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Portugal meningococcal B vaccine (menB) effectiveness study

Submission date
15/05/2019

Recruitment status
No longer recruiting

Registration date
21/05/2019

Overall study status
Completed

Last Edited
02/12/2020

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
Meningococcal group B bacteria are a serious cause of life-threatening infections worldwide, including meningitis and blood poisoning. Developing a vaccine against the most common cause (type B) has been a priority but technically very difficult. Because the disease is so rare it has not been possible to carry out the standard type of study (randomised controlled trial) to prove that these vaccines actually protect people against the disease, instead licensure was based on the pattern of antibodies produced and predicted coverage of the commonest strains of Meningococcal disease.

Who can participate?
All children and adolescents diagnosed with invasive meningococcal disease in Portugal between October 2014 and March 2019 inclusive will be eligible for inclusion. For each case, 2 - 4 age and location matched controls will be identified.

What does the study involve?
Examination of medical records including immunisation history of cases and matched controls

What are the possible benefits and risks of participating?
None

Where is the study run from?
Coimbra, Portugal with participation of multiple hospitals in Portugal

When is the study starting and how long is it expected to run for?
April 2018 to September 2019

Who is funding the study?
The investigators and clinicians providing data are undertaking the study as part of their professional duties. No external funding has been sought or obtained.

Who is the main contact?
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
1.3

Study information

Scientific Title
Case control study to evaluate the effectiveness of the 4CMenB vaccine for protection against invasive meningococcal disease caused by group B Neisseria meningitidis in Portugal

Acronym
PT-BEST

Study objectives
Current study hypothesis as of 03/07/2019:
That rates of full immunisation per licensed schedule for age with Bexsero among children presenting with culture and/or PCR-proven meningococcus group B invasive disease will be significantly lower than among age and gender-matched controls presenting at the same hospitals at around the same time with conditions unrelated to meningococcal infection.

Previous study hypothesis:
That rates of full immunisation per licensed schedule for age with Bexsero will be significantly higher among children presenting with culture and/or PCR-proven meningococcus group B invasive disease will be significantly lower than among age and gender-matched controls presenting at the same hospitals at around the same time with conditions unrelated to meningococcal infection.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 14/05/2018, Ethics Committee from Centro Hospitalar e Universitário de Coimbra (Centro Hospitalar Universitário de Coimbra, Serviço de Doenças Infecciosas, Praceta Mota Pinto, 3000-075 Coimbra, Portugal; +351 239 400 402; jscunha@fmed.uc.pt), ref: CHUC-099-17
National Data Protection authorisation number 306/ 2018

Study design
Multi-centre density case-control study

Primary study design
Observational

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Neisseria meningitidis

Interventions
All children and adolescents diagnosed with invasive meningococcal disease in Portugal between October 2014 and March 2019 inclusive will be eligible for inclusion. For each case, 2-4 age and location matched controls will be identified.

The study involves examination of medical records and extraction of anonymised information.

Intervention Type
Biological/Vaccine

Phase
Phase IV

Drug/device/biological/vaccine name(s)
4CMenB (Bexsero®)

Primary outcome(s)
Effectiveness of the 4CMenB vaccine for protection against invasive meningococcal disease caused by group B Nm in Portugal (partially immunized children considered unvaccinated). Data are extracted from the medical records of cases and matched controls including immunisation history.

Key secondary outcome(s))
1. Effectiveness of the 4CMenB vaccine for protection against invasive meningococcal disease caused by group B Nm in Portugal when partially vaccinated children are excluded from analysis.
2. Effectiveness of one or more doses of 4CMenB vaccine for protection against invasive meningococcal disease caused by group B Nm in Portugal (i.e. partially vaccinated children included in analysis but considered to be vaccinated).
3. Effectiveness of the 4CMenB vaccine, using the 3 approaches summarized above, for protection against all-cause invasive meningococcal disease in Portugal.
Standardised data are extracted from the medical records of cases and matched controls including immunisation history.

Completion date
01/09/2019

Eligibility

Key inclusion criteria

Case participant inclusion criteria:
1. Age > 2 months and 14 days and < 18 years
2. Meningococcal invasive disease confirmed by culture or PCR in a normally-sterile biological sample (blood, CSF, pleural fluid, joint fluid, other)
3. Resident in Portugal at time of presentation
4. Eligible to have received and responded to 4CMenB (age at least 2 months and 14 days, absence of vaccine contraindication)
5. Available information about vaccine status for 4CMenB, MenC and MenACWY from central immunisation records database.

Control participant inclusion criteria:
6. Born within specified time period of matched case participant. If case is less than < 2 years old, controls have to have been born +/- 14 days (minimum age of 2 months and 14 days); if cases are aged 2-5 years, controls have to have been born +/- 60 days, if cases are aged >= 5 years or more, controls have to have been born +/-90 days
7. Eligible to have received and responded to 4CMenB (aged at least ≥ 2 months and 14 days, absence of vaccine contraindication)
8. Living in the same district as the case
9. Same gender as the case
10. Presenting to the same hospital, within the same week of the case (up to 14 days before or after the day when the case was observed), with an illness that was clearly not invasive meningococcal disease (i.e. not meningitis, septicaemia or pyrexia of unknown origin)
11. Available information about vaccine status for 4CMenB, MenC and MenACWY from central immunisation records database

Vaccination status:
For the primary analysis, children who have received the appropriate number of vaccine doses for their age will be considered vaccinated – i.e. those aged 4 to 15 months who have had 2 or more vaccine doses with the second dose at least 14 days before presentation and those aged 16 months or more who have had either 2 or 3 doses before 1 year of age and one dose after 1 year of age (with the booster dose at least 14 days before presentation) or who have had at least 2 vaccine doses after the first birthday (with the second dose at least 14 days before presentation). All children who have received fewer than the appropriate number of doses as defined above will be considered unvaccinated. Children too young to have received two priming doses with the second at least 14 days before presentation (i.e. less than 4 months and 14 days old) will not be included in this analysis.

Participant type(s)

Mixed

Healthy volunteers allowed

No

Age group

Child

Lower age limit

2 months

Upper age limit

18 years

Sex
All

Total final enrolment
98

Key exclusion criteria
1. Unknown vaccine status from centralised immunisation records database
2. Belonging to a risk group for meningococcal invasive disease: asplenia, immunodeficiency including but not restricted to complement deficiency or on treatment with Eculizumab
3. History of invasive meningococcal disease
4. Recent known or suspected contact with a case of meningococcal invasive disease

Date of first enrolment
01/04/2019

Date of final enrolment
01/09/2019

Locations

Countries of recruitment
Portugal

Study participating centre
Hospital Pediátrico - Centro Hospitalar e Universitário de Coimbra
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Study participating centre
Centro Materno Infantil do Norte
Largo da Maternidade de Júlio Dinis
Porto
Portugal
4050-651

Study participating centre
Hospital S. Pedro - Centro Hospitalar Trás-os-Montes e Alto Douro
R. dos Lagoeiros 43

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Portugal
5000-508

Study participating centre
Centro Hospitalar da Póvoa do Varzim/Vila do Conde
Largo da Misericórdia
Póvoa do Varzim
Portugal
4490-421

Study participating centre
Centro Hospitalar de Vila Nova de Gaia
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Portugal
4434-502

Study participating centre
Centro Hospitalar Barreiro Montijo
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2830-003

Study participating centre
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4200-319

Study participating centre
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Study participating centre
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1169-045

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Study participating centre
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Sponsor information

Organisation
Sociedade Portuguese de Pediatria

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded.

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a publically available repository
University of Bristol Research Data Repository
data.bris
https://www.bristol.ac.uk/staff/researchers/data/accessing-research-data/
Anonymised dataset used to calculate effectiveness (both primary and secondary endpoints) including age in months, date of presentation and immunisation history of cases and controls.

Data will become available when study is published and will be available indefinitely.
Data will be open access and users will be able to download and analyse it in whatever way they wish.
This study was a case-control study involving access to personally identifiable information only by managing clinical teams and no identifiers were provided to researchers running the study and undertaking the analysis.
It was not feasible nor deemed necessary by the ethical committee and data protection regulators to obtain consent from cases or controls.
There are no ethical or legal restrictions.

IPD sharing plan summary

Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/12/2020	02/12/2020	Yes	No