



## Clinical trial results: Efficacy and Safety of SAR156597 in the Treatment of Idiopathic Pulmonary Fibrosis (IPF): A Randomized, Double-Blind, Placebo-Controlled, 52-Week Dose-Ranging Study

### Summary

EudraCT number	2014-003933-24
Trial protocol	GB CZ DK DE ES FR GR PT IT
Global end of trial date	14 August 2017

### Results information

Result version number	v1 (current)
This version publication date	25 August 2018
First version publication date	25 August 2018

### Trial information

#### Trial identification

Sponsor protocol code	DRI11772
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02345070
WHO universal trial number (UTN)	U1111-1154-6083
Other trial identifiers	Study Name: ESTAIR

Notes:

#### Sponsors

Sponsor organisation name	Sanofi aventis recherche & développement
Sponsor organisation address	1 avenue Pierre Brossolette, Chilly-Mazarin, France, 91380
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com

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	20 September 2017
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	14 August 2017
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To evaluate, in comparison with placebo, the efficacy of 2 dose levels/regimens of SAR156597 administered subcutaneously during 52 weeks on lung function of subjects with Idiopathic Pulmonary Fibrosis (IPF).

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy:

Subjects were stratified at baseline according to background anti-fibrotic therapy (with or without) either pirfenidone or nintedanib.

Evidence for comparator: -

Actual start date of recruitment	01 May 2015
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	Portugal: 3
Country: Number of subjects enrolled	Spain: 14
Country: Number of subjects enrolled	United Kingdom: 14
Country: Number of subjects enrolled	Czech Republic: 10
Country: Number of subjects enrolled	Denmark: 10
Country: Number of subjects enrolled	France: 44
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Argentina: 23
Country: Number of subjects enrolled	Australia: 31
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Chile: 30
Country: Number of subjects enrolled	Colombia: 5

Country: Number of subjects enrolled	Israel: 24
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	Mexico: 5
Country: Number of subjects enrolled	United States: 49
Country: Number of subjects enrolled	Korea, Republic of: 16
Country: Number of subjects enrolled	Turkey: 26
Worldwide total number of subjects	327
EEA total number of subjects	116

Notes:

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### **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)	98
From 65 to 84 years	227
85 years and over	2

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 110 centres in 19 countries. A total of 652 subjects were screened between May 2015 and May 2016, of whom, 327 subjects were randomized in 1:1:1 ratio to placebo: SAR156597 200 mg q2w: SAR156597 200 mg qw.

### Pre-assignment

Screening details:

Subjects were stratified at the moment of randomization according to background therapy (subjects with background anti-fibrotic therapy with either pirfenidone or nintedanib versus subjects without background anti-fibrotic therapy).

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Placebo qw

Arm description:

Subjects received one injection of placebo (matched to SAR156597) subcutaneously once every week (qw) for 52 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single subcutaneous injection in abdomen.

<b>Arm title</b>	SAR156597 200mg q2w
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Arm description:

Subjects received one injection of SAR156597 200 mg subcutaneously once every 2 weeks (q2w) alternating with placebo (matched to SAR156597) for 52 weeks.

Arm type	Experimental
Investigational medicinal product name	SAR156597
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single subcutaneous injection in abdomen.

<b>Arm title</b>	SAR156597 200mg qw
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Arm description:

Subjects received one injection of SAR156597 200 mg subcutaneously qw for 52 weeks.

Arm type	Experimental
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Investigational medicinal product name	SAR156597
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single subcutaneous injection in abdomen.

<b>Number of subjects in period 1</b>	Placebo qw	SAR156597 200mg q2w	SAR156597 200mg qw
Started	110	109	108
Treated	109	108	108
Completed	90	98	85
Not completed	20	11	23
Other than specified above	6	3	7
Adverse event	12	8	16
Poor compliance to protocol	2	-	-

## Baseline characteristics

### Reporting groups

Reporting group title	Placebo qw
Reporting group description: Subjects received one injection of placebo (matched to SAR156597) subcutaneously once every week (qw) for 52 weeks.	
Reporting group title	SAR156597 200mg q2w
Reporting group description: Subjects received one injection of SAR156597 200 mg subcutaneously once every 2 weeks (q2w) alternating with placebo (matched to SAR156597) for 52 weeks.	
Reporting group title	SAR156597 200mg qw
Reporting group description: Subjects received one injection of SAR156597 200 mg subcutaneously qw for 52 weeks.	

Reporting group values	Placebo qw	SAR156597 200mg q2w	SAR156597 200mg qw
Number of subjects	110	109	108
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	69.0 ± 8.6	67.4 ± 7.2	68.0 ± 7.6
Gender categorical Units: Subjects			
Female	22	32	27
Male	88	77	81
Race Units: Subjects			
White	105	104	99
Black Or African American	0	0	2
Asian	5	5	7
Other	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	21	28	24
Not Hispanic or Latino	89	81	84

Reporting group values	Total		
Number of subjects	327		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	-		
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Gender categorical			
Units: Subjects			
Female	81		
Male	246		
Race			
Units: Subjects			
White	308		
Black Or African American	2		
Asian	17		
Other	0		
Ethnicity			
Units: Subjects			
Hispanic or Latino	73		
Not Hispanic or Latino	254		

## End points

### End points reporting groups

Reporting group title	Placebo qw
Reporting group description: Subjects received one injection of placebo (matched to SAR156597) subcutaneously once every week (qw) for 52 weeks.	
Reporting group title	SAR156597 200mg q2w
Reporting group description: Subjects received one injection of SAR156597 200 mg subcutaneously once every 2 weeks (q2w) alternating with placebo (matched to SAR156597) for 52 weeks.	
Reporting group title	SAR156597 200mg qw
Reporting group description: Subjects received one injection of SAR156597 200 mg subcutaneously qw for 52 weeks.	

### Primary: Absolute Change From Baseline in Percent Predicted Forced Vital Capacity (FVC) at Week 52

End point title	Absolute Change From Baseline in Percent Predicted Forced Vital Capacity (FVC) at Week 52
End point description: FVC is a standard pulmonary function parameter measured by spirometry and used to quantify respiratory capacity (inspiration and expiration). It is a widely used objective measure of disease status in subjects with IPF. The primary variable was recorded as percentage of predicted value, which takes into account the height, gender and age of the subject. The endpoint measured the change in lung function from baseline at week 52. Analysis was performed on modified intent-to-treat (mITT) population that consisted of all subjects who received at least 1 injection of investigational medicinal product (IMP), had a valid baseline percent predicted FVC measurement, and had at least one post-baseline percent predicted FVC measurement. Here, number of subjects analyzed = subjects with available data for this end point.	
End point type	Primary
End point timeframe: Baseline, Week 52	

End point values	Placebo qw	SAR156597 200mg q2w	SAR156597 200mg qw	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	81	89	75	
Units: Percent predicted FVC				
least squares mean (standard error)	-5.81 (± 0.74)	-5.24 (± 0.73)	-6.31 (± 0.75)	

### Statistical analyses

Statistical analysis title	Placebo qw vs. SAR156597 200mg qw
Statistical analysis description: A hierarchical testing procedure was used to control type I error. Testing was then performed sequentially in order the endpoints are reported (qw dose group compared to placebo). Analysis was performed using MMRM with fixed categorical effects of treatment arm, stratification factor (with/without background therapy), time point, treatment-by-time point interaction, stratification factor-by-treatment-	

by-time point interaction, and continuous fixed covariate of % predicted FVC baseline.

Comparison groups	Placebo qw v SAR156597 200mg qw
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority <sup>[1]</sup>
P-value	= 0.6339 <sup>[2]</sup>
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.56
upper limit	1.56
Variability estimate	Standard error of the mean
Dispersion value	1.05

Notes:

[1] - The hierarchical testing sequence continued only when previous endpoint was statistically significant at 0.05 level.

[2] - Threshold for significance at 0.05 level.

<b>Statistical analysis title</b>	Placebo qw vs. SAR156597 200 mg q2w
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Statistical analysis description:

A hierarchical testing procedure was used to control type I error. Testing was then performed sequentially in order the endpoints are reported (q2w dose group compared to placebo). Analysis was performed using MMRM with fixed categorical effects of treatment arm, stratification factor (with/without background therapy), time point, treatment-by-time point interaction, stratification factor-by-treatment-by-time point interaction, and continuous fixed covariate of % predicted FVC baseline.

Comparison groups	Placebo qw v SAR156597 200mg q2w
Number of subjects included in analysis	170
Analysis specification	Pre-specified
Analysis type	superiority <sup>[3]</sup>
P-value	= 0.5874 <sup>[4]</sup>
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.47
upper limit	2.6
Variability estimate	Standard error of the mean
Dispersion value	1.04

Notes:

[3] - The hierarchical testing sequence continued only when previous endpoint was statistically significant at 0.05 level.

[4] - Threshold for significance at 0.05 level.

### **Secondary: Time to Disease Progression: Kaplan-Meier Estimates of Probability of Disease Progression at Week 52**

End point title	Time to Disease Progression: Kaplan-Meier Estimates of Probability of Disease Progression at Week 52
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End point description:

Disease progression was defined as the time from randomization to the first occurrence of any of the following events: decrease in absolute % predicted FVC  $\geq 10\%$ , decrease in absolute % predicted

DLCO $\geq$ 15%, lung transplant, or death. The median time to disease progression was not estimated because the number of occurrence of events was too low in the SAR156597 200mg arms. Analysis was performed on mITT population.

End point type	Secondary
End point timeframe:	
From randomization to disease progression (up to Week 52)	

<b>End point values</b>	Placebo qw	SAR156597 200mg q2w	SAR156597 200mg qw	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	108	108	
Units: probability of disease progression				
number (not applicable)	0.512	0.460	0.537	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Event: Kaplan-Meier Estimates of Probability of All Cause Mortality (Deaths) at Week 52

End point title	Time to Event: Kaplan-Meier Estimates of Probability of All Cause Mortality (Deaths) at Week 52
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End point description:

All-cause mortality was considered for this endpoint which was defined as the time from randomization to the date of death. The median time to event was not estimated because the number of all cause mortality was too low in the SAR156597 200mg arms. Analysis was performed on mITT population.

End point type	Secondary
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End point timeframe:

From randomization up to Week 52

<b>End point values</b>	Placebo qw	SAR156597 200mg q2w	SAR156597 200mg qw	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	108	108	
Units: probability of deaths				
number (not applicable)	0.09	0.08	0.13	

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AE) were collected from signature of the informed consent form up to the end of follow up visit (Week 64) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported AEs are treatment-emergent adverse AEs that is AEs that developed/worsened during treatment period. Reported death are all deaths that occurred during the treatment period. Treatment period is defined as the time from the first administration of the IMP to the last administration of the IMP + 84 days.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

### Reporting groups

Reporting group title	Placebo qw
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Reporting group description:

Subjects received one injection of placebo (matched to SAR156597) subcutaneously qw for 52 weeks.

Reporting group title	SAR156597 200mg q2w
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Reporting group description:

Subjects received one injection of SAR156597 200 mg subcutaneously q2w alternating with placebo (matched to SAR156597) for 52 weeks.

Reporting group title	SAR156597 200mg qw
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Reporting group description:

Subjects received one injection of SAR156597 200 mg subcutaneously qw for 52 weeks.

<b>Serious adverse events</b>	Placebo qw	SAR156597 200mg q2w	SAR156597 200mg qw
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 109 (23.85%)	27 / 108 (25.00%)	46 / 108 (42.59%)
number of deaths (all causes)	9	6	13
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-Cell Lymphoma			
subjects affected / exposed	0 / 109 (0.00%)	1 / 108 (0.93%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangiocarcinoma			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive Ductal Breast Carcinoma			

subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Adenocarcinoma			
subjects affected / exposed	1 / 109 (0.92%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuroendocrine Carcinoma Metastatic			
subjects affected / exposed	1 / 109 (0.92%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Small Cell Lung Cancer Metastatic			
subjects affected / exposed	1 / 109 (0.92%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
T-Cell Polymphocytic Leukaemia			
subjects affected / exposed	0 / 109 (0.00%)	1 / 108 (0.93%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Prostatitis			

subjects affected / exposed	1 / 109 (0.92%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Respiratory, thoracic and mediastinal disorders</b>			
<b>Acute Respiratory Failure</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Dyspnoea</b>			
subjects affected / exposed	0 / 109 (0.00%)	1 / 108 (0.93%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Dyspnoea Exertional</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Haemoptysis</b>			
subjects affected / exposed	1 / 109 (0.92%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Idiopathic Pulmonary Fibrosis</b>			
subjects affected / exposed	10 / 109 (9.17%)	9 / 108 (8.33%)	22 / 108 (20.37%)
occurrences causally related to treatment / all	2 / 11	3 / 13	1 / 26
deaths causally related to treatment / all	2 / 6	0 / 0	0 / 7
<b>Pneumothorax</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Pulmonary Alveolar Haemorrhage</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Pulmonary Embolism</b>			

subjects affected / exposed	2 / 109 (1.83%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Pulmonary Hypertension</b>			
subjects affected / exposed	0 / 109 (0.00%)	2 / 108 (1.85%)	2 / 108 (1.85%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
<b>Respiratory Failure</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	2 / 108 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
<b>Rheumatoid Lung</b>			
subjects affected / exposed	1 / 109 (0.92%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Psychiatric disorders</b>			
<b>Anxiety</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Assisted Suicide</b>			
subjects affected / exposed	0 / 109 (0.00%)	1 / 108 (0.93%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
<b>Investigations</b>			
<b>Ejection Fraction Decreased</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Electrocardiogram Qt Prolonged</b>			
subjects affected / exposed	0 / 109 (0.00%)	1 / 108 (0.93%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>General Physical Condition Abnormal</b>			

subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight Decreased			
subjects affected / exposed	0 / 109 (0.00%)	1 / 108 (0.93%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Post Procedural Haemorrhage			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib Fracture			
subjects affected / exposed	1 / 109 (0.92%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stress Fracture			
subjects affected / exposed	1 / 109 (0.92%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist Fracture			
subjects affected / exposed	0 / 109 (0.00%)	1 / 108 (0.93%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Atrial Septal Defect			
subjects affected / exposed	0 / 109 (0.00%)	1 / 108 (0.93%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute Coronary Syndrome			

subjects affected / exposed	1 / 109 (0.92%)	0 / 108 (0.00%)	2 / 108 (1.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
<b>Acute Right Ventricular Failure</b>			
subjects affected / exposed	0 / 109 (0.00%)	1 / 108 (0.93%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
<b>Arrhythmia</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Arteriosclerosis Coronary Artery</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Atrial Fibrillation</b>			
subjects affected / exposed	0 / 109 (0.00%)	1 / 108 (0.93%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Atrial Flutter</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Cardiac Failure</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Cardiac Failure Congestive</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Congestive Cardiomyopathy</b>			

subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Coronary Artery Stenosis</b>			
subjects affected / exposed	1 / 109 (0.92%)	1 / 108 (0.93%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Myocardial Infarction</b>			
subjects affected / exposed	1 / 109 (0.92%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
<b>Right Ventricular Failure</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
<b>Supraventricular Tachycardia</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Ventricular Fibrillation</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
<b>Nervous system disorders</b>			
<b>Cerebrovascular Accident</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Ischaemic Stroke</b>			
subjects affected / exposed	1 / 109 (0.92%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Postresuscitation Encephalopathy</b>			

subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Quadripareisis</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Syncope</b>			
subjects affected / exposed	0 / 109 (0.00%)	1 / 108 (0.93%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Transient Ischaemic Attack</b>			
subjects affected / exposed	0 / 109 (0.00%)	1 / 108 (0.93%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Blood and lymphatic system disorders</b>			
<b>Anaemia</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Iron Deficiency Anaemia</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Neutropenia</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Gastrointestinal disorders</b>			
<b>Abdominal Pain</b>			
subjects affected / exposed	0 / 109 (0.00%)	1 / 108 (0.93%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Duodenal Obstruction</b>			

subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired Gastric Emptying			
subjects affected / exposed	0 / 109 (0.00%)	1 / 108 (0.93%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal Obstruction			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal Achalasia			
subjects affected / exposed	1 / 109 (0.92%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Volvulus			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis Acute			
subjects affected / exposed	0 / 109 (0.00%)	1 / 108 (0.93%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic Congestion			

subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	2 / 108 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Hepatic Mass</b>			
subjects affected / exposed	0 / 109 (0.00%)	1 / 108 (0.93%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Musculoskeletal and connective tissue disorders</b>			
<b>Musculoskeletal Chest Pain</b>			
subjects affected / exposed	1 / 109 (0.92%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Musculoskeletal Pain</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Osteoporotic Fracture</b>			
subjects affected / exposed	0 / 109 (0.00%)	1 / 108 (0.93%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Infections and infestations</b>			
<b>Bronchitis</b>			
subjects affected / exposed	1 / 109 (0.92%)	0 / 108 (0.00%)	2 / 108 (1.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Bronchitis Bacterial</b>			
subjects affected / exposed	0 / 109 (0.00%)	1 / 108 (0.93%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Diverticulitis</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastroenteritis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis Norovirus			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes Zoster			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 109 (0.92%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower Respiratory Tract Infection			
subjects affected / exposed	1 / 109 (0.92%)	1 / 108 (0.93%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Infection			
subjects affected / exposed	0 / 109 (0.00%)	2 / 108 (1.85%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Metapneumovirus Infection			
subjects affected / exposed	0 / 109 (0.00%)	1 / 108 (0.93%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ophthalmic Herpes Zoster			
subjects affected / exposed	0 / 109 (0.00%)	1 / 108 (0.93%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	4 / 109 (3.67%)	3 / 108 (2.78%)	8 / 108 (7.41%)
occurrences causally related to treatment / all	1 / 4	0 / 3	1 / 9
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 0
<b>Pneumonia Bacterial</b>			
subjects affected / exposed	1 / 109 (0.92%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Pneumonia Klebsiella</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Pneumonia Viral</b>			
subjects affected / exposed	1 / 109 (0.92%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Respiratory Tract Infection</b>			
subjects affected / exposed	1 / 109 (0.92%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Sepsis</b>			
subjects affected / exposed	0 / 109 (0.00%)	1 / 108 (0.93%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Septic Shock</b>			
subjects affected / exposed	2 / 109 (1.83%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 1
<b>Tracheobronchitis</b>			
subjects affected / exposed	0 / 109 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Viral Upper Respiratory Tract Infection</b>			

subjects affected / exposed	1 / 109 (0.92%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

<b>Non-serious adverse events</b>	Placebo qw	SAR156597 200mg q2w	SAR156597 200mg qw
Total subjects affected by non-serious adverse events			
subjects affected / exposed	81 / 109 (74.31%)	86 / 108 (79.63%)	79 / 108 (73.15%)
Investigations			
Weight Decreased			
subjects affected / exposed	9 / 109 (8.26%)	9 / 108 (8.33%)	8 / 108 (7.41%)
occurrences (all)	10	9	8
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 109 (6.42%)	5 / 108 (4.63%)	9 / 108 (8.33%)
occurrences (all)	11	6	11
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	6 / 109 (5.50%)	4 / 108 (3.70%)	3 / 108 (2.78%)
occurrences (all)	7	5	4
Injection Site Erythema			
subjects affected / exposed	3 / 109 (2.75%)	7 / 108 (6.48%)	10 / 108 (9.26%)
occurrences (all)	6	18	18
Injection Site Haematoma			
subjects affected / exposed	2 / 109 (1.83%)	5 / 108 (4.63%)	6 / 108 (5.56%)
occurrences (all)	4	6	11
Injection Site Reaction			
subjects affected / exposed	6 / 109 (5.50%)	11 / 108 (10.19%)	10 / 108 (9.26%)
occurrences (all)	23	30	17
Pyrexia			
subjects affected / exposed	8 / 109 (7.34%)	1 / 108 (0.93%)	0 / 108 (0.00%)
occurrences (all)	8	1	0
Gastrointestinal disorders			

Abdominal Pain			
subjects affected / exposed	1 / 109 (0.92%)	2 / 108 (1.85%)	7 / 108 (6.48%)
occurrences (all)	1	3	9
Diarrhoea			
subjects affected / exposed	16 / 109 (14.68%)	23 / 108 (21.30%)	12 / 108 (11.11%)
occurrences (all)	24	25	15
Gastroesophageal Reflux Disease			
subjects affected / exposed	4 / 109 (3.67%)	6 / 108 (5.56%)	0 / 108 (0.00%)
occurrences (all)	4	6	0
Nausea			
subjects affected / exposed	9 / 109 (8.26%)	9 / 108 (8.33%)	9 / 108 (8.33%)
occurrences (all)	9	10	12
Vomiting			
subjects affected / exposed	6 / 109 (5.50%)	8 / 108 (7.41%)	6 / 108 (5.56%)
occurrences (all)	7	10	6
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	12 / 109 (11.01%)	22 / 108 (20.37%)	18 / 108 (16.67%)
occurrences (all)	14	27	21
Dyspnoea			
subjects affected / exposed	11 / 109 (10.09%)	10 / 108 (9.26%)	13 / 108 (12.04%)
occurrences (all)	11	10	13
Idiopathic Pulmonary Fibrosis			
subjects affected / exposed	10 / 109 (9.17%)	11 / 108 (10.19%)	8 / 108 (7.41%)
occurrences (all)	10	11	9
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 109 (0.00%)	6 / 108 (5.56%)	2 / 108 (1.85%)
occurrences (all)	0	6	2
Back Pain			
subjects affected / exposed	9 / 109 (8.26%)	13 / 108 (12.04%)	9 / 108 (8.33%)
occurrences (all)	11	13	10
Infections and infestations			
Bronchitis			
subjects affected / exposed	12 / 109 (11.01%)	18 / 108 (16.67%)	10 / 108 (9.26%)
occurrences (all)	14	25	21

Lower Respiratory Tract Infection subjects affected / exposed occurrences (all)	2 / 109 (1.83%) 2	11 / 108 (10.19%) 13	6 / 108 (5.56%) 10
Respiratory Tract Infection subjects affected / exposed occurrences (all)	7 / 109 (6.42%) 7	5 / 108 (4.63%) 6	3 / 108 (2.78%) 5
Rhinitis subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1	8 / 108 (7.41%) 9	2 / 108 (1.85%) 3
Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	13 / 109 (11.93%) 17	10 / 108 (9.26%) 12	8 / 108 (7.41%) 10
Urinary Tract Infection subjects affected / exposed occurrences (all)	6 / 109 (5.50%) 7	4 / 108 (3.70%) 4	7 / 108 (6.48%) 9
Viral Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	15 / 109 (13.76%) 19	18 / 108 (16.67%) 22	12 / 108 (11.11%) 18
Metabolism and nutrition disorders Decreased Appetite subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1	7 / 108 (6.48%) 8	2 / 108 (1.85%) 2

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 December 2014	Following amendments were made: - Urine pregnancy tests were added on a monthly basis in women of childbearing potential until the final study visit. - The stability duration of the reconstituted IMP to be injected was updated and 1 hour was replaced by 3 hours. - Method of assigning subjects to treatment group was clarified.
21 July 2015	- Inclusion criterion related to IPF diagnosis was clarified. - A wash out period was added for experimental stem cell therapy if administered prior to study entry. - Safety criterion was added for permanent discontinuation with regards to laboratory abnormalities. - "Acute exacerbation of IPF" was added to the list of medically important events. - Instructions were provided to perform the 6-minute walk test (6-MWT). - Clarified the possibility of a direct to subject shipment of IMPs, from investigational site to subject's home, via a sponsor-approved courier company (in case home administration is done), where allowed by local regulations and approved by the subject. - The rate of subjects with background therapy was capped. - Potential fertility data analysis as interim analysis was added. -An early analysis of the main efficacy endpoints and safety data was performed. Clarified that involvement of subjects with legally acceptable representative is not applicable in this study. The study name was added.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported