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A study to evaluate if RV299 is safe and can treat respiratory syncytial virus infection in healthy adults

Submission date
21/05/2022

Recruitment status
No longer recruiting

Registration date
18/07/2022

Overall study status
Completed

Last Edited
29/06/2022

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
The purpose of this study is to investigate if an experimental drug called RV299 may be useful in treating people infected with Respiratory Syncytial Virus (RSV). RSV spreads from person to person by close contact with infected individuals, through droplets, or through contaminated surfaces. The only approved treatment for RSV infection is a drug called Ribavirin but because of its unwanted side effects, and low effectiveness, it is rarely used. There are vaccines in development for the prevention of RSV, however these are not currently approved for use. Therefore, we need an effective treatment for RSV infection.

Who can participate?
Up to 80 volunteers, 18-55 years of age, who consent to the participation in this research will be invited to a Quarantine unit at hVIVO, to stay for approximately 15 days.

What does the study involve?
Participants will be randomly allocated to one of two treatment groups to receive either RV299 or Placebo. Eligible participants will be administered (inoculated with) the study virus on Study Day 0. To test the study drug, on Study Day 2, we will start to collect and test twice daily nasal wash samples to see if participants have become infected with the study virus. When the nasal wash sample shows that they have become infected, they will receive the first dose of the study drug (or placebo). On Study Day 5, if the nasal wash sample does not yet show infection, all remaining participants will receive the first dose of study drug (or placebo). All participants will receive the study drug or placebo twice daily for 5 consecutive days, a total of 10 doses. After completion of the Quarantine phase, participants will need to return for a final follow up visit approximately 28 days (±3 days) from the date they receive the study virus.

What are the possible benefits and risks of participating?
Benefits:
Not provided at time of registration
Risks:
RV299 has not previously been tested in human subjects infected with RSV and may not provide

any antiviral protection against RSV in humans. Participants will be monitored for severe RSV-related disease throughout the study and managed accordingly.
The most common side effects reported in a previous study of RV299 in adult participants were headache, sore throat and skin itching.
The effects of RV299 on an unborn child are not known, so as a safety precaution, female participants and female partners of male participants must not be pregnant or become pregnant during the study. Participants must follow the contraception guidance in the ICF. We will do pregnancy tests at Screening and during the study.
Participants may experience an allergic reaction to the study drug even though this has not been seen in the previous study. Symptoms of an allergic reaction may include the following; headache, rash, flushing, swelling, shortness of breath, nausea, and vomiting. Participants will be closely monitored for any side effects.
The symptoms of RSV infection are mild and typically mimic the common cold. Symptoms can include runny nose, stuffy nose, sneezing, sore throat, fever, tiredness, malaise, muscle ache, shortness of breath and wheeze. In healthy adults, the illness usually resolves without any treatment, with relief of symptoms occurring naturally within 7 to 10 days. Strict inclusion and exclusion criteria will apply.
Daily medical monitoring will be in place for at least 12 days post challenge virus administration. Suitability for discharge is determined by the PI based on clinical symptoms and, if indicated, a viral diagnostic test.
RSV, like many viruses, can cause more substantial health issues such as myocarditis (inflammation or damage to the heart muscle). Participants will be closely monitored in quarantine. Electrocardiograms will be performed, and cardiac enzymes will be tested at least 7 days and 11 days post-viral challenge.
Blood drawing may cause pain/tenderness, bruising, bleeding, light-headedness, dizziness, fainting and, rarely, infection or nerve damaged. Procedures will be in place to avoid injury. Blood tests may indicate that a participant has an infection or illness. The hVIVO doctor will provide a referral letter to the participants' GP with consent.
Collection of nasal samples may cause discomfort, sneezing, watery eyes, irritated nose or nose bleeding. Sample collection will be performed by appropriately qualified and trained study staff to minimise the discomfort.
If a participant ever had a herpes infection (e.g., cold sores, genital herpes, or shingles), there is a small possibility that this infection could return after challenge. Participants will be instructed to inform the study staff if they currently have an active herpes infection or have had one during the 30 days before enrolment.

Where is the study run from?
ReViral Limited (UK)

When is the study starting and how long is it expected to run for?
May 2022 to October 2022

Who is funding the study?
ReViral Limited (UK)

Who is the main contact?
Dr Victoria Parker, v.parker@hvivo.com

Contact information

Type(s)

Scientific

Contact name
Mr Kingsley Eze

Contact details
Queen Mary BioEnterprises Innovation Centre
42 New Road
London
United Kingdom
E12AX
+44 7876216261
k.eze@hvivo.com

Type(s)
Principal investigator

Contact name
Dr Victoria Parker

Contact details
Queen Mary BioEnterprises Innovation Centre
42 New Road
London
United Kingdom
E12AX
+44 7823739303
v.parker@hvivo.com

Additional identifiers

Integrated Research Application System (IRAS)
1005624

Protocol serial number
REVD002

Study information

Scientific Title
A randomised, phase 1b, double-blind, placebo-controlled study to evaluate the safety, pharmacokinetics and antiviral activity of RV299 against respiratory syncytial virus (RSV) in the viral challenge model

Study objectives
Primary objectives:
1. To assess the antiviral activity of RV299 compared to placebo in healthy adult participants infected with RSV-A Memphis 37b.
2. To evaluate the effect of RV299 compared to placebo in healthy adult participants inoculated with RSV in terms of antiviral effect assessed by:

2.1. Viral-load related endpoints.
2.2. clinical symptom-related endpoints.

Secondary objectives:
1. To evaluate the effect of RV299 on nasal discharge in healthy adult participants inoculated with RSV when compared to placebo.
2. To evaluate the safety of multiple orally administered doses of RV299 when compared to placebo.
3. To monitor the safety of the challenge virus.
4. To characterise the PK profile of RV299 after a single oral dose and after multiple oral doses in plasma from healthy participants inoculated with RSV.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval pending, Fast Track Research Ethics Committee (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, UK; no telephone number provided; fasttrack.rec@hra.nhs.uk), ref: 22/FT/0077

Study design
Interventional double blind randomized parallel group placebo controlled trial

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Respiratory Syncytial Virus

Interventions
Participants will be randomised to one of two study arms (RV299/placebo) in a 1:1 ratio following confirmation of RSV infection . Participants in the active arm (RV299) will be given RV299 50% w/w spray-dried dispersion (SDD) for Oral Suspension, 65 mg as RV299 (i.e., ~130 mg as RV299 50% w/w SDD) reconstituted in 100 mL Ora-Blend® (RV299 50% w/w SDD Oral Suspension), dosed twice daily (~12 hours interval) for 5 consecutive days (a total of 10 doses). Participants in the placebo arm will be given 100 mL matched placebo (Ora-Blend®), dosed twice daily (~12 hours interval) for 5 consecutive days (a total of 10 doses). Participants will be dosed orally in the seated position. A designated unblinded statistician, separate from the conduct or analysis of the study will prepare a computer-generated randomisation schedule. A copy of the randomisation code list will be provided to the unblinded pharmacist/designee preparing the IMP. Individual emergency code break envelopes will be provided to the PI/investigator should it be necessary to break the blind for a participant.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
RV299

Primary outcome(s)
The area under the curve (AUC) for RSV-A Memphis 37b viral load From Dose 1 up to Study Day 12(am).

