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COVID-19 vaccines in pregnancy

Submission date
17/06/2021

Recruitment status
No longer recruiting

Registration date
14/10/2021

Overall study status
Completed

Last Edited
16/10/2024

Condition category
Infections and Infestations

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Ongoing global studies so far have found that pregnant women are more likely to develop severe COVID-19 disease compared to non-pregnant women of the same age. Pregnant women who develop COVID-19 symptoms are two to three times more likely to have their baby early. Pregnant women with COVID-19 also have a higher mortality rate than pregnant women without COVID-19. For these reasons, the current UK guidance on immunisation is that COVID-19 vaccination should be offered to pregnant women at the same time as the rest of the population. However, further pregnancy-specific research is needed on COVID-19 vaccines. This study aims to identify the best interval to be used between doses of COVID-19 vaccines for protecting pregnant women against COVID-19.

Who can participate?
Low-risk pregnant women aged 18-45 years and between 13-34 weeks gestation

What does the study involve?
Once successfully enrolled, participants will be randomly allocated to receive two doses of a COVID-19 vaccine (or only one dose if the participant has already received their first dose) in a short-time interval (4-6 weeks) or a long-time interval (8-12 weeks). For some participants, this means they will receive their second dose after delivery. Participants will be followed up until 1 year after delivery. Blood samples will be taken from participants throughout the study. For some participants, a cord blood sample will be taken after delivery. For all participants, a baby blood sample will be taken between 4 and 12 weeks of age. Participants will be asked to complete a symptom diary and any significant medical events will be investigated. For a sub-group of participants breastmilk samples will also be collected.

What are the possible benefits and risks of participating?
Participating will help the researchers to understand more about the use of vaccines against COVID-19 in pregnancy - specifically their safety and ability to produce an immune response in pregnant women and their babies, as well as whether different dosing intervals make any difference to these immune responses. This research will inform the national immunisation programme in the UK on what advice to give to women already pregnant or planning to become pregnant. Participants will be receiving licensed COVID-19 vaccines and are monitored throughout the duration of the study. This trial involves at least five blood tests from the mother and one blood test from the baby and may include up to two samples of breast milk.

Blood tests can be uncomfortable and may cause slight pain and/or bruising at the site where the needle enters. Some people feel light-headed or even faint when having blood taken. Blood sampling will be performed by an experienced member of the team and participants will be offered a medicated numbing cream for their baby for their blood test.

Where is the study run from?
St George's University of London (UK)

When is the study starting and how long is it expected to run for?
June 2021 to April 2025

Who is funding the study?
The UK Vaccine Taskforce (UK)

Who is the main contact?
1. Dr Eva Galiza, egaliza@sgul.ac.uk
2. Prof. Paul Heath, pheath@sgul.ac.uk

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-003073-60

Integrated Research Application System (IRAS)
301115

ClinicalTrials.gov (NCT)
NCT15279830

Protocol serial number
CPMS 49682, IRAS 301115

Study information

Scientific Title
A Phase II, randomised, single-blind, platform trial to assess safety, reactogenicity and immunogenicity of COVID-19 vaccines in pregnant women in the United Kingdom

Acronym
Preg-Cov

Study objectives
1. To determine whether the immune response in COVID-19 seronegative participants to immunisation with COVID-19 vaccines according to “long” dosing intervals is superior to that observed following immunisation according to “short” dosing intervals.
2. To evaluate the reactogenicity of COVID-19 vaccines, when given as one- or two-dose vaccination regimens, in pregnant participants.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 29/07/2021, Newcastle and North Tynes 1 REC (Newcastle and North Tynes 1 REC, Holland Drive, Newcastle upon Tyne, Tyne and Wear, NE2 4NQ, United Kingdom; +44 (0)207 104 8139, +44 (0)207 104 8285, +44 (0)203 443 6294; newcastlenorthtyneside1.rec@hra.nhs.uk), ref: 21/NE/0114

Study design
Randomized; Interventional; Design type: Treatment, Vaccine

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
COVID-19 (SARS-CoV-2 infection)

Interventions
There are four study cohorts: cohorts 1 and 2 will be the main study cohorts and 3 and 4 will be the sub-study cohorts
Participants in cohorts 2, 3 and 4 can receive the Tdap vaccination from the study team during study visits according to routine recommendations in the UK.

