



## Clinical trial results:

### Evaluation of safety and gene expression with a single dose of pGM169/GL67A administered to the nose and lung of individuals with cystic fibrosis

#### Summary

EudraCT number	2007-004050-85
Trial protocol	GB
Global end of trial date	08 June 2011

#### Results information

Result version number	v1 (current)
This version publication date	07 June 2019
First version publication date	07 June 2019

#### Trial information

##### Trial identification

Sponsor protocol code	cro851
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##### 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
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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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	01 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 June 2011
Global end of trial reached?	Yes
Global end of trial date	08 June 2011
Was the trial ended prematurely?	No

Notes:

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**General information about the trial**

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Main objective of the trial:

To assess the safety and gene transfer resulting from a single dose of pGM169/GL67A to the lungs and nose of patients with cystic fibrosis

Protection of trial subjects:

Patients were fully informed at enrolment of all study procedures

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 February 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	United Kingdom: 35
Worldwide total number of subjects	35
EEA total number of subjects	35

Notes:

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**Subjects enrolled per age group**

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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)	35
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Adults (>16 years) with cystic fibrosis attending the Royal Brompton Hospital fulfilling the inclusion/ exclusion criteria

### Pre-assignment period milestones

Number of subjects started	35
Number of subjects completed	35

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	20ml pGM169/GL67A
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	pGM169/GL67
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal/oromucosal spray, solution, Nebuliser solution
Routes of administration	Inhalation use, Nasal use

Dosage and administration details:

Single nebulised and nasal dose

pGM169/GL67A: Plasmid expressing the human CFTR gene complexed with cationic lipid 67 and helper lipids: 10 ml nebulised and 1 ml nasal administration (n=3) and 20 ml nebulised and 2 ml nasal (n=24)

<b>Arm title</b>	10ml pGM169/GL67A
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	pGM169/GL67
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser solution, Nasal/oromucosal spray, solution
Routes of administration	Nasal use, Inhalation use

Dosage and administration details:

Single nebulised and nasal dose

pGM169/GL67A: Plasmid expressing the human CFTR gene complexed with cationic lipid 67 and helper lipids: 10 ml nebulised and 1 ml nasal administration (n=3) and 20 ml nebulised and 2 ml nasal (n=24)

<b>Arm title</b>	5ml pGM169/GL67A
Arm description: -	
Arm type	Experimental

Investigational medicinal product name	pGM169/GL67
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser solution, Nasal/oromucosal spray, solution
Routes of administration	Inhalation use, Nasal use

Dosage and administration details:

Single nebulised and nasal dose

pGM169/GL67A: Plasmid expressing the human CFTR gene complexed with cationic lipid 67 and helper lipids: 10 ml nebulised and 1 ml nasal administration (n=3) and 20 ml nebulised and 2 ml nasal (n=24)

<b>Number of subjects in period 1</b>	20ml pGM169/GL67A	10ml pGM169/GL67A	5ml pGM169/GL67A
Started	17	10	8
Completed	17	10	8

## Baseline characteristics

### Reporting groups

Reporting group title	20ml pGM169/GL67A
Reporting group description: -	
Reporting group title	10ml pGM169/GL67A
Reporting group description: -	
Reporting group title	5ml pGM169/GL67A
Reporting group description: -	

Reporting group values	20ml pGM169/GL67A	10ml pGM169/GL67A	5ml pGM169/GL67A
Number of subjects	17	10	8
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)	1	0	1
Adults (18-64 years)	16	10	7
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
median	26.7	33.2	32.6
full range (min-max)	17.3 to 50.1	16.4 to 61.6	24.3 to 46.4
Gender categorical Units: Subjects			
Female	5	4	3
Male	12	6	5

Reporting group values	Total		
Number of subjects	35		
Age categorical 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)	2		
Adults (18-64 years)	33		
From 65-84 years	0		
85 years and over	0		

Age continuous Units: years median full range (min-max)	-		
Gender categorical Units: Subjects			
Female	12		
Male	23		

