ISRCTN52318758 https://doi.org/10.1186/ISRCTN52318758

Early protection against meningococcal disease B in infants

Submission date
09/07/2021

Recruitment status
No longer recruiting

Registration date
16/07/2021

Overall study status
Completed

Last Edited
08/10/2025

Condition category
Infections and Infestations

[_] Prospectively registered
[X] Protocol
[X] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
In 2015, the United Kingdom became the first country in the world to introduce the meningococcal group B (Men B) vaccine into its routine schedule for infants. This vaccine has proved to be very effective in protecting against meningitis (infection of the lining of the brain) and septicaemia (blood poisoning) caused by a subgroup (group B) of the meningococcus germ. In the United Kingdom, babies are offered this vaccination at 2, 4, and 12 months.
The aim of this study is to compare two different schedules of Men B vaccination, the standard schedule (at 2, 4, and 12 months) and the early schedule (at 2, 3, and 12 months). Receiving the first two doses of Men B vaccine by 3 months could provide infants earlier protection against Men B disease.

Who can participate?
Babies born at term, aged 56 days to 70 days on the day of the first visit

What does the study involve?
Babies are randomly allocated to one of the two study groups: one group will receive all recommended vaccines according to the standard UK schedule and the other will receive the second dose of Men B vaccine at 3 instead of 4 months and the first dose of PCV13 at 4 instead of 3 months. Both groups will receive an additional dose 'booster' dose of Men B and PCV13 vaccine at 12 months. The researchers will take three blood samples over the study period to check the babies' antibody levels against Meningococcus and Pneumococcus germs, and will ask caregivers to keep a record of any reactions that occur after their vaccinations.

What are the possible benefits and risks of participating?
Participants will have the choice of coming to the study site, or the study team can come to the home of the participants to give the vaccinations and take the blood samples. If participants attend at the local site, reasonable travel expenses will be covered. They will have 24-hour telephone access to a member of the study team if they have any concerns about their baby's vaccinations.
Because the vaccines used in this study are exactly the same ones being used for routine immunisation of other babies in the UK, the researchers do not expect the risk to be any different than with the routinely given vaccines. As with all vaccinations, however, there may

occasionally be some redness and/or swelling at the injection site and fever. Fever is a side effect particularly associated with the Men B vaccination and advice will be given to parents about steps they can take to try to prevent this. Severe allergic reactions, such as anaphylaxis, are extremely rare but can occur with any vaccine. The baby would be observed for 20 minutes following each immunisation and the study staff are specifically trained and equipped to deal with this in the extremely unlikely event that it did occur.
Blood tests may be uncomfortable for infants, but the researchers will try to minimise this by offering a local anaesthetic cream, if appropriate, to numb the skin before taking the blood sample.
It is anticipated that the immune response of the 2-3-month Men B schedule will be similar to that of the 2-4-month schedule, and similarly that the change of timing of the pneumococcal vaccine will have no impact on the protection offered by this vaccine. All participants will have their antibody levels checked following the 12-month vaccinations, which provides an opportunity to identify infants who have a sub-optimal response. If this shows that the baby may have inadequate protection, the research team will contact the participant to discuss the options, including the possibility of a booster dose of vaccine.

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?
April 2021 to October 2024

Who is funding the study?
GlaxoSmithKline (UK)

Who is the main contact?
Dr Natasha Thorn
nthorn@sgul.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Natasha Thorn

Contact details
St George's University of London
Cranmer Terrace
London
United Kingdom
SW17 0RE
+44 (0)208 725 4851
nthorn@sgul.ac.uk

Type(s)
Scientific

Contact name

Prof Paul Heath

Contact details
St George's University of London
Cranmer Terrace
London
United Kingdom
SW17 0RE
+44 (0)2087254851
pheath@sgul.ac.uk

Type(s)
Public

Contact name
Dr Study Team

Contact details
-
-
United Kingdom
-
-
lionmenb@sgul.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2021-001561-21

Integrated Research Application System (IRAS)
265199

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 49304, IRAS 265199

Study information

Scientific Title
Phase IV randomisation study of different Men B vaccine primary immunisation schedules in UK infants

Acronym
LION MenB

Study objectives

This study is being undertaken to compare the immune responses of UK infants who receive their routine immunisations alongside two different 4CMenB primary immunization schedules. Completing the primary 4CMenB schedule by 3 months could provide infants earlier protection against MenB disease since cases peak at 5 months of age and remain high in the second half of the first year before starting to decline (Ladhani et al., 2012). If this clinical trial shows comparable immunogenicity for the main 4CMenB antigens using the two different schedules, then the results could change UK national immunization policy to offer infants earlier protection against this devastating disease and could potentially be adopted by other countries worldwide.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 25/06/2021, North East - Newcastle & North Tyneside 1 Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, United Kingdom; +44 (0)2071048285; newcastlenorthtyneside1.rec@hra.nhs.uk), ref: 21/NE/0093

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

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Meningococcal disease B

Interventions
This study is an open-label, phase IV study which will recruit 220 infants from suitable participating sites.

Recruitment: A variety of recruitment strategies will be used by the different participating centres to recruit eligible participants. Some centres may choose to advertise the study on institutional websites or newsletters, or on posters in the hospital or the community (e.g. in GP practices). Eligible infants may also be identified through the local child health information systems (CHIS) and initially contacted by post. Families expressing an interest in participating in the study by post, email, text, or phone will then be approached by the study team.

Consent: Parents will be asked to give their informed consent to their infant's participation in the study when they have had time to consider the study and ask questions. Consent will be taken at the first study visit.

Randomisation: Infants will be randomised to a treatment group at the first study visit.

Visits will take place either in hospital/university or at home depending on family preference and local strategy.

Visit 1:
Contact details, demographic information, and medical history, including medication, will be collected at this visit and the appropriate CRFs completed. A brief medical examination at this visit will be performed. The infant's temperature will be taken at this visit (preferred route axillary) to confirm that the infant is well for vaccination.

All participants will receive the same vaccinations at this visit:
DtaP/IPV/Hib/HepB, 4CMenB, Rotavirus.

All infants will be observed for 20 minutes following vaccination to ensure they have no adverse reaction. Parents will have the diary (paper or electronic e-diary) explained to them and information will be given as to how to contact the study team if this is needed.

Visit 2 (3 months)
The parents will be asked about the health of the child in the period since their previous vaccinations, the diary will be collected and discussed with the parents. Parents will be asked about any concomitant medication. The infant's temperature will be taken at this visit (preferred route axillary) to confirm that the infant is well for vaccination.

Infants will receive vaccinations according to their study group:
Group 1: DtaP/IPV/Hib/HepB, 4CMenB, Rotavirus.
Group 2: DtaP/IPV/Hib/HepB, PCV13, Rotavirus.

All infants will be observed for 20 minutes following vaccination to ensure they have no adverse reaction. Diary completion instructions will be confirmed at this visit and study staff will check that parents are aware of how to contact the study team.

Visit 3 (4 months)
The parents will be asked about the health of the child in the period since their previous vaccinations, the diary will be collected and discussed with the parents. Parents will be asked about any concomitant medication. The infant's temperature will be taken at this visit (preferred route axillary) to confirm that the infant is well for vaccination.

Infants in Group 1 will have blood taken at this visit. This will ideally be a venous sample, but if this is not possible blood may be obtained by capillary sampling.

Infants will receive vaccinations according to their study group:
Group 1: DtaP/IPV/Hib/HepB, PCV13.
Group 2: DtaP/IPV/Hib/HepB, 4CMenB.

All infants will be observed for 20 minutes following vaccination to ensure they have no adverse reaction.

Diary completion instructions will be confirmed at this visit and study staff will check that parents are aware of how to contact the study team.

Visit 4 (5 months) – Only Group 2
The parents will be asked about the health of the child in the period since their previous vaccinations, the diary will be collected and discussed with the parents. Parents will be asked about any concomitant medication.

Infants in Group 2 will have blood taken at this visit. This will ideally be a venous sample, but if this is not possible blood may be obtained by capillary sampling.

Visit 5 (12 months)
The parents will be asked about the health of the child in the period since their previous vaccinations. Parents will be asked about any concomitant medication. The infant's temperature will be taken at this visit (preferred route axillary) to confirm that the infant is well for vaccination.

All infants will have blood taken at this visit. This will ideally be a venous sample, but if this is not possible blood may be obtained by capillary sampling.

All participants will receive the same vaccinations at this visit:
MCC-TT/Hib-TT, PCV13, 4CMenB, MMR.

All infants will be observed for 20 minutes following vaccination to ensure they have no adverse reaction.

Diary completion instructions will be confirmed at this visit and study staff will check that parents are aware of how to contact the study team.

Visit 6 (13 months)
The parents will be asked about the health of the child in the period since their previous vaccinations, the diary will be collected and discussed with the parents. Parents will be asked about any concomitant medication.

All infants will have blood taken at this visit. This will ideally be a venous sample, but if this is not possible blood may be obtained by capillary sampling.

Intervention Type
Biological/Vaccine

Phase
Phase IV

Drug/device/biological/vaccine name(s)
4CMenB, Bexsero and PCV13, Prevenar

Primary outcome(s)
1. The immunological responses of UK infants between two different primary immunisation schedules of 4CMenB (2 and 3 versus 2 and 4 months of age):
1.1. Antibody geometric mean titers (GMTs) against relevant 4CMenB antigens (fHbp, NadA and PorA) measured by serum bactericidal assay using human complement (hSBA) 4 weeks after 2nd dose of 4CMenB (at 4 months of age for Group 1 versus 5 months of age for Group 2).
1.2. The proportion of infants with antibody titers ≥ 1:4 against relevant 4CMenB antigens (fHbp, NadA and PorA) measured by hSBA assessed at 4 weeks after 2nd dose of 4CMenB (at 4 months of age for Group 1 versus 5 months of age for Group 2)

Key secondary outcome(s))
1. To compare the persistence of immunological responses to 4CMenB at 12 months chronological age after two different primary immunisation schedules of 4CMenB (2 and 3

versus 2 and 4 months of age).
1.1. GMTs against relevant 4CMenB antigens (fHbp, NadA and PorA) measured by hSBA at 12 months of chronological age (pre-booster).
1.2. The proportion of infants with antibody titers ≥ 1:4 against relevant 4CMenB antigens (fHbp, NadA and PorA) measured by hSBA at 12 months of chronological age (pre booster).
2. To compare the immunological responses one month after the 12-month 4CMenB booster in infants who received two different primary immunisation schedules of 4CMenB (2 and 3 versus 2 and 4 months of age).
2.1. GMTs against relevant 4CMenB antigens (fHbp, NadA and PorA) measured by hSBA at 13 months of chronological age (4 weeks post-booster).
2.2. The proportion of infants with antibody titers ≥ 1:4 against relevant 4CMenB antigens (fHbp, NadA and PorA) measured by hSBA at 13 months of chronological age (4 weeks post booster).
3. To compare the persistence of immunological responses to PCV13 at 12 months chronological age after two different primary immunisation schedules of PCV13 (3 versus 4 months of age).
3.1. Serotype specific GMCs against PCV13 serotypes at 12 months of age (pre PCV13 booster).
3.2. The proportion of infants with serotype-specific GMCs ≥ 0.35 µg/ml against PCV13 serotypes at 12 months of age (pre PCV13 booster).
4. To compare the immunological responses to the booster dose of PCV13 given at 12 months in infants who received two different primary immunisation schedules of PCV13 (3 versus 4 months of age).
5.1 Serotype specific GMCs against PCV13 serotypes at 13 months of age (4 weeks post PCV13 booster).
5.2. The proportion of infants with serotype-specific GMCs ≥ 0.35 µg/ml against PCV13 serotypes at 13 months of age (4 weeks post PCV13 booster).

Completion date
31/10/2024

Eligibility

Key inclusion criteria
1. Term infants born at ≥37 weeks gestation
2. Aged ≥56 days to ≤70 days on the day of the first visit
3. No contraindications to vaccination according to the 'Green Book'
4. Willing and able to comply with study procedures
5. Written informed consent

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Child

Lower age limit
56 days

Upper age limit
70 days

Sex
All

Total final enrolment
221

Key exclusion criteria
1. Contraindication to vaccination according to the Green Book
2. Life-limiting congenital abnormality or condition
3. Prior diagnosis of an immunodeficiency syndrome
4. Previous vaccination against meningococcal disease
5. History of Neisseria meningitidis infection, confirmed either clinically, serologically, or microbiologically
6. Considered unlikely to complete the expected follow up until the end of the study
7. Child in care

Date of first enrolment
01/07/2021

Date of final enrolment
22/11/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St George's University Hospitals NHS Foundation Trust
Cranmer Terrace
London
United Kingdom
SW17 0RE

Study participating centre
John Radcliffe Hopsital
Headley Way
Oxford
United Kingdom
OX3 9DU

Study participating centre

Royal Cornwall Hospital
Royal Cornwall Hospitals NHS Trust
Treliske
Truro
United Kingdom
TR1 3LJ

Study participating centre
Portsmouth Hospitals NHS Trust
Southwick Hill Road
Cosham
Portsmouth
United Kingdom
PO6 3LY

Study participating centre
Sheffield Children's NHS Foundation Trust
Western Bank
Sheffield
United Kingdom
S10 2TH

Study participating centre
Southampton General Hospital
University of Southampton and University Hospital Southampton NHS Foundation Trust
Tremona Road
Southampton
United Kingdom
SO16 6YD

Sponsor information

Organisation
St George's, University of London

ROR
https://ror.org/040f08y74

Funder(s)

Funder type
Industry

Funder Name
GlaxoSmithKline; Grant Codes: 213329

Alternative Name(s)
GlaxoSmithKline plc., GSK plc., GlaxoSmithKline plc, GSK

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

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?
Basic results	version 1.0	06/10/2025	08/10/2025	No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	version V2.0	01/06/2021	15/07/2021	No	Yes
Participant information sheet	version 4.0		03/06/2025	No	Yes
Protocol file	version V2.0	02/06/2021	15/07/2021	No	No
Protocol file	version 10	10/09/2024	03/06/2025	No	No
Statistical Analysis Plan	version 1.0	04/07/2024	08/10/2025	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes