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The 6-in-1 Vaccine Study

Submission date
04/03/2019

Recruitment status
No longer recruiting

Registration date
12/03/2019

Overall study status
Completed

Last Edited
06/01/2023

Condition category
Infections and Infestations

[X] Prospectively registered

[X] Protocol

[X] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
In 2017 the hepatitis B vaccine was added to the UK routine immunisation programme. An infection with the hepatitis B virus can cause severe inflammation of the liver and can cause severe long-term damage to the liver. To allow the introduction of the Hepatitis B vaccine to the UK's childhood immunisation schedule without increasing the number of vaccine injections, the previously used '5-in-1' vaccine was replaced by a '6-in-1' vaccine which protects against diphtheria, tetanus, poliovirus, whooping cough (pertussis), hepatitis B and haemophilus influenza B (Hib). There are two licensed '6-in-1' vaccines available and these are called Infanrix-Hexa and Vaxelis. Infanrix-hexa is currently used routinely in the UK. It is known from previous studies that this vaccine works well with the other vaccines in the UK schedule, including the meningococcal B vaccine (MenB, Bexsero), in that it is able to induce a good immune response to all vaccine components and has an acceptable side effect profile. At present this information is not available for the Vaxelis vaccine, and it is important to check this as the components of Vaxelis are slightly different from Infanrix hexa. If it can be shown that immunisation with Vaxelis creates a similar response from the immune system to Infanrix hexa and is just as safe when given in the immunisation schedule along with the MenB vaccine, the NHS will be able to use either vaccine for children in the UK. Having the option to use either of the 6 in 1 vaccines is important to ensure all children continue to be protected even if one vaccine becomes temporarily unavailable. To do this the researchers will enrol 240 infants, 8 to 13 weeks of age, and randomly allocate them to receive either 6 in 1 Infanrix-hexa or Vaxelis along with the routine infant UK immunisation schedule. Blood tests will be taken at 5 and 13 months of age to check the immune responses to these vaccines.

Who can participate?
Infants aged 8-13 weeks who are due to receive their primary immunisations can be enrolled in this study if their parent(s)/legal guardian(s) are over 16 years of age and willing to consent to enrol their child in the study and comply with the study protocol. These infants must live in the Thames Valley where the study is being conducted and have been born ≥ 37 weeks gestational age. Infants with confirmed immunodeficiency, previous anaphylaxis (allergic reaction) to any constituent or excipient in one of the vaccines, a latex allergy or another significant disease which might put the participant at risk will not be eligible to participate in the study.

What does the study involve?
The study involves six visits over approximately 11 months. All study visits are conducted at the

participant's home or at a convenient location. Four of the visits (at 2, 3, 4 and 12 months) involve administering the routine infant immunisations and either Infanrix-hexa or Vaxelis depending on which group the infant is randomly allocated to. Two of the visits (at 5 and 13 months) involve a blood test. Participants are provided with numbing cream to apply to the skin before this procedure to minimise any pain or discomfort. After the vaccine visits parents/legal guardians are asked to complete a 5-day symptom diary.

What are the possible benefits and risks of participating?
The benefits include participants receiving their routine vaccinations in their own home up until 12 months of age. These visits are conducted by trained nurses and doctors and are arranged at a convenient time for the families. The researchers will also test the immune response to the vaccines received, and if any child were to have an inadequate immune response to the Hib component of the 6-in-1 vaccines they arrange for a booster dose of the appropriate vaccine. This information would not otherwise be available. All vaccines (as with any medicine) can sometimes cause side effects. The most common side effects include crying, lethargy, fever, reduced appetite, vomiting and redness/swelling and pain at the site of the injection. Very rarely (less than 1 in 1 million cases) a vaccination can cause a severe allergic reaction (anaphylaxis), which typically occurs soon after vaccine administration. The study team will ensure all participants are observed for 15 minutes after vaccination and are trained and have equipment to treat this should it occur. The blood tests can sometimes cause temporary bruising or tenderness. Discomfort at the time of sampling will be reduced by using anaesthetic cream to numb the skin.