Key secondary outcome(s))
Viral Load:
1.1. Peak viral load measured by qRT-PCR from IMP Dose 1 up to Study Day 12(am)]
1.2. Time (days) to confirmed negative test, after peak viral load measure, in nasal samples measured by qRT-PCR, starting at IMP Dose 1 until the first confirmed undetectable assessment.
1.3. Time (days) to confirmed negative test after peak measure, in nasal samples measured by qRT-PCR, starting from peak qRT-PCR after IMP Dose 1 until first confirmed undetectable assessment.
1.4. Time (days) to peak qRT-PCR in nasal samples, starting from IMP Dose 1.
1.5. Area under the viral load-time curve (VL-AUC) of RSV challenge virus as determined by viral culture on nasal samples, starting at IMP Dose 1 up to planned discharge from quarantine (Day 12, am).
1.6. Peak viral load of RSV determined by viral culture measurements in nasal samples starting from IMP Dose 1 up to planned discharge from quarantine (Day 12, am).
1.7. Time (days) to confirmed negative test by viral culture measurements in nasal samples starting at IMP Dose 1 to first confirmed undetectable assessment after peak measure.
1.8. Time (days) to confirmed negative test by viral culture measurements in nasal samples starting from peak viral culture after IMP Dose 1 to first confirmed undetectable assessment after peak measure.

Clinical Symptom related endpoints (including but not limited to):
2.1. Total clinical symptoms (TSS-AUC)
2.2. Clinical symptoms change from baseline (TSS-AUC-CFB)
2.3. Peak total symptoms diary card score (TSS)
The above clinical symptom-related endpoints are as measured from 10 symptoms within the graded symptom scoring system collected 3 times daily starting from IMP Dose 1 up to planned discharge from quarantine (Day 12, am).

2.4. Peak daily symptom score (individual) from IMP Dose 1 up to planned discharge from quarantine (Day 12, am).
2.5. Time (days) to symptom resolution as measured from 10 symptoms within the graded daily symptom scoring system starting at IMP Dose 1 to time of returning to baseline score.
2.6. Time (days) to symptom resolution as measured from 10 symptoms within the graded daily symptom scoring system starting at peak symptoms after Dose 1 to time of returning to baseline score.
2.7. Time (days) to peak as measured from 10 symptoms within the graded daily symptom scoring system from IMP Dose 1 to the time of peak daily symptom score.

Nasal discharge:
3.1. Total weight of mucus produced, measured by tissue collection from IMP Dose 1 up to planned discharge from quarantine (Day 12, am).
3.2. Total number of tissues used by participants starting at IMP Dose 1 up to planned discharge from quarantine (Day 12, am).

Safety
4.1. Safety data including, but not limited to, occurrence of adverse events (AEs) from IMP Dose 1 up to the Day 28 follow-up.
4.2. Occurrence of serious AEs (SAEs) from IMP Dose 1 up to the Day 28 follow-up.
4.3. Occurrence of AEs related to the viral challenge from viral challenge (Day 0) up to the Day 28 follow up.
4.4. Occurrence of SAEs related to the viral challenge from viral challenge (Day 0) up to the Day 28 follow-up.
4.5. Use of concomitant medications from viral challenge (Day 0) up to the Day 28 follow-up.

Pharmacokinetics:
Time to maximum plasma concentration (tmax), terminal half-life (t1/2), maximum observed plasma concentration (Cmax), area under the plasma concentration-time curve from time zero to the end of the dosing interval (AUC), area under the plasma concentration-time curve over the last 24 hours dosing interval (AUC0-24h) and area under the plasma concentration-time curve from time zero to infinity (AUC0-∞).

