Clinical trial results:
A randomised double-blind placebo-controlled Phase 2B clinical trial of repeated application of gene therapy in patients with cystic fibrosis

Summary

EudraCT number	2011-004761-33
Trial protocol	GB
Global end of trial date	30 May 2014

Results information

Result version number	v1 (current)
This version publication date	08 June 2019
First version publication date	08 June 2019

Trial information

Trial identification

Sponsor protocol code	CRO1881

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Imperial College London
Sponsor organisation address	1b Manresa road, London, United Kingdom, SW3 6LR
Public contact	Samia Soussi, Imperial College, +44 2075947980, s.soussi@imperial.ac.uk
Scientific contact	Samia Soussi, Imperial College, +44 2075947980, s.soussi@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	02 July 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 May 2014
Global end of trial reached?	Yes
Global end of trial date	30 May 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The clinical study has three main objectives:

1. To assess the clinical benefit of pGM169/GL67A when administered on a monthly basis over a period of a year.
2. To assess the safety and tolerability of pGM169/GL67A over the same period.
3. To assess gene expression directed by pGM169/GL67A over the same period.

Protection of trial subjects:

Subjects fully informed prior to enrolment

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 January 2012
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: 116
Worldwide total number of subjects	116
EEA total number of subjects	116

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)	40
Adults (18-64 years)	76
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Pre-dosing visits (all patients or selected ones as indicated)
- Eligibility & Consent (E&C) visit (selected nPD or bronchoscopy subjects only
- Introductory visit (optional, if required for new, non-Run In study subjects only)
- Screening visit (all subjects)
- Pre-dosing nasal PD visits x up to3 (nasal subgroup only- may be before or after Sc

Pre-assignment

Screening details:

Screening visit
This will involve:
Page 18 of 52
Repeated application of gene therapy in CF patients; v06; 21/08/2013
confirmation that patient fulfils inclusion/ exclusion criteria
informed consent signed (if no Introductory Visit)
quality of life questionnaire
full medical history and physical examination including heart rate, resp

Pre-assignment period milestones

Number of subjects started	116
Number of subjects completed	116

Period 1

Period 1 title	Baseline (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo group

Arm description: -

Arm type	Placebo
Investigational medicinal product name	0.9% Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser solution, Nasal spray, solution, Nebuliser suspension
Routes of administration	Nasal use, Inhalation use

Dosage and administration details:

Administration of 5 ml placebo (0.9% saline) via nebuliser to the lungs every 4 weeks for 12 doses
Administration of 2 ml placebo (0.9% saline) via nasal spray to the nose every 4 weeks for 12 doses (subgroup only)

Arm title	pGM169/GL67A group

Arm description: -

Arm type	Active comparator

Investigational medicinal product name	pGM169/GL67A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray, solution, Nebuliser solution, Nebuliser suspension
Routes of administration	Inhalation use, Nasal use

Dosage and administration details:

Administration of 5 ml pGM169/GL67A via nebuliser to the lungs every 4 weeks for 12 doses
Administration of 2 ml pGM169/GL67A via nasal spray to the nose every 4 weeks for 12 doses (subgroup only)

Number of subjects in period 1	Placebo group	pGM169/GL67A group
Started	54	62
Completed	54	62

Baseline characteristics

Reporting groups	
Reporting group title	Placebo group
Reporting group description: -	
Reporting group title	pGM169/GL67A group
Reporting group description: -	

Reporting group values	Placebo group	pGM169/GL67A group	Total
Number of subjects	54	62	116
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)	17	23	40
Adults (18-64 years)	37	39	76
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	26.0	23.6	
standard deviation	± 13.0	± 10.8	-
Gender categorical Units: Subjects			
Female	25	31	56
Male	29	31	60

End points

End points reporting groups

Reporting group title	Placebo group
Reporting group description: -	
Reporting group title	pGM169/GL67A group
Reporting group description: -	
Subject analysis set title	Treatment effect
Subject analysis set type	Per protocol
Subject analysis set description: Treatment effect in pGM169/GL67A group versus placebo group	
Subject analysis set title	Treatment effect
Subject analysis set type	Per protocol
Subject analysis set description: Treatment effect in pGM169/GL67A group versus placebo group	

Primary: FEV1

End point title	FEV1
End point description:	
End point type	Primary
End point timeframe: Absolute treatment effect	

End point values	Treatment effect	Treatment effect		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	62	54		
Units: percent				
arithmetic mean (standard deviation)	3.66 (± 0.39)	3.66 (± 0.39)		

Statistical analyses

Statistical analysis title	ANCOVA-adjusted treatment effect
Statistical analysis description: ANCOVA-adjusted treatment effect in the pGM169/GL67A group versus Placebo at 12 months follow up	
Comparison groups	Treatment effect v Treatment effect
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.046
Method	ANCOVA

Secondary: FVC

End point title	FVC

End point description:

End point type	Secondary

End point timeframe:

Absolute treatment effect

End point values	Treatment effect			
Subject group type	Subject analysis set			
Number of subjects analysed	114			
Units: percent				
arithmetic mean (standard deviation)	3.03 (± 0.42)			

Statistical analyses

No statistical analyses for this end point

Secondary: MEF 25-75

End point title	MEF 25-75

End point description:

End point type	Secondary

End point timeframe:

Absolute treatment effect

End point values	Treatment effect			
Subject group type	Subject analysis set			
Number of subjects analysed	114			
Units: percent				
arithmetic mean (standard deviation)	0.07 (± 0.18)			

Statistical analyses

No statistical analyses for this end point

Secondary: Lung clearence index

End point title	Lung clearence index

End point description:

End point type	Secondary

End point timeframe:

Absolute treatment effect

End point values	Treatment effect			
Subject group type	Subject analysis set			
Number of subjects analysed	110			
Units: unit(s)				
arithmetic mean (standard deviation)	-0.28 (± 0.26)			

Statistical analyses

No statistical analyses for this end point

Secondary: CT Bronchiectasis extent

End point title	CT Bronchiectasis extent

End point description:

End point type	Secondary

End point timeframe:

Absolute treatment effect

End point values	Treatment effect			
Subject group type	Subject analysis set			
Number of subjects analysed	115			
Units: unit(s)				
arithmetic mean (standard deviation)	-0.03 (± 0.11)			

Statistical analyses

No statistical analyses for this end point

Secondary: CT Bronchiectasis severity

End point title	CT Bronchiectasis severity

End point description:

End point type	Secondary

End point timeframe:

Absolute treatment effect

End point values	Treatment effect			
Subject group type	Subject analysis set			
Number of subjects analysed	115			
Units: unit(s)				
arithmetic mean (standard deviation)	-0.08 (± 0.31)			

Statistical analyses

No statistical analyses for this end point

Secondary: CT Wall thickness

End point title	CT Wall thickness

End point description:

End point type	Secondary

End point timeframe:

Absolute treatment effect

End point values	Treatment effect			
Subject group type	Subject analysis set			
Number of subjects analysed	115			
Units: unit(s)				
arithmetic mean (standard deviation)	-0.09 (± 0.28)			

Statistical analyses

No statistical analyses for this end point

Secondary: CT Large airway mucus plugs

End point title	CT Large airway mucus plugs

End point description:

End point type	Secondary

End point timeframe:

Absolute treatment effect

End point values	Treatment effect			
Subject group type	Subject analysis set			
Number of subjects analysed	115			
Units: unit(s)				
arithmetic mean (standard deviation)	-0.03 (± 0.18)			

Statistical analyses

No statistical analyses for this end point

Secondary: CT Small airway mucus plugs

End point title	CT Small airway mucus plugs

End point description:

End point type	Secondary

End point timeframe:

Absolute treatment effect

End point values	Treatment effect			
Subject group type	Subject analysis set			
Number of subjects analysed	115			
Units: unit(s)				
arithmetic mean (standard deviation)	-0.07 (± 0.37)			

Statistical analyses

No statistical analyses for this end point

Secondary: CT Gas trappings

End point title	CT Gas trappings

End point description:

End point type	Secondary

End point timeframe:

Absolute treatment effect

End point values	Treatment effect			
Subject group type	Subject analysis set			
Number of subjects analysed	115			
Units: unit(s)				
arithmetic mean (standard deviation)	-3.49 (± 0.39)			

Statistical analyses

No statistical analyses for this end point

Secondary: C-reactive protein

End point title	C-reactive protein

End point description:

End point type	Secondary

End point timeframe:

Absolute treatment effect

End point values	Treatment effect			
Subject group type	Subject analysis set			
Number of subjects analysed	103			
Units: mg/L				
arithmetic mean (standard deviation)	-4.82 (± 0.39)			

Statistical analyses

No statistical analyses for this end point

Secondary: Erythrocyte sedimentation rate

End point title	Erythrocyte sedimentation rate

End point description:

End point type	Secondary

End point timeframe:

Absolute treatment effect

End point values	Treatment effect			
Subject group type	Subject analysis set			
Number of subjects analysed	114			
Units: mm/hr				
arithmetic mean (standard deviation)	-1.86 (± 0.21)			

Statistical analyses

No statistical analyses for this end point

Secondary: White blood cells

End point title	White blood cells

End point description:

End point type	Secondary

End point timeframe:

Absolute treatment effect

End point values	Treatment effect			
Subject group type	Subject analysis set			
Number of subjects analysed	115			
Units: x10E9/L				
arithmetic mean (standard deviation)	-0.52 (± 0.26)			

Statistical analyses

No statistical analyses for this end point

Secondary: KCOc

End point title	KCOc

End point description:

End point type	Secondary

End point timeframe:

Absolute treatment effect

End point values	Treatment effect			
Subject group type	Subject analysis set			
Number of subjects analysed	112			
Units: unit(s)				
arithmetic mean (standard deviation)	0.03 (± 0.23)			

Statistical analyses

No statistical analyses for this end point

Secondary: TLCOc

End point title	TLCOc

End point description:

End point type	Secondary

End point timeframe:

Absolute treatment effect

End point values	Treatment effect			
Subject group type	Subject analysis set			
Number of subjects analysed	112			
Units: unit(s)				
arithmetic mean (standard deviation)	0.18 (± 0.21)			

Statistical analyses

No statistical analyses for this end point

Secondary: Alveolar volume

End point title	Alveolar volume

End point description:

End point type	Secondary

End point timeframe:

Absolute treatment effect

End point values	Treatment effect			
Subject group type	Subject analysis set			
Number of subjects analysed	113			
Units: unit(s)				
arithmetic mean (standard deviation)	0.07 (± 0.19)			

Statistical analyses

No statistical analyses for this end point

Secondary: Sputum 24h weight

End point title	Sputum 24h weight

End point description:

End point type	Secondary

End point timeframe:

Absolute treatment effect

End point values	Treatment effect			
Subject group type	Subject analysis set			
Number of subjects analysed	49			
Units: gram(s)				
arithmetic mean (standard deviation)	-2.96 (± 0.36)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Post dose	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10

Reporting groups	
Reporting group title	Placebo group
Reporting group description: -	
Reporting group title	pGM169/GL67A group
Reporting group description: -	

Serious adverse events	Placebo group	pGM169/GL67A group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 54 (0.00%)	6 / 62 (9.68%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Respiratory, thoracic and mediastinal disorders			
Admission to hospital with headache, vomiting and viral URTI symptoms			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 54 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post-surgical infection			
subjects affected / exposed	0 / 54 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax after removal of indwelling intravenous access device			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 54 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			

Admission to hospital with acute pancreatitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 54 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Admission to hospital with minor vomiting illness	Additional description: Admitted for assistance with diabetic control		
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 54 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Admission to hospital with severe headache, fever, pulmonary exacerbation and new isolate of MRSA			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 54 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo group	pGM169/GL67A group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 54 (100.00%)	62 / 62 (100.00%)	
General disorders and administration site conditions			
Headache			
subjects affected / exposed	54 / 54 (100.00%)	62 / 62 (100.00%)	
occurrences (all)	54	62	
Other			
subjects affected / exposed	54 / 54 (100.00%)	62 / 62 (100.00%)	
occurrences (all)	54	62	
Blood and lymphatic system disorders			
Haematuria			

subjects affected / exposed	54 / 54 (100.00%)	62 / 62 (100.00%)	
occurrences (all)	54	62	
Isolated raised inflammatory markers			
subjects affected / exposed	54 / 54 (100.00%)	62 / 62 (100.00%)	
occurrences (all)	54	62	
Gastrointestinal disorders			
Gastrointestinal symptoms			
subjects affected / exposed	54 / 54 (100.00%)	62 / 62 (100.00%)	
occurrences (all)	54	62	
Respiratory, thoracic and mediastinal disorders			
Lower airway respiratory symtoms			
subjects affected / exposed	54 / 54 (100.00%)	62 / 62 (100.00%)	
occurrences (all)	54	62	
Upper airway symptoms			
subjects affected / exposed	54 / 54 (100.00%)	62 / 62 (100.00%)	
occurrences (all)	54	62	
Hepatobiliary disorders			
Elevated liver function tests			
subjects affected / exposed	54 / 54 (100.00%)	62 / 62 (100.00%)	
occurrences (all)	54	62	
Infections and infestations			
Fever or flu like symptoms			
subjects affected / exposed	54 / 54 (100.00%)	62 / 62 (100.00%)	
occurrences (all)	54	62	

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

None reported