Screening + study visit 1 (maternal):
This visit will take place between 13+0 – 27+6 gestational weeks (for the earlier gestational weeks group) or between 28+0 – 34+0 gestational weeks (for the later gestational weeks group) at the participating institution.
Eligibility will be confirmed, the study will be discussed in more detail and women will be asked to sign a consent form. They will then be asked about demographic details (including NHS number), past medical history, receipt of any prior dose of a COVID-19 vaccine, details of the current pregnancy including the results of antenatal screening and scans to ensure that they are eligible for the study. The participant's antenatal medical notes will be reviewed. Details will be collected about concomitant medication. A physical examination will be performed, and vital signs, height and weight will be recorded. Immunogenicity blood samples will be obtained.

Cohort 1, 2, 3: Participants will be randomised to a single group to receive one type of COVID-19 vaccine with the first dose to be given at visit 1.
Cohort 4: Participants will receive the same vaccine as given pre-pregnancy or in the first trimester of pregnancy and randomised to either receiving the booster dose before or after 26 weeks gestation.

Vaccination will be given by members of the study team who are trained and experienced in vaccine administration and in emergency procedures in the event of an allergic reaction. They will have access to emergency medication and equipment. The vaccinations will be given according to the advice in the "Green Book" and the Summary of Product Characteristics (SmPC). An eDiary will be set up for the participant and they will be given instructions to complete the diary regularly for 28 days following vaccination. The participant will be observed for a period of 20 minutes following vaccination to assess for allergic adverse events.

Study visit 2 (Maternal) all cohorts
This visit will take place 14 days (10 days – 21 days) after the first vaccination and will be a telephone call.
At this visit adverse events, new medication and the eDiary will be reviewed.

Study visit 3 (Maternal) all cohorts
This visit will take place 28-42 days following the first vaccination at the participating institution.

At this visit adverse events, new medication and the eDiary will be reviewed. A targeted physical examination will be performed if needed and immunogenicity blood samples will be collected

For cohort 1:
Vital signs will be performed pre-vaccination. Vaccination with COVID-19 vaccine if randomised to the short boost or dTaP if randomised to the long boost arm and has not previously received the pertussis vaccine. Participants will be observed for 20 minutes following vaccination.

For cohort 2:
Participants in the short boost group will have vital signs will be performed pre-vaccination and will receive the COVID-19 vaccine. Participants will be observed for 20 minutes following vaccination.

For cohorts 3 and 4:
No vaccination will be received.

Study visit 4 (maternal) cohort 1 and 2 only:
This visit will take place 56-84 days following the first vaccination (or 28-42 days post-short boost dose) at the participating institution.
At this visit adverse events, new medication and the eDiary will be reviewed. A targeted physical examination will be performed if needed and immunogenicity blood samples will be collected.
Vital signs will be performed pre-vaccination.

For cohort 1:
Vaccination with COVID-19 vaccine if randomised to the long boost or dTaP if randomised to the short boost arm and has not previously received the pertussis vaccine. Participants will be observed for 20 minutes following vaccination.

For cohort 2:
Participants in the long boost group will have vital signs will be performed pre-vaccination and will receive the COVID-19 vaccine. Participants will be observed for 20 minutes following vaccination.

Study visit 5 (maternal) cohort 1 and 2 only
This visit will take place 84-112 days following the first vaccination (or 28-42 days post-long boost dose) at the participating institution/participant home
At this visit adverse events, new medication and the eDiary will be reviewed. A targeted physical examination will be performed if needed and immunogenicity blood samples will be collected

Study visit 6 (maternal) cohort 1, 2 and 4 only
This visit will take place 112-140 days following the first vaccination (or 56-84 days post second COVID-19 vaccine dose at the participating institution/participant's home. This visit need only take place if the visit window starts before the due date
At this visit adverse events, new medication and the eDiary will be reviewed. A targeted physical examination will be performed if needed and immunogenicity blood samples will be collected.

Study visit 7 (delivery, maternal/infant) all cohorts
This visit will take place at the time of delivery at the participating institution.
A targeted physical examination will be performed if needed and immunogenicity blood samples will be collected. These samples can be obtained by a member of the study team or a clinical member of staff. If blood sampling is not performed at delivery, women will be asked if a blood sample can be obtained from them within the first week following delivery and if a cord sample

is not obtained parents will be asked if we can take a blood sample from the infant within the first week following delivery. At selected sites a cord blood sample will be taken. Infant examination will be performed by the clinical team.

Study visit 8 (postnatal) breastmilk sub-study and those due vaccination in cohort 3
This visit will take place 0 – 7 days post-delivery where possible at the participating institution for those in the breastmilk sub-study group and those due vaccination in cohort 3
At this visit, adverse events, new medication and the eDiary will be reviewed. A targeted physical examination will be performed if needed for participants in cohort 3 only.

Breastmilk sub-study
At selected sites those participants who have agreed to take part in the breastmilk sub-study will be asked if they still plan to breastfeed and if they are happy to provide a sample of colostrum within the first 72 hours following delivery where possible. If women are still willing to take part in the study, they will be provided with information about colostrum sampling and containers and instructions for the collection of the sample. Participants who are taking part in the breastmilk sub-study will hand express a sample of colostrum from each breast. Participants will be provided with containers and instructions for the collection of subsequent samples

Cohort 3 (28-34 gestational weeks at recruitment)
For those participants in cohort 3 vital signs will be performed pre-vaccination. Vaccination with COVID-19 vaccine for those in cohort 3. These participants will be reviewed for 20 minutes following vaccination. The eDiary will be set up for those receiving a vaccine.

Study visit 9 (postnatal) all cohorts
This visit will take place 12 - 16 days post-delivery where possible at the participating institution for those in the breastmilk sub-study group and those who received vaccination post-delivery in cohort 3. All other participants can be reviewed at this visit by a telephone call.
At this visit adverse events and new medication will be reviewed. A targeted physical examination will be performed if needed and immunogenicity blood samples will be collected. A targeted physical examination will be performed for those participants in cohort 3 only if needed. There will be further randomisation to determine whether the infant bloods are taken at 4-6 weeks after birth or at 10-12 weeks after birth.

Cohort 3
The eDiary will be checked for those who received a vaccine post-delivery.

Breastmilk sub-study
Participants in the breastmilk sub-study sample collection will be asked to provide a sample of breastmilk from each breast. This sample can be collected by the woman in advance and collected by a member of the research team if this is a remote visit.

Study visit 10 (postnatal)
This visit will be performed 28-42 days OR 70-84 days post-delivery at the participating institution/participant's home
At this visit adverse events and new medication will be reviewed. A targeted physical examination will be performed if needed and immunogenicity blood samples will be collected. An infant blood sample will be collected.

Cohort 3
The eDiary will be checked for those who received a vaccine post-delivery.

Study visit 11 (postnatal) all cohorts
This visit will take place 182 days (-/+ 14 days) post-delivery and will be by telephone call.
At this visit adverse events and new medication will be reviewed

Study visit 12 (postnatal)
This visit will take place 364 days (-/+ 14 days) post-delivery at the participating institution /participant's home.
At this visit adverse events and new medication will be reviewed. Immunogenicity blood samples will be collected. Infant neurodevelopmental assessment – "Ages and Stages" Questionnaire- will be performed if not already completed by a healthcare professional during routine care.

Intervention Type
Biological/Vaccine

Phase
Phase II

Drug/device/biological/vaccine name(s)
BNT162b2, mRNA-1273

Primary outcome(s)
1. SARS-COV-2 IgG-specific antibody concentrations measured by ELISA from blood samples collected from vaccinated maternal subjects at delivery
2. Occurrence of solicited local and general adverse events (AEs) that occur during a 7-day follow-up period after each vaccination (i.e., the day of vaccination and 6 subsequent days), measured using diary data entry (solicited AE) from Day 0 to Day 6
3. Occurrence of unsolicited AEs that occur during a 30-day follow-up period after vaccination (i. e., the day of vaccination and 29 subsequent days), measured using diary data entry (unsolicited AE) from Day 0 to Day 29

Key secondary outcome(s))
Maternal:
1. Pregnancy outcomes from Visit 1 up to 6 weeks after delivery. These include live birth with congenital anomalies, miscarriage, fetal death/stillbirth (antepartum or intrapartum), mode of delivery, elective/therapeutic termination. Reviewed at delivery and at 3 days, 14 days, and 42-48 days after delivery.
2. Occurrence of serious adverse events (SAEs), AEs leading to study withdrawal, and medically attended adverse events (MAAEs) from Visit 1 (Day 0) up to 6 weeks after delivery. Notification of SAE/AE/MAAE to site by participant from enrolment to 1 year after delivery/birth
3. Adverse event of special interest (AESI) from Visit 1 up to 6 weeks after delivery (Day 42 post-delivery). These include but are not limited to maternal death, hypertensive disorders of pregnancy (gestational hypertension, pre-eclampsia, pre-eclampsia with severe features including eclampsia), antenatal bleeding (morbidly adherent placenta, placental abruption, caesarean scar pregnancy, uterine rupture), postpartum haemorrhage, fetal growth restriction, gestational diabetes mellitus, non-reassuring fetal status, pathways to preterm birth (premature preterm rupture of membranes, preterm labour, provider-initiated preterm birth), chorioamnionitis, oligohydramnios, polyhydramnios, gestational liver disease (intrahepatic cholestasis of pregnancy, acute fatty liver of pregnancy), maternal sepsis. Notification of AESI to site by participant from enrolment to 6 weeks after delivery for the mother and up to 6 weeks after birth for the infant.
4. SARS-COV-2 IgG-specific antibody concentrations (and neutralizing antibody titres and cellular

