



## 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 to 3 (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
<b>Arm title</b>	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)

<b>Arm title</b>	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)

<b>Number of subjects in period 1</b>	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 ( $\pm$ 0.39)	3.66 ( $\pm$ 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 ( $\pm$ 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 ( $\pm$ 0.18)			

---

**Statistical analyses**

---

No statistical analyses for this end point

---

---

**Secondary: Lung clearance index**

---

End point title	Lung clearance 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 ( $\pm$ 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 ( $\pm$ 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

<b>End point values</b>	Treatment effect			
Subject group type	Subject analysis set			
Number of subjects analysed	115			
Units: unit(s)				
arithmetic mean (standard deviation)	-0.08 ( $\pm$ 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	

<b>End point values</b>	Treatment effect			
Subject group type	Subject analysis set			
Number of subjects analysed	115			
Units: unit(s)				
arithmetic mean (standard deviation)	-0.09 ( $\pm$ 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	

<b>End point values</b>	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	

<b>End point values</b>	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	

<b>End point values</b>	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

<b>End point values</b>	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

<b>End point values</b>	Treatment effect			
Subject group type	Subject analysis set			
Number of subjects analysed	114			
Units: mm/hr				
arithmetic mean (standard deviation)	-1.86 ( $\pm$ 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

<b>End point values</b>	Treatment effect			
Subject group type	Subject analysis set			
Number of subjects analysed	115			
Units: x10E9/L				
arithmetic mean (standard deviation)	-0.52 ( $\pm$ 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

<b>End point values</b>	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

<b>End point values</b>	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

<b>End point values</b>	Treatment effect			
Subject group type	Subject analysis set			
Number of subjects analysed	113			
Units: unit(s)				
arithmetic mean (standard deviation)	0.07 ( $\pm$ 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

<b>End point values</b>	Treatment effect			
Subject group type	Subject analysis set			
Number of subjects analysed	49			
Units: gram(s)				
arithmetic mean (standard deviation)	-2.96 ( $\pm$ 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: -

<b>Serious adverse events</b>	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 %

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