Completion date
31/10/2022

Eligibility

Key inclusion criteria
1. Written informed consent signed and dated by the participant and the investigator obtained before any assessment is performed.
2. Adult male or female aged between 18 and 55 years old inclusive on the day prior to signing the consent form.
3. A total body weight ≥50 kg and body mass index (BMI) ≥18 kg/m2 and ≤ 35kg/m².
4. In good health with no history, or current evidence, of clinically significant medical conditions, and no clinically significant test abnormalities that will interfere with participant safety, as defined by medical history, physical examination, (including vital signs), ECG, and routine laboratory tests as determined by the investigator.
5. Participants will have a documented medical history either prior to entering the study or following medical history review with the study physician at screening.
6. The following criteria are applicable to female participants participating in the study.
6.1. Females of childbearing potential must have a negative pregnancy test prior to enrolment.
6.2. Females of non-childbearing potential:
6.2.1. Post-menopausal females defined as amenorrhea for ≥12 months with no alternative medical cause. A high follicle-stimulating hormone (FSH) level, within appropriate post-menopausal range, may be used to confirm post-menopausal state in the absence of combined hormonal contraception or hormone replacement therapy. If there is <12 months of amenorrhea 2 FSH samples are required at least 4 to 6 weeks apart.
6.2.2. Documented status as being surgically sterile (e.g., tubal ligation, hysterectomy, bilateral salpingectomy, and bilateral oophorectomy).
7. The following criteria apply to female and male participants:
7.1. Female participants of childbearing potential must use one form of highly effective contraception. Hormonal methods must be in place from at least 14 days prior to the first study visit. The contraception use must continue until 90 days after the last dose of IMP. Highly effective contraception is as described below:
7.1.1. Established use of hormonal methods of contraception described below (for a minimum of 14 days prior to the first study visit). When hormonal methods of contraception are used, male

partners are required to use a condom with a spermicide:
7.1.1.1. combined (oestrogen- and progestogen containing) hormonal contraception associated with inhibition of ovulation:
7.1.1.1.1. oral
7.1.1.1.2. intravaginal
7.1.1.1.3. transdermal
7.1.1.2. progestogen-only hormonal contraception associated with inhibition of ovulation:
7.1.1.2.1. oral
7.1.1.2.2. injectable
7.1.1.2.3. implantable
7.1.2. Intrauterine device.
7.1.3. Intrauterine hormone-releasing system.
7.1.4. Bilateral tubal ligation.
7.1.5. Male sterilisation (with the appropriate post vasectomy documentation of the absence of sperm in the ejaculate) where the vasectomised male is the sole partner for that woman.
7.1.6. True abstinence – sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study treatments. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the participant.
7.2. Male participants must agree to the contraceptive requirements below at entry to quarantine and continuing until 90 days after the last dose of IMP.
7.2.1. Use a condom with a spermicide to prevent pregnancy in a female partner or to prevent exposure of any partner (male or female) to the IMP.
7.2.2. Male sterilisation with the appropriate post vasectomy documentation of the absence of sperm in the ejaculate (please note that the use of condom with spermicide will still be required to prevent partner exposure). This applies only to males participating in the study.
7.2.3. In addition, for female partners of childbearing potential, that partner must use another form of contraception such as one of the highly effective methods mentioned above for female participants.
7.2.4. True abstinence – sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study treatments. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical study and the preferred and usual lifestyle of the participant.
7.2.5. In addition to the contraceptive requirements above, male participants must have agreed not to donate sperm following discharge from quarantine until 90 days after the last dose of IMP.
8. Sero-suitable for the challenge virus

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit

55 years

Sex
All

Key exclusion criteria
1. History of, or currently active, symptoms or signs suggestive of upper or lower respiratory tract infection within 4 weeks prior to the first study visit.
2. Any history or evidence of any clinically significant or currently active cardiovascular, respiratory, dermatological, gastrointestinal, endocrinological, haematological, hepatic, immunological (including immunosuppression), metabolic, urological, renal, neurological, or psychiatric disease and/or other major disease that, in the opinion of the investigator may interfere with a participant completing the study and necessary investigations.
3. Any participants who have smoked ≥10 pack years at any time (10 pack years is equivalent to 1 pack of 20 cigarettes a day for 10 years).
4. Females who:
4.1. Are breastfeeding, or
4.2. Have been pregnant within 6 months prior to the study, or
4.3. Have a positive pregnancy test at any point during screening or prior to viral challenge.
5. Lifetime history of anaphylaxis and/or a lifetime history of severe allergic reaction. Significant intolerance to any food or drug in the last 12 months, as assessed by the PI.
6. Venous access deemed inadequate for the phlebotomy and cannulation demands of the study.
7.
7.1. Any significant abnormality altering the anatomy of the nose in a substantial way or nasopharynx that may interfere with the aims of the study and, in particular, any of the nasal assessments or viral challenge (historical nasal polyps can be included, but large nasal polyps causing current and significant symptoms and/or requiring regular treatments in the last month will be excluded).
7.2. Any clinically significant history of epistaxis (large nosebleeds) within the last 3 months of the first study visit and/or history of being hospitalised due to epistaxis on any previous occasion.
7.3. Any nasal or sinus surgery within 3 months of the first study visit.
8.
8.1. Evidence of vaccinations within the 4 weeks prior to the planned date of viral challenge.
8.2. Intention to receive any vaccination(s) before the last day of follow-up (with the exception of vaccinations recommended for Covid-19 as defined by Medicines and Healthcare products Regulatory Agency (MHRA)/government vaccination guidelines).
8.3. No travel restrictions apply after the Day 28 (±3 days) follow-up visit
9. Receipt of blood or blood products, or loss (including blood donations) of 550 mL or more of blood during the 3 months prior to the planned date of viral challenge or planned during the 3 months after the final visit.
10.
10.1 Receipt of any investigational drug within 3 months prior to the planned date of viral challenge.
10.2 Receipt of 3 or more investigational drugs within the previous 12 months prior to the planned date of viral challenge.
10.3 Prior inoculation with a virus from the same virus-family as the challenge virus.
10.4 Prior participation in another HVC study with a respiratory virus in the preceding 3 months, taken from the date of viral challenge in the previous study to the date of expected viral challenge in this study.
11.
11.1. Herbal supplements within 7 days prior to the planned date of Viral Challenge.

11.2. Chronically used medications, vitamins, or dietary supplements, including any medications (including St John’s wort) known to be potent inducers or inhibitors of CYP enzymes, within 21 days prior to the planned date of Viral Challenge.
11.3. Over-the-counter medications (e.g., paracetamol or ibuprofen) where the dose taken over the preceding 7 days prior to the planned date of viral challenge has exceeded the maximum permissible 24-hour dose (e.g., ≥4 grams paracetamol over the preceding week).
11.4. Systemic antiviral administration within 4 weeks of viral challenge.
12.
12.1. Confirmed positive test for drugs of abuse and cotinine on first study visit. One repeat test is allowed at PI discretion.
12.2. History or presence of alcohol addiction, or excessive use of alcohol (weekly intake in excess of 28 units alcohol; 1 unit being a half glass of beer, a small glass of wine, or a measure of spirits), or excessive consumption of xanthine-containing substances (e.g., daily intake in excess of 5 cups of caffeinated drinks, e.g., coffee, tea, cola).
13. A forced expiratory volume in 1 second (FEV1) <80%.
14. Positive HIV, hepatitis B virus, or hepatitis C virus test.
15. Presence of fever, defined as participant presenting with a temperature reading of ≥37.9°C on Day -2, Day -1, and/or pre-challenge on Day 0.
16. Those employed or immediate relatives of those employed at hVIVO or the sponsor.
17. Any other medical, psychiatric, social, or occupational condition and/or responsibility that, in the opinion of the investigator, would interfere with or serve as a contraindication to protocol adherence or the assessment of safety, will deem the participant unsuitable for the study. Any other reason that in the opinion of the investigator raises a concern that the subject will not be able to cope with quarantine requirements.

Date of first enrolment
19/06/2022

Date of final enrolment
16/11/2022

Locations

Countries of recruitment
United Kingdom

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
ReViral Limited

Funder(s)

Funder type
Industry

Funder Name
ReViral Limited

Results and Publications

Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent results publication

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No