### Subject analysis sets

Subject analysis set title	20ml pGM169/GL67A
Subject analysis set type	Per protocol
Subject analysis set description: 20ml pGM169/GL67A	
Subject analysis set title	10ml pGM169/GL67A
Subject analysis set type	Per protocol
Subject analysis set description: 10ml pGM169/GL67A	
Subject analysis set title	5ml pGM169/GL67A
Subject analysis set type	Per protocol
Subject analysis set description: 5ml pGM169/GL67A	

Reporting group values	20ml pGM169/GL67A	10ml pGM169/GL67A	5ml pGM169/GL67A
Number of subjects	17	10	8
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)	1	0	1
Adults (18-64 years)	16	10	7
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years median full range (min-max)	26.7 17.3 to 50.1	33.2 16.4 to 61.6	32.6 24.3 to 46.4
Gender categorical Units: Subjects			
Female			
Male			

## End points

### End points reporting groups

Reporting group title	20ml pGM169/GL67A
Reporting group description: -	
Reporting group title	10ml pGM169/GL67A
Reporting group description: -	
Reporting group title	5ml pGM169/GL67A
Reporting group description: -	
Subject analysis set title	20ml pGM169/GL67A
Subject analysis set type	Per protocol
Subject analysis set description: 20ml pGM169/GL67A	
Subject analysis set title	10ml pGM169/GL67A
Subject analysis set type	Per protocol
Subject analysis set description: 10ml pGM169/GL67A	
Subject analysis set title	5ml pGM169/GL67A
Subject analysis set type	Per protocol
Subject analysis set description: 5ml pGM169/GL67A	

### Primary: Fever Maximum temperature

End point title	Fever Maximum temperature
End point description:	
End point type	Primary
End point timeframe:	
Post dose	

End point values	20ml pGM169/GL67A	10ml pGM169/GL67A	5ml pGM169/GL67A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	6	6	
Units: celsius temperature				
arithmetic mean (standard deviation)	38.6 (± 0.5)	38.0 (± 0.7)	37.4 (± 0.3)	

### Statistical analyses

Statistical analysis title	Three group data analysis
Statistical analysis description: Three group data were compared with analysis of variance, Kruskal-Wallis, or Fisher's extract	
Comparison groups	20ml pGM169/GL67A v 10ml pGM169/GL67A v 5ml pGM169/GL67A

Number of subjects included in analysis	27
Analysis specification	Post-hoc
Analysis type	
P-value	= 0.0002
Method	Kruskal-wallis

### Primary: Blood leukocytes

End point title	Blood leukocytes
End point description:	
End point type	Primary
End point timeframe:	
Post dose	

End point values	20ml pGM169/GL67A	10ml pGM169/GL67A	5ml pGM169/GL67A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	6	6	
Units: x10E9/L				
arithmetic mean (standard deviation)	15.8 (± 3.2)	14.1 (± 4.5)	12.8 (± 3.8)	

### Statistical analyses

Statistical analysis title	Three group data analysis
Statistical analysis description:	
Three group data were compared with analysis of variance, Kruskal-Wallis, or Fisher's extract	
Comparison groups	20ml pGM169/GL67A v 10ml pGM169/GL67A v 5ml pGM169/GL67A
Number of subjects included in analysis	27
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0.22
Method	Kruskal-wallis

### Primary: Blood neutrophils

End point title	Blood neutrophils
End point description:	
End point type	Primary
End point timeframe:	
Post dose	



<b>End point values</b>	20ml pGM169/GL67A	10ml pGM169/GL67A	5ml pGM169/GL67A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	6	6	
Units: x10E9/L				
arithmetic mean (standard deviation)	13.9 (± 3.4)	11.3 (± 4.1)	9.8 (± 3.5)	

## Statistical analyses

<b>Statistical analysis title</b>	Three group data analysis
Statistical analysis description: Three group data were compared with analysis of variance, Kruskal-Wallis, or Fisher's extract	
Comparison groups	20ml pGM169/GL67A v 10ml pGM169/GL67A v 5ml pGM169/GL67A
Number of subjects included in analysis	27
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0.06
Method	Kruskal-wallis

