



Clinical trial results:

A Phase I clinical trial to assess the safety and immunogenicity of HIV DNA-C CN54ENV immunisations administered via the Intramuscular and Intradermal methods with and without electroporation followed by boosting with recombinant HIV CN54gp140 in healthy male and female volunteers

Summary

EudraCT number	2015-001023-23
Trial protocol	GB
Global end of trial date	22 December 2017

Results information

Result version number	v1 (current)
This version publication date	03 November 2018
First version publication date	03 November 2018

Trial information

Trial identification

Sponsor protocol code	CUTHIVAC002
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02589795
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Imperial College London
Sponsor organisation address	South Kensington Campus, London, United Kingdom, SW7 2AZ
Public contact	Tom Cole, Imperial College London, 44 (0)2033136198, t.cole@imperial.ac.uk
Scientific contact	Tom Cole, Imperial College London, 44 (0)2033136198, t.cole@imperial.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	22 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 December 2017
Global end of trial reached?	Yes
Global end of trial date	22 December 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

We aim to assess the safety of the HIV vaccines, and also to assess how well they stimulate responses by the body's immune system, when they are given by intradermal and intramuscular injection with or without electroporation.

Protection of trial subjects:

The wellbeing of trial subjects was monitored closely during the period after each vaccination, through the use of symptom diaries, phone calls, and safety assessments at clinic visits.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	05 October 2015
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
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Subject disposition

Recruitment

Recruitment details:

All trial subjects were recruited at a single site in the UK: the NIHR Imperial Clinical Research Facility, part of Imperial College Healthcare NHS Trust. The first volunteer was screened on 11 Aug 2016, and the final screening visit was on 15 Feb 2017.

Pre-assignment

Screening details:

Trial subjects were screened using criteria designed to select healthy volunteers.

Period 1

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

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
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Arm title	Randomised subjects
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Arm description:

This arm comprised the initial 24 subjects randomised.

Arm type	Experimental
Investigational medicinal product name	DNA-C CN54ENV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use, Intradermal use

Dosage and administration details:

Subjects received 3 doses of DNA-C CN54ENV, at 4-weekly intervals, at Weeks 0, 4 and 8 of the trial.

Subjects in Group 1 received: intradermal (ID) injections of 0.6 mg, with electroporation (EP), into the skin overlying the deltoid; AND intramuscular (IM) injections of 2 mg, without EP, into the anterolateral thigh/vastus lateralis muscle.

Subjects in Group 2 received: ID injections of 0.6 mg, without EP, into the skin overlying the deltoid; AND IM injections of 2 mg, with EP, into the anterolateral thigh/vastus lateralis muscle.

Subjects in Group 3 received: ID injections of 0.6 mg, with EP, into the skin overlying the deltoid; AND IM injections of 2 mg, with EP, into the anterolateral thigh/vastus lateralis muscle.

Investigational medicinal product name	CN54gp140
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

Subjects received a single dose of 50 micrograms of CN54gp140, by intradermal injection into the skin overlying the deltoid, at Week 20 of the trial.

Arm title	Replacement subjects
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Arm description:

This arm comprised the 4 subjects recruited to replace subjects in the 'Randomised subjects' arm.

Arm type	Experimental
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Investigational medicinal product name	DNA-C CN54ENV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intradermal use, Intramuscular use

Dosage and administration details:

Subjects received 3 doses of DNA-C CN54ENV, at 4-weekly intervals, at Weeks 0, 4 and 8 of the trial.

Subjects in Group 1 received: intradermal (ID) injections of 0.6 mg, with electroporation (EP), into the skin overlying the deltoid; AND intramuscular (IM) injections of 2 mg, without EP, into the anterolateral thigh/vastus lateralis muscle.

Subjects in Group 3 received: ID injections of 0.6 mg, with EP, into the skin overlying the deltoid; AND IM injections of 2 mg, with EP, into the anterolateral thigh/vastus lateralis muscle.

Investigational medicinal product name	CN54gp140
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

Subjects received a single dose of 50 micrograms of CN54gp140, by intradermal injection into the skin overlying the deltoid, at Week 20 of the trial.

Number of subjects in period 1	Randomised subjects	Replacement subjects
Started	24	4
Completed	20	3
Not completed	4	1
Consent withdrawn by subject	2	-
Physician decision	-	1
Lost to follow-up	1	-
Protocol deviation	1	-

Baseline characteristics

Reporting groups

Reporting group title	Randomised subjects
Reporting group description: This arm comprised the initial 24 subjects randomised.	
Reporting group title	Replacement subjects
Reporting group description: This arm comprised the 4 subjects recruited to replace subjects in the 'Randomised subjects' arm.	

Reporting group values	Randomised subjects	Replacement subjects	Total
Number of subjects	24	4	28
Age categorical			
In order to be eligible for participation, subjects had to be aged 18-50 years on the day of screening.			
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)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Adults 18-50 years	24	4	28
Age continuous			
In order to be eligible for participation, subjects had to be aged 18-50 years on the day of screening.			
Units: years			
median	27	31	
inter-quartile range (Q1-Q3)	22 to 43	27 to 35	-
Gender categorical			
Units: Subjects			
Female	6	1	7
Male	18	3	21
Ethnicity			
Units: Subjects			
White British	17	2	19
Other white	3	1	4
Other	4	1	5

Subject analysis sets

Subject analysis set title	Randomised subjects, Group 1
Subject analysis set type	Safety analysis
Subject analysis set description: This subject analysis set comprises the randomised subjects allocated to Group 1	
Subject analysis set title	Randomised subjects, Group 2

Subject analysis set type	Safety analysis
Subject analysis set description:	
This subject analysis set comprises the randomised subjects allocated to Group 2	
Subject analysis set title	Randomised subjects, Group 3
Subject analysis set type	Safety analysis
Subject analysis set description:	
This subject analysis set comprises the randomised subjects allocated to Group 3	
Subject analysis set title	Replacement subjects, Group 1
Subject analysis set type	Safety analysis
Subject analysis set description:	
This subject analysis set comprises the replacement subjects allocated to Group 1	
Subject analysis set title	Replacement subjects, Group 3
Subject analysis set type	Safety analysis
Subject analysis set description:	
This subject analysis set comprises the replacement subjects allocated to Group 3	
Subject analysis set title	All Group 1 subjects
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All subjects allocated to Group 1, including both randomised and replacement subjects	
Subject analysis set title	All Group 3 subjects
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All subjects allocated to Group 3, including both randomised and replacement subjects	

Reporting group values	Randomised subjects, Group 1	Randomised subjects, Group 2	Randomised subjects, Group 3
Number of subjects	8	8	8
Age categorical			
In order to be eligible for participation, subjects had to be aged 18-50 years on the day of screening.			
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)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Adults 18-50 years	8	8	8
Age continuous			
In order to be eligible for participation, subjects had to be aged 18-50 years on the day of screening.			
Units: years			
median	31	27	22
inter-quartile range (Q1-Q3)	25 to 34	23 to 43	21 to 47
Gender categorical			
Units: Subjects			
Female	2	2	2
Male	6	6	6

Ethnicity			
Units: Subjects			
White British	6	5	6
Other white	1	0	2
Other	1	3	0

Reporting group values	Replacement subjects, Group 1	Replacement subjects, Group 3	All Group 1 subjects
Number of subjects	1	3	9
Age categorical			
In order to be eligible for participation, subjects had to be aged 18-50 years on the day of screening.			
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)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Adults 18-50 years	1	3	9
Age continuous			
In order to be eligible for participation, subjects had to be aged 18-50 years on the day of screening.			
Units: years			
median	23	35	
inter-quartile range (Q1-Q3)		27 to 48	
Gender categorical			
Units: Subjects			
Female	0	1	
Male	1	2	
Ethnicity			
Units: Subjects			
White British	1	1	
Other white	0	1	
Other	0	1	

Reporting group values	All Group 3 subjects		
Number of subjects	11		
Age categorical			
In order to be eligible for participation, subjects had to be aged 18-50 years on the day of screening.			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		

From 65-84 years	0		
85 years and over	0		
Adults 18-50 years	11		
Age continuous			
In order to be eligible for participation, subjects had to be aged 18-50 years on the day of screening.			
Units: years			
median			
inter-quartile range (Q1-Q3)			
Gender categorical			
Units: Subjects			
Female			
Male			
Ethnicity			
Units: Subjects			
White British			
Other white			
Other			

End points

End points reporting groups

Reporting group title	Randomised subjects
Reporting group description: This arm comprised the initial 24 subjects randomised.	
Reporting group title	Replacement subjects
Reporting group description: This arm comprised the 4 subjects recruited to replace subjects in the 'Randomised subjects' arm.	
Subject analysis set title	Randomised subjects, Group 1
Subject analysis set type	Safety analysis
Subject analysis set description: This subject analysis set comprises the randomised subjects allocated to Group 1	
Subject analysis set title	Randomised subjects, Group 2
Subject analysis set type	Safety analysis
Subject analysis set description: This subject analysis set comprises the randomised subjects allocated to Group 2	
Subject analysis set title	Randomised subjects, Group 3
Subject analysis set type	Safety analysis
Subject analysis set description: This subject analysis set comprises the randomised subjects allocated to Group 3	
Subject analysis set title	Replacement subjects, Group 1
Subject analysis set type	Safety analysis
Subject analysis set description: This subject analysis set comprises the replacement subjects allocated to Group 1	
Subject analysis set title	Replacement subjects, Group 3
Subject analysis set type	Safety analysis
Subject analysis set description: This subject analysis set comprises the replacement subjects allocated to Group 3	
Subject analysis set title	All Group 1 subjects
Subject analysis set type	Intention-to-treat
Subject analysis set description: All subjects allocated to Group 1, including both randomised and replacement subjects	
Subject analysis set title	All Group 3 subjects
Subject analysis set type	Intention-to-treat
Subject analysis set description: All subjects allocated to Group 3, including both randomised and replacement subjects	

Primary: Primary safety endpoint

End point title	Primary safety endpoint
End point description: Grade 3 or above solicited local, systemic or laboratory adverse event, or any grade of adverse event leading to a clinical decision to discontinue immunizations, or any grade of unsolicited adverse event with onset within 7 days of immunization	
End point type	Primary
End point timeframe: From Week 0 up to Week 22	

End point values	Randomised subjects	Replacement subjects	Randomised subjects, Group 1	Randomised subjects, Group 2
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	24	4	8	8
Units: Number of subjects	23	2	7	8

End point values	Randomised subjects, Group 3	Replacement subjects, Group 1	Replacement subjects, Group 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	1	3	
Units: Number of subjects	8	0	2	

Statistical analyses

Statistical analysis title	Primary safety endpoint comparisons
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Statistical analysis description:

The proportions of subjects with primary safety outcomes were compared in a pairwise manner between the three randomised groups, using Fisher's exact tests.

Comparison groups	Randomised subjects, Group 1 v Randomised subjects, Group 2 v Randomised subjects, Group 3
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other ^[1]
P-value	> 0.05 ^[2]
Method	Fisher exact

Notes:

[1] - Inequality test

[2] - All comparisons gave P-values >0.05

Primary: Primary immunogenicity

End point title	Primary immunogenicity
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End point description:

Magnitude of antigen-specific systemic IgG antibody binding responses (ng/mL) to CN54gp140

End point type	Primary
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End point timeframe:

Week 22

End point values	Randomised subjects, Group 2	All Group 1 subjects	All Group 3 subjects	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	9	11	
Units: nanograms per millilitre				
median (inter-quartile range (Q1-Q3))	11292 (9608 to 15568)	13934 (9884 to 38050)	31418 (6304 to 128259)	

Statistical analyses

Statistical analysis title	Primary immunogenicity endpoint comparisons
Statistical analysis description: Kruskal-Wallis test with Dunn's correction for multiple comparisons to compare the levels of antigen-specific serum IgG in the three groups at Week 22.	
Comparison groups	Randomised subjects, Group 2 v All Group 1 subjects v All Group 3 subjects
Number of subjects included in analysis	28
Analysis specification	Post-hoc
Analysis type	other ^[3]
P-value	> 0.05 ^[4]
Method	Kruskal-wallis
Confidence interval	
level	95 %

Notes:

[3] - Inequality test

[4] - All comparisons gave p-values >0.05

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Week 0 to Week 22

Adverse event reporting additional description:

Subjects recorded adverse events using a symptom diary for 7 days after each vaccination, and through regular investigator and laboratory assessments

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.0
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Reporting groups

Reporting group title	Randomised subjects
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Reporting group description:

This arm comprised the initial 24 subjects randomised.

Reporting group title	Replacement subjects
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Reporting group description:

This arm comprised the 4 subjects recruited to replace subjects in the 'Randomised subjects' arm.

Serious adverse events	Randomised subjects	Replacement subjects	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 24 (4.17%)	0 / 4 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Road traffic accident	Additional description: Occurred 5 months after the affected subject's final vaccination		
subjects affected / exposed	1 / 24 (4.17%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Randomised subjects	Replacement subjects	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	1 / 4 (25.00%)	
General disorders and administration site conditions			

Musculoskeletal pain		Additional description: Grade 3 general muscle aches 5 days after the 3rd vaccination; subject in Group 3		
subjects affected / exposed		0 / 24 (0.00%)	1 / 4 (25.00%)	
occurrences (all)		0	1	
Fatigue		Additional description: Grade 3 abnormal tiredness 5 and 6 days after the 3rd vaccination; subject in Group 3		
subjects affected / exposed		0 / 24 (0.00%)	1 / 4 (25.00%)	
occurrences (all)		0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 September 2015	Updates to various documents; submission included Protocol v2.0 and PIS-ICF v2.0
07 December 2015	Updates to various documents; submission included Protocol v3.0 and PIS-ICF v3.0
08 May 2017	Transfer SAE/SUSAR reporting, and monitoring, responsibilities from MRC CTU to ICL; submission comprised Protocol v4.0

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.

We have reported the primary endpoints only.
For non-serious adverse events we have reported only those graded 3 ('severe') or above, and which occurred at a frequency of >5%.

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/30027768>