Clinical trial results:
A Phase 2b, Randomized, Double-Blind, Placebo-Controlled Multi-Center Study Evaluating Antiviral Effects, Pharmacokinetics, Safety, and Tolerability of GS-5806 in Hospitalized Adults with Respiratory Syncytial Virus (RSV) Infection

Summary

EudraCT number	2014-002137-58
Trial protocol	GB BE IT NL
Global end of trial date	12 April 2017

Results information

Result version number	v2 (current)
This version publication date	18 May 2019
First version publication date	12 April 2018
Version creation reason	• Correction of full data set Adding text to "Limitations and Caveats" section

Trial information

Trial identification

Sponsor protocol code	GS-US-218-1227

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02135614
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.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	12 April 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 March 2017
Global end of trial reached?	Yes
Global end of trial date	12 April 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the effects of presatovir (GS-5806) on respiratory syncytial virus (RSV) viral load in RSV-positive adults who have been hospitalized with acute respiratory infectious symptoms.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 June 2014
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	Netherlands: 3
Country: Number of subjects enrolled	Poland: 6
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	France: 35
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Israel: 58
Country: Number of subjects enrolled	United States: 29
Country: Number of subjects enrolled	New Zealand: 18
Country: Number of subjects enrolled	Australia: 16
Country: Number of subjects enrolled	Korea, Republic of: 16
Worldwide total number of subjects	189
EEA total number of subjects	52

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	73
From 65 to 84 years	98
85 years and over	18

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Australia, Europe, Asia, New Zealand, and the United States. The first participant was screened on 09 June 2014. The last study visit occurred on 12 April 2017.

Pre-assignment

Screening details:

833 participants were screened.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Presatovir

Arm description:

Single dose of presatovir

Arm type	Experimental
Investigational medicinal product name	Presatovir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single dose of presatovir 200 mg (4 x 50 mg tablets)

Arm title	Placebo

Arm description:

Single dose of placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single dose of placebo

Number of subjects in period 1[1]	Presatovir	Placebo
Started	92	94
Completed	86	90
Not completed	6	4
Adverse event, serious fatal	1	-
Adverse event, non-fatal	-	1
Withdrew consent	2	2
Lost to follow-up	3	-
Investigator's discretion	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 3 participants (Presatovir = 2; Placebo = 1) who were enrolled but not treated are not included in the subject disposition table.

Baseline characteristics

Reporting groups	
Reporting group title	Presatovir
Reporting group description: Single dose of presatovir	
Reporting group title	Placebo
Reporting group description: Single dose of placebo	

Reporting group values	Presatovir	Placebo	Total
Number of subjects	92	94	186
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	69.4	65.9	
standard deviation	± 14.24	± 13.87	-
Gender categorical Units: Subjects			
Female	50	52	102
Male	42	42	84
Race Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	6	11	17
Black or African American	5	7	12
Native Hawaiian or Pacific Islander	0	2	2
White	72	69	141
Other	2	2	4
Not Permitted	7	2	9
Ethnicity Units: Subjects			
Hispanic or Latino	0	1	1
Not Hispanic or Latino	85	91	176
Not Permitted	7	2	9
Stratification Factor: Disease Status Units: Subjects			
Asthma	22	22	44
Chronic Obstructive Pulmonary Disease	27	30	57
No Chronic Airways or Lung Disease	31	31	62
Other Chronic Airways or Lung Disease	12	11	23
Nasal Viral Load Units: log10 copies/mL			
arithmetic mean	5.58	5.07	
standard deviation	± 2.104	± 2.528	-

Flu-PRO score			
Flu-PRO Score was calculated as the mean of 38 individual scores. Individual scores ranged from 0 (no symptoms) to 4 (worst symptoms).			
Units: units on a scale			
arithmetic mean	1.11	1.04	
standard deviation	± 0.553	± 0.566	-

End points

End points reporting groups	
Reporting group title	Presatovir
Reporting group description: Single dose of presatovir	
Reporting group title	Placebo
Reporting group description: Single dose of placebo	

Primary: Time-Weighted Average Change in Respiratory Syncytial Viral (RSV) Load From Baseline to Day 5

End point title	Time-Weighted Average Change in Respiratory Syncytial Viral (RSV) Load From Baseline to Day 5

End point description:

The time-weighted average change, often referred to as the DAVG, provides the average viral burden change from baseline. The mean values presented were calculated using the ANCOVA model and are adjusted for baseline value and stratification factor.