## Primary: Serum C-reactive protein

End point title	Serum C-reactive protein
End point description:	
End point type	Primary
End point timeframe:	
Post dose	

<b>End point values</b>	20ml pGM169/GL67A	10ml pGM169/GL67A	5ml pGM169/GL67A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	6	6	
Units: mg/L				
median (full range (min-max))	59 (36 to 73)	51 (25 to 88)	38 (5 to 78)	

## Statistical analyses

<b>Statistical analysis title</b>	Three group data analysis
Statistical analysis description: Three group data were compared with analysis of variance, Kruskal-Wallis, or Fisher's extract	
Comparison groups	20ml pGM169/GL67A v 10ml pGM169/GL67A v 5ml pGM169/GL67A
Number of subjects included in analysis	27
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0.4
Method	Kruskal-wallis

### Primary: FEV1 relative % drop

End point title	FEV1 relative % drop
End point description:	
End point type	Primary
End point timeframe:	
Post dose	

<b>End point values</b>	20ml pGM169/GL67A	10ml pGM169/GL67A	5ml pGM169/GL67A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	6	6	
Units: percent				
arithmetic mean (standard deviation)	24.6 (± 9.3)	17.5 (± 7.8)	16.8 (± 4.0)	

### Statistical analyses

<b>Statistical analysis title</b>	Three group data analysis
Statistical analysis description: Three group data were compared with analysis of variance, Kruskal-Wallis, or Fisher's extract	
Comparison groups	10ml pGM169/GL67A v 20ml pGM169/GL67A v 5ml pGM169/GL67A
Number of subjects included in analysis	27
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0.08
Method	Kruskal-wallis

### Primary: FVC relative % drop

End point title	FVC relative % drop
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End point description:

End point type	Primary
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End point timeframe:

Post dose

End point values	20ml pGM169/GL67A	10ml pGM169/GL67A	5ml pGM169/GL67A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	6	6	
Units: percent				
arithmetic mean (standard deviation)	20.7 (± 2.9)	13.7 (± 2.2)	14.7 (± 2.2)	

### Statistical analyses

Statistical analysis title	Three group data analysis
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Statistical analysis description:

Three group data analysis compared with analysis of variance, Kruskal-Wallis, or Fisher's exact tests

Comparison groups	20ml pGM169/GL67A v 10ml pGM169/GL67A v 5ml pGM169/GL67A
Number of subjects included in analysis	27
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0.22
Method	Kruskal-wallis

### Primary: LCI

End point title	LCI
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End point description:

End point type	Primary
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End point timeframe:

Post dose

End point values	20ml pGM169/GL67A	10ml pGM169/GL67A	5ml pGM169/GL67A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	6	6	
Units: unit(s)				
arithmetic mean (standard deviation)	0.75 (± 0.3)	0.32 (± 0.1)	0.32 (± 0.1)	

## Statistical analyses

<b>Statistical analysis title</b>	Three group data analysis
Statistical analysis description:	
Three group data analysis compared with analysis of variance, Kruskal-Wallis, or Fisher's exact tests	
Comparison groups	20ml pGM169/GL67A v 10ml pGM169/GL67A v 5ml pGM169/GL67A
Number of subjects included in analysis	27
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0.03
Method	Kruskal-wallis

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Post dose

Adverse event reporting additional description:

Mild self limiting influenza like systemic response

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	10
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### Reporting groups

Reporting group title	pGM169/GL67A
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Reporting group description: -

Serious adverse events	pGM169/GL67A		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 35 (5.71%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Respiratory, thoracic and mediastinal disorders			
Injury in luvula	Additional description: Injury in luvula sustained from pressure of tube during bronchoscopy 03/04/2009		
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Acute pancreatitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	pGM169/GL67A		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 35 (94.29%)		
Immune system disorders			
Mild self limiting influenza like systemic response			
subjects affected / exposed	33 / 35 (94.29%)		
occurrences (all)	33		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported