Clinical trial results:
A Randomised, Phase 2a, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Pharmacokinetics and Antiviral Activity of Multiple Doses of RV521 Against Respiratory Syncytial Virus infection in the Virus Challenge Model.

Summary

EudraCT number	2017-001282-24
Trial protocol	GB
Global end of trial date	31 October 2017

Results information

Result version number	v1 (current)
This version publication date	19 June 2019
First version publication date	19 June 2019

Trial information

Trial identification

Sponsor protocol code	REVC002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03258502
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ReViral Ltd
Sponsor organisation address	Stevenage Bioscience Catalyst, Gunnels Wood Road, Stevenage, Hertfordshire, United Kingdom, SG1 2FX
Public contact	Director Clinical Operations, ReViral Ltd, +44 1438 906760,
Scientific contact	Chief Operating Officer, ReViral Ltd, +44 1438 906760,

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 June 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 October 2017
Global end of trial reached?	Yes
Global end of trial date	31 October 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the antiviral activity of RV521 compared to placebo in healthy adult subjects inoculated with RSV-A Memphis 37b.

Protection of trial subjects:

This study will be conducted in accordance with the Ethical Principles for Medical Research Involving Human Subjects outlined in the Declaration of Helsinki 19961, the principles of ICH GCP2, current regulatory requirements as detailed in the Medicines for Human Use (Clinical Trial) Regulations (SI 2004/1031)4 and all subsequent amendments, the UK Data Protection Act 19985, any other applicable laws and guidance, and any Sponsor requirements. All ethical and legal requirements will be met before the first subject is enrolled in the study. Safety of the subjects was safeguarded through safety data review and the implementation of study stopping criteria. Safety endpoint measurements included vital signs, 12-lead ECGs, physical examinations, safety laboratory
blood tests (biochemistry, haematology, coagulation and cardiac enzymes) and urinalysis. Adverse events were continuously monitored throughout the study from date of consent until the last follow up assessment.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 July 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 66
Worldwide total number of subjects	66
EEA total number of subjects	66

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)	66
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

66 subjects were enrolled and 65 subjects have completed the study.

Pre-assignment

Screening details:

Subjects were healthy males and/or females, 18 to 45 years of age, who met the eligibility criteria outlined in the Protocol.

Pre-assignment period milestones

Number of subjects started	66
Number of subjects completed	66

Period 1

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

Blinding implementation details:

The study was conducted in a double-blind fashion, whereby subjects and clinical study site staff were blinded to the active or placebo study drug assignment. However, the subjects and clinical study site staff were aware of the dose level that was used in each cohort. As 2 dose levels are used in this study, quarantine staff were to have ensured that each subject remained in their own room without direct contact with any other subject.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo to match RV521 (The placebo group was split equally across the 2 dose groups such that subjects received placebo at dose level 200 mg in Cohort 1 and at 350 mg in Cohort 2).

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

Dosage and administration details:

Placebo capsules at dose level 200 mg (Cohort 1) or 350 mg (Cohort 2), 12 hours apart (± 1 hour) for 10 consecutive doses.

Arm title	200mg RV521

Arm description:

200 mg of RV521 (Cohort 1)

Arm type	Experimental

Investigational medicinal product name	RV521
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

200mg Oral RV521 or placebo, 12 hours apart (± 1 hour) for 10 consecutive doses.

Arm title	350mg RV521

Arm description:

350mg of RV521 (Cohort 2)

Arm type	Experimental
Investigational medicinal product name	RV521
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

350mg Oral RV521 or placebo, 12 hours apart (± 1 hour) for 10 consecutive doses.

Number of subjects in period 1	Placebo	200mg RV521	350mg RV521
Started	22	22	22
Completed	21	22	22
Not completed	1	0	0
Adverse event, non-fatal	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo to match RV521 (The placebo group was split equally across the 2 dose groups such that subjects received placebo at dose level 200 mg in Cohort 1 and at 350 mg in Cohort 2).	
Reporting group title	200mg RV521
Reporting group description:	
200 mg of RV521 (Cohort 1)	
Reporting group title	350mg RV521
Reporting group description:	
350mg of RV521 (Cohort 2)	

Reporting group values	Placebo	200mg RV521	350mg RV521
Number of subjects	22	22	22
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)	0	0	0
Adults (18-64 years)	22	22	22
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	24.6	21.7	24.5
standard deviation	± 5.29	± 3.09	± 5.50
Gender categorical Units: Subjects			
Female	7	9	6
Male	15	13	16

Reporting group values	Total		
Number of subjects	66		
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)	0		

Adults (18-64 years)	66		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	22		
Male	44		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo to match RV521 (The placebo group was split equally across the 2 dose groups such that subjects received placebo at dose level 200 mg in Cohort 1 and at 350 mg in Cohort 2).	
Reporting group title	200mg RV521
Reporting group description:	
200 mg of RV521 (Cohort 1)	
Reporting group title	350mg RV521
Reporting group description:	
350mg of RV521 (Cohort 2)	

Primary: Primary efficacy endpoint

End point title	Primary efficacy endpoint
End point description:	
The analysis of viral load AUC (first dose of IMP to Study Day 12) by nasal wash RT-qPCR, for the ITT-I Analysis Set defined as all randomised subjects who received Challenge Virus and at least one dose of IMP, and met the criterion for laboratory confirmed RSV infection, defined as the presence of viral shedding (measured in nasal wash). The ITT-I analysis set was considered the primary analysis population for efficacy endpoints.	
End point type	Primary
End point timeframe:	
From the last RT-qPCR measurement collected prior to the first dose of IMP until the last RT-qPCR measurement collected up to Study Day 12 (Quarantine discharge).	

End point values	Placebo	200mg RV521	350mg RV521	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	18	16	
Units: log10 PFUe/mL				
log mean (standard error)	501.39 (± 86.57)	224.35 (± 37.60)	185.26 (± 31.17)	

Statistical analyses

Statistical analysis title	Descriptive Statistics
Statistical analysis description:	
AUC descriptive statistics (n, (arithmetic) mean, SD, median, Q1, Q3, minimum and maximum), the Satterthwaite t-test p-value, the difference in mean values (comparison of RV521 dose and placebo) and the associated 95% CI were summarised by treatment group.	
Comparison groups	Placebo v 200mg RV521 v 350mg RV521

Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.007 [1]
Method	Sensitivity Analysis

Notes:

[1] - RV521 resulted in statistically significant reduction in AUC of RT-qPCR RSV viral load compared with placebo; difference in mean values compared with placebo of 55.25% (p=0.007) and 63.05% (p=0.002) for the 200 mg and 350 mg RV521 doses respectively

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Collected from informed consent until final follow up visit.	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0
Reporting groups	
Reporting group title	Overall Summary of Adverse Events for Placebo Group
Reporting group description: -	
Reporting group title	Overall summary of Adverse Events for RV521 200mg group
Reporting group description: -	
Reporting group title	Overall summary of Adverse Events for RV521 350mg group
Reporting group description: -	

Serious adverse events	Overall Summary of Adverse Events for Placebo Group	Overall summary of Adverse Events for RV521 200mg group	Overall summary of Adverse Events for RV521 350mg group
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 22 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Sub-acute myocarditis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 22 (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: 1 %

Non-serious adverse events	Overall Summary of Adverse Events for Placebo Group	Overall summary of Adverse Events for RV521 200mg group	Overall summary of Adverse Events for RV521 350mg group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 22 (59.09%)	12 / 22 (54.55%)	20 / 22 (90.91%)
Cardiac disorders			
Myocarditis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			

Lymphadenopathy			
subjects affected / exposed	1 / 22 (4.55%)	1 / 22 (4.55%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
Catheter site erythema			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Catheter site paraesthesia			
subjects affected / exposed	1 / 22 (4.55%)	1 / 22 (4.55%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Pyrexia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Vessel puncture site bruise			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Eye pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Ocular hyperaemia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Abdominal distension			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	0 / 22 (0.00%)	3 / 22 (13.64%)	4 / 22 (18.18%)
occurrences (all)	0	3	5
Abdominal pain lower			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1

Diarrhoea			
subjects affected / exposed	1 / 22 (4.55%)	4 / 22 (18.18%)	9 / 22 (40.91%)
occurrences (all)	1	4	11
Food poisoning			
subjects affected / exposed	1 / 22 (4.55%)	1 / 22 (4.55%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Lip dry			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	2 / 22 (9.09%)	2 / 22 (9.09%)	12 / 22 (54.55%)
occurrences (all)	2	2	12
Vomiting			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	2 / 22 (9.09%)
occurrences (all)	0	1	2

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

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

A substantial amendment related to the change of the Principle Investigator took place after the End of Trial (LSLV) on the 28th November 2017.

Notes: