Clinical trial results:
A pilot study evaluating the influence of chronobiology on Hepatitis B responses in health-care students attending the University of Salford

Summary

EudraCT number	2014-003756-32
Trial protocol	GB
Global end of trial date	10 April 2017

Results information

Result version number	v1 (current)
This version publication date	07 February 2020
First version publication date	07 February 2020

Trial information

Trial identification

Sponsor protocol code	R03930

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	REC reference: 15/EE/0119

Notes:

Sponsors

Sponsor organisation name	Manchester University NHS Foundation Trust
Sponsor organisation address	29 Grafton Street, Manchester, United Kingdom, M13 9WU
Public contact	Dr Lynne Webster, Head of the Research Office, Manchester University NHS Foundation Trust, +44 01612764125, lynne.webster@mft.nhs.uk
Scientific contact	Dr Lynne Webster, Head of the Research Office, Manchester University NHS Foundation Trust, +44 01612764125, lynne.webster@mft.nhs.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 April 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 April 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Our principal research question is: 'How does the time of day of first vaccination affect the immune response to Hepatitis B vaccine?'

Our primary objectives in the study are

•Establish the procedures for a definitive investigation into time of day and vaccine responses.
•Evaluate the difference in Hepatitis B antibody (Anti-HBs) titres of morning, afternoon and evening vaccination groups after 3 doses of Hepatitis B vaccination.

Protection of trial subjects:

1. Additional blood tests: Trial subjects will undergo additional blood tests. All potential participants will be informed of this prior to recruitment and only those who are willing for the same will be recruited into the trial. These blood tests will be an additional point of contact with the trial personnel.
2. Morning vs evening vaccination: Participants will be required to attend their first appointment within a narrow time window during the morning and late in the evening. This will be discussed in advance with participants. Reasonable travel expenses in order to attend study visits will be reimbursed.
3. Collection of saliva sample: Participants will be expected to provide saliva samples on the night before and immediately on waking the day of vaccination. This will be detailed in the PIL and discussed at the screening visit. Samples are provided by the subject at their home and does not require any additional vaccination.
4. Completion of questionnaires: Potential subjects will be asked to fill in questionnaires (Munich Chronotype Questionnaire and sleep diary). Participants will be informed of the need to do this prior to enrolment and only those prepared to do so will be enrolled.

Background therapy:

N/A

Evidence for comparator:

There is no placebo or control group for this trial.

Actual start date of recruitment	11 August 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 99999

Worldwide total number of subjects	99999
EEA total number of subjects	99999

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	99999
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First year nursing students who were admitted in the spring term and who will require vaccinations prior to entry into the course will be provided information (written and verbal) about the study by Occupational health. Once subjects have expressed interest in the study, details of participants will be provided to the research team with consent.

Pre-assignment

Screening details:

Inclusion:
- Age older than or equal to 16 years
- University student in good health who consent to complete sleep diary,Munich chronotype questionnaire and attend am/pm
appointments

Period 1

Period 1 title	Hepatitis B vaccination (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[1]

Blinding implementation details:

Participants are randomised to receive the Hepatitis B vaccine either in the morning, afternoon or evening. Analysis of the blood samples was conducted by a blinded member of staff.

Arms

Arm title	Hepatitis B vaccination

Arm description:

Participants will receive Engerix B® 20 micrograms/1 ml, give as 3 doses of 20 micrograms at 0, 1 and 6 months.

Arm type	IMP given in morning
Investigational medicinal product name	Engerix B® 20 micrograms/1 ml
Investigational medicinal product code	
Other name	PL 10592/0165
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses of 20 micrograms given at 0,1 and 6 months. The vaccine stimulates the production of Anti Hepatitis B surface antigen antibodies and other components of the immune system. AntiHBs antibody concentrations > 10 IU/l correlate with protection to HBV infection.

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Analysis of blood samples was to be performed by a blinded member of staff. No other staff member was blinded. It was not possible for the patient to be blinded as the randomisation was for time of day to take the drug.

Number of subjects in period 1	Hepatitis B vaccination
Started	99999
Visit 1 - Randomisation & baseline	99999
Visit 2 - Vaccination & blood test	99999
Visit 3 - Vaccination & blood test	99999

Visit 4 - Vaccination & blood test	99999
Visit 5 - Blood test	99999
Completed	99999

Baseline characteristics

Reporting groups

Reporting group title	Hepatitis B vaccination

Reporting group description: -

Reporting group values	Hepatitis B vaccination	Total	
Number of subjects	99999	99999	
Age categorical			
99999			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	99999	99999	
From 65-84 years	0	0	
85 years and over	0	0	
99999	0	0	
Age continuous			
99999			
Units: years			
arithmetic mean	99		
standard deviation	± 99	-	
Gender categorical			
Units: Subjects			
Female	99999	99999	
Male	0	0	

Subject analysis sets

Subject analysis set title	99999
Subject analysis set type	Full analysis

Subject analysis set description:
99999

Reporting group values	99999		
Number of subjects	99999		
Age categorical			
99999			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			

Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over 99999			
Age continuous			
99999			
Units: years arithmetic mean standard deviation	 99 ± 99		
Gender categorical Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	Hepatitis B vaccination

Reporting group description:

Participants will receive Engerix B® 20 micrograms/1 ml, give as 3 doses of 20 micrograms at 0, 1 and 6 months.

Subject analysis set title	99999
Subject analysis set type	Full analysis

Subject analysis set description:

99999

Primary: To establish the procedures we will use in a definitive study of circadian rhythm, the time of day and vaccine responses

End point title	To establish the procedures we will use in a definitive study of circadian rhythm, the time of day and vaccine responses[1]

End point description:

99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants enrolled in the trial.

End point type	Primary

End point timeframe:

99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants enrolled in the trial.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No subjects were enrolled in the trial hence results are not available

End point values	Hepatitis B vaccination			
Subject group type	Reporting group			
Number of subjects analysed	99999[2]			
Units: 99999	0			

Notes:

[2] - No subjects were enrolled in the trial hence results are not available

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

This study concerns an IMP prescribed within its licensed indication, dosage and form for clinical purposes. Subjects will be questioned, at visit 3 only, for reports of Serious Adverse Events.

Adverse event reporting additional description:

These events will be reported to the Sponsor, the MHRA and the REC in accordance with the regulatory guidelines. An Annual Safety Report will be submitted. We do not propose to monitor or record Adverse Event or Adverse Reaction data. No AEs occurred within this trial as it was terminated prior to screening/recruitment.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	0

Frequency threshold for reporting non-serious adverse events: 0 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No patients were screened or entered onto the trial.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 June 2016	A. Protocol amendment: The protocol has been amended to include the following: -Change in Vaccine schedule: The University of Salford study site is adopting the accelerated schedule for Hepatitis B vaccination. Hence the study timeline for vaccination will change from 0, 1 and 6 months to 0, 1 and 2 months. -Study groups and numbers: In addition to morning and evening vaccination, an additional time point to reflect current standard of care (1-2pm) has been added. Study group numbers have been revised from 30 in each group to 20 in each group with a total of 60 subjects. -Additional blood sample: An additional blood sample will be collected opportunistically when subject attends for third dose of the vaccine, hence current venepuncture schedule is 0, 1, 2 and 3 months. B. Patient Information Leaflet and Consent forms have been revised to reflect the above changes C. We have added a section to the protocol to cover adverse event reporting. REC favourable opinion was issued 04/07/2016.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants enrolled in the trial

Notes: