Clinical trial results:
Exploring novel mechanisms of vaccine failure and induction of pulmonary immunity following live attenuated influenza vaccination in HIV infected and uninfected individuals: a pilot study.

Summary

EudraCT number	2014-001924-31
Trial protocol	GB
Global end of trial date	15 June 2015

Results information

Result version number	v1 (current)
This version publication date	27 November 2019
First version publication date	27 November 2019
Summary attachment (see zip file)	Primary Endpoint Data (Primary Endpoint Data.docx)

Trial information

Trial identification

Sponsor protocol code	STH18166

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02266992
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sheffield Teaching Hospitals NHS Foundation Trust
Sponsor organisation address	Trust Headquarters, 8 Beech Hill Road, Sheffield, United Kingdom, S10 2SB
Public contact	Dr Dipak Patel, Sheffield Teaching Hospitals NHS Foundation Trust, sth.ResearchAdministration@nhs.net
Scientific contact	Dr Dipak Patel, Sheffield Teaching Hospitals NHS Foundation Trust, sth.ResearchAdministration@nhs.net

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	15 June 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 June 2015
Global end of trial reached?	Yes
Global end of trial date	15 June 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Do HIV infected individuals have distinct differential early gene expression profiles following intra-nasal live attenuated
influenza vaccine, when compared to age and sex matched HIV negative subjects, thus providing insights into the aberrant immunological response to live vaccines modulated by HIV infection?

Protection of trial subjects:

All participants were given a participant information sheet to read and consider for at least 24 hours before attending for a screening visit for the study. Participants were reviewed by a clinician, or an experienced study nurse who was delegated to this task, according to the strict inclusion and exclusion criteria. All participants give written informed consent prior to enrolment to the study

Background therapy:

Nil therapy

Evidence for comparator:

N/A

Actual start date of recruitment	05 September 2014
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: 28
Worldwide total number of subjects	28
EEA total number of subjects	28

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)	28

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Two groups: HIV-uninfected subjects and HIV-infected subjects. Recruited from Sheffield, UK.
Recruitment period: 05/09/2014 - 31/10/2015

Pre-assignment

Screening details:

HIV infected subjects, on antiretroviral therapy were screened in accordance with the eligibility criteria.

HIV-negative subjects were screened in accordance with eligibility criteria. They must have had history of having received at least one dose of trivalent inactivated influenza vaccine in the past and be a Non-smoker

All were 18 – 49

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Trial was not blinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	HIV Infected Participants

Arm description:

HIV Infected Participants

Arm type	Experimental
Investigational medicinal product name	FLUENZ tetra nasal spray suspension Influenza vaccine (live attenuated, nasal)
Investigational medicinal product code	EMEA/H/C/002617 (European Medicines Agency code)
Other name	FLUENZ tetra nasal spray suspension
Pharmaceutical forms	Nasal spray, suspension
Routes of administration	Nasal use

Dosage and administration details:

One dose (0.1ml divided dose into each nostril)

Arm title	HIV not infected participants

Arm description:

HIV not infected participants

Arm type	Experimental
Investigational medicinal product name	FLUENZ tetra nasal spray suspension Influenza vaccine (live attenuated, nasal)
Investigational medicinal product code	EMEA/H/C/002617 (European Medicines Agency code)
Other name	FLUENZ tetra nasal spray suspension
Pharmaceutical forms	Nasal spray, suspension
Routes of administration	Nasal use

Dosage and administration details:

One dose (0.1ml divided dose into each nostril)

Number of subjects in period 1	HIV Infected Participants	HIV not infected participants
Started	8	20
Day 3	7	20
Day 7	6	20
Completed	4	19
Not completed	4	1
Lost to follow-up	4	1

Baseline characteristics

Reporting groups	
Reporting group title	HIV Infected Participants
Reporting group description: HIV Infected Participants	
Reporting group title	HIV not infected participants
Reporting group description: HIV not infected participants	

Reporting group values	HIV Infected Participants	HIV not infected participants	Total
Number of subjects	8	20	28
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	8	20	28
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	4	10	14
Male	4	10	14

End points

End points reporting groups

Reporting group title	HIV Infected Participants
Reporting group description: HIV Infected Participants	
Reporting group title	HIV not infected participants
Reporting group description: HIV not infected participants	

Primary: Antiinfluenza antibody titres in serum - H1N1

End point title	Antiinfluenza antibody titres in serum - H1N1[1]
End point description: Antiinfluenza antibody titres in serum	
End point type	Primary
End point timeframe: median fold rise in antibody titre from day 0 to day 28 post-vaccination, per influenza antigen included in the vaccine - H1N1	

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: Hypothesis testing was not relevant to the study objectives.
Please note that this is a secondary endpoint, not a primary end point as stated. Unable to submit EudraCT form without a primary end point inputted. See attachment for primary endpoint data.

End point values	HIV Infected Participants	HIV not infected participants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	19		
Units: haemagglutinating units				
median (inter-quartile range (Q1-Q3))	1 (1 to 1.25)	1 (1 to 1)		

Statistical analyses

No statistical analyses for this end point

Primary: Antiinfluenza antibody titres in serum - H3N2

End point title	Antiinfluenza antibody titres in serum - H3N2[2]
End point description: Antiinfluenza antibody titres in serum	
End point type	Primary
End point timeframe: median fold rise in antibody titre from day 0 to day 28 post-vaccination, per influenza antigen included in the vaccine - H3N2	

Notes:

[2] - 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: Hypothesis testing was not relevant to the study objectives.
Please note that this is a secondary endpoint, not a primary end point as stated. Unable to submit EudraCT form without a primary end point inputted. See attachment for primary endpoint data.

End point values	HIV Infected Participants	HIV not infected participants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	19		
Units: haemagglutinating units				
median (inter-quartile range (Q1-Q3))	1 (1 to 1)	1 (1 to 1)		

Statistical analyses

No statistical analyses for this end point

Primary: Antiinfluenza antibody titres in serum - Influenza B

End point title	Antiinfluenza antibody titres in serum - Influenza B[3]

End point description:

Antiinfluenza antibody titres in serum

End point type	Primary

End point timeframe:

median fold rise in antibody titre from day 0 to day 28 post-vaccination, per influenza antigen included in the vaccine - Influenza B

Notes:

[3] - 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: Hypothesis testing was not relevant to the study objectives.
Please note that this is a secondary endpoint, not a primary end point as stated. Unable to submit EudraCT form without a primary end point inputted. See attachment for primary endpoint data.

End point values	HIV Infected Participants	HIV not infected participants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	19		
Units: haemagglutinating units				
median (inter-quartile range (Q1-Q3))	1 (1 to 1)	1 (1 to 1.25)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The reporting period for adverse events was be from the date informed consent is signed until 28 days after administration of IMP.

Adverse event reporting additional description:

Subjects were asked about the appearance of any potential adverse effects on day 3 and 7 following LAIV administration.

No SAEs occured in this trial.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	HIV Infected Participants

Reporting group description:

HIV Infected Participants

Reporting group title	HIV not infected participants

Reporting group description:

HIV not infected participants

Serious adverse events	HIV Infected Participants	HIV not infected participants	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 20 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	HIV Infected Participants	HIV not infected participants	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)	12 / 20 (60.00%)	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 8 (12.50%)	4 / 20 (20.00%)	
occurrences (all)	1	4	
General disorders and administration site conditions			

Fever			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	2	
Eye disorders			
Itchy eyes			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Swollen eyelid			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	0 / 8 (0.00%)	7 / 20 (35.00%)	
occurrences (all)	0	8	
Runny nose			
subjects affected / exposed	0 / 8 (0.00%)	3 / 20 (15.00%)	
occurrences (all)	0	3	
Sore throat			
subjects affected / exposed	0 / 8 (0.00%)	4 / 20 (20.00%)	
occurrences (all)	0	4	
Musculoskeletal and connective tissue disorders			
Generalised Muscle Aches			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

See attachment for primary endpoint data. Secondary endpoint (Influenzaspecific Tcell responses in blood) is not reported upon in this publication as the lung substudy did not start. The T-cell data is not available.

Notes: