gestational diabetes/pre-eclampsia or eclampsia/obstetric cholestasis/pre-term pre labour rupture of membranes (PPROM)/intrauterine growth restriction (IUGR)/others), clinical assessment
25. Intrapartum complications (shoulder dystocia/others), clinical assessment
26. Maternal postnatal complications (admission to HDU or ITU/Abnormal thyroid test within four weeks/referred to psychiatrist or started on antidepressants/others), clinical assessment
27. Neonatal complications (early neonatal death defined as death within 7 days after delivery /late neonatal death defined as death beyond 7 days and before 28 days post-delivery/admission to NNU/SCBU/active resuscitation within first 28 days/surfactant use/mechanical ventilation /intermittent positive pressure ventilation/continuous positive airway pressure/oxygen use /congenital abnormalities/hypoxic ischaemic encephalopathy/retinopathy of prematurity /respiratory distress syndrome/pneumothorax/intraventricular hemorrhage (grade 3 or 4) /necrotizing enterocolitis/early infection/others), clinical assessment
28. Reported symptoms that participant is concerned about at each assessment time (3 months, 6 months, 9 months, 6-8 weeks pregnancy, 16-18 weeks pregnancy and 28 weeks pregnancy)
29. Serious Adverse Events, clinical assessment at 3 months, 6 months, 9 months, 6-8 weeks pregnancy, 16-18 weeks pregnancy and 28 weeks pregnancy

Previous secondary outcome measures (added 29/04/2013):
1. Gestation at delivery
2. Conception (urinary pregnancy) rate
3. Clinical pregnancy at 6 8 weeks
4. On-going pregnancy at 11-13 weeks
5. Miscarriage (delivery before 24 weeks of gestation)
6. Survival at 28 days of neonatal life
7. Thyroid function tests

Overall study start date
10/10/2011

Completion date
15/05/2017

Eligibility

Key inclusion criteria
Current inclusion criteria as of 29/04/2013:
1. Women trying to conceive
2. History of one or more miscarriage(s) or who are being treated for infertility
3. Age 16 40 years at randomisation
4. Biochemically euthyroid (Free T4 and TSH within specified reference ranges)
5. Thyroid Peroxidase Antibody (TPO) positive
6. Willing and able to give written informed consent

Previous inclusion criteria until 29/04/2013:
1. Women trying to conceive
2. History of one or more miscarriage(s)
3. Age 16 40 years at randomisation
4. Biochemically euthyroid (Free T4 and TSH within specified reference ranges)
5. Thyroid Peroxidase Antibody (TPO) positive
6. Willing and able to give written informed consent

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
Planned Sample Size: 900; UK Sample Size: 900

Total final enrolment
952

Key exclusion criteria
Current exclusion criteria as of 29/04/2013:
1. Current or past treatment for thyroid disease
2. Contraindication to levothyroxine treatment
3. Thyrotoxicosis
4. Hypersensitivity to any components tablets
5. Women taking amiodarone or lithium therapy
6. Participants in any other blinded, placebo controlled trials on Investigational Medicinal Products in pregnancy
7. Previous or current diagnosis of cardiac disease

Previous exclusion criteria until 29/04/2013:
1. Current or past treatment for thyroid disease
2. Contraindication to levothyroxine treatment
3. Thyrotoxicosis
4. Hypersensitivity to any components tablets
5. Women taking amiodarone or lithium therapy
6. Participants in any other blinded, placebo controlled trials on Investigational Medicinal

Products in pregnancy
7. Planning to conceive using ovulation stimulation therapy
8. Previous or current diagnosis of cardiac disease

Date of first enrolment
01/11/2011

Date of final enrolment
22/01/2016

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Birmingham Womens Hospital
Birmingham
United Kingdom
B15 2TG

Study participating centre
For full list of centres please see: http://www.birmingham.ac.uk/research/activity/mds/trials/bctu/trials/womens/tablet/investigators/recruitment.aspx
United Kingdom
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Sponsor information

Organisation
University of Birmingham (UK)

Sponsor details
Research Support Group
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Edgbaston
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B15 2TT

Sponsor type
University/education

Website
http://www.bctu.bham.ac.uk/

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
Efficacy and Mechanism Evaluation Programme

Alternative Name(s)
NIHR Efficacy and Mechanism Evaluation Programme, EME

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
1. The protocol is available at: https://www.birmingham.ac.uk/research/activity/mds/trials/bctu/trials/womens/tablet/investigators/documentation.aspx
2. The final report will be published in May 2018

Intention to publish date
01/05/2018

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	04/04/2019		Yes	No
Basic results			28/05/2020	No	No
HRA research summary			28/06/2023	No	No