immune responses in subsets) measured by ELISA from blood samples collected from vaccinated maternal subjects at Day 0 (before vaccination), Day 28-42, Day 56-84, Day 84-112, Day 112-140, at delivery, between 4 weeks and 12 weeks, and at 12 months after delivery
5. SARS-COV-2 IgG-specific antibody concentrations (and neutralizing antibody titres and cellular immune responses in subsets) measured by ELISA from blood samples collected from vaccinated maternal subjects at Day 0 (before vaccination), Day 28-42, Day 56-84, Day 84-112, Day 112-140, at delivery, between 4 weeks and 12 weeks, and at 12 months after delivery

Infant:
6. Occurrence of SAEs, AEs leading to study withdrawal, and MAAEs. Review of SAEs, AEs leading to study withdrawal, and MAAEs at delivery and at 3 days, 14 days, and 42-48 days after delivery, and at 6 months and 12 months.
7. Occurrence of neonatal AEs of special interest (up to 6 weeks after birth). These include but are not limited to small for gestational age, low birth weight including very low birth weight, neonatal encephalopathy, congenital microcephaly (postnatally or prenatally diagnosed), congenital anomalies (major external structural defects, internal structural defects, functional defects), neonatal death (in a preterm live birth or in a term live birth), neonatal infections (bloodstream infections, meningitis, respiratory infection), respiratory distress in the neonate, preterm birth, failure to thrive, large for gestational age, macrosomia. Review of neonatal AESIs at delivery and at 3 days, 14 days, and 42-48 days after delivery, and at 6 months and 12 months.
8. Developmental status assessed by neurodevelopmental assessment at 12 months of age
9. SARS-COV-2 IgG-specific antibody concentration (and neutralizing antibody titres in a subset) against SARS-COV-2 measured by ELISA on the cord blood sample collected at delivery, or on a blood sample collected from the infant within 3 days after birth (if no cord blood sample can be obtained)
10. The ratio between cord blood and maternal SARS-COV-2 IgG-specific antibody concentrations measured by ELISA or an infant blood sample collected within 72 hours after birth (if no cord blood sample can be obtained)
11. SARS-COV-2 IgG-specific antibody concentrations and neutralizing antibody titres against SARS-COV-2 in infants born to vaccinated mothers measured by ELISA at Day 28 to 42 or Day 70 to 84 post- delivery
12. SARS-COV-2 IgG-specific antibody concentration (and neutralizing antibody titres in a subset) against SARS-COV-2 measured by ELISA on the cord blood sample collected at delivery, or on a blood sample collected from the infant within 3 days after birth (if no cord blood sample can be obtained)
13. The ratio between cord blood and maternal SARS-COV-2 IgG-specific antibody concentrations or an infant blood sample collected within 72 hours after birth (if no cord blood sample can be obtained) measured by ELISA
14. SARS-COV-2 IgG-specific antibody concentrations and neutralizing antibody titres against SARS-COV-2 in infants born to vaccinated mothers measured by ELISA at Day 28 to 42 or Day 70 to 84 post- delivery

Exploratory:
Maternal:
15. Levels of maternal IgA and/or IgG (and subtypes) against SARS-CoV-2 in colostrum and breast milk measured by ELISA within 3 days and 14 days where possible
16. Occurrence of COVID-19 up to 12 months post-delivery (mother). Identification and laboratory confirmation by PCR of SARS-CoV-2 infection and symptomatic COVID-19throughout the study.
17. SARS-COV-2 IgG-specific antibody concentrations (and neutralizing antibody titres and cellular immune responses in subsets) measured by ELISA from blood samples collected from vaccinated maternal subjects at Day 0 (before booster vaccination), Day 28-42, Day 56-84, Day

84-112, Day 112-140, at delivery, between 4 weeks and 12 weeks, and at 12 months after delivery
18. SARS-COV-2 IgG-specific antibody concentrations (and neutralizing antibody titres and cellular immune responses in subsets) measured by ELISA from blood samples collected from vaccinated maternal subjects at Day 0 (before vaccination), Day 28-42, Day 56-84, Day 84-112, Day 112-140, at delivery, between 4 weeks and 12 weeks, and at 12 months after delivery
19. SARS-COV-2 IgG-specific antibody concentrations (and neutralizing antibody titres and cellular immune responses in subsets) measured by ELISA from blood samples collected from vaccinated maternal subjects at Day 0 (before vaccination), Day 28-42, Day 56-84, Day 84-112, Day 112-140, at delivery, between 4 weeks and 12 weeks, and at 12 months after delivery

Infant:
20. Occurrence of COVID-19 up to 12 months post-delivery (infant). Identification and laboratory confirmation by PCR of SARS-CoV-2 infection and symptomatic COVID-19 throughout the study

Completion date
30/04/2025

Eligibility

Key inclusion criteria
1. Healthy women ≥18 years of age who are between 13 0/7 and 34 0/7 weeks' gestation on the day of planned vaccination, with an uncomplicated, singleton pregnancy, who are at no known increased risk for obstetric complications
2. Able and willing (in the investigator's opinion) to comply with all study requirements
3. Willing to allow the investigators to discuss the volunteer's medical history with their General Practitioner and access all medical records when relevant to study procedures
4. Willing and able to give informed consent prior to study enrolment
5. No contraindication to the specific vaccine to be administered in the study, according to the Green Book

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
45 years

Sex
Female

Total final enrolment
319

Key exclusion criteria
1. Previous microbiological (based on a positive SARS-CoV-2 NAAT result) diagnosis of COVID-19
2. Administration of immunoglobulins and/or any blood products within the 3 months preceding the planned administration of the study vaccine candidate (with the exception of anti-D immunoglobulin)
3. Previous vaccination with any COVID-19 vaccine (main cohort); prior receipt of one dose of a COVID-19 vaccine is permitted (sub-study)
4. Any confirmed or suspected immunosuppressive or immunodeficient state; chronic administration (defined as more than 14 continuous days) of immunosuppressant medication within the past 3 months, except topical steroids or short-term oral steroids (course lasting ≤14 days)
5. Any contraindication to the specific vaccine to be administered in the study, according to the Green Book or to the Summary of Product Characteristics for a specific vaccine
6. Current major illness of the mother or conditions of the fetus that, in the investigator's judgment, will substantially increase the risk associated with the participant's participation in, and completion of, the study or could preclude the evaluation of the participant's response, including but not limited to the following:
6.1. Uncontrolled gestational hypertension
6.2. Preeclampsia-eclampsia
6.3. Placental abnormality
6.4. Polyhydramnios or oligohydramnios
6.5. Significant bleeding or blood clotting disorder
6.6. Uncontrolled gestational diabetes
6.7. Any signs of premature labor with the current pregnancy or having ongoing intervention (medical/surgical) in the current pregnancy to prevent preterm birth
6.8. Prior stillbirth or neonatal death, preterm delivery (≤34 weeks), or previous infant with a known genetic disorder or major congenital anomaly

Date of first enrolment
03/08/2021

Date of final enrolment
31/05/2022

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
Liverpool Women's Hospital
Crown Street
Liverpool

United Kingdom
L8 7SS

Study participating centre
Milton Keynes University Hospital
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Study participating centre
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SE1 7EH

Study participating centre
St George's University Hospitals NHS Foundation Trust - Preg Cov Covid19 Trials
St. Georges Vaccine Institute
Jenner Wing, St. Georges Hospital
Cranmer Terrace
London
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SW17 0RE

Study participating centre
Lancashire Teaching Hospitals NHS Foundation Trust - Preg Cov Covid19 Trials
Sharoe Green Unit
Royal Preston Hospital
Sharoe Green Lane
Preston
United Kingdom
PR2 9HT

Study participating centre
Manchester University NHS Foundation Trust - Preg Cov Covid19 Trials
St Marys Hospital
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
Birmingham Heartlands Hospital
Bordesley Green East
Bordesley Green
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B9 5SS

Study participating centre
University Hospital Bristol
Bristol Royal Infirmary
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BS2 8HW

Study participating centre
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Du Cane Road
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Study participating centre
Leeds Teaching Hospitals NHS Trust
St. James's University Hospital
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LS9 7TF

Sponsor information

Organisation
St George's, University of London

ROR
https://ror.org/040f08y74

Funder(s)

Funder type
Government

Funder Name
Department for Business, Energy and Industrial Strategy, UK Government

Alternative Name(s)
Dept for BEIS, Department for BEIS, Department for Business, Energy & Industrial Strategy, Department for Business, Energy and Industrial Strategy, Department for Business, Energy & Industrial Strategy, United Kingdom, Department for Business, Energy & Industrial Strategy, UK Government, BEIS

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 5.0	23/07/2021	06/10/2021	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes