A Phase 2b, Randomized, Double-Blind, Placebo-Controlled Study of EDP-938 Administered Orally for the Treatment of Acute Upper Respiratory Tract Infection with Respiratory Syncytial Virus in Ambulatory Adult Subjects (RSVP)

Published: 29-07-2020
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Primary Objective• To evaluate the effect of EDP-938 on the progression of RSV infection by assessment of clinical symptomsSecondary Objectives• To evaluate the antiviral efficacy of EDP-938• To evaluate the pharmacokinetics (PK) of EDP-938• To...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON49803

Source
ToetsingOnline

Brief title
EDP 938-102

Condition

- Viral infectious disorders

Synonym
Respiratory Syncytial Virus, RSV

Research involving

Human

Sponsors and support

Primary sponsor: Enanta Pharmaceuticals, Inc.
Source(s) of monetary or material Support: biotechnologische industrie

Intervention

Keyword: EDP 938-102, Respiratory syncytial virus, RSV

Outcome measures

Primary outcome

Primary Endpoint

• Effect of EDP-938 compared to placebo on RSV infection clinical symptoms measured as the total symptom score (TSS) area under the curve (AUC) from Day 1 through Day 14

Secondary outcome

Secondary Endpoints

• The AUC for RSV RNA viral load measured in nasopharyngeal swab samples by quantitative reverse transcription polymerase chain reaction (RT-qPCR)

• Percentage of subjects with RSV RNA viral load below the lower limit of quantitation in subjects receiving EDP-938 compared to placebo

• Plasma PK concentrations of EDP-938 and its major metabolites (EP-024636, EP-024594, and EP-024595)

• Safety endpoints include, but are not limited to, adverse events (AEs), vital sign measurements, pulse oximetry measurements, and clinical laboratory test results (including chemistry, hematology, and urinalysis)

• Time to RSV RNA viral load below the lower limit of quantitation in subjects

receiving EDP-938 compared to placebo

• RSV RNA viral load change from Baseline

Exploratory Endpoints

• Resistance to EDP-938 in RSV obtained from nasopharyngeal swab samples

• Correlation between EDP-938 plasma concentration and viral load and clinical

symptoms

• The FLU-PRO questionnaire evaluation across visits

• RSV RNA viral load AUC and TSS AUC by RSV subgroup A or B

Study description

Background summary

Respiratory syncytial virus is the leading cause of lower respiratory tract infection and presents a significant health challenge in small children, elderly, and immunocompromised patients. EDP-938 is active against all RSV-A and RSV-B laboratory strains and clinical isolates tested in vitro and has demonstrated in vivo efficacy in the RSV-infected African Green Monkey model. To address the unmet medical need for more effective antiviral therapies for RSV and based on the promising early nonclinical safety and pharmacological profile, EDP-938 is being investigated in humans as a potential treatment for RSV infection. For additional information please refer to the protocol, section 1 (p. 24-28).

Study objective

Primary Objective
• To evaluate the effect of EDP-938 on the progression of RSV infection by assessment of clinical symptoms

Secondary Objectives
• To evaluate the antiviral efficacy of EDP-938
• To evaluate the pharmacokinetics (PK) of EDP-938
• To evaluate the safety of EDP-938

Exploratory Objectives
• To evaluate EDP-938 in terms of emergence of viral resistance
• To evaluate the relationship between the PK of EDP-938 and antiviral activity and clinical symptoms
• To explore the progression of RSV infection using the InFLUenza Patient-Reported Outcome (FLU-PRO) questionnaire
• To evaluate the relationship between RSV subgroup A or B with antiviral and clinical efficacy of EDP-938

Study design

For each subject, the duration of study participation will be approximately 2 weeks and will consist of 3 periods: Screening, Treatment, and Follow-up as follows:
Screening (Day 1): Occurs on Day 1
Treatment (Day 1 to 5): 5 days
Follow-up (Day 6 to 14): 9 days after the last dose
Approximate total duration of participation: 14 days

Screening Period on Day 1: At Screening (on Day 1), subjects will first review and sign the Rapid Viral Screen informed consent form (ICF) prior to RSV and influenza screening. Subjects will undergo a rapid diagnostic test for RSV and influenza virus using respiratory secretions obtained by nasal (or nasopharyngeal) swab collection. Subjects whose swab sample tests are positive for RSV and negative for influenza virus may proceed for further screening. Such subjects will be required to sign the full study ICF prior to performing any further study-specific assessments. After signing the full study ICF, subjects will undergo further screening procedures to determine study eligibility.
All study screening activities should be completed on Day 1. If any assessment is anticipated to fall outside of that window, then the Investigator should consult with the PPD Medical Monitor to determine if the subject can proceed. For subjects who sign the full study ICF and whose swab sample test results are positive for RSV and negative for influenza virus, the first screening activity should be to test subjects for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) using a rapid molecular diagnostic test. Subjects will not be randomized until all screening activities that allow assessment of inclusion/exclusion criteria have been completed to the satisfaction of the Investigator, including the screening electrocardiogram (ECG) and the screening urine pregnancy test. All screening procedures are detailed in the Schedule of Assessments (SoA).

Treatment Period (Days 1 to 5): Subjects who meet all inclusion criteria and none of the exclusion criteria to the satisfaction of the Investigator will be eligible to enter the study and will be randomized 1:1 to receive 800 mg of EDP-938 or placebo. Subject randomization will be stratified by the presence or absence of asthma/COPD.

Eligible subjects must complete the Day 1 biological sample collections (ie, blood, urine, and nasopharyngeal swab[s]) prior to receiving the first dose of EDP-938 or placebo. Day 1 blood and urine samples will be sent to both local (expedited testing and reporting) and central laboratories. Nasopharyngeal swab(s) will be sent to the central laboratory only.
Eligible subjects will receive an electronic data capture handheld device (ERT® electronic clinical outcome assessment [eCOA] Handheld eDiary) to use for the duration of the study. Subjects will use this device to complete the RSV symptom diary (twice daily at the same times each day ±2 hours) and the FLU-PRO questionnaire (once daily at the same time each day ±2 hours), to record when each dose of study drug is taken, and to record acetaminophen use. The device will also serve to alert the subject when it is time for study drug dosing. The subject will receive instruction on the proper use and care of the device, including the recording of the first dose, and the device should be brought to each study site visit. In case the subject is unable to complete any assessments or recordings into the device for technical reasons, the subject will also be provided with a paper diary(ies) as a back-up.
The subject will be instructed on the use of concomitant medications during the study, including the use of acetaminophen as the study-specific analgesic/antipyretic (see Section 5.8 and Section 5.9).
Subjects will receive the first dose of study drug while at the study site. After the first dose, subjects will be instructed to take 800 mg of EDP-938 or placebo once daily at approximately the same time every day (±1 hour) on each of the 4 subsequent days. The subject will also receive instruction on the appropriate storage and transport of study drug.
On Day 3 and Day 5 (end-of-treatment), subjects should bring their study drug with them as part of their study site visit (in the provided cooler system) for drug accountability and for dosing of study drug on Day 5. If a subject is unable to attend the Day 3 and/or Day 5 study site visit, a home visit by a study nurse may be arranged, if feasible; refer to the Study Procedures Manual (SPM) for details.
Subjects who discontinue treatment early (ie, prior to completing 5 days of dosing) should return to the study site within 24 hours and no more than 48 hours later to complete the end-of-study (EOS) procedures.
All study assessments during the Treatment Period, including PK sample collection, are detailed in the SoA.

Follow-up Period (Days 6 to 14): Subjects should return to the study site for follow-up visits on Day 9 and Day 14 (EOS Visit) for post-treatment safety assessments. Visit assessments may be completed at the study site or by a study nurse via a home visit, if feasible; refer to the SPM for details.
Subjects who discontinue the study early (ie, prior to Day 14) should return to the study site within 24 hours and no more than 48 hours later to complete the EOS procedures.
All study assessments during the Follow-up Period are detailed in the SoA.
Throughout the study, safety for each subject in each study period will be evaluated by assessment of clinical laboratory findings, physical examination

findings (as applicable), vital sign measurements, pulse oximetry measurements (only for subjects with asthma or COPD), and AEs.

Intervention

One group receives 800 mg EDP-938 once a day for 5 days, the other group receives placebo once a day for 5 days.
EDP-938 will be supplied as tablets for oral administration in two dose strengths: 150 mg and 200 mg.

Study burden and risks

The potential risks to subjects receiving EDP-938 have been estimated based on reporting of safety data from 5 studies, which are 4 Phase 1 studies in healthy subjects and 115 healthy subjects in the Phase 2 RSV Challenge Study. A total of 282 subjects have been exposed to a single dose of up to 800 mg or multiple doses up to 600 mg per day.

Across these studies, the most commonly reported side effect of EDP-938 was mild headache. No pattern of side effects was observed, and the majority of side effects were mild. Also, there were no severe or serious side effects. One subject stopped participating in the study due to a side effect, a brief irregular heartbeat on an ECG in a single dose study of EDP-938. This subject did not have any symptoms and the irregular heartbeat stopped without treatment. There may also be side effects and discomforts of EDP-938 that are not yet known.

If EDP-938 is effective at treating RSV infection, patients may benefit by a shortened time they feel unwell.

Invasive procedures:
Blood draws
Nasopharyngeal swabs
SARS-CoV-2 test via nasal or nasopharyngeal or oropharyngeal swab if the swab for the RSV/flu test cannot be used.

Contacts

Public
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Watertown MA 02472
US

Scientific
Enanta Pharmaceuticals, Inc.

Arsenal Street 500
Watertown MA 02472
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. A full ICF signed and dated by the subject. (Note: Prior to signing the full ICF, subjects will sign a Rapid Viral Screen ICF as described in inclusion criterion #4.)
2. Male or female individuals aged 18 to 75 years, inclusive.
3. Up to 48 hours of URTI symptoms with at least one of the following symptoms: Nasal discharge, nasal congestion, malaise/tiredness, headache, sinus congestion, sneezing, sore throat, hoarseness, cough, shortness of breath, respiratory wheeze, earache, and/or symptoms of fever.
Note: The duration of symptoms (not more than 48 hours) is to be measured from the estimated time of onset of the first symptom.
4. After signing the Rapid Viral Screen ICF, positive for RSV infection and negative for influenza virus based on rapid diagnostic screen of nasal (or nasopharyngeal) swab samples.
5. Medically stable based on assessment of physical examination, medical history, vital sign measurements, pulse oximetry (only for subjects with asthma or COPD), and 12-lead ECG performed at Screening.
6. A body mass index >=18 kg/m2 and <=40 kg/m2.
7. Negative urine pregnancy test for women of childbearing potential as defined in inclusion criterion #8.
8. A woman of childbearing potential who is sexually active with a male must agree to use two effective methods of contraception from the date of Screening

until 30 days after her last dose of study drug. Effective methods of contraception are defined as:
A condom for the male partner and at least one of the following for the female subject:
a. Intrauterine device
b. Occlusive cap (diaphragm or cervical/vault caps)
c. Oral, injectable, implantable, transdermal, or intravaginal hormonal contraceptive
Note: The above does not apply to a female subject who has a vasectomized male as the sole partner or who is of nonchildbearing potential (ie, physiologically incapable of becoming pregnant) as defined below:
a. Has had a complete hysterectomy >=3 months prior to dosing or
b. Has had a bilateral oophorectomy (ovariectomy) or
c. Has had a bilateral tubal ligation or fallopian tube inserts or
d. Is postmenopausal (a total cessation of menses for at least 2 years; Note: Subjects with a cessation of menses between 1 to 2 years and a follicle-stimulating hormone [FSH] level of >35 mIU/mL will also be considered to be postmenopausal).
9. A male subject who has not had a vasectomy and is sexually active with a woman of childbearing potential must agree to use effective contraception from the date of Screening to 90 days after his last dose of study drug. Effective contraception is defined as a condom and at least one of the following for a female partner:
a. Intrauterine device
b. Occlusive cap (diaphragm or cervical/vault caps)
c. Oral, injectable, implantable, transdermal, or intravaginal contraceptive
Note: For a male subject who has had a vasectomy, use of a condom will still be required.
10. Male subjects must agree to refrain from sperm donation from the date of Screening until 90 days after his last dose of study drug.
11. Must be willing and able to adhere to the study assessments, visit schedules, prohibitions, and restrictions, as described in this protocol.
Additional Inclusion Criteria for Subjects With Asthma
12. Physician-diagnosed asthma and currently receiving Global Initiative for Asthma (GINA) Step 2, 3, or 4 treatment, with stable dosing for at least 4 weeks prior to Screening.
13. Stable prebronchodilator forced expiratory volume in 1 second (FEV1) >=60% of predicted within the prior 12 months of Screening based on historical spirometry medical records.
Additional Inclusion Criteria for Subjects With COPD
14. Physician-diagnosed COPD and currently receiving either short-acting bronchodilators (as required) or up to two maintenance therapies.
15. No change in the background COPD therapy for at least 4 weeks prior to Screening.
16. Stable postbronchodilator FEV1 >50% of predicted and FEV1:forced vital capacity (FVC) ratio <0.7 within the prior 12 months of Screening based on

historical spirometry medical records.

Exclusion criteria

1. Clinical evidence of a lower respiratory tract infection, as determined by the Investigator.
2. Anticipated need for hospitalization or emergency room care within 24 hours of Screening.
3. Receipt of systemic antiviral, antibacterial, antifungal, or antimycobacterial therapy within 7 days of Screening and for the duration of the study.
4. Awareness of concomitant respiratory infections that are viral (other than RSV), bacterial, or fungal, including systemic bacterial or fungal infections, within 7 days of Screening.
5. SARS-CoV-2 positive within 28 days of Screening or at Screening following signature of full ICF.
6. Frailty scale score >=4 at Screening.
7. History of chronic liver disease (eg, hemochromatosis, Wilson*s disease, alpha-1 antitrypsin deficiency, autoimmune hepatitis, nonalcoholic steatohepatitis, and/or alcoholic liver disease); a history of biliary disease (eg, primary sclerosing cholangitis, cholecystitis, choledocholithiasis); or a history of portal hypertension. A diagnosis of hepatic steatosis (fatty liver) is not exclusionary.
8. Heart disease: any congenital heart disease, acute or chronic heart failure, ischemic heart disease, congenital long QT syndrome, or any clinical manifestation resulting in QT interval prolongation. Note: Subjects with controlled hypertension without cardiac compromise will be allowed to enroll. See exclusion criterion #18 for prohibited medications.
9. Neurological and neurodevelopmental disorders (including disorders of the brain, spinal cord, peripheral nerve, and muscle, eg, cerebral palsy, epilepsy [seizure disorders], stroke, muscular dystrophy, or spinal cord injury). Note: Minor neurological disorders (eg, past concussions, headaches, migraine) are allowed.
10. Malignant tumor or history of malignancy that may interfere with the aims of the study or a subject completing the study.
11. Prior receipt or the subject is waiting to receive a bone marrow, stem cell, or solid organ transplantation.
12. Diagnosis of cystic fibrosis.
13. Known positive human immunodeficiency virus, active hepatitis A virus infection, chronic hepatitis B virus infection, and/or current or treated hepatitis C virus infection.
14. Prior or planned ileal resection or bariatric surgery. Note: Subjects who have undergone gastric surgeries that do not affect drug absorption (eg, gastric band or gastric sleeve procedures) will be allowed to participate if they are stable for at least 1 year prior to

Screening. Gastrectomy will be allowed if stable for at least 3 years prior to Screening.
15. Pregnant or nursing female subjects.
16. History of alcohol addiction or current heavy alcohol use defined as: >14 standard drinks per week and/or >=4 standard drinks per occasion for males and >7 standard drinks per week and/or >=3 standard drinks per occasion for females. A standard drink is 12 oz of beer (5% alcohol), 5 oz table wine (12% alcohol), or 1.5 oz of spirits (40% alcohol).
17. Known or suspected, in the opinion of the Investigator, renal disease or renal impairment.
18. Twelve-lead ECG demonstrating a QT interval corrected for heart rate according to Fridericia (QTcF) that is >500 msec or other clinically relevant abnormalities as judged by the Investigator at Screening.
19. Use of or intention to use excluded or contraindicated medication(s) or supplements, including any medication known to be a moderate or potent inducer or inhibitor of the cytochrome P450 3A4 enzyme, within 14 days prior to Screening and for the duration of the study.
20. Receipt of >=14 days of systemic immunomodulator therapy (eg, oral corticosteroids) within 3 months of Screening.
21. Prior to the first dose of study drug and during study participation, the subject has received any vaccine, investigational agent, or biological product within 30 days or 5 times the half-life, whichever is longer. Note: Influenza vaccination within 7 days of
Screening is not allowed.
22. Use of St John*s wort within 28 days prior to the first dose of study drug and for the duration of the study.
23. History of or currently experiencing a medical condition or any other finding (including laboratory test results) that, in the opinion of the Investigator, might confound the results of the study; pose an additional risk in administering study drug to the subject; could
prevent, limit, or confound the protocol-specified assessments; or deems the subject unsuitable for the study.
Additional Exclusion Criteria for Subjects With Asthma
24. Subjects must not have experienced a severe asthma exacerbation (defined as worsening asthma that requires treatment with oral corticosteroids for 3 or more days, or emergency room attendance) or deterioration in asthma requiring an increase in asthma treatment for at least 6 weeks prior to Screening.
25. Subject is receiving more than two maintenance asthma therapies or theophylline preparations for asthma treatment.
26. Pulse oximetry reading of <90% oxygen saturation measured at rest at Screening.
Additional Exclusion Criteria for Subjects With COPD
27. Receipt of theophylline, roflumilast, maintenance oral corticosteroids, or long-term oxygen therapy (defined as prescribed for 12 or more hours per day).
28. Exacerbation of COPD requiring treatment with systemic corticosteroids and/or antibiotics, or emergency room attendance or hospitalization within 6 weeks prior to Screening.

29. More than three COPD exacerbations with the past 12 months.
30. Pulse oximetry reading of <90% oxygen saturation measured at rest at Screening

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	8
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	EDP-938
Generic name:	EDP-938

Ethics review

Approved WMO

Date:	29-07-2020
Application type:	First submission
Review commission:	METC Brabant (Tilburg)

Approved WMO

Date:	07-10-2020
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	26-11-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	30-11-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	23-12-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	17-02-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-05-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-06-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2020-001529-30-NL
ClinicalTrials.gov	NCT04196101
CCMO	NL74572.028.20

Study results

Results posted: 15-12-2022

Summary results
Trial never started

First publication
24-08-2022