Where is the study run from?
The study is being coordinated and carried out by the Oxford Vaccine Group (UK)

When is the study starting and how long is it expected to run for?
Recruitment to the study will start from March 2019 and continue until October 2019. The trial end date is September 2021.

Who is funding the study?
Funding has been received from MCM, the vaccine manufacturer of Vaxelis

Who is the main contact?
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2018-003451-38

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
40864

Study information

Scientific Title
Immunogenicity and reactogenicity of concomitantly administered hexavalent and Group B meningococcal vaccines in infancy

Study objectives
This study involves a comparison of the immunogenicity and reactogenicity of two licensed 6 in 1 vaccines, which protect against diphtheria, tetanus, pertussis, polio, haemophilus influenza B (Hib) and hepatitis B. The first 6 in 1 vaccine is Infanrix-hexa, developed by GlaxoSmithKline, licensed in Europe and routinely used in the UK routine immunisation schedule at 2, 3 and 4 months of age. This vaccine has been widely used internationally with data to support its efficacy and safety. The second 6 in 1 vaccine is Vaxelis, developed jointly by Merck/MSD and Sanofi Pasteur, and licensed in Europe.

The study hypothesis is that Vaxelis is non-inferior to Infanrix-hexa when used as part of the UK routine immunisation schedule at 2, 3 and 4 months of age.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 08/02/2019 by South Central - Oxford A Research Ethics Committee, Bristol Research Ethics Committee Centre, Whitefriars, Level 3 Block B, Lewins Mead, Bristol, BS1 2NT, Tel: +44 (0) 207 104 8041, Email: nrescommittee.southcentral-oxforda@nhs.net, ref: 19/SC/0052

Study design
Randomised; Both; Design type: Prevention, Vaccine, Cross-sectional

Primary study design
Interventional

Study type(s)

Prevention

Health condition(s) or problem(s) studied
Vaccination against diphtheria, tetanus, pertussis, polio, haemophilus influenza B (Hib) and hepatitis B virus (HBV)

Interventions
This study will be an open-label, non-inferiority randomised clinical trial conducted by the Oxford Vaccine Group (OVG). 240 healthy infants, aged between 8 and 13+0 weeks will be recruited in the UK. They will be randomised 1:1 to receive either Infanrix-hexa or Vaxelis (both 6 in 1 vaccines) alongside their routine immunisations resulting in 120 infants in each group.

There will be six visits during the study including four vaccine visits and two blood tests. These visits will take place in participant's homes or a suitable, convenient location. Participation will last for 11 months (from enrolment at 8 weeks minimum to the last blood test at 13 months of age).

Visit 1 (2 months of age): Participants are enrolled after written informed consent from their parents or legal guardians. They will be randomised into one of two groups and will receive PCV13, Men B, rotavirus (as per routine schedule) and either Infanrix-hexa or Vaxelis
Visit 2 (3 months of age): Participants receive rotavirus (as per routine schedule) and either infanrix-hexa or Vaxelis
Visit 3 (4 months of age): Participants receive PCV13, MenB vaccines (as per routine schedule) and either Infanrix-hexa or Vaxelis
Visit 4 (5 months of age): Blood sampling (involves the use of anaesthetic cream to numb the skin)
Visit 5 (12 months of age): Participants receive their routine vaccinations (Hib-MenC, PCV13, MMR, MenB)
Visit 6 (13 months of age): Blood sampling

After each vaccine visit, parents/legal guardians will be asked to complete a 5-day symptom diary to document any reactions following vaccination.

Intervention Type
Biological/Vaccine

Phase
Not Applicable

Primary outcome(s)
The immunogenicity of the Haemophilus influenza type B (Hib) component of 6-in-1 Infanrix-hexa (IH) and 6-in-1 Vaxelis (V) when co-administered with 4CMenB in the UK routine immunisation schedule at 5 months of age; measured using anti-PRP (Hib) IgG concentration by ELISA at 5 months of age
(4-6 weeks after the administration of the participant's 3rd 6-in-1 vaccine)

Key secondary outcome(s))
1. The anti-PRP (Hib) IgG concentrations measured by ELISA at 13 months of age (1 month after the administration of Hib-MenC at 12 months of age) in participants primed with 6-in-1 (IH) and 6-in-1 (V); Timepoint(s): 13 months of age (4-6 weeks after the participant has received their Hib-MenC vaccine at 12 months of age)

2. The immunogenicity of the other antigens in the routine UK infant immunisation schedule at 5 and 13 months of age in participants receiving 6-in-1 (IH) and 6-in-1 (V), measured using:
2.1. IgG concentrations measured at 5 and 13 months of: 1) Diptheria toxoid 2) Tetanus toxoid 3) Hepatitis B 4) Vaccine- serotype pneumococcal capsule antigens 5) Pertussis antigens 6) Poliovirus neutralising antibodies
2.2. Serum bactericidal titres at 5 and 13 months of: 1) 3 reference serogroup B meningococcal strains 2) Serogroup C meningococcus; Timepoint(s): At 5 months (4-6 weeks after completion of primary immunisations) and 13 months (4-6 weeks after receiving the booster Hib-MenC vaccine)
3. The reactogenicity of 6-in-1 (IH) and 6-in-1 (V) when administered in the routine UK immunisation schedule, determined by any solicited local or systemic adverse events within 5 days of each vaccination visit; Timepoint(s): For 5 days after every vaccination visit (2, 3, 4 and 12 months)

Completion date
30/09/2021

Eligibility

Key inclusion criteria
For recruitment to all study groups, participants MUST FULFILL each of the below criterion:
1. Parents/legal guardians are over 16 years of age, and are willing and able to consent to enrol their child/children in the study
2. Parents/legal guardians able to comply with the requirements of the trial protocol and have internet access for the duration of the study
3. Parents/legal guardians are willing to allow their General Practitioner, health visitor and consultant, if appropriate, to be notified of participation in the trial
4. Participants born at greater than or equal to 37 weeks gestation
5. Participants are due to receive their primary immunisations, aged 8 to 13 weeks (i.e. the day the child turns 13 weeks of age) at enrolment

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Neonate

Sex
All

Total final enrolment
194

Key exclusion criteria
The participant may not enter the trial IF ANY of the following apply:
1. Parents/legal guardians of children are on the delegation log of this study
2. Confirmed or suspected immunodeficiency
3. Fulfil any of the contraindications to vaccination as specified in The Green Book

4. Confirmed anaphylactic reaction/s to any constituent/s or excipient/s of the vaccine(s)
5. Confirmed anaphylactic reaction to neomycin, streptomycin or polymyxin B (which may be present in trace amounts in the tetanus vaccine), kanamycin, histidine, sodium chloride or sucrose (which may be present in trace amounts in the Meningococcal B vaccine) or to gelatin (which may be present in trace amounts in the MMR vaccine)
6. Latex hypersensitivity (the syringe cap of the Meningococcal B vaccine, Bexsero may contain natural rubber latex)
7. Any other significant disease or disorder which, in the opinion of the Investigator, may either put the participants at risk because of participation in the trial, or may influence the result of the trial, or the participant's ability to participate in the trial
8. Thrombocytopenia or any other bleeding disorders.
9. Child is currently participating in another interventional clinical trial

Temporary exclusions for all groups
For a vaccination visit only (visit 1, 2, 3, and 5)
1. Administration of any other vaccine within 14 days prior to study vaccines
2. Scheduled elective surgery, planned admission or other procedures requiring general anaesthesia within 7 days of receiving a vaccine
3. Febrile illness (axillary temperature > = 38.0°C) within the previous 24 hours or on the day of vaccination

For a blood sampling visit only (visit 4 and 6)
Have received parenteral or oral antibiotics within the last 7 days

Date of first enrolment
01/07/2019

Date of final enrolment
21/04/2020

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Oxford Vaccine Group
Centre for Clinical Vaccinology and Tropical Medicine (CCVTM)
Churchill Hospital
Old Road
Headington
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United Kingdom
OX3 7LE

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Industry

Funder Name
MCM Vaccine BV

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available. Summary data only will be published. No identifiable personal data will be used.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/01/2023	05/01/2023	Yes	No
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 4.0	17/08/2020	06/10/2022	No	No
Statistical Analysis Plan	version 2.0	02/07/2021	06/10/2022	No	No