The Evaluable Analysis Set included all randomized participants who received at least 1 dose of study medication, had an RSV viral load greater than lower limit of quantification (LLOQ) of the RT-qPCR assay in the Day 1 nasal-swab sample, and had a minimum of 3 quantifiable samples (including baseline) within a 5 day period.

End point type	Primary
End point timeframe: Baseline to Day 5	

End point values	Presatovir	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	74		
Units: log10 copies/mL				
arithmetic mean (standard error)	-0.77 (± 0.113)	-0.89 (± 0.118)		

Statistical analyses

Statistical analysis title	Statistical Analysis - Presatovir vs Placebo
Comparison groups	Placebo v Presatovir
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.46 [1]
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	0.12

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.43

Notes:

[1] - P-value was calculated from the ANCOVA model including baseline values, Clinical Frailty Scale (CFS) score, and stratification factor as covariates.

Secondary: Time-weighted Average Change in the Flu-PRO Score From Baseline to Day 5

End point title	Time-weighted Average Change in the Flu-PRO Score From Baseline to Day 5

End point description:

The Flu-PRO is a patient-reported outcome questionnaire utilized as a standardized method for evaluating symptoms of influenza. Flu-PRO Score was calculated as the mean of 38 individual scores. Individual scores ranged from 0 (no symptoms) to 4 (worst symptoms). The mean values presented were calculated using the ANCOVA model and are adjusted for baseline value and stratification factor.

Participants in the Evaluable Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline to Day 5

End point values	Presatovir	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	74		
Units: units on a scale				
arithmetic mean (standard error)	-0.27 (± 0.029)	-0.35 (± 0.030)		

Statistical analyses

Statistical analysis title	Statistical Analysis - Presatovir vs Placebo
Comparison groups	Presatovir v Placebo
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.046 [2]
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.16

Notes:

[2] - P-value was calculated from the ANCOVA model including the baseline value, CFS score and stratification factor as covariates.

Secondary: Number of Hospitalization-Free Days Following Presatovir Administration

End point title	Number of Hospitalization-Free Days Following Presatovir Administration

End point description:

The Evaluable Analysis Set included all randomized participants who received at least 1 dose of study medication, had an RSV viral load greater than lower limit of quantification (LLOQ) of the RT-qPCR assay in the Day 1 nasal-swab sample, and had a minimum of 3 quantifiable samples (including baseline) within a 5 day period.

End point type	Secondary

End point timeframe:

Up to Day 28

End point values	Presatovir	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	74		
Units: days				
median (inter-quartile range (Q1-Q3))	25 (20 to 27)	25 (20 to 27)		

Statistical analyses

Statistical analysis title	Statistical Analysis - Presatovir vs Placebo
Comparison groups	Presatovir v Placebo
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.39 [3]
Method	Negative Binomial Model

Notes:

[3] - P-value was calculated from the negative binomial model with the stratification factor as covariate.

Secondary: Rate of Unplanned Medical Encounters

End point title	Rate of Unplanned Medical Encounters

End point description:

The adjusted rate of unplanned medical encounters (clinic visits, emergency room visits, urgent care visits, and rehospitalizations) related to a respiratory illness after initial hospital discharge through Day 28 will be assessed. Event rate was calculated as the total number of unplanned medical encounters divided by the total number of participants. The mean values presented were adjusted for stratification factor.

The Evaluable Analysis Set included all randomized participants who received at least 1 dose of study medication, had an RSV viral load greater than lower limit of quantification (LLOQ) of the RT-qPCR assay in the Day 1 nasal-swab sample, and had a minimum of 3 quantifiable samples (including baseline) within a 5 day period.

End point type	Secondary

End point timeframe:

Up to Day 28

End point values	Presatovir	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	74		
Units: encounters per participant				
number (confidence interval 95%)	0.226 (0.133 to 0.384)	0.066 (0.029 to 0.150)		

Statistical analyses

Statistical analysis title	Statistical Analysis - Presatovir vs Placebo
Comparison groups	Presatovir v Placebo
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 [4]
Method	Negative Binomial Model

Notes:

[4] - P-value from the negative binomial model comparing the rate ratio between treatment groups, adjusted for the stratification factor.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Day 28

Adverse event reporting additional description:

Safety Analysis Set: all participants who received 1 dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Presatovir

Reporting group description:

Single dose of presatovir

Reporting group title	Placebo

Reporting group description:

Single dose of placebo

Serious adverse events	Presatovir	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 92 (8.70%)	13 / 94 (13.83%)	
number of deaths (all causes)	2	0	
number of deaths resulting from adverse events			
Investigations			
Troponin increased			
subjects affected / exposed	1 / 92 (1.09%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	2 / 92 (2.17%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 92 (1.09%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Myocardial infarction			
subjects affected / exposed	0 / 92 (0.00%)	1 / 94 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 92 (0.00%)	1 / 94 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 92 (1.09%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Angle closure glaucoma			
subjects affected / exposed	0 / 92 (0.00%)	1 / 94 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 92 (0.00%)	1 / 94 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 92 (1.09%)	2 / 94 (2.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 92 (0.00%)	1 / 94 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			

subjects affected / exposed	1 / 92 (1.09%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 92 (1.09%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary congestion			
subjects affected / exposed	0 / 92 (0.00%)	1 / 94 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 92 (0.00%)	1 / 94 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 92 (0.00%)	1 / 94 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 92 (0.00%)	1 / 94 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 92 (0.00%)	1 / 94 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	1 / 92 (1.09%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Influenza			
subjects affected / exposed	0 / 92 (0.00%)	1 / 94 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 92 (1.09%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device malfunction			
subjects affected / exposed	0 / 92 (0.00%)	1 / 94 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Presatovir	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 92 (36.96%)	31 / 94 (32.98%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	5 / 92 (5.43%)	2 / 94 (2.13%)	
occurrences (all)	5	2	
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 92 (8.70%)	5 / 94 (5.32%)	
occurrences (all)	8	5	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	5 / 92 (5.43%)	1 / 94 (1.06%)	
occurrences (all)	5	1	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 92 (4.35%)	9 / 94 (9.57%)	
occurrences (all)	4	9	
Diarrhoea			

subjects affected / exposed	5 / 92 (5.43%)	7 / 94 (7.45%)	
occurrences (all)	5	7	
Constipation			
subjects affected / exposed	4 / 92 (4.35%)	5 / 94 (5.32%)	
occurrences (all)	4	5	
Vomiting			
subjects affected / exposed	2 / 92 (2.17%)	6 / 94 (6.38%)	
occurrences (all)	2	6	
Abdominal pain			
subjects affected / exposed	5 / 92 (5.43%)	2 / 94 (2.13%)	
occurrences (all)	5	2	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	6 / 92 (6.52%)	3 / 94 (3.19%)	
occurrences (all)	6	3	
Epistaxis			
subjects affected / exposed	2 / 92 (2.17%)	5 / 94 (5.32%)	
occurrences (all)	2	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 March 2014	• Added South Korea to the planned study centers and clarified which European countries had been selected to participate • Clarified PK sampling time points on Days 1, 3, and 5 • Corrected the title of the Frailty Index to the Clinical Frailty Scale (CFS) • Added an exclusion criterion for subjects requiring > 50% O2 when awake at screening • Added an exclusion criteria for subjects scoring > 7 on the CFS at baseline • Added RSV antibody titer blood draws at baseline and Day 14 • Added viral-coinfection testing at baseline, and clarified that RSV and influenza sampling and testing at screening was to follow local laboratory procedures • Clarified the exclusion criteria for chronic systemic immunosuppressive agents and the exclusion criteria related to pneumonia • Deleted the exclusion criteria related to life-expectancy and to heart failure • Removed the Clinical Symptom Score assessment and the European Quality of Life 5-Dimension utility measure (EQ5D-5L) questionnaire • Modified the Flu-PRO secondary endpoint from AUC of change in score from baseline to Day 7 to daily average change in the Flu-PRO score from baseline to Day 5, and updated the Secondary Analysis sections accordingly • Updated the Interim Analysis section to allow for an earlier assessment of futility and allow for study termination at a higher conditional power threshold • Modified the primary endpoint from the AUC of log10 viral load from Day 1 to Day 7 to the daily average change in log10 viral load from Day 1 to Day 5, and updated the assumptions used in the sample size calculation • Deleted the total number of intensive care unit (ICU) transfers exploratory endpoint
05 August 2014	• Modification of contraceptive requirements • Addition of phototoxicity text to the dosage and administration information • Addition of text to address potential for drug-drug interactions (DDI) to the prior and concomitant medication information • Addition of the EudraCT Number and the ClinicalTrials.gov Identifier • Updated the terminology of relevant endpoints from daily averages to time-weighted averages as this term, along with difference between time-weighted average post-baseline and baseline (DAVG), is often used in literature. The definitions and calculations of the endpoints remained the same.

29 August 2014	• Updated the list of countries in which study centers were planned • Modified inclusion criteria to allow hospitalizations due to respiratory or non-respiratory reasons and to clarify that either upper or lower respiratory tract symptoms were acceptable, instead of requiring both • Expanded exclusion criterion related to prednisone use to include similar corticosteroids • Removed exclusion criteria related to history of bleeding disorder and to arrhythmia • Replaced exclusion criterion for HIV/AIDS and hepatitis B or C status with a criterion excluding cluster determinant 4 (CD4) counts indicative of immunocompromised subjects • Modified exclusion criterion related to bacteremia and fungemia • Replaced exclusion criteria related to cerebrovascular accident or stroke, and admission for trauma or planned and emergent surgeries with a broader exclusion criterion to exclude subjects with unstable medical conditions • Modified exclusionary laboratory values for relevance in the elderly patient population • Clarified the 2-part consent process • Clarified the use of admissions records to support enrollment and baseline data • Added telephone visit as an option for Day 28 • Administrative change to relocate collection of demographic information from baseline visit (Day 1) to screening (Day −1) in order to align with electronic data capture (EDC) requirements • Administrative changes to Section 7.0 Adverse Events including rewording and reformatting for clarity • Administrative change to update the sponsor address to the address of Gilead's main headquarters • Administrative change updating the primary medical monitor to Seth Toback, MD
17 November 2015	• Added summary of the definitive embryo-fetal development study • Added a section for ongoing clinical studies • Completely revised the study design section for clarity • Removed food-effect and phototoxicity wording from study drug dosing requirements • Added End of Study and Post Study Care sections to the protocol • Increased the number of study centers where the study was planned and added Hong Kong as a study location • Clarified inclusion criterion for number of symptom days • Added exclusion criterion for Middle East Respiratory Syndrome coronavirus (MERS-CoV) and other coronavirus coinfection • Added moderate cytochrome P450 enzyme (CYP) inducers to the concomitant and prohibited medications • Added recent historical evidence of pleural effusion and arterial blood pH to medical history requirements • Added the option for home visits at Days 2, 3, 5, 7, and 14 • Added Day 21 visit • Updated Flu-PRO instructions • Added the EQ5D-5L • Standardized O2 saturation procedure across protocols • Added Supplemental Oxygen Use Diary • Added an ECG to Day 14 and updated ECG before dosing at baseline to a mandatory requirement • Added requirement for collection of clinical data related to cardiac testing • Added troponin blood draws before and after dosing at baseline and added an additional troponin blood draw at Day 14 • Updated exploratory analyses based on the addition of the EQ5D-5L questionnaire. Analysis methods for other endpoints were also updated to include stratification factors in the model. • Administrative change of all instances of GS-5806 to presatovir, excluding the study title • Corrected typographical error in the EudraCT Number • Administrative clarification that subjects could be discharged 30 minutes after dosing but were still required to complete all after dosing procedures • Administrative addition of text regarding the Eligibility Criteria electronic case report form (eCRF) based off the new protocol template

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

An unplanned review of unblinded clinical trial data was performed in this study that was not prospectively specified in the protocol. There was no impact on the overall integrity or conclusions of the study.

Notes: