Clinical trial results:
Long term antibody response to CMV gB vaccine in patients requiring liver or renal transplant. A Phase II open, single-site study, in participants who received CMV gB vaccine or placebo in previous trial (CTA ref no 20363/0238/001-0010; REC ref no 5476; UCL sponsor no 05/009).

Summary

EudraCT number	2012-002767-95
Trial protocol	GB
Global end of trial date	13 June 2016
Results information	
Result version number	v1 (current)
This version publication date	13 April 2019
First version publication date	13 April 2019
Summary attachment (see zip file)	results for part 2 of this research (Report - RED_00089589 ATR CMC11.pdf) results for part 1 of this research (ReportforfollowupanalysisMR.docx) extra samples text (Extra samples text.docx) extra samples summary (extrasamplessummary.xlsx)

Trial information

Trial identification	
Sponsor protocol code	12/0161
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00299260
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	University College London
Sponsor organisation address	Gower Street, London, United Kingdom, WC1E 6BT
Public contact	Paul Griffiths, University College London, 0207 8302997, p.griffiths@ucl.ac.uk
Scientific contact	Paul Griffiths, University College London, 0207 8302997, p.griffiths@ucl.ac.uk
Sponsor organisation name	University College London
Sponsor organisation address	Gower Street, London, United Kingdom, WC1E 6BT
Public contact	Samim Patel, University College London, 44 207 679 9320 , samim.patel@ucl.ac.uk
Scientific contact	Samim Patel, University College London, 44 207 679 9320 , samim.patel@ucl.ac.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	13 October 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 February 2016
Global end of trial reached?	Yes
Global end of trial date	13 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The Primary objective is in two parts: 1) to see the antibody levels found months to years after patients entered the randomised placebo-controlled trial of a glycoprotein B vaccine against cytomegalovirus and 2) to have the previous samples retested using new and different methods which have been developed in different labs.

Protection of trial subjects:

This refers to the main study:
Negative pregnancy test was required before each vaccine dose

Adverse and serious adverse events were tabulated and presented to a Data Safety Committee on six occasions.

Background therapy:

Immunosuppressive drugs

Evidence for comparator:

This refers to the main study:
Placebo used to assess rate of side effects and immunogenicity

Actual start date of recruitment	03 August 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 31
Worldwide total number of subjects	31
EEA total number of subjects	31

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)	31
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Blood samples collected from UK patients who had previously volunteered for a placebo controlled RCT of CMV gB vaccine (report published Lancet 2011) starting 3 December 2013 and ending 9 February 2016.

Pre-assignment

Screening details:

Patients who had previously volunteered for a placebo controlled RCT of CMV gB vaccine

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

vaccine or matching placebo were dispensed by a pharmacist according to a randomisation code

Arms

Are arms mutually exclusive?	Yes
Arm title	vaccine seropositive

Arm description:

CMV glycoprotein B plus MF59 adjuvant

Arm type	Experimental
Investigational medicinal product name	glycoprotein B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

20 micrograms plus MF59 adjuvant

Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml normal saline

Arm title	placebo seronegative

Arm description:

normal saline

Arm type	Placebo
Investigational medicinal product name	normal saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.9% saline

Arm title	vaccine seronegative

Arm description: CMV glycoprotein B plus MF59 adjuvant	
Arm type	Experimental
Investigational medicinal product name	CMV glycoprotein B plus MF59 adjuvant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous use
Dosage and administration details: 20 micrograms plus MF59 adjuvant	
Arm title	placebo seropositive
Arm description: Normal saline	
Arm type	Placebo
Investigational medicinal product name	Normal saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous use
Dosage and administration details: Normal saline	

Number of subjects in period 1	vaccine seropositive	placebo seronegative	vaccine seronegative
Started	5	10	8
Completed	5	10	8

Number of subjects in period 1	placebo seropositive
Started	8
Completed	8

Baseline characteristics

Reporting groups

Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	31	31	
Age categorical Units: Subjects			
Adults (18-64 years)	31	31	
Gender categorical Units: Subjects			
Female	12	12	
Male	19	19	

Subject analysis sets

Subject analysis set title	Glycoprotein B antibodies
Subject analysis set type	Per protocol

Subject analysis set description:
measurement of titre of antibodies to glycoprotein B

Reporting group values	Glycoprotein B antibodies		
Number of subjects	31		
Age categorical Units: Subjects			
Adults (18-64 years)	31		
Gender categorical Units: Subjects			
Female	12		
Male	19		

End points

End points reporting groups

Reporting group title	vaccine seropositive
Reporting group description: CMV glycoprotein B plus MF59 adjuvant	
Reporting group title	placebo seronegative
Reporting group description: normal saline	
Reporting group title	vaccine seronegative
Reporting group description: CMV glycoprotein B plus MF59 adjuvant	
Reporting group title	placebo seropositive
Reporting group description: Normal saline	
Subject analysis set title	Glycoprotein B antibodies
Subject analysis set type	Per protocol
Subject analysis set description: measurement of titre of antibodies to glycoprotein B	

Primary: Titre of antibodies against glycoprotein B

End point title	Titre of antibodies against glycoprotein B[1]
End point description:	
End point type	Primary
End point timeframe: Months to years following vaccine	

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: Statistical analysis is not possible because of the small numbers, however, examination of the mean values for each group allows some general conclusions to be made. The seronegatives remain seronegative unless they develop viraemia. The seropositives may have a small boost in antibody level from viraemia. Once these effects of viraemia are taken into account, there is no substantial evidence that the vaccine was responsible for increasing antibody levels.

End point values	vaccine seropositive	placebo seronegative	vaccine seronegative	placebo seropositive
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	10	8	8
Units: Antibody titre				
geometric mean (full range (min-max))				
Viraemia	2.496 (2.165 to 2.826)	2.237 (2.223 to 2.467)	2.287 (2.109 to 2.546)	3.083 (2.856 to 3.28)
No viraemia	2.272 (2.065 to 2.707)	0.847 (0.311 to 2.059)	0.852 (0.05 to 2.107)	2.586 (1.935 to 3.061)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
Until end of trial 13 June 2016	
Adverse event reporting additional description:	
SAEs and SUSARS	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups	
Reporting group title	all patients
Reporting group description:	
all patients donating blood	

Serious adverse events	all patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 31 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	all patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 31 (0.00%)		

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: The scope of this sub-study was to look at the long-term antibody response to CMV gB vaccine in patients requiring liver or renal transplant who had participated in the trial: A Phase II Immunogenicity Trial Of Cytomegalovirus Glycoprotein B Vaccine In Allograft Candidate Recipients; CTA ref no 20363/0238/001-0010; REC ref no 5476; UCL sponsor no 05/009. No IMP was administered in the sub-study, one 40ml blood sample taken from the participants was the only intervention.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 September 2014	A substantial amendment was made on 17 September 2014 to the ethics committee to allow use of blood samples from patients recruited from the first study but who had since died and to analyse the samples overseas. This was approved on 10 October 2014.

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.

Note that no clinical trial medication was given to patients during this follow up study. There was no prior hypothesis and only descriptive statistics were used to gain insight into natural history of this infection.

Notes: